



MEDICATION ADHERENCE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: FACTORS, BARRIERS, AND STRATEGIES FOR IMPROVING TREATMENT OUTCOMES

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ABSTRACT

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance, progressive β -cell dysfunction, and persistent hyperglycaemia, imposing a substantial clinical, social, and economic burden worldwide. Effective diabetes management requires long-term pharmacotherapy, lifestyle modification, regular monitoring, and sustained patient engagement. Medication adherence is therefore a critical determinant of therapeutic effectiveness and glycaemic control. This review examines medication adherence in T2DM from clinical, behavioural, pharmaceutical, and healthcare-system perspectives. It discusses the concepts of adherence, compliance, persistence, and non-adherence, along with their prevalence, determinants, barriers, measurement methods, and clinical consequences. Evidence indicates that suboptimal adherence to antidiabetic therapy remains common, although reported rates vary considerably according to study population, treatment regimen, adherence definition, and measurement method. Poor adherence has been associated with inadequate glycaemic control, increased risk of diabetes-related complications, reduced quality of life, and greater healthcare utilization and economic burden. Major determinants include treatment complexity, polypharmacy, adverse effects, socioeconomic constraints, medication cost and availability, psychological factors, limited health literacy, and inadequate healthcare access. Particular emphasis is placed on pharmacist-led interventions, patient education, behavioural strategies, medication counselling, treatment simplification, follow-up, and digital health technologies. Evidence from India further highlights the influence of socioeconomic and healthcare-access barriers on medication-taking behaviour. Overall, medication adherence should be considered a dynamic and multifactorial behaviour rather than solely a patient-related factor. An individualized, patient-centred, and multidisciplinary approach involving pharmacists and other healthcare professionals is essential to improve adherence and optimize diabetes outcomes. Future research should emphasize standardized adherence definitions, validated measurement approaches, culturally appropriate interventions, and longer-term evaluation, particularly within Indian healthcare settings.

KEYWORDS: Type 2 Diabetes Mellitus, Medication Adherence, Medication Non-adherence, Antidiabetic Drugs, Glycaemic Control, Pharmacist, Diabetes Self-management, Digital Health.

Introduction

Overview of Type 2 Diabetes Mellitus

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance, progressive β -cell dysfunction, and persistent hyperglycaemia. Its increasing prevalence has created a substantial clinical, social, and economic burden worldwide. Diabetes management requires sustained lifestyle modification, regular monitoring, and long-term pharmacotherapy; consequently, the effectiveness of treatment depends not only on the pharmacological efficacy of medicines but also on whether patients can obtain, understand, initiate, and continue their prescribed treatment. Medication adherence therefore represents a central component of successful diabetes care. This literature review examines medication adherence in T2DM from clinical, behavioural, pharmaceutical, and health-system perspectives. The review discusses the pathophysiology and treatment of T2DM; definitions of adherence, compliance, persistence, and non-adherence; the prevalence of suboptimal adherence; determinants and barriers; methods used to measure adherence; relationships between adherence and glycaemic control; consequences of non-adherence; and interventions intended to improve medicine-taking behaviour. Particular attention is given to pharmacist-led interventions, behavioural change techniques, digital health approaches, treatment complexity, socioeconomic barriers, and evidence from India. Available evidence demonstrates substantial variability in reported adherence because studies use different definitions, thresholds, populations, treatment regimens, and measurement methods. A systematic review of oral antidiabetic therapy published in 2023 estimated pooled adherence at approximately 54% and found a statistically significant association between good adherence and good glycaemic control[1]. Earlier systematic reviews likewise identified adherence as an ongoing problem and emphasized the heterogeneity of measurement methods[2,3]. Recent evidence from India indicates that non-adherence remains common and is associated with treatment complexity, socioeconomic disadvantage, psychological distress, polypharmacy, and barriers to healthcare access[4]. The evidence also suggests that adherence should not be approached as a simple patient characteristic. It is a dynamic behaviour produced by the interaction of individual capability and motivation, treatment demands, social circumstances, medicine affordability and availability, communication with healthcare professionals, and the organization of care. Contemporary diabetes guidance therefore emphasizes person-centred shared decision-making, consideration of treatment burden, adverse effects, cost and access, comorbidities, and patient preferences when selecting glucose-lowering therapy[5]. Multifaceted interventions involving pharmacists, education, practical support, action planning, and appropriate follow-up show potential, although intervention effects are heterogeneous and long-term sustainability remains an important research gap[6,7].

This review concludes that improving medication adherence in T2DM requires an individualized and multidisciplinary approach. Pharmacists are particularly well positioned to identify medication-related barriers, educate patients, reconcile medicines, support self-management, monitor adherence, and coordinate follow-up. Future research should use standardized adherence definitions, validated and complementary measurement methods, culturally appropriate interventions, and longer follow-up periods, particularly in underrepresented populations and in Indian healthcare settings. Type 2 diabetes mellitus is a chronic metabolic disease resulting from a combination of insulin resistance, inadequate compensatory insulin secretion, progressive pancreatic β -cell dysfunction, abnormal hepatic glucose regulation, and disturbances in multiple metabolic pathways[8]. Unlike type 1 diabetes, in which absolute insulin deficiency predominates, T2DM develops through a heterogeneous interaction of genetic susceptibility, excess adiposity, physical inactivity, ageing, environmental exposure, and other metabolic determinants. The disease is progressive, and many patients eventually require intensification or combination pharmacotherapy to maintain individualized glycaemic targets[5,8]. The clinical significance of T2DM extends beyond hyperglycaemia. Persistent metabolic abnormalities contribute to microvascular complications, including diabetic kidney disease, retinopathy and neuropathy, and to macrovascular disease involving the coronary, cerebral and peripheral arterial systems[8,9]. Consequently, effective diabetes management must integrate glucose lowering with cardiovascular and renal risk reduction, weight management, blood-pressure control, lipid management, smoking cessation, and appropriate screening for complications[5].

Global Burden of Diabetes

Diabetes has become one of the major global public-health challenges of the twenty-first century. The World Health Organization reported that the number of people living with diabetes increased from approximately 200 million in 1990 to 830 million in 2022, with prevalence increasing particularly rapidly in low- and middle-income countries[10]. The Global Burden of Disease analysis has similarly documented a major increase in diabetes prevalence over recent decades and projects continued growth in the coming decades if prevention and treatment strategies are not substantially strengthened[11]. The burden of diabetes is not confined to glucose concentrations. Diabetes contributes to premature mortality, cardiovascular disease, kidney failure, visual impairment and lower-limb amputation and places substantial demands on health systems[10]. The WHO has also emphasized that treatment coverage remains incomplete and that more than half of people living with diabetes did not take diabetes medication in 2022, highlighting the distinction between the availability of effective therapies and their effective use in real-world populations[10].

Diabetes in India

India has a particularly important role in the global diabetes epidemic because of its large population and rapidly changing demographic, nutritional and socioeconomic environment. The ICMR-INDIAB programme has provided large-scale national evidence on metabolic non-communicable diseases, demonstrating the extensive distribution of diabetes and related risk factors across Indian states and population groups[12]. Recent evidence specifically addressing medication adherence in Indian patients with T2DM indicates substantial geographic and methodological heterogeneity. A 2026 systematic review and meta-analysis of Indian studies published between 2020 and 2024 found that non-adherence estimates varied considerably across studies and identified treatment complexity, polypharmacy, psychological distress, socioeconomic disadvantage and healthcare-access barriers among important predictors[4]. The Indian context is particularly relevant to medication adherence because patients may encounter multiple interacting barriers, including out-of-pocket medicine costs, fragmented continuity of care, variable access to medicines, travel requirements for follow-up, differences in health literacy, family responsibilities, and coexistence of traditional and biomedical health practices. These factors should not be interpreted as individual failings; rather, they represent modifiable characteristics of the treatment and healthcare environment as well as patient-level determinants[4,13].

Importance of Medication Adherence

Long-term diabetes therapy is effective only when medicines are taken with sufficient regularity and persistence to produce the intended pharmacological exposure. The WHO has described poor adherence to long-term therapy as a major worldwide problem and emphasized that adherence is influenced by multiple interacting factors rather than by patient behaviour alone[14]. In T2DM, inadequate adherence may contribute to therapeutic failure, higher glycaemic exposure, treatment intensification, avoidable complications, increased healthcare utilization and increased economic burden[1,15]. Medication adherence should therefore be considered a clinical outcome and a quality-of-care issue. It is also an appropriate target for pharmaceutical care because pharmacists can identify medicine-related problems, assess practical barriers, simplify therapy where possible, educate patients, reinforce appropriate medicine use, and monitor response over time[6,7].

