Saudi Pharmaceutical Journal 32 (2024) 102054

HOSTED BY

Contents lists available at ScienceDirect

Saudi Pharmaceutical Journal

journal homepage: www.sciencedirect.com

The prevalence of cardiovascular diseases, chronic kidney disease, and obesity in patients with type 2 diabetes mellitus and the description of concurrent treatments: A two-center retrospective cross-sectional study in Saudi Arabia

Omar A. Alshaya [a,b,c,*], Ghazwa B. Korayem [d], Munirah Alghwainm [b], Wed Alyami [a], Albandari Alotaibi [a], Majed S. Alyami [a,b,c], Omar A. Almohammed [e,f]

[a] Department of Pharmacy Practice, College of Pharmacy, King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia
[b] Pharmaceutical Care Department, King Abdulaziz Medical City, Riyadh, Saudi Arabia
[c] King Abdullah International Medical Research Center, Riyadh, Saudi Arabia
[d] Department of Pharmacy Practice, College of Pharmacy, Princess Nourah Bint Abdulrahman University P.O.Box 84428, Riyadh 11671, Saudi Arabia
[e] Department of Clinical Pharmacy, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia
[f] Pharmacoeconomics Research Unit, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia

ARTICLE INFO

Keywords:
Atherosclerotic cardiovascular diseases
Type 2 diabetes mellitus
Heart failure
Chronic kidney disease
Sodium-glucose co-transporter inhibitors
Glucagon-like peptide 1 receptor agonists

ABSTRACT

Background: Atherosclerotic cardiovascular disease (ASCVD), heart failure (HF), chronic kidney disease (CKD), and obesity are associated with increased morbidity and mortality in patients with type 2 diabetes mellitus (T2DM). Nonetheless, their prevalence among patients with T2DM in Saudi Arabia (SA) remains unknown. As current guidelines recommend, these comorbidities require adding certain antidiabetic agents with cardiorenal benefits. However, the prescribers' adherence to these recommendations remains unclear.

Methods: A two-center retrospective cross-sectional study was conducted including adult patients (≥18 years) with T2DM admitted to hospital or seen at outpatient clinics between January and December 2020. Patients were classified into two groups based on the presence or absence of ASCVD. Patients with no prior ASCVD history were further classified based on the 10-year ASCVD risk estimation. Endpoints of interest included the prevalence of ASCVD, HF, CKD, and obesity in patients with T2DM. We also evaluated the characteristics of the utilized antidiabetic agents, statin, and aspirin therapies..

Results: Of the 1,218 included patients with T2DM, the majority were female (57.0 %), and aged 45–64 years (53.0 %) with a mean age of 59.3 ± 13.1 years. Hypertension and dyslipidemia were the most prevalent comorbidities (67.7 % and 69.0 %, respectively). Among all patients, 18.6 % had an established ASCVD and the prevalence of HF, CKD, and obesity were 5.1 %, 8.7 %, and 58.3 %, respectively. The most common types of ASCVD witnessed were revascularization (42.3 %), myocardial infarction (36.6 %), and stroke (33.9 %); with an increased prevalence of ASCVD as the age increases (52.8 % at age ≥ 65 years). In the non-ASCVD group, the 10-year ASCVD risk was intermediate or high in 62.7 % of these patients. The rates of utilization of guidelines-recommended therapies were 83.6 % for metformin, 9.4 % for GLP-1 RA, 10.8 % for SGLT2i, 35.2 % for aspirin alone or in combination with clopidogrel, and 79.7 % for statin therapy.

Conclusions: ASCVD, HF, CKD, and obesity are common complications in patients with T2DM in SA, with low overall utilization of the recommended guidelines-recommended medical therapies. Multimodal strategies should be utilized to assess T2DM and its complications, and to improve prescribers' adherence to guidelines-recommended therapies.

* Corresponding author at: King Saud bin Abdulaziz University for Health Sciences - College of Pharmacy, P.O. Box 3660, Riyadh 11481, Saudi Arabia.
E-mail address: omaraalshaya@gmail.com (O.A. Alshaya).

https://doi.org/10.1016/j.jsps.2024.102054
Received 24 January 2024; Accepted 27 March 2024
Available online 28 March 2024

1. Introduction

Cardiovascular diseases (CVD) are the main factor contributing to morbidity and mortality in individuals with type 2 diabetes mellitus (T2DM) worldwide (Einarson et al., 2018). In a *meta*-analysis that included more than 4.5 million patients with T2DM representing Europe, the United States (US), and Western Pacific/China, the prevalence of CVD was estimated to be 32.2 % (Einarson et al., 2018). Among those patients, 29.1 % had atherosclerosis, 21.2 % had coronary heart disease, and 14.9 % had heart failure (HF) (Einarson et al., 2018). Moreover, CVD was the leading cause of death in 9.9 % of the included patients (Einarson et al., 2018). In Saudi Arabia (SA), the International Diabetes Federation (IDF) report (from 2000 to 2045) shows that the estimated prevalence of coronary artery disease is at 7.3 %, cerebrovascular disease at 3.1 %, HF at 1.5 %, and nephropathy at 3.7 % in patients with diabetes (International Diabetes Federation, 2022). Nevertheless, the precise year when this prevalence was documented remains unclear. In the crude mortality rate in SA, diabetes mellitus ranks tenth among the top causes of death, with ischemic heart disease being the first and chronic kidney disease (CKD) being fourth (The Centers for Disease Control and Prevention (CDC), 2022). The Saudi Scientific Diabetes Society reports that more than 50 % of patients with T2DM die of CVD (Robert and Al Dawish, 2021). However, the specific prevalence of CVD in patients with T2DM remains limited.

