COST OF ILLNESS, HEALTH-RELATED QUALITY OF LIFE AND COST-EFFECTIVENESS ANALYSIS OF PHARMACIST-LED LIFESTYLE INTERVENTION AMONG DIABETES POPULATION IN PAKISTAN

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UNIVERSITI SAINS MALAYSIA

2024

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by

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Thesis submitted in fulfilment of the requirements
for the degree of
Doctor of Philosophy

April 2024

ACKNOWLEDGEMENT

I want to thank Allah, my Lord, the All-Knowing, the Almighty, the most merciful and the compassionate. I thank Allah Almighty for giving me the inspiration, patience, time, and strength to finish this work.

I wish to extend my sincerest appreciation to the individuals who have contributed towards the successful completion of this work. I am particularly grateful to **Dr. Ong Siew Chin**, my primary supervisor, whose unwavering guidance, profound insights, and unwavering support have been instrumental in ensuring the success of this endeavor. Her mentorship has been invaluable, significantly impacting the outcome of this research and deepening my understanding of the subject matter.

I extend my gratitude to **Prof. Dr Zaheer ud Din Babar**, the co-supervisor. His thorough guidance, insightful suggestions, and scholarly contributions have immensely enhanced the quality and depth of this thesis. His dedication to academic excellence has been a constant source of inspiration.

I am deeply indebted to **Prof. Dr. Muhammad Fawaad Rasool** and **Dr. Muhammad Umar Wahab**, the field supervisor and mentor. Their expertise, encouragement, and thoughtful critiques have been integral to refining the scope and direction of this work. Their mentorship has been a guiding light that has helped me navigate the complexities of my research area.

To my mother, sister, and brother, I am profoundly thankful for their unwavering belief in me. Their encouragement, patience, and sacrifices have been the foundation upon which I've built my academic pursuits.

I reserve a special place of gratitude for my wife. Her boundless patience, unyielding support, and unwavering belief in my abilities have driven my accomplishments. Her courage and understanding sustained me through the challenges of this project.

Lastly, I am grateful to all those who have been a part of my academic journey, providing insights, encouragement, and a helping hand along the way.

In their collective support, I find the strength and motivation to overcome obstacles and reach new heights. My gratitude knows no bounds.

Thank you.

MUHAMMAD DAOUD BUTT

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LIST OF ABBREVIATIONS

ADA	American Diabetes Association
ADA	American Diabetes Association
AFR	African
BGL	Blood Glucose Level
BIDE	Baqai Institute of Diabetes and Endocrinology
BMI	Body Mass Index
CDA	Canadian Diabetes Association
CG	Control Gorup
DASH	Dietary Approaches to Stop Hypertension
DHQ	District Headquarters Hospitals
DIPSI	Diabetes in Pregnancy Society of India
DKA	Diabetic Ketoacidosis
DM	Diabetes Mellitus
DPP	Diabetes Prevention Program
DPP-4	Dipeptidyl Peptidase-4
DSME	Diabetes Self-management Education
EASD	European Association for the Study of Diabetes
EUR	European
FATA	Federally Administered Tribal Areas
FIGO	International Federation of Gynaecology and Obstetrics
GADAs	Glutamic Acid Decarboxylase Autoantibodies
GCT	Glucose Challenge Test
GLP-1 RAs	Glucagon-Like Peptide-1 Receptor Agonists
HbA1c	Glycated Hemoglobin

HDL	High-Density Lipoprotein
HIC	High Income Countries
HIP	Hyperglycaemia in pregnancy.
HLA	Human Leukocyte Antigen
HRQoL	Health-Related Quality of Life
IAAs	Insulin Autoantibodies
IADPSG	International Association of the Diabetes and Pregnancy Study Groups
ICAs	Islet Cell Autoantibodies
IDDM	Insulin-Dependent Diabetes Mellitus
IDF	International Diabetes Federation
IFG	Impaired fasting glucose
IG	Interventional Group
IGT	Impaired glucose tolerance
INS	Insulin Gene
KPK	Khyber Pakhtunkhwa
LADA	Latent Autoimmune Diabetes in Adults
LDL	Low-Density Lipoprotein
LHVs	Lady Health Visitors
LMIC	Low Middle-Income Countries
MCHCs	Maternity & Child Welfare Centres
MCHs	Mother and Child Health Centers
MENA	Middle East and North Africa
mg/dL	Milligram per Decilitres
MODY	Maturity Onset Diabetes Of The Young
NAC	North America and Caribbean

NDDG	National Diabetes Data Group
NICE	National Institute for Clinical Excellence
NIDDM	Non-Insulin-Dependent Diabetes Mellitus
OGTT	Oral Glucose Tolerance Test
RCT	Randomized Controlled Trial
RHCs	Rural Health Centres
SGLT-2	Sodium-Glucose Cotransporter-2
T.B	Tuberculosis
T1DM	Type 1 Diabetes
T2DM	Type 2 Diabetes
THQ	Tehsil Headquarters Hospitals
USD	United States Dollar
WC	Waist Circumference
WHO	World Health Organization
WHR	Waist-To-Hip Ratio
WP	Western Pacific
WTP	Willingness to Pay

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KOS SAKIT, KUALITI HIDUP BERKAITAN KESIHATAN DAN ANALISIS KEBERKESANAN KOS INTERVENSI GAYA HIDUP LED AHLI FARMASI DALAM KALANGAN PENDUDUK DIABETES DI PAKISTAN

ABSTRAK

Diabetes mellitus adalah kebimbangan kesihatan awam yang semakin meningkat di Pakistan, mengenakan beban ekonomi yang besar dan menjejaskan kesihatan individu secara negatif. Intervensi gaya hidup yang diterajui ahli farmasi mungkin menguruskan diabetes, tetapi keberkesanan kosnya di Pakistan tidak diketahui. Kajian ini bertujuan untuk menilai kos Penyakit Diabetes, HRQoL, dan keberkesanan kos rawatan gaya hidup yang diterajui ahli farmasi. Lebih 12 bulan, analisis ekonomi yang meluas dari segi sosial telah dilakukan. Kos kajian penyakit meliputi kos pengurusan diabetes langsung, bukan perubatan dan tidak langsung. Kos penyakit masyarakat telah dikira. Kajian kuantitatif menilai HRQoL dengan EQ-5D-5L dan kesusahan khusus diabetes dengan DAI-10. Tingkah laku ubat dan pengurusan diri telah diperiksa menggunakan MDKT dan DSMQ. Percubaan terkawal rawak meneliti pendidikan diabetes yang diketuai oleh ahli farmasi. Untuk mengira keberkesanan kos tambahan, model analisis keputusan membandingkan perubahan gaya hidup yang diterajui ahli farmasi kepada rawatan standard. Klinik Pesakit Luar Diabetes Pakistan menyediakan 1,839 pesakit kencing manis untuk kajian itu. Tiga daerah telah dipilih dari setiap wilayah, kemudian dari daerah ini hanya bandar metropolitan dipilih, pendekatan persampelan berkelompok digunakan dan 150 peserta telah dimasukkan dari setiap daerah. Dalam Fasa 1 lebih 1,839 pesakit kencing manis klinik pesakit luar Pakistan telah disiasat. Yang membimbangkan, beberapa pesakit mempunyai gula darah yang tidak terkawal, memerlukan rawatan yang lebih