Objectives of the Review

General Objective

To comprehensively review the published literature concerning medication adherence in adults with type 2 diabetes mellitus, with emphasis on determinants, measurement, clinical consequences and interventions.

Specific Objectives

- To describe the clinical and pharmacological context

in which medication adherence is required for T2DM management.

- To define medication adherence, persistence, compliance, implementation and non-adherence and distinguish these concepts.
- To summarize the prevalence and variability of medication adherence reported in T2DM studies.
- To identify patient-, disease-, medication-, socioeconomic-, behavioural- and health-system-related determinants of adherence.
- To compare direct and indirect methods used to measure medication adherence.
- To examine the relationship between adherence, glycaemic control and diabetes-related outcomes.
- To review interventions designed to improve medication adherence, including pharmacist-led, behavioural and digital interventions.
- To discuss the relevance of medication adherence evidence to Indian healthcare settings.
- To identify limitations and research gaps and propose priorities for future research.

Literature Review Methodology

Review Approach

This manuscript was developed as a narrative literature review informed by systematic reviews, meta-analyses, major diabetes guidelines, epidemiological reports and relevant primary studies. Priority was given to peer-reviewed evidence indexed in PubMed/MEDLINE and to authoritative sources such as the World Health Organization and the American Diabetes Association. The search strategy was designed around the core concepts of T2DM, medication adherence, medication persistence, non-adherence, antidiabetic medicines, glycaemic control, pharmacist interventions and digital or behavioural interventions.

Search Concepts

Representative search combinations included: “type 2 diabetes mellitus” AND “medication adherence”; “type 2 diabetes” AND “medication non-adherence”; “antidiabetic drugs” AND adherence; “Morisky” AND diabetes; “pharmacist intervention” AND diabetes AND adherence; and “digital intervention” AND diabetes AND medication adherence. Systematic reviews and meta-analyses were used to identify the breadth of evidence and major determinants, while guideline and epidemiological sources were used to support clinical and population-level context.

Selection Principles

The review prioritizes adult T2DM literature, validated adherence measures, randomized or comparative intervention studies, systematic reviews and meta-analyses, and evidence relevant to real-world diabetes care. Older seminal studies were retained where they established definitions or measurement concepts. Recent evidence was preferentially used for current disease burden, pharmacological management and emerging

intervention approaches. Because adherence outcomes are highly dependent on methodology, reported percentages are interpreted in the context of the measurement method and study population rather than treated as a single universal adherence rate.

Evidence Interpretation

The literature is synthesized descriptively rather than through a new quantitative meta-analysis. Particular attention is paid to heterogeneity arising from different adherence thresholds, questionnaires, pharmacy-claims metrics, treatment classes, follow-up durations and patient populations. Where a study reports an association, the review does not automatically interpret that association as proof of causality. This distinction is important because adherence, glycaemic control, treatment complexity and disease severity can influence one another over time.

Pathophysiology and Clinical Course of T2DM

Type 2 diabetes mellitus (T2DM) is a heterogeneous, chronic metabolic disorder characterized by hyperglycaemia resulting from a progressive loss of adequate pancreatic β -cell insulin secretion, usually occurring in the setting of insulin resistance. The disorder develops through interaction among genetic susceptibility, excess adiposity, environmental exposures, physical inactivity, dietary factors, and other metabolic influences. Contemporary models of T2DM emphasize that abnormalities extend beyond skeletal muscle, liver, and pancreatic β -cells to include adipose tissue, the gastrointestinal tract, pancreatic α -cells, kidneys, and the central nervous system[31,35,36]. The progression from insulin resistance to overt diabetes is gradual and variable. During early disease, increased insulin secretion may compensate for reduced tissue sensitivity. With continued metabolic stress, however, β -cell function

declines, hepatic glucose production becomes inappropriately elevated, postprandial glucose regulation deteriorates, and chronic hyperglycaemia becomes established. The resulting metabolic and vascular injury contributes to microvascular and macrovascular complications and creates a continuing need for individualized long-term pharmacotherapy[31,35,37].

Insulin Resistance and β -Cell Dysfunction

Insulin resistance refers to a state in which normal or increased concentrations of insulin produce a subnormal biological response in target tissues. In T2DM, skeletal muscle, liver, and adipose tissue are major sites of impaired insulin action. Skeletal muscle shows reduced insulin-stimulated glucose uptake and utilization, particularly after meals. In the liver, insulin fails to adequately suppress endogenous glucose production, while adipose tissue shows impaired inhibition of lipolysis and increased release of free fatty acids (FFAs) [31,35,36]. The pancreatic β -cell initially compensates for insulin resistance by increasing insulin secretion. This compensatory response can maintain relatively normal glucose concentrations for a substantial period. However, the increased secretory demand occurs in an environment characterized by nutritional excess, elevated FFAs, oxidative and endoplasmic-reticulum stress, inflammation, and glucotoxicity. Over time, β -cell function deteriorates and insulin secretion becomes inadequate for the prevailing degree of insulin resistance. The current ADA classification therefore describes T2DM as a nonautoimmune progressive loss of adequate β -cell insulin secretion, frequently occurring against a background of insulin resistance[31]. The transition from compensated insulin resistance to overt diabetes is therefore best understood as a dynamic process rather than a single defect. Declining β -cell compensation, together with worsening hepatic and peripheral insulin resistance, produces rising fasting and postprandial plasma glucose concentrations. [31,35]

Table 1: Major pathophysiological components of type 2 diabetes mellitus

Pathophysiological component	Principal abnormality	Immediate metabolic effect	Clinical relevance
Skeletal muscle	Reduced insulin-stimulated glucose uptake	Postprandial hyperglycaemia	Peripheral insulin resistance
Liver	Reduced suppression of glucose output	↑ fasting plasma glucose	Fasting hyperglycaemia
Adipose tissue	↑ lipolysis and inflammatory signalling	↑ free fatty acids; ectopic lipid	Worsening insulin resistance
β -cell	Progressive secretory dysfunction	Relative insulin deficiency	Disease progression
α -cell / glucagon	Inappropriately elevated glucagon activity	↑ hepatic glucose production	Fasting and postprandial hyperglycaemia
Gut / incretin system	Reduced incretin effect or response	Inadequate meal-related insulin response	Postprandial dysglycaemia
Kidney	Continued glucose reabsorption	Reduced urinary glucose loss	Maintenance of hyperglycaemia
Central nervous system	Altered appetite/insulin-related signalling	Abnormal energy regulation	May contribute to obesity and metabolic dysfunction

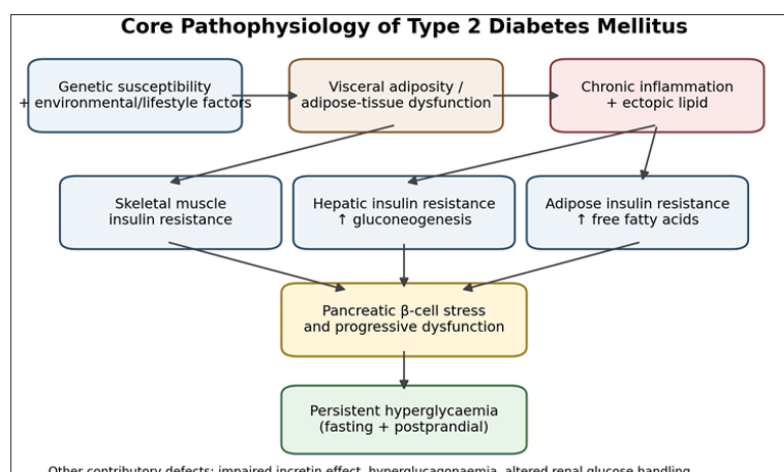


Figure 1. Integrated pathophysiological model of T2DM showing the interaction of insulin resistance, adipose dysfunction, inflammation, hepatic glucose production and progressive β -cell dysfunction. Adapted conceptually from DeFronzo and contemporary classification literature[31,35,36]

