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Perspectives on deprescribing in older people with type 2 diabetes and/or cardiovascular conditions: challenges from healthcare provider, patient and caregiver perspective, and interventions to support a proactive approach

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ABSTRACT
Introduction: For people with type 2 diabetes and/or cardiovascular conditions, deprescribing of glucose-lowering, blood pressure-lowering and/or lipid-lowering medication is recommended when they age, and their health status deteriorates. So far, deprescribing rates of these so-called cardiometabolic medications are low. A review of challenges and interventions addressing these challenges in this population is pertinent.

Areas covered: We first provide an overview of relevant deprescribing recommendations. Next, we review challenges for healthcare providers (HCPs) to deprescribe cardiometabolic medication and provide insight in the patient and caregiver perspective on deprescribing. We summarize findings from research on implementing deprescribing of cardiometabolic medication and reflect on strategies to enhance deprescribing. We have used a combination of methods to search for relevant articles.

Expert opinion: There is a need for rigorous development and evaluation of intervention strategies aimed at proactive deprescribing of cardiometabolic medication. To address challenges at different levels, these should be multifaceted interventions. All stakeholders must become aware of the relevance of deintensifying medication in this population. Education and training for HCPs and patients should support patient-centered communication and shared decision-making. Development of procedures and tools to select eligible patients and conduct targeted medication reviews are important for implementation of deprescribing in routine care.

1. Introduction

Many people with type 2 diabetes (T2D) and/or cardiovascular conditions have a high risk of polypharmacy [1,2]. Polypharmacy is commonly defined as the concurrent use of five or more chronic medications [3]. Such polypharmacy occurs in at least half of people with T2D or cardiovascular diseases [1,4]. Polypharmacy in older people with such diseases is associated with negative outcomes [5]. Polypharmacy in itself is not necessarily inappropriate. The medication prescribed may at some point in time have been indicated. However, reviewing the medication use of older T2D patients on polypharmacy showed that more than 25% received at least one medication identified as potentially inappropriate [2]. Potentially inappropriate medication use is not typical for this population; it has been observed among many older people [6]. In the past decades, education, prescribing audits and medication reviews have been recommended to address potentially inappropriate medication use [7,8]. At first, these initiatives were focused on stopping of specific medication that was considered inappropriate for older people. Tools have been developed to identify potentially inappropriate medication, such as the Beers list and the Screening Tool of Older Persons’ potentially inappropriate Prescriptions (STOPP) criteria [9]. More recently, optimizing medication among older people has evolved into stopping or decreasing medication when the benefits no longer outweigh the risks, a process which is called ‘deprescribing’ [10]. For older people with T2D and/or cardiovascular conditions, deprescribing may include deintensifying of glucose-lowering, blood pressure-lowering, and/or lipid-lowering medication. These are the so-called cardiometabolic medications.

1.1. What is deprescribing?

We define deprescribing as the ‘process of medication withdrawal or reduction, supervised by a healthcare provider (HCP), in the context of an individual’s comorbidity, functional status, treatment goals and preferences, and life expectancy’ [11–13]. Deprescribing thus includes any medication deintensification, that is, medication discontinuation, dose reduction or switch to less potent and lower risk medication. The context of the individual patient is important. Decisions have to be made repeatedly on whether or not to continue medication when the patient’s context...

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changes, for example, due to aging. Consideration of deprescribing should thus be part of routine care. To prevent the onset of medication-related harm and reduce medication burden, a proactive approach is needed [14]. Deciding on whether or not to continue prescribing requires a shared decision-making process, eliciting the patient’s current values and preferences regarding the treatment and relevant outcomes as input for the decision [15]. Several reviews have looked at the impact of deprescribing interventions. Such interventions can result in the reduction of potentially inappropriate medication but did not show clear effects on reduction of falls or hospitalizations [8,10,16]. It has been suggested that deprescribing might reduce mortality, but methodological limitations of the underlying studies, such as small sample size and short follow-up, cast doubt on this inference [17].

1.2. Guidelines to deprescribe cardiometabolic medication

In recent years, the evidence on the benefits and risks of deprescribing cardiometabolic medication has been summarized in clinical practice guidelines [18–20]. This has resulted in recommendations and decision-support algorithms on when deprescribing can be considered, usually focusing on people of 65 or 70 years or older. Generally, deprescribing is not recommended in people who are not frail, have a long life expectancy (>5–10 years), and/or have a high cardiovascular risk. In these people, it is usually beneficial to continue the medication. The benefits of preventive medication, however, can become limited by a reduced life expectancy [21,22]. With advanced age and frailty, the achievement of strict targets with medication is less beneficial and can even become harmful [23–28]. The benefits and risks of deprescribing cardiometabolic medication depend on the patient’s health status, number and type of medication used, and risk factor levels (see also section 3).

1.3. Rates of deprescribing

So far, deprescribing rates of cardiometabolic medication among older people appear to be low, ranging between 14% and 27% in outpatient settings [29,30]. Among potentially overtreated patients in long-term care facilities deintensification rates ranged from 22% to 50% [31–35]. These numbers illustrate that deprescribing of cardiometabolic medication may not be easy to implement.

1.4. Outline of this review

In this paper, we first provide an overview of the current recommendations for deprescribing cardiometabolic medication in older patients. Next, we go into the challenges for HCPs to deprescribe medication, with a particular focus on cardiometabolic medication, and we present what is known about the patient and caregiver perspective on deprescribing. We summarize findings from research on implementing deprescribing of cardiometabolic medication and reflect on models and strategies suggested to enhance deprescribing in clinical practice. With this, we aim to sketch the way forward to optimize deprescribing among older people with T2D and/or cardiovascular conditions.

2. Setting and methods

Our focus is on older patients treated with cardiometabolic medication who are not yet at the end of life. This is a large and diverse group for whom deprescribing recommendations can be difficult to implement. This includes people in ambulatory care, nursing homes and hospital settings but not those in palliative care, hospices or other end-of-life care settings. Although various age cutoffs have been used for defining old age, we included information related to people of 65 years and older. By doing so, the population can range from fit to frail and from those with a long to a relatively short life expectancy. There are differences in life expectancy between high-income and low-income countries, but in general, decreases in life expectancy are seen among people due to chronic conditions like T2D [35].

We used a combination of methods to search for relevant articles and information. First, we used existing reviews on barriers and facilitators of deprescribing, including a chapter we wrote on this topic for the Dutch guidance on deprescribing [36]. For that chapter, we had conducted studies assessing views of HCPs and patients with diabetes and/or cardiovascular diseases on deprescribing [37–39]. Furthermore, we built upon reviews on rates, determinants, and success of implementing deprescribing in people with T2D and/or cardiovascular conditions [29,40,41], and research on improving healthcare and deprescribing for older people with multimorbidity and polypharmacy [42–44]. We used our experiences from research on developing and testing a multicomponent training program for HCPs to support the implementation of deprescribing of cardiometabolic medication [45,46]. We included information presented at the first International Conference in Deprescribing [47], and searched PubMed in September 2023 for recent studies on
guidance and implementation of deprescribing of cardiometabolic medication, using terms related to ‘diabetes medication,’ ‘antihypertensives’ and ‘statins’ (see Appendix for search strategy).

