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Barriers in prescribing antidiabetic medications with cardiovascular benefits: practice, experience, and attitudes of GPs in Croatia

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Abstract

Background The treatment approaches of type 2 diabetes (T2D) are being transformed, due to the availability of novel antidiabetic medications, sodium-glucose co-transporter 2 inhibitors (SGLT2ins), and glucagon-like peptide-1 receptor agonists (GLP-1 RAs). Despite their proven beneficial effects, recent research points to their insufficient prescription. This study aimed to reveal the prescription rates of SGLT2ins and GLP-1 RAs among general practitioners (GPs) in Croatia and to examine factors associated with their low self-confidence in prescribing them.

Methods A self-designed survey questionnaire was used and delivered to the GPs' e-mail addresses in digital format. The data on the number of individuals diagnosed with T2D and prescribed new antidiabetic medications were checked by the respondents in their electronic database. Factors associated with lower GPs` self-confidence in prescribing SGLT2ins and GLP-1 RAs were assessed by bivariate and multivariate logistic regression analyses.

Results The study included 168 GPs (66.1% women; 49.4% specialists in family medicine) and a cohort of 23,036 individuals with T2D. The prescription rates of SGLT2ins and GLP-1 RAs were 21.0% and 14.4%, respectively. Specialists stated a higher level of self-confidence in prescribing these medications, compared to other respondents. In the multivariate models, a factor that was shown to reduce the likelihood of low GPs` self-confidence in prescribing SGLT2ins was "familiarity with the side effects of these medications" (OR = 0.03), while factors that increased this likelihood were: "being familiar with GLP-1 RAs` side effects" (OR = 4.8), "an insufficient knowledge and experience of GPs in adjusting two target outcome measures to the same patient" (OR = 2.2), and "the GPs` assumption that the new guidelines` protocol which separates two target outcome measures is useful only in some cases but not in all" (OR = 5.4). Regarding GLP-1 RAs, only one factor – "familiarity of GPs with GLP-1 RAs side effects", was shown to reduce the probability of GPs` low self-confidence in prescribing this group of medications (OR = 0.27).

Conclusion It is of the utmost importance to identify barriers the GPs face when prescribing these medications, as well as to suggest potential strategies to optimize their prescription.

Keywords Type 2 diabetes, Cardiovascular risk, SGLT2ins, GLP-1 RAs, Prescribing rates, Prescribing barriers, Therapeutic inertia

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Introduction

Due to the high prevalence of type 2 diabetes (T2D), individuals with this disease are often solely under the care of general practitioners (GPs). GPs are the first point of contact and play a crucial role in ongoing management [1]. Current guidelines offer evidence-based recommendations for the diagnosis, treatment, and follow-up of individuals with T2D, helping GPs deliver standardized, high-quality care [2, 3]. The quality of life for T2D patients is significantly affected by various comorbidities and complex care regimens [4]. This poses challenges for healthcare providers, especially GPs, due to their role in providing comprehensive and patient-centered care [5]. To assist GPs in the complex landscape of pharmacological approaches, treatment guidelines provide algorithms that address the efficacy, safety, and cost of medications while considering patient factors like socioeconomic status and existing health conditions such as cardiovascular disease (CVD), chronic kidney disease (CKD), and chronic heart disease (CHD) [2, 3]. These guidelines advocate for shared decision-making with patients, regular monitoring of progress, and adjustments to treatment goals. They also facilitate the integration of the latest advancements in diabetes management, helping GPs stay current in a rapidly evolving field [2, 6].

Haemoglobin A1c (HbA1c) is a key measure of glycaemic control and a standard for quality care in individuals with T2D [7]. Achieving target HbA1c levels is thought to reduce adverse clinical outcomes and is used to guide medication therapy [2]. However, many individuals with T2D still do not meet these glycemic goals [8]. As a major contributing factor to this failure, therapeutic inertia (TI) – the failure to adjust medical therapy as needed—has been addressed [9]. Causes of TI involve factors related to healthcare providers, patients, and the healthcare system, often interacting in complex ways. Previous efforts to address this issue have not been successful [10]. Enhancing qualitative research to tackle TI effectively may provide a better understanding of the problem and lead to targeted strategies tailored to local contexts [9].

The introduction of antidiabetic medications with cardiovascular (CV) and renal benefits, such as glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and sodium-glucose cotransporter-2 inhibitors (SGLT2ins), marked a new era in treating T2D [11]. CV outcome trials (CVOTs), today the required standard in assessing new remedies for curing T2D, have shown that these medications provide significant benefits beyond blood sugar control [12]. The joint guidelines from the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) recommend these treatments for individuals with T2D and established atherosclerotic cardiovascular disease (ASCVD) or those at high risk, regardless of HbA1c levels [2, 3]. For individuals with T2D and CHD or CKD, SGLT2ins take precedence over GLP-1 RAs [2]. Conversely, GLP-1 RAs and the newer insulin secretion-stimulating medication tirzepatide are preferred for weight loss in obese individuals with T2D [13, 14].

The introduction of these new antidiabetic medications has significantly changed the management of T2D. These advancements allow for an integrated approach to managing T2D alongside CVD, fulfilling a long-desired goal in patient care [15]. Treatment can now be personalized based on grading CV risk, and by enabling tailored strategies that address the unique needs of particular individuals with T2D [16]. In addition to meeting glycemic targets, current recommendations also take into account factors such as weight management, the risk of hypoglycemia, and the prevention of CV and kidney complications. Access to medications, their cost, and availability are also important factors to consider in person-centered therapy [2].

Despite the clear health benefits of new antidiabetic medications for T2D, their prescription rates have been reported low [17–19]. This fact revived the importance of research on factors contributing to TI. A key barrier in prescribing these medications was identified to be a lack of understanding of factors influencing treatment outcomes, given the complexity of T2D, which may be a constraint for informed decision-making and personalized management of these individuals [20–22]. Individuals with T2D exhibit considerable heterogeneity in physical characteristics (age, obesity, comorbidities), psychosocial factors (socioeconomic status, health literacy), and disease characteristics (duration, onset, and complications), all of which can affect treatment responses to GLP-1 RAs and SGLT2ins [21, 23, 24]. Additionally, gaps in understanding treatment outcomes partially arise from the inadequate characterization of participants in CVOTs, the evidence from which is used to inform recommendations in the guidelines [25]. It is generally agreed that guidelines should be clearer about how to use these medications in specific situations and better define the clinical contexts for their recommendation [26]. Regarding GPs, they believe that better knowledge translation could enhance their confidence in prescribing these medications and that guidelines should indicate where harm–benefit ratios are unclear or where evidence is insufficient [27].

The lack of clarity in guidelines` recommendations significantly contributes to poor adherence among healthcare providers, particularly GPs, and this was recognized as one of the most important factors of TI [28]. An important reason for the low implementation of clinical guidelines among GPs is that they often do not

fit the GPs` working style, known as holistic, and fail to address unique cases, which limits their applicability in real-life practice. The complexity of guideline manuals and ineffective communication with specialists may also hinder compliance [28]. A general view is that qualitative research among GPs could provide insights into these guideline gaps and implementation barriers [24].

Based on the abovementioned evidence, the reasons for the low uptake of novel antidiabetic medications remain largely under-researched, but they seem to be influenced by various factors, often assembled within the framework of TI. Overall, the most common barriers relate to GP's knowledge and attitudes, guideline comprehensiveness and the rate of implementation, GPs` communications with patients and specialists, and health system organization. This study aimed to determine the novel antidiabetic prescription rates in Croatia and the motivation and confidence of GPs to prescribe them, as well as to investigate the association of these results with potential barriers that GPs encounter in the process of prescribing these medications.