Table 2: Relationship between insulin resistance and β -cell dysfunction

Stage	β -cell response	Metabolic consequence
Early insulin resistance	Compensatory increase in insulin secretion	Glucose may remain near normal
Persistent insulin resistance	High secretory demand with metabolic stress	Postprandial dysglycaemia begins
β -cell dysfunction	Progressively inadequate insulin secretion	Fasting and postprandial hyperglycaemia
Established T2DM	Relative insulin deficiency	Sustained hyperglycaemia and need for treatment intensification

Table 3: Factors associated with increased risk of T2DM

Category	Examples	Pathophysiological link
Genetic	Family history; polygenic susceptibility	Influences β -cell function and insulin sensitivity
Dietary	Excess energy; highly processed foods; excessive refined carbohydrate intake	Promotes weight gain and metabolic stress
Physical activity	Sedentary behaviour; low exercise	Reduces peripheral insulin sensitivity
Adiposity	Visceral and ectopic fat	Promotes insulin resistance, FFAs and inflammation
Age and metabolic ageing	Age-related changes in body composition and insulin sensitivity	Reduces metabolic reserve in susceptible individuals
Other environmental factors	Sleep disturbance and psychosocial stress	May influence appetite, activity and metabolic regulation

Role of Genetic, Environmental, and Lifestyle Factors

T2DM arises from interaction between inherited susceptibility and acquired metabolic stressors. Genetic susceptibility influences insulin secretion, insulin sensitivity, adipose distribution, appetite regulation, and other determinants of glucose homeostasis. The genetic contribution is polygenic and heterogeneous rather than attributable to a single diabetes gene in the majority of patients[31,36]. Environmental and lifestyle factors can amplify this underlying susceptibility. Excess calorie intake, diets with high energy density, low physical activity, sedentary behaviour, insufficient

sleep, stress, and progressive weight gain are associated with greater metabolic risk. Physical activity improves insulin-stimulated glucose uptake in skeletal muscle and supports maintenance of healthy body composition, whereas prolonged inactivity facilitates positive energy balance and insulin resistance[31,34,36]. It is important to recognize that T2DM is not restricted to people meeting conventional body-mass-index definitions of obesity. Some individuals with a normal or modestly elevated BMI may have excess visceral or ectopic fat and significant metabolic dysfunction. Conversely, obesity does not inevitably result in diabetes, demonstrating the role of interindividual differences in genetic susceptibility and adipose-tissue biology[31].

Obesity, Adipose Tissue Dysfunction, and Chronic Inflammation

Adipose tissue is an endocrine and immune-active organ rather than a passive energy store. Expansion of visceral adipose tissue is associated with adipocyte hypertrophy, altered adipokine secretion, increased lipolysis, recruitment and activation of immune cells, and chronic low-grade inflammation. These changes can interfere with insulin signalling in adipose tissue, liver, and skeletal muscle[38,39]. Excess FFAs delivered to the liver and skeletal muscle can promote ectopic lipid accumulation and metabolic dysfunction. At the same time, obesity-related adipose inflammation is characterized by increased production of mediators such as tumour necrosis factor- α and interleukins, together with reduced expression of insulin-sensitizing adipokines such as adiponectin. The resulting inflammatory environment contributes to impaired insulin signalling and may also worsen pancreatic β -cell dysfunction[38,39].

The relationship can therefore become self-reinforcing: adipose expansion increases lipolysis and inflammation; these abnormalities worsen systemic insulin resistance; compensatory insulin secretion increases; and chronic metabolic stress accelerates β -cell dysfunction[35,38,39].

Hepatic Glucose Dysregulation and Increased Gluconeogenesis

The liver is a major determinant of fasting plasma glucose because it supplies glucose during fasting through glycogenolysis and gluconeogenesis. Under normal conditions, insulin suppresses hepatic glucose production after food intake. In T2DM, hepatic insulin resistance reduces this suppression, allowing excessive glucose output to continue despite already elevated plasma glucose[35,36]. Gluconeogenesis uses substrates including lactate, glycerol, and amino acids. Increased adipose lipolysis can increase glycerol availability, while altered lipid metabolism and hepatic acetyl-CoA signalling can stimulate gluconeogenic pathways. The combined effect is excessive hepatic glucose production, which contributes particularly to fasting hyperglycaemia and amplifies overall glucose exposure[36,40]. This abnormality is clinically important because lowering inappropriate hepatic glucose output is one of the major therapeutic principles in T2DM. Hepatic glucose regulation should therefore be considered alongside peripheral insulin resistance and β -cell dysfunction when interpreting the metabolic progression of the disease[32,35].

Incretin Dysfunction and Abnormal Glucagon Secretion

The incretin system links nutrient ingestion in the gastrointestinal tract with pancreatic hormone secretion. The principal incretin hormones are glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). In healthy individuals, oral glucose produces a greater insulin secretory response than an equivalent intravenous glucose stimulus, a phenomenon known as the incretin

effect. This effect is substantially impaired in T2DM[37]. In T2DM, β -cell responses to incretin signalling are abnormal. The response to GIP is markedly reduced, while GLP-1 receptor signalling remains therapeutically exploitable. In addition, glucagon secretion may be inappropriate in relation to prevailing glucose concentrations, promoting hepatic glucose output. These abnormalities help explain why postprandial glucose handling is impaired and why incretin-based therapies, including GLP-1 receptor agonists and DPP-4 inhibitors, have an important place in modern management[32,37].

Renal Glucose Reabsorption and Altered Glucose Homeostasis

The kidneys participate actively in glucose homeostasis. Glucose is freely filtered by the glomeruli and normally reabsorbed in the proximal tubule, predominantly through sodium-glucose cotransporter 2 (SGLT2), with additional contribution from sodium-glucose cotransporter 1 (SGLT1) downstream[35,41]. In the setting of hyperglycaemia, the filtered glucose load increases. Renal glucose reabsorption can consequently contribute to persistence of elevated blood glucose by recovering a large proportion of the filtered glucose rather than allowing it to be excreted. Recognition of this mechanism contributed to development of SGLT2 inhibitors, which reduce proximal tubular glucose reabsorption and increase urinary glucose excretion[32,35,41]. Renal glucose handling is therefore part of the broader network of abnormalities involved in T2DM rather than an isolated consequence of hyperglycaemia. It also demonstrates why pharmacological approaches can target different organs and mechanisms to achieve glucose control and organ protection[32,41].

Progressive Hyperglycaemia and Metabolic Deterioration

The combined effects of insulin resistance, declining β -cell function, increased hepatic glucose production, altered incretin and glucagon activity, adipose dysfunction, and renal glucose handling progressively increase plasma glucose concentrations. Initially, postprandial glucose may rise before fasting glucose becomes clearly abnormal. With further loss of β -cell compensation, both fasting and postprandial hyperglycaemia become persistent[31,35,36]. Chronic hyperglycaemia can itself aggravate β -cell dysfunction through glucotoxic mechanisms involving oxidative stress, altered cellular signalling, protein glycation and other metabolic disturbances. Thus, hyperglycaemia is both a consequence of metabolic dysfunction and a factor that can further sustain that dysfunction[35,36]. The result is a positive-feedback cycle in which insulin resistance increases β -cell demand, β -cell dysfunction reduces compensation, hyperglycaemia increases metabolic stress, and further metabolic stress accelerates disease progression. The rate of progression differs among individuals, making regular reassessment of glycaemic control and treatment needs essential[31,32].