3. Recommendations for deprescribing cardiometabolic medication

Deprescribing glucose-lowering, blood pressure-lowering and lipid-lowering medication includes various options of medication deintensification, i.e. medication discontinuation, dose reduction, or switching to medication with a lower risk of adverse drug effects. In general, the treatment goals and in whom to consider treatment deintensification depend on the patients’ health status [48–51]. Among older patients in good health, that is, with few comorbidities and few limitations in activities of daily living (ADL), treatment goals are relatively strict and medication deintensification should be considered only in those experiencing adverse drug effects and/or with risk factor levels below the treatment target levels. In case of intermediate health status, that is, with at least 3 comorbidities and/or mild cognitive or physical impairment, targets should be more relaxed and medication deintensification could also be considered in those experiencing medication burden or having difficulties to manage certain drugs. In those with poor health, targets can be relaxed further and medication deintensified accordingly.

3.1. Glucose-lowering medication

Continuation of intensive diabetes treatment, particularly with sulfonylureas and insulins, in older and frail people with low glycated hemoglobin A1c (HbA1c) levels increases the risk of hypoglycemia. Simultaneously, the benefits related to a reduction of macro- and microvascular complications decrease in this population. Therefore, it is recommended to reduce glucose-lowering medication in patients at high risk of hypoglycemia and/or in whom benefit is uncertain due to high age, comorbidities, or long diabetes duration [18–20]. Dose reduction or regimen simplification can be considered for people experiencing difficulties regarding the correct use of insulin. It appears that deintensification of medication with a high risk of hypoglycemia is feasible without unacceptable increases in glycemic control [29,40,41,52,53]. This can be effective for reducing the rates of hypoglycemia [29,54].

3.2. Blood pressure-lowering medication

Intensive treatment with antihypertensive agents in older people with low blood pressure levels increases the risk of orthostatic hypotension, falls, and medication-related hospitalization. At the same time, in people with advanced age and low cardiovascular risk without prior vascular diseases, the benefits of continuing medication to reduce vascular events become uncertain. Therefore, it is recommended to relax the blood pressure targets in older and frail patients and deprescribe medication accordingly, particularly in those treated with multiple antihypertensive agents [19,20]. Deprescribing of antihypertensive medication appears feasible with limited and acceptable or temporary increases in blood pressure [53,55–57].

3.3. Lipid-lowering medication

The guidance is less clear for deprescribing of lipid-lowering medication. Recommendations have been made for deprescribing of statins considering time to benefit, frailty, and multimorbidity. For primary prevention, the time to benefit from statins is estimated to be 2–5 years. Deprescribing can be considered in more frail people with limited life expectancy or in those experiencing adverse drug effects [19,20,58]. In people with advanced age (85 years or older), the benefits of statins are substantially reduced [19,20]. Polypharmacy, which is common in older people, increases the risk of drug–drug interactions. Interactions mediated by CYP 450 enzymes can result in increased risk of muscle-related toxicity of statins, which can be a reason for deprescribing [19]. For secondary prevention, statin treatment is recommended despite advanced age, but treatment can be tailored depending on the patient’s health status, prognosis, and preferences.

Considerations for deprescribing cardiometabolic medication are summarized in Table 1.

4. Challenges for healthcare providers

Research on barriers and facilitators experienced by HCPs for implementing deprescribing is dominated by qualitative studies, particularly among physicians. Using focus groups or interviews both challenges and opportunities have been summarized. Some studies used theoretical models for this, such as the Theoretical Domains Framework (TDF) [39,59,60]. In reviews, the TDF [61] and other models or theories have been used, such as the Socio Ecological Model (SEM) [62] and the Normalization Process Theory [63]. Some researchers have developed their own framework or categories to describe their results [64,65].

4.1. Challenges identified in qualitative research

We have summarized the challenges identified in qualitative research in four general domains informed by the TDF (Table 2). We particularly focused on challenges that have been mentioned in relation to deprescribing of cardiometabolic medication [39,61,65]. Some challenges appear specific for primary care HCPs or pharmacists, which is indicated in Table 2. Most HCPs experience a lack of evidence or knowledge on the benefits and risks of deprescribing. There is also uncertainty about when to deprescribe. Primary care HCPs mention they lack skills to explain reasons for stopping these drugs to the patients and their family. Both primary care HCPs and specialists mentioned their limited training on deprescribing. There seems to be clinical inertia and lack of motivation to change cardiometabolic medication when there are no problems. Most HCPs expressed fear of adverse outcomes after stopping medication. Such outcomes felt more as a consequence of their actions than when a negative outcome
would occur with continuation of the medication. These challenges are seen in general, but it seems that some HCPs are particularly reluctant to deprescribe cardiometabolic medication. This may be driven by beliefs about the necessity of these drugs to prevent cardiovascular events and the fear of becoming responsible for such events after stopping. Challenges seen with regard to professional collaboration are similar to those observed for deprescribing in general. Lack of communication and collaboration between HCPs, uncertainty about responsibilities, and not wanting to change medication initiated by other HCPs are often mentioned barriers to deprescribing. Lack of trust from patients to change cardiometabolic medication is perceived by pharmacists. Finally, there are time and financial constraints. Deprescribing is not yet part of routine care for many HCPs. Lack of awareness and overview of patients in need of deprescribing and also lack of support from professional organizations and absence of incentives to deprescribe have been mentioned as barriers. Specific for cardiometabolic medication are the challenges seen regarding lack of access to blood pressure and other clinical measures by pharmacists and lack of remuneration for close monitoring during follow-up by physicians.

4.2. Challenges identified in surveys

Quantification of these findings has been limited and it should be noted that some challenges may be typical for the period or the population included. Given that deprescribing guidelines have been published in more recent years in countries like Canada, Australia, and the Netherlands, one can expect that lack of guidance is less seen as a challenge by HCPs in these countries nowadays. There have been a few studies using questionnaires or case vignettes to quantify HCP barriers, attitudes, and willingness to deprescribe [66–69]. A recent survey study observed that pharmacists had higher knowledge and awareness of deprescribing benefits but perceived more external barriers than physicians [68]. Other studies show that there are differences in perceived barriers to deprescribing cardiometabolic medication between countries, disciplines, medication classes, and patient characteristics. For example, concerns about interfering with other physicians when deprescribing cardiovascular medication was reported by around 70% of general internists and geriatricians and by just over 50% of cardiologists [66]. Patient reluctance was reported as barrier by around 60% of geriatricians and 40–45% of general internists and cardiologists. Barriers reported by less than 40% of these specialists included patients’ lack of understanding of deprescribing, insufficient time to explain deprescribing to patients, medico-legal concerns, insufficient evidence of benefits, concern about upsetting patient and/or family, insufficient time to engage in complex decision-making, and deprescribing not being reimbursable [66]. Limited training was mentioned by general internists (16%). Regarding specific medication, it was found that geriatricians were more prone to deprescribe antihypertensives and statins than cardiologists [66]. For general practitioners (GPs), important factors influencing their

