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REVIEW

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Economic burden and cost of non-adherence in type 2 diabetes: a systematic review of middle- and high-income countries

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Abstract

Background Type 2 diabetes mellitus (T2DM) poses a growing economic burden in middle- and high-income countries due to its high prevalence and long-term complications. This study aimed to quantify and compare the annual per-capita direct and indirect costs of T2DM in adults of middle- and high-income countries, and to examine how treatment adherence relates to complications, hospitalizations, and costs, while also assessing the completeness of economic reporting.

Main A PRISMA-guided systematic review (January 2014—March 2024) searched MEDLINE (via PubMed), Embase, PsycINFO, and EconLit for adult studies reporting T2DM costs; reporting completeness was appraised with Consolidated Health Economic Evaluation Reporting Standards (CHEERS). All costs were standardized to annual per-person 2024 United States dollars (USD) adjusted for PPP (PPP-USD) using local Consumer Price Index (CPI) inflation and Purchasing Power Parity (PPP) conversion. When necessary, per-person values were derived from aggregated cost data. Fifteen studies met inclusion criteria.

Direct costs varied widely, ranging from USD 17.74 per person-year in Pakistan to USD 623 in Spain, while indirect costs were reported in 5 of 15 (33.3%) studies and were highest in South Korea (USD 1,068) and China (USD 929.5), mainly from productivity losses and premature mortality. Higher adherence was associated with fewer complications and hospitalizations despite higher pharmacy spending, and adherence was frequently shaped by education, geographic context, and emotional distress.

Conclusion Beyond direct medical spending, the economic burden of T2DM is strongly influenced by indirect costs, especially productivity losses and premature mortality, which remain under-measured. Strengthening adherence and adopting standardized, societal-perspective costing with routine reporting of indirect costs, alongside near-term policy levers such as primary-care adherence support and targeted out-of-pocket relief, could improve comparability, equity, and efficiency by redirecting resources from avoidable hospitalizations toward sustained adherence support.

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Trial registration The study protocol was registered in the International prospective register of systematic reviews PROSPERO database under registration number CRD42024519296 (Gómez-Torres et al, Int J Environ Res Public Health 20:328, 2024)

Keywords Type 2 diabetes mellitus, Economic burden, Direct costs, Indirect costs, Treatment adherence, Systematic review

Background

Diabetes mellitus (DM) is one of the most prevalent chronic diseases worldwide and is associated with complications that drive excess mortality, disability, reduced life expectancy, and substantial healthcare spending [58]. In 2021, an estimated 537 million people were living with DM, with a global prevalence exceeding 10%, which is projected to increase by approximately 46% by 2045. The largest growth is expected to occur in middle-income countries, particularly China and India, driven by rising obesity, population aging, and urbanization [24]. There is broad consensus that DM imposes a substantial burden on society through increased direct medical costs, productivity losses, premature mortality, and intangible costs such as reduced life expectancy [48]. Consequently, countries and healthcare systems worldwide face major political and economic challenges, largely driven by the cost of treating DM and its associated complications, including cancer, cardiovascular disease, and the onset of other chronic conditions [48].

This review focuses on Type 2 diabetes mellitus (T2DM) which is characterized by insulin resistance and progressive β-cell dysfunction. Clinical diagnosis commonly relies on fasting plasma glucose (FPG), the 2-h plasma glucose during a 75-g oral glucose tolerance test (OGTT), or glycated hemoglobin (HbA1c) as per contemporary clinical guidance. Management combines lifestyle modification (nutrition, physical activity, weight control) with stepwise pharmacotherapy [1, 43].

The standard economic approach to cost analysis in DM focuses on attributable direct medical costs, representing the opportunity costs of medical resources used to manage the disease, its complications, and comorbidities (e.g., inpatient care, outpatient visits, emergency services, rehabilitation, services from other healthcare professionals, nursing home and palliative care, diagnostic testing, prescription medications, and medical supplies) [49]. Despite the large clinical burden of T2DM, indirect costs are inconsistently defined and reported across studies, limiting comparability and policy relevance. Non-adherence further amplifies costs via preventable complications. This review addresses these gaps by standardizing cost definitions and emphasizing the economic implications of adherence. However, the true societal burden extends beyond healthcare spending to indirect costs (e.g., productivity loss, disability, premature death) and other non-medical consequences that degrade quality of life [22, 33]. Despite their policy relevance, indirect costs remain underreported and inconsistently measured across studies, complicating cross-country comparisons and obscuring the full economic footprint of T2DM [22, 33].

