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Deprescribing oral antidiabetics in elderly patients: Do electronic leaflets across the world address it?

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ABSTRACT

Diabetes caused 6.7 million deaths in 2021, equating to one death every five seconds, with its global financial burden projected to rise from $1.32 trillion in 2015 to $2.12 trillion by 2030. Severe hypoglycemia necessitates interventions like deprescribing, behavioral strategies, and technology for prevention. Deprescribing aims to reduce unnecessary medication use, enhance rational prescribing, prevent prescribing cascades, and improve health outcomes in elderly patients. Evaluating electronic leaflets can support deprescribing based on patient-centered care and shared decision-making.

Objective: To analyze information on deprescribing in oral antidiabetic leaflets from national medicines regulatory authorities, focusing on elderly patients with type 2 diabetes.

Methods: This documental study analyzed electronic leaflets of oral antidiabetics from the official websites of nine Medicines Regulatory Authorities: Australia, Brazil, Canada, New Zealand, Singapore, South Africa, UK, USA, and EU, covering drugs listed in the WHO's Essential Medicines List 2023. The analysis focused on the alignment of deprescribing information with the Ontario deprescribing algorithm for oral antidiabetics developed by the Bruyère Institute in Canada.

Results: Out of 72 expected leaflets, 64 (88.9 %) were retrieved. Only 18 leaflets (28.1 %) explicitly discussed deprescribing oral antihyperglycemics. Hypoglycemia and drug interaction risks were addressed in 55 leaflets (85.9 %). Caution for use in patients over 65 was mentioned in 32 leaflets (50 %), and 23 leaflets (35.9 %) addressed the risks of tight glucose and HbA1c targets.

Conclusion: Despite a high retrieval rate, 11.1 % of leaflets were missing, and those available contained inconsistent deprescribing information. There are significant disparities in guidance across regulatory authorities. Standardized, updated leaflets that address deprescribing in frail older patients could enhance prescribers' confidence and support shared decision-making

1. Introduction

The global trend of an aging population presents substantial challenges in healthcare, particularly in the management of medications for elderly individuals with multiple chronic conditions.[1] Among older adults, prevalent health issues include hearing impairment, cataracts, musculoskeletal pain, osteoarthritis, chronic obstructive pulmonary disease, diabetes, depression, and dementia.[2] Diabetes is particularly common, with over a quarter of those aged 65 and above diagnosed with the condition, and half with prediabetes.[3] Managing these conditions frequently necessitates the use of many medications also termed polypharmacy, defined as the concurrent use of five or more medications, which increases the risk of inappropriate prescriptions.[4] This issue is more prevalent in older populations, affecting approximately 45 % of individuals aged 65 or older, compared to 27 % of those under 65.[5] Studies focused on qualitative (rational) prescribing define polypharmacy not just as the simultaneous use of more than five medications to treat chronic conditions, but primarily as the use of inappropriate medications where the side effects outweigh the benefits.[6]

Rational medication use requires a systematic approach tailored to individual health conditions because inappropriate prescribing can lead to adverse drug reactions, increased healthcare costs, and diminished

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quality of life.[7] Polypharmacy complicates the management of type 2 diabetes in the elderly due to the various physiological changes that occur with aging. These changes can significantly impact drug pharmacokinetics and pharmacodynamics, thereby increasing the risk of adverse drug events, particularly hypoglycemia.[8] Adverse drug reactions from polypharmacy can trigger prescribing cascades, where new medications are used to treat a new medical condition caused by these side effects, complicating rational prescribing practices.[9] Severe hypoglycemia, which can lead to confusion, falls, fractures, seizures, and coma, necessitating hospitalization in elderly patients, underscores the need for clear and meticulous information, especially considering the rapid global population aging process.[10] Moreover, Drug-induced hypoglycemia is a significant barrier to achieving glycemic targets. Various guidelines recommend individualized care and less stringent glycemic targets for older patients at high risk of hypoglycemia, as the frequency and severity of hypoglycemic episodes can significantly diminish quality of life. This, in turn, increases the fear of future episodes, leading to reduced self-care and poorer glucose control.[11]