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<tbody>
<tr>
<td>Good health, no physical/cognitive impairment, independent</td>
<td>HbA1c below 6.5%-7%</td>
<td>[19, 20, 26, 49–51]</td>
<td>Blood pressure below 130/80 mmHg</td>
<td>[50*]</td>
<td>Use of high intensity statin, aim for 50% LDL reduction</td>
<td>[50*]</td>
</tr>
<tr>
<td>Intermediate health, mild physical/cognitive impairment, partially dependent on assistance for ADL</td>
<td>HbA1c below 7%-8%</td>
<td>[20, 26, 49–51]</td>
<td>Blood pressure below 140/90 mmHg</td>
<td>[50*, 57]</td>
<td>Use of statin for primary prevention and life expectancy less than time to benefit (2–5 year)</td>
<td>[19,20,48,58]</td>
</tr>
<tr>
<td>Poor health, moderate-severe physical/cognitive impairment dependent for ADL</td>
<td>HbA1c below 7.5%-8.5%</td>
<td>[20, 26, 49,50]</td>
<td>Blood pressure below 150/90 mmHg</td>
<td>[50*, 57]</td>
<td>Depending on life expectancy, clinical judgment and patient preferences</td>
<td>[19, 20, 48, 50*, 58]</td>
</tr>
<tr>
<td>Other considerations</td>
<td>Hypoglycemic events</td>
<td>[19,20,26,49,51]</td>
<td>Hypotension related adverse effects</td>
<td>[19,20,57]</td>
<td>Muscle-related adverse effects when treated with statins</td>
<td>[19,20,48,58]</td>
</tr>
<tr>
<td></td>
<td>Treated with insulin or sulfonylurea</td>
<td>[20, 26, 51]</td>
<td>Treated with multiple antihypertensives and SBP &lt;130 mmHg</td>
<td>[20]</td>
<td>Treated with high intensity statin</td>
<td>[50*]</td>
</tr>
<tr>
<td></td>
<td>Advanced age (e.g. ≥80 year) or &lt;10 year life expectancy</td>
<td>[19,26,51]</td>
<td>Advanced age (e.g. ≥80–85 year)</td>
<td>[19,20]</td>
<td>Advanced age (e.g. ≥85 year) depending on cardiovascular risk</td>
<td>[20, 50*]</td>
</tr>
<tr>
<td></td>
<td>Impaired renal function</td>
<td>[26,51]</td>
<td>Diastolic blood pressure &lt;60–70 mmHg</td>
<td>[20,57]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Long duration diabetes (e.g. ≥20 years)</td>
<td>[26,51]</td>
<td></td>
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</tr>
</tbody>
</table>

* For older people with type 2 diabetes; Ref, References; ADL, Activities of Daily Living; HbA1c, glycated hemoglobin A1c; SBP, Systolic Blood Pressure; LDL, Low Density Lipoprotein.
Table 2. Key challenges for deprescribing cardiometabolic medication perceived by healthcare providers as derived from qualitative research.

<table>
<thead>
<tr>
<th>Domain</th>
<th>Challenge in general and toward cardiometabolic medication</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence &amp; expertise (TDF domains: Knowledge; Skills; Beliefs about capabilities)</td>
<td>Insufficient data/lack of evidence on benefits and risks</td>
<td>[39,62–65]</td>
</tr>
<tr>
<td></td>
<td>Single-disease guidelines focus on prescribing #</td>
<td>[62,63]</td>
</tr>
<tr>
<td></td>
<td>Lack of deprescribing guidelines #</td>
<td>[39,62,63]</td>
</tr>
<tr>
<td></td>
<td>Lack of knowledge/uncertainty when or how to taper and/or stop specific medication #</td>
<td>[61–65]</td>
</tr>
<tr>
<td></td>
<td>Insufficient knowledge about newer medications to stop them #*</td>
<td>[39]</td>
</tr>
<tr>
<td></td>
<td>Lack of communication skills to discuss and explain reasons for stopping with patients and family #</td>
<td>[39,61,62]</td>
</tr>
<tr>
<td>Beliefs &amp; fears (TDF domains: Motivation and goals; Social influences; Beliefs about consequences; Emotion)</td>
<td>Inertia to change medication; lack of interest in deprescribing; not motivated when there is no problem</td>
<td>[39,63–65]</td>
</tr>
<tr>
<td></td>
<td>Maintaining status quo feels safer/is easier; negative outcomes of stopping weigh more than negative outcomes of continuing prescribing</td>
<td>[39,63,64]</td>
</tr>
<tr>
<td></td>
<td>Uncertainty/fear of adverse outcomes; anticipated regret</td>
<td>[39,62–65]</td>
</tr>
<tr>
<td></td>
<td>Strong belief in continuation of medication; cardiometabolic medication is often needed *</td>
<td>[39,61,63,64]</td>
</tr>
<tr>
<td></td>
<td>Belief that patients or caregivers do not want medication stopped</td>
<td>[39,61–65]</td>
</tr>
<tr>
<td></td>
<td>Fear that patients or family perceive deprescribing as being ‘given up’</td>
<td>[39,63,65]</td>
</tr>
<tr>
<td></td>
<td>Negative previous experience</td>
<td>[63,65]</td>
</tr>
<tr>
<td></td>
<td>Fear of legal implications or complaints from family #</td>
<td>[62–64]</td>
</tr>
<tr>
<td></td>
<td>Lack of communication between HCPs</td>
<td>[62–65]</td>
</tr>
<tr>
<td></td>
<td>Lack of collaboration or support of other HCPs and/or medical specialists #</td>
<td>[39,61–64]</td>
</tr>
<tr>
<td></td>
<td>Devolved responsibility or uncertain about responsibility/tasks</td>
<td>[39,61–64]</td>
</tr>
<tr>
<td></td>
<td>Not wanting to change medication started by specialist #</td>
<td>[39,62,63,65]</td>
</tr>
<tr>
<td></td>
<td>no interference with other HCPs’ treatment plan</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lack of trust of patient (for pharmacists) */poor patient-provider relationship</td>
<td>[39,61–63,65]</td>
</tr>
<tr>
<td></td>
<td>Lack of time or opportunity; insufficient time to manage complex process of deprescribing; lack of awareness/not in routine process</td>
<td>[39,61–65]</td>
</tr>
<tr>
<td>Professional collaboration &amp; interpersonal factors (TDF domains: Professional role &amp; identity; Nature of behavior)</td>
<td>Lack of tools for patient education and risk communication with patients #</td>
<td>[62,63]</td>
</tr>
<tr>
<td></td>
<td>Lack of systems or templates to aid initiation of deprescribing and communication to other HCPs (for pharmacists) #</td>
<td>[61–63]</td>
</tr>
<tr>
<td></td>
<td>Lack of simple and time-efficient tools for risk assessment and (electronic) clinical decision-support #</td>
<td>[39,63]</td>
</tr>
<tr>
<td></td>
<td>Lack of reimbursement, including remuneration for close monitoring when tapering or stopping medication; more incentives to prescribe; reduced income (for pharmacists) #</td>
<td>[39,62–65]</td>
</tr>
<tr>
<td></td>
<td>Lack of information exchange between HCPs; lack of access to blood pressure and other clinical measurements (for pharmacists) # *</td>
<td>[39,62–65]</td>
</tr>
<tr>
<td></td>
<td>Insufficient overview/no reminders of patients in need of deprescribing #</td>
<td>[39,63,64]</td>
</tr>
<tr>
<td></td>
<td>Professional associations do not give attention to deprescribing #</td>
<td>[39]</td>
</tr>
</tbody>
</table>

#Reported mostly by primary care providers; * reported particularly for cardiometabolic medication; HCP, HealthCare Provider; TDF, Theoretical Domains Framework.

deprescribing decisions included fear of potential negative outcomes (95%), difficult communication with patients/relatives (70%), interprofessional collaboration and communication (79% and 78%), existence of deprescribing guidelines and tools (76% and 70%), and expenditure of time (48%) [67].

