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Systematic Review

Determinants of Medication Adherence in Older Adults with Type 2 Diabetes: A Systematic Review Based on the WHO Five-Dimensional Framework

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Abstract

Introduction: Medication non-adherence in elderly patients with type 2 diabetes mellitus contributes to poor disease control and complications. This systematic review aimed to systematically identify and classify the determinants of medication adherence in older adults with type 2 diabetes according to the WHO five-dimensional framework.

Methods: This systematic review was conducted in accordance with PRISMA guidelines. A comprehensive search of PubMed, ScienceDirect, Web of Science, SAGE Journals, the Cochrane Library, Google Scholar, and Scopus were performed for English-language studies published from January 2000 to December 2024. Observational and qualitative studies conducted among adults aged ≥ 60 years with type 2 diabetes were included if medication adherence was assessed using validated instruments or defined self-report measures. Study quality and risk of bias were evaluated using standardized appraisal tools. Due to substantial methodological heterogeneity across study designs and adherence measures, findings were synthesized narratively.

Results: Of 1,143 identified records, 29 studies met the inclusion criteria. Factors associated with non-adherence, as reported in the included studies, included socio-demographic characteristics (younger age, male sex, single status, low income or education, and alcohol use), patient-related barriers, psychological comorbidities (anxiety and depression), and healthcare system constraints. Factors promoting adherence included structured healthcare support, better quality of life, simpler medication regimens, reduced medication costs, higher self-efficacy, stronger social support, spiritual coping, greater health literacy, positive treatment attitudes, and engagement in self-care behaviors.

Conclusion: This review highlights modifiable barriers and facilitators to medication adherence in elderly patients with type 2 diabetes, supporting interventions like mental health integration and treatment simplification to improve outcomes.

Introduction

Type 2 diabetes mellitus (T2DM), which accounts for more than 90% of diabetes cases worldwide, is a chronic metabolic disorder characterized by persistent hyperglycemia and associated with serious long-term complications, including cardiovascular disease, kidney failure, neuropathy, and visual impairment.[1,2] In 2021, an estimated 536.6 million adults worldwide were living with diabetes (10.5% prevalence), and this number is projected to rise to 783.2 million (12.2%) by 2045. Prevalence is highest among older adults and is increasing most rapidly in middle-income countries. In addition to its growing epidemiological burden, diabetes imposes substantial economic costs, with global health expenditures reaching 966 billion USD in 2021.[2] These trends highlight the urgent need for effective long-term disease management.

Older adults (≥ 60 years) represent a rapidly growing segment of the diabetic population. Age-related physiological decline, multimorbidity, cognitive impairment, and functional limitations increase both the prevalence and management complexity of T2DM in this group.[3,4] Optimal diabetes control requires sustained engagement in multiple self-management behaviors, including adherence to dietary recommendations, regular physical activity, stress management, glucose monitoring, and pharmacological treatment.[5,6] However,

Research Highlights

What is the current knowledge?

- T2DM prevalence is rising globally, particularly among the elderly due to aging populations and declining capacities.
- Medication adherence in T2DM patients is often weak to moderate, influenced by factors like gender, age, self-efficacy, social support, and affordability.
- The WHO five-dimensional model classifies adherence determinants into socio-economic, patient-related, condition-related, therapy-related, and healthcare/system factors.
- Prior studies have explored specific adherence factors in elderly patients with type 2 diabetes; however, to the best of our knowledge, a comprehensive application of the WHO model has not been fully addressed.
- Higher age is variably associated with adherence levels across studies.

What is new here?

- This systematic review applies the WHO framework to synthesize factors affecting medication adherence specifically in elderly T2DM patients, addressing a key literature gap.
- This study highlights key barriers (e.g., younger age, low income/education, anxiety/depression, complex treatment regimens, and healthcare system obstacles) and facilitators (e.g., social support, self-efficacy, simplified treatments, and health literacy) associated with adherence.
- This study synthesizes evidence on associations across different dimensions, with socio-economic and patient-related factors being the most frequently examined, while healthcare/system-level factors remain relatively underexplored.
- This study highlights variability in adherence rates (low in > 50% of participants in some studies and moderate/good in ≥ 50% in others); however, these differences should be interpreted cautiously because different measurement tools and cut-off thresholds were used across studies. It also suggests interventions such as mental health screening, regimen simplification, and patient education.
- This study suggests potential strategies to enhance adherence and may help inform targeted interventions, while highlighting cultural and societal differences in the impact of these factors.

adherence to lifestyle recommendations and medication regimens remains suboptimal among many patients with T2DM.[7] Medication adherence defined as the extent to which patients take medications as prescribed is particularly critical for glycemic control and prevention of complications. [8, 9]

Medication adherence defined as the extent to which patients take medications as prescribed is a key determinant of treatment effectiveness and complication prevention.[10] In older adults with T2DM is influenced by a complex interplay of socio-demographic, psychological, clinical, and health system factors. Variables such as age, gender, self-efficacy, social support, treatment complexity, and affordability have been shown to affect adherence behaviors.[11-13] Notably, the association between older age and medication adherence remains inconsistent across studies, with some reporting improved adherence among older individuals, while others suggest the opposite.[11-13] This inconsistency underscores the need for a structured framework to systematically categorize and interpret adherence determinants.

The World Health Organization (WHO) five-dimensional adherence model provides a comprehensive framework for understanding factors influencing medication adherence.[14] This model classifies determinants into five domains: socio-economic factors, This model classifies determinants into five domains: socio-economic factors, patient-related factors, condition-related factors, therapy-related factors, and healthcare system/team-related factors.[10] Unlike behavior-specific models such as the COM-B framework, which conceptualizes behavior in terms of capability, opportunity, and motivation, the WHO model offers a broader, health-system-oriented structure suitable for synthesizing heterogeneous determinants across diverse study designs and populations. Its disease-agnostic and multidimensional structure makes it particularly appropriate for systematic reviews examining adherence in complex chronic conditions.

To the best of our knowledge, no prior systematic review has comprehensively synthesized determinants of medication adherence among older adults with T2DM using the WHO five-dimensional framework. Therefore, this study aimed to systematically identify and classify the determinants of medication adherence in older adults (≥ 60 years) with type 2 diabetes mellitus according to the WHO adherence model.

Materials and Methods

This systematic review was conducted and reported following the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, utilizing its checklist to enhance clarity and quality. The protocol for this review was not registered in any protocol registry, including PROSPERO.

Data Sources and Search Strategy

Articles were searched in the databases PubMed, Science Direct, Web of Science, SAGE Journals, Cochrane Library, Google Scholar, and Scopus using a search strategy derived from a review of the literature in this field and Medical Subject Headings (MeSH). The search strategy was adapted for each database based on its specific indexing system and search syntax. The following keywords were used in this search strategy and are presented in Appendix A, adapted for the Web of Science database.

Also, to ensure reproducibility, a defined screening limit was applied when using Google Scholar. For each search query, only the first 10 pages of results (approximately the first 100 records) were screened. This approach aligns with common recommendations and practices in systematic searches, considering Google Scholar's ranking algorithm and the absence of advanced filtering options.

Study selection

The study's eligibility criteria (both for inclusion and exclusion) were established by adhering to the PRISMA guidelines.

Inclusion criteria

Study type: Cross-sectional, case-control, cohort, and qualitative studies were considered for inclusion.

Study topic: Studies that examined medication adherence among patients with type 2 diabetes mellitus (T2DM) were included.

Study population: Individuals aged 60 years or older with T2DM.

Study outcomes: Medication adherence was assessed using validated measurement tools with established psychometric properties, such as the 8-Item Morisky Medication Adherence Scale (MMAS-8), Medication Possession Ratio (MPR), and Proportion of Days Covered (PDC) or reliable self-reported measures. Adherence had to be defined in behavioral terms such as treatment discontinuation, dose omission, or partial compliance.

