Contents lists available at ScienceDirect

Saudi Pharmaceutical Journal

journal homepage: www.sciencedirect.com

Original article

Prescribing patterns of antidiabetics in type 2 diabetes and factors affecting them

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ARTICLE INFO

Article history: Received 2 November 2021 Accepted 27 December 2021 Available online 31 December 2021

Keywords: Prescribing pattern Type 2 diabetes Factors affecting prescribing Guidelines awareness Guidelines adoption



Introduction: There are limited studies that address the use of newer antidiabetics by prescribers in Saudi Arabia and their adoption of the newer diabetes guidelines. The primary aim of our study was to explore the prescribing patterns of first- and second-line agents for the management of type 2 diabetes and the factors affecting them.

Methods: A cross-sectional self-administered survey was designed to collect responses from the prescribers in the Makkah Region of Saudi Arabia from 16 February through 16 June 2021. The questionnaire was developed in the English language, piloted, and tested for validity. Participants were recruited on a convenience sampling basis, and the data were collected by visiting them in-person.

Results: A total of 103 prescribers responded to the survey. The majority of the respondents were male (69%), Saudi nationals (54%), practicing in Makkah city (62%), working in the government sector (62%), and had the prescribing experience of 1–5 years (37%). Metformin (95%) was the respondents' most preferred first-line drug of choice, followed by sulfonylureas (5%). When the first-line was contraindicated, sulfonylureas (30%) were considered the most preferred drug of choice, followed by DPP4 inhibitors (25%) and SGLT2 inhibitors (16%), respectively. When the first-line was not sufficient to control diabetes, sulfonylureas (32%) and DPP4 inhibitors (31%) were considered the most preferred drugs of choice as an add-on therapy. SGLT2 inhibitors (31%) and metformin (24%) were considered the preferred first-line choices if the patient had an established cardiovascular disease.

Conclusion: Sulfonylureas were found to be the most considered choice as second-line therapy. There is a need to provide targeted education to the prescribers related to the newer diabetes guidelines in order to promote the use of more evidence-based and safer antidiabetics.

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1. Introduction

Diabetes mellitus is a metabolic disease that, if not wellcontrolled, can lead to several microvascular and macrovascular

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complications (Schuster and Duvuuri, 2002). There are 537 million adults with diabetes in the world. In the Middle East North Africa (MENA) region, 73 million adult people are diagnosed with diabetes. Saudi Arabia has the fifth-highest prevalence of diabetes, with 18.7% in the MENA region, following Pakistan, Kuwait, Egypt and Qatar. In Saudi Arabia, total cases of diabetes in adults exceed 4 million (IDF, 2021).

The management of patients with type 2 diabetes depends on several factors, including the physician's knowledge of national and international management guidelines, the institutional practice, and the physician choices that are influenced by patient satisfaction, safety, efficacy, and tolerability (Al-Rubeaan et al., 2020). Evidence suggests that clinical practice guidelines are among the most critical factors for improving the quality of care (Grimshaw

https://doi.org/10.1016/j.jsps.2021.12.019

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Peer review under responsibility of King Saud University.

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and Russell, 1993). Clinical practice guidelines are defined as developed statements that help practitioners and patients to decide on their healthcare in specific clinical circumstances (Woolf et al., 1999). These guidelines are developed and implemented with the aim of improving the quality of healthcare services (Woolf et al., 1999). The two widely used guidelines for the management of diabetes are the American Diabetes Association (ADA) guidelines and the European Society of Cardiology (ESC) guidelines. ADA guidelines 2021 recommend metformin as the first-line choice for patients with type 2 diabetes. ESC guidelines recommend metformin as the first-line choice with overweight and type 2 diabetes without cardiovascular disease (Cosentino et al., 2020). Sodium-glucose transport 2 inhibitors (SGLT-2) and glucagon-like peptide-1 inhibitors (GLP-1) are recommended in patients with a high risk of cardiovascular events and type 2 diabetes (Cosentino et al., 2020).