In elderly patients with type 2 diabetes mellitus (T2 DM), hypoglycemia is the most common type of blood glucose dysfunction associated with neuronal damage,[12] and it is proven that severe hypoglycemia can cause diminished consciousness, falls, motor vehicle accidents, seizures, coma, and death.[13] Recurrent hypoglycemia is a critical medical issue that requires interventions such as deprescribing unnecessary or inappropriate medications, behavioral interventions, and sometimes technology to assist with hypoglycemia prevention and identification.[14] A large cohort study indicated that older adults with type 2 diabetes and a history of hypoglycemia have a greater risk of cognitive impairment and dementia.[15] For all these reasons, deprescribing appears as a significant solution to minimize medication use, prevent prescribing cascades, reduce the risk of geriatric syndromes, enhance health outcomes, and ultimately improve the quality of life.[16]

The term “deprescribing” was first introduced by Michael Wood in 2003, his study brought to light the increasing number of elderly people with polypharmacy. He affirmed that the fundamentals of deprescribing comprise: assessing all of the patient’s current medications, determining which ones should be discontinued, replaced, or cut back on, working with the patient to create a deprescribing plan, and carrying out frequent reviews with continuing assistance.[17] This concept was further described as the suspension or reduction of medications that cause harm or offer no benefit to the patient. In addition, deprescribing as one of the crucial interventions for managing chronic conditions like T2 DM, especially in frail elderly patients, requires a planned, supervised, and collaborative process to be successfully achieved.[18] This process is considered safe for reducing, tapering, or discontinuing medications and can effectively prevent inappropriate prescribing and the resulting prescribing cascade.[19]

Recently, many researchers have introduced various information tools on deprescribing, such as algorithms, pamphlets, and infographics, to enable awareness of either prescribers or patients.[20] These tools highlight the necessity and safety of the deprescribing process, emphasizing the importance of sharing the best available knowledge with patients. By doing so, they aim to overcome multiple barriers that previously made deprescribing an Overwhelming or scary task.[21] Medication leaflets can support patient-centered care by empowering their shared decision-making (SDM) capability that aligns with their preferences, beliefs, and values, therefore facilitating deprescribing strategies.[22] In the era of evidence-based medicine, there has been increasing interest in using deprescribing research to reduce overtreatment and overprescribing, thereby mitigating medication-related harm. Evidence indicates that approximately 10 % of all medications are overprescribed, imposing a substantial burden on patients and healthcare services through preventable medication-related harm, and resulting in significant costs to healthcare systems globally.[23]

To the best of our knowledge, no studies address the necessity of evaluating electronic leaflets regarding the availability of information and guidance on deprescribing oral antihyperglycemics in elderly patients with type 2 diabetes. This issue is of urgent importance, as diabetes caused 6.7 million deaths in 2021, corresponding to one death every five seconds.[24] Furthermore, the global financial burden of diabetes is projected to increase from $1.32 trillion in 2015 to $2.12 trillion by 2030.[25] This challenging scenario prompted us to critically examine the information contained in electronic leaflets of oral antihyperglycemic medications marketed worldwide regarding their deprescribing in elderly patients.

1.1. Objective

To systematically assess the content of electronic leaflets for oral antihyperglycemic medications from various national regulatory authorities worldwide, with a specific focus on whether these leaflets provide guidance on deprescribing in elderly patients with T2 DM. The study aims to evaluate the extent to which the leaflets address important aspects of deprescribing, such as dose reduction, withdrawal, risk of hypoglycemia, and tailored recommendations for elderly patients while comparing the information against established deprescribing protocols for oral antidiabetics in older populations.

2. Methods

This documental study analyzed electronic leaflets of oral antihyperglycemic medications available on the official websites of nine national medicines regulatory authorities’ websites: Australia, Brazil, Canada, New Zealand, Singapore, South Africa, the United Kingdom, the United States of America, and the European Union (as it has one medicine regulatory authority); including drugs listed on the WHO’s Essential Medicines List 2023.

A full reading of all the oral antidiabetic electronic leaflets collected was duplicated (K.T.B and S.J.E.C.J) to search for the content of deprescribing. Afterward, the results were compared to assess the reliability of the analysis. Noteworthy, the reading was carried out individually to avoid influence on the interpretation of the leaflets.