Timeframe: Studies published from 2000 onwards were included.

Language: Only studies published in English were considered.

Setting: Studies conducted among outpatients in healthcare settings were included.

Exclusion criteria

Articles with non-standard formats, unclear or insufficient reporting of sample characteristics, or studies not focusing on medication adherence in older adults with T2DM were excluded. Randomized controlled trials (RCTs) and quasi-experimental studies were also excluded because these designs typically evaluate interventions rather than naturalistic factors influencing medication adherence, which were the primary focus of this review. Additionally, review articles and conference abstracts were excluded.

Data extraction and screening

Articles retrieved from the specified databases were sorted and scrutinized using EndNote management software. One researcher conducted the article search from the databases. Once duplicates were removed, the titles and abstracts of the articles were assessed for suitability. Following that, the full text of the articles was examined, and pertinent data from the qualifying articles were logged in a data extraction table. This process was carried out independently by two researchers. If there was a disagreement on the remaining articles between the two researchers, a third researcher would step in to review and provide their viewpoint to settle the dispute. Additionally, the reference list of the leftover and related articles was also inspected (Figure 1).

Narrative synthesis

A meta-analysis of the results was not possible due to substantial diversity in key methodological elements across the included studies. These variations encompassed sampling methods, participants' age ranges, study settings, study designs, and the instruments used to measure medication adherence. The process of data extraction was conducted based on several predefined criteria, including the lead author's name, the year and country of publication, the study design (type of study, study objective, setting, sampling method, sample size, and inclusion and exclusion criteria), the tools used to assess medication adherence, the independent variables examined in relation to adherence, the level of medication adherence, and the main findings (as presented in Tables 1 and 2).

Following data extraction, study findings were mapped

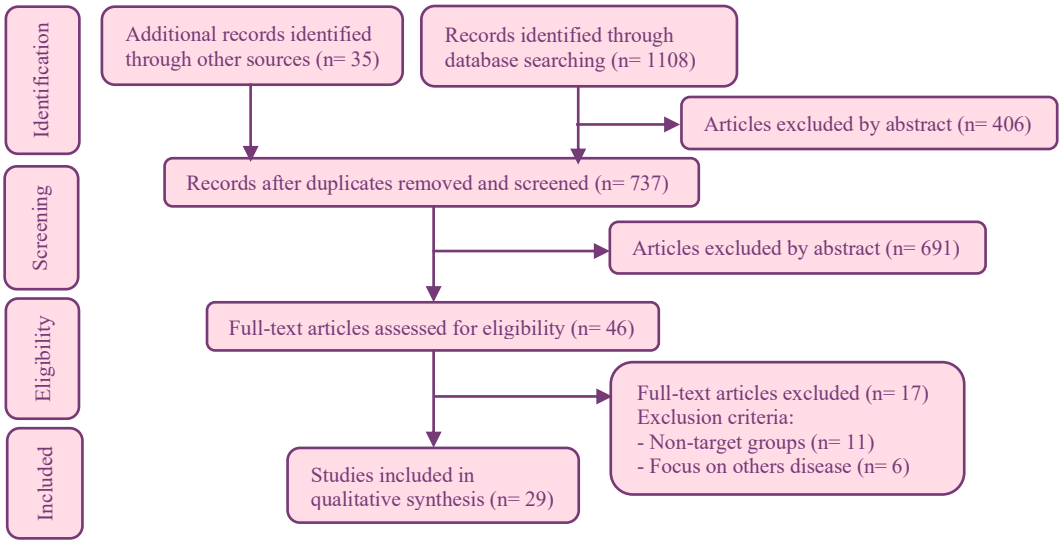

Figure 1. Flow diagram for the identification, screening, eligibility, and inclusion of studies

Table 1. Description of the studies

First author/ Country (year)	Study design						Risk-of-bias
	Research design	Objective	Sampling location	Sampling technique	Sample size	Eligibility criteria	
Balkrishnan et al[15]/ USA (2003)	Longitudinal cohort study	To examine the relationship between self-reported health status data, subsequent anti-diabetic medication adherence, and health care service utilization	Medicare health maintenance organization	Convenience sampling	775	Inclusion: Participants were required to be over 65 years old, use anti-diabetic drugs, and be continuously enrolled in a health maintenance organization for 1 to 5 years.	Moderate
Nicklett & Liang[16]/ USA (2010)	Longitudinal cohort study	To examine the relationship between socio-demographic and social support, adherence, and health decline	Community-dwelling individuals	Random sampling	1788	Inclusion: individuals over the age of 60 years with type 2 diabetes mellitus	Good
Park et al[17]/ Korea (2010)	Observational (cross-sectional)	To evaluate the factors affecting medication adherence in geriatric diabetic patients	Private clinics and hospitals	Not reported	265	Inclusion: Patients older than 65 years and patients who had been taking diabetes medication for longer than 6 months	Moderate
Manan et al[18]/ Malaysia (2014)	Observational (cross-sectional)	To assess the level of hypoglycemic medication adherence, the factors associated with adherence and the quality of life	Non-Communicable Disease Clinic	Convenience sampling	179	Inclusion: patients aged 60 years and/or above, having T2DM since at least one year (being diagnosed in the clinic), and documentation of past HbA1c measurements with the details of oral hypoglycemic medications Exclusion: patients who have cognitive, verbal problems or have difficulty to respond to the instruments of the study	Moderate
Gentil et al[19]/ Canada (2017)	Observational (cross-sectional)	To document the impact of depression and anxiety disorders on adherence to oral hypoglycemic	Community-dwelling individuals	Random sampling	301	Inclusion: patients taking oral hypoglycemic medication alone during the 2 years of follow-up Exclusion: Patients who did not have at least two consecutive prescriptions of oral hypoglycemic drugs	Moderate
MacEwan et al[20]/ USA (2017)	Retrospective study	To examine the relationship between medication adherence, cost sharing measured as out-of-pocket spending, and total annual spending in Medicare beneficiaries with type 2 diabetes	Medicare claims data	Random sampling	12305	Inclusion: Patients with a T2D diagnosis or anti-diabetics medication use in the year prior to the first observed claim in the database if the patient's index date was less than 1 year after the date of Medicare enrollment Exclusion: Patients with a follow-up period of less than 1 year after the index date or those who were pregnant or less than 6 months post-partum	Good
Wallace et al[21]/ USA (2017)	Qualitative (ethnographic approach)	To examine the intersections of drug abuse histories and medication adherence among urban, older African Americans with T2D	Community-dwelling individuals	Not reported	83	Inclusion: Older adults living in Baltimore City	Moderate
Borba et al[22]/ Brazil (2018)	Observational (cross-sectional)	To identify factors associated with medication compliance in elderly type 2 diabetic patients	Elderly Care Center	Not reported	47	Inclusion: Patients with type 2 diabetes aged 65 years or older who had not developed diabetic complications, or symptoms of complications, who self-managed their oral medications, did not have cognitive problems, and were able to complete the questionnaire without assistance	Moderate
Caballero et al[23]/ USA (2018)	Observational (cross-sectional)	To investigate potential cognitive and demographic correlates of medication non adherence in older Hispanic adults with type 2 diabetes	Healthcare clinics, community centers, and the local community	Not reported	40	Inclusion: Hispanic ethnicity, an age of 65 years or older, and a diagnosis of type 2 diabetes Exclusion: cognitive impairment requiring pharmacotherapy and severe psychiatric illness that would impair the ability to provide consent	Moderate
Mendes et al[24]/ Portugal (2019)	Observational (cross-sectional)	To identity predictors of medication non-adherence	Hospital	Not reported	94	Inclusion: aged≥65 years old and diagnosis of diabetes	Moderate
Saffari et al[25]/ Iran (2019)	Longitudinal cohort study	To investigate the impact of religiosity on medication adherence and Health Related Quality of Life (HRQoL)	Outpatient Diabetic Unit of university hospitals	Convenience sampling	793	Inclusion: a confirmed diagnosis of T2D for at least 1 year before the study; aged 65 years or older; taking anti-diabetes medications regularly, and; agreeing to participate in the study Exclusion: Had a severe cognitive impairment, were not able to read and speak Persian, or were not responsible for taking their medications	Moderate

Table 1. Continued.