The most common cause of death in Saudi Arabia is cardiovascular disease (CDC, 2019). However, the most commonly prescribed first-line antidiabetic agent in Saudi Arabia is metformin. This was reflected in the findings of the study by Al-Rubeaan and colleagues, which explored the physician choices for the firstand second-line management of type 2 diabetes in Saudi Arabia. They found that metformin was the most commonly prescribed first-line agent and sitagliptin was the most commonly prescribed second-line agent, followed by gliclazide, glibenclamide, and glimepiride (Al-Rubeaan et al., 2020). However, this study did not include patient-related factors that could influence the prescribing pattern. Moreover, at the time of this study, some of the newer antidiabetic agents that are available now in Saudi Arabia, were not available. These include alogliptin, vildagliptin, canagliflozin, empagliflozin, and dulaglutide (Saudi Food & Drug Authority, 2021).

SGLT2 inhibitors and GLP-1 agonists have recently gained favor due to their favorable effects on cardiovascular outcomes. However, there are limited studies addressing the use of these drugs by practitioners in Saudi Arabia and their adoption of the newer diabetes guidelines. In addition to following the guidelines, prescribing antidiabetic agents depends on several other patientand drug-related factors (Montvida et al.,2018). The primary aim of our study was to explore the prescribing patterns of first- and second-line agents for the management of type 2 diabetes and the factors affecting them. We also aimed to determine the physicians' awareness and willingness to adopt the newer diabetes guidelines.

2. Methods

2.1. Design of the study and setting

A cross-sectional self-administered survey was designed to collect responses from physicians employed in private and government hospitals and primary healthcare centers in the Makkah Region of Saudi Arabia. We targeted two cities in this region (Makkah and Jeddah) for the ease of data collection. The data were collected from 16 February through 16 June 2021.

2.2. Instrument

We developed the questionnaire based on a comprehensive literature review (Al-Rubeaan et al., 2020; Montvida et al., 2018). It consisted of closed-ended and open-ended questions and was divided into four sections. Section 1 was about demographic characteristics such as participants' job position, specialty, gender, workplace, and the number of years of prescribing antidiabetic agents. Section 2 was aimed to collect the data regarding the most commonly prescribed first-line antidiabetic agent and the factors affecting this choice. The participants were also asked to rank their top three choices of factors. Section 3 was designed to collect the data regarding the most commonly prescribed second-line antidiabetic agent and the factors affecting this choice. In this section also, the participants were asked to rank their top three choices of factors. Section 4 was intended to gather the data regarding the guideline the participants follow to prescribe antidiabetic agents, assess their awareness about the updated guidelines, and determine their willingness to adopt the new guidelines. This section also aimed to capture the physicians' antidiabetic agent preference in the presence of established cardiovascular disease. The questionnaire was developed and administered in the English language. An online version of the questionnaire was also developed using a free web-based survey program (JotForm).

2.3. Validity and reliability of the instrument

Face validity: The questions were reviewed by three experts (one physician, one pharmacist, and one academic researcher) to ensure their relevance, reasonability, and that no ambiguity existed. Content validity: The experts also checked the overall content and flow of the questionnaire to ensure that the instrument's content was logical and easy to understand. Since the questionnaire was not designed as a scale and the responses were not intended to be scored, we did not plan to conduct the reliability analysis of the questionnaire. Subsequently, the questionnaire was piloted with four physicians, and minor amendments were made following the piloting.

2.4. Sampling and sample size

Participants were recruited using the convenience sampling method. The data were collected from the potential participants by visiting them in-person in government hospitals and healthcare centers, and private hospitals and healthcare centers in the two cities using the paper version of the questionnaire. The participants were also given the choice of completing the questionnaire online by using the QR code on the questionnaire. All prescribing physicians who had at least one year of experience prescribing antidiabetic agents were considered eligible for participating in the study. Sample size calculation was conducted based on the number of physicians in Makkah and Jeddah (MoH, 2020), by using an online sample calculator (Raosoft; http://www.raosoft.com/samplesize. html), with a chosen accepted error margin of 20%, 80% confidence interval, and 50% response distribution within the described population. The required sample size was calculated to be 162.

2.5. Ethical considerations

The study was reviewed and approved by the Institutional Review Board (IRB) of Umm Al-Qura University, Saudi Arabia (approval number: 143623). The physicians were informed that their participation was voluntary and that the anonymity and confidentiality of the collected data would be ensured. They were also informed that they had the right to withdraw their responses from the research at any time. Completion of the questionnaire by the participants was considered their consent to participate in the research.