In 2008, the US Food and Drug Administration (U.S. FDA) mandated that manufacturers must evaluate all new antidiabetic drugs to assess their cardiovascular safety after several reports of the adverse cardiovascular effect of some of the commonly used antidiabetic agents (Low Wang et al., 2019). This mandate has resulted in many cardiovascular outcome trials (CVOTs) that demonstrated a reduction in major adverse cardiovascular events (MACE), CKD, incidence of HF and HF-related hospitalization, and body weight. These benefits were heavily demonstrated in two new antidiabetic classes: sodium-glucose co-transporter-2 inhibitors (SGLT2i) and glucagon-like peptide 1 receptor agonists (GLP-1 RA). Effective glucose control is not always associated with a clinically significant reduction in the risk of undesirable cardiovascular events (Scirica et al., 2013, Green et al., 2015). Therefore, T2DM treatment guidelines encourage using these two new classes, especially in patients with a history or at high risk of atherosclerotic cardiovascular disease (ASCVD), CKD, HF, or obesity (Davies et al., 2022, de Boer et al., 2022).

A *meta*-analysis that evaluated 8 CVOTs of SGLT2i demonstrated a statistically significant reduction in MACE by 10 % compared to a placebo group (McGuire et al., 2021). This reduction was more evident in patients with ASCVD than without ASCVD (11 % reduction vs. 6 % reduction, respectively). On the other hand, a *meta*-analysis of 8 CVOTs of GLP-1 RA showed an overall reduction of MACE by 16 % in patients with a history of CVD compared to patients without a history of CVD (6 %) (Giugliano et al., 2021). In the real world, a large report using US administrative claims data in 2015 for more than one million patients with T2DM showed that 45.2 % had established ASCVD with low overall use of SGLT2i or GLP-1 RA (<12 %), and this was even lower (<9%) in the ASCVD group (Weng et al., 2019). Additionally, statin with lifestyle therapy and aspirin are recommended for individuals of all ages with T2DM and history of ASCVD secondary prevention of CVD. Furthermore, current guidelines recommend the addition of statin with lifestyle therapy for patients with T2DM and aged 40–75 years for primary prevention of CVD (Davies et al., 2022, de Boer et al., 2022).

The prevalence of CVD and renal diseases among patients with T2DM in SA is poorly reported (Al Slail et al., 2016). At the same time, the utilization of guideline-recommended therapy in managing T2DM and comorbidities has yet to be evaluated in SA. Therefore, this study aimed to evaluate the prevalence of patients with T2DM in SA with or at high risk of ASCVD, HF, CKD, and obesity, as well as describe the characteristics of the most utilized antidiabetic agents, statin, and aspirin therapy.

2. Methods

2.1. Study design and setting

This study is a two-center retrospective observational study conducted at King Abdulaziz Medical City (KAMC) and King Abdullah Bin Abdulaziz University Hospital (KAAUH) in Riyadh, SA. The institutional review board (IRB) at King Abdullah International Medical Research Center (KAIMRC) and KAAUH granted ethical approval to conduct this study with reference numbers SP20/477/R and 21–0291, respectively. The study data inclusion period started from January 2020 to December 2020.

2.2. Study population and data collection

All patients who visited the outpatient endocrinology, cardiac, internal medicine, nephrology, family medicine, and obesity/bariatric clinics or were admitted to KAMC or KAAUH during the study period were assessed for inclusion in the study. Patients were eligible if they were at least 18 years old and had an established diagnosis of T2DM. Included patients were divided into two groups based on the presence or absence of ASCVD (i.e., coronary heart disease (CHD) manifested by myocardial infarction (MI), angina, cerebrovascular diseases such as transient ischemic attack (TIA), ischemic stroke, peripheral artery disease (PAD), revascularization including stent or coronary artery bypass graft (CABG), or aortic atherosclerotic disease) as defined by the American College of Cardiology (ACC) (The American College of Cardiology, 2022a). Patients without ASCVD were further classified based on their 10-year risk of ASCVD according to the ACC risk estimator tool (The American College of Cardiology, 2022b). Patients younger than 18 and those with other types of diabetes were excluded.

We conducted a chart review and collected the following patient information: baseline demographics, past medical history (most importantly ASCVD, HF, CKD, and obesity), medication history, type of hospital visit, utilization of antidiabetic agents, including SGLT2i and GLP-1 RA, statin, and aspirin therapies.. For SGLT2i, dapagliflozin was available at both KAMC, and KAAUH, and empagliflozin was available at KAAUH. For GLP-1 RA, liraglutide and semaglutide were available at both KAMC and KAAUH, and dulaglutide was available at KAAUH. The definition of CKD was based on the Kidney Disease Improving Global Outcomes (KDIGO) criteria (de Boer et al., 2022), the obesity definition was based on the World Health Organization (WHO) criteria (The World Health Organization, 2022), and we characterized HF according to the definition provided by the AHA/ACC/HFSA, wherein an ejection fraction (EF) of $\leq$ 40 % is categorized as HF with reduced EF, and EF between 41 and 49 % is classified as HF with moderately reduced EF. We chose an EF threshold of less than 45 % to encompass the majority of patients diagnosed with HF with reduced ejection fraction or those who were closely approaching this threshold (Heidenreich et al., 2022).

2.3. Study endpoints

The endpoints of interest in this study were the prevalence of ASCVD, HF, CKD, and obesity among patients with T2DM. As well as the characteristics of the prescribed antidiabetic agents, statin, and aspirin therapies.

2.4. Statistical analysis

Descriptive statistics were performed to report the data about patients' characteristics and study endpoints. Means with standard deviation (SD) were used for continuous data and frequencies with percentages for categorical data. The Research Electronic Data Capture (REDCap®) software (version 7.3.6) was used to organize the data collected from the patients' medical records. The data were coded and analyzed using SAS software (version 9.4; SAS Institute Inc., Cary, NC).

3. Results

3.1. Patients' baseline characteristics

Among the included 1,218 patients with T2DM, the mean age was 59.3 ± 13.1 years, with the majority being between 45 and 64 years old (53.0 %). The majority had no ASCVD (81.4 %, n = 991), while 18.6 % of these patients had established ASCVD (n = 227). The patients in the ASCVD group were older than patients in the non-ASCVD group (65.2 ± 11.7 vs. 58.0 ± 13.0 years). Female gender was more prevalent in our cohort at 57.0 %, with more females in the non-ASCVD group (59.8 % vs. 44.5 %). The mean body mass index (BMI) was 31.9 ± 6.5, with more patients being obese with a BMI ≥ 30.0 Kg/m^2 (58.3 %). Active smoking was reported in 7.6 % of the included patients, with a higher prevalence among patients in the ASCVD group (13.2 %). Hypertension and dyslipidemia were the most reported comorbid condition in our cohort at 67.7 % and 69.0 %, respectively; with a higher proportion of patients with hypertention among those with ASCVD (89.0 % vs. 62.9 %). Patients' characteristics are summarized in Table 1.

