



**Evaluation of discharge patients with T2DM based on target goals of therapy
at a private hospital in sana'a, Yemen**

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2021-2022

1443

Accreditation

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Dedication

**We dedicate our research, firstly to Allah who help us to
done**

This Modest study.

To our families for their endless support and love.

To our friends and every one supported us in our life.

To all those who love Yemen

Acknowledgements

First and last, all thanks to Allah for his strength, kindness and support to complete this work. I would like to acknowledge my **Supervisor/Dr. Ali**

Alyahwai who was the soul and activator for our team research.

Special thanks for **University of Science and Technology Hospital** who kept no effort to support success of this research work.

Special thanks for **the Chief of 21 September University of Medical &Applied Science and Medical Council / Prof. Mogahed Maisar.**

Special thanks for all employees in pharmacy Deanery specially **Dr / Abdulmalik Abudenia.**

Lastly thanks for all students in my college.

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List of Abbreviations

A1c	Hemoglobin A1c
AACE	American Association of Clinical Endocrinologists
ACCORD	Action to Control Cardiovascular Risk in Diabetes
ACC/AHA	American College of Cardiology/American Heart Association
ACE	Angiotensin-converting enzyme
ADA	American Diabetes Association
ADVANCE	Action in Diabetes and Vascular Disease
AIDS	Acquired immune deficiency syndrome
ALT	Alanine aminotransferase
ARB	Angiotensin II receptor blocker
ASCVD	Atherosclerotic cardiovascular disease
ATP	Adenosine triphosphate
BG	Blood glucose
BMI	Body mass index
BP	Blood pressure
BUN	Blood urea nitrogen
CAD	Coronary Artery Disease
CDC	Centers for Disease Control and Prevention
CHD	Chronic Heart Disease
CKD	Chronic Kidney Disease
Cl	Chloride
CrCl	Creatinine clearance
CSII	Continuous subcutaneous insulin infusion
CVD	Cardiovascular Disease
CVOTs	Cardiovascular outcomes trials
DCCT	Diabetes Control and Complications Trial
DKA	Diabetic ketoacidosis
DKD	Diabetic Kidney Disease
DM	Diabetes mellitus
DPP-4	Dipeptidyl peptidase-4
ECG	Electrocardiogram
eGFR	Estimated glomerular filtration rate
FBG	Fasting blood glucose
FDA	Food and Drug Administration
FPG	Fasting plasma glucose
GDM	Gestational diabetes mellitus
GI	Gastrointestinal
GIP	Glucose-dependent insulintropic peptide
GLP-1	Glucagon-like peptide-1
HDL	High-density lipoprotein
HF	Heart Failure
HHS	Hyperosmolar hyperglycemic state
Hgb	Hemoglobin
HIV	Human immunodeficiency virus
HTN	Hypertension
IFG	Impaired fasting glucose

IGT	Impaired glucose tolerance
IM	Intramuscular
ISF	Interstitial fluid
IV	Intravenous
K	Potassium
LADA	Latent autoimmune diabetes in adults
LDL	Low-density lipoprotein
MACE	Major Adverse Cardiovascular Events
Mg	Magnesium
MNT	Medical nutrition therapy
Na	Sodium
NGSP	National Glycohemoglobin Standardization Program
NPH	Neutral protamine Hagedorn
OGTT	Oral glucose tolerance test
PAD	Peripheral arterial disease
PCO ₂	partial pressure of carbon dioxide
PCSK9	Proprotein Convertase subtilisin/Kexin
PPAR- γ	Proxisome proliferator-activated receptor gamma
PPC	Professional practice Committee
PPG	Postprandial glucose
SC	Subcutaneous
SCr	Serum creatinine
SGLT2	Sodium-dependent glucose cotransporter-2
SMBG	Self-monitoring of blood glucose
SPSS	Statistical Package Social Science
SU	Sulfonylurea
T1DM	Type 1 diabetes mellitus
T2DM	Type 2 diabetes mellitus
TGs	Triglycerides
TLC	Therapeutic lifestyle change
TZD	Thiazolidinedione
UKPDS	United Kingdom Prospective Diabetes Study
ULN	Upper limit of normal
UTI	Urinary tract infection
VADT	Veterans Affairs Diabetes Trial
WHO	World Health Organization

Abstract

Objective : The management of type 2 diabetes mellitus (T2DM) is complex , requiring continuous medical care by health care professionals and considerable self-care efforts by patients. Clinical pharmacy have important role in team of health care in management the therapy, reinforce patient education, resolution of drug-related problems(DRPs), This study also aims to draw attention to important clinical pharmacy in periodically evaluation for medication problems of discharge patient with T2DM.

Methods: The study was a clinical retrospective study performed on discharge patient with T2DM in private Hospital in Sana'a city between December 4,2021 and January 4,2022.

Results: A total of 150 diagnosed cases of T2DM were studied . Male patients were 87 (58.0%) and female patients were 63 (42.0%) . The age of patients with T2DM ranged between 20 and 82 years . The results of the patient study showed that most patients with T2DM aged above 41 years (92.0%). The patient lipid profile labs were categorized into three category : normal 29 (19.3%) ,abnormal 51(34.0%) and non-available 70(46.7%). The fasting blood glucose (FBG) range were minimum range were (75 mg / dl). And maximum range were (622 mg /dl).

HBA1C labs minimum range were (5.7 mmol / L). And maximum range were (14.5 mmol / L). The most patients of T2DM were without comorbidity 77(51.3%), 56(37.3%) with hypertension and 15(10%) with cardiovascular disease. Almost patients of T2DM were without major drug-drug interaction 145(96.7%) . According to ADA 2022 guideline 47 (31.3%) of patients of T2DM were acceptable, most

percent 74(49.3%) without statin recommendation and less percent 12(8%) without ACEI and 14(9.3%) without ACEI and statin .

Conclusions:

According to the results of this study the clinical outcomes of discharge patient of T2DM not acceptable to some extent according to the recommendation of ADA guideline , so activate the role of clinical pharmacy improvement from clinical outcomes for patients.

Chapter-I

1. Introduction and Review of Literature

1.1. Definition of Diabetes mellitus (DM) :

Diabetes mellitus (DM) describes a group of chronic metabolic disorders , caused by an absolute lack of insulin or relative lack of insulin as a result of impaired insulin secretion and action. DM is characterized by symptomatic glucose intolerance resulting in hyperglycemia and alterations in lipid and protein metabolism. In the long term these metabolic abnormalities contribute to the development of complications such as cardiovascular disease(CVD),retinopathy, nephropathy , and neuropathy and a higher risk of cancer^(1,2).

The management of type 2 diabetes mellitus is complex, requiring continuous medical care by health care professional and considerable self-care efforts by patients. Clinical pharmacist care programs have been shown to help patients with diabetes succeed in achieving treatment goals and improving clinical outcomes. Clinical pharmacist care is a new health care concept in Yemen ⁽²⁾.

In randomized controlled study in Northern Cyprus demonstrated that clinical pharmacist care program in a public hospital's outpatient diabetes was associated with significant improvement in reducing A1c and other secondary outcomes (blood pressure, lipid profile, medication adherence, body mass index and self-care activities) for patient with T2DM over 12-month period ⁽²⁾.

This study therefore demonstrate important role of clinical pharmacist in evaluation and improvement clinical result for patient with T2DM.

1.2. Epidemiology :

- Both the number of cases and the prevalence of diabetes have been steadily increasing over the past few decades ⁽³⁾.

According to International Diabetes Federation Middle East and North Africa (IDF MENA) region about 463 million people have diabetes in the world , In Yemen 572,700 persons have diabetes or 3.9% ⁽⁴⁾.

1.3. Classification Diabetes :

Diabetes can be classified into the following general categories:

1. Type 1 diabetes (due to autoimmune b-cell destruction, usually leading to absolute insulin deficiency, including latent autoimmune diabetes of adulthood) .
2. Type 2 diabetes (due to a progressive loss of adequate b-cell insulin secretion frequently on the background of insulin resistance) .
3. Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young), diseases of the exocrine pancreas (such as cystic fibrosis and pancreatitis), and drug- or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation) .
4. Gestational diabetes mellitus (diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation)⁽⁵⁾.

Type 1 diabetes and type 2 diabetes are heterogeneous diseases in which clinical presentation and disease progression may vary considerably. Classification is

important for determining therapy, but some individuals cannot be clearly classified as having type 1 or type 2 diabetes at the time of diagnosis⁽⁶⁾.

Most people with diabetes have type 2 diabetes, a heterogeneous disorder that is characterized by obesity, β cell dysfunction, resistance to insulin action, and increased hepatic glucose production. Both the incidence and prevalence of diabetes increase dramatically with age and obesity⁽⁷⁾.

1.4. Screening and Diagnostic Tests for Prediabetes and Type 2

Diabetes

The diagnostic criteria for diabetes and prediabetes are shown in Table 1^(8,9,10).

Table 1 Criteria for the Screening and Diagnosis of Prediabetes and Diabetes ^(8,9,10)		
	Prediabetes	Diabetes
• A1C	5.7–6.4% (39–47 mmol/mol)	≥ 6.5% (48 mmol/mol)
• Fasting plasma glucose	100–125mg/dL (5.6–6.9 mmol/L)	≥ 126 mg/dL (7.0 mmol/L)
• 2-hour plasma glucose during 75-g OGTT	140–199mg/dL (7.8–11.0 mmol/L)	≥ 200 mg/dL (11.1 mmol/L)
• Random plasma glucose	—————	≥ 200 mg/dL (11.1 mmol/L)

Screening criteria for adults and children are listed in Table 2⁽¹¹⁾. Screening for prediabetes and type 2 diabetes risk through an informal assessment of risk factors or with an assessment tool, Marked discrepancies between measured A1C and plasma glucose levels should prompt consideration that the A1C assay may not be reliable for that individual, and one should consider using an A1C assay without interference or plasma blood glucose criteria for diagnosis. (An updated list of A1C assays with interferences is available at ngsp.org/interf.asp). If the patient has a test result near the margins of the diagnostic threshold, the clinician should follow the patient closely and repeat the test in 3–6 months. If using the oral glucose tolerance test (OGTT), fasting

or carbohydrate restriction 3 days prior to the test should be avoided, as it can falsely elevate glucose levels. Certain medications such as glucocorticoids, thiazide diuretics, some HIV medications, and atypical antipsychotics are known to increase the risk of diabetes and should be considered when deciding whether to screen ⁽¹²⁾.

Table 2. American Diabetes Association (ADA) Screening Recommendations For Diabetes⁽¹¹⁾.
<p>Asymptomatic Type 2</p> <ol style="list-style-type: none"> 1. The ADA recommends screening for T2DM every 3 years in all adults beginning at 45 years of age 2. Testing should be considered for persons younger than 45 years of age or more frequently in individuals who are overweight (BMI ≥ 25 kg/m² for the general population and ≥ 23 kg/m² for Asian Americans) and have additional risk factors: <ul style="list-style-type: none"> • Habitually inactive • First-degree relative with diabetes • Member of a high-risk ethnic population (eg, African American, Latino, Native American, Asian American, Pacific Islander) • Previous diagnosis of GDM • Hypertensive ($\geq 140/90$ mm Hg or on therapy) • HDL cholesterol level < 35 mg/dL (0.91 mmol/L) and/or triglyceride level > 250 mg/dL (2.83 mmol/L) • Polycystic ovary syndrome • Previous IGT or IFG or A1c $\geq 5.7\%$ (0.057 or 39 mmol/mol Hgb) • Other clinical conditions associated with insulin resistance (eg, acanthosis nigricans) • History of cardiovascular disease. <p>Type 2 in Children and Adolescents</p> <p>Criteria:</p> <ul style="list-style-type: none"> • Overweight (BMI > 85th percentile for age and sex, weight for height > 85th percentile, or weight $> 120\%$ of ideal for height) <p>Plus any two of the following risk factors:</p> <ul style="list-style-type: none"> • Family history of T2DM in first- or second-degree relatives • Race or ethnicity (Native American, African American, Latino or Hispanic American, Asian American, Pacific Islander) • Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, or polycystic ovary disease) • Maternal history of diabetes or GDM during child's gestatio

1.5. Pathogenesis

- **Normal Carbohydrate Metabolism**

The body's main fuel source is glucose. Cells metabolize glucose completely through glycolysis and the Krebs cycle, producing adenosine triphosphate (ATP) as energy⁽¹³⁾. Glucose is stored in the liver and muscles as glycogen. Glycogenolysis converts stored glycogen back to glucose⁽¹⁴⁾. Glucose also may be stored in adipose tissue, which may subsequently undergo lipolysis yielding free fatty acids⁽¹³⁾. In the fasting state, free fatty acids supply much of the energy needs for the body except for the central nervous system, which requires glucose to function normally⁽¹⁴⁾. Proteins also can be converted to glucose through gluconeogenesis⁽¹³⁾. Homeostasis is achieved through a balance of the metabolism of glucose, free fatty acids, and amino acids to maintain a BG level sufficient to provide an uninterrupted supply of glucose to the brain⁽¹⁴⁾.