baik. Jumlah kos tahunan penjagaan diabetes ialah USD 740.1. Kos meliputi kos pengurusan diabetes langsung, bukan perubatan dan tidak langsung. Penghospitalan dan ubat-ubatan menyumbang sebahagian besar daripada perbelanjaan langsung USD 646.7. Pengurusan diabetes adalah 1.67% daripada KDNK Pakistan. Dalam Fasa 2 kajian majoriti peserta mempunyai profil demografi bandar dengan purata umur 48±12.4 tahun, kebanyakannya perempuan. Secara amnya, 60.1% pesakit mempunyai gula darah puasa yang tidak terkawal dan 66.5% gula darah rawak. Pesakit kelihatan kurang pendidikan untuk memahami terapi diabetes dan penjagaan diri. 52.1% pesakit mempunyai glukosa darah yang tidak terkawal walaupun mengambil 5.08 ubat, menggariskan keperluan untuk pematuhan dan pengurusan ubat yang lebih baik. Hubungan yang signifikan telah diwujudkan antara kawalan glisemik dan BMI, pengubahsuaian gaya hidup, dan penggunaan ubat ($p<0.05$). Dalam percubaan Kawalan Rawak Fasa 3 didapati tiada perbezaan yang ketara dalam jantina, umur, BMI, tabiat merokok, pendidikan, sejarah keluarga, status bekerja, tempoh diabetes, jenis terapi anti-diabetes, atau nilai min HbA1c merentas kumpulan ($p<0.05$).). Berbanding dengan kumpulan kawalan, intervensi pendidikan diabetes yang diketuai ahli farmasi selama 12 bulan menunjukkan peningkatan yang ketara pada pemakanan, gaya hidup, penjagaan kaki dan pengurusan diri. RCT mengukur pembolehubah klinikal dan kuantitatif sebelum dan selepas campur tangan. Kumpulan intervensi mengalami penurunan ketara dalam tahap HbA1c ($p<0.001$) 1.1% iaitu 3 kali lebih besar daripada kumpulan kawalan 0.26%, penurunan HbA1c secara signifikan dikaitkan dengan pengetahuan diabetes yang lebih tinggi ($p<0.01$), dan peningkatan kemahiran pengurusan diri. ($p<0.05$). Keberkesanan kos ICER berbeza mengikut parameter klinikal. Setiap peningkatan HbA1c, ICER ialah PKR 4565.20 (USD 18.1). ICER serupa PKR 292.99 (USD 1.16) seunit peningkatan dilihat dalam bacaan glukosa

darah rawak. Kajian itu menandakan keperluan untuk merasionalkan pendekatan pengurusan diabetes untuk meningkatkan kawalan glisemik dalam pesakit diabetes Jenis 2 di Pakistan. Ia juga menekankan keperluan untuk penglibatan Ahli Farmasi dalam pasukan Pelbagai Disiplin untuk pengurusan diabetes. Di samping itu adalah potensi besar untuk program pendidikan Awam yang boleh menjadi penting bagi penghidap diabetes yang mempunyai pengetahuan yang rendah tentang pengurusan diabetes. Walaupun pelbagai rejimen ubat, ramai pesakit bergelut dengan glukosa darah yang tidak terkawal, menekankan kepentingan pematuhan dan terapi peribadi. Pakistan memerlukan pelan pengurusan diabetes yang komprehensif yang menyepadukan pendidikan, kepatuhan, dan terapi yang disesuaikan untuk meningkatkan hasil dan mengurangkan beban penyakit. Intervensi pendidikan diabetes terutamanya meningkatkan hasil klinikal dan HRQoL. Analisis keberkesanan kos memberikan pandangan yang berharga untuk pembuat keputusan penjagaan kesihatan.

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ABSTRACT

Diabetes mellitus is a growing public health concern in Pakistan, imposing a substantial economic burden and negatively affected individuals' health. Pharmacist-led lifestyle interventions may manage diabetes, but their cost-effectiveness in Pakistan is unknown. This study aims to evaluates Diabetes cost of Illness, HRQoL, and pharmacist-led lifestyle treatment cost-effectiveness. Over 12 months, a socially extensive economic analysis was done. The cost of illness study covered direct, non-medical, and indirect diabetes management costs. The societal cost of illness was calculated. The quantitative study assessed HRQoL with the EQ-5D-5L and diabetes-specific distress with the DAI-10. Medication behavior and self-management were examined using the MDKT and DSMQ. A randomized controlled trial examined pharmacist-led diabetes education. To calculate incremental cost-effectiveness, a decision-analytic model compared pharmacist-led lifestyle changes to standard treatment. Pakistani Diabetes Outpatient Clinics provided 1,839 diabetics for the study. Three districts were selected from each province, afterwards from these districts only metropolitan cities were selected, clustered sampling approach was used and 150 participants were included from each districts. In Phase 1 over 1,839 Pakistani outpatient clinic diabetic patients were investigated. Alarmingly, several patients had uncontrolled blood sugar, requiring improved treatment. The annual total cost of diabetes care was USD 740.1. The cost covered direct, non-medical, and indirect diabetes management costs. Hospitalization and medication accounted for a significant

proportion of direct expenditures USD 646.7. Diabetes management was 1.67% of Pakistan's GDP. In the Phase 2 of the study majority of participants were having urban demographic profile with an average age of 48±12.4 years, predominantly female. Concerningly, 60.1% of patients had uncontrolled fasting blood sugar and 66.5% random blood sugar. Patients appear to lack the education to understand diabetic therapy and self-care. 52.1% of patients had uncontrolled blood glucose despite taking 5.08 medications, underlining the need for better drug adherence and management. Significant relationships were established between glycemic control and BMI, lifestyle modifications, and medication usage ($p<0.05$). In the Phase 3 Randomized Control trial it was observed no significant differences in gender, age, BMI, smoking habits, education, family history, working status, diabetes duration, anti-diabetic therapy types, or mean HbA1c values across groups ($p<0.05$). Compared to the control group, the 12-month pharmacist-led diabetes education intervention demonstrated significant improvement on nutrition, lifestyle, foot care, and self-management. The RCT measured clinical and quantitative variables pre-and post-intervention. The intervention group experienced significant decreases in HbA1c levels ($p<0.001$) 1.1% which is 3 times greater than the control group 0.26%, drop in HbA1c was significantly associated with higher diabetes knowledge ($p<0.01$), and improved self-management skills ($p<0.05$). The cost-effectiveness of ICERs varied by clinical parameter. Per HbA1c improvement, ICER was PKR 4565.20 (USD 18.1). A similar ICER of PKR 292.99 (USD 1.16) per unit improvement was seen in random blood glucose readings. The study signifies the need for rationalizing the diabetes management approach to improved glycemic control in Type 2 diabetes patients in Pakistan. It also highlighted the need for the involvement of Pharmacist in the Multidisciplinary team for diabetes management. Alongside the is a huge potential for Public education programs which

could be vital for people living with diabetes having low knowledge about diabetes management. Despite diverse drug regimens, many patients struggle with uncontrolled blood glucose, emphasizing the importance of adherence and personalized therapy. Pakistan requires a comprehensive diabetes management plan integrating education, adherence, and tailored therapy to enhance outcomes and reduce the disease burden. The diabetes education intervention notably improved clinical outcomes and HRQoL. Cost-effectiveness analysis provided valuable insights for healthcare decision-makers.

CHAPTER 1

INTRODUCTION

Diabetes is a chronic metabolic disorder characterized by elevated blood glucose levels resulting from defects in insulin secretion, insulin action, or both. There are different types of diabetes, including type 1 diabetes (T1DM), type 2 diabetes (T2DM), gestational diabetes, and other less common forms. T1DM is an autoimmune condition where the body's immune system mistakenly attacks and destroys the insulin-producing cells in the pancreas. T2DM is characterized by insulin resistance and impaired insulin secretion, often associated with lifestyle factors such as obesity and physical inactivity. Gestational diabetes occurs during pregnancy and usually resolves after childbirth (Petersmann, Müller-Wieland et al. 2019).