2.6. Statistical analysis

The data collected from the online version of the questionnaire were exported as a Microsoft Excel file. The data collected from visiting the physicians in-person were manually entered in a separate Excel file. The two files were merged and later imported into IBM SPSS (version 26.0) for descriptive and inferential analysis. The descriptive analysis illustrated participants' demographic characteristics and responses in terms of frequencies and percentages. The inferential analysis was conducted to determine any statistically significant association between the participants' demographic characteristics and other responses by employing the chi-square test. The statistical significance was set at a p-value of less than 0.05.

3. Results

3.1. Demographics

A total of 103 prescribers responded to the survey. The majority of the respondents were male (69%), Saudi nationals (54%), and practicing in Makkah city (62%). Family medicine was the most encountered specialty among the respondent prescribers, followed by internal medicine. More than half of the respondents were working in the government sector (62%). The majority of them had the prescribing experience of 1–5 years (37%). Table 1 represents more details regarding the demographic characteristics of the respondents.

3.2. Choice of drug treatment

Metformin (95%) was the respondents' most preferred first-line drug of choice, followed by sulfonylureas (5%). When the first-line was contraindicated, sulfonylureas (30%) were considered the most preferred drug of choice, followed by DPP4 inhibitors (25%) and SGLT2 inhibitors (16%), respectively. When the first-line was not sufficient to control diabetes, sulfonylureas (32%) and DPP4 inhibitors (31%) were considered the most preferred drugs of choice as an add-on therapy. SGLT2 inhibitors (31%) and metformin (24%) were considered the preferred first-line choices if the patient had an established cardiovascular disease. More details regarding the drug treatment choices are present in Table 2.

Prescribers from all specialties were significantly more likely to prescribe metformin as first-line drug treatment than other antidiabetics (p = 0.014). Family medicine prescribers were significantly more likely to prescribe sulfonylureas as second-line drug treat-

Table 1

Demographic characteristics of the participants (n = 103).

Demographic characteristic	Number of participants (%)
Specialty	
Internal medicine	20 (19.4)
General medicine	12 (11.7)
Cardiology	3 (2.9)
Endocrinology	12 (11.7)
Family medicine	45 (43.7)
General practitioner	4 (3.9)
Missing	7 (6.8)
Nationality	
Saudi	55 (53.5)
Non-Saudi	48 (46.5).
City	
Makkah	70 (61.9)
Jeddah	33 (29.2)
Gender	
Male	71 (68.9)
Female	32 (31.1)
Workplace	
Government sector	63 (61.5)
Private sector	40 (38.5)
Prescribing experience	
1–5 years	38 (36.9)
6–10 years	29 (28.2)
More than 11 years	36 (35.0)

ment when first-line is insufficient to control diabetes (p < 0.001). Prescribers from Makkah were significantly more likely to prescribe sulfonylureas as second-line when the first-line is contraindicated (p = 0.009) and when the first-line is not sufficient (p = 0.019) compared to the prescribers from Jeddah. Similarly, prescribers from the government sector were significantly more likely to prescribe sulfonylureas as second-line when the first-line is not sufficient (p = 0.001) compared to the prescribers from the government sector were significantly more likely to prescribe sulfonylureas as second-line when the first-line is contraindicated (p = 0.007) and when the first-line is not sufficient (p = 0.001) compared to the prescribers from the private sector. Figs. 1-4 illustrate the drug treatment choices based on demographic characteristics.

3.3. Factors affecting the drug treatment choices

Last measured HbA1c was the topmost considered factor among the patient-related factors when selecting the first-line (65%) and second-line (66%) drugs of choice. Weight was the second topmost considered factor when selecting the first-line drug of choice (53%), and renal function was the second topmost considered factor when selecting the second-line drug of choice (56%). Among the nonpatient-related factors, guidelines compliance and drug effectiveness were the most considered factors when selecting the firstline (80% and 62%) and second-line (83% and 75%) drugs of choice. More details regarding factors affecting the drug treatment choices are present in Table 3.