Table 4: Incretin and glucagon abnormalities in T2DM

Physiological pathway	Abnormality in T2DM	Metabolic consequence
GIP signalling	Reduced β -cell responsiveness	Less glucose-dependent insulin secretion
GLP-1 signalling	Endogenous incretin effect reduced; receptor remains therapeutically responsive	Reduced meal-related insulin support and impaired appetite/emptying regulation
Glucagon	Inappropriate secretion relative to glucose level	$\uparrow$ hepatic glucose production
Overall	Disordered gut-pancreas-liver communication	Postprandial and fasting hyperglycaemia

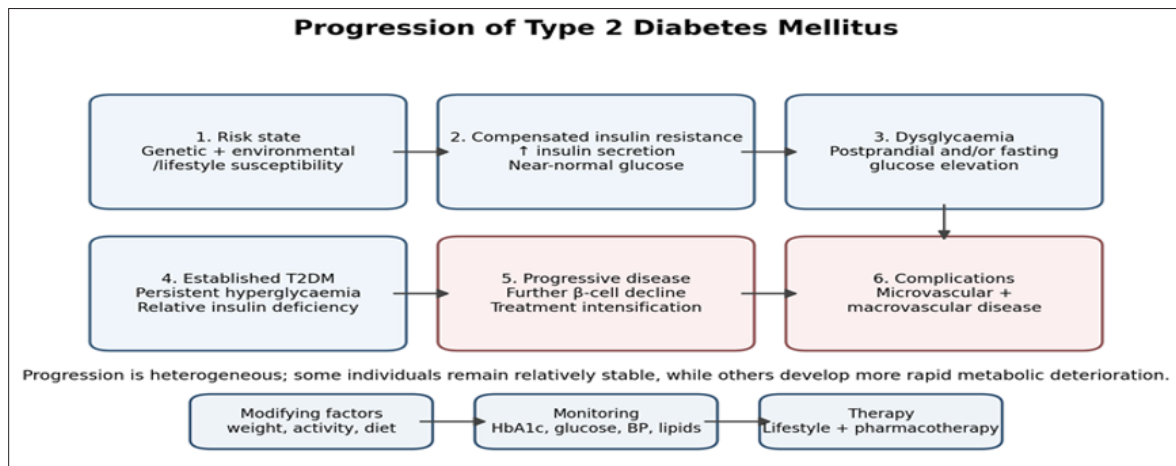


Figure 2. Simplified clinical progression of T2DM from susceptibility and compensated insulin resistance to dysglycaemia, established diabetes, treatment intensification and complications. Progression is heterogeneous among individuals[31,35,36]

Clinical Course and Progression of T2DM

The clinical course of T2DM commonly evolves over years. A person may have substantial insulin resistance with compensatory hyperinsulinaemia before diagnostic glucose criteria are met. A period of impaired glucose regulation may follow, during which postprandial glucose excursions become more pronounced and β -cell reserve becomes progressively limited. Once overt T2DM develops, persistent hyperglycaemia may continue to worsen unless

the metabolic drivers are addressed. [31,36] The presentation is heterogeneous. Some people remain relatively stable with lifestyle modification and one medication, whereas others experience more rapid decline in β -cell function or develop clinically important cardiovascular, kidney or other comorbidities that alter treatment priorities. Consequently, the clinical course should be understood as a continuum rather than a fixed sequence with identical timing in every patient. [31,32]

Table 5: Simplified clinical stages in the natural history of T2DM

Stage	Predominant abnormality	Typical glycaemic pattern	Therapeutic implication
Susceptibility	Genetic and environmental risk	Normal glucose may be present	Risk reduction and screening
Compensated insulin resistance	↑ insulin demand with preserved compensation	Near-normal or mildly altered glucose	Lifestyle intervention; risk-factor management
Dysglycaemia	Emerging β-cell dysfunction	Postprandial and/or fasting glucose elevation	Active prevention of progression and treatment where indicated
Established T2DM	Relative insulin deficiency + insulin resistance	Persistent hyperglycaemia	Individualized pharmacotherapy + lifestyle
Progressive T2DM	Further loss of β-cell function and/or increasing comorbidity	Rising HbA1c or glucose despite prior regimen	Therapy reassessment and intensification/simplification as appropriate
Complicated T2DM	Vascular/organ complications	Variable	Complication-specific and risk-reduction strategies

Development of Microvascular and Macrovascular Complications

Long-standing diabetes is associated with injury to small and large blood vessels. Hyperglycaemia contributes through advanced glycation end-product formation, oxidative stress, endothelial dysfunction, inflammatory signalling, and other metabolic pathways. Blood pressure, dyslipidaemia, smoking, duration of diabetes, obesity and kidney dysfunction can further modify vascular risk[33,34,42]. Microvascular complications include diabetic retinopathy, diabetic kidney disease and diabetic neuropathy. These conditions are particularly related to chronic metabolic exposure and can lead to visual impairment, chronic kidney disease, loss of protective sensation, foot ulceration and other morbidity. The ADA recommends structured surveillance for these complications, including foot assessment and appropriate screening for eye and kidney disease[33]. Macrovascular complications include coronary artery disease, cerebrovascular disease and peripheral arterial disease. T2DM frequently coexists with hypertension, dyslipidaemia, obesity and other cardiovascular risk factors, so the vascular burden reflects cumulative metabolic and cardiovascular risk rather than hyperglycaemia alone[34,42].

Implications of Disease Progression for Long-Term Pharmacotherapy and Medication Adherence

Because T2DM is progressive and mechanistically heterogeneous, long-term pharmacotherapy must be periodically reviewed. The ADA 2026 Standards recommend person-centred selection of glucose-lowering

medicines with consideration of glycaemic efficacy, cardiovascular and kidney effects, weight, hypoglycaemia risk, adverse effects, cost and access, and individual preferences. Combination therapy may be appropriate when it helps patients reach individualized treatment goals more efficiently[32]. Treatment intensification should not automatically be interpreted as failure of a previous medicine. It may reflect the natural history of progressive β -cell dysfunction, changes in weight, development of comorbidities, or a change in therapeutic priorities. Similarly, deintensification or regimen simplification may be appropriate when treatment burden, hypoglycaemia risk, adverse effects or other factors outweigh the incremental benefit of a complex regimen[32]. Medication adherence is a major determinant of real-world effectiveness. Barriers include regimen complexity, cost, treatment burden, adverse effects, fear of hypoglycaemia, forgetfulness, inadequate understanding of the purpose of therapy, competing life demands, and limited access to medicines or healthcare. Poor adherence may lead to prolonged hyperglycaemia and delayed treatment adjustment[32,43]. For pharmacy practice, this progression highlights the importance of medication counselling, adherence assessment, identification of adverse effects, reinforcement of self-management skills, and timely referral when glycaemic control remains inadequate. A sustainable treatment plan should balance efficacy with practical feasibility, because a theoretically effective regimen cannot provide its intended benefit when it is difficult for the patient to use consistently[32,43].

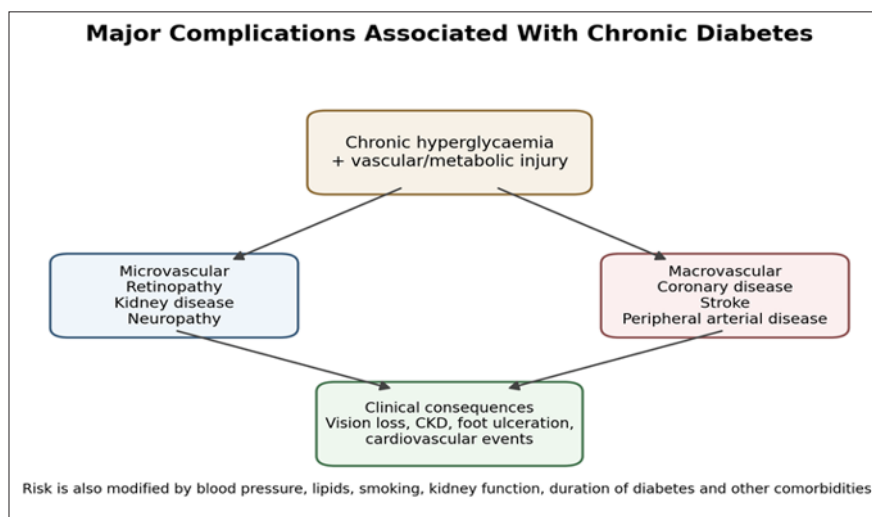
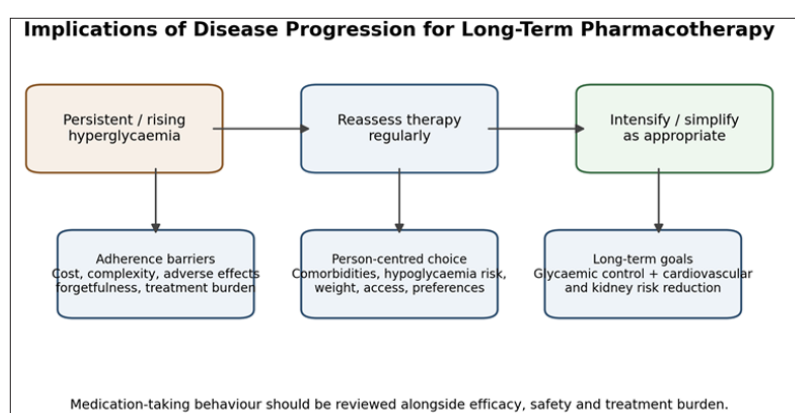