3.2. Prevalence of ASCVD, HF, CKD, and obesity

ASCVD was reported in 227 patients (18.6 %), with more male patients than females (24.0 % vs. 14.6 %). The most common types of ASCVD were revascularization, including stent or CABG (42.3 %), MI (36.6 %), and stroke (33.9 %). The prevalence of ASCVD increased as the age increased in our cohort, with 52.8 % of these patients aged ≥ 65 years (Fig. 1). In the group without ASCVD, 32.1 % and 30.6 % of these patients were estimated to be at intermediate and high risk of ASCVD, respectively (Fig. 2). The prevalence of HF was reported in 5.1 % of the total cohort, with more prevalence in the ASCVD group compared to the non-ASCVD group (17.2 % vs. 2.3 %). In addition, CKD was reported in 8.7 % of the included patients, and again it was more prevalent in the ASCVD group (19.8 % vs. 6.2 %). Table 2 summarizes the data on the prevalence of ASCVD, HF, CKD, and obesity.

3.3. Characteristics of the prescribed antidiabetic agents, statin, and aspirin therapies

The majority of the included patients utilized one or two oral antidiabetic drugs (OAD) (43.1 % and 27.0 %, respectively), with only 17.3 % utilizing ≥ three OADs. The rate of metformin use was reported at 83.6 %, with less utilization in the ASCVD group (76.2 % vs. 85.3 %). Insulin therapy was used in 41.3 % of all patients; it was utilized as a single therapy in 6.4 % of the patients, while being used more in combination with OAD in 31.9 %, and less frequently with SGLT2i (6.2 %) or GLP-1 RA (5.1 %). SGLT2i was prescribed to 10.8 % of the patients with more utilization in the non-ASCVD group (11.2 % vs. 8.8 %). In addition, GLP-1 RA was prescribed in 9.4 % of the patients with more utilization in the non-ASCVD group (10.0 % vs. 7.0 %). Aspirin use alone or in combination with clopidogrel was reported in 35.2 % of the patients with more utilization in the ASCVD group (70.1 % vs. 27.1 %). Statin therapy was reported in 79.7 % of the patients with more utilization in the ASCVD group (90.3 % vs. 77.3 %). Table 3 summarizes the data on the most common medications used by our cohort.

Table 1
Baseline characteristics of patients with T2DM stratified based on history of ASCVD.

Variable	All patients n = 1218	ASCVD Status	
		Non ASCVD n = 991 (81.4 %)	ASCVD n = 227 (18.6 %)
Age, year, mean (SD)	59.3 ± 13.1	58.0 ± 13.0	65.2 ± 11.7
Age categories, n (%)			
18–44	160 (13.1)	147 (14.8)	13 (5.7)
45–64	646 (53.0)	552 (55.7)	94 (41.4)
≥ 65	412 (33.8)	292 (29.5)	120 (52.9)
Gender, n (%)			
Female	694 (57.0)	593 (85.4)	101 (14.6)
Male	524 (43.0)	398 (76.0)	126 (24.0)
Weight, mean (SD)	82.4 ± 17.1	82.6 ± 17.2	81.4 ± 17.1
BMI, mean (SD)	31.9 ± 6.5	32.0 ± 6.5	31.6 ± 6.6
BMI > 30, n (%)	701 (58.3)	576 (59.0)	125 (55.6)
Type of visit, n (%)			
Hospital admission	188 (15.5)	134 (13.6)	54 (24.0)
Clinic visit	1024 (84.5)	853 (86.4)	171 (76.0)
Smoking, n (%)	93 (7.6)	63 (6.4)	30 (13.2)
Past medical history, n (%)			
Hypertension	825 (67.7)	623 (62.9)	202 (89.0)
Dyslipidemia	841 (69.0)	684 (69.0)	157 (69.2)
Hypothyroidism	161 (13.2)	138 (13.9)	23 (10.1)
Hyperthyroidism	13 (1.1)	11 (1.1)	2 (0.9)
Retinopathy	57 (4.7)	46 (4.6)	11 (4.8)
Neuropathy	35 (2.9)	25 (2.5)	10 (4.4)
Laboratory findings, mean (SD)			
Systolic blood pressure, mmHg	134.2 ± 15.9	134.1 ± 15.6	134.7 ± 17.2
Diastolic blood pressure, mmHg	70.7 ± 10.9	71.1 ± 10.8	69.0 ± 11.3
Heart rate, bpm	82.2 ± 12.5	83.0 ± 12.2	78.9 ± 13.5
HgbA1C, %	8.1 ± 1.9	8.0 ± 1.9	8.5 ± 2.0
Fasting blood sugar, mmol/L	9.2 ± 3.7	9.1 ± 3.7	9.4 ± 3.8
Random blood sugar, mmol/L	10.4 ± 4.9	10.2 ± 5.0	11.1 ± 4.5
Total cholesterol, mmol/L	4.4 ± 1.2	4.5 ± 1.2	4.1 ± 1.2
LDL, mmol/L	2.8 ± 7.3	2.7 ± 1.0	3.5 ± 16.6
HDL, mmol/L	1.1 ± 0.4	1.1 ± 0.4	1.0 ± 0.5
Triglyceride, mmol/L	1.9 ± 5.6	1.9 ± 6.2	1.9 ± 1.6
Serum creatinine, mmol/L	81.6 ± 59.6	76.8 ± 49.5	102.7 ± 88.3
Creatinine clearancea, ml/min	94.5 ± 38.6	98.5 ± 38.3	77.3 ± 35.1
eGFRb, ml/min/1.73 m^2	90.4 ± 32.2	93.8 ± 31.5	77.1 ± 31.3
> 60 ml/min/1.73 m^2, n (%)	985 (85.4)	824 (89.5)	161 (69.4)
< 60 ml/min/1.73 m^2, n (%)	168 (14.6)	102 (11.0)	66 (29.5)
Plasma albumin, g/L	38.9 ± 5.2	39.1 ± 5.2	38.0 ± 5.1
BUN, mmol/L	6.8 ± 17.4	6.6 ± 18.3	8.0 ± 12.4
Vitamin D, nmol/L	72.7 ± 161.9	74.8 ± 174.5	59.7 ± 29.5
Vitamin B12, pmol/L	407.4 ± 294.6	409.8 ± 307.0	396.0 ± 227.4