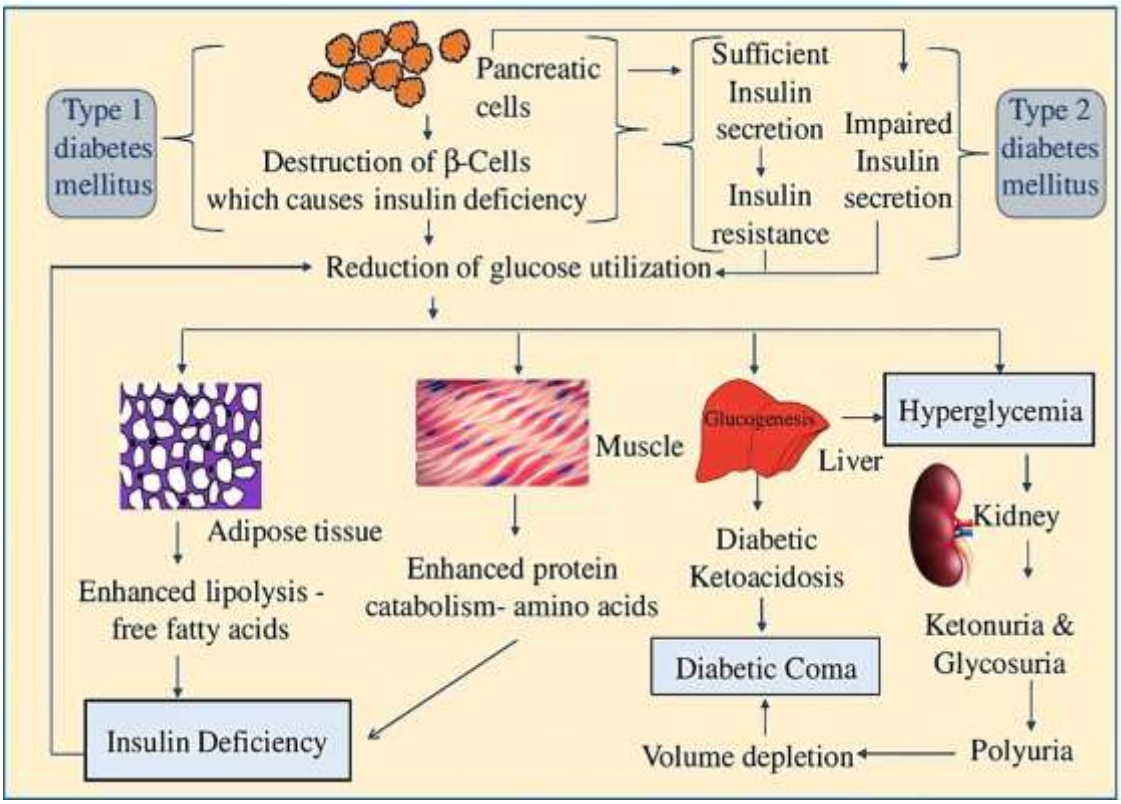


Figure 1.1 Pathophysiology of Diabetes Mellitus

1.1 Type 1 Diabetes Mellitus

An autoimmune illness, type 1 diabetes mellitus (T1DM) or insulin-dependent diabetes mellitus (IDDM) accounts for 5-10% of all diabetes cases. The condition involves T-cells destroying pancreatic β-cells, resulting in insulin insufficiency and hyperglycemia. Genetic and environmental factors influence immune-mediated destruction (Katsarou, Gudbjörnsdottir et al. 2017).

Individuals progress differently with T1DM. Rapid β-cell loss in infants and teenagers can lead to diabetic ketoacidosis (DKA) as the initial symptom of the condition. Others develop the condition slowly, with minor fasting blood glucose rises. Physiological stress from infections or other illnesses can cause severe hyperglycemia or ketoacidosis. Adults with T1DM may initially have some β-cell activity but become insulin-dependent when insulin insufficiency worsens (Dai BD, Huang et al. 2022).

T1DM is characterized by autoantibodies. Glutamic acid decarboxylase, islet cell, and insulin autoantibodies are linked to β-cell death. T1DM autoantibodies are mostly GADAs, then ICAs. IAAs are more common in infants and young children at diagnosis and can impair insulin action in insulin-treated individuals (Jahromi and Al-Ozairi 2019).

In adults with late-onset T1DM, autoantibodies are essential for diagnosis. LADA, or late-onset autoimmune diabetes, can mimic type 2 diabetes but is detected by autoantibodies. LADA is the most frequent adult-onset autoimmune diabetes (Keshavarzi, Noveiry et al. 2022).

In addition to β-cell loss, T1DM is linked to autoimmune disorders such myasthenia gravis, Addison's disease, celiac disease, vitiligo, and thyroid problems.

T1DM and other autoimmune illnesses are linked by HLA genes, particularly HLA-DR3 and HLA-DR4.

The insulin gene (INS) region and other non-HLA genes contribute to T1DM risk, although HLA haplotypes and INS gene variants are important genetic determinants. Few people with T1DM are obese at diagnosis (Ilonen, Lempainen et al. 2019).

1.1.1 Diagnosis of Type 1 Diabetes

Type 1 diabetes, diagnosed in children, adolescents, and young adults, has particular diagnostic criteria to reliably identify it. Hyperglycemia symptoms like extreme thirst, frequent urination, and unexplained weight loss are combined with a random plasma glucose level of 200 mg/dL (11.1 mmol/L) or greater. A fasting plasma glucose level of 126 mg/dL (7.0 mmol/L) or higher or a 2-hour plasma glucose level of 200 mg/dL (11.1 mmol/L) or higher during an oral glucose tolerance test can also confirm diagnosis. A1C levels of 6.5% (48 mmol/mol) or above are another sign. To accurately diagnose and treat type 1 diabetes, these criteria should be repeated on a different day without hyperglycemia (Kahanovitz, Sluss et al. 2017, Balaji, Duraisamy et al. 2019).

1.1.1(a) Complications associated with T1DM.

Diabetic ketoacidosis (DKA) is a severe condition characterized by high blood glucose levels, ketone production, and metabolic acidosis. Hypoglycemia, on the other hand, involves low blood glucose levels due to excessive insulin or inadequate carbohydrate intake. Long-term complications of diabetes include damage to small blood vessels in the eyes, kidneys, and nerves (microvascular complications), as well as an increased

risk of heart disease, stroke, and peripheral artery disease (macrovascular complications). These complications highlight the critical need for vigilant management and comprehensive care to mitigate both immediate and long-term risks associated with diabetes(Bhattarai, Godsland et al. 2019).

1.2 Type 2 Diabetes Mellitus

Type 2 diabetes mellitus (T2DM), non-insulin-dependent diabetes mellitus (NIDDM), or adult-onset diabetes accounts for 90-95% of all diabetes cases. It is characterized by insulin resistance and β-cell dysfunction. Cells in peripheral tissues like muscle, liver, and adipose tissue become insulin resistant. To regulate blood glucose levels, β-cells initially increase insulin production, leading to hyperinsulinemia. However, β-cell activity reduces over time, causing insulin insufficiency and hyperglycemia. T2DM rarely causes DKA unless extreme stress or certain drugs are present (Gao, Yang et al. 2019).

Slow-moving T2DM is commonly undiagnosed until symptoms including weight loss, blurred eyesight, polyuria, and polydipsia occur. The complex aetiology of T2DM comprises genetic and environmental variables. Aging, obesity, family history of diabetes, physical inactivity, modern lifestyles, hypertension, dyslipidemia, and certain racial or ethnic backgrounds are risk factors. Unlike T1DM, T2DM does not involve immune-mediated pancreatic β-cell death. (Arslanian, Bacha et al. 2018).

Obesity plays a significant role in T2DM, contributing to insulin resistance and hyperglycemia. Abdominal or visceral obesity is mainly associated with T2DM. Patients with T2DM often present with cardiovascular risk factors such as hypertension and abnormal lipoprotein metabolism. T2DM is a chronic condition that can lead to various

microvascular and macrovascular complications due to prolonged hyperglycemia (Zatterale, Longo et al. 2020).

1.2.1 Diagnosis of Type 2 Diabetes

Type 2 diabetes is the most common form of diabetes and is often diagnosed in adults, although it is increasingly being diagnosed in children and adolescents. The diagnostic criteria for type 2 diabetes include:

- A fasting plasma glucose level of 126 mg/dL (7.0 mmol/L) or higher, or
- A 2-hour plasma glucose level of 200 mg/dL (11.1 mmol/L) or higher during an OGTT
- An A1C level of 6.5% (48 mmol/mol) or higher.