Figure 3. Major microvascular and macrovascular complications associated with chronic diabetes. The clinical burden is modified by duration of diabetes and coexisting cardiovascular and metabolic risk factors[33,34,42]

Table 6: Major complications of T2DM and their principal clinical manifestations

Category	Complication	Major pathological process	Important clinical outcome
Microvascular	Retinopathy	Retinal microvascular injury, ischemia and vascular permeability changes	Visual impairment and vision loss
Microvascular	Diabetic kidney disease	Glomerular and renal vascular injury	Albuminuria and progressive CKD
Microvascular	Neuropathy	Metabolic and vascular nerve injury	Pain, numbness, sensory loss and foot complications
Macrovascular	Coronary artery disease	Accelerated atherosclerotic and vascular injury	Angina, myocardial infarction, heart failure risk
Macrovascular	Cerebrovascular disease	Large-vessel atherosclerotic disease	Transient ischemic attack or stroke
Macrovascular	Peripheral arterial disease	Peripheral arterial atherosclerosis	Claudication, ischemia and increased foot risk

**Figure 4. Relationship between disease progression, treatment reassessment, person-centred medicine selection and medication adherence in long-term T2DM management[32,43]****Table 7: Common medication-adherence barriers and practical pharmacy considerations**

Barrier	Potential impact	Pharmacy / clinical consideration
Complex regimen	Missed or incorrectly timed doses	Simplify regimen where clinically appropriate; use clear schedules
Cost / access	Interruption or rationing of medicines	Discuss affordable options and access barriers
Adverse effects	Intentional dose skipping or discontinuation	Identify, document and communicate adverse effects; review alternatives
Fear of hypoglycaemia	Under-dosing, especially with insulin or secretagogues	Education on symptoms, monitoring and safe dose use
Forgetfulness/ routine disruption	Missed doses	Link doses to routines and use reminders where helpful
Low perceived need	Reduced motivation when symptoms are absent	Explain long-term benefits and complication prevention in understandable terms
Treatment burden	Reduced persistence with long-term therapy	Prioritize essential therapies and review burden at follow-up

Integrated Summary

The pathophysiology of T2DM can be viewed as an interconnected network of defects rather than a single abnormality. Genetic susceptibility and lifestyle factors

may promote visceral adiposity and metabolic dysfunction. Insulin resistance then develops in skeletal muscle, liver and adipose tissue, initially compensated by increased insulin secretion. Progressive β -cell dysfunction reduces this compensation, while hepatic glucose production,

inappropriate glucagon activity, impaired incretin effect and altered renal glucose handling further increase glucose exposure[31,35-37]. Persistent hyperglycaemia promotes additional metabolic and vascular injury, which contributes to microvascular and macrovascular complications. Because the underlying abnormalities can progress over time, long-term pharmacotherapy requires periodic reassessment, attention to comorbidities and individualized selection of medicines. Medication adherence is integral to achieving the intended benefit of treatment and should be addressed as a clinical variable rather than assumed[32-34,43].

From Risk Factors to Long-Term Management

T2DM develops through interconnected metabolic abnormalities. Insulin resistance in skeletal muscle, adipose tissue and liver reduces glucose uptake and alters hepatic glucose production. In the early stages, pancreatic β -cells may increase insulin secretion sufficiently to compensate. Over time, however, β -cell function progressively deteriorates, resulting in inadequate insulin secretion relative to metabolic demand[8]. The clinical phenotype therefore changes during the disease course, and treatment frequently requires intensification rather than remaining static.

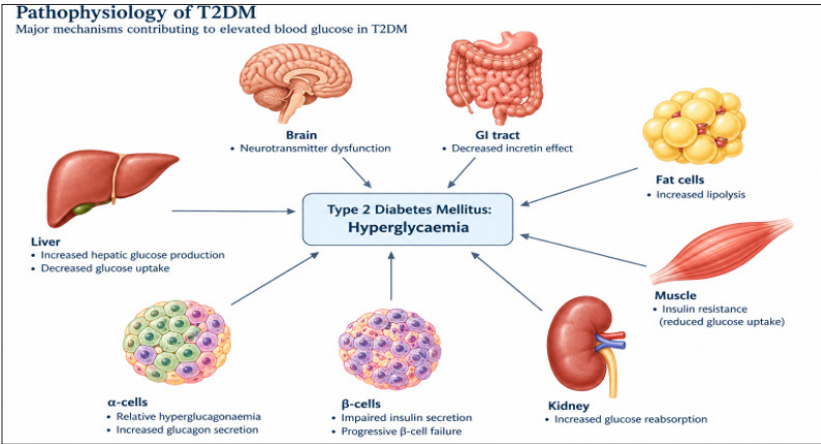


Figure 5. Chapter summary flowchart illustrating the broad progression from risk factors to metabolic deterioration, complications and long-term management[31,32,35]

Drug/Class	Examples	Mechanism of Action	Main Effect	Ref.
Biguanide	Metformin	Reduces hepatic gluconeogenesis and improves peripheral insulin sensitivity	↓ Blood glucose	[26,27]
Sulfonylureas	Glimepiride, Glipizide	Stimulate pancreatic β -cells by closing ATP-sensitive K^+ channels, increasing insulin secretion	↑ Insulin release	[26,27]
Meglitinides	Repaglinide, Nateglinide	Stimulate rapid, short-duration insulin secretion through β -cell K^+ -channel modulation	↓ Postprandial glucose	[26,27]
DPP-4 inhibitors	Sitagliptin, Linagliptin	Inhibit DPP-4, thereby prolonging endogenous GLP-1/GIP activity and enhancing glucose-dependent insulin secretion	↓ Blood glucose	[26,27]
GLP-1 receptor agonists	Semaglutide, Liraglutide	Activate GLP-1 receptors, increasing glucose-dependent insulin secretion, reducing glucagon secretion and slowing gastric emptying	↓ Glucose; ↓ body weight	[26,28]
SGLT2 inhibitors	Empagliflozin, Dapagliflozin	Inhibit renal SGLT2-mediated glucose reabsorption, increasing urinary glucose excretion	↓ Blood glucose; cardiorenal benefits	[26,29]
Thiazolidinediones	Pioglitazone	Activates PPAR- γ and improves insulin sensitivity in adipose tissue, skeletal muscle and liver	↓ Insulin resistance	[26,27]
α -Glucosidase inhibitors	Acarbose, Voglibose	Delay intestinal carbohydrate digestion and glucose absorption	↓ Postprandial glucose	[27,30]
Insulin	Regular insulin, Lispro, Glargine	Activates insulin receptors, increasing glucose uptake and reducing hepatic glucose production	↓ Blood glucose	[26,27]
Dual GIP/GLP-1 receptor agonist	Tirzepatide	Activates GIP and GLP-1 receptors, enhancing glucose-dependent insulin secretion and reducing glucagon secretion and appetite	↓ Glucose; ↓ body weight	[26,28]

Progressive Treatment Requirements

The progressive nature of T2DM has direct implications for adherence. A patient may initially take one medicine once daily and later receive multiple agents with different administration requirements, monitoring needs and adverse-effect profiles. Treatment burden may therefore increase even when individual medicines are appropriate. Current ADA guidance recommends person-centred shared decision-making and consideration of treatment burden, adverse effects, cost and access, comorbidities and patient preferences when selecting therapy[5].

Pharmacological Management of T2DM

General Principles

Pharmacological management of T2DM is individualized according to glycaemic goals, cardiovascular and kidney disease, weight considerations, hypoglycaemia risk, tolerability, cost, access and patient preferences[5]. Contemporary treatment therefore extends beyond a simple “first-line drug” model. Metformin remains widely used because of its efficacy, safety, low cost and availability, while agents such as SGLT2 inhibitors and GLP-1 receptor agonists may be selected when cardiovascular, renal or weight-related benefits are clinically relevant[5].

Major Drug Classes and Adherence Considerations

Real-world comparative evidence shows that adherence and persistence differ among glucose-lowering therapies, although the magnitude and direction of differences depend on the method used to define adherence. A systematic review and meta-analysis of 48 studies found variability among drug classes and emphasized that definitions of adherence and persistence were highly heterogeneous[15]. A more recent systematic review of real-world studies similarly reported wide ranges in adherence and persistence across antidiabetic therapies and linked these outcomes with clinical and economic endpoints[16].