Insulin and glucagon are produced in the pancreas by cells in the islets of Langerhans. β -Cells make up 70% to 90% of the islets and produce insulin and amylin, whereas α -cells produce glucagon⁽¹³⁾. The main function of insulin is to decrease BG levels. Glucagon, along with other counter regulatory hormones such as growth factor, cortisol, and epinephrine, increases BG levels⁽¹⁴⁾. Although BG levels vary, the opposing actions of insulin and glucagon, along with the counter regulatory hormones, normally maintain fasting values between 79 and 99 mg/dL (4.4–5.5 mmol/L).

- **Normal Insulin Action**

Fasting insulin levels in the circulation average from 43 to 186 pmol/L (6–26 μ IU/mL)⁽¹³⁾. After food is consumed, BG levels rise, and the insulin-secretion response occurs in two phases.

An initial burst, known as first phase insulin response, lasts approximately 5 to 10 minutes and serves to suppress hepatic glucose production and cause insulin-mediated glucose disposal in adipose tissue. This bolus of insulin minimizes hyperglycemia during meals and during the postprandial period. The second phase of insulin response is characterized by a gradual increase in insulin secretion, which lasts 60 to 120 minutes and stimulates glucose uptake by peripheral insulin-dependent tissues, namely muscle. Slower release of insulin allows the body to respond to the new glucose entering from digestion while maintaining BG levels. Basal insulin secretion is the low rate of continuous insulin secreted by the pancreas to maintain normal FBG levels⁽¹⁾.

Amylin is a naturally occurring hormone that is cosecreted from β -cells with insulin. People with DM have either a relative or complete lack of amylin. Amylin has three major mechanisms of action: suppression of postmeal glucagon secretion; regulation of the rate of gastric emptying from the stomach to the small intestine, which increases satiety; and regulation of plasma glucose concentrations in the bloodstream⁽¹⁾.

Impaired Insulin Secretion A pancreas with normal β -cell function is able to adjust insulin production to maintain normal BG levels⁽¹⁴⁾. In T2DM, more insulin is secreted to maintain normal BG levels until eventually the pancreas can no longer produce sufficient insulin⁽¹³⁾. The resulting hyperglycemia is enhanced by extremely

high insulin resistance, pancreatic burnout in which β -cells lose functional capacity, or both. Impaired β -cell function results in a reduced ability to produce a first-phase insulin response sufficient to signal the liver to stop producing glucose after a meal⁽¹⁵⁾. Progressive β -cell decline is hypothesized to result from ongoing glucotoxicity and lipotoxicity. A recent study showed that early resolution of glucotoxicity through use of basal insulin in those at risk for developing DM reduced the incidence of diabetes diagnosis⁽¹⁶⁾.

Insulin Resistance Insulin resistance is the primary factor that differentiates T2DM from other forms of diabetes. Insulin resistance may be present for several years prior to the diagnosis of DM and can continue to progress throughout the course of the disease⁽¹³⁾. Resistance to insulin occurs in adipose tissue, skeletal muscle, and the liver⁽¹⁷⁾. Insulin resistance in the liver poses a double threat because the liver becomes nonresponsive to insulin for glucose uptake, and hepatic production of glucose after a meal does not cease, leading to elevated fasting and postmeal BG levels⁽¹⁾.

Metabolic Syndrome Insulin resistance has been associated with a number of other cardiovascular risks, including abdominal obesity, hypertension, dyslipidemia, hypercoagulation, and hyperinsulinemia⁽¹⁸⁾. The clustering of these risk factors has been termed metabolic syndrome. Criteria defining the metabolic syndrome as established by the International Diabetes Federation are summarized in Table 3⁽¹⁸⁾. Patients having these additional risk factors are at much higher cardiovascular risk than would be expected from individual components of the syndrome.

Table 3. Five Components of Metabolic Syndrome ⁽¹⁸⁾ .	
Risk Factor	Defining Level
1. Abdominal obesity the following: 2. Triglycerides treated 3. HDL cholesterol • Men treated • Women 4. Blood pressure 5. Fasting glucose type 2 diabetes	Based on ethnic group ^a Plus any two of ≥ 150 mg/dL (1.70 mmol/L) or < 40 mg/dL (1.03 mmol/L) or < 50 mg/dL (1.29 mmol/L) or treated ≥ 130 or ≥ 85 mm Hg or treated ≥ 100 mg/dL (5.6 mmol/L) or diagnosed
^a 102 cm (40 in) for males and 88 cm (35 in) for females likely to be used clinically. HDL, high-density lipoprotein.	

1.6. Management Of DM Type-2

1.6.1 Prevention Or Delay Of Type 2 Diabetes And Associated Comorbidities

A. Lifestyle Behavior Change for Diabetes Prevention.

The strongest evidence supporting lifestyle intervention for diabetes prevention in the U.S. comes from the DPP (Diabetes Prevention Program) trial, which demonstrated that intensive lifestyle intervention could reduce the risk of incident type 2 diabetes by 58% over 3 years. Evidence suggests that there is not an ideal percentage of calories from carbohydrate, protein, and fat to prevent diabetes^(19,20).

B. Pharmacologic Interventions.

Various pharmacologic agents have been evaluated for diabetes prevention, and metformin has the strongest evidence base and demonstrated long-term safety as pharmacologic therapy for diabetes prevention. However, no agents have been approved by the U.S. Food and Drug Administration (FDA) for diabetes prevention^(19, 21).

C. Prevention of Vascular Disease and Mortality.

Prediabetes is associated with heightened cardiovascular (CV) risk; therefore, screening for and treatment of modifiable risk factors for cardiovascular disease (CVD) are suggested⁽²²⁾.

D. Patient-Centered Care Goals.

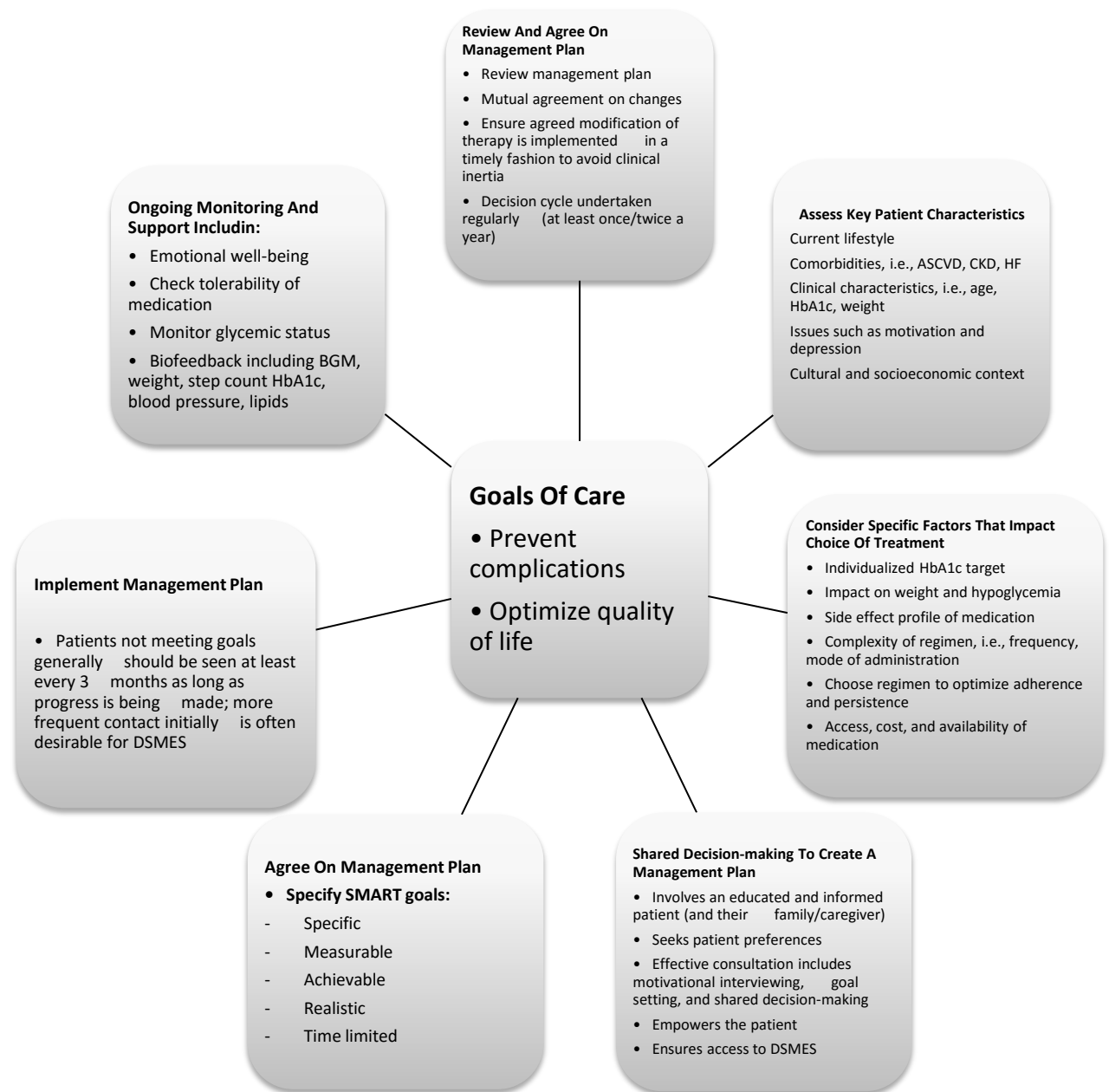
In adults with overweight/obesity at high risk of type 2 diabetes, care goals should include weight loss or prevention of weight gain, minimizing progression of hyperglycemia, and attention to CV risk and associated comorbidities⁽²²⁾.

1.6.2 Comprehensive Medical Evaluation And Assessment Of Comorbidities.

A. Patient-Centered Collaborative Care

successful medical evaluation depends on beneficial interactions between the patient and the care team. Individuals with diabetes must assume an active role in their care. The person with diabetes, family or support people, and health care team should together formulate the management plan, which includes lifestyle management, to improve disease outcomes and wellbeing⁽²³⁾.

The goals of treatment for diabetes are to prevent or delay complications and optimize quality of life (Figure 1)⁽²⁴⁾. The use of person-centered, strength based, empowering language that is respectful and free of stigma in diabetes care and education can help to inform and motivate people. Language that shames and judges may undermine this effort. Use language that is person-centered (e.g., “person with diabetes” is preferred over “diabetic”)⁽²³⁾.



ASCVD = Atherosclerotic Cardiovascular Disease

CKD = Chronic Kidney Disease

HF = Heart Failure

DSMES = Diabetes Self-Management Education and Support

BGM = Blood Glucose Monitoring

FIGURE1. Decision cycle for patient centered glycemic management in type 2 diabetes . HbA1c ,glycated hemoglobin⁽²⁴⁾ .

B. Comprehensive Medical Evaluation

The comprehensive medical evaluation includes the initial and follow-up evaluations, assessment of complications, psychosocial assessment, management of comorbid conditions, and engagement of the patient throughout the process. While a comprehensive list is provided in Table 4⁽²³⁾.

Table 4- Components of the comprehensive diabetes medical evaluation at initial, follow-up, and annual visits⁽²³⁾.		Initial Visit	Every Followup Visit	Annual Visit
Past Medical And Family History	Diabetes history			
	• Characteristics at onset (e.g., age, symptoms)	✓		
	• Review of previous treatment regimens and response	✓		
	• Assess frequency/cause/severity of past hospitalizations	✓		
	Family history			
	• Family history of diabetes in a first-degree relative	✓		
	• Family history of autoimmune disorder	✓		
	Personal history of complications and common comorbidities :			
	• Common comorbidities (e.g., obesity, OSA, NAFLD)	✓		✓
	• High blood pressure or abnormal lipids	✓		✓
	• Macrovascular and microvascular complications	✓		✓
	• Hypoglycemia: awareness/frequency/causes/timing of episodes	✓	✓	✓
	• Presence of hemoglobinopathies or anemias	✓		✓
	• Last dental visit	✓		✓
	• Last dilated eye exam	✓		✓
	• Visits to specialists	✓	✓	✓
	Interval history			
	• Changes in medical/family history since last visit		✓	✓
Behavioral Factors	• Eating patterns and weight history	✓	✓	✓
	• Assess familiarity with carbohydrate			

	counting (e.g., type 1 diabetes, type 2 diabetes treated with MDI)	✓		✓
	• Physical activity and sleep behaviors	✓	✓	✓
	• Tobacco, alcohol, and substance use	✓		✓
Medications And Vaccinations	• Current medication regimen	✓	✓	
	• Medication-taking behavior	✓	✓	✓
	• Medication intolerance or side effects	✓	✓	✓
	• Complementary and alternative medicine use	✓	✓	✓
	• Vaccination history and needs	✓		✓
Technology Use	• Assess use of health apps, online education, patient portals, etc	✓		✓
	• Glucose monitoring (meter/CGM): results and data use	✓	✓	✓
	• Review insulin pump settings and use, connected pen and glucose data	✓	✓	✓
Social Life Assessment	Social network			
	• Identify existing social supports	✓		✓
	• Identify surrogate decision maker, advanced care plan	✓		✓
	• Identify social determinants of health (e.g., food security, housing stability & homelessness, transportation access, financial security, community safety)	✓		✓
Physical Examination	• Height, weight, and BMI; growth/pubertal development in children and adolescents	✓	✓	✓
	• Blood pressure determination	✓	✓	✓
	• Orthostatic blood pressure measures (when indicated)	✓		
	• Fundoscopic examination (refer to eye specialist)	✓		✓
	• Thyroid palpation	✓		✓
	• Skin examination (e.g., acanthosis nigricans, insulin injection or insertion sites, lipodystrophy)	✓	✓	✓
	• Comprehensive foot examination			
	• Visual inspection (e.g., skin integrity, callous formation, foot deformity or ulcer, toenails)**	✓		✓
	• Screen for PAD (pedal pulses—refer for ABI if diminished)	✓		✓
	• Determination of temperature, vibration or pinprick sensation, and 10-g monofilament exam	✓		✓

