Aalborg Universitet



### Deprescribing in primary care without deterioration of health-related outcomes: A reallife, quality improvement project

Olesen, Anne Estrup: Væver, Tanja Joest: Simonsen, Martin: Simonsen, Peter Gaardbo; Høj, Kirsten

Published in: Basic & Clinical Pharmacology & Toxicology

DOI (link to publication from Publisher): 10.1111/bcpt.13925

Creative Commons License CC BY-NC-ND 4.0

Publication date: 2024

Document Version Publisher's PDF, also known as Version of record

Link to publication from Aalborg University

Citation for published version (APA):

Olesen, A. E., Væver, T. J., Simonsen, M., Simonsen, P. G., & Høj, K. (2024). Deprescribing in primary care without deterioration of health-related outcomes: A real-life, quality improvement project. *Basic & Clinical* Pharmacology & Toxicology, 134(1), 72-82. Advance online publication. https://doi.org/10.1111/bcpt.13925

#### General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
  You may not further distribute the material or use it for any profit-making activity or commercial gain
  You may freely distribute the URL identifying the publication in the public portal -

#### Take down policy

If you believe that this document breaches copyright please contact us at vbn@aub.aau.dk providing details, and we will remove access to the work immediately and investigate your claim.

Revised: 29 June 2023

ORIGINAL ARTICLE



## Deprescribing in primary care without deterioration of health-related outcomes: A real-life, quality improvement project

Anne Estrup Olesen <sup>1,2</sup> 💿	Tanja Joest Væver <sup>3</sup>	Martin Simonsen <sup>4</sup>
Peter Gaardbo Simonsen <sup>4</sup>	Kirsten Høj <sup>1,5</sup> 🝺	

<sup>1</sup>Department of Clinical Pharmacology, Aalborg University Hospital, Aalborg, Denmark

<sup>2</sup>Department of Clinical Medicine, Aalborg University, Aalborg, Denmark

<sup>3</sup>Centre for Health and Care, Municipality of Frederikshavn, Frederikshavn, Denmark

<sup>4</sup>General practitioner practice 'Lægeklinikken Frederikshavn', Frederikshavn, Denmark

<sup>5</sup>Research Unit for General Practice, Aarhus, Denmark

#### Correspondence

Anne Estrup Olesen, Aalborg University Hospital, Department of Clinical Pharmacology, Mølleparkvej 8a, 9000 Aalborg, Denmark. Email: aneso@rn.dk

**Funding information** No funding was received.

#### Abstract

Medication reviews focusing on deprescribing can reduce potentially inappropriate medication; however, evidence regarding effects on health-related outcomes is sparse. In a real-life quality improvement project using a newly developed chronic care model, we investigated how a general practitioner-led medication review intervention focusing on deprescribing affected healthrelated 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 the 105 included patients, 87 completed the follow-up. From baseline to follow-up, 255 medication changes were made, of which 83% were deprescribing. Mean self-reported health status increased (0.55 [95% CI: 0.22 to 0.87]); the proportion with general condition rated as 'average or above' was stable (0.06 [95% CI: -0.02 to 0.14]); and the proportion with functional level 'without any disability' was stable (-0.05 [95% CI: -0.09 to 0.001]). In conclusion, this general practitioner-led medication review intervention was associated with deprescribing and increased self-reported health status without the deterioration of general condition or functional level in real-life primary care patients. The results should be interpreted carefully given the small sample size and lack of control group.

#### K E Y W O R D S

chronic disease management, deprescribing, medication review, polypharmacy, primary care

#### **1** | INTRODUCTION

The growing population of older people with multiple chronic conditions and polypharmacy challenges healthcare systems worldwide.<sup>1,2</sup> The term polypharmacy has no single agreed definition, but the most reported is the daily use of five or more medications.<sup>3</sup> Polypharmacy can provide significant health benefits to patients; however, it also

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

<sup>© 2023</sup> The Authors. Basic & Clinical Pharmacology & Toxicology published by John Wiley & Sons Ltd on behalf of Nordic Association for the Publication of BCPT (former Nordic Pharmacological Society).

increases the risk of medication-related harm.<sup>3</sup> Therefore, increasing focus is being placed on differentiating between appropriate and inappropriate medication rather than the number of medications alone.<sup>4</sup>

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, for example, because of drug–drug interactions and agerelated alterations in pharmacokinetics and pharmacodynamics.<sup>5</sup> Adverse effects can have serious implications for patients in terms of reduced quality of life, hospital admission and premature death.<sup>6</sup> 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'.<sup>6</sup>