Methods

Study design

The study employed a quantitative survey research design targeting GPs in Croatia. Data collection occurred in two phases, each lasting about 6 months: a pilot phase, conducted from October 2023 to March 2024, and a second phase, conducted from June to November 2024. We concluded the survey after the second phase due to declining interest among potential participants and to avoid biases from an extended study period, as our topic is a rapidly evolving area of medical practice, which confirms a lot of evidence-based position statements from this field regularly emerging [29]. GPs in Croatia are periodically exposed to educational activities organized by the Croatian Endocrine Society and pharmaceutical representatives. To enhance visibility, we presented our initial findings of this study at national and international conferences, ensuring that the study remained relevant to GPs. For all these reasons, the responding GPs could have rapidly changed their attitudes towards prescribing these medications.

Respondents (GPs) and the study population of individuals with T2D

Currently, 2,169 GPs are employed in Croatia, of whom 63% are women [30]. The planned sample size was 180, or about 8.3% of this population. The final sample of 168 surveyed GPs constitutes 7.8% of the total working population of GPs in Croatia (Fig. 1).

The general characteristics of respondents are presented in Table 1. Of the total number of respondents, 111 (66.1%) were women (Table 1). The respondents` age range was 25 to 67 years, with a median age of 45

Table 1 General characteristics of respondents (GPs)

Characteristics	N (%)
Total	168 (100.0)
Gender	
Male	57 (33.9)
Female	111 (66.1)
Academic degree	
Doctor without specialization	53 (31.5)
Family medicine resident	29 (17.3)
Family/general medicine specialist	83 (49.4)
Specialist in another field	3 (1.8)
Place of practice	
Urban area	114 (67.9)
Rural area	54 (32.1)

N – *number of respondents*

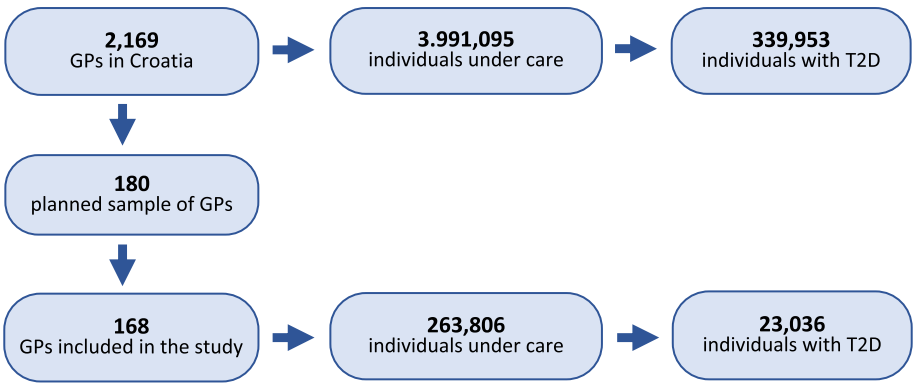

Fig. 1 National record data of GPs, a total of individuals under GPs` care, and individuals diagnosed with T2D, compared to the study data. GPs – *general practitioners*, T2D – *type 2 diabetes*

Table 2 The age stratification of individuals with T2D covered by the study and inter-practice variation

	N (%)	Minimum–maximum range	Median (IQR)
Individuals with T2D in the study	23,036 (100.0)	15—370	133 (95—179)
< 60 years	6,535 (28.4)	5—150	31 (20—50)
60–80 years	12,903 (56.0)	4—300	70 (50—102)
> 80 years	3,598 (15.6)	0—98	20 (10—30)

N Number of respondents, *IQR* Interquartile range, *T2D* Type 2 diabetes

years, interquartile range (IQR) 33–57. Their length of service varied from 0 to 42 years with a median length of 19 years (IQR 8–30). A major part of respondents, 114 (67.9%), worked in the urban area. Regarding the academic degree, 83 (49.4%) were specialists in general/family medicine, and 53 (31.5%) were GPs without specialization (Table 1).

GPs in Croatia care for 3.991,095 people (Fig. 1) [31]. Those diagnosed with T2D count 339,953, making the prevalence of T2D in Croatia of 8.5% [32]. GPs included in this survey ($N = 168$) care for 263,806 individuals, which makes up 6.6% of the insured population (Fig. 1). The number of those with T2D was 23,036, or 8.7% of the total population registered at the respondent GPs (Fig. 1, Table 2). The number of insured individuals in particular GP practices ranged from 500 to 2500, with a median of 1594 (IQR 1315–1850). The number of individuals with T2D among practices varied from 15–370, with a median of 133 (IQR 95–179) (Table 2). Looking at the age groups, most individuals with T2D were aged between 60 and 80 years (Table 2).

Regarding the associated CV comorbidities in individuals with T2D, the highest proportions accounted for arterial hypertension (58.6%), and CAD (20.0%) (Table 3).

Looking at the magnitude of prescriptions for certain antidiabetic medications with cardio-metabolic benefits, 35.0% of individuals with T2D were prescribed dipeptidyl peptidase-4 inhibitors (DPP-4ins), 21.0% were given SGLT2ins, and 14.4% were given GLP-1 RAs. The rates at which these medications were prescribed by individual GPs participating in the survey varied significantly (Table 4).

The data collection procedure

GPs from all over Croatia were involved in the survey. The total territory of Croatia is divided into 6 regions, named: Western, Eastern, Northern, Southern, Central, and the city of Zagreb [33]. The survey questionnaire was sent to GPs online via publicly available e-mail addresses of their practices and health centers from all over Croatia. Respondents have approached the survey on a volunteer basis, completely anonymously via Google Form platform.

Table 3 CV comorbidities in individuals with T2D covered by the study and inter-practice variation

	N (%)	Minimum–maximum range	Median (IQR)
Individuals with T2D in the study	23,036 (100.0)	15—370	133 (95—179)
with associated **arterial hypertension**	13,493 (58.6)	0—180	80 (50—100)
with associated **CAD**	4,622 (20.0)	0—92	22 (10—40)
with associated **CKD (eGFR < 60 mL/min)**	4,001 (17.4)	0—90	20 (10—34)
with associated **acute HF in the last year**	1,164 (5.0)	0—50	4 (2—8)

N Number of respondents, *IQR* Interquartile range, *eGFR* Estimated glomerular filtration rate, *CAD* Coronary artery disease, *CKD* Chronic kidney disease, *HF* Heart failure

Table 4 Individuals with T2D who were prescribed certain antidiabetic medication and inter-practice variation

	N (%)	Minimum–maximum range	Median (IQR)
Individuals with T2D in the study	23,036 (100.0)	15—370	133 (95—179)
who were prescribed **DPP-4ins**	8,068 (35.0)	3—130	43 (30—64)
who were prescribed **SGLT2ins**	4,828 (21.0)	1—80	25 (15—40)
who were prescribed **GLP-1 RAs**	3,324 (14.4)	0—93	15 (10—25)
who were prescribed **GLP-1 RAs** and **SGLT2ins combined**	1,641 (7.1)	0—60	6 (3—12)

N Number of respondents, *IQR* Interquartile range, *DPP-4ins* Dipeptidyl peptidase-4 inhibitors, *GLP-1 RAs* Glucagon-like peptide-1 receptor agonists, *SGLT2ins* Sodium-glucose co-transporter 2 inhibitors

The Cover Letter has been sent to potential respondents together with the online survey form, to explain the purpose of the survey and provide them with instructions for data collection and answering the questions. We also asked the respondents for their consent to use data obtained from the survey for publication.