While selecting first-line drug treatment, prescribers from the government sector were significantly more likely to consider last measured HbA1c (p = 0.004) as compared to the prescribers from the private sector, prescribers from the private sector were significantly less likely to consider dietary habits (0.037), patient request (p < 0.001), pre-prandial glucose (p = 0.007) and significantly more likely to consider renal function (p = 0.005) as compared to the prescribers from the government sector, and prescribers from both government and private sector were significantly less likely to consider hospital/clinic formulary/protocol compliance (p = 0.001). While selecting second-line drug treatment, prescribers from government and private sectors were significantly less likely to consider hospital/clinic formulary/protocol compliance (p < 0.001).

While selecting first-line drug treatment, prescribers who had 1–5 years and 6–10 years of experience were significantly more likely to consider last measured HbA1c (p = 0.002), prescribers who had more than 11 years of experience were significantly more like to consider weight (p = 0.034) and renal function (p = 0.011), prescribers who had 6–10 years and more than 11 years of experience were significantly less like to consider the patient request (p = 0.005) and pre-prandial glucose (p = 0.048), and prescribers with 1–5 years of experience were significantly less likely to consider renal function (p = 0.011). While selecting second-line drug treatment, all the prescribers were significantly less likely to consider hospital/clinic formulary/protocol compliance (p = 0.017) and significantly more likely to consider guidelines compliance (p = 0.042).

3.4. Preferred diabetes guidelines followed by the participants

The majority of the participants (69%) said that they follow ADA guidelines when managing patients with Type 2 diabetes and 13% follow ADA guidelines in conjunction with other guidelines (Table 4). However, only 36% of all the participants were aware of the EASD guidelines. The questionnaire highlighted the summary of EASD guidelines to the participants, following which only less than half of the respondents (40%) said their prescribing practice was likely to be changed by the EASD guidelines (Table 5). Fig. 5 and Fig. 6 illustrate the participants' awareness of 2019 EASD guidelines and their willingness to change the prescribing practice based on these guidelines.

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Table 2

Preferred drug treatment choices of the participants (multiple choice question).

Drug class	First-line choice ¹	Second-line choice when the first-line is contraindicated ²	Second-line choice when the first-line is insufficient to control diabetes ³	First-line choice if the patient has established CVD ⁴
Alpha-glucosidase inhibitors	0	0	1 (1%)	0
DPP-4 inhibitors	0	26 (25.2%)	32 (31.1)	7 (6.8%)
GLP-1 receptor agonists	0	11 (10.7%)	5 (4.9%)	15 (14.6%)
Insulin	0	3 (2.9%)	2 (1.9)%	8 (7.8%)
Meglitinides	0	2 (1.9%)	2 (1.9%)	0
Metformin	99 (98%)	1 (1%)	3 (2.9%)	25 (24.3%)
Sulfonylureas	2 (2%)	31 (30.1%)	33 (32%)	0
SGLT2 inhibitors	0	16 (15.5%)	12 (11.7%)	32 (31.1%)
Thiazolidinediones	0	2 (1.9%)	1 (1%)	1 (1%)

¹ Two participants' data were excluded as they selected multiple responses

² Eleven participants' data were excluded as they selected multiple responses

³ Twelve participants' data were excluded as they selected multiple responses

⁴ Fifteen participants' data were excluded as they selected multiple responses



Fig. 1. Choice of drug treatment based on participants' nationality



Fig. 2. Choice of drug treatment based on participants' gender

Family medicine prescribers (p < 0.001), Saudi prescribers (p = 0.031), prescribers from Makkah (p < 0.001), prescribers from the government sector (p = 0.005), prescribers who had 1–5 years of experience (p < 0.001), were significantly less aware of the change in 2019 EASD guidelines. In contrast, internal medicine prescribers were significantly more aware of the change in 2019 EASD guidelines (p < 0.001). Internal medicine prescribers (p = 0.002), non-Saudi prescribers (p = 0.004), prescribers from the private sector (p = 0.002), and prescribers with more than 11 years of experience (p < 0.001) were significantly more likely to change or had changed their practice based on the 2019 EASD guidelines.

More detailed results of all inferential analyses can be requested by contacting the authors.

3.5. Miscellaneous

Participants' responses to the open-ended questions such as situations considered when metformin is not the good choice as firstline therapy for Type 2 diabetes management, situations when the participants consider adding a second-line antidiabetic drug therapy, situations when the participants consider adding or initiating insulin for Type 2 diabetes patients and opinions regarding the



Fig. 3. Choice of drug treatment based on participants' workplace



Fig. 4. Choice of drug treatment based on participants' prescribing experience

Table 3

Factors affecting the preferred drug treatment choices of the participants (multiple response questions).