2.1. Eligibility criteria

Based on the online essential medicines list (EML) provided by the World Health Organization (WHO), we considered all electronic oral antihyperglycemic leaflets eligible for this study.[26]

The analysis used electronic leaflets available on different websites included in this study from the 8th of June to the 15th of November 2023 for canagliflozin, dapagliflozin, empagliflozin, glibenclamide, gliclazide, glimepiride, metformin, and pioglitazone.

The leaflets for generic oral antihyperglycemics (when available) and their brand names (when generics were unavailable) were selected, ensuring comprehensive coverage of the entire class of oral antidiabetic medications and providing the most complete and up-to-date information for analysis. Only leaflets available on the official websites of the selected countries and particularly intended for healthcare professionals were considered eligible for this study.

Countries where access to these websites was possible and where the leaflets were available on their respective medicines regulatory authorities’ websites were included in the study. Further information is provided in Table 1.

2.2. Exclusion criteria

The online leaflets for combined oral antihyperglycemics were excluded to avoid duplicating information about the selected medications.

Electronic leaflets from regulatory authorities within the European Union, other than those from the European Medicines Agency (EMA), were not selected, as they are considered already covered by the EMA.

Table 1
National Medicines regulatory authorities and their websites.

Country	National Medicines Regulatory Authority	Official Website
Canada	Drugs and Health Products	www.canada.ca
United States of America (USA)	Food Drug Administration (FDA)	www.fda.gov
Brazil	Agência Nacional de Vigilância Sanitária (ANVISA)	www.gov.br/anvisa/pt-br
Europe	European Medicines Agency (EMEA)	www.ema.europa.eu
New Zealand	Medsafe	www.medsafe.govt.nz
Australia	The Therapeutic Goods Administration (TGA)	www.health.gov.au/contacts/therapeutic-goods-administration-tga
South Africa	South African Health Products Regulatory Authority (SAHPRA)	www.sahpra.org.za
United Kingdom	Medicines and Healthcare Products Regulatory Agency (MHPRA)	www.gov.uk/medicines-and-healthcare-products-regulatory-agency
Singapore	Health Sciences Authority (HAS)	www.hsa.gov.sg/therapeutic-products

Countries worldwide where access was unavailable or leaflets were inaccessible despite available access were excluded from the study.

2.3. Analysis of information available in electronic leaflets

The following keywords were used to identify the content: "deprescribing", "withdrawal", "tapering", and "dose reduction" (in Portuguese for Anvisa leaflets and in English for the rest of the national regulatory authorities).

Each retrieved antidiabetic electronic leaflet was analyzed for the following information:

1. Systematized information and guidance on the deprescribing process
2. Time-to-benefit and uncertainty in clinical benefits
3. Caution for using oral antidiabetics in patients over 65
4. Recommendations for tight fasting blood glucose (FG) control and a glycated hemoglobin (HbA1C) target ≤6.5 % in elderly patients
5. Risk of hypoglycemia and drug interactions

Finally, an examination was conducted to assess whether the deprescribing information found in the electronic leaflets aligned with the deprescribing protocol of oral antidiabetics in elderly patients developed by the Bruyère Institute in Ontario-Canada.[27] This protocol recommends deprescribing oral antihyperglycemic in the following situations.:

a. If the elderly patient is at risk of hypoglycemia due to advanced age, multimorbidity, tight glycemic control, drug interactions, hypoglycemia history or unawareness, impaired renal function, or if they are on sulfonylureas or insulin therapy
b. If the elderly patient is experiencing or at risk of adverse effects from oral antihyperglycemics
c. If there's uncertainty in clinical benefits (due to frailty, dementia, or limited life expectancy).

3.3. Data analysis.

To summarize, analyze, and interpret the data obtained, it was described in.

absolute (n) and relative (%) frequency form and presented in tables.

3. Results

Out of an anticipated total of seventy-two oral antihyperglycemics electronic leaflets, sixty-four (100 %) were retrieved from the respective national medicines regulatory authorities' websites for analysis.