Polypharmacy interventions as, for example, medication reviews are considered valuable to reduce potentially inappropriate medications through deprescribing recommendations.<sup>7</sup> 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.<sup>8</sup> 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.<sup>9</sup>

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.<sup>10</sup> 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.<sup>10</sup> 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 hospitalisation).<sup>8,9</sup> There is limited evidence of the effectiveness of the interventions on clinical outcomes of importance to patients.<sup>10</sup>

Therefore, based on a primary care settled real-life quality improvement (QI) project aiming to deprescribe medication through a medication review intervention, we investigated how the implemented medication changes affected health-related outcomes in patients with chronic diseases and polypharmacy. We hypothesised that medication changes, hereof expected mainly deprescribing, could be performed without deterioration of health-related outcomes.

#### 2 | METHODS

#### 2.1 | Study design

The QI project formed part of a larger initiative in the Municipality of Frederikshavn, Denmark, focusing on polypharmacy and communication inspired by the World Health Organisations global initiative 'Medication without harm'.<sup>11</sup> As part of this initiative, a new local chronic care model (hereafter CCM) was drawn up (Figure 1). The medication review intervention performed in this QI project was embedded in the CCM. The approach chosen for assessing the impact of the medication review intervention was a one group, before-and-after design. The whole initiative (including the present QI project) was implemented and evaluated in the 2-year period from January 2020 to December 2021. The study was protocoled before initiation and all data were collected and managed using Research Electronic Data Capture (REDCap) hosted at Aalborg University Hospital, Aalborg, Denmark.<sup>12</sup> In this paper, we describe the CCM and report the quantitative findings related to the medication review intervention with health-related patient outcomes as the main outcomes of interest. The reporting is based on the Revised Standards for Quality Improvement Reporting Excellence (SOUIRE 2.0).



**FIGURE 1** The annual consultation flow in the chronic care model (CCM). The new local CCM consisted of three consultations conducted with four-month 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.

## 2.2 | Setting

Danish healthcare is mainly tax-financed and includes free-of-charge access to services.<sup>13</sup> 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.<sup>14</sup>

The current QI project was conducted in a close collaboration between the Centre for Health and Care in the Municipality of Frederikshavn and a large GP clinic in Frederikshavn (hereafter GPF). The Centre for Health and Care runs 12 care homes, of which 11 are covered by a specific GP practice. The GPF is an affiliated care home doctor in four care homes in the municipality. The GPF is a large clinic with a strategic focus on older patients and patients with chronic diseases and has a close collaboration with the municipal and regional health services. The GPF has an affiliated population of approximately 8900 patients, of which more than 2300 citizens are older than 65 years. The GPF employs eight GPs, 10 nurses, 10 medical students or GP trainees, a social and health assistant, a pharmaconomist (professional with expertise in pharmaceuticals with a 3-year tertiary degree) and a physiotherapist.

#### 2.3 | The CCM

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, for example, the size of the clinic and the competencies in the staff group.<sup>15</sup> The established CCM in this QI project targeted 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 CCM consisted of three consultations conducted with four-month intervals as illustrated in Figure 1.

In addition to the CCM, 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 specialised geriatric department at the hospital every second week.

#### 2.4 | Intervention

In this QI project, a fixed procedure for the annual CCM consultation focusing on pharmacological treatment constituted the intervention. This procedure included (1) a structured review of the patient's health state; (2) a structured medication review with a focus on appropriate medication and deprescribing and (3) fixed points to be discussed in the consultation (when relevant) concerning treatment plans for addictive drugs, dose dispensing, resuscitation, life-prolonging treatment and terminal care. The participants were not assigned to the intervention; they received it as part of their routine chronic care.

Both GPs and nurses were involved in the delivery of the intervention. Two GPs responsible for the chronic care management in the GPF performed all medication reviews. In care home residents, the GPs also carried out the related consultation focusing on pharmacological treatment. In community-dwelling patients, the GPs delegated part of the intervention delivery to three experienced nurses (between 10 to 40 years of clinical experience) from the GPF. These nurses delivered the consultations focusing on pharmacological treatment with the GPs as close support. The nurses used the notes from the GPs medication review in their consultation and decided on a deprescribing plan together with the patient. If in doubt, the nurses were able to contact the GP.