	<ul style="list-style-type: none"> • Screen for depression, anxiety, and disordered eating Consider assessment for functional performance* 	✓		✓
	<ul style="list-style-type: none"> • Consider assessment for functional performance 	✓		✓
Laboratory Evaluation	<ul style="list-style-type: none"> • A1C, if the results are not available within the past 3 months 	✓	✓	✓
	<ul style="list-style-type: none"> • If not performed/available within the past year 	✓		✓
	<ul style="list-style-type: none"> • Lipid profile, including total, LDL, and HDL cholesterol and triglycerides# 	✓		✓
	<ul style="list-style-type: none"> • Liver function tests 	✓		✓
	<ul style="list-style-type: none"> • Spot urinary albumin-to-creatinine ratio 	✓		✓
	<ul style="list-style-type: none"> • Serum creatinine and estimated glomerular filtration rate 	✓		✓
	<ul style="list-style-type: none"> • Thyroid-stimulating hormone in patients with type 1 diabetes# 	✓		✓
	<ul style="list-style-type: none"> • Vitamin B12 if on metformin 	✓		✓
	<ul style="list-style-type: none"> • Serum potassium levels in patients on ACE inhibitors, ARBs, or diuretics 	✓		✓

C. Immunizations

The importance of routine vaccinations for people living with diabetes has been elevated by the coronavirus disease 2019 (COVID-19) pandemic. Preventing avoidable infections not only directly prevents morbidity but also reduces hospitalizations, which may additionally reduce risk of acquiring infections such as COVID-19. Children and adults with diabetes should receive vaccinations according to age-appropriate recommendations^(25,26).

D. Cancer

Patients with diabetes should be encouraged to undergo recommended age- and sex-appropriate cancer screenings and to reduce their modifiable cancer risk factors (obesity, physical inactivity, and smoking) ⁽²⁷⁾.

E. Cognitive Impairment/Dementia

In the presence of cognitive impairment, diabetes treatment regimens should be simplified as much as possible and tailored to minimize the risk of hypoglycemia ^(28,29,30,31).

F. Nonalcoholic Fatty Liver Disease

Patients with type 2 diabetes or prediabetes and elevated liver enzymes or fatty liver on ultrasound should be evaluated for presence of nonalcoholic steatohepatitis and liver fibrosis ^(32,33,34,35).

1.6.3. Facilitating Behavior Change And Well-Being To Improve

Health Outcomes

Building positive health behaviors and maintaining psychological well-being are foundational for achieving diabetes treatment goals and maximizing quality of life ^(36,37). Essential to achieving these goals are diabetes self-management education and support (DSMES), medical nutrition therapy (MNT), routine physical activity, smoking cessation counseling when needed, and psychosocial care ⁽³⁸⁾.

A. Diabetes Self-Management Educations DSMES

In accordance with the national standards for DSMES, all people with diabetes should participate in diabetes self-management education and receive the support needed to facilitate the knowledge, decision-making, and skills mastery for diabetes self-care. There are four critical times to evaluate the need for diabetes self-management education to promote skills acquisition in support of regimen implementation, MNT, and well-being: at diagnosis, annually and/or when not meeting treatment targets, when complicating factors develop (medical, physical, psychosocial), and when transitions in life and care occur. DSMES should be patient-centered, may be offered in group or individual settings, and should be communicated with the entire diabetes care team. Digital coaching and digital self-management interventions can be effective methods to deliver DSMES ⁽³⁹⁾.

B. Evidence for the Benefits

Studies have found that DSMES is associated with improved diabetes knowledge and self-care behaviors^(40,41) lower A1C^(40,42,43) lower self-reported weight⁽⁴⁴⁾, improved quality of life ^(45,46), reduced all-cause mortality risk⁽⁴⁷⁾, positive coping behaviors^(48,49), and reduced health care costs^(50,51). Better outcomes were reported for DSMES interventions that were >10hours over the course of 6–12months ⁽⁵²⁾.

C. Management Nutrition Therapy MNT

Nutrition therapy plays an integral role in overall diabetes management , and people with diabetes should be actively engaged in education , self-management , and treatment planning with their health care team , including the Collaborative development of an individualized eating plan^(53,54). MNT delivered by a registered

dietitian nutritionist is associated with A1C absolute decreases of 1.0–1.9% for people with type 1 diabetes and 0.3–2.0% for people with type 2 diabetes ⁽⁵⁵⁾.

D. Weight Management

Studies have demonstrated that a variety of eating plans, varying in macronutrient composition, can be used effectively and safely in the short term (1–2 years) to achieve weight loss in people with diabetes ⁽⁵⁶⁾.

E. Physical Activity

Physical activity is a general term that includes all movement that increases energy use and is an important part of the diabetes management plan. Exercise has been shown to improve blood glucose control, reduce cardiovascular risk factors, contribute to weight loss, and improve well-being ⁽⁵⁷⁾. Children and adolescents with type 1 or type 2 diabetes or prediabetes should engage in 60 minutes/day or more of moderate- or vigorous intensity aerobic activity, with vigorous muscles strengthening and bone-strengthening activities at least 3 days/week ⁽³⁹⁾.

Most adults with type 1 and type 2 diabetes should engage in 150 minutes or more of moderate- to vigorous-intensity aerobic activity per week, spread over at least 3 days/week, with no more than 2 consecutive days without activity. Shorter durations (minimum 75 minutes/week) of vigorous-intensity or interval training may be sufficient for younger and more physically fit individuals ⁽³⁹⁾.

E.1 Hypoglycemia

Physical activity may cause hypoglycemia if the medication dose or carbohydrate consumption is not adjusted for the requirement of exercises from glucose. Patients need to be educated to check blood glucose levels before and after periods of exercise

and about the potential prolonged effects of exercise, depending on its intensity and duration^(58,59).

E.2. Smoking Cessation: Tobacco and Cigarettes

People with diabetes who smoke have a heightened risk of CVD, premature death, microvascular complications, and worse glycemic control when compared with those who do not smoke^(60,61). Smoking may have a role in the development of type 2 diabetes^(62,63). Advise all patients not to use cigarettes and other tobacco products or e-cigarettes. After identification of tobacco or e-cigarette use, include smoking cessation counseling and other forms of treatment as a routine component of diabetes care⁽³⁹⁾.

F. Psychosocial Issues

Complex environmental, social, behavioral, and emotional factors, known as psychosocial factors, influence living with diabetes, both type 1 and type 2, and achieving satisfactory medical outcomes and psychological well-being. Thus, individuals with diabetes and their families are challenged with complex, multifaceted issues when integrating diabetes care into daily life⁽⁶⁴⁾. So psychosocial screening, follow-up and assessment for symptoms of diabetes distress, depression, anxiety, disordered eating, and cognitive capacity should be recommended for all patients with diabetes⁽³⁹⁾.

1.6.4. Glycemic Targets

Glycemic control is assessed by A1C measurement, continuous glucose monitoring (CGM), and blood glucose monitoring (BGM). Clinical trials primarily use A1C to demonstrate the benefits of improved glycemic control. CGM serves an increasingly

important role in managing the effectiveness and safety of treatment in many patients with type 1 diabetes and selected patients with type 2 diabetes ⁽⁶⁵⁾. Assess glycemic status (A1C) at least two times a year in patients who are meeting treatment goals or have stable glycemic control and at least every 3 months and as needed in patients whose therapy has recently changed and/or who are not meeting glycemic goals ⁽⁶⁶⁾.

For many people with diabetes, glucose monitoring is key for achieving glycemic targets. It allows patients to evaluate their individual response to therapy and assess whether glycemic targets are being safely achieved ⁽⁶⁷⁾.

A. Glycemic Goals

An A1C goal for many nonpregnant adults of <7% (53 mmol/mol) without significant hypoglycemia is appropriate. On the basis of provider judgment and patient preference, achievement of lower A1C levels than the goal of 7% may be acceptable and even beneficial if it can be achieved safely without significant hypoglycemia or other adverse effects of treatment. Less stringent A1C goals (such as <8% [64 mmol/mol]) may be appropriate for patients with limited life expectancy or where the harms of treatment are greater than the benefits. In the Table 5 summary of glycemic goals for many nonpregnant adults ⁽⁶⁸⁾.

Table 5. Summary Of Glycemic Recommendations For Many Nonpregnant Adults With Diabetes⁽⁶⁸⁾	
A1C	<7.0%
Preprandial capillary plasma glucose	80–130 mg/dL
Peak postprandial capillary plasma glucose†	<180 mg/dL (10.0 mmol/L)

B. Hypoglycemia

Hypoglycemia is the major limiting factor in the glycemic management of type 1 and type 2 diabetes. The classification of hypoglycemia level is summarized in Table 6

^(69,70). Occurrence and risk for hypoglycemia should be reviewed at every encounter and investigated as indicated. Glucose (approximately 15–20 g) is the preferred treatment for the conscious individual with blood glucose <70 mg/dL (3.9 mmol/L), although any form of carbohydrate that contains glucose may be used. Fifteen minutes after treatment, if BGM shows continued hypoglycemia, the treatment should be repeated. Once the BGM or glucose pattern is trending up, the individual should consume a meal or snack to prevent recurrence of hypoglycemia. Glucagon should be prescribed for all individuals at increased risk of level 2 or 3 hypoglycemia, so that it is available should it be needed. Caregivers, school personnel, or family members providing support to these individuals should know where it is and when and how to administer it. Glucagon administration is not limited to health care professionals. Hypoglycemia unawareness or one or more episodes of level 3 hypoglycemia should trigger hypoglycemia avoidance education and reevaluation and adjustment of the treatment regimen to decrease hypoglycemia. Insulin-treated patients with hypoglycemia unawareness, one level 3 hypoglycemic event, or a pattern of unexplained level 2 hypoglycemia should be advised to raise their glycemic targets to strictly avoid hypoglycemia for at least several weeks in order to partially reverse hypoglycemia unawareness and reduce risk of future episodes. Ongoing assessment of cognitive function is suggested with increased vigilance for hypoglycemia by the clinician, patient, and caregivers if impaired or declining cognition is found ⁽⁶⁸⁾.

Table 6 Classification of Hypoglycemia ^(69,70).	
	Glycemic Criteria/Description
Level 1	Glucose <70 mg/dL and ≥54 mg/dL
Level 2	Glucose <54 mg/dL
Level 3	A severe event characterized by altered mental and/or physical status requiring assistance for treatment of hypoglycemia

1.6.5.Obesity And Weight Management For The Prevention And Treatment Of Type 2 Diabetes

Strong evidence exists that obesity management can delay the progression from prediabetes to type 2 diabetes⁽⁷¹⁾ and is highly beneficial in the treatment of type 2 diabetes⁽⁷²⁾. Modest weight loss improves glycemic control and reduces the need for glucose lowering medications,⁽⁷³⁾ and more intensive dietary energy restriction can substantially reduce A1C and fasting glucose and promote sustained diabetes remission through at least 2years^(74,75). Metabolic surgery strongly improves glycemic control and often leads to remission of diabetes, improved quality of life, improved CV outcomes, and reduced mortality⁽⁷⁶⁾.

There are three treatment options for overweight and obesity in type 2 diabetes .

1-Diet, Physical Activity, and Behavioral Therapy

Diet, physical activity, and behavioral therapy to achieve and maintain $\geq 5\%$ weight loss is recommended for most people with type 2 diabetes and overweight or obesity. Additional weight loss usually results in further improvements in control of diabetes and CV risk⁽⁷⁷⁾.