1.2.1(a) Complications associated with T2DM.

Type 2 diabetes poses significant risks to cardiovascular health, including heightened susceptibility to heart disease, heart attacks, strokes, and related complications. Hypertension is also prevalent among those with type 2 diabetes, exacerbating cardiovascular concerns. Moreover, dyslipidemia commonly accompanies this condition, marked by imbalanced lipid profiles that elevate LDL cholesterol and triglycerides while lowering HDL cholesterol (Viigimaa, Sachinidis et al. 2020). Prolonged hyperglycemia can lead to retinopathy, causing damage to the retina and potentially resulting in vision impairment. Additionally, diabetic nephropathy can lead to kidney damage, progressing to chronic kidney disease and end-stage renal failure. Neuropathy, affecting nerves and causing symptoms like numbness and pain, is another complication. Foot complications, stemming from nerve damage and poor

circulation, can lead to ulcers, infections, and even amputations. Furthermore, type 2 diabetes increases the risk of various other conditions, including certain cancers, sleep apnea, cognitive decline, and depression. Managing these complexities requires comprehensive care to mitigate risks and improve quality of life for individuals with type 2 diabetes (Faselis, Katsimardou et al. 2020).

*Adopted with permission from the International Diabetes Federation. IDF Diabetes Atlas, 10th edn. Brussels, Belgium: International Diabetes Federation, 2021. http://www.diabetesatlas.org

Figure 1.2 Modified diagnostic criteria for diabetes.

1.3 Gestational Diabetes

Gestational diabetes develops during pregnancy and is characterized by high blood glucose levels. If not properly managed, it can pose risks to both the mother and the baby. Women with gestational diabetes are at higher risk of developing type 2 diabetes later in life(Choudhury and Rajeswari 2021).

1.3.1 Diagnosis of Gestational Diabetes

Gestational diabetes is a type of diabetes that develops during pregnancy. The diagnostic criteria for gestational diabetes include:

Initially, a 50-gram glucose challenge test (GCT) 1-hour plasma glucose level of 180 mg/dL (10.0 mmol/L) or greater suggests gestational diabetes. If the GCT is positive, a 3-hour OGTT is done. If at least two of the following plasma glucose values are met or exceeded during the OGTT, gestational diabetes is confirmed: fasting level of 95 mg/dL (5.3 mmol/L), 1-hour level of 180 mg/dL (10.0 mmol/L), 2-hour level of 155 mg/dL (8.6 mmol/L), or 3-hour level of 140 mg/dL or higher. This diagnostic approach detects and treats gestational diabetes early to protect mother and fetal health (Rani and Begum 2016).

Table 1.1 Diagnostic criteria in studies used for estimating hyperglycaemia in pregnancy.

Criteria	Fasting		1-hour		2-hour		3-hour	
	mg/dL	mmol/L	mg/dL	mmol/L	mg/dL	mmol/L	mg/dL	mmol/L
NDDG (USA)*	105	5.9	190	10.6	165	9.2	145	8.1
Carpenter Coustan(USA)*	95	5.3	180	10	155	8.6	140	7.8
CDA	95	5.3	191	10.6	160	9	–	–
WHO 1985	140	7.8	–	–	140	7.8	–	–
WHO 1999	126	7	–	–	140	7.8	–	–
IADPSG/ADA WHO/FIGO	92	5.1	180	10	153	8.5	–	–
(DIPSI non-fasting)	–	–	–	–	–	7.8	–	–
NICE (UK)	–	5.6	–	–	–	7.8	–	–

ADA = American Diabetes Association; NDDG = National Diabetes Data Group; CDA = Canadian Diabetes Association; DIPSI = Diabetes in Pregnancy Society of India; WHO = World Health Organization; IADPSG = International Association of the Diabetes and Pregnancy Study Groups. NICE = National Institute for Clinical Excellence; FIGO = International Federation of Gynaecology and Obstetrics.

* after 50g glucose challenge test-if positive, use 100g glucose load, at least two need to be positive

1.3.2 Complications associated.

Gestational diabetes introduces several risks during pregnancy and beyond. One notable concern is the increased likelihood of needing a caesarean section for delivery. Additionally, babies born to mothers with uncontrolled gestational diabetes may develop macrosomia, characterized by larger-than-average size, potentially complicating delivery and raising the risk of birth injuries. Furthermore, infants born to mothers with gestational diabetes may experience neonatal hypoglycemia, wherein their blood glucose levels drop shortly after birth. Importantly, gestational diabetes also carries implications for the mother's future health, as women who have experienced it have a heightened risk of developing type 2 diabetes later in life. These risks underscore the importance of monitoring and managing gestational diabetes to ensure the health and well-being of both mother and child (Farahvar, Walfisch et al. 2019).

1.4 Other Specific Types

Diabetes encompasses various specific types, including those stemming from genetic defects in beta-cell function or insulin action, pancreatic diseases, endocrine disorders, drug-induced factors, and infections. Each type presents unique complications and management considerations. The World Health Organization (WHO) classifies diabetes into specific categories such as monogenic and secondary diabetes. Monogenic diabetes, caused by single gene mutations, often mimics type 1 or type 2 diabetes but requires tailored therapy and complication risk assessment. It includes forms like neonatal diabetes and maturity-onset diabetes of the young (MODY), with new subtypes continually emerging through genome-wide studies. Approximately 1.5-2.0% of all cases are attributed to monogenic diabetes, although it

is often misdiagnosed. Secondary diabetes can arise from underlying conditions listed in the WHO's recent classification, highlighting the diverse nature of diabetes and the need for individualized approaches to diagnosis and treatment (Singh, Bansal et al. 2023).

1.5 Global Prevalence of Diabetes

Diabetes is a significant global health concern, with its prevalence steadily increasing in recent years. According to the International Diabetes Federation (IDF), Atlas 1st edition published in 2000, the number of adults aged 18 years and older living with D.M. was 151 million. In IDF Atlas 10th edition 2021, the global prevalence of diabetes among adults aged 20-79 was estimated to be 10.5%, with approximately 537 million individuals living with the condition. By 2030, this number is projected to increase to 643 million (11.3% of the population), and by 2045, it is expected to reach 783 million (12.2% of the population) (Sun, Saeedi et al. 2022).

Table 1.2 Projected global adult (20–79 years) diabetes prevalence for 2021, 2030, and 2045.

At a glance	2021	2030	2045
Diabetes estimates (20-79 y)			
People with diabetes, in 1,000s	536,600	642,800	783,700
Age-adjusted comparative prevalence of diabetes, %	9.8	10.8	11.2
People with undiagnosed diabetes, in 1,000s	-	-	-
Proportion of people with undiagnosed diabetes, %	44.7	-	-
Impaired glucose tolerance (IGT) estimates (20-79 y)			
People with IGT, in 1,000s	541	623	730
Age-adjusted comparative prevalence of IGT, %	10.2	10.8	11.2
Impaired fasting glucose (IFG) estimates (20-79 y)			
People with IFG, in 1,000s	319	369.7	440.8
Age-adjusted comparative prevalence of IFG, %	5.7	6	6.3

Table 1.2 (Continued)