As shown in Table 2, the leaflets of gliclazide, glimepiride, and glibenclamide were absent in most countries. However, Brazil, Canada, and the United Kingdom stand out as the exception, having all of these leaflets available. The majority of the leaflets addressed the risks of hypoglycemia and drug interaction. From Table 3, it's possible to assert that Australia had a 100 % proportion of leaflets that addressed the risk of hypoglycemia and drug interactions followed by Brazil, New Zealand, the European Union, and the United Kingdom with 87.5 % each. Results of Table 4 confirm that less than one-third of the retrieved leaflets explicitly discussed deprescribing oral antidiabetics in elderly patients, offering recommendations for gradual dose reduction and systematic instructions. Likewise, a low proportion of the leaflets provided information on how and when to deprescribe. Notably, Australia, the European Union, New Zealand, and the United Kingdom led in discussing deprescribing, each accounting for around 40 % of the leaflets. Table 5 illustrates that less than half of the leaflets addressed caution in using oral antihyperglycemics in patients over 65 years. Canada was prominent in discussing this matter, with a prevalence close to 90 %, followed by Brazil, while Singapore, South Africa, and the United Kingdom had the lowest prevalence rates. According to Table 6, one-third of the leaflets addressed the Risks of Tight Fasting glucose and HbA1C target ≤6.5 % in elderly patients. In this regard, Australia has the highest prevalence, followed by Brazil and we notably noticed the absence of this information from Singapore's electronic leaflets. Table 7 shows that less than 10 % of leaflets mentioned the time-to-benefit and uncertainty clinical benefits, and Brazil headed the list in this regard. Lastly, Table 8 presents that almost half of the leaflets discussed oral antihyperglycemics temporary treatment cessation. The United Kingdom had the highest proportion of leaflets covering this topic, while the European Union, Singapore, and South Africa had the lowest rate of leaflets that addressed this matter.

4. Discussion

The examination of electronic oral antihyperglycemics leaflets from various national regulatory authorities offers valuable insights into deprescribing practices for elderly patients with T2DM. This study shed light on a comprehensive effort to access worldwide medicines regulatory authorities' information and databases. However, sulfonylureas leaflets were notably lacking in most results, potentially impacting deprescribing decisions. The analysis revealed a notable absence of sulfonylurea leaflets in many of the results, which may hinder informed deprescribing decisions. During data collection across various regulatory authorities, it was observed that the European Medicines Agency (EMA) specifies on its website that certain medications may be authorized through national procedures within individual Member States,

Table 2
Descriptive Analysis of Retrieved and Missing oral antidiabetics electronic leaflets by Country.

Name of the country	Number of leaflets expected	Number of Leaflets retrieved	Names of the missing leaflets
Australia	8	8 (100 %)	None
Brazil	8	8 (100 %)	None
Canada	8	7(87.5 %)	glibenclamide
European Union	8	7 (87.5 %)	gliclazide
New Zealand	8	7(87.5 %)	glimepiride
Singapore	8	7 (87.5 %)	glimepiride
South Africa	8	6 (75 %)	canagliflozin and pioglitazone
United Kingdom	8	8 (100 %)	None
USA	8	6 (75 %)	glibenclamide and gliclazide
TOTAL	**72(100 %)**	**64 (88.9 %)**	

Table 3
Descriptive analysis of oral antidiabetics electronic leaflets by country that addressed the risks of hypoglycemia and drug interactions.

Name of the country	Number of the leaflets that addressed the risks of hypoglycemia and drug interactions?	Names of the leaflets
Australia	8 (100 %)	canagliflozin, dapagliflozin, empagliflozin, glibenclamide, gliclazide, glimepiride, metformin, and pioglitazone
Brazil	7 (87.5 %)	canagliflozin, dapagliflozin, empagliflozin, glibenclamide, gliclazide, glimepiride and pioglitazone
Canada	3 (37.5 %)	glibenclamide, metformin and pioglitazone
European Union	6 (75 %)	canagliflozin, dapagliflozin, empagliflozin, glibenclamide, glimepiride, and pioglitazone
New Zealand	7 (87.5 %)	canagliflozin, dapagliflozin, empagliflozin, glibenclamide, gliclazide, metformin and pioglitazone
Singapore	5 (62.5 %)	canagliflozin, dapagliflozin, empagliflozin, glibenclamide and gliclazide
South Africa	6 (75 %)	dapagliflozin, empagliflozin, glibenclamide, gliclazide, glimepiride, and metformin
United-Kingdom	7 (87.5 %)	canagliflozin, empagliflozin, glibenclamide, gliclazide, glimepiride, metformin and pioglitazone
USA	6 (75 %)	canagliflozin, dapagliflozin, empagliflozin, glimepiride, metformin, and pioglitazone
TOTAL	**55 (85.9 %)**	

Table 4
Descriptive analysis of electronic leaflets by country that addressed deprescribing, how and when to deprescribe oral antidiabetics in elderly patients.

