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REVIEW ARTICLE

Deprescribing, Polypharmacy and Prescribing Cascades in Older People with Type 2 Diabetes: A Focused Review

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Abstract | Deprescribing is the process by which medications are reduced without compromising safety to the patient (Jude et al. in 2022 Diabetes Ther 13: 619–634, 2022). The purpose of this narrative review is to discuss deprescribing as a topic, firstly discussing the benefits and pitfalls to such pharmacological interventions along with the current barriers and enablers to such a controversial topic, and then discussing deprescribing with respect to preventive medications, namely those that reduce the long term impacts of a condition or disease. Research that has previously focused on reducing polypharmacy has highlighted the benefits of such interventions, including reduction of adverse reactions or complications, improved patient satisfaction and quality of life, and improved cost effectiveness and drug compliance. Some potential harms that have been highlighted include an increased number of complications, increased symptoms of previously dampened conditions, and negligible changes in patient satisfaction that have stressed the importance of this intervention being patient centred and individualized to each patient. The implementation of deprescribing processes could drastically change the way people think about deprescribing and could be extremely beneficial to older patients living with type 2 diabetes worldwide. Developments in preventive medication deprescribing could pave the way for this intervention to become more common place improving the quality of life in patient's final years.

Keywords: *Type 2 diabetes mellitus, Cardiometabolic, Deprescribing, Elderly, End of life, United Kingdom*

1 Introduction

Deprescribing is a systematic process which can safely reduce medications in clinical practice through deintensification whereby they are simplified, reduced, or completely withdrawn in an effort to prevent the risk of polypharmacy[1]. With the term being first introduced back in 2003 by Michael Woodward in his article in the *Journal of Pharmacy Practice and Research*, many studies have identified the increasing incidence of polypharmacy in those with type 2 diabetes highlighting the importance of deprescribing as part of good prescribing practices. Deprescribing can be undertaken using four main intervention models, (1) a complete withdrawal of a medication, (2) tapering of a dose regime, (3) reducing the dose of a medication or (4) switching to an alternative medication which has a better benefit to harm ratio[2]. Deprescribing has the potential to reduce the number of adverse drug reactions (ADEs), reverse the potential iatrogenic harms of inappropriate polypharmacy, and reduce inappropriate or ineffective medicines, known as pill burden. Current evidence suggests that 64% (95% CI 45–80%) of older people with type 2 diabetes are taking more than five medications which is

Deprescribing: Reducing medication without compromising safety.

De-intensification: Medication is simplified, reduced or completely withdrawn in an effort to prevent the risk of polypharmacy and its associated adverse events, or alternatively, as complete withdrawal, discontinuation, reducing dosage, conversion, or substitution of at least one medication

Polypharmacy: The use of multiple medications.

Iatrogenic: Illness or disease induced by a medical examination or treatment.

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Table 1: Deprescribing approaches currently being used or developed within clinical practice[5,6].

Deprescribing approach	Main focus
STOPP/START	Identification of high risk outcomes and problems when prescribing in elderly patients, with respect to reduction of medication burden and the addition of beneficial interventions and therapies
Beers Criteria	Identification of medications that have an increased incidence of adverse events and outcomes in elderly patients due to multi-morbidity, ageing and altered pharmacokinetics
IMPACT tool	Improvement of Medicines and Polypharmacy Appropriateness Clinical Tool
7-Steps Approach	Guidance around polypharmacy centred around the individual
NO TEARS	Need and indication, Open questions, Tests and Monitoring, Evidence and guidelines, Adverse events, Risk reduction or prevention, Simplification, and switches
Deprescribing Rainbow	Conceptual framework which includes clinical, psychological, social and physical considerations
Bruyere Guidelines	Drug-specific guidelines
MedStopper	Web-based system which provides information on a medications benefits and risks
Good Palliative Geriatric Practice (GP-GP)	Determines the appropriateness of a medication and advises on the possible deprescribing approach to take

directly associated with negative outcomes including poor glycaemic control, increased hypoglycaemic events, increased incidences of falls and hospitalisations, and an increased mortality rate[3], with a study undertaken in Saudi Arabia on 8932 adults showing that polypharmacy is twice as prevalent in patients with coexisting cardiovascular conditions (83.4%, $p < 0.001$)[4]. To date, limited articles have been published focusing on the impacts of polypharmacy and its associated prescribing cascades in older patients with type 2 diabetes and assessed the specific risks that place an individual at risk of it, along with discussing deprescribing interventions and approaches that can be utilised in this vulnerable population.

Patient Decision Aids: Tools that enable the patient to become involved in the decision-making process during a medical consultation, by providing information about the available options and possible outcomes of the treatment.

2 Deprescribing Approaches

Enacting deprescribing practices within clinical practice has proven to be difficult. To date, multiple tools have been published to aid in the deprescribing process (Table 1). These approaches vary in their form and include basic frameworks, drug-specific deprescribing guidelines and deprescribing tools that can assist in a specific part of the deprescribing process, such as the identification of potentially inappropriate medications.

Deprescribing should be undertaken as a partnership between the patient and the healthcare provider and requires regular patient consultations and support from the prescribing practitioner. Discussions surrounding deprescribing need to be individualised and should only be undertaken with the patient's full understanding and acceptance. Patient decision aids (PDA's) can be of significant value when considering the shared decision making process and become useful when there are multiple possible courses of action that could be considered[7]. PDA's allow patients to weigh up the information and assess both the advantages and disadvantages of the different treatment options[8]. A commonly used PDA to capture how patient's feel about deprescribing is the Patient's Attitudes Towards Deprescribing (PATD) questionnaire and has been validated in many studies in recent years[7].