At a glance	2021	2030	2045
Mortality attributable to diabetes (20-79 y)			
Deaths attributable to diabetes	6,700,000	-	-
Proportion of diabetes-related deaths in people under 60 y, %	32.6	-	-
Type 1 diabetes estimates in children and adolescents			
New cases of type 1 diabetes (0-14 y), in 1,000s	108.3	-	-
New cases of type 1 diabetes (0-19 y), in 1,000s	149.5	-	-
Type 1 diabetes (0-14 y), in 1,000s	651.2	-	-
Type 1 diabetes (0-19 y), in 1,000s	1,211.90	-	-
Hyperglycaemia in pregnancy (HIP) (20-49 y)			
Live births affected by HIP	21,060,499	-	-
Prevalence of gestational diabetes mellitus (GDM), %	16.7	-	-
Live births affected by other types of diabetes first detected in pregnancy	2,112,148	-	-
Live births affected by other types of diabetes detected prior to pregnancy	2,460,478	-	-
Diabetes-related health expenditure			
Total diabetes-related health expenditure, USD million	966,000	1,027,600	1,053,700
Total diabetes-related health expenditure, ID million	1,421,852	1,549,800	1,630,100
Diabetes-related health expenditure per person, USD	1,838	-	-
Diabetes-related health expenditure per person, ID	2,707	-	-
Demographics			
Total adult population (20-79 y), in 1,000s	51,134,598	5,700,000	6,400,000
Population of children (0-14 y), in 1,000s	1,991,356	-	-
Population of children and adolescents (0-19 y), in 1,000s	2,607,712	-	-

In 2021, diabetes prevalence was notably higher in middle-income countries compared to low-income ones, with approximately 80.6% (432.7 million) of individuals with diabetes residing in these regions. Looking forward to 2045, middle-income countries are projected to experience the most significant relative increase in prevalence, followed by high-income and low-income countries (21.1% vs. 12.2% vs. 11.9% increase, respectively), with over 200 million more adults expected to have diabetes in middle-income countries alone. Among world regions, the Middle East and

North Africa (MENA) had the highest comparative prevalence at 18.1%, while Africa (AFR) had the lowest at 5.3%. Despite this, both AFR and MENA regions are projected to undergo the most significant relative growth in diabetes prevalence in the coming years(Haimanot 2022).

In terms of absolute numbers, the Western Pacific (W.P.) region currently has the highest number of individuals with diabetes, totaling 206 million. Looking ahead, the African (AFR) and Middle East and North Africa (MENA) regions are expected to experience the most significant relative growth in diabetes cases, while regions like Europe (EUR), North America and the Caribbean (NAC), and the Western Pacific (W.P.) are anticipated to have comparatively smaller increases. This data underscores the global challenge of diabetes, highlighting the need for intensified efforts in prevention, awareness, and management strategies across all regions, particularly in areas with the highest prevalence rates like Pakistan, French Polynesia, and Kuwait. Effective public health measures are essential to combatting this growing epidemic and improving outcomes for affected populations worldwide (Ogurtsova, Guariguata et al. 2022, Sun, Saeedi et al. 2022).

Table 1.3 Top 10 countries or territories for number of adults (20–79 years) with diabetes in 2021 and 2045

2021			2045		
Rank	**Country or territory**	**Comparative prevalence (%)**	**Rank**	**Country or territory**	**Comparative prevalence (%)**
1	Pakistan	30.8	1	Pakistan	33.6
2	French Polynesia	25.2	2	Kuwait	29.8
3	Kuwait	24.9	3	French Polynesia	28.2
4	New Caledonia	23.4	4	Mauritius	26.6
5	Northern Mariana Islands	23.4	5	New Caledonia	26.2

6	Nauru	23.4	6	Northern Mariana Islands	26.2
7	Marshall Islands	23.0	7	Nauru	26.2
8	Mauritius	22.6	8	Marshall Islands	26.0
9	Kiribati	22.1	9	Kiribati	24.1
10	Egypt	20.9	10	Egypt	23.4

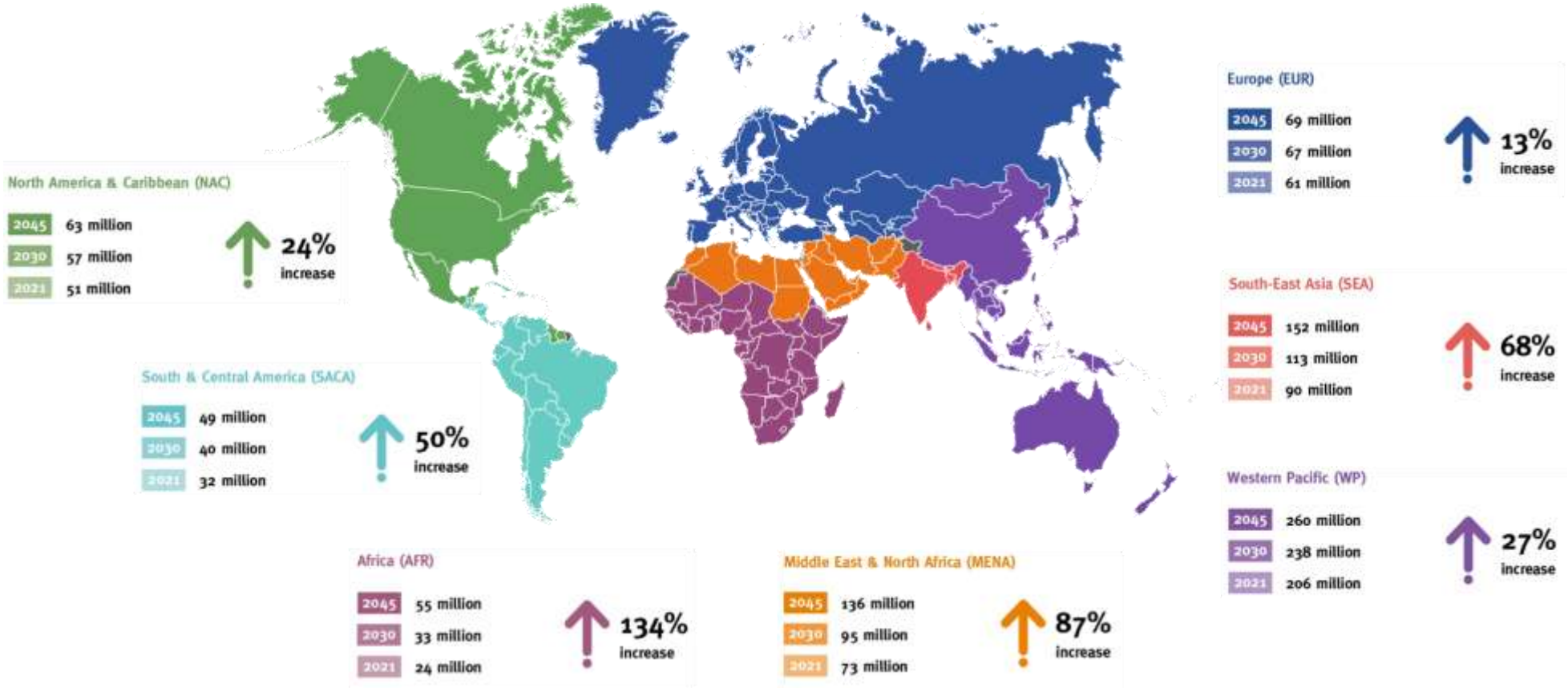
*Adopted from International Diabetes Federation. IDF Diabetes Atlas, 10th edn. Brussels, Belgium: International Diabetes Federation, 2021. http://www.diabetesatlas.org

These statistics in table 1.3 and figure1.3 highlight the urgent need for global attention and concerted efforts to combat the rising prevalence of diabetes. Strategies such as public health campaigns, improved access to healthcare, and lifestyle interventions can help reduce the burden of diabetes and its associated complications in these countries and worldwide (Sun, Saeedi et al. 2022).

1.6 Diabetes Prevalence in Pakistan

Diabetes prevalence in Pakistan is a significant public health concern, with the country experiencing a high disease burden. The latest available data suggests a considerable increase in diabetes prevalence over the years, highlighting the urgent need for prevention, early detection, and effective management strategies.

According to the International Diabetes Federation (IDF), Pakistan had an estimated diabetes prevalence of 30.8% among adults aged 20-79 years in 2021, translating to approximately 32.9 million people affected by the disease. This number is projected to rise to 42.8 million by 2045 if appropriate measures are still needed to address the issue (Wang, Li et al. 2022).