For most of the answers, respondents had to fill in the survey questionnaire based on their experience and attitudes. For some questions, like the number and demographic data of individuals diagnosed with T2D who are registered on their list, the number of those with particular CV comorbidity, or those who were prescribed a certain antidiabetic medication – responding GPs needed to find data from their electronic (e-) health records. These simplified summaries of data can be easily extracted automatically, through a search engine of the IT system that groups ensured individuals according to the type of diagnosis and prescribed medications. For information about HbA1c and renal function, measured by the estimated glomerular filtration rate (eGFR), respondents could also take a look at the panel for supporting T2D surveillance in e-health records. They were advised to use data not older than a year. Although a majority of GPs in Croatia are holding this panel, it is not mandatory and is subject to incentive.

Although we could not directly control this procedure, in the Cover Letter we included a statement where we appealed to responding GPs to their conscience and professional honesty and asked them to certainly check the required data in single patients` e-health records or the summary data of patients` e-health profiles.

Description of the instrument (survey questionnaire)

The instrument used in this research was a survey questionnaire consisting of two thematically related parts designed specifically for the needs of this research but integrated into one online document. The principal and a senior researcher created the questionnaire. The survey data included also information on respondents` characteristics (gender, age, seniority, academic status, place of work, the distance of the GP office from the hospital, the total number of insured individuals on the list, and the number of those diagnosed with T2D).

Questions were of the close-ended type, including both single-selection and multiple-selection question types. Some questions contained a 5-point Likert Scale. There were also questions with a ranking score scale, asking respondents to rank the offered answers in order of importance from 1 to 3 or 1 to 5.

A part of the questions were open-ended questions. Those were questions where respondents were required to provide data from e-health records. It is necessary to mention that the data from e-health records in Croatia have the purpose of creating statistical and financial reports and are not specifically intended for research. This affected the limitations in the type of data collected because, knowing our IT system, we listed as required data in the survey those that we knew were present in e-health records (such as disease diagnoses, prescribed medications, and demographic data of insured individuals). The data indicating HbA1c and eGFR were obtained from e-health records or the panel of individuals with T2D. For this reason, we did not apply any standard report recommendations for using data from e-health records, such as, e.g., the RECORD checklist [34].

The survey questionnaire was composed of two parts. The first part contained a set of questions aimed at examining the current routine of GPs in prescribing antidiabetic medications, with special emphasis put on prescribing antidiabetic medications with CV benefits. Another set of questions in this part aimed at getting insights into the quality of the process of care for individuals with T2D, including the routes of communication with specialists.

The second part of the survey questionnaire focused on barriers to effective prescribing of new antidiabetic medications. These questions were developed based on the theoretical framework of TI but were tailored to address the specific conditions of the Croatian healthcare system. The focus was primarily on issues related to prescribing new antidiabetic medications, rather than barriers to transitioning from oral medications to insulin, which is the more commonly discussed topic in the published literature within the TI research area. The questions included issues such as the GPs` knowledge of recommendations from the guidelines, their practice in making decisions in specific clinical situations, characteristics of the healthcare system that may hamper optimal prescribing of these medications, as well as communication with specialists and the patients.

In seeking constructive criticism of the created survey questionnaire, we asked two specialist diabetologists, professors at our University, and two assistants at the Department of Family Medicine – one PhD and one doctoral student – to check it. In a joint discussion, some incorrect formulations were corrected and parts that were misunderstood were harmonized.

This paper presents the study results related to barriers to prescribing new antidiabetic medications.

Data analysis methods

To detect a significant mean difference between continuous variables in two independent groups (high/low level of self-confidence) with a medium effect size ($d = 0.5$), a sample size of 128 respondents was estimated, assuming a significance level of 0.05 and a statistical power of 0.8.

For bivariate and multivariate regression analysis, a minimum of 10 respondents per predictor is required. Consequently, the total minimum sample size was determined to be 180 respondents. This calculation was conducted using the G*Power software (version 3.1.9.2.), developed by Franz Faul at the University of Kiel, Germany.

Categorical data were presented as absolute and relative frequencies. Differences between categorical variables were tested using the χ^2 test, and, when necessary, Fisher's exact test. The normality of distribution for continuous variables was assessed using the Shapiro–Wilk test. Continuous data were described using the median and interquartile range boundaries. Associations were evaluated using Spearman's correlation coefficient ρ (Rho). Logistic regression, both bivariate and multivariate (stepwise method), was employed to assess the influence of multiple factors on the likelihood of lower self-confidence of GPs for prescribing antidiabetic medications with CV benefits [35, 36]. The high level of confidence was considered if the GPs chose the Likert grades 4 and 5, and the low level of confidence corresponded with points 1, 2 and 3 on the Likert Scale. In Croatia, the prescribing of SGLT2ins has been liberalized so that GPs can indicate their prescription independently of the specialists` recommendations. It is not yet allowed for GLP-1 RAs, but GPs often express their initiatives and readiness for doing so.

All P-values were two-tailed, with the significance level set at alpha = 0.05. Statistical analyses were performed using the MedCalc® Statistical Software version 23.0.6 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2024). The study report was prepared following guidelines for reporting research findings in biomedicine and health sciences [37].

Validation procedures

In the pilot study, we tested respondent response, and data relevance, and performed early data processing. The pilot phase included 86 respondents, comprising approximately 12,000 individuals with T2D. To check the reliability of the data collected in this phase, we compared the number of people with T2D in proportion to the share of surveyed GPs in the total number of GPs employed in Croatia with the total number of people with T2D registered in Croatia (as shown in Fig. 1 for the full-size data). In addition, we compared the data indicating proportions of individuals with T2D prescribed with particular types of new antidiabetic medications with the available data from other studies (as demonstrated in Discussion). We estimated the internal consistency of the data related to GPs` attitudes, and Cronbach`s α was 0.78. After that initial review, we concluded that we can proceed with data collection.

At the end of the survey, we repeated similar validity procedures for data representing numbers (facts) (as demonstrated in Fig. 1) and data indicating attitudes. The Cronbach`s α for the whole sample was 0.76.

We prove the representativeness of the sample by the fact that it involves respondents from all counties of Croatia, with a predominance of respondents from larger cities, where the concentration of GP teams is higher compared to rural areas. In addition, the ratio of male to female respondents (66% women) corresponds to that ratio in the entire population of GPs (63% women). Furthermore, GPs of both younger (< 45) and older (≥ 45) ages were included.

Since the sample is representative, we believe that the slightly smaller than calculated sample did not affect the validity of the research. Additionally, we placed emphasis on the examination of attitudes and subjective perceptions of GPs of the level of self-confidence in prescribing, rather than examining the magnitude of the problem of TI.

Results

The self-assessment of the level of confidence in prescribing SGLT2ins and GLP-1 RAs

Regarding the self-assessment of the level of confidence of surveyed GPs in prescribing antidiabetic medications with CV benefits, 128 (76.2%) respondents declared a high level of self-confidence (Likert grades 4 and 5) in prescribing SGLT2ins, and 90 (53.6%) respondents claimed that they are highly confident in prescribing GLP-1 RAs (Table 5).

Table 5 The self-assessment of the level of confidence of GPs for prescribing medications from the groups of SGLT2ins and GLP-1 RAs

	N (%)					
	Likert grade 1	**Likert grade 2**	**Likert grade 3**	**Likert grade 4**	**Likert grade 5**	**Total**
SGLT2ins	1 (0.6)	8 (4.8)	31 (18.5)	55 (32.7)	73 (43.5)	168 (100)
GLP-1 RAs	2 (1.2)	19 (11.3)	57 (33.9)	48 (28.6)	42 (25.0)	168 (100)

N number of respondents, *SGLT2ins* Sodium-glucose co-transporter 2 inhibitors, *GLP-1 RAs* Glucagon-like peptide-1 receptor agonists, Likert grade 1, 2 and 3 – *Low level of self-confidence*; *Likert grade 4 and 5 – High level of self-confidence*

Differences in GPs` general characteristics according to their declared high or low level of self-confidence in prescribing SGLT2ins and GLP-1 RAs

Greater confidence in prescribing SGLT2ins (Fisher's exact test, $P = 0.03$) and GLP-1 RAs (Fisher's exact test, $P = 0.02$) is significantly more expressed by specialists in general/family medicine, compared to respondents belonging to other classes of academic degrees, while there is no significant difference in the distribution of respondents regarding gender and place of work (Table 6).