A valuable tool when assessing the older patient with type 2 diabetes is The American Geriatrics Society published Guiding Principles on the Care of Older Adults with Multimorbidity which was designed to aid clinicians in making patient-centred decisions when faced with uncertainty during a consultation and can help the clinician create an individualised management plan that aligns with the patient's health preferences and concerns. Along with generic tools, more specific guidelines include the antihyperglycaemics deprescribing guideline which suggests that antihyperglycaemics that are known to contribute to hypoglycaemia should be deprescribed, clinicians should also consider deprescribing in patients who are at high risk of adverse events, and glycaemic targets should be individualised to goals of care and with consideration to the time to benefit being noted.

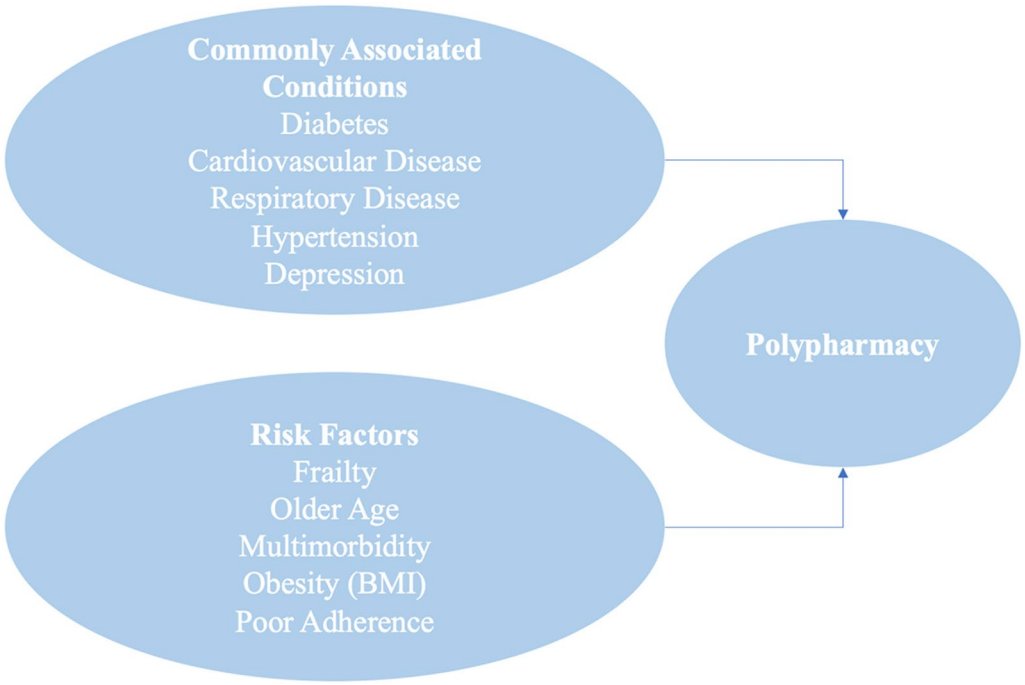

Figure 1: Determinants of polypharmacy.

3 Polypharmacy

Polypharmacy is commonly defined as the use of five or more medications being used by an individual[9], with its increased prevalence being largely related to the increasing ageing population worldwide and the ever increasing burden of multimorbidity. Global studies have suggested that on average elderly patients are consuming between 2 and 9 medications per day[10], and in those with type 2 diabetes is associated with multiple factors including sex, age, diabetes complications and aggressive diabetes overtreatment [11]. Increased incidences of prescribing are significantly associated with unsafe prescribing practices and rates of adverse events[12]. Studies have shown that one-third of the total population are using five or more drugs, and this was significantly associated with a 21% increased rate of falls over a 2 year period[13]. Polypharmacy is of major concern with the older population living with type 2 diabetes as clinicians feel responsible for treating microvascular and macrovascular complications to prevent further disease progression, with older patients being of particular risk due to multimorbidity, renal and hepatic disease and lack of adherence. For such patients, the implementation or continuation of preventive medications may no longer be rational, may increase the risks of adverse drug events (ADEs), a greater incidence of falls (with the higher the number of medications, the greater the incidence of falls) and may no longer align with the patients preferences, displaying the importance for pharmacovigilance in this patient population[13]. Figure 1 shows a few of the possible adverse outcomes and risk factors associated with polypharmacy.

It is also determined that a significant portion of the population receive repeat prescriptions with this proportion significantly increasing with the ageing population. With repeat prescriptions being generated automatically without the need for any GP consultations, medication reviews and medication optimisation rarely occurs within clinical practice for the older population. The implication of automated repeat prescriptions in this population represents a lack of prescribing quality, resulting in increased ADEs and increasing amounts of drug-related hospital admissions.[14] Repeat prescriptions raise into question the issues surrounding prescribing momentum, where medications are continued beyond their therapeutic need, and is a critically important risk when considering the management of this frail and vulnerable cohort of patients[15].

4 Prescribing Cascades

A prescribing cascade is a clinical situation whereby a set of signs and symptoms is incorrectly interpreted as a disease and as such is treated with the introduction of a new

Pharmacovigilance: The practice of assessing the effects of medical interventions after they have been initiated.

Multiple long-term conditions (Multimorbidity): The presence of two or more long-term diseases or conditions in the same individual.