*Adopted from International Diabetes Federation. IDF Diabetes Atlas, 10th edn. Brussels, Belgium: International Diabetes Federation, 2021. http://www.diabetesatlas.org

Figure 1.3 Number of people with diabetes worldwide and per IDF Region in 2021–2045 (20–79 years)

The first community based national HbA1c study in Pakistan included 18,856 people, making it the largest in the area. The prevalence of type 2 diabetes was 16.98% (with a 95% confidence interval of 16.44 to 17.51) and prediabetes was 10.91%. This prevalence is much greater than in the sole previous nationwide survey in 1999, which used an OGTT and comprised 5,433 participants (Adnan and Aasim 2020).

Interestingly, the study accepted Basit et al.'s results of rising diabetes and prediabetes rates. Basit et al. used OGTT, while this study used HbA1c. Despite discrepancies in prevalence rates, both studies showed that diabetes and prediabetes are more common than previously thought (Basit, Fawwad et al. 2020).

The current study included working men throughout the day, making it more representative than the 1999 survey. OGTT, the gold standard for diabetes screening, is logistically difficult due to fasting and transit stability, especially in warm areas like South Asia. Direct HbA1c testing in the field helped the study overcome these issues. We also compared studies from neighbouring countries. A capillary fasting blood glucose research in India found 4% to 13.6% prevalence (Atre, Deshmukh et al. 2020). Family history, age, obesity, and socioeconomic position were shared risk factors despite methodological variances. Using capillary fasting levels, a Bangladeshi study reported 4.3% type 2 diabetes prevalence, underlining common risk factors (Akter 2023).

Pakistani regions have variable diabetes rates. Urban areas have higher prevalence than rural areas, according to several research. Diabetes is rising in metropolitan areas due to lifestyle changes, bad diets, and sedentary lifestyles (Basit, Tanveer et al. 2020).

Pakistani diabetes prevalence is also affected by age, gender, and socioeconomic position. Older persons are at higher risk for the condition. Diabetes is increasingly impacting teenagers and young adults due to lifestyle and genetic factors. Diabetes prevalence is higher in women than males. This discrepancy may be due to biological, hormonal, and gender-specific healthcare-seeking (Adnan and Aasim 2020).

The impact of diabetes in Pakistan goes beyond the individual level, as the disease imposes a significant economic burden on individuals, families, and the healthcare system. The cost of diabetes management, including medications, regular check-ups, and potential complications, can financially strain many individuals, especially those from lower socioeconomic backgrounds (Singh, Narayan et al. 2019).

Uncontrolled diabetes poses a considerable risk for complications, including cardiovascular diseases, kidney disease, neuropathy, and retinopathy. These complications can significantly affect the quality of life and increase mortality among individuals with diabetes (Lotfy, Adeghate et al. 2017).

Table 1.4 Pakistan Estimated total number of adults (20–79 years) with diabetes in 2021, 2030 and 2045.

At a glance	2021	2030	2045
Diabetes estimates (20-79 y)			
People with diabetes, in 1,000s	32,964.50	42,850.70	62,018.50
Age-adjusted comparative prevalence of diabetes, %	30.8	32.8	33.6
People with undiagnosed diabetes, in 1,000s	8,864.90	-	-
Proportion of people with undiagnosed diabetes, %	26.9	-	-
Impaired glucose tolerance (IGT) estimates (20-79 y)			
People with IGT, in 1,000s	10,573.30	13,358.80	18,727.90
Age-adjusted comparative prevalence of IGT, %	9.4	9.9	10.2

Table 1.4 (Continued)

At a glance	2021	2030	2045
Impaired fasting glucose (IFG) estimates (20-79 y)			
People with IFG, in 1,000s	2,412.40	3,007.50	4,215.40
Age-adjusted comparative prevalence of IFG, %	2.1	2.1	2.1
Mortality attributable to diabetes (20-79 y)			
Deaths attributable to diabetes	396,625.40	-	-
The proportion of diabetes-related deaths in people under 60 y, %	17.5	-	-
Type 1 diabetes estimates in children and adolescents			
New cases of type 1 diabetes (0-14 y), in 1,000s	0.8	-	-
New cases of type 1 diabetes (0-19 y), in 1,000s	1.1	-	-
Type 1 diabetes (0-14 y), in 1,000s	3.3	-	-
Type 1 diabetes (0-19 y), in 1,000s	5.6	-	-
Hyperglycaemia in pregnancy (HIP) (20-49 y)			
Live births affected by HIP	643,356.40	-	-
Prevalence of gestational diabetes mellitus (GDM), %	4	-	-
Live births affected by other types of diabetes first detected in pregnancy	153,561.80	-	-
Live births affected by other types of diabetes detected prior to pregnancy	417,724.70	-	-
Diabetes-related health expenditure			
Total diabetes-related health expenditure, USD million	2,639.90	3,271.90	4,354.50
Total diabetes-related health expenditure, ID million	10,975.30	13,602.90	18,103.50
Diabetes-related health expenditure per person, USD	80.1	99.3	132.1
Diabetes-related health expenditure per person, ID	332.9	412.7	549.2
Demographics			
Total adult population (20-79 y), in 1,000s	123,526.40	152,157.60	204,214.20
Population of children (0-14 y), in 1,000s	77,987.30	-	-
Population of children and adolescents (0-19 y), in 1,000s	100,158.20	-	-

*Adopted from International Diabetes Federation. IDF Diabetes Atlas, 10th edn. Brussels, Belgium: International Diabetes Federation, 2021. http://www.diabetesatlas.org

Policymakers, healthcare providers, and relevant stakeholders must recognize the economic impact of diabetes and work towards implementing policies and programs that ensure affordable and accessible diabetes care for all individuals in Pakistan. Investing in preventive measures, education, and comprehensive healthcare services can mitigate the burden of diabetes-related healthcare expenditure, leading to improved outcomes and better quality of life for individuals with diabetes (Basit, Riaz et al. 2015).

1.7 Economic Burden of Diabetes

Diabetes costs countries, healthcare systems, diabetics, and their families a lot. Direct diabetes costs are healthcare expenses for controlling and treating the illness. According to the International Diabetes Federation (IDF) Diabetes Atlas, global diabetes health expenditure has increased significantly. It rose 316% in 15 years from USD 232 billion in 2007 to USD 966 billion in 2021 for adults aged 20–79. The IDF expects diabetes-related health spending to climb to USD 1.03 trillion by 2030 and USD 1.05 trillion by 2045. Compared to 2021, these forecasts are up 66.4% and 9.1%. Diabetes expenditures are predicted to rise due to population expansion, aging, sex distribution, and urbanization (Sun, Saeedi et al. 2022).

North America and Caribbean (NAC) had the greatest diabetes-related health expenditure, 42.9% of the global total in 2021. It is followed by the Western Pacific (W.P.) area with USD 241.3 billion and Europe (EUR) with USD 189 billion. South and Central America (SACA), Middle East and North Africa (MENA), Africa (AFR), and South-East Asia (SEA) account for 12.5% of worldwide diabetes-related health expenditure despite a large diabetes population. NAC has the greatest diabetes-related health spending per adult with diabetes, followed by EUR, SACA, and W.P. However,

MENA, AFR, and SEA have lower diabetic health costs per person (Williams, Karuranga et al. 2020).

Diabetes accounts for 11.5% of worldwide health expenses. SACA has the greatest diabetes-related health spending (18.4%), followed by MENA (16.6%). EUR has the lowest (8.6%). Diabetes in Pakistan has a significant economic impact on individuals, families, and the healthcare system. Recent studies show that diabetes care in Pakistan is expensive. Diabetes care costs 332.0 USD per patient per year, mostly due to healthcare, pharmaceutical, and consultation costs. These prices are cheaper than those in India, China, Singapore, Iran, and the U.S (Khowaja, Khuwaja et al. 2007, Gillani, Aziz et al. 2018).

The direct cost of diabetes in Pakistan is estimated at 37.9 billion PKR, roughly 69.2% greater than the national health budget. Diabetes care costs the lowest-income households 19% of their income. Rural residents had higher direct costs than urban residents. Diabetes care costs more for people with greater socioeconomic class and longer disease duration. Complex therapies include insulin and oral hypoglycemic medications and comorbidities increased costs. Diabetes medication prices made for 60.4% of diabetes care costs (Gillani, Aziz et al. 2018).