4.3. Willingness to deprescribe cardiometabolic medication

A recent survey study conducted among physicians in the United States explored factors influencing deprescribing sulfonylureas or insulin [70]. It was found that 71–74% of these physicians would be willing to deintensify when a patient experienced hypoglycemia or a decline in health, whereas 49–62% were willing to do so because of old age, polypharmacy, or when a patient desired less medication. Most physicians, however, would not deintensify this medication for older patients with complex and poor health who had HbA1c levels between 7.3% and 7.7%, as was recommended by American Diabetes Association (ADA) guidelines [71]. This indicates that physicians may be uncomfortable with relaxing HbA1c targets. Others studied willingness to deprescribe antihypertensives in primary prevention patients with high levels of ADL dependency and reported rates between 6% and 49%, depending on type of medication and specialty [66,67]. Rates were lower for angiotensin-converting-enzyme-inhibitors as compared to other antihypertensives and higher for geriatricians compared to general internists and cardiologists. Willingness to deprescribe statins in such patients was generally higher, with rates ranging from 23% for cardiologists to 77% for GPs [66,67].

5. Patient and caregiver perspective

5.1. Barriers and facilitators to deprescribing in general

Reeve et al. summarized the barriers and facilitators in relation to the patients’ willingness to have their medication deprescribed [72]. They clustered factors around five themes: appropriateness, fear, process, influences, and dislike. Barriers included beliefs about the necessity, fear of missing out on future benefits, mistrust of recommendations to stop, fears about negative outcomes when stopping medication, lack of physician support or time, previous bad experiences with stopping, and discouragement by a physician, family, or friends. Later reviews identified similar barriers [73,74]. Complexity of the healthcare system with multiple medical providers and lack of communication
between HCPs were added as barriers perceived by patients [74]. Regarding chronic disease management, changes in treatment targets were identified as barrier [74]. The belief that medication taken for a long time must be appropriate was reported as a barrier for caregivers [73]. Some caregivers expressed fear or uncertainty about initiating medication conversations with the HCP [73].

Facilitators toward deprescribing for patients include a general dislike of medication, beliefs about lack of effectiveness, experiencing or fearing side effects, availability of support, and having the option to restart [72]. Several reviews mentioned trust in the HCP, carefully planning the deprescribing process, and having a monitoring process in place as facilitators for both patients and caregivers [73,74]. Shared decision-making and deprescribing education were further identified as facilitators [74].

5.2. Barriers and facilitators to deprescribing cardiometabolic medication

Several studies focused on barriers and facilitators for patients and caregivers to deprescribing of cardiometabolic medication [37,75,76]. Beliefs about appropriateness and necessity of such medication were reported as barriers. This perceived need was linked to expectations regarding better health, improvement of risk factor levels, disease control, and survival. Some patients, however, may have unrealistic views of the benefits of their medication [76]. Other barriers were having experienced a cardiovascular event or having a family history of cardiovascular diseases. Also, fear of experiencing a cardiovascular event after deprescribing and uncertainty about risks and benefits were reported as barriers. The uncertainty raised by changing or conflicting treatment targets formed a barrier to deprescribing cardiometabolic medication [75]. Some patients and caregivers became confused about changing targets and would distrust proposals from other HCPs than the original prescriber to discontinue cardiometabolic medication [37]. Deprescribing contrasted with the belief that this medication should be taken until end of life. As such, there was ignorance of the concept of deprescribing [61]. Experiencing no side effects was a barrier for some patients to changing their cardiovascular medication [65].

Several facilitators related to deprescribing cardiometabolic medication were similar as those reported for deprescribing in general. This included a dislike of medication, experiencing or fearing side effects, positive experiences with deprescribing, and trusting the HCP who advised deprescribing. Facilitators more specific for cardiometabolic medication included close monitoring of risk factor levels, beliefs that the disease was under control and/or cardiovascular risk was low, perceiving no improvement or change in risk factors while being on medication, and a lack of understanding the concept of risk reduction with cardiometabolic medication [65,76].

Crutzen et al. mapped the barriers and facilitators in four themes related to (1) beliefs and fears about the medication, (2) beliefs and fears about stopping medication, (3) relationship with the HCP, (4) conditions to stop [37]. Based on their findings among 18 patients, a deprescribing typology was proposed of patients with a positive opinion about medication and unwilling to stop, patients with a positive opinion about medication but willing to stop, patients with a negative/ambivalent opinion about medication and willing to stop, and patients indifferent toward both medication taking and stopping. This was similar to a typology suggested by Weir et al. for deprescribing in general [77].

5.3. Attitudes toward deprescribing

Quite a number of studies have quantified patients’ attitudes toward deprescribing, often using the Patients Attitudes Toward Deprescribing (PATD) or revised Patients Attitudes Toward Deprescribing (rPATD) questionnaire [78]. These questionnaires include a general question on the willingness of patients to stop medication when their doctor would recommend this and additional subscales assessing attitudes related to perceived ‘appropriateness of medication,’ ‘burden of medication,’ ‘concerns about stopping,’ and ‘involvement in decisions about medication.’ The willingness to stop one or more of their regular medications was generally high, with percentages of patients agreeing between 68% and 97% [78]. Percentages of patients willing to stop medication were lower in low-middle-income countries compared to high-income countries [79]. The rPATD questionnaire was also used to assess patients attitudes and willingness to stop cardiometabolic medication [38,80]. Both studies illustrated that a general willingness to stop medication does not mean that a patient has an intrinsic desire to try stopping specific cardiometabolic medication. Patients may be more open to reducing the dose of such medication instead of stopping it altogether [80]. The percentage of patients that would like to try stopping a sulfonylurea agent was 19%, for stopping insulin this was 12%, for stopping antihypertensive medication this was also 12%, whereas 32% would like to try stopping their statin [38]. Of note, there were no clear differences in concerns about stopping these specific medications. Differences were, however, seen regarding their perceived appropriateness of these medications.

6. Implementing deprescribing of cardiometabolic medication

6.1. Simple interventions

Research on the development and evaluation of interventions to enhance the implementation of deprescribing is rapidly expanding, but the number of studies on deprescribing cardiometabolic medication is still limited. Several single-arm studies have been conducted to evaluate the feasibility and effects of protocols, reminders, and decision support tools for such deprescribing (Table 3). For example, one pilot study evaluated the feasibility of implementing a protocol for deprescribing blood pressure-lowering medication in primary care [81]. Although this seemed feasible, the number of general practices and patients that consented to participate was low. This indicates that more needs to be done to prepare practice organizations and patients for implementing deprescribing protocols in clinical practice. Three studies explored the effect of making HCPs aware of diabetes patients eligible for deprescribing. It was observed that automated alerts or
reminders can lead to deintensification of glucose-lowering treatment in 10%–26% of the patients, with higher rates when patients reported hypoglycemic symptoms [82,83]. When HCPs received a notification of a limited number of patients that were potentially overtreated with the encouragement to reevaluate treatment, deintensification was initiated in 56% of these patients [84]. This process of deprescribing was considered to be time-consuming [84]. A clinical decision support tool added to a screening tool was tested in the HypoPrevent study [85]. The decision support tool and instructional guide were intended for use during patient consultations. The HCPs were trained to use the tool to individualize HbA1c goals together with the patient. This study showed that setting individual goals was feasible for most patients, but glucose-lowering treatment was deintensified in only 20% of the patients. The authors concluded that this demonstrated the difficulty of deprescribing these drugs despite available guideline recommendations and support tools [85].