Medication Adherence: Concepts and Definitions

Medication Adherence

Medication adherence refers to the extent to which a person’s medication-taking behaviour corresponds with the agreed recommendations of a healthcare professional. The concept is broader than simply “taking tablets” because it includes initiation of therapy, implementation of the prescribed regimen and persistence over time. The WHO framework emphasizes that adherence is a multidimensional phenomenon influenced by socioeconomic factors, healthcare-system factors, disease characteristics, therapy-related factors and patient-related factors[14].

Adherence, Compliance and Persistence

The term “compliance” traditionally implies that the patient follows instructions, whereas “adherence” is preferred because it emphasizes an agreed therapeutic plan and recognizes patient participation in treatment decisions. Persistence refers to the duration of time a patient continues a therapy before discontinuation. A patient can therefore have good day-to-day implementation but poor persistence, or may persist with a medicine while taking it inconsistently. These distinctions are essential when interpreting research outcomes[15,16].

Intentional and Unintentional Non-Adherence

Unintentional non-adherence may arise from forgetfulness, misunderstanding, difficulty organizing medicines, visual or cognitive limitations, or practical access problems. Intentional non-adherence occurs when a person deliberately modifies or stops therapy because of concerns about adverse effects, perceived lack of benefit, cost, beliefs about medicines, treatment burden or competing priorities. Interventions must therefore be matched to the underlying mechanism; reminders may help with forgetfulness but are unlikely to resolve a deliberate decision to avoid a medicine because of adverse-effect concerns.

Drug/class	Principal role	Adherence-relevant considerations	Reference
Metformin	Glucose lowering; commonly used in T2DM	Gastrointestinal adverse effects, dosing frequency and long-term continuation can affect use.	[44]
Sulfonylureas	Increase insulin secretion	Hypoglycaemia and dosing considerations may influence willingness and persistence.	[44]
DPP-4 inhibitors	Glucose lowering with generally low hypoglycaemia risk	Oral administration may be convenient, but real-world adherence remains incomplete.	[44]
SGLT2 inhibitors	Glucose lowering with cardiovascular/renal benefits in selected patients	Genitourinary adverse effects, cost and access may affect persistence.	[44]
GLP-1 receptor agonists	Glucose lowering and weight-related benefits; selected agents reduce cardiovascular risk	Injection/device burden, gastrointestinal effects, cost and persistence are relevant.	[44]
Insulin	Essential when endogenous insulin is inadequate or when clinically indicated	Injection burden, hypoglycaemia concerns, regimen complexity and storage requirements may affect adherence.	[44,45]

Prevalence and Epidemiology of Medication Non-Adherence

Reported adherence in T2DM varies markedly across studies. Krass and colleagues reviewed 27 studies and found adherence estimates ranging from 38.5% to 93.1%, while only a minority of studies reported adherence of at least 80%[2]. A later meta-analysis of oral antihyperglycaemic agents estimated a pooled mean medication possession ratio of 75.3% and found that 67.9% of patients met an MPR threshold of at least 80%, again demonstrating that a substantial proportion of patients did not meet the commonly used threshold[3].

More recent evidence continues to demonstrate suboptimal adherence. A 2023 systematic review and meta-analysis involving 156 studies and more than 10 million participants estimated the pooled proportion of adherent patients taking oral antidiabetic drugs at 54% (95% CI 51–58%) and found that good adherence was associated with good glycaemic control (OR 1.33, 95% CI 1.17–1.51).[1] A 2024 systematic review restricted to larger cross-sectional studies estimated overall adherence to oral antidiabetic drugs at 55.53% (95% CI 44.22–66.85%)[17]. These estimates should not be directly compared as if they measured the same construct: the studies used different instruments, populations, thresholds and definitions. In India, a 2026 systematic review and meta-analysis of studies published from 2020 through 2024 found overall non-adherence estimates ranging from 11% to 68%; among studies using MMAS-8, the pooled prevalence of non-adherence was 48% (95% CI 18–79%)[4]. The wide confidence interval and geographic concentration of studies demonstrate the uncertainty surrounding a single national adherence estimate. Nevertheless, the consistency of evidence that a substantial proportion of patients experience adherence problems supports the need for routine assessment in diabetes care.

Factors Influencing Medication Adherence

Patient-Related Factors

Patient characteristics can influence medication-taking behaviour, but associations are rarely uniform across studies. Age, education, health literacy, beliefs about medicines, forgetfulness, psychological distress, perceived benefit, perceived risk and social support may all influence adherence. Importantly, these variables interact with treatment demands and healthcare access. Recent evidence using the COM-B framework indicates that adherence interventions are more likely to be understandable when capability, opportunity and motivation are considered together rather than treating adherence as a single psychological trait[18].

Disease-Related Factors

The asymptomatic or minimally symptomatic nature of T2DM can reduce the immediate perceived benefit of medication. A patient may feel well despite elevated glucose and therefore have difficulty connecting daily medicine-taking with future risk reduction. Conversely, disease complications or poor

glycaemic control may increase treatment intensity and consequently increase treatment burden. This bidirectional relationship makes it difficult to interpret adherence solely as a cause of poor control.

Medication-Related Factors

Medication-related determinants include dosing frequency, number of medicines, pill burden, route of administration, adverse effects, hypoglycaemia risk, cost, storage requirements and complexity of instructions. Treatment complexity becomes especially relevant in people with multimorbidity and polypharmacy. The 2026 ADA pharmacologic guidance explicitly includes treatment burden, adverse reactions, cost and access among factors that should inform person-centred medication selection[5].

Socioeconomic Factors

Medication adherence is influenced by the affordability and accessibility of treatment. Cost may lead patients to delay refills, reduce doses, skip doses or choose between medicines and other household needs. Krass and colleagues identified medication cost as a consistent and potentially modifiable predictor in the literature they reviewed[2]. In India, socioeconomic disadvantage and healthcare-access barriers have also been identified as predictors of non-adherence[4].

Healthcare-System Factors

Continuity of care, communication, waiting times, availability of medicines, appointment accessibility and medication reconciliation influence whether patients can implement treatment plans. Poor communication can result in uncertainty about dosing, misunderstanding of adverse effects or inappropriate discontinuation. Safe transitions between hospital and outpatient care are also important; current ADA hospital-care guidance emphasizes medication reconciliation, structured communication and education at discharge[19].

Cultural and Family Factors

Family support can facilitate medicine-taking routines, clinic attendance and healthy lifestyle practices, whereas conflicting advice or reliance on unverified treatment claims may create uncertainty. In India, systematic evidence also suggests that traditional medicines and self-medication practices may influence diabetes treatment behaviour, making respectful and non-judgmental communication essential[13].

Major Barriers to Medication Adherence

The central implication of these barriers is that adherence interventions should be matched to cause. A single intervention cannot reasonably address all adherence mechanisms. For example, a reminder application may be appropriate for an unintentional lapse caused by forgetting, but a patient who deliberately avoids a medicine because of hypoglycaemia concerns requires a different intervention involving discussion of perceived risks, adverse effects and alternative treatment options.

Measurement of Medication Adherence

Barrier	How it may affect adherence	Potential response	Reference
Forgetfulness	Missed doses despite intention to follow therapy	Pill organizers, reminders, routine linkage and follow-up.	[46,47]
Adverse effects	Intentional dose reduction or discontinuation	Counselling, adverse-effect management and regimen review.	[46,47]
Cost	Skipped doses, delayed refills or discontinuation	Generic alternatives, affordability review and assistance where available.	[46,48]
Complex regimen	Confusion and increased cognitive burden	Regimen simplification and medication reconciliation.	[46,47]
Low perceived benefit	Reduced motivation for asymptomatic disease	Education linking adherence with individualized goals and outcomes.	[46,47]
Health-system access	Interrupted supply and missed follow-up	Refill coordination, accessible services and continuity of care.	[46,48]
Psychological distress	Reduced self-management capacity or intentional avoidance	Screening, supportive communication and referral when indicated.	[46,49]
Low health literacy	Misunderstanding instructions or risks	Plain-language counselling and teach-back.	[46,50]

Direct Methods

Direct approaches include measurement of drug concentrations, metabolites or pharmacological effects and directly observed administration. These methods can provide strong evidence that a medicine was taken but may be expensive, invasive, difficult to repeat and affected by pharmacokinetic variability. They are therefore less commonly used for routine community assessment of chronic antidiabetic medication adherence.