According to Baryakova et al. [9] and Zakeri et al. [68], specifically in the case of T2DM, poor treatment adherence constitutes a significant economic burden. Evidence indicates that adherence to prescribed therapies remains suboptimal [30], with the extent and nature of non-adherence varying across regions and populations [16, 23, 61]. In the United States alone, non-adherence is estimated to cost the healthcare system between United States dollars (USD) 100 billion and USD 300 billion annually, mainly due to avoidable hospitalizations, emergency department visits, and the management of preventable complications [9]. However, the economic burden is not limited to healthcare systems. Patients themselves also bear a substantial portion of the costs. Non-adherence can result in higher expenditures due to additional physician visits, increased medication costs, and the need for more intensive care to manage complications.

In general, the cost of non-adherence in chronic diseases such as diabetes, mental illness, and cardiovascular disease was reported in 2018 to range from USD 949 to USD 52,341 [51]. This is especially concerning for low-income patients, for whom the cost of managing chronic diseases already represents a significant financial strain [14]. Since many diabetes-related complications can be prevented, mitigated, or delayed through proper treatment adherence, the overall economic impact could be significantly reduced by prioritizing preventive strategies aimed at improving adherence. In addition, the influence of certain socioeconomic determinants on treatment adherence has been highlighted in multiple studies [4, 56]. Therefore, the management of T2DM must be multifactorial, incorporating not only clinical risk factors but also social determinants such as income level, education, gender, and healthcare system structure [62].

Given the rising global prevalence of T2DM and its important burden on healthcare systems across countries with varying income levels, there is a growing need to better understand the economic costs associated with its management, from the healthcare system, patient and societal perspectives. For example, in 2024, in Germany, 0.87% of the Gross Domestic Product (GDP) was allocated to diabetes-related health care (USD 40.4 billion), whereas in Pakistan, it was 0.73% of the GDP (USD 2.7 billion). Although the proportion of diabetes-related expenditure appears modest (< 1%), it represents a substantial burden in middle- and high-income countries [24, 66].

In this context, the present systematic review aims to analyze and compare the economic burden of T2DM in middle- and high-income countries, focusing on its direct and indirect costs. Furthermore, it seeks to explore the role of treatment adherence in modulating these costs, while also considering a range of socioeconomic determinants. To achieve this, we synthesized and examined studies published over the past decade that quantified T2DM-related expenditures, to identify patterns, disparities, and potential areas for targeted intervention that could optimize resource allocation and improve health outcomes. Across income settings, the economic footprint of T2DM reflects both disease prevalence and the financing capacity of health systems. Middle- and high-income countries more often report detailed cost components, including indirect costs, enabling cross-study comparability, whereas low-income settings face limited reporting and distinct financing structures. Accordingly, this review focuses on middle- and high-income countries to ensure methodological comparability and data completeness, while acknowledging that separate syntheses are warranted for low-income settings.

Methodology

Study design and protocol registration

This systematic review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [42]. The study protocol was registered in the International prospective register of systematic reviews (PROSPERO) database under registration number CRD42024519296 [21, 24].

Eligibility criteria

Quantitative cost studies, cost analyses or cost-of-illness (COI) designs, published in English or Spanish between January 2014 and March 2024 were eligible if they reported direct and/or indirect costs associated with T2DM in adults (≥ 18 years). Studies had to be conducted in countries classified by the World Bank [65] as middle- or high-income for fiscal year 2024. Meta-analyses, qualitative studies, case reports, letters to the editor, conference abstracts, and publications in languages other than English or Spanish were excluded.

Rationale for the 2014—2024 window. This period was selected because it reflects contemporary treatment patterns and prices, aligns with updated reporting standards, and ensures availability of consistent Consumer Price Index (CPI) and Purchasing Power Parity (PPP) series for price-year alignment and cross-country harmonization. Earlier studies were excluded to avoid outdated therapeutic contexts and non-comparable price years.

Rationale for focusing on middle- and high-income countries. These settings more consistently reported price year, currency, perspective (e.g., health-system or societal), and indirect-cost components (e.g., productivity losses, premature mortality), improving comparability and data completeness. Low-income settings often require tailored methods and merit a separate synthesis.