Factors	Considered for first-line choice	Considered for second-line choice
Patient-related factors		
Age	46 (44.7%)	54 (52.4%)
Comorbidities	50 (48.5%)	57 (55.3%)
Dietary habits	25 (24.3%)	32 (31.1%)
Exercise habits	27 (26.2%)	28 (27.2%)
General health	17 (16.5%)	22 (21.4%)
Hepatic function	27 (26.2%)	29 (28.2%)
History of cardiovascular	36 (35%)	51 (49.5%)
disease(s)		
Last-measured HbA1c	67 (65%)	68 (66%)
Lipid profile	15 (14.9%)	22 (21.4%)
Weight	55 (53.4%)	51 (49.5%)
Medication adherence	18 (17.5%)	32 (31.1%)
behavior		
Patient request (patient	25 (24.3%)	20 (19.4%)
choice)		
Patient's ability to tolerate	23 (22.3%)	28 (27.2%)
side effects		
Post-prandial glucose levels	20 (19.4%)	21 (20.4%)
Pre-prandial glucose levels	33 (32%)	22 (21.4%)
Renal function	50 (48.5%)	58 (56.3%)
Other factors		
Advertisements by	6 (5.8%)	5 (4.9%)
pharmaceutical company		
Cost	33 (32%)	38 (36.9%)
Drug effectiveness	64 (62.1%)	77 (74.8%)
Hospital/clinic formulary/	15 (14.6%)	18 (17.5%)
protocol compliance		
Guideline's compliance	82 (79.6%)	85 (82.5%)
Morbidity and mortality	49 (47.6%)	62 (60.2%)
reduction		

change in 2019 EASD guidelines are presented in supplementary data.

4. Discussion

This study was carried out with the aim to explore the prescribing patterns of first- and second-line agents for the management of type 2 diabetes and the factors affecting them. We also aimed to determine the physicians' awareness and willingness to adopt the newer diabetes guidelines in the Makkah region in Saudi Arabia.

The most commonly prescribed first-line antidiabetic was found to be metformin, followed by sulfonylurea. This finding is similar to the prescribing patterns reported in the studies from India and the United States (Boccuzzi et al., 2001; Das et al., 2011). This finding may be explained by the fact that metformin and sulfonylureas are less expensive and readily available in most healthcare facilities in Saudi Arabia. Moreover, metformin is the recommended first-line choice, unless contraindicated, in the updated ADA and EASD guidelines (Davies et al., 2018). Furthermore, in our study, sulfonylureas were found to be the most commonly prescribed second-line antidiabetic in Saudi Arabia followed by DPP-4 inhibitors. Sulfonylureas and DPP-4 inhibitors were also found to be the most commonly prescribed second-line antidiabetics when the first-line is insufficient to control diabetes in Europe (Overbeek et al., 2017). More reasons for the high prescribing of sulfonylureas are its local production in the country, hence leading to the low market price and easy availability in private and governmental healthcare institutes in the Makkah region. However, sulfonylureas are known to be associated with an increased risk of

Table 4

Diabetes guidelines followed by the participants.

Number of participants following these guidelines
71 (68.9%)
2 (1.9%)
4 (3.9%)
0
2 (1.9%)
2 (1.9%)
3 (2.9%)
4 (3.9%)
4 (3.9%)
1 (1%)
1 (1%)
9 (8.7%)

Table 5

Likelihood of changing the prescribing practice based on EASD guidelines.

Likelihood	Number of participants changing the practice
Likely	41 (39.8%)
Neutral	40 (38.8%)
Unlikely	19 (18.4)
Missing	3 (3.0)

severe hypoglycemia and myocardial infarction (Douros et al, 2018). Further studies should explore the association of high prescribing of sulfonylureas with these adverse effects.