Indirect Methods

Indirect methods include patient self-report, pill counts, pharmacy refill records, medication possession ratio (MPR), proportion of days covered (PDC), electronic monitoring and validated questionnaires. Each method measures a different aspect of adherence. Pharmacy claims can quantify possession but do not prove ingestion, while self-report is inexpensive and can reveal reasons for non-adherence but may be affected by recall and social-desirability bias[2,20].

Medication Possession Ratio and Proportion of Days Covered

MPR is generally calculated as the total days' supply obtained during a defined period divided by the number of days in that period, whereas PDC is generally capped at 100% and is designed to avoid counting overlapping supplies more than once. A threshold of 80% is frequently used in observational research, but this is a convention rather than a universal biological threshold for every medicine or patient[3,16].

Morisky Medication Adherence Scale

The eight-item Morisky Medication Adherence Scale (MMAS-8) is widely used as a self-report screening measure. Validation studies in diabetes populations have examined reliability, construct validity and relationships with glycaemic

control[21,22]. However, psychometric performance can vary by language, population and adaptation, and the scale should not be treated as a perfect objective measure. Researchers should report the version used, permission requirements where applicable, scoring method and threshold and should avoid presenting self-reported adherence as equivalent to pharmacy-based measures.

Complementary Measurement

Because no single method captures every dimension of adherence, combining approaches can be advantageous. For example, a self-report questionnaire can identify reasons for non-adherence, while pharmacy refill data can provide an objective record of medicine acquisition. Combining behavioural and utilization measures can distinguish "cannot take," "does not want to take," and "cannot obtain" patterns more effectively than any single metric.

Medication Adherence and Glycaemic Control

The clinical rationale for improving adherence is strongly linked to the relationship between medication exposure and glycaemic control. The 2023 meta-analysis of oral antidiabetic adherence found a significant association between good adherence and good glycaemic control, although the pooled effect was modest and observational evidence cannot establish that adherence alone causes improved glycaemic outcomes[1]. Real-world systematic reviews have also reported associations between adherence and clinical outcomes, hospitalization and healthcare costs, but the direction and magnitude of associations vary by therapy and study design[16].

HbA1c is particularly useful in adherence research because it reflects average glycaemic exposure over approximately the preceding two to three months. However, HbA1c is not

a pure adherence biomarker. Diet, physical activity, disease progression, renal function, treatment intensification, steroid exposure, anaemia and other factors may affect glycaemic outcomes. Consequently, a low adherence score and elevated HbA1c should be interpreted as complementary pieces of evidence rather than as proof of a simple causal pathway.

The relationship can also operate in the opposite direction. Poor glycaemic control may lead clinicians to intensify therapy, resulting in more medicines and greater treatment burden. Patients with long-standing or complicated disease may therefore appear less adherent partly because their treatment is more complex. This illustrates why adherence should be interpreted within the broader context of disease severity and treatment trajectory.

Consequences of Medication Non-Adherence

Clinical Consequences

Suboptimal adherence can reduce the effective exposure to glucose-lowering therapy and contribute to inadequate glycaemic control. Over time, sustained hyperglycaemia is associated with microvascular and macrovascular complications[9]. Non-adherence may also lead to treatment escalation, avoidable clinical visits and, in some circumstances, hospitalization[16].

Economic Consequences

Non-adherence can increase costs through disease complications, treatment intensification and healthcare utilization. The economic effect is particularly relevant for chronic diseases because small daily deviations in treatment may accumulate over years. The WHO has highlighted the waste of healthcare resources associated with poor adherence to long-term therapy[14].

Psychosocial Consequences

Diabetes management itself can impose substantial self-management demands. Repeated treatment failure, fear of complications, medication side effects and complex routines may contribute to distress and reduced confidence in self-management. An adherence-focused approach should therefore avoid blame and instead identify practical and psychological barriers that can be addressed collaboratively.

Interventions to Improve Medication Adherence

Patient Education and Counselling

Education is a foundational intervention because patients need to understand what a medicine is for, how it should be taken, what adverse effects may occur and what to do when a dose is missed. Effective counselling should be interactive rather than limited to providing written instructions. Teach-back, individualized examples and discussion of patient concerns can improve the likelihood that information translates into behaviour.

Regimen Simplification

Reducing unnecessary treatment complexity may improve implementation, particularly in people receiving multiple medicines. Potential strategies include once-daily dosing where clinically appropriate, fixed-dose combinations, synchronized refills and medication reconciliation. Simplification must not compromise safety or individualized therapeutic goals; the decision should be made with the prescriber and patient[5].

Reminder and Messaging Interventions

Electronic reminders, text messages and brief messaging interventions have been studied as methods for supporting medication-taking behaviour. Evidence suggests that messaging can be useful in some circumstances, but effects are not uniformly consistent, and interventions that are not tailored to the underlying barrier may have limited impact[23].

Behaviour Change Techniques

A 2024 systematic review of 55 randomized studies identified several behaviour change techniques commonly present in interventions associated with improved adherence, including use of a credible source, instruction on how to perform the behaviour, practical social support, action planning and information about health consequences.[18] The same review emphasized important weaknesses in the literature, including limited reporting of theoretical foundations, intervention fidelity, context and post-intervention follow-up. This supports a shift from generic education toward structured, theory-informed and barrier-specific interventions.

Pharmacist-Led Interventions

Pharmacists can contribute through medication review, adherence assessment, counselling, adverse-effect management, refill monitoring, education, goal setting and communication with prescribers. A systematic review of 36 randomized trials found that pharmacist interventions improved several clinical outcomes and had positive effects on medication adherence and health-related quality of life in most studies that measured these outcomes.[6] A separate systematic review and meta-analysis of 59 studies found beneficial effects from pharmacy-led interventions, with education and printed or digital materials among the strategies associated with favourable outcomes[7].

Digital Health

Digital tools can support reminders, glucose monitoring, teleconsultation, education and feedback. Diabetes technology is increasingly integrated into routine care, and current ADA standards recognize technology as an important component of diabetes self-management[24]. However, technology should be viewed as a delivery mechanism rather than a universal solution. Digital interventions may be less effective when patients have limited digital literacy, limited connectivity, low engagement or barriers that are primarily

financial or treatment-related.

Multicomponent Interventions

Because adherence is multidimensional, interventions combining education, practical support, treatment review, reminders and follow-up may be more appropriate than isolated approaches. The goal is not simply to increase the number of intervention components but to align each component with an identified barrier. A patient with cost-related non-adherence needs affordability solutions; a patient with forgetfulness needs routine-based supports; and a patient with intentional non-adherence requires exploration of beliefs, concerns and treatment preferences.

Role of the Pharmacist in Medication Adherence

Medication Reconciliation and Review

Medication reconciliation allows the pharmacist to identify duplicate therapies, discontinued medicines that remain on lists, dosing discrepancies and opportunities for simplification. This is especially important during transitions of care. Current ADA hospital standards recommend medication reconciliation and patient education at discharge to reduce gaps and errors in diabetes therapy[19].

Adherence Assessment

Pharmacists can use a brief validated questionnaire together with refill history, patient interview and clinical indicators. The purpose should be to identify barriers rather than merely assign an adherence label. Asking open questions such as “What makes it difficult to take this medicine regularly?” can uncover cost, adverse effects, misunderstanding or competing responsibilities.

Education and Behavioural Support

Pharmacists can explain the purpose of each medicine, administration technique, expected effects, common adverse effects and practical strategies for integrating treatment into daily routines. The evidence base supports pharmacist participation in multidisciplinary diabetes care and suggests potential improvements in adherence and clinical outcomes[6,7].

Follow-Up

Adherence should be reassessed over time because barriers change. Follow-up may identify new adverse effects, medication changes, affordability problems or declining motivation. Continuity also allows pharmacists to evaluate whether counselling produced a measurable improvement in medicine use and clinical outcomes.

Special Populations

Older Adults

Older adults may experience polypharmacy, cognitive or sensory limitations, complex comorbidities and difficulties

with physical access to medicines. Interventions should therefore consider regimen simplicity, caregiver involvement where appropriate, and clear communication.

Patients with Polypharmacy

Polypharmacy increases the number of daily tasks and may make it difficult to distinguish medicines by purpose or timing. Medication review and regimen simplification are particularly important in this group.

Patients Using Insulin or Injectable Therapy

Injectable therapy can introduce additional barriers, including injection discomfort, fear of hypoglycaemia, technique requirements, storage and social inconvenience. Education and device training should be individualized and reinforced during follow-up.