Factors associated with GPs` self-confidence in prescribing SGLT2ins and GLP-1 RAs

The results of the Spearman's correlation analyses indicated that respondents who have a larger total number of insured individuals in their practice (Rho = 0.208) and a higher number of individuals with T2D (Rho = 0.176) tend to exhibit greater self-confidence in prescribing SGLT2ins (Additional file 1). Additionally, a greater number of individuals with T2D prescribed SGLT2ins (Rho = 0.315) was shown to be a factor positively correlated with increased GPs` self-confidence to prescribe this group of medications. Conversely, a larger proportion of individuals with T2D aged 80 years and older relative to the total number of individuals with T2D (Rho = − 0.171) was shown to negatively influence the GPs` self-confidence in this term.

Several factors were also found to influence the increased level of self-confidence among GPs when prescribing GLP-1 RAs (Additional file 1). These factors include the older age of the respondents (Rho = 0.162), a greater number of years of work experience (Rho = 0.159), and a larger total number of insured individuals in their practice (Rho = 0.198). However, there is an inverse association of a proportion of individuals with T2D aged 80 years and older with the level of self-confidence for prescribing this group of antidiabetic medications (Rho = − 0.228). Interestingly, the proportion of individuals with T2D prescribed SGLT2ins showed

Table 6 Differences in GPs` general characteristics according to their declared high or low level of self-confidence in prescribing SGLT2ins and GLP-1 RAs

	N (%) with different levels of self-confidence			*P**
	High level of self-confidence	Low level of self-confidence	Total	
When prescribing SGLT2ins				
Gender				
Men	48 (38)	9 (23)	57 (34)	0.08
Women	80 (63)	31 (78)	111 (66)	
Academic degree				
GP without specialization	39 (30)	14 (35)	53 (32)	**0.03**†
Family medicine resident	17 (13)	12 (30)	29 (17)	
Specialist in general/family medicine	70 (55)	13 (33)	83 (49)	
Specialist of another specialization	2 (2)	1 (3)	3 (2)	
Place of work				
Urban area	90 (70)	24 (60)	114 (68)	0.22
Rural area	38 (30)	16 (40)	54 (32)	
When prescribing GLP-1 RAs				
Gender				
Men	35 (39)	22 (28)	57 (34)	0.08
Women	55 (61)	56 (72)	111 (66)	
Academic degree				
GP without specialization	25 (28)	28 (36)	53 (32)	**0.02**†
Family medicine resident	10 (11)	19 (24)	29 (17)	
Specialist in general/family medicine	53 (59)	30 (38)	83 (49)	
Specialist of another specialization	2 (2)	1 (1)	3 (2)	
Place of work				
Urban area	61 (68)	53 (68)	114 (68)	0.98
Rural area	29 (32)	25 (32)	54 (32)	

* χ^2 test; †Fisher's exact test, *N* number of respondents, *SGLT2ins* Sodium-glucose co-transporter 2 inhibitors, *GLP-1 RAs* Glucagon-like peptide-1 receptor agonists, *GP* General practitioner

positive correlations (albeit weak) with GPs` self-confidence in prescribing also GLP-1 RAs, in addition to SGLT2ins.

Associations of TI-related factors with low self-confidence when prescribing medications from the SGLT2ins and GLP-1 RAs groups

To examine associations of different factors related to TI with the low level of self-confidence of GPs in prescribing SGLT2ins and GLP-1 RAs, bivariate and multivariate logistic regressions have been performed. The frequency distribution of TI-related factors is presented in Additional file 2.

Regarding the low level of self-confidence in prescribing SGLT2ins, in the bivariate logistic regression, several factors were indicated as being more pronounced than the others, including unfamiliarity with the EASD/ADA guidelines` recommendations for prescribing antidiabetic medications with cardio- and reno-protective effects (OR = 5.5), the opinion that the protocol in the recently updated guidelines greatly complicates decision-making because of the need to compare different treatment options within the specific clinical and social contexts of a particular individual (OR = 5.5), and the answer that GPs are not sure whether the new guidelines` protocol that considers a dual target goal provides any help in decision making (OR = 5.7). Other significant factors associated with low self-confidence in prescribing SGLT2ins, as obtained by the bivariate regression analysis, are shown in Additional file 3.

Among a large number of examined factors, only a few were chosen as significantly associated with low GPs` self-confidence in prescribing SGLT2ins in the multivariate model (Table 7). The model is entirely significant (χ^2 test = 76.3, $P < 0.001$) and explains from 40% (by Cox&Snell R^2) to 60% (by Negelkerke R^2) of the variance of low self-confidence in prescribing SGLT2ins and correctly classifies 83% of cases.

It can be realized from Table 7 that a greater number of individuals with T2D with already prescribed SGLT2ins, although with a weak likelihood ratio (OR = 0.96), as well as having detailed information about their side effects (OR = 0.03), reduce the probability of low confidence of GPs in prescribing this group of medications. On the contrary, being familiar with GLP-1 RAs` side effects in a great part contributes to the probability of low self-confidence among GPs when prescribing SGLT2ins (OR = 4.8). Of other barriers in prescribing SGLT2ins, this model points out an insufficient knowledge and experience of GPs in adjusting two target outcome measures to the same patient, by combining the principle of achieving HbA1c target values and determining increased CV risk (OR = 2.2). This factor is further emphasized by the assumption of GPs that the new guidelines` protocol that separates these two target outcome measures is likely to be useful only in some cases but not in the majority of them (OR = 5.4).

Similarly, many potential factors were identified in the bivariate logistic regression models as to be associated with low GPs'self-confidence in prescribing GLP-1 RAs (Additional file 4). These factors were from three main groups of TI-related factors, including insufficient GPs` knowledge of the guidelines` content, shortcomings of the guidelines in providing support to GPs in their decision-making, as well as characteristics of the GPs` communication with patients. Several obtained factors showed to be more pronounced than others, including unfamiliarity with the EASD/ADA guidelines` recommendations on prescribing antidiabetic medications with cardio- and reno-protective effects (OR = 5.2), the opinion that the new guidelines` protocol vastly complicates decision-making because of the need to compare

Table 7 The multivariate logistic regression model of low GPs` self-confidence in prescribing SGLT2ins

	β	Wald	*P*	OR	95% confidence interval
A greater number of individuals with T2D with already prescribed SGLT2ins	− 0.04	6.57	**0.01**	0.96	0.92 to 0.98
Barriers – knowledge It is difficult for me to apply the principle of achieving HbA1c target values and determining increased CV risk to one patient	0.76	7.09	**0.008**	2.2	1.22 to 3.73
Barriers – guidelines:					
Familiarity with GLP-1 RAs` side effects	1.57	5.43	**0.02**	4.8	1.28 to 17.9
Familiarity with SGLT2ins` side effects	− 3.41	18.5	**< 0.001**	0.03	0.01 to 0.16
The new guidelines` protocol that uses a double criterion for assessing the quality of T2D control helps in some cases, in some, it doesn't) vs. (yes, it sure helps)	1.69	7.4	**0.006**	5.4	1.61 to 18.05
Constant	3.86	7.2	**0.007**		

β Regression coefficient, *OR* Odds ratio, *T2D* Type 2 diabetes, *GLP-1 RAs* Glucagon-like peptide-1 receptor agonists, *SGLT2ins* Sodium-glucose co-transporter 2 inhibitors, *HbA1c* Glycated hemoglobin, *CV* Cardiovascular

different treatment options within the specific clinical and social contexts of a particular individual (OR = 7.4), thus making the decision difficult (OR = 6.0).