[a] Calculated by using the Cockcroft-Gault equation.
[b] Calculated by using the CKD-EPI equation.
Abbreviations: T2DM: type 2 diabetes mellitus; ASCVD: atherosclerotic cardiovascular disease; SD: standard deviation; BMI: body mass index; HgbA1C: glycated hemoglobin; LDL: low-density lipoprotein; HDL: high-density lipoprotein; eGFR: estimated glomerulus filtration rate; BUN: blood urea nitrogen.

4. Discussion

This retrospective descriptive study aimed to assess the prevalence of ASCVD, HF, CKD, and obesity in individuals with T2DM in SA. The investigation was prompted by the limited available data on the prevalence of these significant complications associated with T2DM. Additionally, the study provided a detailed evaluation of the characteristics of the antidiabetic agents, statin, and aspirin therapies used in the cohort.

Within our cohort, we noted a lower prevalence of ASCVD at 18.6 %, in contrast to the 45.2 % reported in the United States (Weng et al., 2019). However, it is essential to acknowledge the comparatively smaller sample size in our study. Comparing our findings to the IDF report on Saudi Arabia, we observed a higher prevalence of HF (1.5 % vs. 5.1 %) and CKD (3.7 % vs. 8.7 %) (International Diabetes Federation, 2022). Generally, the prevalence of HF in individuals with T2DM has been estimated to range from 9 % to 22 %, which is four times higher than in the general population (Nichols et al., 2004, Dunlay et al., 2019).

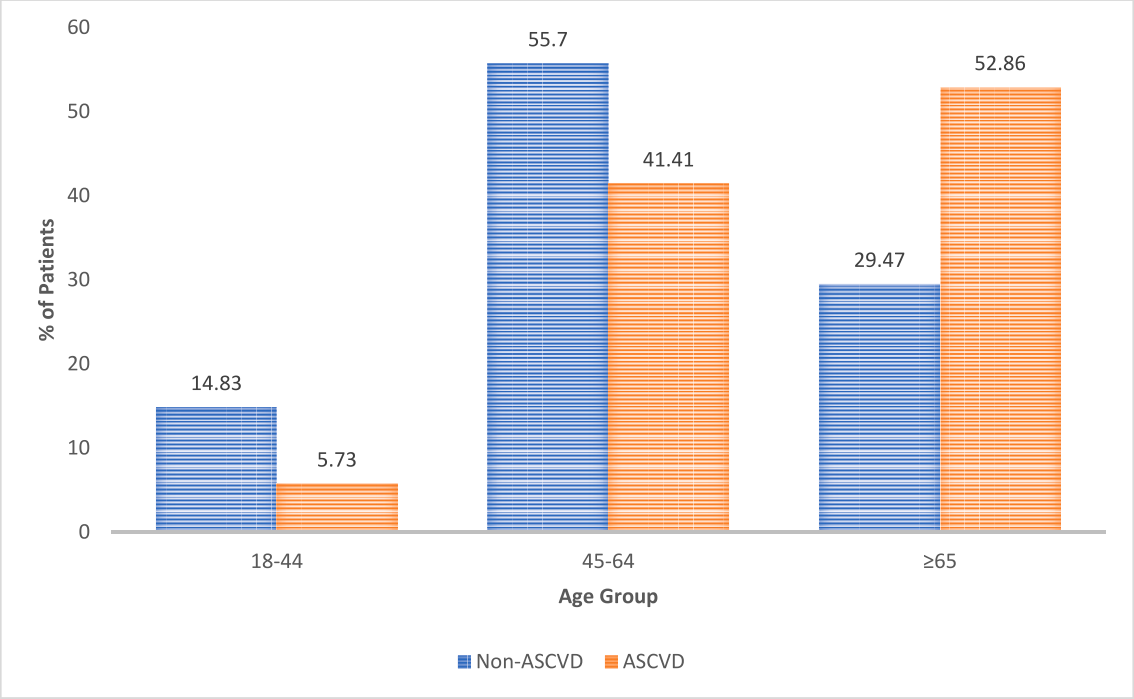

Fig. 1. Prevalence of ASCVD among patients with T2DM stratified by age groups Abbreviations: ASCVD: atherosclerotic cardiovascular disease; T2DM: type 2 diabetes mellitus.