2-Pharmacotherapy

A meta-analysis of 227 randomized controlled trials of glucose-lowering treatments in type 2 diabetes found that A1C changes were not associated with baseline BMI, indicating that people with obesity can benefit from the same types of treatments for diabetes as normal-weight patients⁽⁷⁸⁾. When choosing glucose-lowering medications for people with type 2 diabetes and overweight or obesity, consider the medication's effect on weight . Agents associated with varying degrees of weight loss include metformin, α -glucosidase inhibitors, sodium–glucose cotransporter 2 inhibitors,

glucagon-like peptide 1 receptor agonists, and amylin mimetics. Dipeptidyl peptidase 4 inhibitors are weight neutral. In contrast, insulin secretagogues, thiazolidinediones, and insulin are often associated with weight gain. Whenever possible, minimize medications for comorbid conditions that are associated with weight gain⁽⁷⁹⁾. If a patient's response to weight loss medication is effective (>5% weight loss after 3 months' use), further weight loss is likely with continued use. When early response is insufficient (<5% weight loss after 3 months' use) or if there are significant safety or tolerability issues, consider discontinuation of the medication and evaluate alternative medications or treatment approaches^(80,82). Five weight loss medications are FDA approved for long-term use (>12 weeks) in adult patients with BMI ≥ 27 kg/m² with one or more obesity associated comorbid condition (e.g., type 2 diabetes, hypertension, and/or dyslipidemia) who are motivated to lose weight include orlistat, phentermine/topiramate ER, naltrexone/bupropion ER, liraglutide 3 mg, and semaglutide 2.4 mg⁽⁸³⁾.

3-Metabolic Surgery

Data from numerous large cohort studies and randomized controlled clinical trials, demonstrates that metabolic surgery achieves superior glycemic control and reduction of cardiovascular risk in patients with type 2 diabetes and obesity compared with nonsurgical intervention⁽⁸⁴⁾. In addition to improving glycemia, metabolic surgery reduces the incidence of microvascular disease⁽⁸⁵⁾, improves quality of life^(86,87), decreases cancer risk, and improves cardiovascular disease risk factors and longterm cardiovascular events.^(88,89) Cohort studies that match surgical and nonsurgical subjects strongly suggest that metabolic surgery reduces all-cause mortality^(90,91).

People who undergo metabolic surgery should receive long-term medical and behavioral support and routine monitoring of micronutrient, nutritional, and metabolic status. Table 7 summarizes treatment options for overweight and obesity in type 2 diabetes⁽⁹²⁾.

Table 7 Treatment Options for Overweight and Obesity in Type 2 Diabetes BMI Category, kg/m ² ⁽⁹²⁾ .			
Treatment	25.0–26.9 (or 23.0–24.9*)	27.0–29.9 (or 25.0–27.4*)	≥30.0 (or ≥27.5*)
Diet, physical activity, and behavioral counseling	↑	↑	↑
Pharmacotherapy		↑	↑
Metabolic surgery			↑
*Recommended cut points for Asian-American individuals (expert opinion). †Treatment may be indicated for select motivated patients			

1.6.6. Pharmacologic Therapy for Adults With Type 2 Diabetes

Table 8 and Figure 3 provide details for informed decision-making on pharmacologic treatment for the management of glycemia in type 2 diabetes.

Initial Therapy

First-line therapy depends on comorbidities, patient-centered treatment factors, and management needs but will generally include metformin and comprehensive lifestyle modification. Pharmacotherapy should be started at the time type 2 diabetes is diagnosed unless there are contraindications; for many patients this will be metformin monotherapy in combination with lifestyle modifications. Additional and/or alternative agents may be considered in special circumstances, such as in individuals with established or increased risk of cardiovascular or renal complications. Metformin is effective and safe, is inexpensive, and may reduce risk of cardiovascular events and death⁽⁹³⁾. Metformin is available in an immediate-release form for twice-daily dosing or as an extended-release form that can be given once daily. Compared with

sulfonylureas, metformin as first-line therapy has beneficial effects on A1C, weight, and cardiovascular mortality⁽⁹⁴⁾; there is little systematic data available for other oral agents as initial therapy of type 2 diabetes.

In patients with contraindications or intolerance to metformin, initial therapy should be based on patient factors; consider a drug from another class depicted in Fig. 1.3. When A1C is $\geq 1.5\%$ (12.5 mmol/mol) above the glycemic target many patients will require dual combination therapy to achieve their target A1C level⁽⁹⁵⁾. Insulin has the advantage of being effective where other agents are not and should be considered as part of any combination regimen when hyperglycemia is severe, especially if catabolic features (weight loss, hypertriglyceridemia, ketosis) are present. It is common practice to initiate insulin therapy for patients who present with blood glucose levels ≥ 300 mg/dL (16.7 mmol/L) or A1C $>10\%$ (86 mmol/mol) or if the patient has symptoms of hyperglycemia (i.e., polyuria or polydipsia) or evidence of catabolism (weight loss) (Fig. 1.4). As glucose toxicity resolves, simplifying the regimen and/or changing to noninsulin agents is often possible. However, there is evidence that patients with uncontrolled hyperglycemia associated with type 2 diabetes can also be effectively treated with a sulfonylurea⁽⁹⁶⁾.

Combination Therapy

Because type 2 diabetes is a progressive disease in many patients, maintenance of glycemic targets with monotherapy is often possible for only a few years, after which combination therapy is necessary. Traditional recommendations have been to use stepwise addition of medications to metformin to maintain A1C at target. The advantage of this is to provide a clear assessment of the positive and negative effects of new drugs and reduce potential side effects and expense⁽⁹⁷⁾. However, there are

data to support initial combination therapy for more rapid attainment of glycemic goals ^(98,99) and later combination therapy for longer durability of glycemic effect ⁽¹⁰⁰⁾. The VERIFY (Vildagliptin Efficacy in combination with metfoRmIn For early treatment of type 2 diabetes) trial demonstrated that initial combination therapy is superior to sequential addition of medications for extending primary and secondary failure, These results have not been generalized to oral agents other than vildagliptin, but they suggest that more intensive early treatment has some benefits and should be considered through a shared decision-making process with patients, as appropriate ⁽¹⁰¹⁾. Recommendations for treatment intensification for patients not meeting treatment goals should not be delayed, The choice of medication added to initial therapy is based on the clinical characteristics of the patient and their preferences. Important clinical characteristics include the presence of established ASCVD or indicators of high ASCVD risk, HF, CKD, other comorbidities, and risk for specific adverse drug effects, as well as safety, tolerability, and cost. A comparative effectiveness meta-analysis suggests that each new class of noninsulin agents added to initial therapy with metformin generally lowers A1C approximately 0.7–1.0% .⁽¹⁰²⁾⁽¹⁰³⁾ For patients without established ASCVD, indicators of high ASCVD risk, HF, or CKD, the choice of a second agent to add to metformin is based on efficacy, avoidance of side effects (particularly hypoglycemia and weight gain), cost, and patient preferences.⁽¹⁰⁴⁾ Similar considerations are applied in patients who require a third agent to achieve glycemic goals. The need for the greater potency of injectable medications is common, particularly in people with a longer duration of diabetes. The addition of basal insulin, either human NPH or one of the long-acting insulin analogs, to oral agent regimens is a well-established approach that is effective for many patients. In addition, recent evidence supports the utility of GLP-1 RAs in patients not at glycemic goal ^(105,106).

Cardiovascular Outcomes Trials

There are now multiple large randomized controlled trials reporting statistically significant reductions in cardiovascular events in patients with type 2 diabetes treated with an SGLT2 inhibitor or GLP-1 RA (see table 8,fig. 3)^(107,108).

		Efficacy	Hypoglycemia	Weight change	CV effects		Cost	Oral/SQ	Renal effect		Additional considerations
					ASCVD	HF			Progression of DKD	Dosing/use considerations	
Metformin		High	No	Neutral (potential for modest loss)	Potential benefit	Neutral	low	Oral	Neutral	Contraindicated with eGFR <30 mL/min/1.73 m ²	Gastrointestinal side effects common (diarrhea, nausea) Potential for B12 deficiency
SGLT2 inhibitors		Intermediate	No	Loss	Benefit: empagliflozin [†] , canagliflozin	Benefit: empagliflozin [‡] , canagliflozin, dapagliflozin [‡] , ertuglifloz	High	Oral	Benefit: canagliflozin [§] , empagliflozin, dapagliflozin	See labels for renal dose considerations of individual agents Glucose-lowering effect is lower for SGLT2 inhibitors at lower eGFR	Should be discontinued before any scheduled surgery to avoid potential risk for DKA DKA risk (all agents, rare in T2D) Risk of bone fractures (canagliflozin) Genitourinary infections Risk of volume depletion, hypotension LDL cholesterol Risk of Fournier's gangrene
GLP-1 RAs		High	No	Loss	Benefit: dulaglutide [†] , liraglutide [†] , semaglutide (SQ)	Neutral	High	SQ; oral (semaglutide)	Benefit on renal end points in CVOTs, driven by albuminuria outcomes: liraglutide, semaglutide (SQ), dulaglutide	See labels for renal dose considerations of individual agents No dose adjustment for dulaglutide, liraglutide, semaglutide Caution when initiating or increasing dose due to potential risk of nausea, vomiting, diarrhea, or dehydration. Monitor renal function in patients reporting severe adverse GI reactions when initiating or increasing dose of therapy	FDA Black Box: Risk of thyroid C-cell tumors in rodents; human relevance not determined (liraglutide, dulaglutide, exenatide extended release, semaglutide) GI side effects common (nausea, vomiting, diarrhea) Injection site reactions Pancreatitis has been reported in clinical trials but causality has not been established. Discontinue if pancreatitis is suspected.
DPP-4 inhibitors			No	Neutral	Neutral: exenatide once weekly, lixisenatide	Potential risk: saxagliptin	High	Oral	Neutral	Renal dose adjustment required (sitagliptin, saxagliptin, alogliptin); can be used in renal impairment No dose adjustment required for linagliptin	Pancreatitis has been reported in clinical trials but causality has not been established. Discontinue if pancreatitis is suspected. Joint pain
Thiazolidinediones		High	No	Gain	Potential benefit: pioglitazone	Increased risk	low	Oral	Neutral	No dose adjustment required Generally not recommended in renal impairment due to potential for fluid retention	FDA Black Box: Congestive heart failure (pioglitazone, rosiglitazone) Fluid retention (edema; heart failure) Benefit in NASH Risk of bone fractures Bladder cancer (pioglitazone) LDL cholesterol (rosiglitazone)
Sulfonylureas (2nd generation)		High	Yes	Gain	Neutral	Neutral	low	Oral	Neutral	Glyburide: generally not recommended in chronic kidney disease Glipizide and glimepiride: initiate conservatively to avoid hypoglycemia	FDA Special Warning on increased risk of cardiovascular mortality based on studies of an older sulfonylurea (tolbutamide)
Insulin	Human insulin	High	Yes	Gain	Neutral	Neutral	Low (SQ)	SQ; inhaled	Neutral	Lower insulin doses required with a decrease in eGFR; titrate per clinical response	Injection site reactions Higher risk of hypoglycemia with human insulin (NPH or premixed formulations) vs. analogs
	Analog						High	SQ			

Table 8. Drug-specific and patient factors to consider when selecting antihyperglycemic treatment in adults with type 2 diabetes ^(107,108).

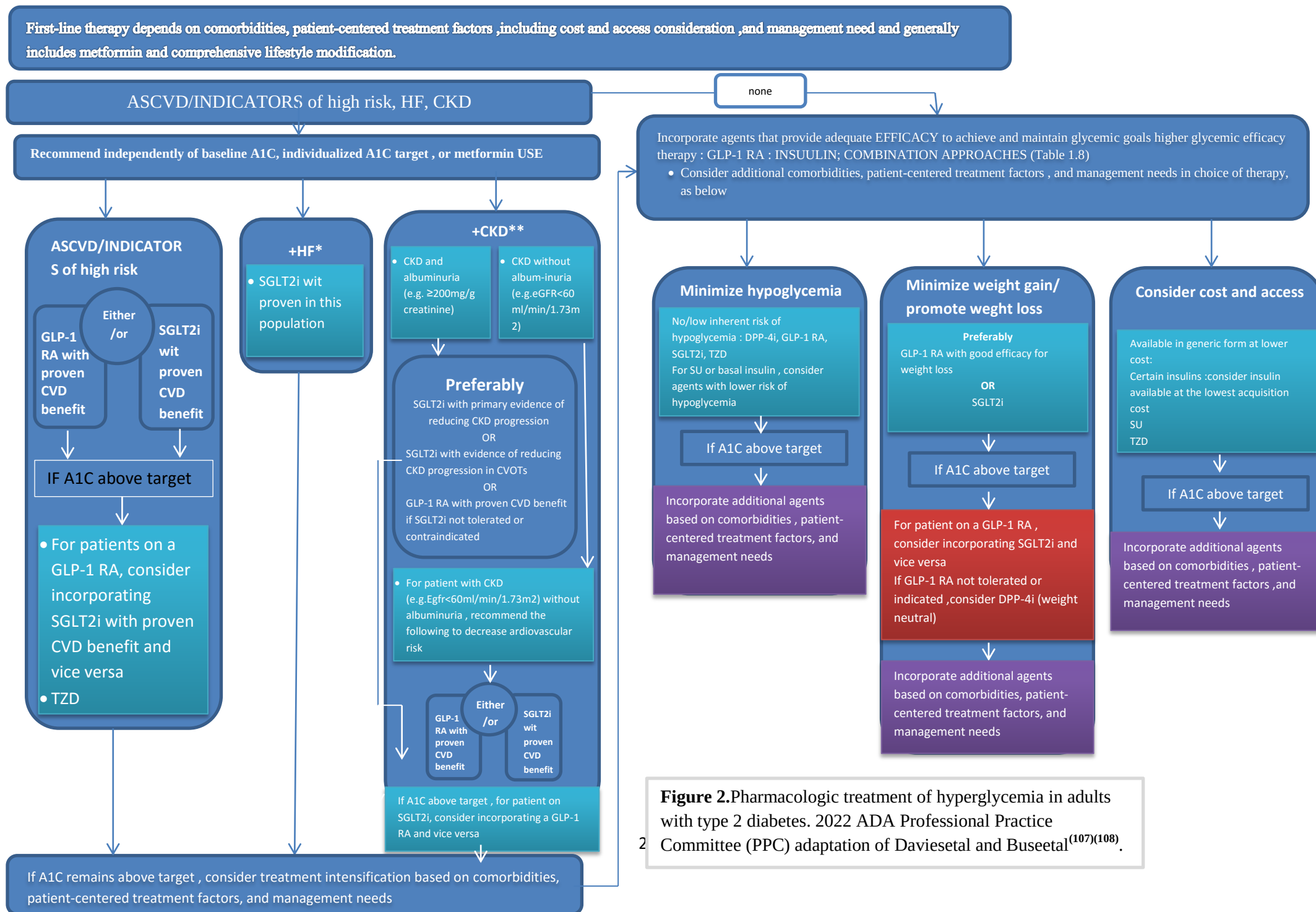


Figure 2. Pharmacologic treatment of hyperglycemia in adults with type 2 diabetes. 2022 ADA Professional Practice Committee (PPC) adaptation of Davies et al and Buse et al⁽¹⁰⁷⁾⁽¹⁰⁸⁾.