Microvascular: Vessels within the circulatory system that measure less than 0.3mm in diameter and include capillaries and venules.

Macrovascular: Vessels within the circulatory system that are larger (macro) in diameter and include the arteries and the aorta.

Table 2: Examples of prescribing cascades.

Medication 1	Side effect	Medication 2	Side effect	Medication 3
Amlodipine	Ankle oedema**Oedema**: Accumulation of excess watery fluid within the tissue cavities of the body	Furosemide	Hypokalaemia	Sando K
Diltiazem	Ankle oedema	Chlorthalidone	Hyperglycaemia	Glyburide
Quetiapine	Tremor	Levodopa	Hypertension	Lisinopril
Amlodipine	Ankle oedema	Furosemide	Urinary Frequency	Tamsulosin

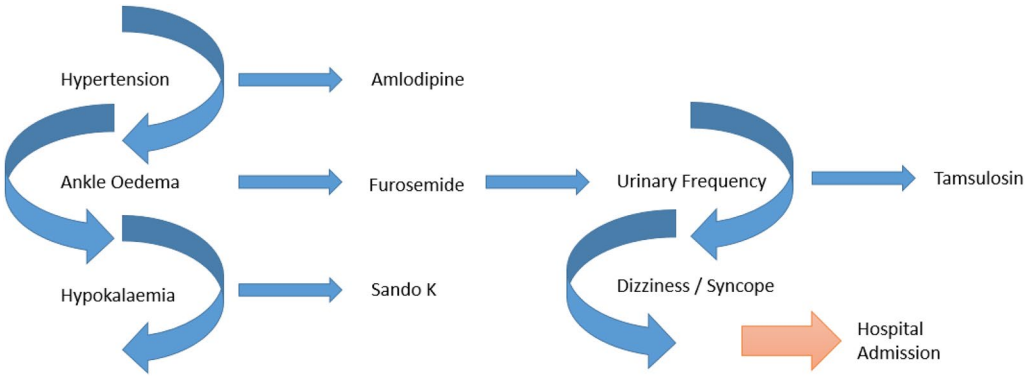

Figure 2: Diagrammatic example of a prescribing cascade.

medication, instead of performing a medication review and identifying the new signs and symptoms as negative side effects of a medication previously prescribed. Such prescribing cascades were first depicted by The Lancet in 1995, which was later reviewed by the BMJ in 2020 stating that it's a clinical situation whereby 'a drug is prescribed, an adverse drug event occurs that is misinterpreted as a new medical condition and a subsequent drug is prescribed'[16], with numerous examples of them being described since. Having a healthcare professional initiate and oversee the deprescribing process can result in fewer ADEs from occurring and can resolve many symptoms and complications that have occurred as a result[17]. Table 2 shows some simple examples of prescribing cascades, depicting how the use of one medication results in a new symptom which in turn leads to the addition of a new medication and so on and so forth.

A study looking into prescribing cascades by Farrell et al. showed that patients were unaware of the term and few patients recognised the side effects of their regularly used medications. Patients stated feelings of confusion surrounding their medications as these were regularly changed especially under stressful circumstances such as during an episode of hospitalisation. Other patients stated that they had *"lost track"* of their medications as their health had declined and the number of their regular medications used increased, with one patient stating "*I just take whatever I take and I don't worry about it now*".[18] These results show the lack of patient awareness towards their regular medications and their side effects which exacerbates the prescribing cascade problem, leaving healthcare clinician's to quickly determine the cause of new signs and symptoms under strict time constraints (Fig. 2).

Problematic polypharmacy and prescribing cascades in the older population is a global issue, with strict time constraints and fragmented care plans in place, along with the difficulties surrounding differentiating drug side effects and new medical conditions that are significant hurdles when considering safe de-prescribing practices. The prescribing concept is part of the wider problematic polypharmacy conundrum and aids in depicting drugs eligible to undergo deprescribing interventions. With new drugs continuously entering the medical market, leading to new and unknown prescribing cascades, it is vitally important that we get on top of well-known cascades now. Rochon and Gurwitz described three

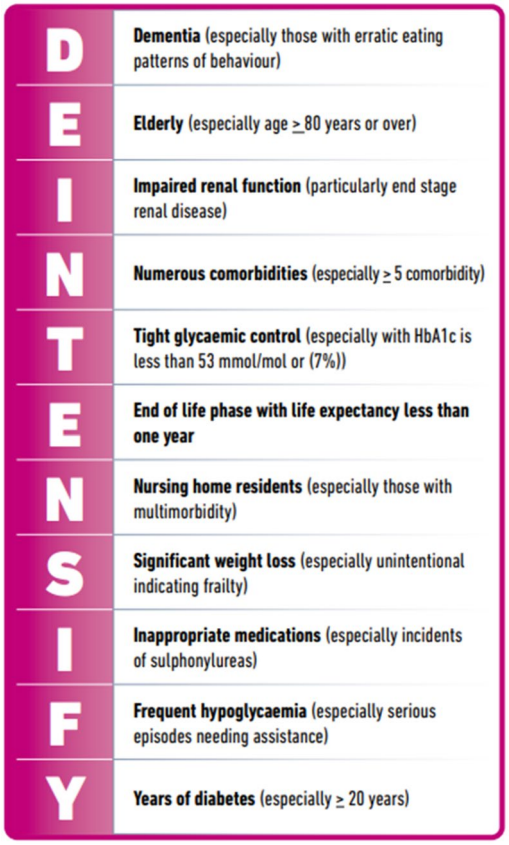

Figure 3: A mnemonic to help identify patients with diabetes who may be eligible to undergo deprescribing interventions[22].

clinically important questions to ask when considering a potential prescribing cascade, namely, is a new drug being prescribed to address an adverse drug event? Is the initial therapy that led to the cascade really needed? And finally, what are the benefits and harms of continuing the medication that led to the cascade?[16]

With the increasing incidence of automatically generated repeat prescriptions, untimely medication reviews and increased hospital admissions due to prescribing cascades that go unnoticed for prolonged periods of time, the need for deprescribing interventions to be comfortably implemented within clinical practice is needed urgently and deserve far greater attention by healthcare professionals than it currently receives.