Rural and Socioeconomically Disadvantaged Populations

In populations with limited healthcare access, adherence can be constrained by medicine availability, transportation, cost and reduced continuity of care. Indian evidence indicates that socioeconomic disadvantage and health-system access are important contributors to non-adherence[4]. Interventions should therefore include system-level strategies rather than focusing exclusively on patient education.

Evidence from India

Indian adherence research is clinically important because the country combines a large diabetes population with substantial regional, socioeconomic and healthcare-system diversity. The ICMR-INDIAB programme has documented the broad national burden of metabolic disease[12], while recent adherence-specific synthesis indicates that non-adherence remains common and that the evidence base is geographically uneven[4].

The 2026 Indian systematic review included 16 studies published between 2020 and 2024. The authors reported non-adherence estimates ranging from 11% to 68% overall and a pooled non-adherence prevalence of 48% among studies using MMAS-8. Predictors included older age, socioeconomic disadvantage, substance use, treatment complexity, psychological distress, polypharmacy and health-system access barriers[4]. The authors also noted that studies were disproportionately concentrated in parts of India, limiting national generalizability[4].

These findings support a shift toward context-specific adherence services. In Indian pharmacy practice, adherence assessment could be integrated into medication counselling, chronic disease clinics and community-pharmacy encounters. However, implementation should account for medicine affordability, availability of generic alternatives, local languages, health literacy and continuity between primary, secondary and tertiary care.

Synthesis of Major Literature

Design/Scope	Principal contribution	Interpretive point	Reference
Systematic review; 27 studies	Adherence ranged 38.5–93.1%; depression and medication cost were consistent potentially modifiable predictors.	Large variability reflects heterogeneous measures and populations.	[2]
Meta-analysis; 40 studies with relevant endpoints	Pooled mean MPR 75.3%; 67.9% met MPR $\geq 80\%$; persistence was variable.	MPR is a proxy for possession, not ingestion.	[3]
Systematic review/meta-analysis; 156 studies, >10 million patients	Pooled oral-drug adherence 54%; good adherence associated with good glycaemic control.	Association does not establish causality.	[1]
Systematic literature review; 92 real-world studies	Adherence and persistence varied widely and were linked in some studies with clinical/economic outcomes.	Evidence was predominantly retrospective and often US-based.	[16]
Systematic review/meta-analysis; 26 studies, 69,366 patients	Estimated OAD adherence at 55.53%.	Large studies still showed substantial heterogeneity.	[17]
Indian systematic review/meta-analysis; 16 studies	Non-adherence 11–68%; MMAS-8 pooled non-adherence 48%; multiple predictors identified.	Geographic diversity and reporting limitations restrict national inference.	[4]
Systematic review of 36 RCTs	Pharmacist interventions improved several outcomes and often adherence/quality of life.	Interventions were heterogeneous.	[6]
Systematic review/meta-analysis; 59 studies	Pharmacy-led interventions improved diabetes-related outcomes; education/digital materials were useful.	Effects differed by intervention type and outcome.	[7]
Systematic review; 55 RCTs	Identified behaviour-change techniques and highlighted reporting/tailoring gaps.	Intervention context and sustainability require better study design.	[18]

Future Perspectives

Future adherence care is likely to become more individualized. Rather than classifying patients simply as adherent or non-adherent, clinicians may increasingly identify the specific mechanism of difficulty and match the intervention to that mechanism. Digital reminders, electronic dispensing records, remote consultations and patient-reported outcomes may support continuous monitoring, while clinical pharmacists can interpret these data within the broader medication and disease context. Behavioural science also provides an important future direction. The COM-B framework and behaviour-change technique taxonomy can help researchers describe why an intervention should work and which mechanism it targets.[18] This may improve reproducibility and enable stronger comparisons between interventions. In parallel, healthcare systems should address structural determinants such as affordability, medicine availability and continuity of care because behavioural counselling cannot fully compensate for inaccessible treatment. In India, future work should prioritize multicentre studies spanning different regions and healthcare settings, culturally and linguistically adapted interventions, community-pharmacy involvement, and evaluation of cost-effectiveness. Research should also

examine how adherence services can be integrated into routine primary care without creating excessive workload for patients or healthcare professionals.

Discussion

The evidence reviewed in this paper establishes medication adherence as a central determinant of effective T2DM management, but it also demonstrates why adherence should not be reduced to a single percentage. The prevalence of adherence varies substantially depending on whether the study measures self-reported behaviour, medicine possession, persistence or another construct. Consequently, apparently different estimates across studies often reflect differences in methodology rather than genuine contradictions[1-3,16,17]. The clinical importance of adherence is nevertheless clear. Good adherence is associated with better glycaemic control in large observational evidence syntheses[1], while broader real-world literature connects adherence and persistence with clinical and economic outcomes[16]. The relationship should be interpreted cautiously because disease severity and treatment complexity can influence both adherence and outcomes.

The intervention literature supports a multidisciplinary

approach. Pharmacist involvement has repeatedly been associated with improvements in diabetes-related outcomes, and several systematic reviews indicate favourable effects on adherence[6,7]. Behaviour-change research further suggests that interventions incorporating credible professional support, practical instruction, action planning, social support and health-consequence information may be useful[18]. However, the absence of one universally effective intervention is itself an important finding. Adherence barriers are heterogeneous, so intervention design should be individualized and theoretically informed.

For B.Pharm practice, the topic has direct relevance. Pharmacists are uniquely positioned at the interface between medicines and patient behaviour. Their contribution should extend beyond dispensing to medication reconciliation, adherence assessment, counselling, adverse-effect identification, regimen review and communication with prescribers. The objective is not to police medicine-taking but to identify and remove barriers to safe and effective therapy.

Conclusion

Medication adherence is a fundamental component of successful type 2 diabetes management. The available literature consistently demonstrates that a substantial proportion of patients do not take or continue glucose-lowering medicines as intended, although the reported magnitude varies because adherence is measured in different ways[1-3,17]. Non-adherence is multidimensional and may arise from forgetfulness, treatment complexity, adverse effects, cost, health beliefs, psychological distress, social circumstances, medicine availability and healthcare-system barriers[2,4,14,18].

Good medication adherence is associated with better glycaemic control and may reduce the clinical and economic consequences associated with inadequate treatment exposure[1,16]. Nevertheless, adherence should not be interpreted as a fixed patient characteristic or a matter of blame. It is a dynamic behaviour shaped by the interaction between individuals, medicines, healthcare professionals and the broader healthcare environment.

Effective adherence management should therefore combine patient-centred education, shared decision-making, treatment simplification when appropriate, affordability and access considerations, behavioural support, follow-up and technology where useful. Pharmacists have an important role in delivering and coordinating these interventions[6,7]. Future research should standardize adherence measurement, improve reporting of intervention mechanisms and context, extend follow-up, and strengthen evidence from diverse populations, particularly in India[4,18].

Recommendations

For Patients

- Understand the purpose and expected benefit of each

prescribed medicine.

- Discuss adverse effects, cost concerns or difficulties rather than stopping medicines without professional advice.
- Use practical routines, reminders or organizers when forgetfulness is a problem.
- Attend scheduled monitoring and follow-up appointments.

For Pharmacists

- Incorporate routine adherence screening into diabetes medication review.
- Identify the specific reason for non-adherence before selecting an intervention.
- Use plain-language counselling and teach-back.
- Review adverse effects, drug interactions, dosing schedules and opportunities for simplification.
- Coordinate with physicians and other healthcare professionals when treatment changes are required.
- Use refill history and other objective information where available to complement self-report.

For Prescribers

- Use shared decision-making and consider treatment burden, adverse effects, cost, access and patient preferences[5].
- Review adherence before automatically escalating therapy when clinically appropriate.
- Provide clear instructions and reassess the treatment plan after initiation or intensification.

For Healthcare Systems

- Improve continuity of diabetes care and medicine availability.
- Strengthen medication reconciliation during care transitions[19].
- Support pharmacist integration into multidisciplinary diabetes services.
- Develop accessible and culturally appropriate adherence-support programmes.

For Researchers

- Use clearly defined and validated adherence measures.
- Report both adherence and persistence separately.
- Combine subjective and objective measures where feasible.
- Evaluate sustainability beyond the active intervention period.
- Include diverse Indian populations and report regional and socioeconomic characteristics.

Conflict of Interest

The authors declare that they have no conflicts of interest.

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