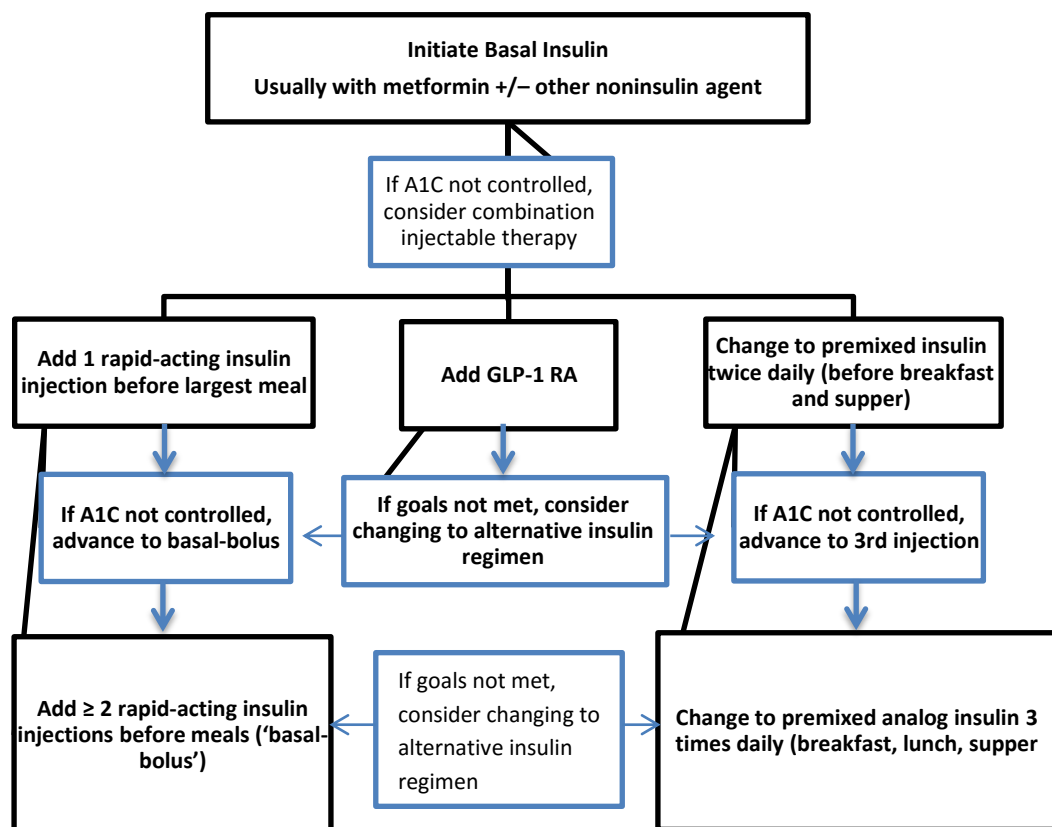


Figure 3. Intensifying to injectable therapies in type 2 diabetes⁽¹⁰⁷⁾.

1.6.7. Treatment of comorbidity Conditions

The ADA standards of medical care address many of the common comorbid conditions, as well as complications that result from the progression of DM.

1.6.7.1. CVD And Risk Management

For patients with diabetes and hypertension, blood pressure targets should be individualized through a shared decision-making process that addresses CV risk, potential adverse effects of antihypertensive medications, and patient preferences. For individuals with diabetes and hypertension at higher CV risk (existing ASCVD or 10-year ASCVD risk $\geq 15\%$), a blood pressure target of $<130/80$ mmHg may be appropriate, if it can be safely attained. For individuals with diabetes and hypertension at lower risk for CVD (10-year ASCVD risk $<15\%$), treat to a blood pressure target of $<140/90$ mmHg⁽¹⁰⁹⁾.

Pharmacologic treatment.

Patients with confirmed office-based blood pressure $\geq 140/90$ mmHg should, in addition to lifestyle therapy, have prompt initiation and timely titration of pharmacologic therapy to achieve blood pressure goals⁽¹⁰⁹⁾. Patients with confirmed office-based blood pressure $\geq 160/100$ mmHg should, in addition to lifestyle therapy, have prompt initiation and timely titration of two drugs or a single-pill combination of drugs demonstrated to reduce CV events in patients with diabetes⁽¹¹⁰⁾. Treatment for hypertension should include drug classes demonstrated to reduce CV events in patients with diabetes. ACE inhibitors or angiotensin receptor blockers (ARBs) are recommended first-line therapy for hypertension in people with diabetes and coronary artery disease (CAD)^(111,112) Multiple-drug therapy is generally required to achieve

blood pressure targets. However, combinations of ACE inhibitors and ARBs and combinations of ACE inhibitors or ARBs with direct renin inhibitors should not be used^(113,114).

For patients treated with an ACE inhibitor, ARB, or diuretic, serum creatinine/estimated glomerular filtration rate (eGFR) and serum potassium levels should be monitored at least annually⁽¹¹⁶⁾.

Antiplatelet Agents

Aspirin has been shown to be effective in reducing cardiovascular morbidity and mortality in high-risk patients with previous MI or stroke (secondary prevention) and is strongly recommended. In primary prevention, however, among patients with no previous cardiovascular events, its net benefit is more controversial^(117,118). Use aspirin therapy (75–162 mg/day) as a secondary prevention strategy in those with diabetes and a history of ASCVD. For patients with ASCVD and documented aspirin allergy, clopidogrel (75 mg/day) should be used. Dual antiplatelet therapy (with low-dose aspirin and a P2Y₁₂ inhibitor) is reasonable for a year after an acute coronary syndrome and may have benefits beyond this period. Long-term treatment with dual antiplatelet therapy should be considered for patients with prior coronary intervention, high ischemic risk, and low bleeding risk to prevent major adverse cardiovascular (MACE) events. Combination therapy with aspirin plus low-dose rivaroxaban should be considered for patients with stable CAD and/or PAD and low bleeding risk to prevent major adverse limb and CV events. Aspirin therapy (75–162 mg/day) may be considered as a primary prevention strategy in those with diabetes who are at increased CV risk, after a comprehensive discussion with the patient on the benefits versus the comparable increased risk of bleeding⁽¹¹⁹⁾.

1.6.7.2. Lipid Management

Primary Prevention:

Patients with type 2 diabetes have an increased prevalence of lipid abnormalities, contributing to their high risk of ASCVD. Multiple clinical trials have demonstrated the beneficial effects of statin therapy on ASCVD outcomes in subjects with and without CHD^(120,121). For patients with diabetes aged 40 years and older without ASCVD, use moderate-intensity statin therapy in addition to lifestyle therapy^(122,123). For patients with diabetes aged 20–39 years with additional ASCVD risk factors, it may be reasonable to initiate statin therapy in addition to lifestyle therapy. In patients with diabetes at higher risk, especially those with multiple ASCVD risk factors or aged 50–70 years, it is reasonable to use high intensity statin therapy⁽¹²⁴⁾. In adults with diabetes and 10-year ASCVD risk of 20% or higher, it may be reasonable to add ezetimibe to maximally tolerated statin therapy to reduce LDL cholesterol levels by 50% or more⁽¹²⁵⁾.

Secondary Prevention:

For patients of all ages with diabetes and ASCVD, high-intensity statin therapy should be added to lifestyle therapy^(126,127). Over the past few years, there have been multiple large randomized trials investigating the benefits of adding nonstatin agents to statin therapy, including those that evaluated further lowering of LDL cholesterol with ezetimibe⁽¹²⁸⁾ and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors⁽¹²⁹⁾.

Treatment of Other Lipoprotein Fractions or Targets

For patients with fasting triglyceride levels ≥ 500 mg/dL, evaluate for secondary causes of hypertriglyceridemia and consider medical therapy (fibric acid derivatives and/or fish oil) to reduce the risk of pancreatitis. In patients with ASCVD or other CV risk factors on a statin with controlled LDL cholesterol but elevated triglycerides (135–499 mg/dL), the addition of icosapent ethyl can be considered to reduce CV risk^(130,131).

1.6.8. Treatment of Acute Complications

1.6.8.1. Diabetic Ketoacidosis (DKA)

DKA is a reversible but potentially life-threatening medical emergency that results from a relative or absolute deficiency in insulin. Diagnostic criteria for DKA include hyperglycemia (> 250 mg/dL [13.9 mmol/L]), ketosis (anion gap > 12 mEq/L [mmol/L]), and acidosis (arterial pH ≤ 7.3). Typical fluid deficit is 5 to 7 L or more, and major deficits of serum sodium and potassium are common. DKA severity depends on the magnitude of the decrease in arterial pH, serum bicarbonate levels, and mental state rather than the magnitude of hyperglycemia. Treatment goals of DKA consist of reversing the underlying metabolic abnormalities, rehydrating the patient, and normalizing serum glucose. Fluid replacement with normal saline at 1 to 1.5 L/hour for the first hour is recommended to rehydrate the patient and ensure the kidneys are perfused. Potassium and other electrolytes are supplemented as indicated by laboratory assessment. The use of sodium bicarbonate in DKA is controversial and generally only recommended when the pH is less than 7. Regular insulin at 0.1 unit/kg/hour by continuous IV infusion is the preferred treatment in DKA to regain metabolic control rapidly. When plasma glucose values drop below 250 mg/dL (13.9

mmol/L), dextrose 5% should be added to IV fluids. During the recovery period, it is recommended to continue administering insulin and allow patients to eat as soon as possible. Dietary carbohydrates combined with insulin assist in the clearance of ketones⁽¹³²⁾.

1.6.8.2. Hyperosmolar Hyperglycemic State (HHS)

HHS is a life-threatening condition similar to DKA that also arises from inadequate insulin, but HHS occurs primarily in older patients with T2DM. DKA and HHS also differ in that HHS lacks the ketonemia and acidosis associated with DKA. Patients with hyperglycemia and dehydration lasting several days to weeks are at greatest risk of developing HHS. Infection, silent myocardial infarction, cerebrovascular accident, mesenteric ischemia, acute pancreatitis, and use of medications that affect carbohydrate metabolism including steroids and thiazide diuretics are known precipitating causes of HHS. Two main diagnostic criteria for HHS are a plasma glucose value of greater than 600 mg/dL (33.3 mmol/L) and a serum osmolality of greater than 320 mOsm/kg (mmol/kg). The extreme hyperglycemia and large fluid deficits resulting from osmotic diuresis are major challenges to overcome with this condition. Similar to DKA, the treatment of HHS consists of aggressive rehydration, correction of electrolyte imbalances, and continuous insulin infusion to normalize serum glucose. BG levels should be reduced gradually to minimize risk of cerebral edema⁽¹³²⁾.

1.6.9.Treatment of Long-Term Complications

1.6.9.1. Retinopathy

Diabetic retinopathy occurs when the microvasculature that supplies blood to the retina becomes damaged. This damage permits leakage of blood components through the vessel walls. The ADA recommends that patients with T2DM receive a dilated eye examination at the time of diagnosis by an ophthalmologist or optometrist. Examinations should begin within 5 years of diagnosis of T1DM. Once one or more normal examinations occur, the dilated eye examination is recommended to be repeated at least every 2 years. In patients with documented retinopathy, an annual dilated eye examination is recommended. Glucose and BP control are the best strategies for decreasing risk and slowing the progression of retinopathy⁽¹³³⁾.