6.2. Complex interventions

Two studies have evaluated more complex interventions, where deprescribing of cardiometabolic medication was embedded in tailored clinical medication reviews (CMR). One was a cluster-randomized trial in Norwegian nursing homes, where a two-day education seminar was offered to ‘ambassadors’ in the intervention group focusing on optimizing blood pressure-lowering treatment [86]. The education included knowledge and skills training about communication and shared decision-making with patients and relatives. The ambassadors were responsible for short daily training sessions with the rest of the staff and CMRs were planned for consenting patients. This multicomponent intervention led to reduced blood pressure-lowering medication regimes in 32% of the intervention patients compared to 10% in the control group [86]. Another was a quasi-experimental study conducted in the Netherlands to assess the potential effects of a pharmacy-led multicomponent intervention aimed at deprescribing cardiometabolic medication in a targeted CMR in primary care [45]. Participating community pharmacists received a six-hour training covering the following topics: problems related to hypoglycemia, deprescribing guidelines for cardiometabolic medication, and patient counseling about deprescribing. During the training, attention was paid to barriers perceived by patients and HCPs. The participants received several supportive tools: a conversation aid to guide patient consultations about deprescribing, an agreement card for patients to document medication changes that were discussed, and a summary of the deprescribing guidelines with information on how and when to deprescribe specific cardiometabolic medication [45]. In 48% of the patients at least one cardiometabolic medication was deintensified after the CMR, which was significantly more in comparison to 31% in the control group [45]. This study was accompanied with a process
evaluation study [46]. Both the pharmacists and the patients were positive about the CMRs focusing on deprescribing of cardiometabolic medication. Suggestions for improvement included: adaptation of the patient selection tool to include less patients not eligible for deprescribing, specific training and tools for discussing deprescribing with patients who do not perceive negative effects of the medication themselves or who have a stable health condition, and more explicit local collaboration and agreements on deprescribing [46]. Furthermore, it was noted that more training in shared decision-making could be useful.

6.3. Generic interventions

There are many generic interventions aimed at reducing inappropriate polypharmacy, which have been evaluated in trials [44]. Reduction of cardiometabolic medication has been observed in some of these interventions. For example, a GP-led intervention – including a five-hour deprescribing training for GPs and a patient-centered CMR with support of pharmacists – resulted in deprescribing of statins, oral glucose-lowering medication, and diuretics [87].

7. Addressing the challenges

As said, challenges for HCPs include lack of evidence on the benefits of deprescribing cardiometabolic medication, fears about negative outcomes, lack of guidelines and tools, lack of communication skills and training, lack of interprofessional collaboration and communication, and finally, lack of time and reimbursement. For patients, perceived need to continue such medication, fear about negative outcomes, and confusion about changes are barriers to overcome. To address these challenges, one can make use of facilitators reported for deprescribing of cardiometabolic medication [39,61,65] and learn from intervention strategies developed to address perceived barriers toward deprescribing in general [88–90]. The interventions that have been tested are quite heterogenous, which limits the ability to draw conclusions on optimal interventions. To identify key components of interventions and map them to barriers and facilitators, different framework or models have been used [91–94]. We use the socio-ecological model to group barriers and facilitators at different levels: societal/system level, organizational/institutional level, interpersonal level, and individual level (Figure 1). Within each level, subdivisions can be made. For example, the interpersonal level includes the interactions between HCPs from different disciplines as well as interactions between HCPs and patients. The individual level includes barriers and facilitators for HCPs and those for patients and caregivers.

7.1. Societal/system level

More high-level evidence is needed on the benefits and risks of discontinuation or deintensification of specific medication as compared to continuation of the medication. Currently, there are few randomized controlled trials (RCT) assessing the benefits and risks of discontinuation or deintensification of glucose-lowering medication in older people with T2D and most are of poor quality [52]. There has been one RCT assessing the noninferiority of reducing antihypertensive medication among older patients treated with multiple antihypertensives [95]. This RCT demonstrated that the

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Figure 1. Barriers and facilitators at different levels of the socio-ecological-model.
proportion of patients with a systolic blood pressure <150 mmHg after 12 weeks did not differ between the intervention and control group. Also, no differences in harms were observed. One RCT evaluated discontinuation of statins among patients in a palliative care setting and showed that this did not result in differences in harmful effects within 60 days [96]. More RCTs are clearly needed with longer follow-up and inclusion of other patient populations. Of note, the evidence on the benefits and risks of continuing cardiometabolic medication in older people with frailty or multimorbidity is also limited. Trials focusing on effects of such medication in older patients include relatively healthy individuals [97]. Information from well-designed observational studies remains valuable, for example, using a propensity score-matched cohort design [54]. Goyal et al. suggested that N-of-1 trials can provide relevant evidence for deprescribing in individuals, while allaying concerns that may inhibit participation in an RCT [98]. Internationally, there are several deprescribing research networks and organizations that aim to develop and disseminate evidence about deprescribing for older adults [99]. On their websites guidelines and tools can be found that can support deprescribing of cardiometabolic medication [19,20,100]. It has been stressed that existing clinical guidelines should also include recommendations on deprescribing [101]. A good example is the ADA Standards of Care in Diabetes, which includes a chapter with schemes and considerations for treatment regimen simplification and deintensification in older adults with diabetes [102].

Reimbursement and incentives to deprescribe may be important, but little is known about their impact. It has been posed that in countries where pharmacists are involved and receive reimbursement for assisting in CMRs, deprescribing interventions are more feasible [89]. Incentives could be related to prescribing quality measures. Currently, these indicators support prescribing instead of deprescribing [103]. One measure for assessing potential overtreatment among patients 80 years and older with an HbA1c level <53 mmol/mol was included in a previously developed quality indicator set for T2D [104]. With longitudinal data, this can be transformed into a deprescribing indicator assessing the proportion of eligible patients in whom glucose-lowering medication is deintensified within a certain period [105].

There is also a need for a change in culture at societal and system level [42]. Prescribing of medication has been an important part of the identity of many clinicians and stopping treatment may be associated with adequate care only at the end of life. An overall awareness and acceptance that deprescribing is part of good prescribing is needed. As such, deprescribing should be incorporated in competency frameworks for healthcare curricula [106]. Also, professional organizations can support the implementation of deprescribing, for example, by endorsing deprescribing guidelines and offering platforms and courses to disseminate deprescribing recommendations. Public awareness needs to increase as well. Survey studies in Canada illustrated that public awareness for deprescribing was 8.2% in 2020 and had not substantially increased since 2016 [107].

### 7.2. Organizational/institutional level

Fragmented care and lack of information exchange between HCPs can lead to unwanted continuation of medication treatment, inappropriate addition of medication or unintended restarts [108,109]. It has become clear that both primary and secondary care physicians are reluctant to change medication started by another HCP. Among GPs and community pharmacists, there is reluctance to initiate deprescribing of cardiometabolic medication that was started by a specialist. Not knowing the indication for the medication may decrease their confidence to take a proactive role. Part of this challenge might be addressed at organizational or institutional level, for example, with ICT systems to share patient information and support information exchange between HCPs [83,110]. Efficient communication between HCPs has been considered essential for co-management of cardiovascular medication [22]. Electronic portals to share information, easy access to expert advice, and user-friendly decision support have been suggested as interventions to support deprescribing [110]. Multidisciplinary teams can support the process of deprescribing, making use of different expertise and increasing the efficiency of the process [14,111]. It has been acknowledged that team-based efforts -including clinicians, pharmacists and nurses- are among the more effective interventions to overcome clinical inertia in diabetes care [112]. In particular, pharmacist-physician collaboration for conducting medication reviews is an effective strategy to support deprescribing [111,113]. It has been shown that pharmacy-led CMRs can increase deprescribing of cardiometabolic medication [45]. Furthermore, agreements can be made at an organizational level about general principles of deprescribing, for example, which patient groups will be targeted for deprescribing.