Name of the country	Number of the leaflets that explicitly addressed deprescribing oral antidiabetics in elderly patients	Number of the leaflets that addressed when and/or how to deprescribe	Names of the leaflets
Australia	3 (37.5 %)	3 (37.5 %)	glibenclamide, glimepiride, and Metformin
Brazil	3 (37.5 %)	3 (37.5 %)	gliclazide, glibenclamide and glimepiride
European Union	3 (37.5 %)	3 (37.5 %)	glibenclamide, glimepiride and pioglitazone
New Zealand	3 (37.5 %)	3 (37.5 %)	canagliflozin, empagliflozin and metformin
South Africa	1 (12.5 %)	1 (12.5 %)	
Singapore	1 (12.5 %)	1 (12.5 %)	empagliflozin
United Kingdom	2 (25 %)	2 (25 %)	dapagliflozin and empagliflozin
USA	02 (25 %)	02 (25 %)	glimepiride and metformin
Total	**18 (28.1 %)**	**18 (28.1 %)**	

rather than centrally by the EMA. As a result, only those medicines evaluated by the EMA are included on its platform, potentially limiting the completeness of available leaflets for specific conditions.[28] This limitation was identified as a constraint in the data collection process for the current study.

Table 5
Descriptive analysis of the leaflets by country that addressed caution of using oral antidiabetics in patients ≥65 years old.

Names of countries	Number of the leaflets addressing caution of use in patients older than 65-year-old	Names of the leaflets
Australia	4 (50 %)	canagliflozin, dapagliflozin, empagliflozin, and metformin
Brazil	6 (75 %)	canagliflozin, empagliflozin, gliclazide, glibenclamide, metformin and pioglitazone
Canada	7 (87.5 %)	canagliflozin, dapagliflozin, empagliflozin, glibenclamide, gliclazide, metformin and pioglitazone
New Zealand	3(37.5 %)	canagliflozin, empagliflozin, and metformin
Singapore	2 (25 %)	Glibenclamide, and gliclazide
South Africa	2 (25 %)	empagliflozin and metformin
United Kingdom	3 (37.5 %)	Canagliflozin,glibenclamide and pioglitazone
USA	5 (62.5 %)	canagliflozin, empagliflozin, glimepiride, metformin, and pioglitazone
TOTAL	**32 (50 %)**	

Table 6
Descriptive analysis of oral antidiabetics electronic leaflets by country that addressed the Risks of Tight Fasting glucose and HbA1C target ≤6.5 % in elderly patients.

Name of the country	Number of leaflets that addressed the risks of tight FG and HbA1C target ≤ 6.5 % in elderly patients	Names of the leaflets
Australia	7 (87.5 %)	canagliflozin, dapagliflozin, empagliflozin, gliclazide, glibenclamide, glimeperide and metformin
Brazil	4 (50 %)	gliclazide, glimeperide, metformin and pioglitazone
Canada	1 (12.5 %)	pioglitazone
European Union that mentioned	3 (37.5 %)	dapagliflozin, empagliflozin and glibenclamide
New Zealand	1 (12.5 %)	gliclazide
South Africa	1(12.5 %)	empagliflozin
United Kingdom	3 (37.5 %)	dapagliflozin, gliclazide and glimepiride
USA	3 (37.5 %)	canagliflozin, dapagliflozin and metformin
TOTAL	**23(35.9 %)**	

Table 7
Descriptive analysis of oral antidiabetics electronic leaflets by country that addressed the treatment time-to-benefit and uncertain clinical benefits in elderly patients.

Names of countries	Number of leaflets that addressed time-to-benefit and uncertain clinical benefits	Names of the leaflets
Australia	1 (12.5 %)	glimepiride
Brazil	2 (25 %)	gliclazide, and metformin
United Kingdom	1 (12.5 %)	pioglitazone
USA	1 (12.5 %)	pioglitazone
TOTAL	**5 (7.8 %)**	

In alignment with the protocol used in this study (i.e., the Bruyère Institute protocol) on deprescribing oral antihyperglycemics in elderly

Table 8
Descriptive analysis of leaflets by country that addressed temporary treatment cessation of oral antidiabetics.