Search strategy

A comprehensive search was conducted in MEDLINE (via PubMed), Embase, PsycINFO, and EconLit for studies published from January 1, 2014, to March 1, 2024. Boolean operators (AND/OR) combined terms for population (adults; middle-/high-income countries), condition (diabetes; T2DM), adherence/non-adherence where relevant, and economic outcomes (economic burden; direct/indirect cost; expenditure; cost per capita). Full strategies are provided in Supplementary Table S1.

Study selection

Two independent reviewers conducted a three-phase selection process: removal of duplicates, screening of titles and abstracts, and full-text review. Discrepancies were resolved by consensus with a third reviewer. References were managed in Mendeley© (Elsevier Publishing, Amsterdam, Netherlands).

Data extraction and cost harmonization

Costs were extracted as direct or indirect and summarized as annual cost per capita categorized by type and region. Monetary values were harmonized to 2024 USD adjusted for PPP; hereafter, (PPP-USD 2024) using a predefined protocol: (i) extraction of currency, price year, perspective, and cost components; (ii) inflation in the study's local currency using national CPI to the stated price year; (iii) conversion using PPP factors; and (iv) update to PPP-USD 2024. When annual per-person costs were not directly reported, totals were annualized and per-person values were derived from the reported population denominators, applying the same CPI/PPP steps.

Transparency (AI use)

A large-language-model tool (ChatGPT) was used only for routine arithmetic (e.g., inflation updates, currency conversions, annualization) under researcher supervision. No AI was used for study selection, data extraction, synthesis, or interpretation. All AI-assisted calculations were independently verified by two reviewers (see Supplementary Material—Appendix 1).

Sensitivity analysis

Pre-specified sensitivity analyses varied PPP and CPI inputs by ± 10%, re-expressed results in 2024 euros (EUR), and explored alternative productivity-loss valuations (human-capital vs. friction-cost) and wage inputs (mean vs. minimum), where applicable. PPP/CPI ± 10% did not alter the rank-ordering of countries or the qualitative pattern that adherence shifts costs from hospitalizations to pharmaceuticals. Varying wage assumptions and switching between human-capital and friction-cost approaches changed indirect-cost levels but not the conclusion that productivity losses are material where reported.

Quality assessment

Methodological quality was assessed using the Spanish version of the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist [7]. The seven-item checklist aims to improve completeness and transparency in economic evaluations. Studies were categorized as having "high/moderate" quality (≥ 4 points) or "low" quality (≤ 3 points) to flag reports with insufficient detail for cost extraction and standardization. Because CPI/PPP harmonization requires clearly reported currency, price year, perspective, and cost components, studies scoring ≤ 3/7 were excluded from the synthesis to avoid relying on non-transparent imputations; scoring details are reported in Table S2.

Results

The initial database search identified 1,931 articles. After removing 1,005 duplicates, 926 unique records remained. Screening of titles and abstracts led to the exclusion of 814 studies. A total of 112 full-text articles were assessed for eligibility. Of these, 17 met the inclusion criteria, but 2 were excluded due to low methodological quality [47, 67]. Ultimately, 15 studies were included in the final synthesis (5/15 were indirect cost studies). The description of indirect cost components (productivity loss, premature mortality, informal care) was expanded, and inequalities by occupation and urban/rural setting were identified. Where reported, we noted whether studies used human-capital or friction-cost approaches.

A detailed flowchart of the selection process is presented in Fig. 1.

The included studies evaluated the economic burden of T2DM in adults from middle- and high-income countries. Sample sizes ranged from 101 participants in Saudi Arabia [5] to over 4 million individuals in South Korea [46]. The studies employed diverse methodological designs, including cross-sectional analyses, observational studies, descriptive cost assessments, and economic modeling. This heterogeneity allowed for a multifaceted understanding of the cost structures and influencing factors associated with T2DM. Unless otherwise stated, all cost figures refer to annual per-capita (per patient per year) costs.

Findings were organized into three key categories: (A) direct costs, (B) indirect costs, and (C) the economic impact of treatment adherence. Three studies reported both direct and indirect costs [20, 32, 34, 60], therefore, category counts are not mutually exclusive. Most studies were conducted in Asian countries (9/15; 60.0%): China (3), Indonesia (1), Pakistan (1), South Korea (1), Saudi Arabia (1), and Singapore (2) and in Europe (4/15; 26.7%): Spain (1), Germany (2), the Netherlands (1). Overall, 5/15 (33.3%) were conducted in middle-income countries and 10/15 (66.7%) in high-income countries.

A Direct Costs T2DM

Most included studies (10/15; 66.7%) reported estimates of direct annual per capita costs associated with T2DM. Substantial variability was observed between middle- and high-income countries (see Supplementary Material—Table S3).