### 7.3. Interpersonal level

To prevent inefficient care and frustration, agreements about roles and responsibilities are important [111]. This may overcome also part of the reluctance to change medication started by somebody else. Moreover, deprescribing can be a complex and time-consuming process, where task delegation and changes in workflow can help to overcome some of the perceived barriers. Agreements regarding the role of a pharmacist or a dedicated nurse in the deprescribing process can be included in local agreements that may already be in place to manage medication for older people with polypharmacy. Besides more structural changes focusing on efficient information exchange at organizational level, it is important that there is constructive communication between individual HCPs responsible for the same patient [111]. Maintaining good relationships with colleagues and patients can be at stake [110]. Collaboration and partnership between HCPs has been mentioned as facilitator to deprescribing cardiometabolic medication [39].

Furthermore, constructive communication with and trust of patients is key to successful implementation of deprescribing [111]. Training in motivational interviewing, patient-centered communication and shared decision-making can be part of
existing healthcare curricula. Applying these skills in the process of deprescribing may require further training. Relevant models used in such training include the Calgary Cambridge consultation model and the three-talk model for shared decision-making developed by Elwyn et al. [114,115]. These models have been used to develop a communication training program to involve older people in decisions to deprescribe cardiometabolic medication [116]. Also, electronic deprescribing tools have been developed aimed at facilitating patient-centered deprescribing by promoting information exchange for a shared decision-making process and to empower patients [117]. There are decision aids and option grids for engaging patients in deprescribing conversations [99,118]. Finally, especially community pharmacists have expressed the challenge that some patients do not trust them to propose changes in cardiometabolic medication [39]. To build trust, it should be clear for the patient that their physician supports the initiative of the pharmacist.

Interprofessional education and training in deprescribing has been recommended [106]. Such education can be useful to understand and practice how, for example, physicians, pharmacists and nurses can collaborate with patients and caregivers in the deprescribing process. Various learning activities have been suggested, such as interprofessional discussions on responsibilities and practicalities of implementing deprescribing, applying deprescribing concepts to patient cases, and working through simulated interprofessional case studies [106].

### 7.4. Individual level

Knowledge, beliefs, and fears about the benefits and risks of continuation and discontinuation of medication are important factors to be considered at individual level. For example, the knowledge that hypoglycemia is a greater risk in older and frail patients than not achieving strict target levels is important for deprescribing glucose-lowering medication [39]. Similarly, the belief that it is okay for blood pressure levels to increase after discontinuation of antihypertensives is relevant for deprescribing such medication [39]. General beliefs or attitudes toward the need to prevent overtreatment and reduce polypharmacy can be drivers of taking action [39,65]. Education and tools have been developed to increase knowledge, awareness, and motivation to initiate deprescribing [100]. Training of HCPs is relevant to increase their skills and confidence and to support appropriate use of tools for deprescribing [39,92,111]. The Behavior Change Techniques framework has been used to classify components included in various interventions [91,92]. Components more often included in effective interventions are: (a) goal setting and action planning, (b) instructions and guidance on how to perform deprescribing, and (c) information about consequences [91]. Exchanging positive experiences, practicing communication skills, and making use of social influences can be of help [39,65,111]. One example of a successful intervention is D-PRESCRIBE, which was a pharmacist-led intervention to educate both older people and their physicians about reducing inappropriate medication, such as glyburide [119]. Deprescribing decisions are decisions under uncertainty creating cognitive and emotional stress, which can be diminished by a patient-centered and multidisciplinary approach [93,120].

Building on the Transtheoretical Stages of Change model, strategies can be developed to support individuals to adopt, implement, and maintain new behavior [121]. In their review of deprescribing interventions, Coe et al. observed that there are interventions focusing on all stages of change [122]. This includes strategies to engage HCPs in deprescribing activities, for example, in multidisciplinary workshops or practice recruitment and training. As mentioned before, reminder and alert systems have been developed to raise awareness and identify T2D patients eligible for deprescribing. Selection of patients most likely to benefit from deprescribing can be difficult. When patients were selected on an algorithm including demographic and medication information, HCPs felt this was not optimal [46]. It was suggested that longitudinal information on recent medication reviews and recent medication changes could improve the selection process. Furthermore, there are consumer-targeted interventions focusing on the early stages of change. Preparing patients for conversations about deprescribing may be necessary. Brochures have been developed that include quizzes and questions people can ask themselves about their medication and information relevant for deprescribing decision-making, for example, on sulfonylureas [123]. In a pilot study, mailing this brochure to patients two weeks before a scheduled primary care visit led to more discussions about the medication and more deprescribing compared to a control group [124]. Other brochures, fact sheets and videos have been developed to inform people about deprescribing, but few are available for cardiometabolic medication [99,118]. For deprescribing glucose-lowering medication, one information pamphlet and an infographic are available in English and French [100]. Interventions focusing on the later stages of change, in particular addressing relapse and maintenance, include audit and feedback for HCPs [122].

Several step-by-step approaches have been proposed for the process of deprescribing at individual level [125]. We have grouped them in five keys steps for a patient-centered deprescribing process (Table 4). Each of these step can be supported with training and tools for HCPs and patients [122,125]. There are generic step-by-step guides, algorithms, and protocols for deprescribing [126,127]. Consideration of a patient’s history and eliciting a patient’s goals and preferences are important in the early steps of deprescribing [94]. There are implicit and explicit tools that identify medication that is usually considered potentially inappropriate for older people [99]. Some explicit tools include recommendations for stopping cardiometabolic medication [128,129]. There are also algorithms with questions guiding the medication review and software applications that support automated assessment of the medication [125]. One example of a web-based decision support system, which is publicly available, is MedStopper [130]. This can be used to prioritize medication eligible for deprescribing and to find tapering schemes for specific cardiometabolic medication. For patients and caregivers, discussing a monitoring and follow-up plan with agreements on when to restart medication is essential [37,125].
8. Conclusion

Deprescribing for older people with T2D and/or cardiovascular conditions is restricted by barriers perceived by HCPs, patients, and caregivers. Deprescribing of cardiometabolic medication is currently more reactive (e.g. when patients report adverse drug effects) than proactive. Our review illustrates that many of the barriers are similar to those identified for deprescribing in general, but some may be of more importance for cardiometabolic medication. Strong beliefs regarding the need for such medication until the end of life may inhibit proactive deprescribing. Also, the initiation and intensification of cardiometabolic medication is guided by strict treatment targets, such as HbA1c or blood pressure levels to be achieved. The concept that at some point in time achieving these strict targets is no longer needed and medication can be deintensified is not yet widely acknowledged. Intervention strategies are needed to further implement deprescribing of cardiometabolic medication. There are currently few well-designed studies that can provide information on the best intervention strategy. Single component interventions are unlikely to lead to meaningful changes. Multicomponent approaches are recommended, focusing on HCPs, patients and caregivers. In addition, changes are needed at societal and organizational level to support deprescribing becoming part of routine care.

9. Expert opinion

9.1. Interventions for behavior change

There is a need for rigorous development and evaluation of intervention strategies aimed at proactive deprescribing for people with T2D and/or cardiovascular conditions in routine care. To address challenges perceived at different levels by HCPs, patients and caregivers, these need to be multicomponent, modular interventions. Interventions should include training and tools for different stages of the deprescribing process both for HCPs from various disciplines and for patients with different levels of readiness to change. Modular interventions provide the necessary flexibility, since not all components need to be delivered or applied to all stakeholders at the same time. Intervention strategies should pay attention to adoption, implementation, and maintenance of changes in deprescribing behavior.