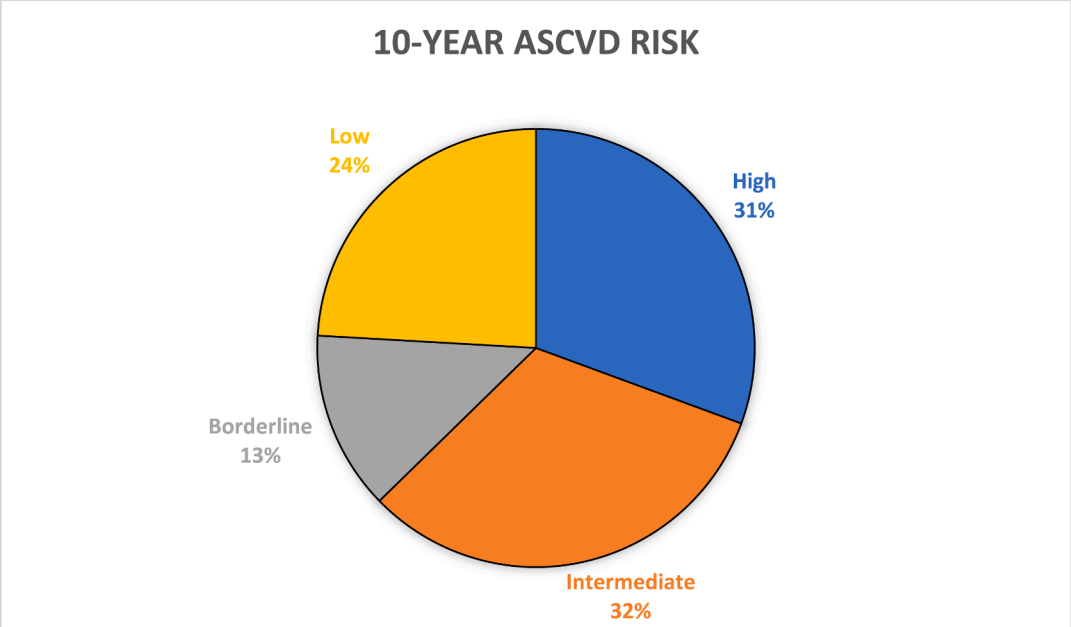

Fig. 2. Estimated 10-year ASCVD risk among non-ASCVD patients with T2DM Definitions of ASCVD risk: low: <5%, borderline: 5 to < 7.5 %, intermediate: 7.5 to < 20 %, high: ≥ 20 % Abbreviations: ASCVD: atherosclerotic cardiovascular disease; T2DM: type 2 diabetes mellitus.

Additionally, a large *meta*-analysis in the Middle East, encompassing 59,395 patients, reported a higher prevalence of CKD in patients with T2DM at 28.96 % (Naser et al., 2021). In our cohort, the prevalence of HF and CKD was higher in the ASCVD group, with rates of 17.2 % and 19.8 %, respectively, and more than half of these patients were obese (55.4 %).

Furthermore, within our cohort, 30.6 % of individuals in the non-ASCVD group exhibited a high risk for ASCVD. This subgroup of patients is recognized for their increased susceptibility to CVD and poorer clinical outcomes (American Diabetes Association Professional Practice Committee, 2022). The prevalence of obesity in our cohort was notable, with 58.3 % of individuals affected, aligning with similar reports in SA where obesity rates in individuals with T2DM were documented as 62 % in Al-Khobar and 57.9 % in Bisha cities (AlShahrani, 2021, Jatoi et al., 2022).

Moreover, the prevalence of smoking in our study was 7.6 % overall, with a higher prevalence observed in the ASCVD group at 13.2 %. Comparatively, other cross-sectional studies in SA reported smoking

Table 2
Prevalence of ASCVD, HF, CKD, and obesity in patients with T2DM.

Disease state	All patients n (%)	ASCVD Status Non ASCVD n (%)	ASCVD n (%)
ASCVD, n (%)	1218 (100.0)	991 (81.4)	227 (18.6)
Revascularization including stent or CABG	96 (7.9)	–	96 (42.3)
Myocardial infraction	83 (6.8)	–	83 (36.6)
Stroke	77 (6.3)	–	77 (33.9)
Transient ischemic attack	46 (3.8)	–	46 (20.3)
Unstable angina	18 (1.5)	–	18 (7.9)
Stable angina	10 (0.8)	–	10 (4.4)
Peripheral arterial disease	6 (0.5)	–	6 (2.6)
Obesity[a], n (%)	700 (58.3)	571 (59.0)	129 (55.4)
Chronic kidney disease[b], n (%)	106 (8.7)	61 (6.2)	45 (19.8)
Heart failure[c], n (%)	62 (5.1)	23 (2.3)	39 (17.2)

[a] Based on obesity definition by the World Health Organization
[b] Based on KDIGO criteria.
[c] Defined as heart failure with reduced ejection fraction of < 45 %.
Abbreviations: ASCVD: atherosclerotic cardiovascular disease; HF: heart failure; CKD: chronic kidney disease; T2DM: type 2 diabetes mellitus; CABG: coronary artery bypass graft.

rates in individuals with diabetes at 9.4 % in 2005 (Saeed, 2012), and 13.2 % in 2021 (Almubark et al., 2022). Additionally, a higher prevalence of smoking was noted at 25.7 % in patients with diabetes in the US (Clair et al., 2013). It's important to note that smoking has been linked to an elevated risk of CVD in individuals with diabetes compared to those without diabetes (HR 1.45; 95 % CI: 1.17–1.78) (Yang et al., 2022).

The usage of SGLT2i in our study was relatively low, standing at 10.8 %, and even lower in the ASCVD group compared to the non-ASCVD group (8.8 % vs. 11.2 %). This pattern mirrors findings from the study by Weng et al., where SGLT2i utilization was reported at 8.8 % in the ASCVD group compared to 11.8 % in the non-ASCVD group (Weng et al., 2019). Similarly, the utilization of GLP-1 RA was modest at 9.4 %, with an even lower prevalence in the ASCVD group compared to the non-ASCVD group (7.0 % vs. 10 %), consistent with observations in the Weng et al. study (7.9 % vs. 9.2 %). This low utilization of SGLT2i and GLP-1 RA in patients with established ASCVD who need them the most requires further investigation. The combined use of either SGLT2i or GLP-1 RA in our cohort was 18.4 %, which exceeds the overall usage reported in the Weng et al. study (<12 %). This difference could be attributed to the fact that the study by Weng et al. was based on older data from 2015. A broader study involving 95,569 patients with T2DM from Cleveland Clinic demonstrated lower rates of GLP-1 RA and SGLT2i utilization in patients with CVD (4.1 % vs. 2.5 %, respectively) (Pantalone et al., 2018). However, it is noteworthy that this study was conducted in 2016, predating the current guidelines that emphasize the use of such therapies. In a more recent evaluation based on data from the US Department of Veterans Affairs and among 537,980 patients with T2DM and established ASCVD, 11.2 % utilized SGLT2i and 8.0 % utilized GLP-1 RA underscoring the continuous low utilization of these new antidiabetic agents (Mahtta et al., 2022).