Name of the country	Number of the leaflets address temporary treatment cessation	Names of the leaflets
Australia	4 (50 %)	dapagliflozin, empagliflozin, glibenclamide and metformin
Brazil	6 (75 %)	canagliflozin, dapagliflozin, empagliflozin, glibenclamide, glimepiride, and metformin
European Union	3 (37.5 %)	glibenclamide, glimepiride and pioglitazone
New Zealand	4 (50 %)	canagliflozin, dapagliflozin, empagliflozin, gliclazide
Singapore	3 (37.5 %)	canagliflozin, dapagliflozin and metformin
South Africa	3 (37.5 %)	dapagliflozin, glimepiride, and metformin
United Kingdom	7 (87.5 %)	canagliflozin, dapagliflozin, empagliflozin, glibenclamide, gliclazide, metformin and pioglitazone
TOTAL	**30 (46.9 %)**	

patients with T2 DM, the risk of hypoglycemia emerges as a significant concern, and it's prominently addressed within electronic leaflets collected. This highlights the significance of comprehensive leaflets in empowering patients' informed decision-making and their adherence to the deprescribing plan. Furthermore, the social and emotional impact of hypoglycemia can make individuals hesitant to intensify therapy, promoting the deprescribing of unnecessary medications. Clear information in leaflets about deprescribing as part of rational prescribing can support this approach.[29]

The study on deprescribing benzodiazepines in Brazilian electronic leaflets, confirms that recent guidelines recommend a gradual and structured withdrawal of medications, especially in frail older adults with limited life expectancy on polypharmacy.[30] However, the electronic leaflets for oral antidiabetics found in this study still fall short of achieving this important goal. The study highlights the significance of improving the communication quality of electronic leaflets to effectively facilitate deprescribing in elderly patients with T2DM. Enhancements in clarity, the use of appropriate terminology, and the provision of comprehensive yet concise content are vital for promoting rational medication use and guiding the deprescribing process for frail adults as necessary. Terminology related to deprescribing, such as "withdrawal" and "tapering," was frequently either absent or inadequately explained, undermining the effectiveness of the leaflets as educational resources. Although some leaflets demonstrated conciseness, they often omitted critical information essential for understanding the deprescribing process. Thus, achieving a balance between brevity and comprehensive coverage of key information is imperative.

Whereas a quarter of the leaflets provided guidance on deprescribing, there's room for improvement in standardized guidance across countries. Australia and New Zealand demonstrated leadership in discussing deprescribing, while Canada stood out for acknowledging age-related considerations. Australia's leadership in including information for deprescribing oral antihyperglycemics for elderly patients in their electronic leaflets highlights the nation's commitment to rational prescribing and efficient healthcare practices. These results stress the Australian health system's dedication to optimizing health outcomes for frail older adults while managing costs. A recent study confirms that deprescribing in the elderly population is a cost-effective intervention that does not compromise quality of life.[31] Following a newly released study conducted in Australia for over twelve months, the savings from deprescribed medications amounted to $328.90 per participant in the blinded intervention group and $164.00 per participant in the open intervention group. Extrapolating these findings to the entire Australian population suggests potential net savings for the national health system ranging from $1 million to $16 million annually.[32]

Only a few electronic leaflets have discussed concerns regarding the time-to-benefit of oral antihyperglycemics treatment and uncertainty in clinical benefits, and Brazil has been a leader in these aspects. Including information regarding the estimated time-to-benefit in leaflets may draw prescribers' attention to the necessity of considering deprescribing unnecessary medications or avoiding irrational prescribing, especially for frail older adults with complex medical conditions and short life expectancy. In this population, the benefits of aggressive treatments are less certain due to multiple drug interactions leading to disability, and reducing the likelihood of them surviving long enough to benefit from the treatment.[33] Despite numerous recommendations for treatment adjustments in older patients with T2DM, the current study found that closer to one-third of the leaflets addressed the risks of tight fasting glucose control and targeting HbA1C levels $\leq$6.5 % in elderly patients. Though guidelines on glycemic targets differ slightly, evidence shows that for older individuals with a life expectancy of less than 10 years, aiming for an HbA1c level $\leq$ 6.5 % can be more harmful than beneficial. This is because microvascular complications generally take more than a decade to develop, and strict glycemic control in older adults is associated with increased morbidity and mortality.[34]