First author/ Country (year)	Study design						Risk-of-bias
	Research design	Objective	Sampling location	Sampling technique	Sample size	Eligibility criteria	
Taber et al[26]/ USA (2019)	Longitudinal cohort study	To evaluate the impact on medication adherence for veterans with dual health care system use when obtaining prescription antihyperglycemic medications to treat diabetes	Clinical and administrative files from the Veterans Health Administration and Centers for Medicare	Not reported	254267	Inclusion: Veterans with type 2 diabetes, completed at least 2 fills of a specific antihyperglycemic class during 1 or more years	Good
Hussain et al[27]/ Pakistan (2020)	Observational (cross-sectional)	To evaluate associations that occur between the level of health literacy and medication adherence	Hospital	Convenience sampling	524	Inclusion: Females older than 60 years with diabetes and concurrent cardiovascular disease Exclusion: Any evidence of psychosis or dementia and the presence of any other current diabetic complication such as neuropathy, retinopathy, nephropathy, and chronic pain	Moderate
Xu et al[28]/ China (2020)	Observational (cross-sectional)	To examine the prevalence of medication non-adherence among older adults with diabetes mellitus	Community-dwelling individuals	Random sampling	1002	Inclusion: Older adults with diabetes mellitus and were taking anti-diabetic medication/had taken anti-diabetic medication	Moderate
Bonikowska et al[29]/ Poland (2021)	Observational (cross-sectional)	To analyze the impact of disease acceptance and selected demographic and clinical factors on the adherence to treatment recommendations in elderly type 2 diabetes mellitus patients	Primary health care centers	Convenience sampling	200	Inclusion: Age ≥ 60 years, time from the diagnosis of T2DM of at least one-year, written consent to conduct the study, practical means of contact with the patient, no diagnosis of severe mental disorders requiring psychiatric treatment.	Moderate
Gomez-Peralta et al[30]/ Spain (2021)	Observational (cross-sectional)	To investigate the prevalence of low adherence to anti-diabetic treatments and the frequency of unrecognized hypoglycemic events in people with T2DM attended at community pharmacies	Community-dwelling individuals	Not reported	618	Inclusion: adult participants receiving pharmacologic anti-diabetic treatment, following the same therapeutic regimen for at least 12 months, with an e-prescription in the previous 6 months and who agreed to participate in the study. Exclusion: Participants who were unable to understand the procedures of the study or complete the questionnaires	Moderate
He et al[31]/ USA (2021)	Observational (cross-sectional)	To examine associations between factors and medication non-adherence among Medicare beneficiaries with type 2 diabetes	Community-dwelling individuals	Multistage sampling	1430	Inclusion: Medicare beneficiaries aged 65 years and older with reported type 2 diabetes	Moderate
Temma et al[32]/ Thailand (2021)	Observational (cross-sectional)	To estimate the prevalence of glycemic control and determine its associated factors among elderly patients with T2DM	Hospital	Convenience sampling	307	Inclusion: T2DM outpatients diagnosed by medical doctors; aged ≥ 60; who can read and write Japanese and are willing to participate in the study. Patients who were hospitalized; using insulin for treatment	Moderate
Wakui et al[33]/ Japan (2021)	Observational (cross-sectional)	To identify factors associated with medication compliance in elderly type 2 diabetic patients	Community-dwelling individuals	Not reported	47	Inclusion: patients with type 2 diabetes aged 65 years or older who had not developed diabetic complications, or symptoms of complications, who self-managed their oral medications, did not have cognitive problems, and were able to complete the questionnaire without assistance.	Moderate
Bonikowska et al[34]/ Poland (2022)	Observational (cross-sectional)	To assessing the impact of frailty syndrome on the level of adherence to medication in elderly patients with type 2 diabetes	Primary health care centers	Not reported	175	Inclusion: age ≥ 60, at least a year since diabetes was diagnosed, a written consent for the participation in the study and physical ability to fill in the questionnaire Exclusion: Participants who have neoplastic disease, chronic heart failure, acute respiratory disease, ischemic heart disease	Moderate
Lara-Morales et al[35]/ Spain (2022)	Observational (cross-sectional)	To explore the influence of anxiety/depression symptoms and social risk in patients older than 65 years with type 2 diabetes mellitus both in non-adherence to pharmacological treatment and in poor control	Primary care centers	Not reported	884	Inclusion: Adults over 65 years of age with type 2 Diabetes Mellitus	Moderate

Table 1. Continued.

First author/ Country (year)	Study design						Risk-of-bias
	Research design	Objective	Sampling location	Sampling technique	Sample size	Eligibility criteria	
Rosli et al[36]/ Malaysia (2022)	Observational (cross-sectional)	To determine the relationship between self-efficacy in medication understanding and quality of life, and the factors associated with QOL in elderly with type 2 diabetes mellitus	Primary care centers	Convenience sampling	321	Inclusion: aged ≥ 60 years old, intact cognitive function, have been diagnosed with T2DM for at least one-year duration, received follow up care at institutional PCSC for at least once within the last one year, on polypharmacy which is ≥ 5 medications and was able to read and communicate in either Malay or English language	Moderate
Jeyalakshmi et al[37]/ India (2023)	Observational (cross-sectional)	To investigate the determinants of medication non-adherence among rural elderly with co-morbid chronic conditions of hypertension (HTN) and type 2 diabetes mellitus (T2DM) in India	Primary health centers	Probability proportional to size sampling	360	Inclusion: elderly aged 60 years and above Exclusion: the elderly with chronic illnesses who had a previous experience of being part of any other project related to drug compliance and also elderly with any other major diagnosed co-morbid illness	Moderate
Maghsoudi et al[38]/ Iran (2023)	Qualitative study	To determine the barriers to treatment adherence among older adults with type 2 diabetes	Diabetes clinics, health centers and local health facilities	Purposive sampling	25	Inclusion: Patients who had been diagnosed with T2D by a Specialist (Internist) and sub- specialist (Endocrinologist) according to WHO criteria; with a history confirming T2D for more than 1 year, age over 60 years, ability to communicate, no other chronic disease and no cognitive impairment.	Moderate
Maghsoudi et al [39]/ Iran (2023)	Qualitative study	To identify the concept of treatment adherence and its associated factors in older people with type 2 diabetes	Diabetes clinics, health centers and local health facilities	Purposive sampling	20	Inclusion: Patients who had been diagnosed with T2D by a Specialist (Internist) and sub- specialist (Endocrinologist) according to WHO criteria; with a history confirming T2D for more than 1 year, age over 60 years, ability to communicate, no other chronic disease and no cognitive impairment.	Moderate
Udupa et al[40]/ India (2023)	Observational (cross-sectional)	To estimate the proportion of medication adherence among diabetic patients above 60 years of age attending a tertiary care hospital in Southern India	Hospital	Consecutive sampling	101	Inclusion: Elderly individuals (>60 years old) who were previously diagnosed with T2DM and were on anti-diabetic medication for at least 1 month	Moderate
Upamali & Rathnayake[41]/ Sri Lanka (2023)	Qualitative study	To explore the perspectives of older people with uncontrolled type 2 diabetes mellitus towards medication adherence	Diabetic Clinic, Hospital, community-dwelling individuals	Snowball sampling	14	Inclusion: Participants aged 60 years and over who were diagnosed with DM by a physician with uncontrolled type 2 diabetes	Moderate
Wu et al[42]/ China (2023)	Observational (cross-sectional)	To investigate the mediation and moderation effects of self-efficacy on the relationship between medication beliefs and adherence in elderly patients with type 2 diabetes	Hospital	Bootstrapping sampling	309	Inclusion: patients aged 65 years or older with type 2 diabetes who had been treated with antidiabetic agents for at least 3 months and were admitted to the internal medical unit, including the endocrinology department, nephrology department, respiratory department, gastrology department, neurology department, and cardiology department Exclusion: patients with type 1 diabetes and other specific types of diabetes, diabetic ketoacidosis, or diabetic coma, and those who could not communicate	Moderate
Yang et al[43]/ China (2023)	Observational (cross-sectional)	To explore the associations among depressive symptoms, medication adherence and QOL in older adults with T2DM	Hospital	Not reported	300	Inclusion: patients with age ≥ 60 years old who meet the WHO diagnostic criteria for T2DM with the course of T2DM ≥ 1 year Exclusion: Patients who suffered from serious diseases such as cancer, heart disease, liver disease and kidney failure that may affect their QOL, and those who were diagnosed with dementia or schizophrenia	Moderate