The two GPs had 10 to 40 years of clinical experience as physicians and 3 to 30 years of experience as specialists in general practice. In Denmark, GPs receive training in medication review and medicines optimisation as part of their specialist training. Furthermore, all members of the Danish Organisation of Physicians annually receive an updated version of a national deprescribing list published by the Danish Health Authority.<sup>16</sup> Therefore, no additional training or deprescribing guideline were provided as part of the intervention. All health care professionals followed the fixed procedure, and documentation of the activities was recorded in the patient's electronic medical record.

#### 2.5 | Participants

The participants 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 four care homes affiliated with the GPF accommodated 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). Among these

74



eligible patients, the GPs had already started deprescribing interventions in some of them before study initiation. Only patients who were not recently exposed to deprescribing were offered the intervention. From 24 March 2020 to 16 June 2021, the intervention was provided consecutively to new residents who moved into the care home and to residents that had not yet attended a consultation focusing on pharmacological treatment in the CCM. No systematic difference was expected between eligible patients that were included or not included.

The GPF had 1800 community-dwelling patients with chronic diseases listed in the period of 2020–2021. From 3 June 2020 to 16 November 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 period. All patients fulfilled the criteria in the CCM (i.e., one or more chronic conditions).

#### 2.6 | Data collection and outcomes

Before and 3–4 months after the CCM consultation focusing on pharmacological treatment, information regarding medication changes and health-related outcomes was collected. The primary outcomes of interest were changes from baseline to 3–4 months follow-up in (1) selfreported health status (on a scale from 1 to 10); (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'). These simple outcomes were purposively developed with inspiration from Garfinkel<sup>17</sup> to ensure a feasible outcome assessment in the busy, real-life clinical setting. Additionally, data on medication were collected. Medication changes were registered by the GPs or nurses during consultations. Subsequently, these were categorised as deprescribing (dose reduction or stopping/ pausing of medications), new prescription and other medication changes (e.g., dose increase or change in dosing interval) by a project pharmacist. Additionally, all medication changes were categorised according to the Anatomical Therapeutic Classification (ATC) classification system.

General condition and functional level were determined by clinical evaluation. In care home residents, the two GPs filled out all baseline questionnaires in close collaboration with the care home staff for the outcomes general condition and functional level. Self-reported health status was assessed by the resident, a relative or the resident's contact person from the care home staff. At followup, the care home nurse was responsible for the followup questionnaires that were filled out together with the resident and/or relatives. For community-dwelling patients, the nurse affiliated with the Centre for Health and Care filled out questionnaires on general condition and functional level. All community-dwelling patients filled out the self-reported health status questionnaire themselves. No specific training or blinding was provided to the staff assessing the outcomes.

#### 2.7 | Statistical analysis

The intervention was planned to be delivered to as many patients as possible as part routine care during the allocated project period. Therefore, no a priori sample size was calculated. Descriptive data are presented as mean  $\pm$  standard deviation, median (25–75% fractiles) or as absolute numbers and percentages. Paired *t*-test was used to compare means of self-reported health status at baseline and follow-up. The distributions were examined using QQ-plots with standard Gaussian quantiles, and the distributions were similar. McNemars test was used when

75

76

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 'rail'. A sensitivity analysis was performed, in which missing data were handled by the last observation carried forward. Additionally, we performed explorative subgroup analyses for the three main outcomes in care home residents and community-dwelling patients. Statistical analyses were performed in STATA 17. Statistical significance was indicated by a two-tailed p value of 0.05.

## 2.8 | Ethics

The project was approved by the Management in the Municipality of Frederikshavn. According to the 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 QI 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.<sup>18</sup> The study is in compliance with the General Data Protection Regulation<sup>19</sup> and a part of the North Denmark Region's record of processing activities (K2023-008). The study is registered in Clinical-Trials.gov (https://clinicaltrials.gov/) (NCT05721534).

#### 3 | RESULTS

In total, 105 patients were included, of which 87 completed the follow-up (Figure 2). The study population contained two sub-groups: care home residents (33%) and community-dwelling patients with chronic diseases (67%). Baseline characteristics of the included study population and the two sub-groups are provided in Table 1.

TABLE 1 Baseline characteristics of the study populat	tion.
---	-------

During the intervention period, 18 patients were lost to follow-up for various reasons, hereof, eight care home residents and 10 community-dwelling patients. Four residents died before follow-up. By clinical evaluation, it was determined that none of the deaths were directly related to the medication review intervention (e.g., one of the residents died from/with COVID-19). Another four residents were unable to collaborate on follow-up questionnaires. None of the included residents were admitted to the hospital between the inclusion and follow-up. Among community-dwelling patients, five did not show up for the consultation. For another five patients, the follow-up questionnaire was not completed for unspecified reasons. Four of the 60 included patients were admitted to the hospital during the intervention period. By clinical evaluation, it was determined that none of the admissions were directly related to the medication review intervention.