All in all, the adoption of new guidelines-recommended therapies for patients with T2DM was notably low in this study. Several factors could contribute to this observation, including limited awareness among clinicians, medication availability, associated therapy costs, concerns about increased side effects, especially in elderly patients, the risk of hypoglycemia, and the presence of comorbidities that may contraindicate the use of these therapies (Pantalone et al., 2018, Khunti et al., 2022). The assessment conducted in this study gains particular significance in light of the recent updates to joint guidelines by major professional organizations. These updates emphasize the utilization of

Table 3
Utilization of antidiabetic medications and other therapies stratified based on ASCVD status.

Variable, n (%)	All patients n = 1218	ASCVD Status Non ASCVD n = 991 (81.4 %)	ASCVD n = 227 (18.6 %)
Number of OAD[a]			
NO OAD	153 (12.6)	105 (10.6)	48 (21.1)
1 OAD	525 (43.1)	432 (43.6)	93 (41.0)
2 OAD	329 (27.0)	276 (27.8)	53 (23.4)
≥ 3 OAD	211 (17.3)	178 (18.0)	33 (14.5)
Type of OAD			
Sulphonylurea	384 (31.5)	315 (31.8)	69 (30.4)
Dipeptidyl peptidase-4 inhibitor	440 (36.1)	376 (37.9)	64 (28.2)
Thiazolidinedione	19 (1.6)	15 (1.5)	4 (1.8)
Metformin	1018 (83.6)	845 (85.3)	173 (76.2)
Insulin	503 (41.3)	379 (38.2)	124 (54.6)
Insulin only	78 (6.4)	50 (5.0)	28 (12.3)
Insulin + OAD	389 (31.9)	305 (30.8)	84 (37.0)
Insulin + SGLT2i	76 (6.2)	61 (6.2)	15 (6.6)
Insulin + GLP-1 RA	62 (5.1)	51 (5.1)	11 (4.8)
GLP-1 RA + SGLT2i	22 (1.8)	17 (1.7)	5 (2.2)
SGLT2i	131 (10.8)	111 (11.2)	20 (8.8)
Dapagliflozin	119 (90.8)	99 (89.2)	20 (100.0)
Empagliflozin	12 (9.2)	12 (10.8)	0 (0.0)
GLP-1RA	115 (9.4)	99 (10.0)	16 (7.0)
Liraglutide	81 (70.4)	70 (70.7)	11 (68.8)
Semaglutide	33 (28.7)	28 (28.3)	5 (31.3)
Dulaglutide	1 (0.9)	1 (1.0)	0 (0.0)
Aspirin only	349 (28.7)	261 (26.3)	88 (38.8)
Aspirin + Clopidogrel	79 (6.5)	8 (0.8)	71 (31.3)
Patients treated for dyslipdemia			
Statin therapy	971 (79.7)	766 (77.3)	205 (90.3)
Ezetimibe	28 (2.3)	15 (1.5)	13 (5.7)
PCSK9 inhibitors	9 (0.7)	6 (0.6)	3 (1.3)
Blood pressure-lowering agents			
ACEI	281 (23.1)	203 (20.5)	78 (34.4)
ARB	398 (32.7)	319 (32.2)	79 (34.8)
CCB	363 (29.8)	261 (26.3)	102 (44.9)
Beta blocker	258 (21.2)	129 (13.0)	129 (56.8)
Thiazide diuretics	99 (8.1)	72 (7.3)	27 (11.9)
Loop diuretics	95 (7.8)	46 (4.6)	49 (21.6)
Aldosterone antagonists	19 (1.6)	6 (0.6)	13 (5.7)

Abbreviations: ASCVD: atherosclerotic cardiovascular disease; OAD: oral antidiabetic drug; SGLT2i: sodium-glucose co-transporter-2 inhibitors; GLP-1 RA: glucagon-like peptide 1 receptor agonists; PCSK9: Proprotein convertase subtilisin/kexin type 9; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker.
a Including: metformin, sulphonylurea, dipeptidyl peptidase-4 inhibitor, and thiazolidinedione.

SGLT2i and GLP-1 RA as first-line therapy for patients at high risk or with established ASCVD, HF, CKD, and obesity (Davies et al., 2022, de Boer et al., 2022).

The profile of other antidiabetic agents used in this study revealed that the majority of patients were undergoing metformin therapy (83.6 %), and a considerable proportion were on two or more OADs (44.3 %). Notably, patients with established ASCVD had lower usage of metformin than patients without ASCVD which could be attributed to the higher rate of CKD in patients with established ASCVD limiting the usage of metformin in this population. The overall high prevalence of metformin use aligns with adherence to previous guidelines that underscored the initiation of metformin as the first-line therapy for T2DM (Davies et al., 2018, American Diabetes Association, 2021). Anticipating a notable shift in these practices in the years to come, we expect increased adoption of SGLT2i and GLP-1 RA as first-line therapies. This shift is supported by accumulating evidence demonstrating their benefits beyond glucose-lowering activity. However, implementing this paradigm change in the management of T2DM will necessitate extensive

efforts in continuous medical education for healthcare providers. Additionally, the involvement of stakeholders in facilitating access to these therapies, along with the expansion of prescribing privileges to healthcare providers, will be crucial components of this evolving landscape.

Moreover, cardioprotective agents such as statin therapy and aspirin were employed in 79.7 % and 35.2 % of the study participants, respectively. Within the non-ASCVD group, 77.3 % received statin therapy for primary prevention in alignment with guideline recommendations (American Diabetes Association Professional Practice Committee, 2022). However, it is noteworthy that 14.8 % of non-ASCVD patients were under the age of 45, and guidelines typically do not recommend initiating statin therapy for primary prevention in patients < 40 years old. This indicates an estimated missed opportunity in roughly 7.9 % of these patients. Conversely, in the ASCVD group, the utilization of statin therapy for secondary prevention was high at 90.3 %, with underutilization observed in 9.7 % of the patients. A comparable but higher proportion of statin nonusers (18.9 %) was reported in patients with T2DM in Malaysia (Hammad et al., 2019).. Among the ASCVD group in this study, only 70.1 % were on aspirin therapy, underscoring the underutilization of aspirin in 29.9 % of these high-risk patients. Similarly, in a large cross-sectional analysis from 2011 to 2018 in the US, aspirin was utilized in only 70.3 % of patients with T2DM and a history of CVD (Liu et al., 2021). However, the presence of contraindications and side effects (such as myopathies and a history of bleeding) may have contributed to the lower reported rates of statin and aspirin utilization in the literature. The challenge lies in the poor documentation of these contraindications and side effects. Therefore, it is crucial to evaluate strategies aimed at reducing undesirable cardiovascular outcomes, aligning with guidelines and recommendations, to enhance overall clinical outcomes (American Diabetes Association Professional Practice Committee, 2022).