Type 2 diabetes mellitus; T2DM, Quality of life; QOL, Type 2 diabetes; T2D

Table 2. Summary of findings

First author (year of study)	Measure of medication adherence	Independent variables tested	Medication adherence of sample	Statistically significant findings
Balkrishnan et al[15]/ USA (2003)	Medication Possession Ratio (MPR)	1. Socioeconomic factors (a. Age; b. Gender) 2. Lifestyle 3. Quality of life 4. Depression 5. Costs	Not reported	- Increased anti-diabetic medication adherence, measured by Medication Possession Ratio (MPR), was strongly associated with decreased total annual health care costs. - For every 10% increase in MPR, there was an 8.6% to 28.9% decrease in annual health care costs.
Nicklett & Liang[16]/ USA (2010)	Self-reported adherence to the six diabetic regimen components	1. Socioeconomic factors (a. Age; b. Gender; c. educational degree; d. Race/ethnicity) 2. Social Support 3. Patient–provider interaction	Not reported	- Support for diabetes care boosts adherence to health-promoting activities but doesn't necessarily improve perceived health status.
Park et al[17]/ Korea (2010)	MMAS-4	1. Socio-demographic status and lifestyle variables (a. Age; b. Gender; c. educational level; d. residence; e. financial level; f. smoking state) 2. The characteristics associated with disease and medication (a. the number of currently ailing diseases; b. the number of medical institutions visited for the current ailment; c. time since diabetes diagnosis; d. the number of diabetes drugs) 3. Health Belief Model (a. Susceptibility seriousness; b. cue to action; c. self-efficacy; d. benefit and barrier)	Hospital patients: 61.1% adherence Private clinic patients: 43.2% adherence	- Influential factors varied by setting, with drug storage and self-efficacy being crucial in hospitals, while financial status were key in clinics.
Manan et al[18]/ Malaysia (2014)	MMAS-8	1. Socioeconomic factors (a. Age; b. Gender; c. Ethnicity; d. Marital status; e. Education level; f. Income g. BMI) 2. Clinical characteristics (a. Duration of diabetes; b. Number of medication) 3. Quality of life	52.0% = low adherence, 48.0% = high adherence	- Medication adherence was associated with gender and quality of life
Gentil et al[19]/ Canada (2017)	Medication possession ratio (MPR)	1. Socioeconomic factors (a. Age) 2. Andersen's behavioral model (a. Need factors (Depression and anxiety disorders, Index Comorbidity, Charlson); b. Predisposing factors (Gender, Education level); c. Enabling factors (Income, Marital status)	Not reported	- Significant difference in oral hypoglycemic medication adherence with depression and anxiety disorders. - Significant difference in oral hypoglycemic medication adherence with levels of education.
MacEwan et al[20]/ USA (2017)	The proportion of days covered (PDC)	1. Cost sharing	Not reported	- The most adherent group also had 64% lower medical spending ($7692 vs $21,421) than the least adherent group.
Wallace et al[21]/ USA (2017)	McGill Illness Narrative Interview (MINI)	1. Socioeconomic factors (a. age; b. gender; c. Living situation) 2. Knowledge about diabetes experience and their self-management 3. Spirituality 4. Lifestyle	Not reported	- Medication adherence was associated with lifestyle - There was a difference in knowledge of blood glucose goals between those who adhered to their medication regimen and those who did not.
Borba et al[22]/ Brazil (2018)	Medication management questionnaire	1. Socioeconomic factors (a. Sex; b. Age) 2. The characteristics associated with disease and medication (a. duration of diabetes; b. number of medications taken) 3. Knowledge of drug effects, and side effects 4. Quality of life	Not reported	- Knowledge of drug effects, knowledge of side effects, medication storage, and the life rating scale (SF-12) subscale physical functioning were strongly associated with medication adherence.
Caballero et al[23]/ USA (2018)	Visual analog scale (VAS)	1. Socioeconomic factors (a. Age; b. Gender; c. educational level) 2. Time diagnosis of diabetes	Not reported	- Time diagnosis of diabetes, and educational level were strongly associated with medication adherence.
Mendes et al[24]/ Portugal (2019)	The measure treatment adherence (MTA)	1. Socio-Demographic factors (a. Age; b. Gender; c. Marital status; d. Living situation; e. Education; f. Occupation; g. Income; h. BMI) 2. Anxiety and depression	14.9% = non-adherent, 14.9% = Partially adherent, 70.2 % = Adherent	- Higher anxiety and depression levels correlated with increased medication non-compliance.
Saffari et al[25]/ Iran (2019)	MARS-5	1. Socioeconomic factors (a. Age; b. Gender; c. Employment; d. educational level; e. Religiosity) 2. Spiritual coping strategy 3. Perceived social support 4. Quality of life	Not reported	- Religious coping, quality of life and social support significantly mediate the impact of religiosity on medication adherence.
Taber et al[26]/ USA (2019)	Proportion of days covered (PDC)	1. Socioeconomic factors (a. Age; b. Gender; c. Marital status; d. Disability; e. Race/Ethnicity; f. Location of residence) 2. Number of comorbidities	Adherence to diabetes prescriptions 75% of VA-only users 63% of dual users	- Adherence decreased with each additional diabetes medication prescribed
Hussain et al[27]/ Pakistan (2020)	Brief Adherence Rating Scale (BARS test)	1. Socioeconomic factors (a. Age; b. Annual income; c. Education) 2. The characteristics associated with disease and medication (a. Age of diagnosis of diabetes; b. Presence of diabetic complications) 3. Health literacy 4. Health status	Medication adherence score (average): 3.1	- Higher health literacy levels correlated with increased medication compliance.

Table 2. Continued.