#### 3.1 | Medication changes

#### 3.1.1 | 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 ([25%–75% fractiles]) 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.

### 3.1.2 | 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

, I I			
	Total population ( <i>n</i> = 105)	Care home residents (n = 35)	Community-dwelling patients ( $n = 70$ )
Age, median [25–75% fractiles]	81 [71-88]	88 [82-92]	75.5 [69–83]
Gender (females), n (%)	62 (59)	23 (66)	39 (56)
Number of medications <sup>a</sup> , median [25%–75% fractiles]	9 [7–12]	11 [8.5–13]	8 [6-12]

<sup>a</sup>Number of medications was counted as all prescriptions registered in the patients' electronic medication record (the Danish Shared Medication Record).

(n = 2) (dose increase) (Figure 3A). The most commonly deprescribed medication classes were vitamins and mineral supplements, analgesics and diuretics. 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.

## 3.1.3 | 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

BCDT

interval) (Figure 3B). The most commonly deprescribed medication classes included cardiac therapy, diuretics and vitamins and mineral supplements. 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.

#### 3.2 | 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. These results were robust in the sensitivity analysis. The explorative subgroup analyses showed







**FIGURE 3** Medication changes by medication classes according to the Anatomical Therapeutic Classification (ATC) classification system. Number of deprescriptions, new prescriptions and other medication changes in (A) care home residents and (B) communitydwelling patients with chronic diseases. The term 'other medication changes' includes, for example, increased dose or change in dosing time. The term 'other drugs' includes medications with  $\leq 2$  medication changes, for example, antiemetics, antihistamines and nonsteroidal anti-inflammatory drugs.

40

OLESEN ET AL
--------------

17427843, 2024, 1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/hcpt.13925 by Danish Regions North Denmark, Wiley Online Library on [16/01/2024]. See the Terms and Conditions (https://onlinelibrary.wiley nditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

similar trends in self-reported health status and functional level. Noteworthy, among care home residents, the proportion of patients with general condition rated as 'average or above' increased non-significantly with 19% points, in contrast to no difference among communitydwelling patients.

#### DISCUSSION 4

#### Main findings 4.1

In this study, the medication review intervention with focus on deprescribing was feasible as part of the locally developed CCM 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 approximately 90% of the 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- and health-related measures.

#### Comparison with existing literature 4.2

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<sup>20</sup> or in different settings such as hospitals,<sup>21</sup> nursing homes<sup>22,23</sup> or primary care.<sup>24,25</sup> Overall, the existing evidence suggests that deprescribing is feasible, safe and, generally, effective in reducing the number of inappropriate prescriptions.<sup>24,26</sup> However, 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%.<sup>24</sup> This variation may be explained by various factors relating to, for example, the class of medication, the setting and the characteristics of the GP and the patient. This QI project focused on medications in the primary care setting. The patients were well-known to the GPs delivering the intervention, and their comorbidities were considered but not registered in the project because of feasibility and resources.

It has been demonstrated that certain medication classes such as vitamins, minerals, analgesics and proton pump inhibitors can be deprescribed with high success.<sup>27</sup> This was also seen in the present study where vitamins and minerals were deprescribed in both groups. Analgesics was the second most prevalent deprescribed drug

Changes from baseline to follow-up in health-related outcomes for complete cases. TABLE 2

	Total popul	ation ( <i>n</i> = 87)		Care home	esidents ( <i>n</i> -	= 27)	Community	/-dwelling pa	tients $(n = 60)$
	BL	FU	Difference (95% CI)	BL	FU	Difference (95% CI)	BL	FU	Difference (95% CI)
Self-reported health, mean (SD) <sup>a</sup>	7.3 (±2.0)	7.9 (±1.7)	0.6 (0.2–0.9)*	6.4 (土2.4)	7.1 (±2.0)	$0.7 \left(-0.2 - 1.7\right)$	7.7 (±1.6)	8.2 (±1.4)	0.5 (0.2–0.7)*
General condition rated as 'average or above', %	74.7	80.5	5.7 (-3.4-14.9)	63.0	81.5	18.5 (-3.1-40.1)	80.0	80.0	0.0 (-9.7-9.7)
Functional level rated as 'without any disability', %	58.6	54.0	$-4.6\left(-10.1-1.0 ight)$	14.8	7.4	-7.4 (-21.0-6.2)	78.3	75.0	-3.3 (-9.5-2.9)

Abbreviations: BL, baseline; CI, confidence interval; FU, follow-up; SD, standard deviation.