Asia

In China, Long Q. et al. [36] reported an annual cost of USD 265.7, whereas H.-F. Li et al. [34] and Lim et al. [35] reported lower values of USD 110 and USD 170.19, respectively. The highest estimate by Long Q. et al. [36] may reflect the inclusion of complication-related expenses. In Indonesia, Suri Ari et al. [60] reported a per capita cost of USD 40.3, encompassing hospitalization and outpatient services. In Pakistan, Gillani et al. [20] reported the lowest estimate at USD 17.74, despite including inpatient and laboratory costs.

Europe

In Spain, Aguirre Rodríguez et al. [3] reported a notably high annual per capita expenditure of USD 623. This contrasts with lower estimates from Germany -USD 351.7 [29] and USD 217.52 [17]- and from the Netherlands, where Geurten et al. [19] reported a per capita cost of USD 316.96, similar to that in Germany and significantly lower than in Spain.

Interregional comparison: Asia vs. Europe

Per capita costs in Pakistan and Indonesia ranged from USD 17.70 to USD 51.56—significantly lower than those in China, Germany, and the Netherlands, where estimates ranged from USD 170.19 to USD 351. Spain reported the highest per capita cost among all countries, at USD 623 [3, 17, 19, 20, 29, 32, 34–36, 60].

B Indirect Costs of T2DM

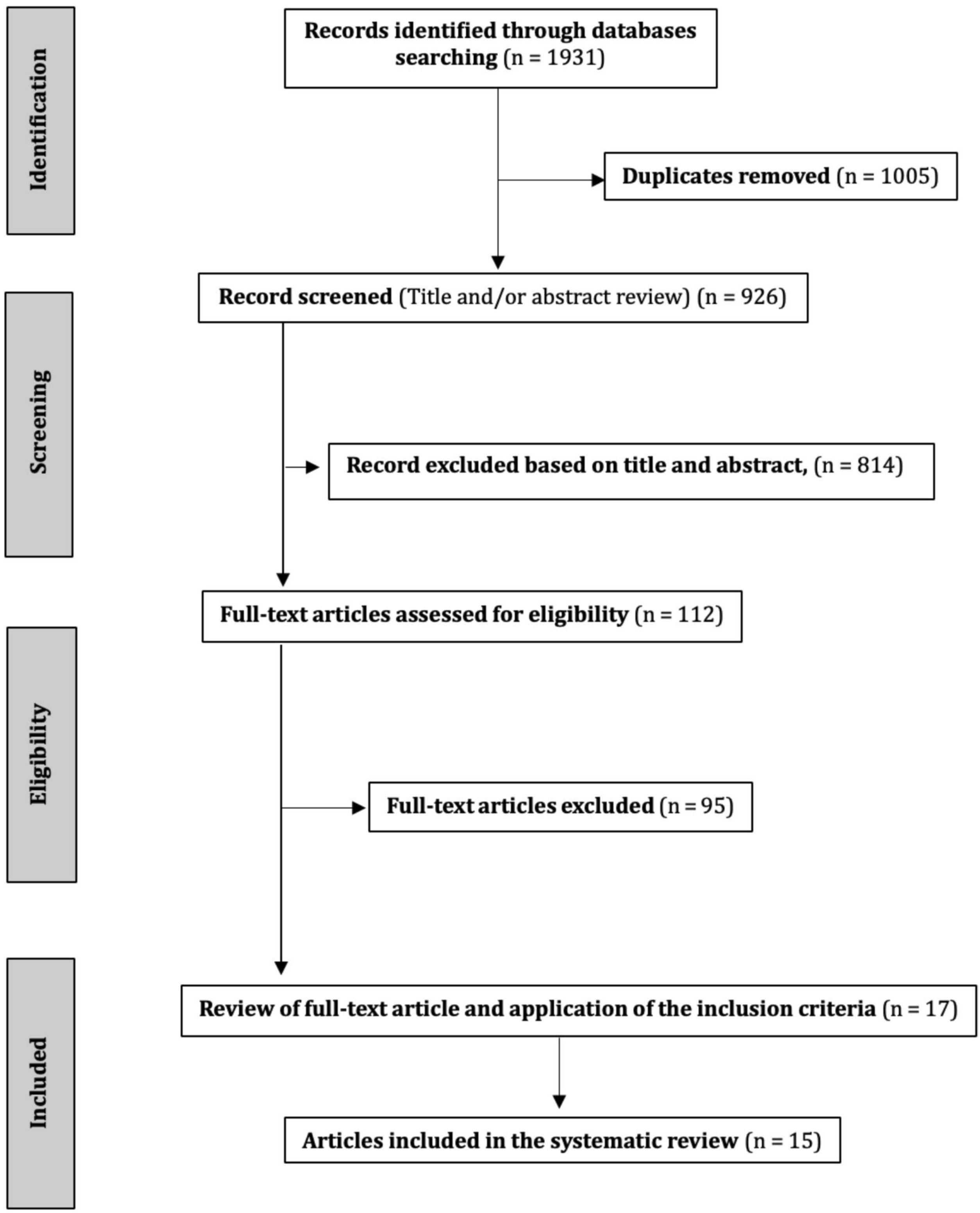

Fig. 1 PRISMA Flow Diagram

All studies (5/15; 33.3%) that reported indirect costs were conducted in Asian countries: one in South Korea [46], two in China [32, 34, 59], one in Indonesia [60] and one in Pakistan [20]. Common indicators used included productivity loss, morbidity, premature mortality, and informal care. Productivity loss due to morbidity was the most frequently assessed dimension. Detailed data are presented in Supplementary Material—Table S4.

Country-specific findings

In China, Li et al. [32, 34] estimated per capita productivity-related costs at USD 929.5, representing 4.4% of the total cost burden in 2016. In Indonesia, Suri Ari et al. [60] reported a per capita indirect cost of USD 145.6, based on employed populations. In Pakistan, Gillani et al. [20] found a per-person cost of USD 223.2 among working-age adults. South Korea had the highest estimated cost, at USD 1,068 per person, according to Oh et al. [46]. Additionally, X. Sun et al. [59], documented ethnic disparities in China, with per capita costs of USD 60.6 for the Han population and USD 16.5 for the Hui population, with higher burdens in urban areas.