In the multivariate logistic regression model, however, only one factor was shown to be truly relevant in determining low GPs` self-confidence for prescribing GLP-1 RAs (Table 8). This factor is from the guidelines-associated barriers and indicates familiarity of GPs with GLP-1 RAs side effects, which if more detailed, reduces the probability of their low confidence in prescribing this group of medications (OR = 0.27).

The model is entirely significant (χ^2 test = 39.6, $P < 0.001$) and explains from 22% (by Cox&Snell R^2) to 30% (by Negelkerke R^2) of the variance of low confidence in prescribing GLP-1 RAs and correctly classifies 76% of cases (Table 8).

Discussion

The results obtained in this study offer valuable insight into the process of prescribing novel antidiabetic medications with CV benefits and the challenges that GPs face in this process. Although the survey was designed to explore the main concepts of TI, it was somewhat adapted to better match the topic. Furthermore, the outcome measure of the multivariate analysis was identified as the confidence level of GPs in prescribing medications. Consequently, the results have revealed some personal characteristics of GPs in Croatia which have a significant influence on how confident they are in their decisions while prescribing these medications. This approach is highly intimate and reveals some of the deep uncertainties and ambiguities that GPs process during their decision-making. Therefore, it provides a new perspective on the problem of inertia in prescribing medications – that which is highly manageable, as it can easily guide the strategies for these medications` prescription optimization.

The general analysis of the cohort of over 20,000 individuals with T2D indicates significant variability in the proportion of individuals with T2D in the total number of insured people registered with individual GPs. This fact, as will be mentioned later, might have differently influenced the level of confidence of GPs in prescribing new antidiabetic medications. Some possible reasons for this variation include differences in the prevalence of T2D among the counties of Croatia, variations in the size of individual practices, and the fact that more pediatric patients are registered in outpatient clinics in rural areas compared to urban areas, where there is a higher concentration of pediatric specialists [32].

Another characteristic of the cohort covered by this study is an older age, with the peak prevalence of T2D in the age group of 60 to 80 years. This age profile can help explain the results of the study, indicating concerns about the side effects of new antidiabetic medications as most relevant in determining the level of confidence in their prescribing. Such an age profile of individuals with T2D aligns with the data for Eastern European countries [38]. Although there are no exact data for Croatia, the recently published paper indicates that prediabetes and undiagnosed T2D prevalence in Croatia increase with age, reaching the maximum at the age of 60 to 70 years [39].

Given that CVD is a leading cause of mortality among individuals with T2D elsewhere, and that they have several times higher CV risk compared to the general population, it is essential to examine the CV risk parameters in these individuals and record CV comorbidities systematically and regularly [3]. For their proper risk stratification and customized treatment, it is also important to know that T2D and CVD, and comorbidities such as arterial hypertension, obesity (in particular of the abdominal type), and CKD share common pathophysiology backgrounds [40]. In this study, we found that the most frequent comorbidities in individuals with T2D are arterial hypertension, with more than half of them affected, and CAD, with a fifth of them affected. According to the available data, CAD, hypertensive disease, and diabetes are the top-ranked causes of death in Croatia, and Croatia is among countries in the EU whose CV and total mortality rates are above the average for the EU. Specifically, standardized and cumulative mortality rates for T2D are held above the average for the EU [41].

When taking into account these facts, together with the fact that the Croatian population is among "old populations", the conclusion arises that targeting common pathways of T2D and CVD, together with high blood pressure, would be the best means for declining the excess of mortality in Croatia. In addition, Croatia is currently a leader in the EU in the prevalence of obesity, with more than 50% of adults being obese or overweight, which implies that priority should be given also to preventing and treating obesity [42].

Within this context, we should consider our results about the extent of the prescribing of new antidiabetic

Table 8 The multivariate logistic regression model of low GPs` self-confidence in prescribing GLP-1 RAs

	β	Wald	*P*	OR	95% confidence interval
Barriers – guidelines:					
Familiarity with GLP-1 RAs side effects	− 1.32	27.6	**< 0.001**	0.27	0.16 to 0.44
Constant	4.47	24.9	**< 0.001**		

β Regression coefficient, *OR* Odds ratio, *GLP-1 RAs* Glucagon-like peptide-1 receptor agonists

medications among the target T2D cohort. With numbers indicating prescription rates for SGLT2ins and GLP-1 RAs of 21.0% and 14.4%, respectively, and for their combination of 7.1%, Croatia seems to be comparable with some economically more developed European countries, like Sweden and Germany [18, 19]. Considering Croatia's higher standardized mortality rate for CVD, the prescription rates for these medications are relatively less beneficial compared to those in developed countries, which are generally regarded as insufficient. For instance, data from the Swedish National Diabetes Register indicated that only one-third of individuals with T2D that are eligible for treatment with SGLT2ins or GLP-1 RAs, according to the common guidelines of the EASD and ADA, and the European Society of Cardiology (ESC), received these medications [18]. Although in Croatia the National Diabetes Register was established 25 years ago, it is not completed for data that is necessary for such assessment [32].

The results of this study, on the contrary, indicate the necessity of establishing systematic screening of CV risk factors and CV comorbidities in routine diabetes care and their recording in e-health records and Diabetes Register. In this regard, establishing a structured model of care that includes standardized elements of the care process has demonstrated benefits for the quality of care, clinical outcomes, and cost-effectiveness [43]. Non-systematically record-keeping of the renal status of individuals with T2D and/or non-regular eGFR checks is supposed to explain a less-than-expected proportion of individuals with decreased renal function (eGFR < 60 ml/min) found in this study (of 17.4%) when compared with the data from the global statistics for T2D (20–30%) or the prevalence of CKD in the general population of Croatia (7.9%) [44, 45]. We also recognized a potential limitation in our data collection, as the information was gathered through a survey of GPs rather than directly extracted from patient registers. The variations in the sample characteristics may also be taken into account.

Overall, the GPs in Croatia are more self-confident in prescribing SGLT2ins than GLP-1 RAs. It can be due to differences in the prescribing regimen between the two. For SGLT2ins, GPs can make indications on their own, while for GLP-1 RAs they need the specialist`s recommendations. In addition, a broader range of indications for GLP-1 RAs, but without a clear protocol in the guidelines of when to use and when to avoid this group of medications, alongside a long list of possible adverse reactions, which frequency and severity of outcomes in the treated population are poorly declared – may contribute to higher GPs` concerns about their prescribing [46, 47]. As we will show later, uncertainties about prescribing GLP-1 RAs are likely to importantly impact the GPs` decision process for prescribing also SGLT2ins.

This study identified certain characteristics of the GPs that significantly impact their prescribing behaviors. They can be assembled under the common denominator of working experience, which aligns with the abovementioned context. For instance, GPs who are family medicine specialists reported a higher level of self-confidence when prescribing medications from both SGLT2ins and GLP-1 RAs groups, compared to other respondents, such as family medicine residents or GPs without specialization. Regarding SGLT2ins, factors shown to significantly influence GPs to be more confident when prescribing them include a larger total number of insured people on the list and a greater number of those with T2D. For GLP-1 RAs, these factors include longer working experience and a larger overall patient load. The finding that a greater number of individuals with T2D of advanced age (old 80 years and over) under the care of particular GPs is likely to reduce their confidence in prescribing both SGLT2ins and GLP-1 RAs, indicates that GPs do not stay well with the safety profiles of these medications, specifically for vulnerable patient groups such as the elderly of very old age. This concern is expected to be resolved with the results of real-life studies currently underway [46, 48, 49].