This cross-sectional analysis is subject to certain limitations that warrant consideration. Firstly, the study is constrained by the small sample size, focusing exclusively on patients with T2DM from two healthcare centers located in the central region of SA. The limited geographic scope may impact the generalizability of the findings to a broader population. Furthermore, the absence of an evaluation of clinical outcomes constitutes a notable limitation. Without such assessments, the complete understanding of the impact of these epidemiological findings, as well as the variation in the prescription patterns of cardiorenal protective antidiabetic agents, remains incomplete. A comprehensive analysis of clinical outcomes would have provided valuable insights into the effectiveness of different therapeutic approaches and their implications for patient health. Therefore, while the study sheds light on certain aspects of T2DM management, it is essential to interpret the findings with caution, considering the constraints imposed by the small sample size and the absence of clinical outcomes' evaluation. Future research endeavors with larger and more diverse cohorts, along with a comprehensive assessment of clinical outcomes, would contribute to a more robust understanding of the implications of prescribing patterns in this context.

5. Conclusions

ASCVD, HF, CKD, and obesity are prevalent complications in patients with T2DM in SA. It is imperative that collaborative efforts be undertaken by both governmental and nongovernmental entities to address these diseases and enhance overall clinical outcomes. Recent consensus guidelines recommend the use of SGLT2i and GLP-1 RA (depending on specific patient's characteristics, availability of medication, and failure of initial management strategies such as lifestyle modifications) as first-line therapies in T2DM. Thus, there is a need for concerted efforts to implement and monitor adherence to these recommendations among healthcare professionals. Additionally, attention should be focused on cardioprotective therapies, such as statins and aspirin, during outpatient clinic visits for patients with T2DM. These therapies should be employed whenever feasible, particularly in the absence of contraindications or side effects. By addressing these aspects comprehensively and collaboratively, there is an opportunity to improve the management of T2DM and reduce the burden of associated complications, ultimately leading to better clinical outcomes for patients in SA.

Declarations.

Funding.

The author (OAA) received a fund from the Researcher Supporting Project number (RSP2024R77), King Saud University, Riyadh, Saudi Arabia. The funding agency plays no role in designing the study, conducting the analysis, interpreting the data, or writing the manuscript.

CRediT authorship contribution statement

Omar A. Alshaya: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Ghazwa B. Korayem:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Munirah Alghwainm:** Supervision, Validation, Writing – original draft, Writing – review & editing, Data curation, Investigation, Project administration. **Wed Alyami:** Data curation, Investigation, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Albandari Alotaibi:** Data curation, Investigation, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Majed S. Alyami:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Omar A. Almohammed:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Acknowledgment

The authors would like to extend their appreciation to King Saud University for funding this work through the Researcher Supporting Project (RSP2024R77), King Saud University, Riyadh, Saudi Arabia.

References

Al Slail, F.Y., Abid, O., Assiri, A.M., et al., 2016. Cardiovascular risk profiles of adults with type-2 diabetes treated at urban hospitals in Riyadh. Saudi Arabia. J Epidemiol Glob Health. 6, 29–36. https://doi.org/10.1016/j.jegh.2015.07.004.

Almubark, R.A., Althumairi, N.A., Alhamdan, A.A., et al., 2022. Socioeconomic and behavioral Disparities among diabetics in Saudi Arabia: a nation-wide descriptive study. Diabetes Metab Syndr Obes. 15, 2693–2703. https://doi.org/10.2147/dmso.S352769.

AlShahrani, M.S., 2021. Prevalence of obesity and overweight among type 2 diabetic patients in bisha, Saudi Arabia. J Family Med Prim Care. 10, 143–148. https://doi.org/10.4103/jfmpc.jfmpc_1349_20.

American Diabetes Association 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes-2021 Diabetes Care. 44 2021 S111 S24 10.2337/dc21-S009.

C. Clair J.B. Meigs N.A. Rigotti Smoking behavior among US adults with diabetes or impaired fasting glucose Am J Med. 126 2013 541.e515 548 10.1016/j.amjmed.2012.11.029.

American Diabetes Association Professional Practice Committee, 2022. 10. Cardiovascular disease and risk Management: Standards of medical Care in Diabetes-2022. Diabetes Care 45, S144–S174. https://doi.org/10.2337/dc22-S010.

Davies, M.J., D'Alessio, D.A., Fradkin, J., et al., 2018. Management of hyperglycaemia in type 2 diabetes, 2018. a consensus report by the American Diabetes Association (ADA) and the european Association for the Study of diabetes (EASD). Diabetologia 61, 2461–2498. https://doi.org/10.1007/s00125-018-4729-5.