Indirect expenditures, including productivity losses, averaged 223.20 USD per patient yearly. These costs are lesser than in other nations, yet they nevertheless add to Pakistan's diabetes cost. Comprehensive methods to reduce the economic effect of diabetes must include cost-saving measures, increasing diabetes treatment affordability and accessibility, and encouraging preventative actions to reduce disease prevalence and consequences. Pakistan's diabetes-related health spending would reach USD 1.03 trillion by 2030 and USD 1.05 trillion by 2045, according to the IDF

(Magliano, Boyko et al. 2021). These data show that diabetes prevention and management are needed to reduce the economic burden on individuals, families, and healthcare systems.

Table 1.5 Healthcare Cost of Diabetes Management

Rank	Country or Territory	Diabetes-related health expenditure (USD) per person with diabetes (20–79 years)
1	Switzerland	12,828
2	United States of America	11,779
3	Norway	11,166
4	Iceland	8,401
5	Luxembourg	8,193
6	Denmark	7,844
7	Ireland	7,843
8	Sweden	7,675
9	Germany	6,661
10	Austria	6,575

*Adopted from International Diabetes Federation. IDF Diabetes Atlas, 10th edn. Brussels, Belgium: International Diabetes Federation, 2021. http://www.diabetesatlas.org

1.8 Management of Diabetes

The management of diabetes requires a comprehensive approach that addresses glycemic control, cardiovascular risk factors, and individual patient needs. The American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) collaborate to provide evidence-based guidelines for managing diabetes.

1.8.1 Individualized Treatment Approach

Diabetes management should be tailored to the individual patient, considering their preferences, comorbidities, and socioeconomic factors. The treatment goals

should focus on achieving and maintaining glycemic control, preventing complications, and improving quality of life (Chung, Erion et al. 2020).

1.8.2 Lifestyle Modifications

Lifestyle modifications play a crucial role in diabetes management. The ADA and EASD recommend a healthy eating pattern, such as the Mediterranean, Dietary Approaches to Stop Hypertension (DASH), or plant-based diets. These diets emphasize whole foods, fruits, vegetables, whole grains, lean proteins, and healthy fats. Regular physical activity is also recommended, aiming for at least 150 minutes of moderate-intensity aerobic activity per week, along with resistance training (Hattersley 2020, Davies, Aroda et al. 2022).

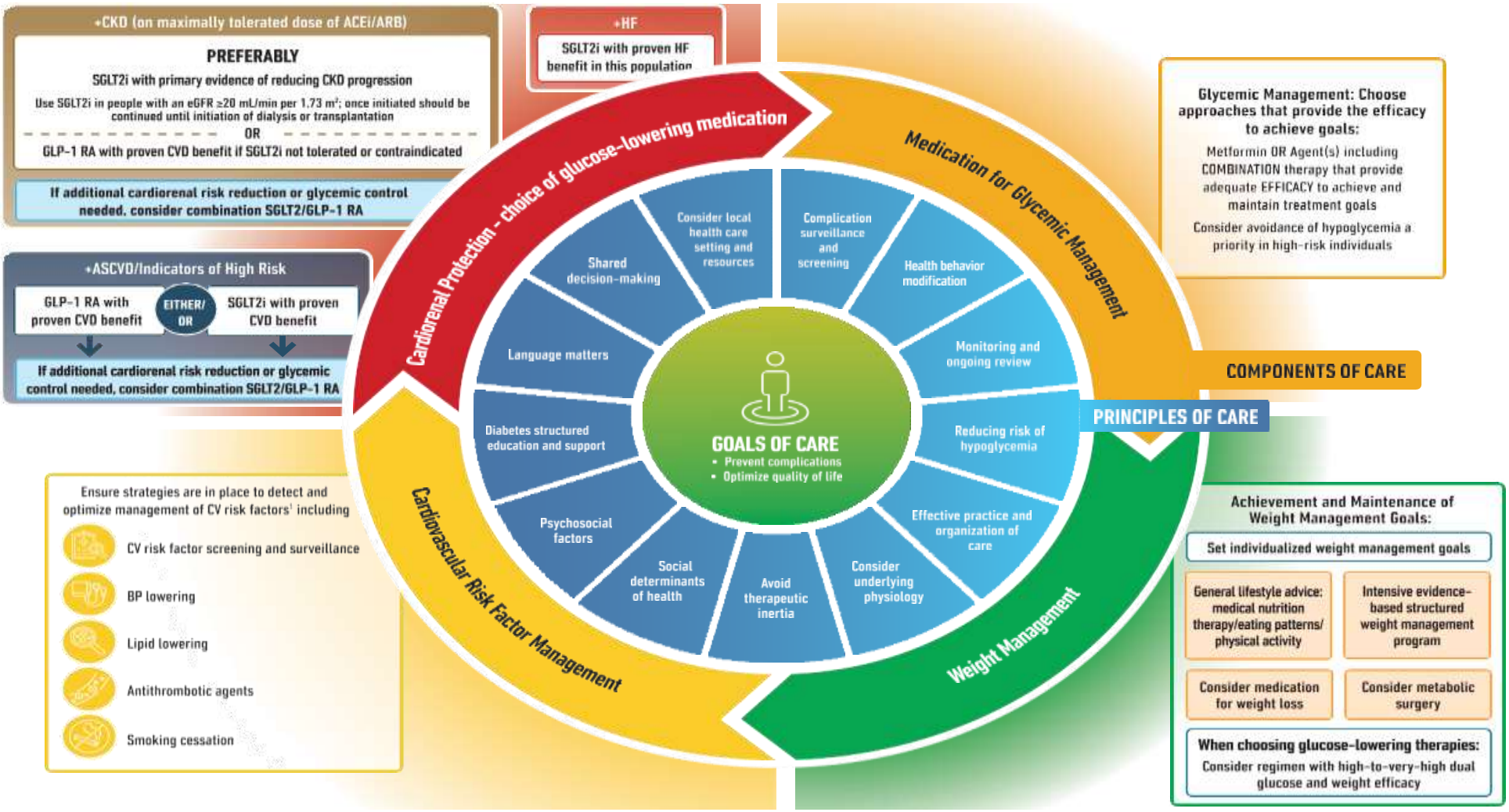


Figure 1.4 Holistic patient Centric Approach for Diabetes management.