First author (year of study)	Measure of medication adherence	Independent variables tested	Medication adherence of sample	Statistically significant findings
Xu et al[28]/ China (2020)	Morisky Green Levine (MGL)	1. Socioeconomic factors (a. Age; b. Gender; c. Residence; d. Marital status; e. Employment status; f. educational level; g. Annual income) 2. Therapy-related factors (a. Duration of the disease; b. Incidence of complication; c. Type of medication) 3. Patient-related factors (a. Perceived importance of medication adherence)	46.2% = Highly adherence 33.9% = Moderate adherence 19.9% = Low adherence	- Female respondents were more likely to experience medication non-adherence. - Those with a disease duration of five years or longer were less likely to experience non-adherence. - Respondents who perceived medication adherence as unimportant were more likely to be non-adherent.
Bonikowska et al[29]/ Poland (2021)	Adherence in Chronic Diseases Scale (ACDS)	1. Socioeconomic factors (a. Age; b. Gender; c. Place of residence; d. educational level; e. Marital status; g. BMI) 2. Clinical variables (a. Duration of the disease; b. Diabetes treatment method; c. Presence and type of comorbidities; d. Number of diabetes tablets per day) 3. Anxiety and depression 4. Self-care	22% = Highly adherence 57% = Moderate adherence 21% = Low adherence	- The complexity of the medication regimen, the duration of diabetes, and Self-care affected adherence.
Gomez-Peralta et al[30]/ Spain (2021)	MMAS-8	1. Socioeconomic factors (a. Age; b. Gender; c. Employment status; d. educational level) 2. Number of treatments per patient and type of pharmacy	40.6% = High adherence 35.1% = Medium adherence 24.3% = Low medication	- The main determinants of low adherence were identified as the level of education, the number of treatments per patient, and the type of pharmacy.
He et al[31]/ USA (2021)	Questionnaire	1. Socioeconomic factors (a. Age; b. Gender; c. Marital status; d. educational degree; e. Race; f. Income; g. Residing area) 2. Health-related covariates (a. Number of reported chronic conditions; b. Physical/functional limitations) 3. Prescription drug coverage satisfaction 4.Costs	10.3% reported medication non-adherence.	- The risk of non-adherence was higher in those dissatisfied with their medication costs
Temma et al[32]/ Thailand (2021)	Diabetes Self-Management Questionnaire (DSMQ)	1. Socioeconomic factors (a. Age; b. Gender; c. Marital status; d. Living situation; e. Education level; f. Occupation; g. Income; h. Smoking and alcohol drinking; i. BMI) 2. Clinical variables (a. Duration of disease; b. Complications; c. Co-morbidities; d. Family history) 3. Social support	Not reported	- Higher social support levels and non-alcoholism correlated with increased medication compliance.
Wakui et al[33]/ Japan (2021)	Questionnaire of medication management situation	1. Socioeconomic factors (a. Age; b. Gender) 2. Knowledge of drug effects and side effects 3. Quality of life 4. Diabetes Treatment Satisfaction	Not reported	- Higher knowledge of drug effects and side effects levels and quality of life correlated with increased medication compliance.
Bonikowska et al[34]/ Poland (2022)	Adherence in chronic disease scale questionnaire (ACDS)	1. Socioeconomic factors (a. Age; b. Professional activity; c. Marital status; d. Education, e. Residence) 2. Clinical variables (Frailty)	The average indicator of adherence to medication was 23.13 ± 3.72	- Patients with low medication adherence showed higher frailty, especially physically and psychologically, as shown by the Tilburg frailty indicator. - Male gender and the number of daily medications taken were identified as independent predictors of non-adherence.
Lara-Morales et al[35]/ Spain (2022)	Morisky Green Levine (MGL)	1. Socioeconomic factors (a. Age; b. Region; c. Economic situation; d. BMI; e. Gender) 2. Time with diabetes 3. Depression/ anxiety symptoms 4. Social risk	Non- adherence to medication: 4.4%	- In men, symptoms of anxiety/ depression were associated with a higher risk of non- adherence to medication. - In women, social risk was associated with a higher risk of non- adherence to medication.
Rosli et al[36]/ Malaysia (2022)	Self- Efficacy in Medication Understanding (MUSE)	1. Socioeconomic factors (a. Age; b. Gender; c. Ethnic; d. educational level; e. Marital status; f. Income) 2. Clinical data (a. the number of prescribed medications; b. duration of T2DM)	Not reported	- Higher self-efficacy, quality of life, income and longer medication duration correlated with increased medication compliance.
Jeyalakshmi et al[37]/ India (2023)	Hill-bone	1. Socioeconomic factors (a. Age; b. Occupation; c. Living status; d. educational level; e. Gender; f. Income status) 2. Clinical Variables (a. Duration of diabetic illness; b. Presence of other co-morbid illnesses)	More than 50% were non-adherent to their prescribed medications and the remaining 44.4% of them were adherent	- Income correlated with decreased medication compliance
Maghsoudi et al[38]/ Iran (2023)	Questionnaire	1. Socioeconomic factors (a. Age; b. Occupation; c. Living status; d. educational level; e. Gender; f. Income status) 2. Knowledge, attitudes, practice and barriers 3. Health care provider system specific barriers	Not reported	- Knowledge, attitudes, practice and barriers correlated with medication compliance. - Healthcare provider- and healthcare system-specific barriers correlated with medication compliance

Table 2. Continued.

First author (year of study)	Measure of medication adherence	Independent variables tested	Medication adherence of sample	Statistically significant findings
Maghsoudi et al[39]/ Iran (2023)	Questionnaire	1. Socioeconomic factors (a. Age; b. Gender; c. Marital status; d. educational level; e. Occupational status) 2. Duration of disease 3. Health Literacy 4. Social support 5. Responsibility	Not reported	- Health Literacy: Understanding of diabetes and its treatment. - Support Umbrella: The role of family, healthcare providers, and social networks in supporting treatment adherence. - Responsibility: The personal commitment of the individuals to adhere to their treatment regimen.
Udupa et al[40]/ India (2023)	MARS-5	1. Socioeconomic factors (a. Age; b. Gender; c. Religion; d. Socioeconomic class; e. Education; f. Occupation)	72% = Adherent 25% = Partially adherent 3% = non-adherent	- It also highlighted the noticeable impact of gender and literacy on medication adherence. - Factors associated with medication non-adherence included being in the age group 18-30 years, male, unmarried, and having lower income
Upamali & Rathnayake[41]/ Sri Lanka (2023)	Questionnaire	1. Socioeconomic factors (a. Age; b. Religion; c. Gender; d. Marital status; e. educational level; e. Occupational status; f. Living status) 2. The number of years of diabetes	Not reported	- Knowledge, attitudes and practices significantly influence medication adherence. - Treatment-related barriers and age-related changes pose a challenge to adherence. - Support systems, including healthcare professionals, play a critical role in improving adherence.
Wu et al[42]/ China (2023)	Adherence to Refills and Medications Scale (ARMS)	1. Socioeconomic factors (a. Age; b. Gender; c. Income; d. Health insurance; e. educational level; f. household income) 2. Self-Efficacy	Not reported	- Self-efficacy for medication use was found to act as both a moderator and a partial mediator in the relationship between general harm medication beliefs and medication adherence.
Yang et al[43]/ China (2023)	MMAS-8	1. Socioeconomic factors (a. Age; b. Gender; c. Marital status; d. Education level; e. Smoking) 2. Depressive 3. Quality of Life 2. Clinical characteristics of the participants (a. other diseases; b. family history of diabetes)	MMAS-8, Mean (SD): 6.08(1.80)	- Depressive symptoms in patients were found to significantly reduce adherence to treatment. - Depressive symptoms led to lower medication adherence, which in turn was associated with lower quality of life.

MMAS-8, Morisky Medication Adherence Scale; Hill-Bone, Hill-Bone Compliance Scale; MGL, Four-Item Morisky, Green, and Levine (MGL) scale; ARMS, the Adherence to Refills and Medications Scale; MUSE, Malay version of the Medication Understanding in Self-Efficacy.

onto the WHO five-dimensional framework for medication adherence through a structured and systematic approach. All identified barriers and facilitators were coded using an initial coding guide derived from the five WHO domains (patient-related, therapy-related, condition-related, health system–related, and socioeconomic factors). Consistent with the overall screening process described earlier, two reviewers independently performed all coding activities, and a third reviewer was available to resolve any disagreements. After comparing coding outcomes, discrepancies were addressed through discussion; when consensus could not be reached, adjudication by the third reviewer ensured accuracy and consistency. Inter-rater agreement was assessed using percentage agreement (and Cohen's kappa when applicable) to confirm the reliability and robustness of the coding process. The final mapped categories were then refined and organized within the five WHO dimensions.