Informed by our review of challenges, implementation strategies, and mapping to behavioral change techniques, relevant intervention components at different levels of the socio-ecological model are:

1. **System/individual level**: dissemination of evidence-based guidelines and recommendations; education, training, and tools for HCPs on why, how, and when to deprescribe specific cardiometabolic medication in light of a patient’s individual condition; audit and feedback on deprescribing behavior; endorsement and reimbursement of deprescribing activities;

2. **Organizational/interpersonal level**: multidisciplinary team-based initiatives; clarity on roles and agreements on information exchange and continuity of care (e.g. who will do what for which patients at which point in time); electronic systems to share information (e.g. access to relevant HbA1c or blood pressure measurements to identify and prioritize medication eligible for deprescribing); procedures or systems to align care for individual patients (e.g. incorporating consultations of other HCPs into the workflow);

3. **Interpersonal/individual level (HCPs)**: training and tools for a structured and patient-centered deprescribing process, including goal setting and action planning; (re)design workflows to incorporate patients’ goals and preferences; consider to continue or discontinue cardiometabolic medication for older patients regularly as part of routine care;

4. **Interpersonal/individual level (HCPs)**: training and tools for constructive patient consultation and shared decision-making (e.g. communication training, conversation and decision aids to explore views and preferences of patients or caregivers);

5. **Interpersonal/individual level (patients and caregivers)**: educational materials and tools for patient engagement throughout the deprescribing process, from contemplating the idea of deprescribing to being informed about benefits and risks of options, being involved in decision-making and follow-up (e.g. agreements about monitoring and when to restart).

Currently, a multidisciplinary training program for primary care HCPs, including many of the above mentioned components to support deprescribing of cardiometabolic medication in people of 75 years and older, is being evaluated in the cluster-randomized CO-DEPRESCRIBE trial [116]. Key components focus on patient-centered communication and shared decision-making within routinely conducted structured CMRs. Additional components pay attention to content and organizational aspects relevant for deprescribing cardiometabolic medication. E-learning and face-to-face
training sessions are offered to HCPs, in particular community pharmacists. The following tools and training are included: a patient leaflet preparing patients for discussing possibilities to deprescribe; an aid for navigating a conversation about deprescribing cardiometabolic medication; an aid for eliciting patient’s preferences, concerns, and experiences; an aid for following the steps of shared decision-making; an aid to elicit patient’s prioritization of treatment goals; practice using relevant risk calculators. By a comprehensive evaluation of this carefully designed training program, covering an effect and process evaluation at HCP and patient level as well as an economic evaluation, this study will increase knowledge needed for sustainable implementation of deprescribing cardiometabolic medication in a primary care setting.

There are other planned and ongoing studies aimed at assessing the effects of implementing deprescribing among people with T2D. For example, the OMed2 trial in the Netherlands [131], the D-MED study in the United Kingdom [132], the RETRO-DM study in the United States [133] and the DIAL study in Canada [134]. These studies will also contribute to the evidence on effective strategies to support deprescribing of glucose-lowering medication. Similar implementation studies are needed for deprescribing of cardiovascular medication. Ultimately, this may allow for reviews or meta-analyses to provide information on successful components of intervention strategies. There may be a need of adaptive randomized trials with multiple arms to determine which elements of a multicomponent intervention are most promising. Additionally, qualitative and quantitative research to elucidate when and how deprescribing decisions are made in clinical practice can point toward the components most relevant for HCPs and patients [103,135].

Aside from interventions in clinical practice, it is important to incorporate the concept of deprescribing and the competencies needed in healthcare curricula [106]. In medical curricula that work with the World Health Organization (WHO)-6-step method for rational prescribing, the 6th step of monitoring treatment should include repeated evaluation of the need to continue or discontinue chronic medication, particularly in older people [136].

9.2. Improving feasibility, efficiency, and cost-effectiveness

Lack of time and resources are an important barrier for change. This is true for the conduct of medication reviews in general, but the process of deprescribing may require additional time and resources. Further development of easy to use procedures and tools is an important area for making the implementation of deprescribing in routine care more feasible. The majority of interventions or activities for deprescribing focus on the key steps for a patient-centered deprescribing process [122]. Tools and training have been developed and tested for the conduct of CMRs, identification of medication eligible for deprescribing, planning and initiation of deprescribing, monitoring, and follow-up. Prior to this, patients eligible for this deprescribing process need to be selected. This is usually incorporated in study procedures when evaluating interventions, but this should become part of routine practice. Selecting patients eligible for deprescribing of specific medication is not yet part of routine care. It is important that screening and selection algorithms become available for clinical practice. Not much research has been conducted on optimizing selection procedures to identify patients who are likely to benefit from deprescribing specific medication. One example making use of machine learning techniques developed an algorithm including demographic and medication data to identify patients potentially eligible for deprescribing of glucose-lowering medication [137]. This algorithm, which was applied on community pharmacy information systems, was not very specific. Particularly, patients were included for whom medication was recently intensified or for whom deprescribing had already been suggested or conducted [46].

Furthermore, explaining the concept of deprescribing to patients and involving them in a shared decision-making process may not fit within a regular patient consultation and not all patients will be open for this. Specific challenges of shared decision-making with older adults include their situational complexity, evidence gaps, and difficulties in sharing information [138]. For some patients, changing the medication may be too difficult to understand [103]. There are concerns about the feasibility of starting deprescribing conversations with all potentially eligible patients in routine care. For proactive deprescribing of cardiometabolic medication, one could focus on those patients who are most willing to discontinue or deintensify their medication. This aligns with the considerations presented in Table 1. Some research has been conducted to evaluate which screening questions can discriminate on patients’ willingness [139]. Also, research on patient typologies might be of help to identify these patients [37,77]. As important, when clinicians initiate cardiometabolic medication they should explain that over time it may be needed to first intensify and later deintensify the medication according to the patient’s condition.

Tapering of medication may take time. While most glucose-lowering medication and also statins can be discontinued at once, blood pressure-lowering medication and insulin usually need to be deintensified in smaller steps. Additional monitoring of the effects on blood glucose or blood pressure levels is recommended. To reduce the burden and costs of the deprescribing process, task delegation can be of help. By forming multidisciplinary teams, including physicians, pharmacists, and support staff (e.g. nurses, nurse practitioners, pharmaceutical consultants and assistants), tasks can be divided. For example, collecting medication history can be conducted by a pharmaceutical consultant, conversations with patients by a pharmacist in consultation with the physician, and monitoring by a nurse or nurse practitioner. Nonetheless, changes in reimbursement may be necessary to enable the conduct of deprescribing.

Another area where more research is needed concerns economic evaluations. We need to assess which intervention strategies are cost-effective and what the economic impact is when interventions are implemented on a broad, nation-wide scale. Very few cost-effectiveness studies have been conducted for deprescribing interventions in real-world settings. For the pharmacist-led D-PRESCRIBE intervention, two cost-utility analyses have been completed
Compared to usual care it was estimated that this intervention was cost-effective for deprescribing of sedatives and of non-steroidal anti-inflammatory drugs. Cost-effectiveness of implementation strategies depends on changes in the rate of deprescribing achieved. With minimum success rates of 20–25% in sensitivity analyses, the D-PRESCRIBE intervention remained cost-effective [140,141]. Of note, cost savings were driven more by anticipated reductions in adverse events than by reductions in medication costs. For medications used by people with T2D and/or cardiovascular conditions, these estimates can be quite different. In several of the ongoing studies focusing on deprescribing of cardiometabolic medication, economic evaluations are planned. Finally, more research should be conducted to assess long-term effects of interventions. Interventions can show an immediate effect that wanes off after several months [142].