The concept of oral antidiabetics temporary treatment cessation was extensively discussed, especially in the United Kingdom. Nevertheless, the context in which it was mentioned primarily related to scenarios such as elective major surgery, pregnancy, breastfeeding, and occasionally in response to serious adverse drug reactions. It is important to note that these discussions did not typically cover the context of the deprescribing process. Given that deprescribing should be approached as a trial process, temporary treatment cessation serves as a viable strategy to achieve the successful withdrawal of unnecessary medications in elderly patients with T2DM.[35] The academic debate surrounding medication review and deprescribing in older adults underscores the necessity of enhancing the comprehensiveness and specificity of deprescribing plans available to patients.[36]

Encouragement is given to the development of standardized leaflets that serve as accessible resources for both healthcare providers and patients, facilitating communication regarding medication adjustments and management strategies. These documents should encompass various elements such as indications, treatment objectives, anticipated duration, care goals, patient preferences, tapering protocols, and monitoring procedures of deprescribing endeavors.[37] An investigation led by The Royal Australian College of General Practitioners found that 84–90 % of patients were willing to withdraw one or more medications when suggested by their prescriber.[38] We believe that providing comprehensive and concise information on deprescribing in the leaflets may significantly boost multidisciplinary communication among healthcare providers, and reduce patient reluctance towards the deprescribing process, one of many other barriers. Previous clinical studies have shown that a strong collaboration between pharmacists and physicians using electronic leaflets for oral antidiabetics is vital for the successful deprescribing process in elderly patients with T2DM.[39] Pharmacists can conduct thorough medication reviews to identify potential drug interactions, duplicate therapies, or medications that may no longer provide meaningful benefits, and communicate these findings to physicians. This teamwork enables safer alternatives or dose adjustments, particularly for medications with heightened hypoglycemia risks, ensuring patient safety.[40]

In agreement with these recommendations, utilizing leaflets as a dependable resource is believed to ease prescribers' concerns about medication withdrawal syndrome that might come from deprescribing and consequently contribute to promoting meaningful and engaged communication between patients and healthcare practitioners, which is crucial for effective healthcare delivery and the improvement of healthcare services.[41] Although some countries have rules for producing medication leaflets, these are created by the pharmaceutical companies

themselves, highlighting a need for change. The research agenda is biased, as sponsors of trials for new drugs rarely study the effects of deprescribing.[42] Public supervision and regulatory authorities should mandate well-designed deprescribing studies for medication registration, which would enhance the quality and safety of healthcare.[43]

Some study's limitations also deserve pinpointing. Since around 11 % of the anticipated leaflets were missing, the study was constrained by the availability of leaflets on regulatory authorities' websites, consequently restraining data collection for the current research. This underscores several critical issues, including the lack of access to medicines' electronic leaflets globally, and outdated leaflets that do not reflect the most recent guidelines for managing T2DM, particularly in elderly patients. Our study found that the recommended timeline for updating leaflet information after introducing a drug to the market exhibits considerable variation across different countries.[44] Nevertheless, guidelines advocate that Product information is updated whenever new data becomes available, such as information about the medicine's efficacy, safety, appearance, or stability.[45] However, our findings reveal a notable discrepancy from this ideal. The European Medicines Agency asserts that reviewing and updating electronic leaflets will ensure patients are better informed about their medications and this revision will empower prescribers and patients by providing them with updated comprehensive information.[46]

In the "World Population Ageing 2019" report, the United Nations (UN) defines older individuals as those aged 60 or 65 years and above. The World Health Organization (WHO) similarly categorizes older individuals in developed economies as those aged 65 or older.[47] Unfortunately, in this research, most analyzed electronic leaflets inconsistently addressed the caution required when using oral antihyperglycemics in older individuals. These leaflets often failed to reference the specific age ranges defined above, resulting in a lack of accuracy in the information provided for the targeted patient group.[48] Addressing these gaps and limitations can significantly improve the quality and comprehensiveness of deprescribing guidance in electronic leaflets for oral antidiabetics. The Food Drug Administration (FDA) recommends that authorized dispensers, such as pharmacists, provide FDA-approved Patient Medication Information (PMI) to patients receiving prescription drug products on an outpatient basis. Patients should have the option to receive PMI in either paper or electronic format, with paper being the default method unless the patient requests electronic delivery.[49] By standardizing, updating, and providing comprehensive information, these leaflets can improve the deprescribing process for elderly patients with T2DM, and empower them to make informed decisions, by enhancing their awareness and at last improving health outcomes.