Missing observations in dataset. n = 24 for care home residents and n = 84 for total population, as self-reported health status was unavailable for three patients. Significant difference (p < 0.05)

class in care home residents; whereas, in communitydwelling patients, deprescribing of analgesics was not prevalent. Drugs for acid-related disorders (e.g., proton pump inhibitors) were only deprescribed in communitydwelling patients. It has also been suggested that deprescribing may be more successful in long-term care compared with the outpatient setting.<sup>27</sup> The present study included only long-term care patients, which may have contributed to the high average number of deprescribed medications per patient. Other deprescribing studies have shown average discontinuations per patient between 2.8 and 4.4.<sup>28-31</sup> Our study did not provide sufficient data to calculate success rates for each drug class. Our aim was not to investigate success rates but to elucidate how the implemented medication changes affected health-related outcomes.

Both GP and patient characteristics can also influence deprescribing decisions.<sup>32</sup> It has been demonstrated that older GPs, GPs regularly treating patients aged 70 years or more with polypharmacy and GPs regularly dealing with the topic of deprescribing are more likely to make deprescribing decisions.<sup>32</sup> Moreover, the odds of deprescribing are higher in patients with high age and in patients with a higher level of dependency in activities of daily living.<sup>32</sup> In our study, two GPs with special interest in chronic care and deprescribing were responsible for the intervention in a complex setting, including patients with high age and high level of dependency in activities of daily living. Thus, the odds of deprescribing were favourable in our setting.

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 minimised or even be prevented using a patientcentred deprescribing process with planning, tapering and close monitoring during and after medication withdrawal.<sup>33</sup> This was possible in our study where a patientcentred 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. Thus, several factors likely contributed to the success rate of deprescribing in our study.

In terms of health-related outcomes, we found that self-reported health status increased from baseline to follow-up. Additionally, general condition and functional level remained stable. However, these results should be interpreted with caution due to the small sample size and lack of control group. The explorative subgroup analyses showed similar trends in health-related outcomes among care home residents and community-dwelling patient. BCPT

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.<sup>34</sup> 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 the quality of life measured by the EQ-5D-5L or on the 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.<sup>26</sup> 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 the quality of life.<sup>26</sup> The latter echoes previous findings across a range of studies conducted in primary care using various quality-of-life measures.<sup>10,35-37</sup> 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.

# 4.3 | 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.<sup>38</sup> In this real-life QI project, the GPs in the GPF decided to construct a new local CCM, including the person-centred medication review intervention, to systematise the care of patients with chronic diseases. Limited time and competing priorities are frequently reported barriers to deprescribing in primary care,<sup>39,40</sup> and 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.<sup>41</sup> Thus, the developed CCM 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, the GPs soon realised that it was preferable to conduct the medication review themselves. This simplified the process, as the GPs were responsible for the final decision on deprescribing. Moreover, medication reviews are a part of their clinical duties. Therefore, the GPs 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.<sup>41</sup> 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.<sup>41</sup> In our study, this was attempted through the cross-sectoral communication model that was established alongside the CCM.

The approach taken in our study might be inspirational to other Danish municipalities as well as other countries with a similar organisation 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 organisation (e.g., home care, care homes and general practices) and health care providers (e.g., nurses, pharmacists and GPs).<sup>42</sup> Furthermore, both private and public stakeholders exist in most countries and may be highly dissimilar in their organisation 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.<sup>41</sup>