5 Deprescribing in Diabetes with Severe Frailty

The shift in management in frail older patients should move from reducing the long term risks to improving the quality of patient's lives and reducing treatment burden. Appropriate deprescribing of antihyperglycaemics and the omission of diabetes related assessments that no longer improve the quality of patient's lives should be the mainstay of focus of diabetes related management plans in the frail older population. Older patients living with type 2 diabetes and multiple long term conditions may not prioritise improvements in microvascular and macrovascular benefits of long term management, even though they could benefit from outcomes such as a reduced risk of stroke and increased renoprotective mechanisms in those using glucagon-like peptide-1 receptor agonists (GLP-1) or sodium glucose co-transporter-2 (SGLT2)-inhibitors just as in the young[19,20]. Identification of eligible patients is vital, and Fig. 3 shows some examples of when patients with diabetes should be considered for such deprescribing approaches[21].

Target setting should be individualised to take into account the needs of the presenting individual but in those with an end of life status or significant frailty and co-morbidities, the aim of treatment should focus on improving the quality of life by reducing symptoms and hospitalisations, along with maintaining functional status. Targets such as HbA1c should be reduced and consideration into the benefits of statin and BP therapy in the individual should be thought about. Recommended targets should focus on maintaining HbA1c levels below 8.5% (< 69 mmol/l), with fasting plasma glucose of between 7.0 and 10.0 mmol, whilst blood pressure readings should be increased to a new goal of < 150/90[23].

Proposed deprescribing interventions in frail elderly people at risk of hypoglycaemia could include stopping sulphonylureas and considering the use of long-acting insulin analogues, such as insulin glargine U300 or insulin degludec, which have strong evidence of lower incidences of hypoglycaemia. The use of prandial rapid-acting insulins can be considered when blood sugar levels rise above the pre-agreed target of 15.0 mmol/l[24].

It is important to be aware of contraindications to well-known anti-diabetic medications such as metformin which is contraindicated in those with severe renal impairments (eGFR < 30 ml/min/1.73m^2) and used with caution in those with impaired hepatic functions, due to the potentially fatal risk of lactic acidosis, whilst thiazolidinediones (TZDs) should be avoided in those with symptomatic heart failure. For older patients, it is prudent to regularly monitor renal and hepatic function, for example every 3–6 months, in the frail and end of life

Renoprotective: protection of the kidneys from harmful effects or damage.

HbA1c: Glycated haemoglobin; used as a measurement to quantify the amount of glucose (sugar) attached to the haemoglobin within the blood stream over the last 2–3 months.

Prandial: relating to food or eating.

Lactic acidosis: A process by which the production of lactic acid exceeds the clearance of lactic acid

