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Research Letter

Deprescribing Glucose-Lowering Therapy in Older Adults with Diabetes: A Systematic Review of Recommendations

To the Editor:

Overtreatment by glucose-lowering treatment (GLT) is frequent, and may induce harmful hypoglycemic events in older people with type 2 diabetes (T2D), significantly increasing morbidity and mortality.[1] Avoiding overtreatment by GLT, either by prescribing appropriate GLT according to their individual risks-benefits balance or by deprescribing GLT, is therefore a key issue in the management of older patients, as recommended by various scientific societies these last years.[2] Nevertheless, there is currently no consensus on the definition of GLT overtreatment in older people,[3] which prevents a clear statement on which patients should undergo deprescribing of GLT. It is therefore worthwhile to define the profiles of patients for whom GLT should be deprescribed. This systematic review of clinical practice guidelines (CPGs) aimed to compare the recommendations defining profiles of older patients in whom deprescribing GLT is recommended.

Methods

This systematic review included all CPGs focused on older people (≥65 years old), related to some aspects of T2D management, providing distinct recommendation(s) addressing the deprescription of GLT, endorsed by scientific societies or expert groups from Europe or North America, and published in English or French from 2015 onward. Literature databases were comprehensively searched (MEDLINE, EMBASE, and CINAHL complete) using research equations, as well as websites of CPG repositories or scientific societies of geriatrics or endocrinology. After removing duplicates, we selected eligible CPGs following a 2-step strategy (step 1: title-and-abstract review; step 2: full-text review of the remaining records after step 1) independently by 2 reviewers. All conflicts were adjudicated by a third reviewer. We assess the methodologic quality of included CPGs using the AGREE-II score.[4] Finally, we extracted the content of all recommendations defining profiles of patients to be targeted for deprescribing GLT, as well as their level of evidence. This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, and its protocol was prospectively registered in PROSPERO (CRD42022320298). The detailed methodology is available in Supplementary Material 1.

This study was supported by a postdoctoral grant (Bourse d'Excellence WBI. world) awarded to Antoine Christiaens from Wallonie-Bruxelles International, Belgium (ref. SUB/2021/515794). The funding body played no part in the design of the study; collection, analysis, and interpretation of data; or in writing the manuscript.

The authors declare no conflicts of interest.

Results

Of the 2270 records identified, 5 CPGs were included: those from the European Geriatric Medicine Society and the European Diabetes Working Party for Older People in 2022 (EuGMS-EDWPOP22),[5] the American Diabetes Association in 2022 (ADA22),[6] the Endocrine Society in 2019 (ES19),[7] the Diabetes Canada Clinical Practice Guidelines Expert Committee in 2018 (DC18),[8] and the network Deprscribing.org in 2017 (Deprescribing.org17)[9] (Table 1). They were all of "high methodological quality" according to AGREE-II scoring. However, the domains related to stakeholders' involvement, applicability of the recommendations, and rigor of the CPG development were lacking in all CPGs. All CPGs provided a list of different profiles of patients for whom deprescribing GLT is recommended, either because those patients have an important risk of hypoglycemia [patients with advancing age, tight glycemic control, prescription of hypoglycemic medications (sulfonylureas, glinides, or insulins), multiple comorbidities, frequent hypoglycemia, impaired renal function, polypharmacy, or long duration of diabetes] or because the benefit of GLT is uncertain (patients with severe neurocognitive disorder, frailty, limited life expectancy, or patients living in nursing home). These profiles are heterogeneous between CPGs, and their definitions were unclear (Table 1). EuGMS-EDWPOP22 and Deprescribing.org17 provided the most comprehensive lists of profiles, whereas ES19 only suggest deprescribing for patients with severe neurocognitive disorder. The extracted recommendations were of very low level of evidence (mainly based on observational studies, or opinions of experts).

Discussions

This systematic review demonstrated the existence of specific recommendations defining the profiles of patients in whom deprescribing is suggested, which is reassuring given the challenge of avoiding overtreatment by GLT in older patients. However, there is room for improvement in some aspects of the methodological development of these guidelines, such as improving the diversity of experts involved in drafting the guidelines (eg, experts in geriatrics and nursing), empowering patients, and providing more clear and precise recommendations to increase their easier use in daily clinical practice.[10] We have also highlighted a lack of consistency in the content of recommendations between the CPGs and a poor level of evidence of these recommendations. There is indeed a significant lack of evidence in the area of T2D in older people, especially in relation to overtreatment, and even more so to deprescribing GLT.[1] This critically prevents the availability of quality recommendations in this crucial area.