9.3. Relevant outcomes

A challenge when assessing the impact of deprescribing concerns the choice of outcome measures. Martin-Kerry et al. developed a core outcome set for hospital deprescribing trials and identified six outcomes as important and feasible for this setting [143]. This set included: the number of prescribed medicines stopped, the number of prescribed medicines with dosage reduced, quality of life, mortality, adverse drug events, and number of hospital stays. Most deprescribing studies are not powered to assess differences in the latter four outcomes. A recent systematic review summarized the outcomes included in 36 deprescribing implementation studies and found that most studies include a medication outcome as primary outcome [144]. This review included one study focusing on cardiometabolic medication, which used the number of antihypertensive drugs prescribed as the primary outcome [86]. For deprescribing cardiometabolic medication, however, a composite medication outcome might be more appropriate [145]. A composite outcome can account for reductions in dosing as well as intensity due to medication switches that can be considered deintensification. In the quasi-experimental study from Crutzen et al., a composite measure was used to assess the proportion of patients for whom one or more cardiometabolic medication was stopped or reduced in dose [45]. How best to define and assess deprescribing from electronic health records is an area for future research. Although previous work on how to assess medication non-adherence and non-persistence may be of help, it also illustrates that looking only at prescription or dispensing data is of little use, since it is impossible to distinguish between patients deciding to stop taking their medication themselves and patients for whom this was conducted as part of deprescribing.

When implementation studies focus primarily on addressing specific barriers toward deprescribing, a different range of outcomes can be used to assess whether the implementation strategy was successful. For example, changes in knowledge, skills, or in perceived uncertainty or fears can be outcomes of interest. In the ongoing CO-DEPRESCRIBE trial, with key intervention components focusing on patient-centered communication and shared decision-making, the communication skills of HCPs, involvement of patients in decision-making, and patients’ attitudes toward deprescribing are included as secondary outcomes [116].

For cost-effectiveness studies, utility and disutility values can be used related to specific health states and adverse events relevant for medication continuation and discontinuation. It has been suggested to add novel patient-centered value elements [146]. These could be related to reducing the burden of taking many medications or aligning treatment plan with an individual’s goals [147]. Also, among older and frail people with T2D and/or cardiovascular conditions patient-reported outcomes related to symptom reduction, like dizziness, may be important to include.

9.4. The way forward

Awareness and acceptance that deprescribing of cardiometabolic medication is part of rational prescribing is fundamental to foster change. Up to now, the need of cardiometabolic medication is often named or perceived as ‘for the rest of your life.’ This results in a view that cardiometabolic medication should only be stopped or deintensified when adverse drug effects occur. We expect that this dogma will change in the coming five years, given the increase in initiatives and activities that promote a more proactive approach toward deprescribing of medication [147]. In the next five years, results will become available from several implementation studies focusing on deprescribing in people with T2D. Also, lessons learned from implementing deprescribing other medication can accelerate the development of successful strategies for deprescribing of cardiometabolic medication [148]. Particularly, initiatives to create public awareness and to train HCPs on how to conduct deprescribing consultations can be of help. Successful and cost-effective strategies can be adopted in regional or national programs for rational drug use and Choosing Wisely initiatives [149].

Currently, several initiatives focus on deintensification of glucose-regulating medication with the goal to reduce the risk of hypoglycemia in older and particularly frail people. More initiatives can be expected focusing on deprescribing of cardiovascular medication, with additional aims to reduce medication burden and discontinue medication with lack of evidence of efficacy in this population. Tools that are used in initiatives for deprescribing, such as the STOPP and the STOPP/FAIL (Screening Tool of Older Persons’ Prescriptions in Frail adults with limited life expectancy), already include criteria for deprescribing statins and antihypertensives [150,151]. Furthermore, with an increase in evidence on benefits and risks of deprescribing cardiometabolic medication, updates of treatment guidelines including recommendations for such deprescribing can be anticipated within the coming years [152].

Solving challenges at healthcare system and organizational level can take time. Where some countries and organizations are frontrunners in policies and programs to promote appropriate use of medication and embrace the concept of deprescribing, others lag behind. Currently, financial incentives for
appropriate prescribing and pay-for-performance programs do not include quality indicators for deprescribing cardiometabolic medication [148]. As a first step, deprescribing quality indicators can be expected for local audit and feedback. Policy changes are needed to allow for information exchange and to reimburse time that goes into deprescribing and compensate for loss of income. Changes are anticipated due to broader initiatives for adopting deprescribing in routine practice [14]. Incorporating health information technology that can support the deprescribing process in an efficient workflow needs further attention.

Finally, deprescribing of cardiometabolic medication should be conducted following an informed discussion with the patient and/or caregiver about uncertain benefits and harms of continuing versus discontinuing such medication. With a newer generation of HCPs who are better trained in shared decision-making, this can become more integrated in routine care consultations with patients.

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**References**

Papers of special note have been highlighted as either of interest (·) or of considerable interest (–) to readers.


- Paper explicitly addressing proactive deprescribing and how this is different from reactive deprescribing.


- Review illustrating that deprescribing in people with T2D is feasible, but support is needed for further implementation in clinical practice.


- One of the few studies assessing older people’s attitudes towards deprescribing specific cardiometabolic medications, illustrating that their willingness to have a particular medication deprescribed can be much lower than their willingness in general.


- Example of a quasi-experimental study evaluating an intervention focusing on deprescribing of cardiometabolic medication, showing the potential of a pharmacist-led intervention.


- Practical guide on how to identify eligible patients, how to conduct deprescribing conversations, and how to deintensify diabetes treatment.


- Review of evidence suggesting that deprescribing glucose-lowering medication may reduce rates of adverse events without deterioration of diabetes control while acknowledging the need for more well-designed studies.


66. Review of barriers and enablers for deprescribing cardiovascular medication from both patients' and healthcare providers' perspective, resulting in a proposal for an intervention using behavioural theory.


71. • Study that quantifies physicians’ intentions to deintensify or switch hypoglycemia causing medication, illustrating high levels of inaction in most clinical scenarios.


80. • Review of research using ‘Patient Attitudes Towards Deprescribing’ questionnaires, showing heterogeneity for patients and caregivers in their willingness to have a medication deprescribed, which could not be well predicted using participant characteristics.


Example of a randomized trial evaluating a complex intervention embedded in an existing care pathway, showing this can decrease the use of antihypertensives in nursing home patients.

- Review focusing on implementation of deprescribing in clinical practice, summarising barriers and enablers at patient, provider, system level and stressing the need for alignment of interventions with existing care processes.

- Systematic review and meta-analysis of deprescribing interventions, using a classification based on behaviour change techniques to identify components included in effective interventions and stressing the need for further research on determinants of success.


- Review that maps intervention activities to key steps in a patient-centered deprescribing process, starting with engaging HCP staff and patients for deprescribing with feedback on deprescribing actions.


- Review of generic tools linked to the subsequent steps for conducting deprescribing, showing similarities between different instruments and a lack of a practical and user-friendly tools.


131. Consequences of reducing hypoglycemia-inducing glucose-lowering medication (medication that lowers glucose [sugar] levels in the blood and can cause low blood sugar) in people with type 2 diabetes of 70 years or older [Internet]. ISRCTN registry - ISRCTN50000062. [cited 2024 Feb 28]. Available from: https://www.isrctn.com/ISRCTN50000062