#### 4.4 | 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.<sup>43</sup> In our study, communitydwelling patients were randomly and consecutively included in the month of their birthday during the study period. Likewise, all new care home residents and those who had not recently been exposed to deprescribing received the intervention in the study period. Thus, no systematic difference between included and non-included patients was expected. In contrast to the highly selected patient groups often included in randomised controlled trials, our study population more likely represents an unselected real-world patient population, which strengthens the generalizability of our results. Further, the

study 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 CCM and include both care home residents and community-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. Consequently, no causal links can be made between the intervention and our results. Another important limitation was that the QI project was unpowered to detect relevant differences in general condition and functional level because of the modest sample size obtained during the allocated project period. Thus, these results should be interpreted with caution. Additionally, the use of purposively developed outcome measures limited the comparability with other studies, but because of limited resources, more comprehensive outcome measures were considered infeasible. Moreover, the staff assessing the outcomes were not trained specifically for this assessment. As the outcome measures were very simple, this was not considered to be necessary. We did not attempt any blinding in this study as this was considered too complicated in this real-life setting. However, a systematic review on deprescribing interventions among older residents in nursing homes showed that the absence of blinding was common because of the nature of the intervention and the setting.<sup>22</sup> Other factors as, for example, mood and cognitive function may have influenced the outcomes. Unfortunately, in this QI project, we were unable to collect sufficient and valid data on, for example, mood and cognitive function. However, the mentioned factors are somehow included in the assessment of general condition and functional level. An additional limitation was the followup period of 3-4 months. As medical conditions in older patients are unstable,<sup>43</sup> more medications change, including potential restarts as well as additional deprescribing, which 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-month 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.<sup>44</sup>

#### 5 | CONCLUSION

In this real-world QI study settled in primary care, we found that a systematic GP-led medication review

intervention was associated with deprescribing and increased self-reported health status without a deterioration of the general condition or functional level among care home residents and community-dwelling patients with chronic diseases. Our results should be interpreted with caution given the small sample size and the lack of a control group. Yet, the results add a new aspect to the existing literature and suggest 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. Statistician Martin Jensen from the Department of Research Data and Statistics, Aalborg University Hospital, is acknowledged for his assistance with the statistical analyses.

#### CONFLICT OF INTEREST STATEMENT

None declared.

#### ORCID

Anne Estrup Olesen D https://orcid.org/0000-0001-9365-1918

*Kirsten Høj* bttps://orcid.org/0000-0001-6591-0548

#### REFERENCES

- Canio WC. Polypharmacy in older adults. *Clin Geriatr Med.* 2022;38(4):621-625. doi:10.1016/j.cger.2022.05.004
- Jyrkkä J, Enlund H, Korhonen MJ, Sulkava R, Hartikainen S. Patterns of drug use and factors associated with polypharmacy and excessive polypharmacy in elderly persons: results of the Kuopio 75 study: a cross-sectional analysis. *Drugs Aging*. 2009; 26(6):493-503. doi:10.2165/00002512-200926060-00006
- Masnoon N, Shakib S, Kalisch-Ellett L, Caughey G. What is polypharmacy? A systematic review of definitions. *BMC Geriatr*. 2017;17(1):230. doi:10.1186/s12877-017-0621-2
- O'Donnell LK, Ibrahim K. Polypharmacy and deprescribing: challenging the old and embracing the new. *BMC Geriatr*. 2022;22(1):734. doi:10.1186/s12877-022-03408-6
- Baruth JM, Gentry MT, Rummans TA, Miller DM, Burton MC. Polypharmacy in older adults: the role of the multidisciplinary team. *Hosp Pract.* 2020;48(sup1):56-62. doi:10. 1080/21548331.2019.1706995
- Rochon PA, Gurwitz JH. Optimising drug treatment for elderly people: the prescribing cascade. *BMJ*. 1997;315(7115):1096-1099. doi:10.1136/bmj.315.7115.1096
- Scott IA, Hilmer SN, Reeve E, et al. Reducing inappropriate polypharmacy: the process of deprescribing. *JAMA Intern Med.* 2015;175(5):827-834. doi:10.1001/jamainternmed.2015.0324
- Beuscart J-BB, Pont LG, Thevelin S, et al. A systematic review of the outcomes reported in trials of medication review in older patients: the need for a core outcome set. *Br J Clin Pharmacol.* 2017;83(5):942-952. doi:10.1111/bcp.13197
- 9. Dalin DA, Frandsen S, Madsen GK, Vermehren C. Exploration of symptom scale as an outcome for Deprescribing: a

BCPT

medication review study in nursing homes. *Pharmaceuticals*. 2022;15(5):1-13. doi:10.3390/ph15050505