WHO has proposed a five-dimensional model to assess the independent variables that influence medication adherence in patients with chronic diseases, including type 2 diabetes (as depicted in Figure 2). This model suggests that medication adherence is a multifaceted phenomenon shaped by five key factors: 1) socio-economic elements, 2) aspects related to the health care team and health system, 3) factors tied to the disease itself, 4) elements related to the therapy, and 5) factors specific to the patient. The impact of these factors on treatment adherence can differ across various societies and cultures.[14]

Thematic synthesis plan

In this systematic review, data on factors influencing medication adherence among patients with diabetes were extracted from a diverse range of studies. Considerable heterogeneity was observed across studies due to variations in adherence measurement methods (e.g., Medication Possession Ratio)MPR(, Morisky Medication Adherence Scale (MMAS-4 and MMAS-8), Proportion of Days Covered (PDC), and Medication Adherence Report Scale (MARS-5), the wide range of independent variables examined (including socioeconomic factors, clinical characteristics, quality of life, and psychological factors), and differences in outcome reporting formats (e.g., percentages, statistically significant associations, or results without quantitative metrics).

Due to these substantial differences in study design, outcome measures, and reporting methods, statistical pooling was not considered methodologically appropriate. Therefore, no meta-analysis was performed, and the findings were synthesized using a narrative approach within a mixed-methods framework.

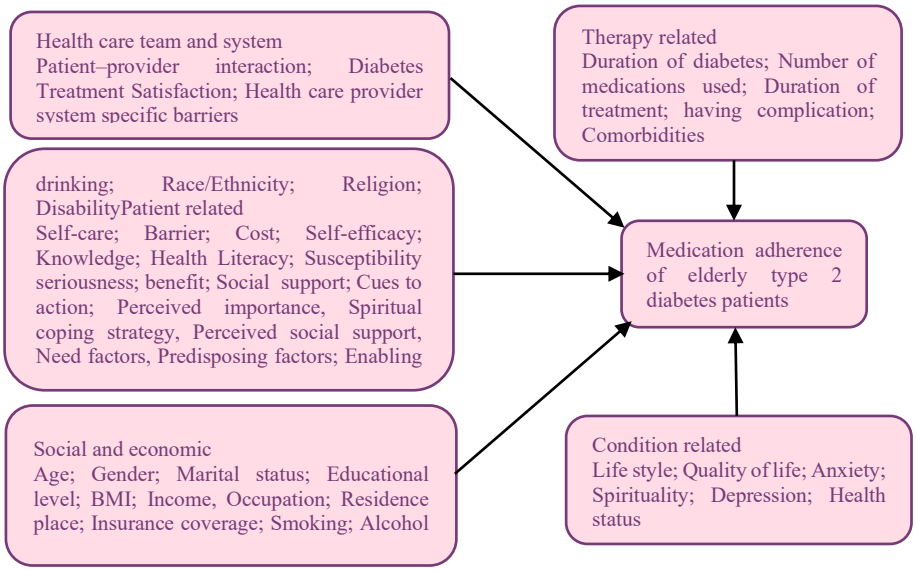

Figure 2. Factors that are associated with medication adherence among elderly patients with type 2 diabetes mellitus

Risk-of-bias assessment

In this study, considering the diversity of research designs included, standardized and validated tools appropriate for each study type were used for quality assessment. For cross-sectional studies, the National Heart, Lung, and Blood Institute (NHLBI) quality assessment tool was applied. This instrument contains 14 items evaluating aspects such as study population, participation rate, measurement validity, and control of confounding. Based on NHLBI guidance, studies meeting 10–14 criteria were classified as good quality, those meeting 5–9 criteria as fair quality, and those meeting 0–4 criteria as poor quality.

For cohort and case-control studies, the Newcastle–Ottawa Scale (NOS) was used. This scale evaluates methodological quality across three domains: participant selection (maximum 4 stars), comparability of study groups (maximum 2 stars), and outcome or exposure assessment (maximum 3 stars), with a total possible score of 9 stars. Studies scoring 7–9 stars were categorized as high quality, 4–6 stars as moderate quality, and 0–3 stars as low quality.

For qualitative studies, the Critical Appraisal Skills Programme (CASP) checklist was employed. This checklist includes 10 questions assessing methodological rigor, credibility of findings, and relevance. Studies addressing 8–10 criteria were considered high quality, those meeting 5–7 criteria moderate quality, and those fulfilling 0–4 criteria low quality. Using these predefined thresholds allowed for a consistent classification of study quality across different assessment tools.

All risk-of-bias and quality assessments were conducted independently by two reviewers. Any disagreements between reviewers were resolved through discussion, and when necessary, by consultation with a third reviewer to reach consensus.

Results

Selection of the studies

Through electronic search engines and strategies, a total of 1143 (1108 database, 35 other sources), articles were recognized. During the initial evaluation of duplicate and title, 406 of these articles were excluded as they did not meet the inclusion criteria. After screening 737 abstracts, 691 were excluded, and 46 full texts were assessed. Seventeen were excluded (11 non-target groups, 6 focused on other diseases), leaving 29 studies (Figure 1). A proportion-meta-analysis was considered for studies using MMAS-8 but deemed infeasible due to inconsistent reporting of adherence rates.

Study characteristics

Table 1 summarizes the characteristics of the studies included in this research. Most of these studies were published post-2017, with only four published between 2003 and 2014.[15-18]

Four longitudinal cohort studies,[15, 16, 25, 26] one retrospective study,[20] four qualitative studies,[21, 38, 39, 41] and twenty cross-sectional studies[17-19, 22-24, 27-37, 40-42] were identified for this study. The cumulative number of participants in the study was 276,681 individuals over the age of 60. Seven studies were conducted in primary healthcare centers,[15, 29, 34-37] seven studies were conducted on community-dwelling individuals,[16, 19, 21, 28, 30, 31, 33] one study was based on health information,[20] one study was conducted in clinics,[18] seven studies were conducted in hospitals,[24, 25, 27, 32, 40, 42, 43] one study was conducted in a senior care center,[22] and five studies were conducted in a combination of the mentioned centers.[17, 26, 38, 39, 41]

The results in Table 2 indicate that medication adherence in the included studies was assessed using both self-reported questionnaires and objective pharmacy refill–based measures. While the majority of studies relied on self-report instruments, several studies used objective indicators such as the Medication Possession Ratio (MPR) [15, 19] and the Proportion of Days Covered (PDC). [20, 26] A wide range of instruments was employed to assess medication adherence across the included studies. Among standardized self-report tools, the 8-item and

4-item Morisky Medication Adherence Scales (MMAS) were the most frequently used, applied in three[18, 30, 43] and one[17] studies, respectively. Other validated self-report instruments included the Visual Analog Scale (VAS),[23] as well as several researcher-developed questionnaires designed for specific study contexts.[16, 17, 38, 39, 41]

A qualitative tool, the McGill Illness Narrative Interview (MINI), [21] was also utilized in one study to provide deeper insight into patients' experiences. Additionally, the Medication Adherence Rating Scale (MARS-5) was used in two studies,[22, 35] while the Morisky-Green-Levine (MGL) questionnaire was applied in two others. [21, 36] Further validated measures included the Hill-Bone Compliance Scale,[15] the Brief Adherence Rating Scale (BARS),[28] and the Adherence to Refills and Medications Scale (ARMS).[29]

Some studies used tools designed for specific chronic conditions, such as the Diabetes Self-Management Questionnaire (DSMQ),[43] the Adherence in Chronic Diseases Scale (ACDS),[27, 31] and the Medication Management Questionnaire.[40, 44] Moreover, a number of studies employed more comprehensive instruments such as the Measure Treatment Adherence (MTA) questionnaire[42] and the Self-Efficacy in Medication Understanding (MUSE) questionnaire[30] which assess both behavioral and cognitive aspects of adherence.