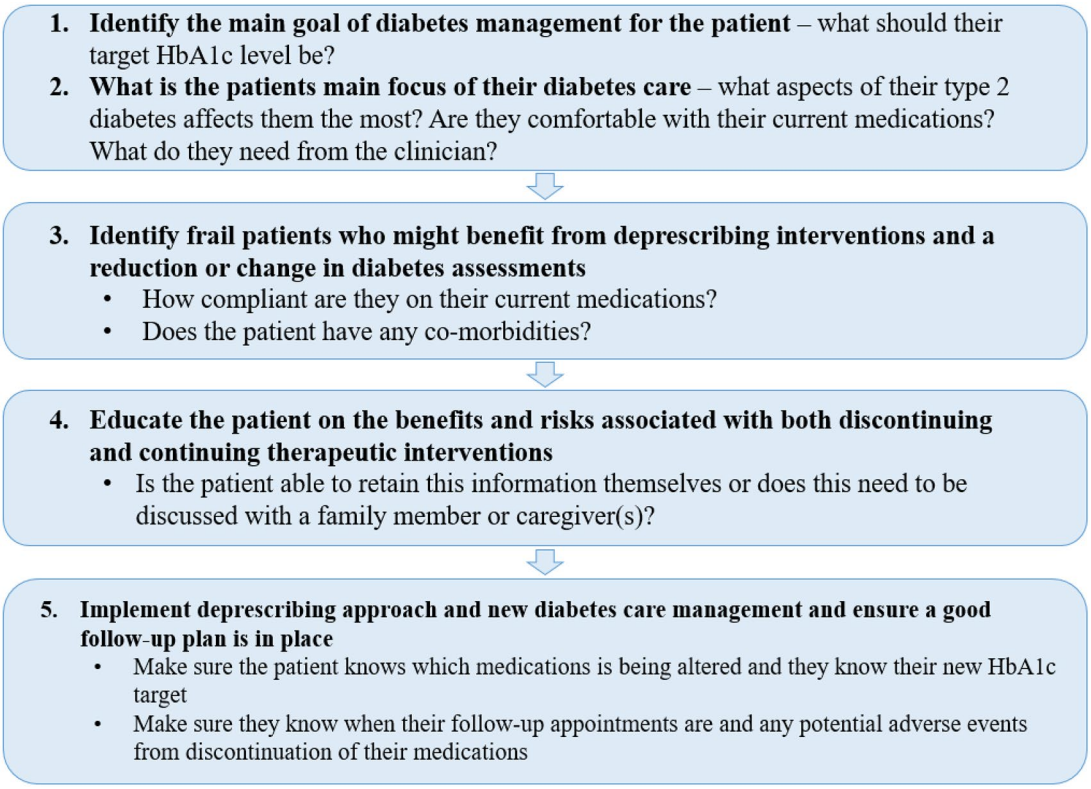

Figure 4: Flow diagram for the management of type 2 diabetes in frail and elderly patients.

population. Figure 4 depicts a flow chart that can be considered when identifying eligible patients for deprescribing.

When a patient becomes extremely frail, such as those with significant comorbidities, functional deficits and those with a markedly reduced life expectancy, their medications should be re-evaluated further, along with a re-evaluation of their functional and frailty status. Since avoidance of long term complication may no longer be a goal of treatment, medications such as metformin and GLP-1 RA's could be stopped, along with discontinuing TZD's (which could be substituted with dipeptidyl peptidase IV inhibitors (DPP4-i)), and sulfonylureas should be discontinued due to their increased risk of hypoglycaemia. This approach may just be enough to prevent acute hyperglycaemic excursions in addition to avoiding the side effects of these drugs that could compromise quality of life. Having regular consultations with the patient can also aid in the deprescribing process, showing the patient and the family member, that the approaches are aimed at improving quality of life symptoms and the focus is on comfort care in their final few days, with a reduction in polypharmacy hopefully improving pill burden.

6 The Role of Deprescribing in Avoiding Hyper- and Hypo- glycaemia

Older patients with type 2 diabetes are more likely to develop hypoglycaemia due to a number of factors including polypharmacy, weight loss, frailty, missing meals, cardiovascular disease, renal dysfunction, and endocrine deficits[24]. Whilst hypoglycaemia is more commonly remembered and included in patient care, hyperglycaemia and its associations can sometimes be overlooked. Medications that can cause hyperglycaemic events should be looked at with care when considering the management of diabetes in the older population, especially towards the end of life. Table 3 shows a list of medications that clinicians should be aware of to reduce the impacts of hyperglycaemia.

Table 3: Medications that can cause hyperglycaemia[22].

Type of medication	Examples
Corticosteroids	Prednisolone Dexamethasone Methylprednisolone Hydrocortisone
Antipsychotics–second generation	Olanzapine Clozapine Risperidone Quetiapine
Protease Inhibitors	Ritonavir Tipranavir Darunavir Etha-noate
Quinolones	Ciprofloxacin Moxifloxacin
Beta-blockers	Bisoprolol Atenolol Propranolol
Thiazide diuretics	Indapamide Chlorothiazide
Thiazide-like diuretics	Loop diuretics Thiazide Doxazosin
Calcineurin inhibitors	Tacrolimus Cyclosporine

When presented with a high risk patient who is taking one of the above medications (be aware that this list is not extensive), due to the risk of hyperglycaemia, the anti-diabetic medication that is being concomitantly used should be altered in dosage to account for the changes in blood sugars when stopping one of the medications listed in Table 3.

Potential drug interactions are a huge concern for older patients taking antihyperglycaemics alongside other commonly used medications as drug-drug interactions can commonly occur which can result in hypoglycaemic or hyperglycaemic events. Table 4 shows commonly used antihyperglycaemic medications and some common interactions that clinicians should be aware of.

7 Case Study

A hypothetical situation that iterates the importance of deprescribing interventions in the older population is one that many clinicians will be able to resonate with. A 78-year-old man is seen by his regular general practitioner with an elevated HbA1c level than previously recorded, rising from 65 to 82 mmol/mol (8.1–9.7%). He was started on and SGLT2-I (Empagliflozin) for concomitant heart failure with a reduced ejection fraction. Following the initiation of this new medication, he returned to his GP a few weeks later with a genitomycotic infection, for which he is prescribed a course of topical clotrimazole; this fungal infection proves to be refractive and so is given further courses systemic the antifungal treatment. The patient returned a months later with new onset dysuria, polyuria and nocturia, and complains of dark, strong smelling urine. For these new symptoms, the patient is given a course of the antibiotic nitrofurantoin. He continually represents over the next few weeks with continuing symptoms of a urinary tract infection and is started on prophylactic antibiotics to combat the refractory infection. With his constant complaints of polyuria, and urinary frequency, the patient is started on the antimuscarinic tolterodine immediate release.

The hypothetical case study presented shows how one new sign or symptom can quickly lead to the introduction of a new medication, which over time leads to the development of a prescribing cascade. At this stage, it becomes very difficult to differentiate between what is medication related and what is a new disease or condition and as such the whole problem is overlooked and the patient is continued on all of the newly prescribed medications contributing to the increased prevalence of polypharmacy in the diabetic population.

8 Attitudes and Beliefs Towards Deprescribing

Through qualitative studies, it has been shown that three themes have emerged surrounding problematic polypharmacy, namely, varying levels of awareness surrounding medication uses and side effects, varying thoughts on who is responsible for medication reviews and finally a lack of accessibility to resources and the correct environment to conduct medication education and conduct such reviews[25].