- Ali MU, Sherifali D, Fitzpatrick-Lewis D, et al. Interventions to address polypharmacy in older adults living with multimorbidity. *Can Fam Physician*. 2022;68(7):E215-E226. doi:10. 46747/cfp.6807e215
- WHO. WHO. Global campaign: Medication Without Harm. 2019. https://www.who.int/patientsafety/medication-safety/ campaign/en/
- Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42(2):377-381. doi:10.1016/j.jbi.2008.08.010
- Pedersen KM, Andersen JS, Snødergaard J. General practice and primary health care in Denmark. *J am Board Fam Med.* 2012;25(SUPPL. 1):34-38. doi:10.3122/jabfm.2012.02.110216
- Pottegård A, Olesen M, Christensen B, Christensen MB, Hallas J, Rasmussen L. Who prescribes drugs to patients: a Danish register-based study. *Br J Clin Pharmacol.* 2021;87(7): 2982-2987. doi:10.1111/bcp.14691
- Praktiserende Lægers Organisation. Læge- Og Praksispopulationen 1977–2020. Nøgletal Fra Medlemsregisteret [General Practioners and General Practice Clinics 1977–2020]. Key Figures from the Member Register; 2020.
- Danish Health Authority. Seponeringslisten 2023. 2023. Accessed May 24, 2023. https://www.sst.dk/da/viden/Laegemidler/ Rationel-Farmakoterapi/Medicingennemgang/Seponeringslisten
- Garfinkel D. Poly-de-prescribing to treat polypharmacy: efficacy and safety. *Ther Adv Drug Saf.* 2018;9(1):25-43. doi:10. 1177/2042098617736192
- Tveden-Nyborg P, Bergmann TK, Jessen N, Simonsen U, Lykkesfeldt J. BCPT policy for experimental and clinical studies. *Basic Clin Pharmacol Toxicol*. 2021;128(1):4-8. doi:10.1111/ bcpt.13492
- 19. General Data Protection Regulation (GDPR). Compliance Guidelines. https://gdpr.eu/
- Rankin A, Cadogan CA, Patterson SM, et al. Interventions to improve the appropriate use of polypharmacy for older people. *Cochrane Database Syst Rev.* 2018;9(9):CD008165. doi:10.1002/ 14651858.CD008165.pub4
- Thillainadesan J, Gnjidic D, Green S, Hilmer SN. Impact of deprescribing interventions in older hospitalised patients on prescribing and clinical outcomes: a systematic review of randomised trials. *Drugs Aging*. 2018;35(4):303-319. doi:10.1007/ s40266-018-0536-4
- Kua C-H, Mak VSL, Huey Lee SW. Health outcomes of deprescribing interventions among older residents in nursing homes: a systematic review and meta-analysis. *J am Med Dir Assoc.* 2019;20(3):362-372. doi:10.1016/j.jamda.2018.10.026
- Almutairi H, Stafford A, Etherton-Beer C, Flicker L. Optimisation of medications used in residential aged care facilities: a systematic review and meta-analysis of randomised controlled trials. *BMC Geriatr.* 2020;20(1):1-19. doi:10.1186/s12877-020-01634-4
- Thio SL, Nam J, van Driel ML, Dirven T, Blom JW. Effects of discontinuation of chronic medication in primary care: a systematic review of deprescribing trials. *Br J Gen Pract.* 2018; 68(675):e663-e672. doi:10.3399/bjgp18X699041
- 25. Ulley J, Harrop D, Ali A, Alton S, Fowler DS. Deprescribing interventions and their impact on medication adherence in

#### 2 BCDT Basic & Clinical Pharmacology & To

community-dwelling older adults with polypharmacy: a systematic review. *BMC Geriatr*. 2019;19(1):1-13. doi:10.1186/s12877-019-1031-4