One study used the Health Belief Model[17] and one study used the Anderson Behavioral Model[19] to investigate the factors affecting medication adherence. However, 27 studies did not use health education models to examine the factors influencing medication adherence.

Five interacting dimensions affect adherence

A. Social and economic factors

Twenty-eight studies examined the socio-economic factors affecting medication adherence. The most frequently occurring variables in the studies were, in order: age (28 studies), gender (24 studies), level of education (23 studies), income (14 studies), marital status (12 studies), occupation (11 studies), place of residence (11 studies), ethnicity/race (7 studies), body mass index (5 studies), smoking (3 studies), religion (3 studies), disability, insurance, and alcohol consumption (each in one study).

B. Health care team and system-related factors

Few studies examined the health care team/ factors related to the health system. Only four studies examined this dimension. One study addressed specific obstacles in the health care delivery system,[38] one study addressed satisfaction with prescription drug insurance coverage,[31] one study addressed patient-provider interaction,[16] and another study examined satisfaction with diabetes treatment and its impact on medication adherence.[33]

C. Condition-related factors

In twelve studies, they had examined the aspect of Condition-related factors. In one study, they examined the lifestyle, quality of life, depression of patients,[15] in one study they examined lifestyle and spirituality,[21] Clinical variables (Frailty),[34] in five studies they examined the quality of life,[18, 22, 25, 33, 43] four other studies examined the anxiety and depression of individuals,[24, 29, 35, 43] and in one study, they examined the health status[27] of patients.

D. Therapy-related factors

Seventeen studies had examined factors related to treatment. In one study, they examined the number of currently ailing diseases; the number of medical institutions visited for the current ailment; time since diabetes diagnosis; the number of diabetes drugs.[17] In one study, they examined the duration of diabetes; number of medications.[18] In two studies, they examined the duration of diabetes; number of medications taken.[22, 36] In four studies, they examined the duration of time since diabetes diagnosis.[23, 35, 38, 41] In one study, they examined the number of comorbidities.[26] In one study, they examined the age of diagnosis of diabetes; presence of diabetic complications; duration of the disease; incidence of complication; type of medication.[28] In one study, they examined the duration of the disease; diabetes treatment method; presence and type of comorbidities; number of diabetes tablets per day.[29] In one study, they examined the number of treatments per patient and type of pharmacy.[30] In one study, they examined the number of reported chronic conditions; physical/functional limitations.[31] In one study, they examined the duration of disease; complications; co-morbidities; family history.[32] In one study, they examined the duration of diabetic illness; presence of other co-morbid illnesses.[37] And in one study, they examined other diseases; family history of diabetes.[43]

E. Patient-related factors

In eighteen studies, they had examined factors related to the patient. In one study, they examined self-care,[29] in three studies they examined cost,[15, 20, 31] in one study they examined perceived importance,[28] in one study they examined health literacy,[27] in one study they examined self-efficacy,[42] in two studies they examined social support,[16, 32] in one study they examined social risk (adverse social conditions such as low socioeconomic status, limited social support, or poor access to healthcare),[35] in one study they examined social support, responsibility and health literacy,[39] in three studies they examined awareness,[21, 22, 33] in one study they examined awareness, attitude, behavior and barriers,[38] in one study they examined the strategy of spiritual adaptation and perceived social support,[25] in one study they examined the constructs of Anderson's behavioral model including need factors, predisposing factors and enabling factors,[19] and in one study they examined the constructs of the health belief model including susceptibility seriousness, guide to action, self-efficacy, benefits and barriers.[17]

Medication adherence

The percentage or average adherence to medication

therapy was not reported at all in fifteen studies. In four studies, the percentage of adherence to medication therapy was low or weak in more than 50% of the patients participating in the studies.[18, 27, 34, 37] Also, the percentage of adherence to medication therapy was moderate and good in approximately 50% or more of the patients participating in ten studies.[17, 24, 26, 28-31, 35, 40, 43] (Table 2)

Types of determinants and their effects

A. Social and economic factors

The factors that were found in the studies to have a statistically significant relationship with non-adherence to medication therapy were younger age,[40, 41] being single,[40] male gender,[18, 34, 35, 40] lower income,[17, 36, 37, 40] lower level of education,[19, 23, 30, 40] and alcohol consumption.[32]

B. Health care team and system-related factors

The factor that was found in the studies to have a statistically significant negative relationship with adherence to medication therapy was healthcare provider- and healthcare system-specific barriers.[38] Also, the factor that was found in the studies to have a statistically significant positive relationship with adherence to medication therapy was Support systems.[41]

C. Condition-related factors

The factors that were found in the studies to have a statistically significant relationship with non-adherence to medication therapy were anxiety and depression disorders.[19, 24, 35, 43] Also, the factors that were found in the studies to have a statistically significant positive relationship with adherence to medication therapy were lifestyle[21] and quality of life.[18, 22, 33, 36, 43]

D. Therapy-related factors

The factors that were found in the studies to have a statistically significant relationship with adherence to medication therapy were a long duration of diabetes history,[23, 28, 29, 34] fewer number of drugs/less complexity in treatment,[26, 29, 30, 34] and the type of pharmacy.[30]

E. Patient-related factors

The factors that were found in the studies to have a statistically significant negative relationship with adherence to medication therapy were barriers.[38, 41] Also, the factors that were found in the studies to have a statistically significant positive relationship with adherence to medication therapy were cost reduction,[15, 20, 31] self-efficacy,[17, 36, 42] social support,[16, 32, 39, 25] spiritual coping strategy,[25] social risk,[35] health literacy,[27, 39] attitude,[38, 41] awareness,[21, 22, 33, 38, 41] behavior,[38, 41] responsibility,[39] perceived importance of medication adherence,[28] and self-care.[29]

Figure 2 illustrates all the elements that have been investigated in connection with adherence to medication, following the structure suggested by the WHO. In these investigations, a variety of factors were scrutinized within each dimension. The dimension pertaining to the team and healthcare system was examined in a limited manner in a few instances, but the factors associated with the remaining four dimensions, particularly the dimension of factors related to treatment and factors associated with diabetic patients, received a more comprehensive examination.

Discussion

To the best of our knowledge, no previous study has comprehensively examined the factors influencing medication adherence among elderly patients with diabetes using the five-dimensional model proposed by the WHO. Therefore, this study aimed to identify factors affecting medication adherence based on the WHO model.

This review explored factors influencing medication adherence in elderly patients (aged 60 and above) with type 2 diabetes, based on the WHO's five-dimensional model. Half of the included studies did not report adherence rates. Among those that did, four reported low adherences, while ten indicated moderate to good adherence. This difference may be due to differences in the demographic characteristics of the participants in different studies. Also, the range of therapeutic services and the quality of the health and treatment system in countries are different from each other.

The key findings indicate that numerous factors, including socio-economic factors, patient-related factors, condition-related factors, treatment-related factors, and team/health system-related factors, influence adherence to medication therapy in this population. Significant factors that were found in the studies to be associated with medication adherence include: (1) Socio-economic factors, (2) Team/health system-related factors: Support systems, (3) Condition-related factors: Quality of life and lifestyle, (4) Treatment-related factors: Long duration of diabetes history, fewer number of drugs/less complex treatment, and type of pharmacy, (5) Patient-related factors: Cost reduction, self-efficacy, social support, Spiritual coping strategy, Social risk, health literacy, attitude, awareness, behavior, responsibility, Perceived importance of medication adherence, and self-care.

Socio-economic factors are one of the factors that have been examined in almost all studies. The findings of this study show that younger age, being single, male gender, lower income, lower level of education, and alcohol consumption were associated with non-adherence to medication therapy. In a study conducted during the Corona pandemic, it was observed that younger ages had less adherence to medication therapy.[44] However, another study estimated memory impairment associated with increasing age as a major barrier to medication adherence, which contradicts the results of our study.[41] Also, the results of a study that confirms our results showed that participants who were uneducated or did not have reported education were less adherent to anti-diabetic treatments.[30] This could indicate the importance of health education in increasing medication adherence. In line

with low income, in a study, the lack of enough money to buy medicine was associated with non-adherence to medication, and patients preferred daily living expenses over buying medicine.[41] These results show how financial issues can directly affect health decisions.