Older patients often feel reluctant to discontinue medications due to a lack of understanding of the deprescribing process and often feel 'left out' of the decision making process[25]. Patient understanding is vital to ensure the deprescribing process goes smoothly, with a study conducted in Singapore showing that out of 1,057 participants, 83% of older adults and 87.1% of caregivers would be willing to stop one or more of their medications if their doctor agreed it was possible[26], showing the power of effective communication during deprescribing consultations. Few patients are able to coherently specify the

Ejection fraction: A measurement of the quantity of blood the left ventricle pumps around the body with each contraction, expressed as a percentage.

Dysuria: Pain upon urination, often expressed as a discomfort or burning sensation.

Polyuria: Increased frequency and/or volume of urination.

Nocturia: Increased urination at night.

Concomitant: associated with or naturally occurring with.

Table 4: Table showing potential drug-drug interactions when taking antihyperglycaemics and other commonly used medications[22].

Diabetes medications	Examples	Potential drug interactions
Biguanides	Metformin	Cephalexin Digoxin Procainamide Cimetidine Quinidine Quinine Trimethoprim Vancomycin Anticholinergics (oxybutynin/dicyclomine)
Sulphonylureas	Glyburide Glipizide	Azole antifungals Tricyclic antidepressants ACE inhibitors Beta blockers Calcium channel blockers Oral contraceptives Thiazide diuretics
Meglitinides	Repaglinide Nateglinide	Azole antifungals Corticosteroids Calcium channel blockers Beta blockers Oestrogen Oral contraceptives Thyroid supplements NSAIDs
Thiazolidinediones	Pioglitazone Rosiglitazone	Fluoxetine Ketoconazole Rifampin Trimethoprim
Alpha-glucosidase Inhibitors	Acarbose	Digoxin Warfarin
DPP-4 Inhibitors	Linagliptin Sitagliptin Saxagliptin	Ritonavir Clarithromycin Rifampin Diltiazem Ketoconazole
SGLT2 Inhibitors	Dapagliflozin Empagliflozin	Rifampin

exact reason they were started on a medication and many state they follow the advice of their healthcare professional with no true understanding of why they are using it in the first instance[27]. These points raise significant patient safety issues and demonstrate the great lack of education being promoted towards patients during the initial consultation where the medication is firstly prescribed[28].

Healthcare professionals seem rather reluctant to make what appears to be quite radical changes to established therapeutic regimens, as they often feel more comfortable continuing what has always been the safe prescribing zone for the patient[29] (Table 5). It is also commonly said that type 2 diabetes is a progressive condition which requires continuous escalation until the patient is within the clinically defined 'safe' HbA1c targets. Whilst there has been evidence-based guidance produced on how to manage elderly patients aged 65 years or more, and even further guidance on how to manage those living with severe frailty, there is limited practical guidance or evidence to aid clinicians in individualising diabetes therapies in those living with severe frailty and coming towards the end of their lives, which inevitably contributes towards the clinical inertia in this treatment area[24].

Some clinicians feel that this goal-setting mentality overshadows the need for appropriate action and grossly under-recognises the importance of basic communication between patient and clinician. The result is that management leads to intensification of type 2 diabetes management until glycaemic control has been lost, complications arise, and immediate intervention is

Clinical inertia: A reluctance to increase treatment intensification even when the patient is not at the evidence-based goals for care.

De-escalation Changing from more intensive to less intensive insulin regimens

Table 5: Summary of attitudes and perceptions towards deprescribing interventions[30].

	Barriers	Enablers
Patients and caregivers	Fear of unknown outcomes following deprescribing interventions Lack of communication on potential benefits of deprescribing leading to reduced patient empowerment and decision making	Feeling of empowerment to deprescribed when successfully explained to patient and backed by a healthcare provider Reduction in number of used medications improving quality of life indicators
Healthcare professionals	Lack of evidence based guidance to aid in the decision making process of deprescribing Difficult to communicate with specialists Lack of knowledge on deprescribing processes – more education required No clinical pathways to guide the management of deprescribing Primary care providers reluctant to deprescribe medications started by specialists Lack of RCT's assessing long term outcomes and safety of deprescribing Time constraints on completing medication reviews on patient visits Fear of unknown consequences of deprescribing a medication	Shared workload when shared decision making is in place involving the multidisciplinary team Observational and retrospective studies assessing the feasibility of deprescribing interventions Reduction in polypharmacy
Health Organisations	Limited studies into the roles of multidisciplinary healthcare professionals and their roles in deprescribing Clinical inertia – belief that stopping a medication is not as beneficial as continuing one Fragmented transitions of care between primary and secondary teams	Studies assessing the cost saving efforts of deprescribing are encouraging Reduced hospital admissions due to adverse drug interactions and polypharmacy

required[31]. With epidemiological data showing that for every 20 people with type 2 diabetes with a HbA1c value 1% above target will suffer a microvascular complication within 5 years, an LDL level 30 mg/dl above goal will result in an myocardial infarction (MI) or stroke, and for every 20 patients with a BP 10 mmHg above target, 1 will experience an MI or stroke[31], it again supports the reluctance of clinicians to initiate deprescribing strategies. However, in the severely frail and end of life population, these adverse outcomes are unlikely to occur due to the predicted time frames of life expectancy.

Healthcare providers feel like they lack the relevant knowledge and guidance which limits them to make adequate clinical decisions surrounding medication optimisation, and whilst many admit to feeling accountable for patients medication use and their related care, state that they do not act on it due to time constraints and limited knowledge.