1.6.9.2. Neuropathy

Peripheral neuropathy is a possible complication of DM. The most common types of peripheral neuropathy include chronic sensorimotor distal peripheral neuropathy, which can cause pain, tingling, and numbness in the feet and hands, and autonomic neuropathy, which can lead to hypotension, gastroparesis, sexual dysfunction, and autonomic failure in response to hypoglycemia⁽¹³³⁾. pregabalin and duloxetine, have been approved for relief of distal peripheral neuropathy pain⁽¹³⁴⁾. A number of other drugs are also sometimes used including venlafaxine, gabapentin, carbamazepine, tramadol, topical capsaicin, and tricyclic antidepressants^(135,136).

1.6.9.3. Foot Ulcers

Lower extremity amputations are one of the most feared and disabling sequelae of long-term uncontrolled DM. A foot ulcer is an open sore that develops and penetrates

to the subcutaneous tissues. Complications of the feet develop primarily as a result of peripheral arterial disease (PAD), neuropathies, and foot deformations⁽¹³⁷⁾. Pharmacologic intervention with antiplatelet therapy (aspirin 160–325 mg/day or clopidogrel 75 mg/day) is indicated in patients with PAD ⁽¹³⁸⁾. For those that remain symptomatic, cilostazol 100 mg twice daily may be useful to improve blood flow and reduce the symptoms of PAD. ADA recommends daily in Neuropathies visual examination of the feet and a foot check performed at every provider visit as well as a comprehensive foot evaluation each year with Neuropathy ⁽¹³³⁾. Sensory testing with a 10-gauge monofilament can detect areas of neuropathy. Treatment consists of glycemic control, preventing infection, debriding dead tissues, applying dressings, treating edema, and limiting ambulation ⁽¹³⁹⁾.

Chapter-II

2. Aims of the study:

2.1. General objectives:

Evaluation of discharge patients with T2DM based on target goals of therapy at a private hospital in sana,a, Yemen

2.2. Specific objectives:

1. To study extent of commitment to implementing the treatment plan in discharge patient with T2DM according to 2022 ADA guideline .
2. To study the presence of drug-drug interaction in the list of drugs for discharge patients with T2DM .

To study the impact of cardiovascular disease and lipid management on the therapeutic plain for discharge patient with T2DM

Chapter-III

3. Methodology:

3.1 Study protocol:

The study was a clinical retrospective study performed on discharge patient with T2DM in University of Science & Technology Hospital in Sana'a city between December 4,2021 and January 4,2022.

3.2 Study population:

The study population constitutes of 150 cases taken from 4977 cases for discharge patients have been diagnosed with T2DM. All cases for patients admitted to hospital in 2021 and extracted from the electronic health record (HER) database to obtain the required data. Patients were enrolled in the study after making sure that there were medication to treat diabetes and the presence of the necessary tests to assess the patient's condition .

3.3 Data collection:

The collected data including age , gender (male or female) , fasting blood sugar or randomized blood sugar , Hemoglobin A1c, lipid profile (high-density lipoprotein cholesterol [HDL],low-density lipoprotein cholesterol [LDL], Total Cholesterol test , Triglyceride test [TGs]) as normal, abnormal or non-available, Serum-Creatinine Sr.Cr ,stage of chronic kidney disease based on MDRD eGFR calculator and list of discharge medication and each medication generic name, dose, frequency, dosage form, duration of medication and route of administration . The selection of these variables was based on previous similar studies .

3.4 Statistical analysis:

Following data, data was analyzed using statistical package for social science (collection SPSS) version 21. Continuous variables were presented as mean and standard deviation. Categorical variables were presented as frequencies and percentages.

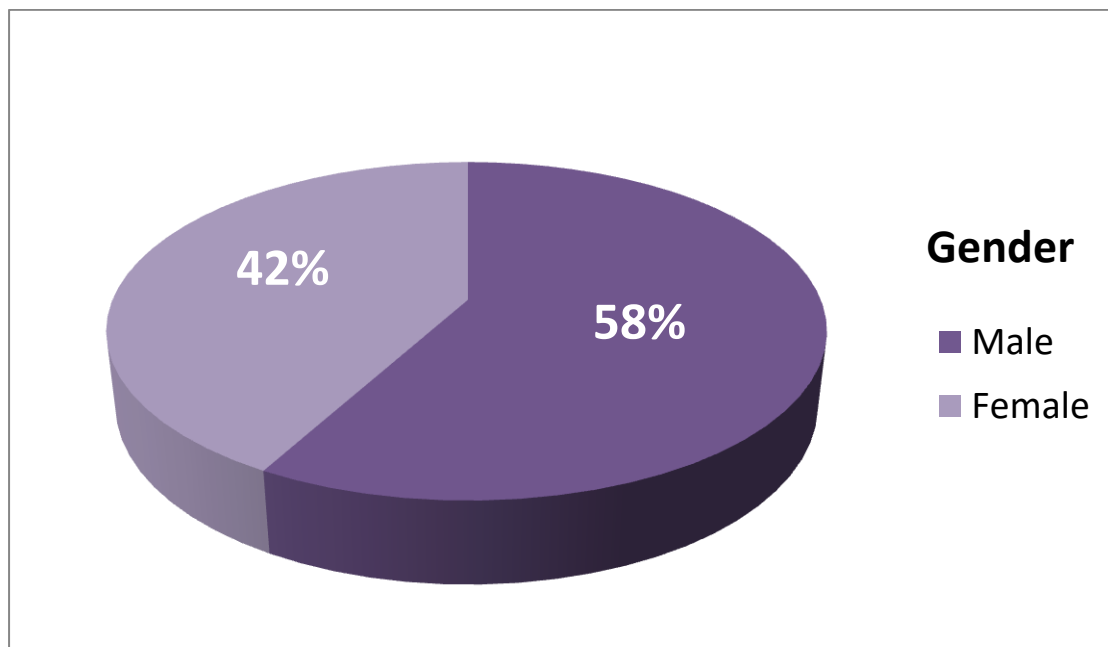
Chapter-IV

4.Result

4.1.Gender distribution

During the period of this study a total of 150 out-patients records were reviewed, among which majority were males and the remaining were female, The gender distribution of the sample is represented in [Table 9] and graphically illustrated in [Figure 4]

[Table 9] Gender distribution		
	Frequency	(%) Percent
Male	87	58.0%
Female	63	42.0%
Total	150	100.0%

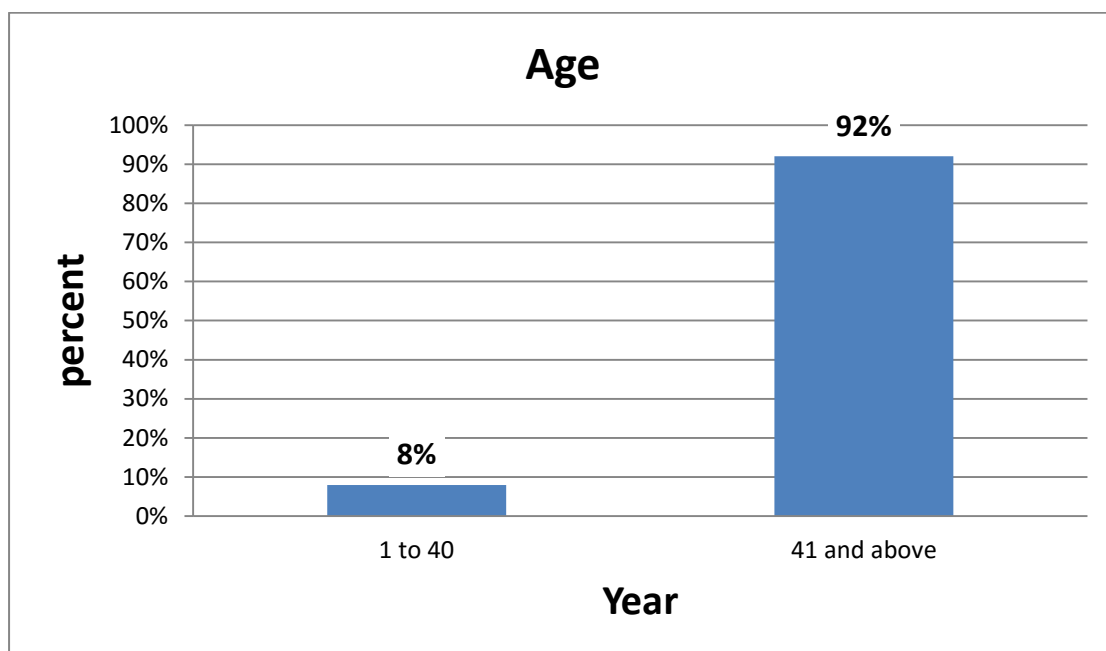


[Fig. 4] Gender Distribution

4.2.Age distribution

It was found that age of the patients involved varied from 20 to 82 years. The age groups were categorized into two: 1-40 years, and 41 years and above. The Age distribution of the sample is represented in [Table 10] and graphically illustrated in [Figure 5]

[Table 10] Age distribution		
	Frequency	(%) Percent
1-40	12	8.0%
41 and above	138	92.0%
Total	150	100.0%

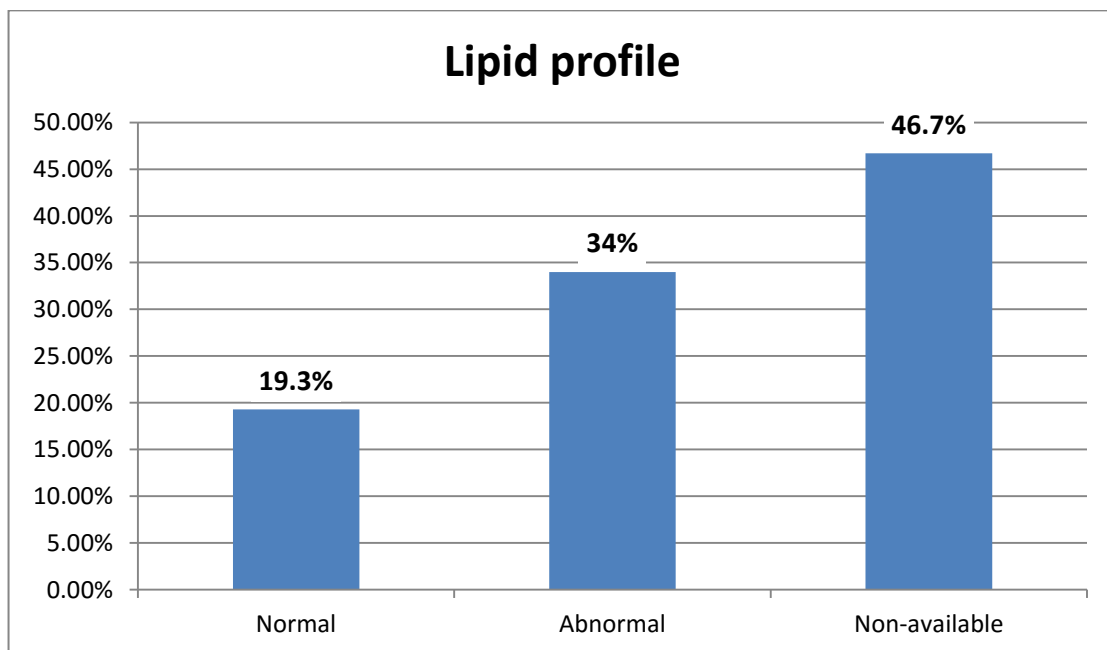


[Figure 5] Age Distribution

4.3.Lipid Profile distribution

It was found that Lipid profile of the patients ,were categorized into three: Normal, Abnormal and Non-available. The Lipid Profile distribution of the sample is represented in [Table 11] and graphically illustrated in [Figure 6]

[Table 11] Lipid profile distribution		
	Frequency	(%) Percent
Normal	29	19.3%
Abnormal	51	34%
Non-available	70	46.7%
Total	150	100.0%

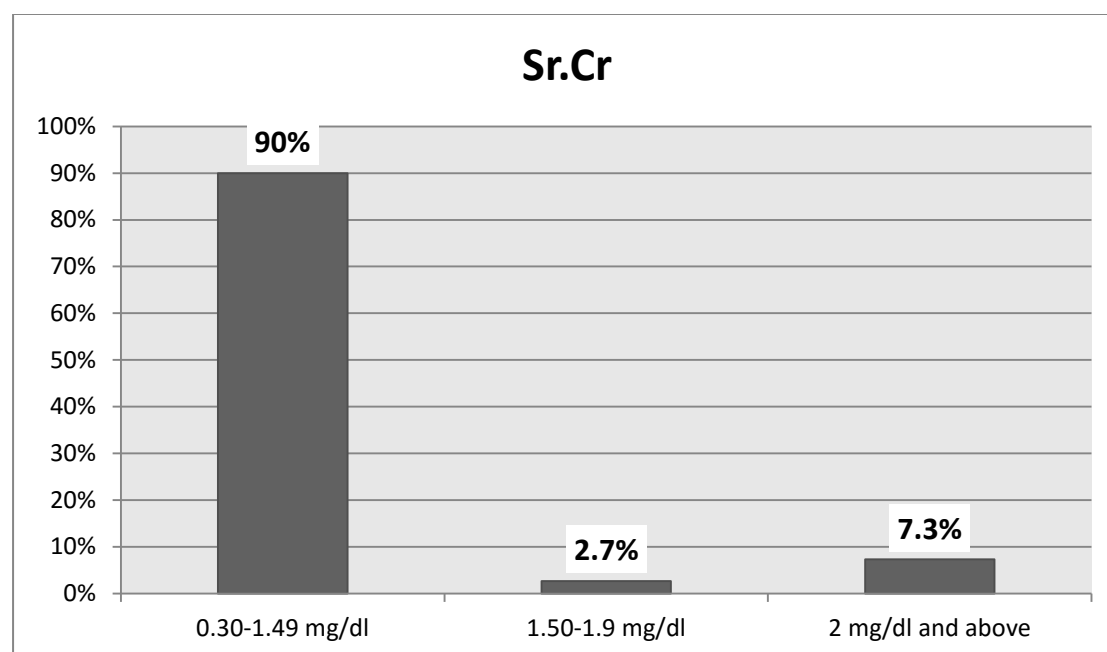


[Figure 6] Lipid Profile distribution

4.4.Sr.Cr distribution

Existing Data for Sr.Cr were as the following: (90%) for (0.30-1.49 mg/dl), (2.7%) for (1.50-1.9 mg/dl) and (7.3%) for (2.0 mg/dl and above). The Sr.Cr distribution of the sample is represented in [Table 12] and graphically illustrated in [Figure 7]