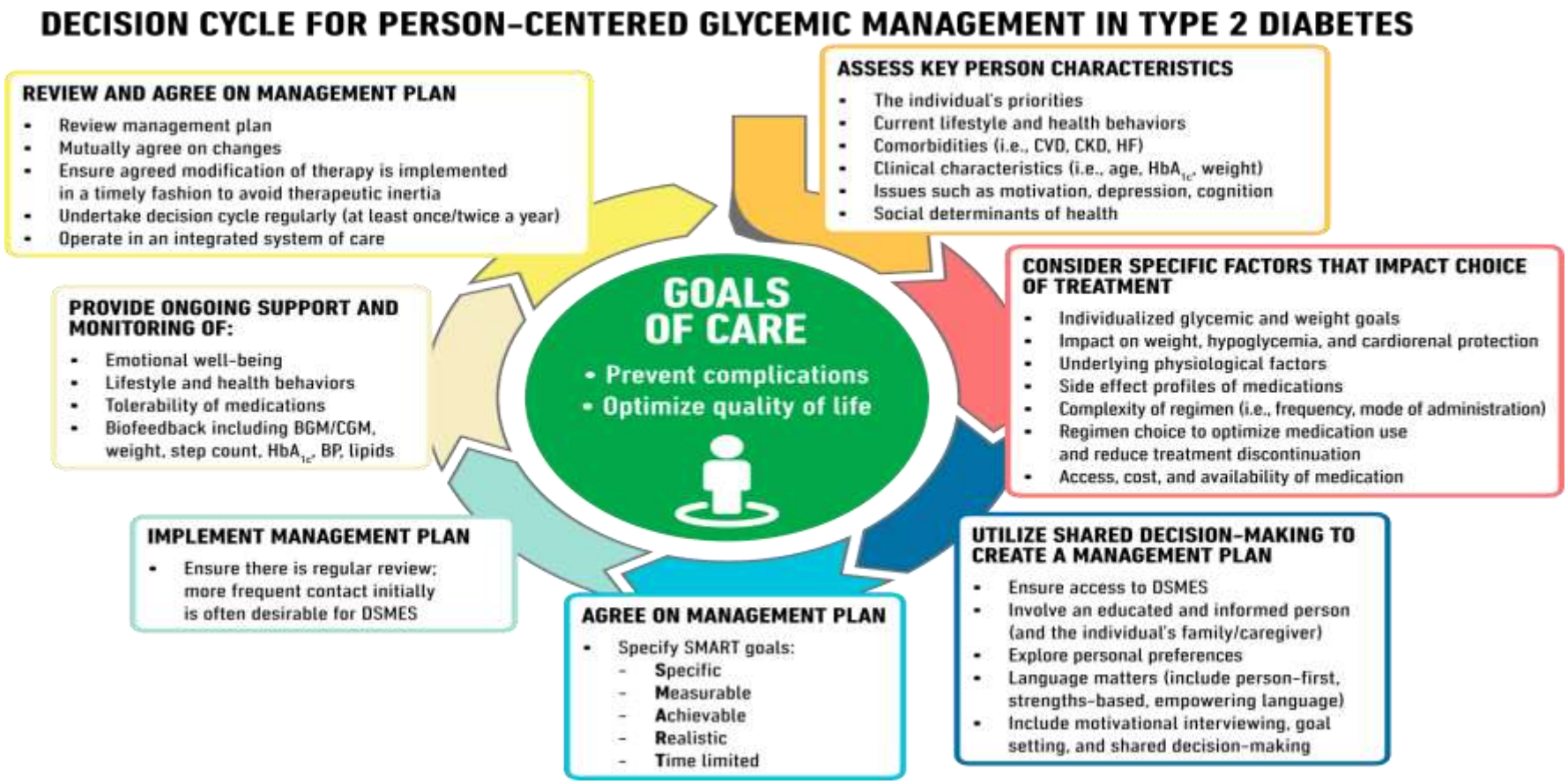


Figure 1.5 Decision cycle for person-centered glycemic management in type 2 diabetes.

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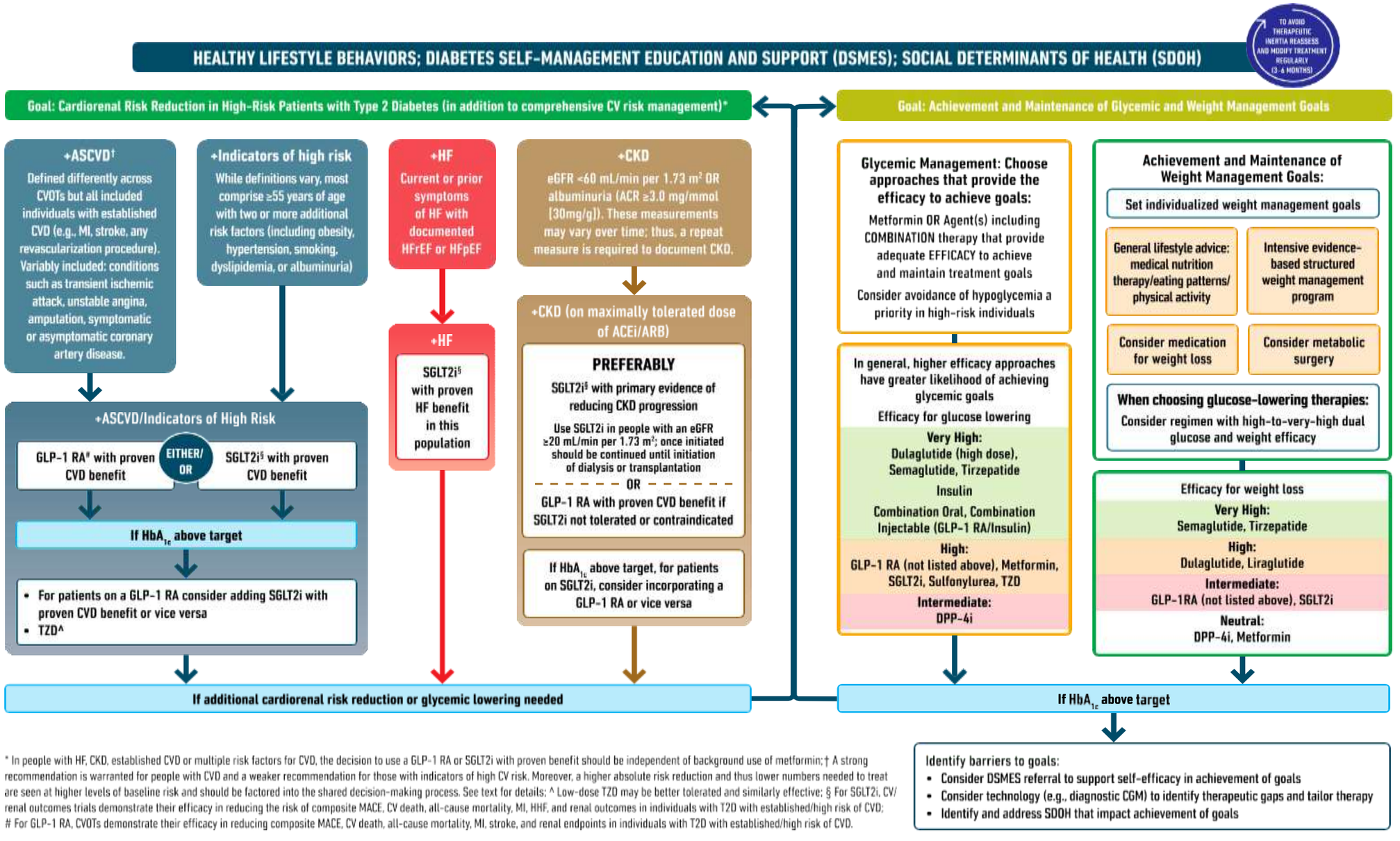
1.8.3 Pharmacological Therapy

The choice of pharmacological therapy should be individualized based on patient characteristics and preferences. The ADA and EASD recommend metformin as the first-line pharmacological agent for most patients with type 2 diabetes unless contraindicated (Katsiki, Ferrannini et al. 2020). Additional medications may be added based on the patient's clinical profile, including sodium-glucose cotransporter-2 (SGLT-2) inhibitors, glucagon-like peptide-1 receptor agonists (GLP-1 RAs), dipeptidyl peptidase-4 (DPP-4) inhibitors, and basal insulin. Medication selection should consider their efficacy, side effect profile, cardiovascular benefits, hypoglycemia risk, and patient preferences (Gourdy, Darmon et al. 2023).

1.8.4 Cardiovascular Risk Management

Given the increased risk of cardiovascular disease in individuals with diabetes, aggressive management of cardiovascular risk factors is essential. Blood pressure control is crucial, with a target of <130/80 mmHg for most individuals. Lipid management aims to reduce low-density lipoprotein cholesterol levels with statins and lifestyle modifications (Bays, Taub et al. 2021). Antiplatelet therapy with low-dose aspirin is recommended for individuals with established cardiovascular disease. Smoking cessation is also vital to reduce cardiovascular risk (Aimo, Ridker et al. 2020).



* In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin; † A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details; ^ Low-dose TZD may be better tolerated and similarly effective; § For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF, and renal outcomes in individuals with T2D with established/high risk of CVD; # For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and renal endpoints in individuals with T2D with established/high risk of CVD.

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Figure 1.6 Use of glucose-lowering medications in the management of type 2 diabetes.