9 Questions to Consider when Identifying Deprescribing Approaches

Identifying suitable patients and suitable medications can be challenging and has been commonly identified as a recurring barrier to deprescribing interventions, with time pressures increasing these difficulties. Clinicians need to focus their thought processes on five main areas of concern, namely, the disease, the medications, the patient, adherence, choice, and costs effectiveness. Table 6 highlights some main questions that should be considered prior to initiating deprescribing interventions in a frail patient with type 2 diabetes.

Epidemiological: The assessment of the distribution of diseases and the incidence of factors relating to health in a defined population.

10 The Ethics of Deprescribing in Clinical Practice

The Four Principles of ethics as outlined by Beauchamp and Childress 2012, namely, beneficence, non-maleficence, justice, and autonomy should guide medical practitioners when considering medication deprescribing. Informed consent is the process by which information is efficiently presented to the patient and time allowed for the patient to reflect on the information provided. It also implies that the consent can be withdrawn at any time. These principles provide a good pragmatic framework for clinicians to apply to patients and make decisions that are morally acceptable to both the clinician and the patient.

Anderson et al. described medication deprescribing as an "active medical decision" influenced by barriers and enablers[32], with uncertainties and fears regarding negative consequences hindering current deprescribing practices. In deprescribing, the clinician needs to provide adequate

Table 6: Questions to consider during the deprescribing process consultation[5].

Area	Questions
Disease	1. Are the presenting symptoms due to a new condition or disease or are they side effects of a medication the patient is currently using? 2. Is the patient moving towards the end of their life? 3. Has the patients clinical frailty status changes since your last consultation with them?
Medications	1. Is there a clear and justifiable indication for the medication you wish to prescribe or deprescribe? 2. Are there any significant or possible drug interactions? 3. Are there any significant or possible adverse events? 4. Could the dose be titrated down to a lower dose, or should the medication be stopped?
Patient	1. Will the patient adhere to medication discontinuation? 2. Are all other medications currently being used dosed correctly? 3. Is the patient comfortable with the medications they are taking? 4. What will be the significance of discontinuation for this patient? 5. Does the patient acknowledge and understand the aims of deintensification? 6. Could a PDA tool be used to aid in the deprescribing process?
Adherence	1. Have you discussed how long it will take for any adverse events to become apparent? 2. Have you explained how long it will take for the benefits and outcomes to become apparent? 3. Can the pharmacist aid in this process? 4. Could a medication review consultation be booked in advance to check adherence?
Choice	1. Have you discussed the benefits and risks of medication deprescribing for the patient? 2. Have you used any PDA's or tools to support the patient understand the proposed outcomes and weigh up all of the available information? 3. Does the patient require time away to contemplate the information you have given them?
Cost	1. If switching to an alternative medication, does the benefits outweigh the increased cost of the new medication? 2. Is there a more cost-effective alternative that carries the same benefits?

information to the patient on both the risks and benefits of deprescribing and place this within the context of the patients current care goals[33] When considering both beneficence and non-maleficence, it becomes slightly more complex as it must be deduced whether deprescribing is seen as an *action* or the *discontinuation of a previous action*[34]. If seen as the former, it creates a stronger moral duty to the deprescribing clinician.

Justice refers to not only the appropriate use of resources but also the right to equal treatment[35]. With ageing comes the reduced benefit to many medications, increased risks and adverse events, and an increased risk of mortality. Given this, there becomes a shift between the benefits and the risks of the medication being used[34], and as such it is important to recognise that deprescribing is not the omission of a medication but the optimisation of a patients management plan.

When considering deprescribing interventions, it is of paramount importance to be aware of the patient's level of capacity, their beliefs, and preferences, as well as their current clinical condition. Deprescribing is another tool for clinicians to use but should be used alongside the theory of "principlism" and be used with clinical judgement at all times. Improvement in evidence to better understand the relationship between polypharmacy and deprescribing with health outcomes in the elderly diabetic population should be a priority to optimise medication management in this population.

Principlism: An ethical approach that is used in medicine and the healthcare sciences to emphasize the four universal and basic aspects of ethics, namely justice, autonomy, beneficence, and non-maleficence.

11 Legal Aspects of Deprescribing

With emerging evidence supporting the necessity of deprescribing, many clinicians are concerned with the possibility of litigation. One of the key aspects of tort law is to protect patients by deterring clinicians from providing substandard clinical care which has the ability to cause harm to the patient[36]. The ideas of clinical negligence and a lack of informed consent in deprescribing are just some of the possible contributors to tort law cases.

To prevent negligence claims, clinicians must ensure they are complying with up to date standards of care, however, given the continually evolving field of medicine resulting in the standard of care being dynamic, the law relies on the medical professionals expertise, training, and expert testimony[36].

It is foreseen that deprescribing malpractice claims will be split into two categories, (1) a failure to deprescribe when necessary or (2) deprescribing in violation of the standard of care, but these claims will only be successful should harm befall upon the patient. When considering litigation, there are four key aspects of clinical

malpractice that need to be considered, namely, duty of care, breach of duty, harm, and causation.

A prescriber may act upon their clinical judgement to deprescribe medications without a patients consent, such as when an opioid or a corticosteroid is tapered based on clinical guidelines, for fear of potential liability for not deprescribing the medication. Thus, the law does not always implicitly require that a patient consents to deprescribing initiatives, especially when deemed to be clinically appropriate; this is the idea of assent, where a patient agrees with a clinicians professional judgement and is the foundation of good doctor-patient relationships[36].