Deprescribing should be one of the core components of clinical care for older adults, as it is essential for promoting rational prescribing and enhancing their quality of life.[50] However, achieving this goal requires active patient involvement, as deprescribing is a patient-centered care strategy.[51] Hence, it should be approached as a trial and a collaborative process between healthcare providers and patients involving a collaborative process where clinicians and patients engage in discussions about the various treatment options, supported by the best available evidence.[52] This partnership also empowers patients by providing them with knowledge and increasing their awareness regarding the reduction, alteration, or discontinuation of medications that, although previously beneficial, may become inappropriate and detrimental to their quality of life due to age and physiological changes.[53]

Shared Decision-making (SDM) includes clinical plans and tests, balancing anticipated outcomes and risks with patient values and preferences. Unlike the paternalistic informed model, SDM is recommended and favored in numerous healthcare policies worldwide.[54] It has emerged as a widely accepted and preferred approach during clinical consultations, particularly when multiple treatment options are available.[55] Therefore, by stressing the importance of explicit deprescribing guidance in electronic leaflets, the study underlines the role of these documents in empowering doctors and patients to make informed decisions. Electronic oral antihyperglycemics leaflets are considered enablers to a successful deprescribing process, they focus on a patient-centered care approach and are substantial for enhancing better healthcare outcomes that would consequently improve the quality of life for elderly patients with T2 DM.[56]

5. Conclusion

The study highlights global regulatory efforts in accessing electronic leaflet databases but notes the absence of Sulfonylureas leaflets in various national medicines regulatory authorities, indicating a potential gap. Outdated leaflets in most medicines' regulatory authorities, and their fluctuations in availability, indicate significant regulatory issues.

Among the various Medicines Regulatory Authorities, there are significant disparities regarding the deprescribing guidance, and only a minority of leaflets addressed this concern. This highlights the need for standardized leaflets, as seen in Australia, New Zealand, and Canada, which also addressed age-related considerations. Explicit deprescribing instructions are crucial, especially for patients with multimorbidity, polypharmacy, and limited life expectancy, with hypoglycemia being a major concern. Despite clear guidance, inconsistencies suggest room for improvement because clear and detailed leaflets can be essential and contribute to informed treatment decisions.

Aligned with Ontario protocol recommendations, the study stresses the hypoglycemia risk in elderly patients, requiring clear information for shared decision-making. The social and emotional impacts of hypoglycemia emphasize the need for leaflets accommodating less stringent glycemic goals in frail elderly patients.

Even more, efforts should focus on enhancing the specificity and comprehensiveness of deprescribing plans, using leaflets as communication tools. Up-to-date information on regulatory websites and detailed leaflets are crucial for facilitating the deprescribing process and building prescriber confidence. Therefore, public oversight and deprescribing studies during medication registration can be necessary to understand the potential consequences between time-to-benefit and clinical uncertainty, especially for frail elderly patients with limited life expectancy.

In conclusion, deprescribing should be a core component of clinical care for older adults, promoting rational prescribing and improving quality of life. The study advocates for comprehensive, standardized, and updated electronic leaflets with clear deprescribing guidance, empowering healthcare providers and patients for informed decision-making. Oral antihyperglycemics leaflets can play a critical role in facilitating the deprescribing process by reassuring prescribers, mitigating their apprehension, and enhancing their communication confidence. This approach supports shared decision-making, fostering a collaborative process that considers patient values and preferences, ultimately improving healthcare outcomes for elderly patients with T2DM.

CRediT authorship contribution statement

Kitete Tunda Bunnel: Writing – review & editing, Writing – original draft, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Silvio José Elisei Carvalho:** Data curation. **Mariana Linhares Pereira:** Conceptualization. **René Oliveira Couto:** Formal analysis. **André Oliveira Baldoni:** Methodology.

Declaration of competing interest

The authors declare no conflicts of interest.

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