Based on the bivariate logistic regression analysis, many factors can influence the GPs` level of confidence in prescribing new antidiabetic medications, but with varying strength. The factors that contribute most to the GPs` low-level confidence for both SGLT2ins and GLP-1 RAs are those associated with the lack of knowledge of the content of the EASD/ADA guidelines, and those that refer to the quality of the guidelines to support their decision-making, meaning that the recommendations in the guidelines make the decisions harder, rather than easier. This especially refers to the need to apply a dual aim of treatment to the same individual, and the lack of clear recommendations on how to approach every individual with T2D. In addition, the need to compare different treatment options depending on the clinical and social context of a particular individual with T2D greatly complicates decision-making. For these reasons, the recommendations from the guidelines the surveyed GPs assumed helpful in some cases, but not in others. Alternatively, unfamiliarity with the guidelines made GPs rather indifferent toward their helpfulness.

This problem —— designing a person-centered treatment for individuals with T2D who are characterized by extreme complexity, has been supposed to be a major barrier to the optimal uptake of new antidiabetic medications [20, 47, 49]. However, in-depth studies, exploring the attitudes of the prescribers, notably GPs, have not yet been performed. Such studies, however, allowing researchers to learn more about the wider context of the problem under investigation, would be essential for

designing effective interventions. Since the developers of the guidelines are usually clinical experts – this study, by providing a view on this issue that reflects the typical GPs` way of thinking – may have a significant impact on future guidelines designing and as a facilitator of in-depth research. Within the same context of knowledge about the guidelines, our results highlight familiarity with SGLT2ins` and GLP-1 RAs` side effects and indications for their prescription as factors that can reduce the GPs` low confidence in prescribing these medications.

These results highlight the necessity for ongoing education for GPs and the adjustment of guidelines to better align with their practical needs, as previously indicated in the literature. These methods are essential for enhancing guidelines adherence among GPs [28]. Providing case studies and clinical examples in the guidelines could make recommendations clearer in terms of how to use these medications in specific situations. Based on our results, educative activities should target especially younger GPs, with little working experience, and non-specialists, as well as those with small-sized practices, and with a low number of individuals with T2D under their care. Another measure to improve guidelines to better fit real-life situations would be by intensifying research in terms of conducting "post-hoc" analyses targeting narrower, well-defined patient subgroups. Such studies could help justify treatment indications and identify adverse reactions tailored to specific patient groups [25]. The need for better CV risk communication with individuals with T2D and shared decisions about pharmacological treatments are also emphasized in this study as factors that can reduce the low confidence of GPs in prescribing these medications. This factor is well-known from the previous studies about TI [10]. There is a hope that the emerging digital technology could provide new means of communication of GPs with both specialists and patients [50].

The multivariate models further narrowed the number of factors associated with the low GPs` confidence in prescribing GLP-1 RAs and SGLT2ins. If GPs were allowed to independently prescribe GLP-1 RAs—familiarity with their safety profile was shown to be a unique factor that could strongly reduce the GPs` low confidence when prescribing them. This point reflects a concern of GPs on how to handle this group of medications and suggests a need for knowledge improvement about the risk–benefit profile of these medications. An effective way would be the possibility of learning from real-life examples, including various clinical contexts and different target groups [46]. This GPs`concern might have been amplified in their perception as an “unknown threat”, beyond the real risk level, due to their lack of personal experience in handling these medications, as they do not take full responsibility for their prescription. However, this simplified probability model is likely to inspire initiatives to explore new theories regarding the causes of inertia in prescribing GLP-1 RAs. In this regard, this model was shown to explain only 30% of the variance of the GPs` low confidence in prescribing GLP-1 RAs.

A somewhat different situation is with SGLT2ins, for which GPs in Croatia got permission for their independent prescription shortly before the start of this study so that they could have changed for a little their perception about the circumstances in which to indicate them. Similarly, as with GLP-1 RAs, they highly value knowledge about the safety profile of SGLT2ins as a factor in reducing their low confidence in prescribing these medications. At first glance paradoxically, however, it is their feeling that the familiarity with GLP-1 RAs` side effects contributes to their low confidence in prescribing SGLT2ins. This perception becomes yet reasonable when taking into account that GLP-1 RAs and SGLT2ins share some common indication fields for individuals with T2D and complement each other in indications such as low renal function and old age of over 75 years [48, 51]. This lack of clarity in a division between indications of these two types of medications becomes even more pronounced in situations of an insufficient experience of GPs in handling these medications, as emphasized in this study. This especially applies to GLP-1 RAs, for their broader range of indications, and for which GPs in Croatia need to ask permission for their prescription from the specialists, which ultimately hinders their opportunity to gain personal experience in handling them. It is even more so when these uncertainties are put within the context of older age of individuals with T2D, as is the characteristic of the target cohort in this study. In this term, our results support the opinion that economic reasons should not justify the restrictive prescribing policy of GLP-1 RAs and that holding the medical indications is the most important factor in optimizing their prescription. In this context, introducing health policy providers to pharmacoeconomic analyses is likely to be crucial [43, 52].

Close to the above discussion is an explanation for two other statements that were demonstrated in the multivariate model of SGLT2ins. They relate to the inability of the guidelines to translate the requirement for achieving a dual aim, including both the glycemic target and beneficial CV outcomes, in high-risk individuals with T2D, to the full-spectrum diversity of the real-life situations that GPs face daily. Intensifying training for GPs in the guidelines` recommendations, including learning on real-life cases, or allowing GPs easy access to resources that can help support their decision-making in concrete situations, are likely to mitigate their concerns [46, 53]. There are opinions from previous studies that

implementation of the guidelines in a primary care setting should be a part of a broader knowledge translation process, which should include the development of practical pathways and protocols [54, 55]. The development of the guidelines that are intended to be used specifically in primary care, could also be an option. To support this knowledge translation strategy, there are suggestions to establish an ongoing monitoring programme of the efficacy and safety of these medications, alongside the side effect registry.

Conclusions

Results were presented from a comprehensive online survey performed among GPs in Croatia aimed at getting insights into the barriers to prescribing new antidiabetic medications with proven CV/renal benefits. We explored factors influencing GPs` decision-making based on their self-confidence levels, which allowed a perspective on this problem from the point of view of GPs. The obtained results are very instructive and can be used to inform mitigation strategies and strengthen practice. There is a need to intensify the educational activities among GPs, particularly for those with less working experience, non-specialists, and with a small number of people under care. Streamlined authorization for GLP-1 RAs or full abolition of prescribing restriction would allow GPs to get more personal insights into the risk-effect characteristics of these medications, which could have implications on enhancing the GPs` confidence in prescribing both GLP-1 RAs and SGLT2ins. In addition, strengthening inter-professional collaboration with specialist endocrinologists and cardiologists through more direct communication channels (face-to-face meetings, telephone or digital communication) could reduce the GPs` uncertainty in prescribing these medications and ultimately lead to an increase in their prescribing rates. Striving toward better communication with patients could be also helpful in empowering GPs in their decision-making about pharmacological treatment. One of the measures in the strategy to improve care for individuals with T2D, as indirectly suggested by our results, would be to maintain a systematic record of the data necessary for T2D surveillance. Finally, the results of this study encourage guideline developers and policymakers to pay more attention to aligning the recommendations with the working style of GPs.