[Table 12] Sr.Cr distribution		
	Frequency	(%) Percent
0.30-1.49 mg/dl	135	90%
1.50-1.9 mg/dl	4	2.7%
2.0 mg/dl and above	11	7.3%
Total	150	100.0%

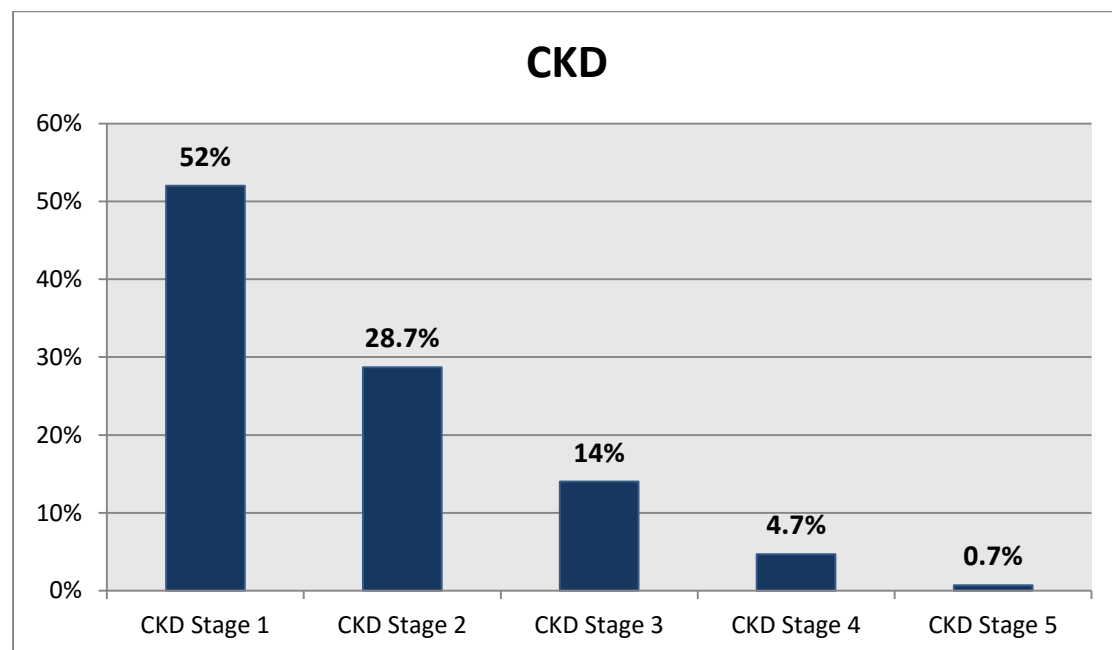


[Figure 7] Sr.Cr Distribution

4.5. CKD distribution

Based on GFR category 150 out- patients were screened for chronic kidney disease stages and the results were as followed. The CKD distribution of the sample is represented in [Table 13] and graphically illustrated in [Figure 8]

[Table 13] CKD according to GFR distribution		
	Frequency	(%) Percent
CKD Stage 1	78	52%
CKD Stage 2	43	28.7%
CKD Stage 3	21	14%
CKD Stage 4	7	4.7%
CKD Stage 5	1	0.7%
Total	150	100.0%

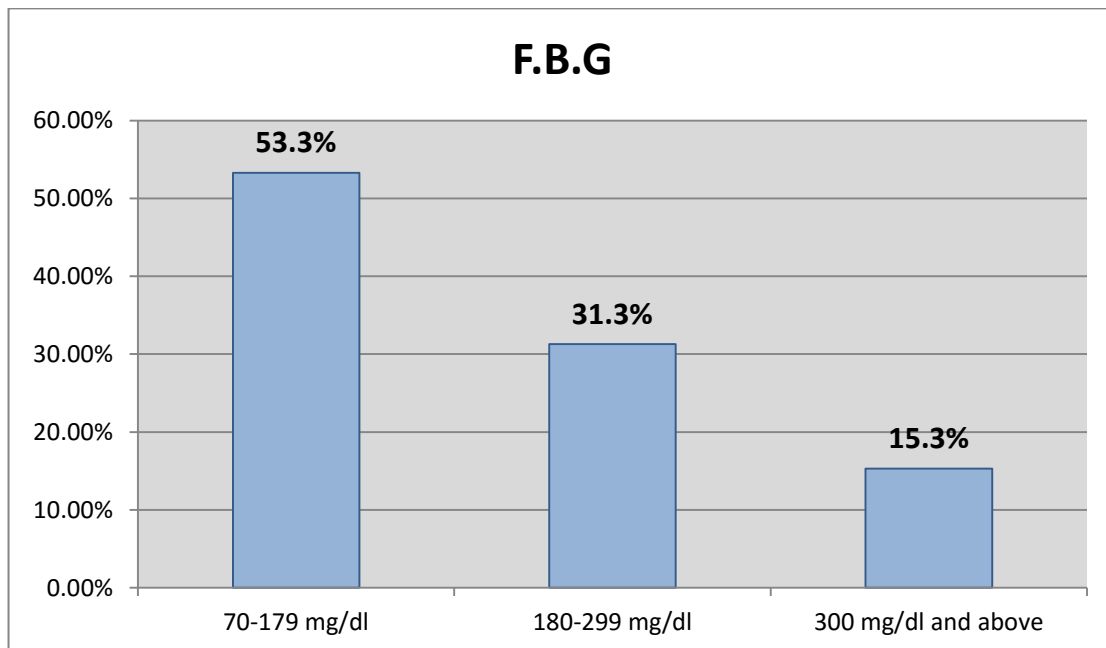


[Figure 8] CKD Distribution

4.6.FBG distribution

When were taken and follow the existing cases found that F.B.G of the patients involved varied from 72 to 622 md/dl, FBG groups were categorized into three: (70-180 mg/dl) , (181 - 299 mg/d) .And (300 mg/dl and above). The F.B.G distribution of the sample is represented in [Table 14] and graphically illustrated in [Figure 9]

[Table 14] FBG distribution		
	Frequency	(%) Percent
70-180 mg/dl	80	53.3%
181 - 299 mg/dl	47	31.3%
300 mg/dl and above	23	15.3%
Total	150	100.0%

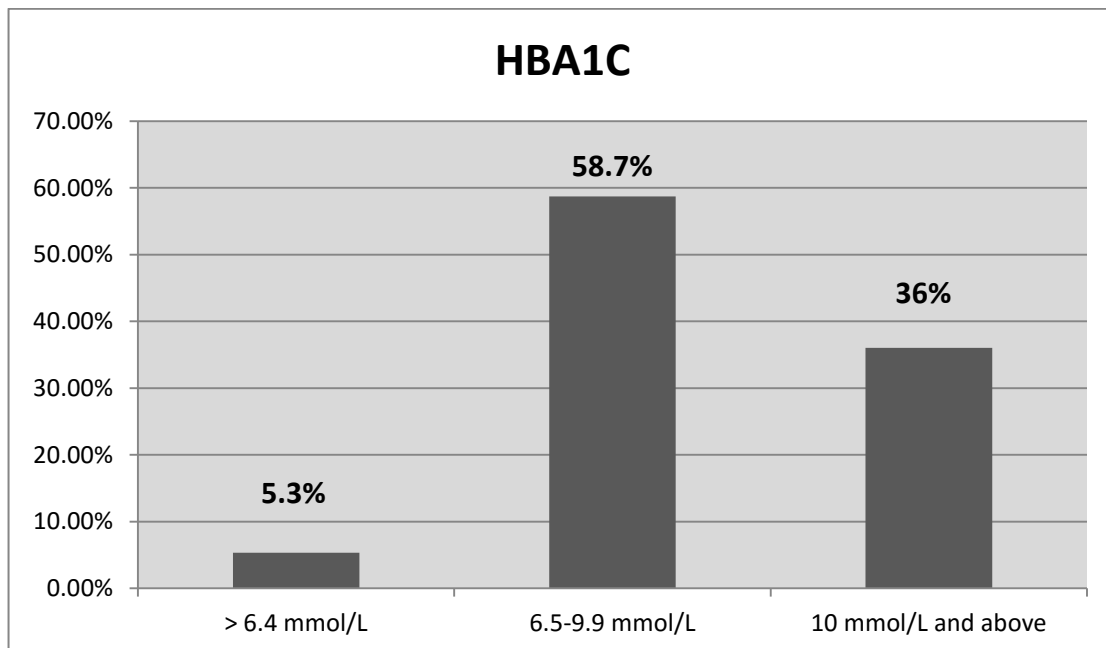


[Figure 9] FBG Distribution

4.7.HBA1C distribution

Distribute HBA1C ranged between 5.7 –14.5 mmol / L . Where 8 (5.3%) of total patients HBA1C between (less than 6.4 mmol / L), 88 (58.7%) HBA1C between (6.5 – 9.9 mmol / L),and 54 (36%) HBA1C (10 mmol / L and above) . The HBA1C distribution of the sample is represented in [Table 15] and graphically illustrated in [Figure 10]

[Table 15] HBA1C distribution		
	Frequency	(%) Percent
Less than 6.4 mmol/L	8	5.3%
6.5 - 9.9 mmol/L	88	58.7%
10 mmol/L and above	54	36%
Total	150	100.0%

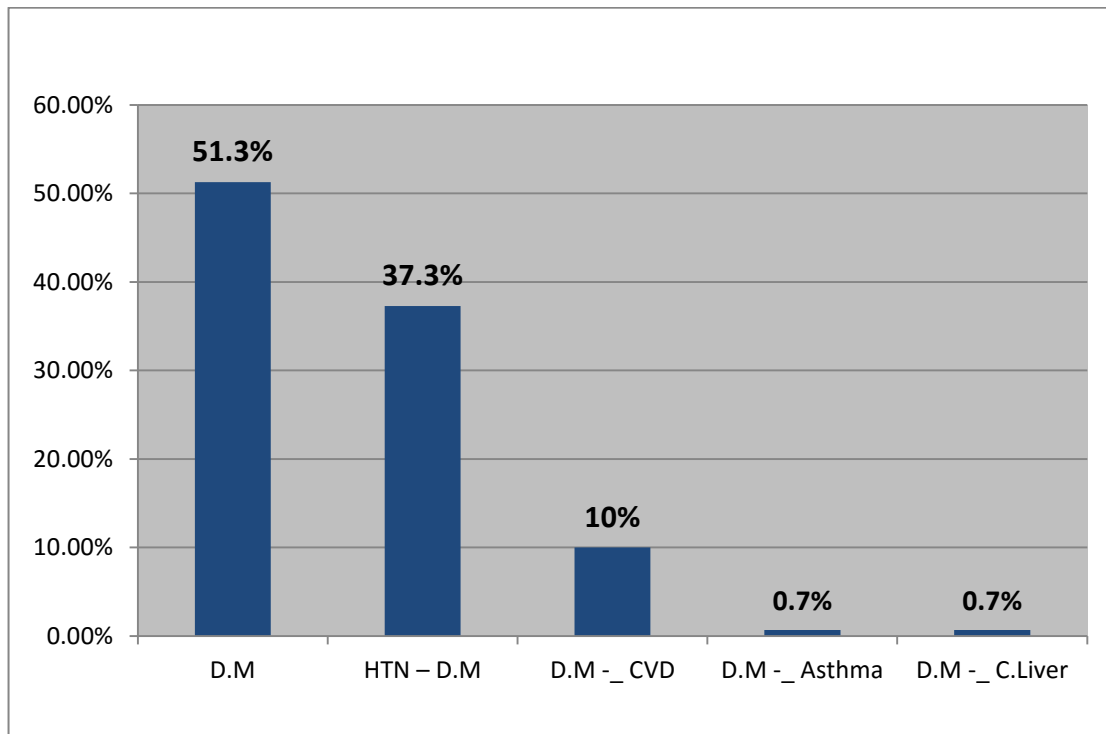


[Figure 10] HBA1C Distribution

4.8.Chronic Disease distribution

The major morbidity pattern Diabetes mellitus 51.3%, which were the most.And 37.3% of morbidity included HTN and CVD. The Chronic Disease distribution of the sample is represented in [Table 16] and graphically illustrated in [Figure 11]