Therefore, there is an urgent need for high-quality evidence in this field, necessary to establish trustworthy recommendations, leading to the avoidance of overtreatment, and to better care of older patients with type 2 diabetes.

Supplementary Data

Supplementary data related to this article can be found online at https://doi.org/10.1016/j.jamda.2022.12.018.

Table 1
Profiles of Patients to Be Targeted for Deprescribing GLT According to the Recommendations of the 5 CPGs

CPG	EuGMS-EDWPOP22[5]	ADA22[6]	ES19[7]	DC18[8]	Deprescribing.org17[9]
	European Geriatric Medicine Society; European Diabetes Working Party for Older People	American Diabetes Association (ADA)	Endocrine Society	Diabetes Canada	Deprescribing.org Network
Year	2022	2022	2019	2018	2017
Country or region	Europe	USA	USA (and Europe)	Canada	Canada
No. of recommendations*	3/133	1/20	1/35	2/13	3/3
Patients at risk of hypoglycemia	Multiple comorbidities (esp. ≥5 comorbidities)	—	—	Multiple comorbidities	Multiple comorbidities
	Tight glycemic control†	—	—	—	Tight glycemic control
	Frequent hypoglycemia (esp. serious episodes needing assistance)	Wide glucose excursions or severe or recurrent hypoglycemia on sulfonylureas or glinides‡	—	—	Hypoglycemia history or lack of awareness
	Inappropriate medications (esp. insulin or sulfonylureas)	Sulfonylureas or glinides (+ cognitive dysfunction, depression, anorexia, or inconsistent eating pattern)	—	—	Taking a sulfonylurea or insulin
	—	Polypharmacy‡	—	—	Drug interactions
	Impaired renal function§	—	—	—	Impaired renal function
	Advancing age (≥80 y)	—	—	—	Advancing age
	Long duration of diabetes (>20 y)	—	—	—	—
Patients in whom benefit is uncertain	Dementia, especially those with erratic eating pattern and abnormal behavior	Cognitive dysfunction, depression, anorexia, or inconsistent eating pattern (with sulfonylureas or glinide)	Cognitive impairment (ie, mild cognitive impairment or dementia)	—	Dementia
	Significant weight loss, especially unintentional indicating frailty	—	—	Frailty	Frailty
	End of life, especially those with ≤1 y life expectancy	If taking any medications without clear benefits in approving symptoms and/or comfort (in patients at the end of life)	—	—	Limited life expectancy
	Nursing home residents, especially those with multiple comorbidities	—	—	—	—
Other	—	—	—	—	Patients at risk of other GLT adverse effects

esp., especially.
*Number of recommendations extracted / total number of recommendations provided in the CPG.
†HbA_{1c} <6.5% or <7.0% in patients with frailty.
‡In patients in good or intermediate health status.
§Especially those with end stage renal disease.

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Long-Term Care Needs and Incidence of End-Stage Kidney Disease: A Retrospective Cohort Study

To the Editor:

End-stage kidney disease (ESKD) requiring renal replacement therapy is a public health problem with an economic burden.[1] The aging of the population has increased the number of older patients with ESKD worldwide.[2,3] Several studies have shown that poor performance in activities of daily living (ADL) is a predictor of cardiovascular diseases[4] and all-cause mortality.[5] However, few studies have assessed the association between ADL performance and incidence of ESKD.

The present retrospective cohort study, the **Neyagawa Health checkups and Health care in Kokuho database (NHHK)** study,[6] aimed to assess the association between long-term care needs certification,[7] which is correlated with the Barthel ADL index,[8] and the incidence of ESKD.

Methods

The methods of the present study are described in detail in Supplementary Methods. Briefly, eligible participants comprised 146,519 beneficiaries of the National Health Insurance or the Late-stage Medical Care System for the Elderly in **Neyagawa city, Osaka prefecture**, Japan, who had an insured period between September 2012 and March 2017 (Supplementary Figure 1). The present study included 7873 participants aged ≥65 years who received long-term care-needs certification for the first time during the insured period. Each participant with care needs certification was matched to

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