Limitations

This study has several limitations. It included a smaller number of participants than estimated, which might have caused an overestimation of the effect size in differences and regression analyses. In addition, the participant selection procedure only partially aligned with the rules of randomization, which might have had an impact on the variable selection in the regression models. Yet, logistic regression models do not require the principles of linear regression models, and randomization does not justify the assumptions behind the model. Also alleviating circumstances are that the sample is rather representative of the population of GPs in Croatia and that participating GPs in the study are all exposed to similar education processes and all employ similar strategies in managing T2D. Another limitation is that respondent GPs sought the numerical data in their e-health records by themselves or according to personal assessment, which might have affected the data accuracy.

Abbreviations

T2D	Type 2 diabetes
SGLT2 ins	Sodium-glucose cotransporter-2 inhibitors
GLP- 1 RAs	Glucagon-like peptide-1 receptor agonists
GP	General practitioner
CVD	Cardiovascular disease
CKD	Chronic kidney disease
CHD	Chronic heart disease
TI	Therapeutic inertia
HbA1c	Glycated haemoglobin
CV	Cardiovascular
CVOT	Cardiovascular outcome trials
ADA	American Diabetes Association
EASD	European Association for the Study of Diabetes
ASCVD	Atherosclerotic cardiovascular disease
CAD	Coronary artery disease
eGFR	Estimated glomerular filtration rate
HF	Heart failure
DPP- 4ins	Dipeptidyl peptidase-4 inhibitors
ESC	European Society of Cardiology

Supplementary Information

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Additional file 1. Associations of variables indicating age, length of service, the number of insured individuals in the practice, and the percentage of individuals with T2D in the total number of insured individuals with the level of GPs` confidence for prescribing antidiabetic medications with CV benefits

Additional file 2. Barriers in prescribing antidiabetic medications with CV benefit

Additional file 3. Factors predicting the probability of low GPs` self-confidence for prescribing SGLT2 ins (bivariate logistic regression – significant factors are shown)

Additional file 4. Factors predicting the probability of low confidence for prescribing GLP- 1 RAs (bivariate logistic regression - significant factors are shown)

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Authors' contributions

TK – made substantial contributions to the conception, design of the work, the acquisition, analysis, interpretation of data, prepared tables, have drafted the work and substantively revised it. DŠ – made substantial contributions to literature analysis, writing the draft and revised it. IBĆ – made substantial contributions to the design of the work, revised the survey and methodology,

interpretation of data and substantively revised the draft. SCV – made substantial contributions to the design of the work, revised the survey and methodology, interpretation of data and substantively revised the draft. LJTM – made substantial contributions to the conception, design of the work, conceptualization of the survey and methodology, the analysis and interpretation of data, have drafted the work and substantively revised it.

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Data availability
This comprehensive research yields a wealth of data, which will be published in several publications. To enhance the understanding of the collected data and clarify the content of the study, all data generated or analyzed in this part of the research are included in this published article, along with its additional files.

Declarations

Ethics approval and consent to participate
This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Faculty of Medicine, the Josip Juraj Strossmayer University of Osijek (No. 641–01/24–01/04), dated March 5, 2024.
Each respondent who participated in the research completed an informed consent form in which they were informed of the conditions of participation and the reasons and method of conducting the research.

Consent for publication
All respondents were asked for their consent to use the data obtained by the survey for publication.

Competing interests
The authors declare no competing interests.

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References

1. Marcussen M, Titlestad SB, Lee K, Bentzen N, Søndergaard J, Nørgaard B. General practitioners' perceptions of treatment of chronically ill patients managed in general practice: an interview study. Eur J Gen Pract. 2021;27(1):103–10.
2. Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, et al. Management of hyperglycemia in type 2 diabetes, 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care. 2022;45(11):2753–86.
3. Marx N, Federici M, Schütt K, et al. 2023 ESC guidelines for the management of cardiovascular disease in patients with diabetes. Eur Heart J. 2023;44(39):4043–140.
4. Jing X, Chen J, Dong Y, et al. Related factors of quality of life of type 2 diabetes patients: a systematic review and meta-analysis. Health Qual Life Outcomes. 2018;16(1):189.
5. Kolesnyk P, Bayen S, Shushman I, et al. Identification and ranking of core values in family medicine: a mixed methods study from Ukraine. Front Med. 2021;8: 646276.
6. Bode B, King A, Russell-Jones D, Billings LK. Leveraging advances in diabetes technologies in primary care: a narrative review. Ann Med. 2021;53(1):805–16.
7. ElSayed NA, Aleppo G, Aroda VR, et al. 6. glycemic targets: standards of care in diabetes-2023. Diabetes Care. 2023;46(Suppl 1):97–110.
8. Newson RS, Divino V, Boye KS, et al. Glycemic control and obesity among people with type 2 diabetes in Europe and Australia: a retrospective cohort analysis. Diabetes Ther. 2024;15(6):1435–49.
9. Rodriguez P, San Martin VT, Pantalone KM. Therapeutic inertia in the management of type 2 diabetes: a narrative review. Diabetes Ther. 2024;15(3):567–83.
10. Powell RE, Zaccardi F, Beebe C, et al. Strategies for overcoming therapeutic inertia in type 2 diabetes: a systematic review and meta-analysis. Diabetes Obes Metab. 2021;23(9):2137–54.
11. Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes: a patient-centered approach: position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care. 2013;35(6):1364–79.
12. McGuire DK, Marx N, Johansen OE, Inzucchi SE, Rosenstock J, George JT. FDA guidance on antihyperglyacemic therapies for type 2 diabetes: one decade later. Diabetes Obes Metab. 2019;21(5):1073–8.
13. Lundgren JR, Janus C, Jensen SBK, et al. Healthy weight loss maintenance with exercise, liraglutide, or both combined. N Engl J Med. 2021;384(18):1719–30.
14. Jastreboff AM, Aronne LJ, Ahmad NN, et al. Tirzepatide once weekly for the treatment of obesity. N Engl J Med. 2022;387(3):205–16.
15. Mitchell S, Malanda B, Damasceno A, et al. A roadmap on the prevention of cardiovascular disease among people living with diabetes. Glob Heart. 2019;14(3):215–40.
16. Rodriguez-Valadez JM, Tahsin M, Fleischmann KE, et al. Cardiovascular and renal benefits of novel diabetes drugs by baseline cardiovascular risk: a systematic review, meta-analysis, and meta-regression. Diabetes Care. 2023;46(6):1300–10.
17. Schernthaner G, Shehadeh N, Ametov AS, et al. Worldwide inertia to the use of cardiorenal protective glucose-lowering drugs (SGLT2i and GLP-1 RA) in high-risk patients with type 2 diabetes. Cardiovasc Diabetol. 2020;19(1):185.
18. Lim CE, Pasternak B, Eliasson B, Danaei G, Ueda P. Use of sodium-glucose co-transporter 2 inhibitors and glucagon-like peptide-1 receptor agonists according to the 2019 ESC guidelines and the 2019 ADA/EASD consensus report in a national population of patients with type 2 diabetes. Eur J Prev Cardiol. 2023;30(8):634–43.
19. Barth SD, Kostev K, Krensel M, Mathey E, Rathmann W. Do glucagon-like peptide-1 receptor agonist and sodium-glucose co-transporter 2 inhibitor prescriptions in Germany reflect recommendations for type 2 diabetes with cardiovascular disease of the ADA/EASD consensus report? Exp Clin Endocrinol Diabetes. 2023;131(3):153–61.
20. Young KG, McInnes EH, Massey RJ, et al. Treatment effect heterogeneity following type 2 diabetes treatment with GLP1-receptor agonists and SGLT2-inhibitors: a systematic review. Commun Med. 2023;3(1):131.
21. Bellary S, Kyrou I, Brown JE, Bailey CJ. Type 2 diabetes mellitus in older adults: clinical considerations and management. Nat Rev Endocrinol. 2021;17(9):534–48.
22. Chung WK, Erion K, Florez JC, et al. Precision medicine in diabetes: a Consensus Report from the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia. 2020;63(9):1671–93.
23. Zoungas S, Woodward M, Li Q, et al. Impact of age, age at diagnosis and duration of diabetes on the risk of macrovascular and microvascular complications and death in type 2 diabetes. Diabetologia. 2014;57(12):2465–74.
24. Rushforth B, McCrorie C, Glidewell L, Midgley E, Foy R. Barriers to effective management of type 2 diabetes in primary care: qualitative systematic review. Br J Gen Pract. 2016;66(643):e114–27.
25. Schnell O, Battelino T, Bergenstal R, et al. CVOT Summit 2022 report: new cardiovascular, kidney, and glycemic outcomes. Cardiovasc Diabetol. 2023;22(1):59.
26. Gimeno JA, Cánovas G, Durán A. Factors associated with adherence to clinical practice guidelines for patients with type 2 diabetes mellitus: results of a Spanish Delphi Consensus. J Diabetes Res. 2021;2021:9970859.