Informed consent may be implicitly needed in situations where there is a lack of clinical guidelines or trust based policies. In such instances, shared decision making is required and patient decision aids and deprescribing tools can be used to aid in the decision making process and can ensure the patients values and preferences are upheld.

Legally, deprescribing is no different to prescribing, in that ongoing monitoring and reviews are required for safe patient care, with all decisions needing to be discussed in full with the patient to ensure the requirements of informed consent are met. As deprescribing becomes more common place within clinical practice, failing to fully inform the patient on the possible benefits and adverse events of medication deprescribing may expose clinicians to clinical negligence claims, however, the process of stopping, changing, or reducing a medication is fundamentally no different to that of initiating a new medication[37].

Deprescribing is an area where there is potential for medical malpractice liability, but it has not yet been embraced by litigators, likely due to the lack of clinical guidelines and trust based policies. As evidence begins to emerge for this field, litigators may become more receptive to bringing medical malpractice and informed consent deprescribing claims to light where appropriate. Legal and policy reforms must be made to firmly position deprescribing within the overall prescribing process and reduce preventable patient harms from polypharmacy[36]. When deprescribing is performed in partnership with the patient and/or caregiver, supported by the appropriate knowledge and skills, and considering the values and beliefs of each patient, the law presents no barriers to deprescribing practices[38].

12 Plans Moving Forward

There are many valuable ways that deprescribing interventions can be more commonplace within the clinical setting. Some possible actions that could be considered to implement such interventions can be seen in Table 7.

Accountability needs to be present when new medications are prescribed and the rationale for prescribing needs to be justified. Nevertheless, there needs to be assistance for medical practitioners to ensure they feel empowered when making new prescribing choices and new clinical

Table 7: Possible approaches to implement deprescribing practices within the clinical practice setting[18].

Actions to aid in the deprescribing process
1. Increase education for medical professionals surrounding optimisation of medications and undertaking meaningful medication reviews, which can be performed during the diabetic review consultation
2. Spread the workload by involving ANP's and pharmacist's to aid in the medication review process
3. Dedicated appointments for medication reviews allowing patients to openly discuss any new or ongoing symptoms, which can be performed by the wider medical team
4. Improved prescribing documentation that could include the reason the medication was initially prescribed and how long it is foreseen that the medication will be required for. Updated sections could include reasons for stopping, withdrawing, or changing the medication
5. Improved electronic health systems to alert the prescribing practitioner of potential side effects and drug-drug interactions, along with signs and symptoms to be monitored to try and prevent prescribing cascades
6. Empower medical professionals to undertake deprescribing initiatives by producing new proformas and training/education services
7. Increased follow up appointments to assess if any new signs or symptoms are present following the initiation of a new medication
8. Public education and increasing awareness of medication side effects – this could come in the form of an electronic pamphlet or leaflet highlighting signs and symptoms to look out for
9. Empower patients to come forward should they have any concerns regarding their medications by opening up new appointments dedicated to this

pathways should be put in place to aid in the deprescribing process[39]. The process needs to be clearly outlined and justified by evidence-based guidance for clinicians to feel competent with this new approach to medical optimisation.

13 Summary

The outcomes of deprescribing interventions in patients living with multiple long term conditions and frailty and type 2 diabetes is limited and much research is needed within this field to help develop guidelines to assist clinicians in taking deprescribing initiatives and involving it within the diabetic patient's management plan. When we consider preventive medications, we need to be aware of valid assessments and educate individuals to give their use appropriate weight and therefore justify their continued use, particularly when considering evidence surrounding their continued use with respect to efficacy and safety is seldom derived from randomised control trials (RCTs) under current clinical practice.

Preventive medications: Medications that are prescribed to proactively prevent the occurrence of long-term health complications associated with a disease or condition.

Current literature grossly underestimates the devastating impacts problematic polypharmacy has on the ageing population living with type 2 diabetes and multimorbidity and underestimates the sheer size of the current global problem not only to patient safety, but to patient satisfaction, quality of life, cost effectiveness and the burden on the healthcare system.

Future research should focus on the level of hyperglycaemia that causes harm in the older population, optimisation of glycaemic targets, treatment effectiveness, patient preferences towards individualised glycaemic targets, optimisation of deprescribing approaches and regimes, and the short term benefits and risks of continuing and discontinuing antihyperglycaemics.

14 Key Messages

- There is strong evidence supporting the need for deprescribing interventions to be commonplace within the clinical setting, especially for those with type 2 diabetes and other cardiometabolic conditions
- Management for patients with type 2 diabetes needs to be individualised, and if appropriate, blood pressure and cholesterol lowering targets relaxed during frailty and end of life, with medications stopped or altered accordingly
- There is lack of evidence based practice and formal guidance to aid healthcare professionals decisions on the best targets for individuals
- During end of life care, or those with severe frailty, all invasive assessments should be stopped or minimised, especially those that do not improve quality of life.
- Barriers to deprescribing include a lack of healthcare provider knowledge and awareness, patient resistance and a lack of evidence-based guidance and clinical pathways
- As of the 2019/20 General Medical Services contract Quality and Outcome Frameworks, higher glycaemic targets in this population have been identified as appropriate
- Future research should focus on identifying high risk cohorts and undertaking RCT's to aid in the production of clinical guidance and pathways

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Declarations

Conflict of Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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