- Ibrahim K, Cox NJ, Stevenson JM, Lim S, Fraser SDS, Roberts HC. A systematic review of the evidence for deprescribing interventions among older people living with frailty. *BMC Geriatr.* 2021;21(1):1-16. doi:10.1186/s12877-021-02208-8
- Dharmarajan TS, Choi H, Hossain N, et al. Deprescribing as a clinical improvement focus. *J am Med Dir Assoc*. 2020;21(3): 355-360. doi:10.1016/j.jamda.2019.08.031
- Garfinkel D, Mangin D. Feasibility study of a systematic approach for discontinuation of multiple medications in older adults: addressing polypharmacy. *Arch Intern Med.* 2010; 170(18):1648-1654. doi:10.1001/archinternmed.2010.355
- van der Velde N, Stricker BHC, Pols HAP, van der Cammen TJM. Risk of falls after withdrawal of fallrisk-increasing drugs: a prospective cohort study. *Br J Clin Pharmacol.* 2007;63(2):232-237. doi:10.1111/j.1365-2125.2006. 02736.x
- Potter K, Flicker L, Page A, Etherton-Beer C. Deprescribing in frail older people: a randomised controlled trial. *PLoS ONE*. 2016;11(3):1-21. doi:10.1371/journal.pone.0149984
- Garfinkel D, Zur-Gil S, Ben-Israel J. The war against polypharmacy: a new cost-effective geriatric-positive approach for improving drug therapy in disabled elderly people. *Isr Med Assoc J.* 2007;9(6):430-434.
- 32. Jungo KT, Mantelli S, Rozsnyai Z, et al. General practitioners' deprescribing decisions in older adults with polypharmacy: a case vignette study in 31 countries. *BMC Geriatr.* 2021;21(1):1-12. doi:10.1186/s12877-020-01953-6
- Reeve E, Moriarty F, Nahas R, Turner JP, Kouladjian O'Donnell L, Hilmer SN. A narrative review of the safety concerns of deprescribing in older adults and strategies to mitigate potential harms. *Expert Opin Drug Saf.* 2018;17(1):39-49. doi: 10.1080/14740338.2018.1397625
- 34. Verdoorn S, Kwint HF, Blom JW, Gussekloo J, Bouvy ML. Effects of a clinical medication review focused on personal goals, quality of life, and health problems in older persons with polypharmacy: a randomised controlled trial (DREAMER-study). *PLoS Med.* 2019;16(5):1-18. doi:10.1371/ journal.pmed.1002798
- 35. McCarthy C, Clyne B, Boland F, et al. GP-delivered medication review of polypharmacy, deprescribing, and patient priorities in older people with multimorbidity in Irish primary care (SPPiRE study): a cluster randomised controlled trial. *PLoS Med.* 2022;19(1):1-19. doi:10.1371/journal.pmed.1003862

- 36. Salisbury C, Man MS, Bower P, et al. Management of multimorbidity using a patient-centred care model: a pragmatic cluster-randomised trial of the 3D approach. *Lancet*. 2018; 392(10141):41-50. doi:10.1016/S0140-6736(18)31308-4
- Schäfer I, Kaduszkiewicz H, Mellert C, et al. Narrative medicine-based intervention in primary care to reduce polypharmacy: results from the cluster-randomised controlled trial MultiCare AGENDA. *BMJ Open.* 2018;8(1):1-14. doi:10.1136/ bmjopen-2017-017653
- Trenaman SC, Kennie-Kaulbach N, d'Entremont-MacVicar E, et al. Implementation of pharmacist-led deprescribing in collaborative primary care settings. *Int J Clin Pharm* Published online. 2022;44(5):1216-1221. doi:10.1007/s11096-022-01449-w
- Schiøtz ML, Høst D, Christensen MB, et al. Quality of care for people with multimorbidity - a case series. *BMC Health Serv Res.* 2017;17(1):1-9. doi:10.1186/s12913-017-2724-z
- Riordan DO, Byrne S, Fleming A, Kearney PM, Galvin R, Sinnott C. GPs' perspectives on prescribing for older people in primary care: a qualitative study. *Br J Clin Pharmacol.* 2017; 83(7):1521-1531. doi:10.1111/bcp.13233
- Wang T, Tan JYB, Liu XL, Zhao I. Barriers and enablers to implementing clinical practice guidelines in primary care: an overview of systematic reviews. *BMJ Open*. 2023;13(1): e062158. doi:10.1136/bmjopen-2022-062158
- 42. Baumgartner A, Kunkes T, Clark CM, et al. Opportunities and recommendations for improving medication safety: understanding the medication management system in primary care through an abstraction hierarchy. *JMIR Hum Factors*. 2020; 7(3):e18103. doi:10.2196/18103
- Macias FM, Ramsay RE, Rowan AJ. Recruitment and retention in clinical trials of the elderly. *Int Rev Neurobiol*. 2007;81: 265-272. doi:10.1016/S0074-7742(06)81017-2
- Reilev M, Lundby C, Jensen J, Larsen SP, Hoffmann H, Pottegård A. Morbidity and mortality among older people admitted to nursing home. *Age Ageing*. 2019;49(1):67-73. doi: 10.1093/ageing/afz136

**How to cite this article:** Olesen AE, Væver TJ, Simonsen M, Simonsen PG, Høj K. Deprescribing in primary care without deterioration of healthrelated outcomes: A real-life, quality improvement project. *Basic Clin Pharmacol Toxicol.* 2024;134(1): 72-82. doi:10.1111/bcpt.13925