According to the study results, factors related to the health team/system, including barriers related to healthcare providers and the healthcare system, were associated with non-adherence to medication therapy. On the other hand, support systems were associated with adherence to medication therapy. The results of other study also show that support and services received from healthcare workers are one of the reported support mechanisms. However, some participants reported that when their blood sugar level was high, they were afraid to talk to doctors.[41] Limited access to healthcare facilities is also another barrier to adherence to medication therapy.[37] These results indicate that improving access to healthcare facilities can help increase adherence to medication therapy.

Among the condition-related factors in this study, anxiety disorders and depression were associated with non-adherence to medication therapy. Also, lifestyle and quality of life had a statistically significant relationship with adherence to medication therapy. Yang et al[43] in a study confirmed the direct role of depression on medication adherence and also showed that this depression can also reduce the quality of life in elderly patients with type 2 diabetes. In another study, patients who were not adherent to medication experienced higher depression and anxiety than adherent patients.[35] Evidence from another study indicated that anxiety and depressive symptoms in men may be associated with reduced adherence to medication [24]. These findings suggest the potential value of integrating mental health evaluation into routine diabetes management, particularly among male patients. Approaches including systematic psychological screening, established referral pathways for counseling services, and tailored educational or self-management interventions may contribute to improved medication adherence in this population.

Factors associated with the treatment of long-term diabetes history, fewer drugs/less complexity in treatment, and the type of pharmacy were related to adherence to medication treatment. These results suggest that improving diabetes management, simplifying the treatment regimen, and choosing the right pharmacy may be associated with increased adherence to medication treatment. Other study results show that taking medications every day is a stressful experience for most participants, and frequent medication use is an unpleasant experience for some.[41] In the study of Balkrishnan et al[15] the use of injectable drugs was associated with non-adherence to medication treatment. This result shows that the type of drug can affect adherence to medication treatment. In another study, awareness of drug effects had the most significant relationship with medication adherence.[33] This result shows that patients' awareness and knowledge about drug effects, side effects, and how to store drugs can help increase adherence to medication treatment. Taber and colleagues showed that adherence to medication significantly worsened with each additional diabetes drug and significantly decreased over time.[26] This result shows that the complexity of the treatment regimen can be a barrier to adherence to medication treatment. In another study, having a doctor who knew all types of consumed drugs could also help increase adherence to medication treatment.[45] This result suggests that effective communication with the healthcare team may be associated with increased adherence to medication treatment.

Factors related to the patient such as reducing costs, self-efficacy, social support, spiritual coping strategy, social risk, health literacy, attitude, awareness, behavior, responsibility, perceived importance of medication adherence, and self-care were associated with adherence to medication treatment, and obstacles were also related to non-adherence to treatment. Other study results show that most participants believe that adhering to medication can prevent them from getting sick.[40] This result shows that awareness and beliefs related to the benefits of medication can affect adherence to medication treatment. In a study, the level of disease acceptance in the high adherence group was significantly higher than the low and medium adherence group.[34]

This result suggests that acceptance of the disease condition may be associated with increased adherence to medication treatment. In other studies, the relationship between medication adherence and self-efficacy was confirmed,[17, 25, 42] indicating the importance of this factor in increasing adherence to medication treatment. Wu and his colleagues explained that those who believe that drugs have less public harm may have higher self-efficacy, which in turn leads to a higher level of medication adherence.[42] Attitude and empowerment have also been mentioned in other studies as important factors for medication adherence.[46] Other studies have also identified the role of religious coping and social support as important mediators between religiosity and medication adherence.[25] The role of lower cost, with more adherence to medication treatment, has been confirmed.[15] Other studies have also confirmed that the risk of non-adherence to medication among people who were dissatisfied with the amount paid for drugs was higher compared to those who were satisfied [31]. About reducing costs, a study confirmed the relationship of higher out-of-pocket costs with lower adherence.[20] Like our study, which identified health literacy as a factor associated with medication adherence, other study have also reported that individuals with sufficient health literacy, compared with those with limited health literacy, were more likely to remember to take their medications and less likely to change their medication doses without a doctor's recommendation.[27]

This systematic review synthesizes factors influencing medication adherence in elderly T2DM patients using the WHO 5-dimensional model. Unlike prior reviews

focusing on specific factors (e.g., socio-economic), this study integrates all dimensions, addressing a gap in comprehensive analyses. Socio-economic barriers (e.g., low income, education) align with findings from non-elderly T2DM populations, but age-related contradictions (e.g., younger age linked to non-adherence) suggest unique challenges in the elderly, possibly due to cognitive decline or differing priorities.[44] Qualitative synthesis revealed that self-efficacy and social support enhance adherence by fostering confidence and accountability, while anxiety and complex regimens deter it through emotional and cognitive overload.[18, 43, 44]

Limitations of study

Limitations include reliance on self-reported adherence, which may introduce recall bias, and the exclusion of non-English studies, potentially omitting relevant evidence. The predominance of cross-sectional designs also limits causal inferences, and publication bias may over represent significant findings. In addition, adherence was measured using different tools and cut-off values across studies, which introduces heterogeneity and may affect the comparability of reported adherence levels. The absence of a meta-analysis further limits the ability to quantify pooled effects. Moreover, the inclusion of studies with heterogeneous designs (e.g., cross-sectional, cohort, and qualitative) may introduce variability in how determinants of adherence are categorized or interpreted. There may also be potential inconsistencies in the reporting of study selection. Different methodologies capture distinct aspects of adherence behavior, complicating synthesis and potentially leading to non-comparable conclusions.

Future research should prioritize longitudinal studies to better clarify causal relationships and should employ more standardized adherence measurement approaches. Interventions targeting modifiable factors such as regimen complexity, mental health support, and patient education may help improve adherence. Policymakers may also consider addressing socio-economic barriers through cost-reduction programs and improved access to healthcare services.

Conclusion

This review highlights diverse factors influencing medication adherence in elderly T2DM patients. Key barriers include socio-economic challenges, anxiety, depression, and complex regimens, while facilitators like social support, self-efficacy, and simpler treatments offer actionable targets. Healthcare providers should integrate mental health screening, simplify prescriptions, and leverage support systems to enhance adherence. Future research should focus on longitudinal studies and interventions to address modifiable determinants, improving outcomes for this vulnerable population.

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Conflict of Interests

The authors declared no potential conflicts of interest regarding the research, authorship, and/or publication of this article.

Data Accessibility Statement

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Ethical Approval

This study was approved by the Ethics Committee of Hamadan University of Medical Sciences (approval code: IR.UMSHA.REC.1403.055).

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Appendix A. Search strategy for Web of Science database

Domains	Search string
Medication adherence	"Patient Compliance" (TOPIC) OR "Patient Adherence" (TOPIC) OR "Medication Compliance" (TOPIC) OR "Medication Adherence" (TOPIC) OR "Adherence to Medication " (TOPIC) OR "Drug Adherence" (TOPIC) OR "Drug Compliance"
AND	
Older Adults	Aged OR aging OR elderly OR geriatric OR senior OR "old age" OR aged OR older OR "older people" OR "older adults" OR elder OR pensioner OR senile OR senescent.
AND	
Type 2 Diabetes	"Type 2 Diabetes Mellitus" OR "Type 2 Diabetes" OR "Diabetic Patients" OR T2DM OR "Diabetes Mellitus" OR "Type II Diabetes Mellitus" OR "Type II Diabetes"
Filters in search	
Date	2000-2024
Language	English
Document Types	Article