Davies, M. J., V. R. Aroda, B. S. Collins, et al., 2022. 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. DOI: 10.2337/dci22-0034.
de Boer, I.H., Khunti, K., Sadusky, T., et al., 2022. Diabetes Management in Chronic Kidney Disease: a consensus report by the American Diabetes Association (ADA) and kidney disease: improving global outcomes (KDIGO). Diabetes Care. https://doi.org/10.2337/dci22-0027.
Dunlay, S.M., Givertz, M.M., Aguilar, D., et al., 2019. Type 2 diabetes mellitus and Heart failure: a scientific statement from the American Heart Association and the Heart Failure Society of America: this statement does not represent an update of the 2017 ACC/AHA/HFSA heart failure guideline update. Circulation 140, e294–e324. https://doi.org/10.1161/cir.0000000000000691.
Einarson, T.R., Acs, A., Ludwig, C., et al., 2018. Prevalence of cardiovascular disease in type 2 diabetes: a systematic literature review of scientific evidence from across the world in 2007–2017. Cardiovasc Diabetol. 17, 83. https://doi.org/10.1186/s12933-018-0728-6.
Giugliano, D., Scappaticcio, L., Longo, M., et al., 2021. GLP-1 receptor agonists and cardiorenal outcomes in type 2 diabetes: an updated meta-analysis of eight CVOTs. Cardiovasc Diabetol. 20, 189. https://doi.org/10.1186/s12933-021-01366-8.
Green, J.B., Bethel, M.A., Armstrong, P.W., et al., 2015. Effect of sitagliptin on Cardiovascular outcomes in type 2 diabetes. N Engl J Med. 373, 232–242. https://doi.org/10.1056/NEJMoa1501352.
Hammad, M.A., Syed Sulaiman, S.A., Aziz, N.A., et al., 2019. Prescribing statins among patients with type 2 diabetes: the clinical gap between the guidelines and practice. J Res Med Sci. 24, 15. https://doi.org/10.4103/jrms.JRMS_100_18.
Heidenreich, P.A., Bozkurt, B., Aguilar, D., Allen, L., et al., 2022. AHA/ACC/HFSA guideline for the Management of Heart Failure: a report of the American College of Cardiology/American Heart Association joint committee on clinical Practice guidelines. J Am Coll Cardiol. https://doi.org/10.1016/j.jacc.2021.12.012.
International Diabetes Federation Saudi Arabia Diabtese Report 2000–2045 Retrieved Ocotober 1 2022 From https://www.diabetesatlas.org/data/en/country/174/sa.html.
Jatoi, N.A., Al-Qassab, R.M., Al Salem, F.H., et al., 2022. Prevalence of obesity and Cardiovascular risk factors among type 2 diabetes mellitus patients in al-Khobar. Saudi Arabia. Cureus. 14, e30539.
Khunti, K., Jabbour, S., Cos, X., et al., 2022. 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. 24, 1187–1196. https://doi.org/10.1111/dom.14684.
Liu, E.Y., Al-Sofiani, M.E., Yeh, H.C., et al., 2021. Use of preventive aspirin among older US adults with and without diabetes. JAMA Netw Open. 4, e2112210.
Low Wang, C.C., Everett, B.M., Burman, K.D., et al., 2019. Cardiovascular safety trials for all new diabetes mellitus drugs? Circulation 139, 1741–1743. https://doi.org/10.1161/circulationaha.118.038771.
Mahtta, D., Ramsey, D.J., Lee, M.T., Chen, L., et al., 2022. Utilization rates of SGLT2 inhibitors and GLP-1 receptor agonists and their facility-level Variation among patients with atherosclerotic Cardiovascular disease and type 2 diabetes: insights from the Department of Veterans Affairs. Diabetes Care 45 (2), 372–380. https://doi.org/10.2337/dc21-1815.
McGuire, D.K., Shih, W.J., Cosentino, F., et al., 2021. Association of SGLT2 inhibitors with Cardiovascular and kidney outcomes in patients with type 2 diabetes: a meta-analysis. JAMA Cardiol. 6, 148–158. https://doi.org/10.1001/jamacardio.2020.4511.
Naser, A.Y., Alwafi, H., Alotaibi, B., et al., 2021. Prevalence of chronic kidney diseases in patients with diabetes mellitus in the Middle East: a systematic review and meta-analysis. Int J Endocrinol. 2021, 4572743. https://doi.org/10.1155/2021/4572743.
Nichols, G.A., Gullion, C.M., Koro, C.E., et al., 2004. The incidence of congestive heart failure in type 2 diabetes: an update. Diabetes Care 27, 1879–1884. https://doi.org/10.2337/diacare.27.8.1879.
Pantalone, K.M., Misra-Hebert, A.D., Hobbs, T.M., et al., 2018. Antidiabetic treatment patterns and specialty care utilization among patients with type 2 diabetes and cardiovascular disease. Cardiovasc Diabetol. 17, 54. https://doi.org/10.1186/s12933-018-0699-7.
Robert, A.A., Al Dawish, M.A., 2021. Cardiovascular disease among patients with diabetes: the current Scenario in Saudi Arabia. Curr Diabetes Rev. 17, 180–185. https://doi.org/10.2174/1573399816666200527135512.
Saeed, A.A., 2012. Association of tobacco products use and diabetes mellitus-results of a national survey among adults in saudi arabia. Balkan Med J. 29, 247–251. https://doi.org/10.5152/balkanmedj.2012.035.
Scirica, B.M., Bhatt, D.L., Braunwald, E., et al., 2013. Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus. N Engl J Med. 369, 1317–1326. https://doi.org/10.1056/NEJMoa1307684.
The American College of Cardiology. ACC Handbook on ASCVD and Type 2 Diabetes. Retrieved October 1, 2022, From https://www.acc.org/~/media/2b4c1477f1434c37bd0b3812d23564b1.pdf.
The American College of Cardiology. ASCVD Risk Estimator Tool. Retrieved October 1, 2022, From https://tools.acc.org/ldl/ascvd_risk_estimator/index.html#!/calulate/estimator/.
The Centers for Disease Control and Prevention (CDC). Global Health in Saudi Arabia. Retrieved October 1, 2022, From https://www.cdc.gov/globalhealth/countries/saudi_arabia/default.htm.
The World Health Organization. Obesity and Overweight. Retrieved October 1, 2022, From https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight#:~:text=%2Fm2).-,Adults,than%20or%20equal%20to%2030.
Weng, W., Tian, Y., Kong, S.X., et al., 2019. The prevalence of cardiovascular disease and antidiabetes treatment characteristics among a large type 2 diabetes population in the United States. Endocrinol Diabetes Metab. 2, e00076.
Yang, Y., Peng, N., Chen, G., et al., 2022. Interaction between smoking and diabetes in relation to subsequent risk of cardiovascular events. Cardiovasc Diabetol. 21, 14. https://doi.org/10.1186/s12933-022-01447-2.