[Table 16] CD distribution		
	Frequency	(%) Percent
D.M	77	51.3%
HTN – D.M	56	37.3%
D.M _ CVD	15	10%
D.M _ Asthma	1	0.7%
D.M _ C.Liver	1	0.7%
Total	150	100.0%

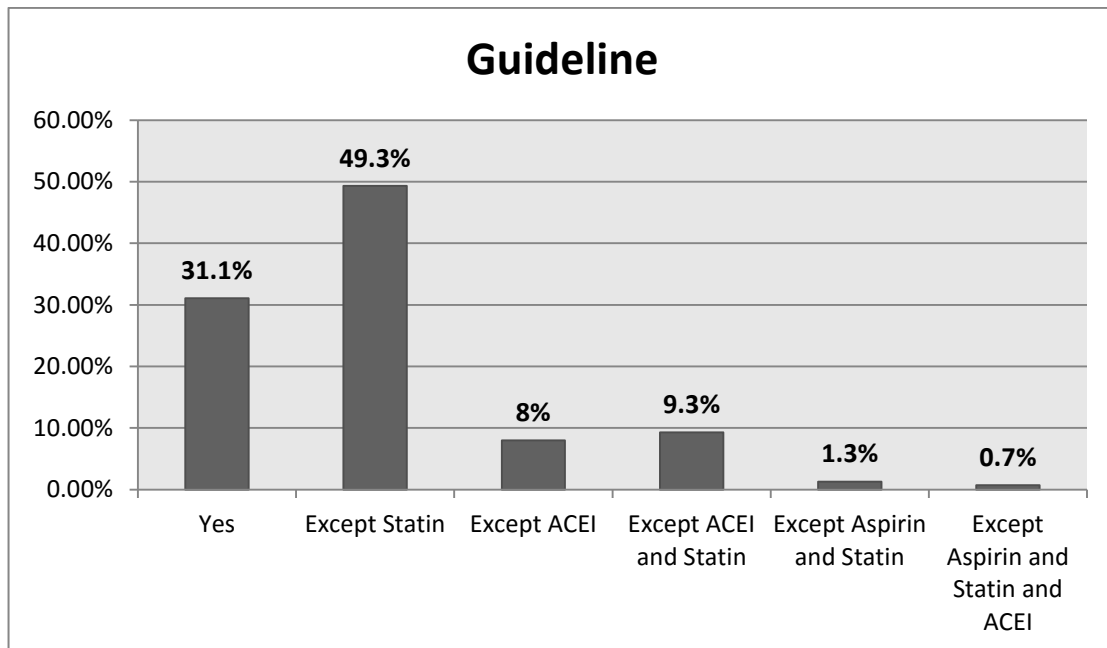


[Figure 11] Chronic Disease Distribution

4.9. According to Guideline distribution

On guideline 2021 to all 150 prescription, it had been found that 47 patients yes and were followed accord to guideline . The According to Guideline distribution of the sample is represented in [Table 17] and graphically illustrated in [Figure 12]

[Table 17] Guideline distribution		
	Frequency	(%) Percent
Yes	47	31.3%
Except Statin	74	49.3%
Except ACEI	12	8%
Except ACEI and Statin	14	9.3%
Except Aspirin and Statin	2	1.3%
Except Aspirin and Statin and ACEI	1	0.7%
Total	150	100.0%

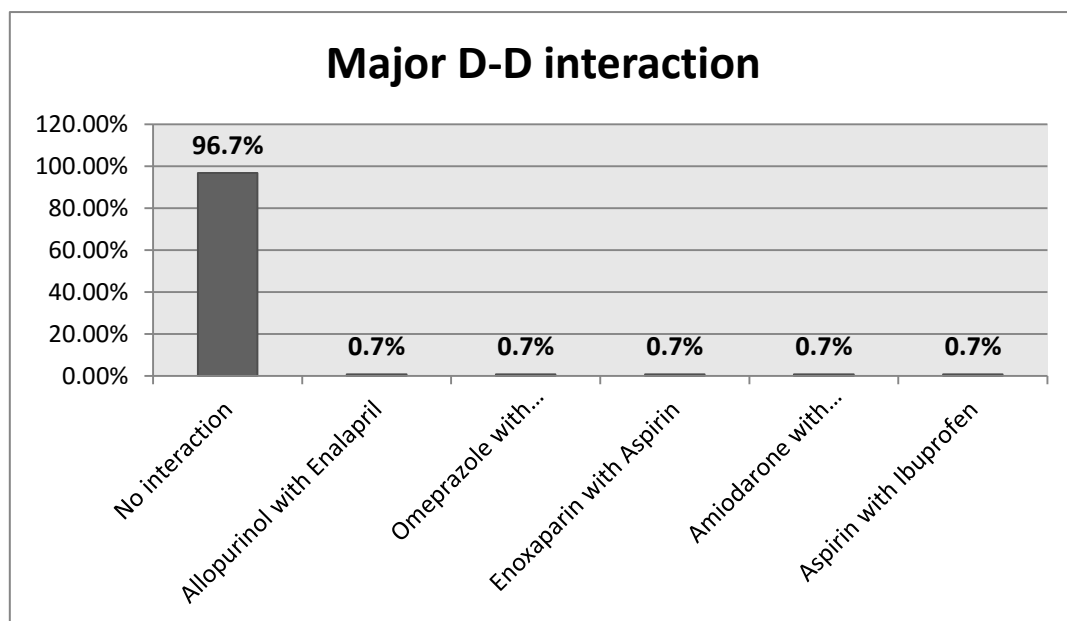


[Figure 12] Guideline Distribution

4.10. Major D-D interaction distribution

The results also revealed that 145 (96.7%) of patients had no major drug –drug interaction on discharge. The Major D-D interaction distribution of the sample is represented in [Table 18] and graphically illustrated in [Figure 13]

[Table 18] Major D-D interaction distribution		
	Frequency	(%) Percent
No interaction	145	96.7%
Allopurinol with Enalapril	1	0.7%
Omeprazole with Clopidogrel	1	0.7%
Enoxaparin with Aspirin	1	0.7%
Amiodarone with Ondansetron	1	0.7%
Aspirin with Ibuprofen	1	0.7%
Total	150	100.0%



[Figure 13] Major D-D interaction Distribution

Chapter-V

5. Discussion:

This is the first Yemeni study and one of the few global and international studies that evaluates of medications use in discharge patients with type II D.M based on the latest version of Guideline ^(140,141).

It was found that Lipid profile of the patients in private hospital which majority were Non-available and the remaining were Available[Table 11].

For the patients in the study fasting blood glucose (F.B.G) minimum range were (75 mg / dl). And maximum range were (622 mg /dl).

In this study, the presence of HBA1C,minimum range were (5.7 mmol / L). And maximum range were (14.5 mmol / L).

In this study, the presence of certain chronic conditions. The most common morbidity resulting in hospitalization was HTN and CVD [Table 16].

For patients in this study major drug-drug interactions on discharge as mentioned in [Table 18].In drug-drug interactions the majority were 145 (96.7%) of patients with No drug-drug interaction,1 (0.7%) were interaction between Omeprazole and Clopidogrel where Omeprazole decreases effects of clopidogrel by affecting hepatic enzyme CYP2C19 metabolism so clopidogrel efficacy may be reduced.

The prevalence of drugs used based on guideline in private hospital were (49.3%) except statin,(31.3%) yes to following according to guideline, (9.3%) were Except ACEI and with Statin. And (8%) were Except ACEI. [Table 17].

5.1.Limitations of the study:

The study is subjected to some limitations. One of the study limitations is that not all recommendation of guideline are available in the hospital formulary. Also, this study is done over one hospital only, one department and the study duration was short so, the results may be not representative of all T2DM in Yemen .

This study only used guideline as the tool for evaluation medications used in discharged patients with type II D.M.

Chapter-VI

6. Conclusion and Recommendation

6.1. Conclusion:

From the results of the present study, it could be concluded that:

- Discharge patients with T2DM is more prevalent in male patients than female patients.
- Discharge patients with T2DM is more prevalent in patients over 40 years of age.
- Discharge patients with T2DM have a deficiency in lipid management.
- The clinical outcomes of discharge patient of T2DM not acceptable to some extent with the recommendation of ADA guideline.
- There are a very small percentage of major drug-drug interaction for discharge patients with T2DM.

6.2. Recommendations:

According to the results obtained in this work, the following recommendations are proposed:

- The studies should be done on all departments of Yemen's hospitals.
- Physicians should be aware and given more attention during prescribing of drugs.
- Clinical pharmacists should be present in all branches of the hospitals in order to correct any errors.

Chapter VII

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الخلاصة

الموضوع: إدارة النوع الثاني من مرض السكري يكون معقد ويتطلب الرعاية الصحية المستمرة بواسطة أعضاء الرعاية الصحية و الأخذ بالاعتبار تأثيرات رعاية المريض لنفسه . الصيدلي السريري لديه دور مهم في فريق الرعاية الصحية في إدارة العلاج وتعزيز توعية المريض و إزالة المشاكل المتعلقة بالدواء. هذي الدراسة تهدف أيضا إلى لفت الانتباه لأهمية الصيدلة السريرية في التقييم الدوري لمشاكل الادوية للنوع الثاني لمرض السكري للمرضى الخارجين من المستشفى .

الطريقة: الدراسة عبارة عن دراسة سريرية سابقة نفذة على المرضى الخارجين من المستشفى لمرضى النوع الثاني لمرض السكري في مستشفى خاص بأمانة العاصمة صنعاء في الفترة ما بين ال 4 من ديسمبر 2021 حتى ال 4 من يناير 2022.

النتائج: تمت دراسة 150 حالة مشخصة من النوع الثاني لمرض السكري ، بلغ عدد المرضى الذكور 87(58.0%) ، والمرضى الإناث 63(42.0%) تراوحت أعمار المرضى من النوع الثاني لمرض السكري بين 20 و 82 سنة، أظهرت نتائج الدراسة الحالية أن معظم مرضى النوع الثاني لمرض السكري تتراوح أعمارهم فوق 41 سنة بنسبة (92.0%) . النتائج المخبرية لملف الدهون للمرضى كانت على ثلاث فئات: نتائج طبيعية 29(19.3%) ، نتائج غير طبيعية 51(34.0%) ، نتائج غير متوفرة 70(46.7%) . تراوحت النتائج المخبرية لفحص سكر الدم للمرضى الصائمين (FBG) بين حد أدنى (75mg/dl) وحد أعلى (622mg/dl) .وتراوح أيضا نتائج فحص HBA1C بين حد أدنى(5.7mmol/L) وحد أعلى (14.5mmol/L) . معظم مرضى النوع الثاني من مرض السكري كانوا بدون أي أمراض مزمنة مصاحبة 77(51.3%) ، والمرضى الذي كانوا يعانون من مرض ارتفاع ضغط الدم 56(37.3%) ، والمرضى الذي كانوا يعانون من أمراض القلب الوعائية 15(10%). غالبية مرضى النوع الثاني من مرض السكري كانوا بدون أي تداخلات دوائية خطيرة 145(96.7%) . وفقا لتوصيات الجمعية الامريكية لمرضى السكري(ADA) لعام 2022 كانت نتائج الدراسة كتالي: 47(31.3%) من المرضى متوافقين مع التوصيات و النسبة الاكبر 74(49.3%) بدون توصيات أخذ أدوية خفض الدهون(statin) و بنسبة أقل 12(8.0%) بدون توصيات أخذ دواء ال ACEI لخفض ارتفاع ضغط الدم ، و 14(9.3%) بدون توصيات أخذ ال ACEI و statin.

الاستنتاج: وفقا لنتائج هذي الدراسة فإن النتائج السريرية للمرضى الخارجين من المستشفى لمرضى النوع الثاني من مرض السكري غير متوافقة الى حدما مع توصيات الجمعية الامريكية لمرضى السكري (ADA)، وهذا يدل على أهمية تفعيل دور الصيدلي السريري لتحسين النتائج السريرية للمرضى .



الجمهورية اليمنية

وزارة التعليم العالي والبحث العلمي

جامعة ٢١ سبتمبر للعلوم الطبية
والتطبيقية

كلية الصيدلة السريرية

تقييم المرضى الخارجين من المستشفى مع مرض السكري النوع الثاني بالاعتماد على الهدف العلاجي
في مستشفى خاص في صنعاء في اليمن

مقدم من

محمد عبدالرحمن المعمري	زكريا يحيى محمد الشطبي
محمد عبدالباسط احمد المريسي	علي إبراهيم محمد ابودنيا
محمد عبداللطيف محمد الجمالي	علامة محمد احمد السيد
موسى مصلح محمد الوجبة	نصر محمد علي مشرح
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تحت إشراف:

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استاذ مشارك – الصيدلة السريرية و المعالجة

رئيس قسم الصيدلة السريرية ، جامعة سباء

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