Diabetes affects people from all cultures, races, and ethnic backgrounds but some more than others (Caballero, 2017). The care and management of people with diabetes are influenced by cultural factors and so are the prescribing patterns (Tripp-Reimer et al., 2001; Pawa, 2003). However, some factors affecting the drug choice by the physicians may be similar across different cultures, countries, and races. Last measures HbA1c was the most considered factor in our study while selecting first- and second-line drug treatments. This resonates with a similar study from Japan which reported that HbA1c is the most influential factor while selecting first-line oral antidiabetic (Murayama et al., 2018) This study also reported that the key factor which influenced the first-line selection of antidiabetic in their country is the renal function which was also one of the dominant driving factors in our study. Interestingly, prescribers from all sectors in our study were significantly less likely to consider adherence as a factor affecting the prescribing. In contrast, the study by Campbell and colleagues concluded that adherence is the key factor that determines the duration of first-line treatment and drops off considerably within the first three months of the first-line treatment initiation (Campbell et al., 2021).

We found some significant differences in the factors affecting the prescribing patterns between different demographic characteristics. It was found that the majority of the Saudi prescribers generally do not consider weight or dietary habits as one of the factors that might affect prescribing. Jeddah is a metropolitan city with a high number of prescribers from various nationalities, and the prescribers from there were significantly less likely to consider dietary habits. There is an increased need for the importance of health awareness among the prescribers while prescribing. Young pre-



Fig. 5. Participants' awareness of 2019 EASD guidelines



Fig. 6. Likelihood of changing the prescribing practice based on 2019 EASD guidelines

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scribers (with less than ten years of prescribing) were significantly more likely to consider last measured HbA1c than more experienced prescribers who were significantly more likely to consider the weight and renal of the patient while prescribing. This reflects the broader and holistic approach of the experienced prescribers considering the patient's overall health compared to only taking into account the glycemic control.

We found that less than half of the prescribers were aware of the EASD guidelines. This reflects the high prescribing rate of metformin and sulfonylureas and less consideration of the patient's cardiovascular status. If the prescribers are aware of the EASD guidelines, they are more likely to consider the cardiovascular status of the patient and more likely to prescribe other agents (such as SLT2 inhibitors and GLP1 agonists) in the patients with cardiovascular disease. This is similar to the findings from a study in Riyad (Saudi Arabia) which reported that the prescribers were less aware of the guidelines (Amin et al., 2016). An encouraging finding is that on making the prescribers aware of the EASD guidelines, only a few were not likely to change their practice. The majority of them either were likely to change their practice or remained neutral. This highlights the need to educate the prescribers more regarding different guidelines in order to promote better prescribing practices and thus better diabetes management.

Our study is unique as it is the first study to be conducted in the Makkah region, exploring factors affecting physician choices regarding antidiabetics and assessing their awareness about newer guidelines. For better external validity, prescribers from different specialties, age groups, and sectors were included. However, the COVID-19 pandemic restricted access to the prescribers leading to a limited response rate. This also explains our inability to achieve the required sample size, hence, the results should be interpreted with caution. Moreover, some physicians may not show their unawareness about the newer guidelines for selecting antidiabetics for patients with cardiovascular disease and renal impairment treatment. In addition, a survey questionnaire could limit the options presented to the prescribers and force them to choose only selected responses.

5. Conclusions

Following metformin as first-line antidiabetic therapy, sulfonylureas and DPP4 inhibitors were found to be the most considered choices as second-line antidiabetic therapy respectively when the first-line was contraindicated or not sufficient to control diabetes. SGLT2 inhibitors and metformin were considered the preferred choices for patients with established cardiovascular disease. The majority of the prescribers were not aware of the EASD guidelines; however, they were likely to change their practice or remain neutral on being aware of these guidelines. There is a need to provide targeted education to the prescribers related to the newer diabetes guidelines in order to promote the use of more evidence-based and safer antidiabetics. We expect that our findings will help understand the rational use of antidiabetics for patients with type 2 diabetes. Larger-scale further research is warranted to validate our findings. Further research should also be undertaken to provide an insight into the reasons for variation in prescribers' choices regarding the selection of antidiabetics via different methods such as interviews or focus groups.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors would like to thank all the prescribers and academic staff who helped in piloting and validating the survey questionnaire and all the prescribers who responded to the survey.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

MaA conceived and designed the study. All authors (except NA) were involved in data collection, analysis, and interpretation. MaA and NA supervised the project. All authors contributed to the drafting and critical review of the manuscript and have approved the final draft of the manuscript.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jsps.2021.12.019.

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