27. Wangler J, Jansky M. What is the significance of guidelines in the primary care setting? Results of an exploratory online survey of general practitioners in Germany. Wien Med Wochenschr. 2021;171(13–14):321–9.
28. Brenner S, Oberaigner W, Stummer H. In guidelines physicians trust? Physician perspective on adherence to medical guidelines for type 2 diabetes mellitus. Heliyon. 2020;6(8): e04803.
29. European association for the study of diabetes: statements and guidelines. https://www.easd.org/guidelines/statements-and-guidelines.html. Accessed 12 Mar 2025.
30. Hrvatska liječnička komora: Atlas liječništva HLK - PZZ. https://atlas.hlk.hr/atlas/. Accessed 12 Mar 2025.
31. Hrvatski zavod za zdravstveno osiguranje: Broj osiguranih osoba HZZO-a. 2024. https://hzzo.hr/hzzo-za-partnere/broj-osiguranih-osoba-hzzo. Accessed 12 Mar 2025.
32. Hrvatski zavod za javno zdravstvo: Dijabetes. 2023. https://www.hzjz.hr/sluzba-epidemiologija-prevencija-nezaraznih-bolesti/odjel-za-koordinaciju-i-provodenje-programa-i-projekata-za-prevenciju-kronicnih-nezaraznih-bolest/dijabetes/. Accessed 20 Oct 2024.
33. Kern J, Polasek O, Milanović SM, et al. Regional pattern of cardiovascular risk burden in Croatia. Coll Antropol. 2009;33(Suppl 1):11–7.
34. Benchimol EI, Smeeth L, Guttmann A, et al. The REporting of studies conducted using observational routinely-collected health data (RECORD) statement. PLoS Med. 2015;12(10): e1001885.
35. Wayne DW. Biostatistics: a foundation for analysis in the health science. USA: John Wiley & Sons, Inc; 2012.
36. Armitage P, Berry G, Matthews JNS. Statistical methods in medical research. USA: Wiley-Blackwell; 2001.
37. EQUATOR Network: Enhancing the QUAlity and Transparency Of Health Research. 2024. https://www.equator-network.org. Accessed 26 Nov 2024.
38. GBD 2021 Diabetes Collaborators. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet. 2023;402(10397):203–34.
39. Lapić I, Rogić D, Nikolac Gabaj N, et al. Haemoglobin A1c-based screening for prediabetes and diabetes mellitus: a multi-center study in Croatian adult population. Biochem Med. 2022;32(1): 010903.
40. Roden M, Shulman GI. The integrative biology of type 2 diabetes. Nature. 2019;576(7785):51–60.
41. Reiner Ž, Jelaković B, Miličić D, Bubaš M, Balint I, Jukić NB, et al. Effective strategies and a ten-point plan for cardio-kidney-metabolic health in Croatia: an expert opinion. J Clin Med. 2024;13(23): 7028.
42. Global nutrition report: country nutrition profiles. 2022. https://globalnutritionreport.org/resources/nutrition-profiles/europe/southern-europe/croatia/. Accessed 11 Mar 2025.
43. Höglinger M, Wirth B, Carlander M, Caviglia C, Frei C, Rhomberg B, et al. Impact of a diabetes disease management program on guideline-adherent care, hospitalization risk and health care costs: a propensity score matching study using real-world data. Eur J Health Econ. 2023;24(3):469–78.
44. Koye DN, Magliano DJ, Nelson RG, Pavkov ME. The global epidemiology of diabetes and kidney disease. Adv Chronic Kidney Dis. 2018;25(2):121–32.
45. Jelaković A, Radunović D, Josipović J, Vrkić TŽ, Gellineo L, Domislović M, et al. Prevalence, characteristics, and awareness of chronic kidney disease in Croatia: the EH-UH 2 study. J Clin Med. 2024;13(22): 6827.
46. Guerci B, Charbonnel B, Gourdy P, Hadjadj S, Hanaire H, Marre M, et al. Efficacy and adherence of glucagon-like peptide-1 receptor agonist treatment in patients with type 2 diabetes mellitus in real-life settings. Diabetes Metab. 2019;45(6):528–35.
47. Melo M, Gavina C, Silva-Nunes J, Andrade L, Carvalho D. Heterogeneity amongst GLP-1 RAS cardiovascular outcome trials results: can definition of established cardiovascular disease be the missing link? Diabetol Metab Syndr. 2021;13(1):81.
48. Scheen AJ. Cardiovascular and renal outcomes with SGLT2ins: real-life observational studies in older patients with type 2 diabetes: SGLT2ins in elderly and real life. Diabet Epidemiol Manag. 2023;10:10.
49. Khunti K, Jabbour S, Cos X, Mudaliar S, Mende C, Bonaca M, et al. Sodium-glucose co-transporter-2 inhibitors in patients with type 2 diabetes: barriers and solutions for improving uptake in routine clinical practice. Diabetes Obes Metab. 2022;24(7):1187–96.
50. Fitzpatrick PJ. Improving health literacy using the power of digital communications to achieve better health outcomes for patients and practitioners. Front Digit Health. 2023;5:1264780.
51. Karagiannis T, Tsapas A, Athanasiadou E, Avgerinos I, Liakos A, Matthews DR, et al. GLP-1 receptor agonists and SGLT2ins for older people with type 2 diabetes: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2021;174: 108737.
52. Farcher R, Graber SM, Thüring N, Blozik E, Huber CA. Does the implementation of an incentive scheme increase adherence to diabetes guidelines? A retrospective cohort study of managed care enrollees. BMC Health Serv Res. 2023;23(1):707.
53. De Angelis G, Davies B, King J, McEwan J, Cavallo S, Loew L, et al. Information and communication technologies for the dissemination of clinical practice guidelines to health professionals: a systematic review. JMIR Med Educ. 2016;2(2): e16.
54. De Belvis AG, Pelone F, Biasco A, Ricciardi W, Volpe M. Can primary care professionals' adherence to evidence based medicine tools improve quality of care in type 2 diabetes mellitus? A systematic review. Diabetes Res Clin Pract. 2009;85(2):119–31.
55. Qumseya B, Goddard A, Qumseya A, Estores D, Draganov PV, Forsmark C. Barriers to clinical practice guideline implementation among physicians: a physician survey. Int J Gen Med. 2021;14:7591–8.

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