Only one study, Oh et al. [46] explicitly addressed premature mortality as an indirect cost, while Gillani et al. [20] included income loss. Oh et al. [46] also considered informal care and non-medical expenses, including food and transportation, in South Korea. Occupation type influenced the extent of productivity loss: higher losses were observed among skilled workers compared to unpaid or lower-paid workers.

III.Economic impact of treatment adherence

Four studies assessed how treatment adherence influences direct medical costs, including medication use, outpatient visits, and hospitalizations, using varied methodologies across geographic contexts.

In Singapore, Lum et al. [37] found that poor glycemic control (potentially linked to low adherence) was associated with significantly higher costs (USD 1,093.31 ± 483.38) compared to suboptimal control (USD 924.71 ± 384.85). Poor control also increased costs related to care manager consultations, visits with other professionals, and medications. High levels of diabetes-related distress were associated with lower adherence and poorer glycemic control. In Saudi Arabia, Alomar et al. [5] found that well-informed patients incurred lower medication costs (USD 265.37) than poorly informed patients (USD 332.44). Adherence to a low-sugar diet and regular physical activity also led to reduced healthcare costs (USD 254.08 vs. USD 355.21,USD 260.47 vs. USD 322.43, respectively).

In the United States, Eby et al. [15] examined patients on basal insulin (BI) or basal insulin plus bolus correction (BI + BC). Adherent patients in both groups had higher pharmacy costs -USD 7,120 (BI) and USD 11,021 (BI + BC)- than non-adherent patients (USD 3,474 and USD 5,644, respectively). However, they also incurred lower hospitalization and outpatient care costs. In the BI group, adherent patients had hospitalization costs of USD 2,273 compared to USD 3,482 in non-adherent patients. In the BI + BC group, hospitalization costs were USD 2,226 versus USD 4,150, respectively. Chinthammit et al. [12] reported that adherent patients using non-insulin antidiabetic medications had higher overall annual treatment costs (USD 10,159 vs. USD 8,785), driven by higher medication costs (USD 3,384 vs. USD 1,874). However, adherent patients had lower hospitalization costs (USD 2,047 vs. USD 2,273), while outpatient costs were similar between groups.

Studies conducted in the United States, Saudi Arabia, and Singapore, have shown that the reductions in hospitalisation and outpatient care costs observed among adherent patients, despite higher pharmaceutical expenditure, reflect a magnitude of potential savings. These savings are relevant to healthcare resource allocation and models of integrated care (primary care, pharmacy, endocrinology and community).

Discussion

The study of costs associated with T2DM is increasingly relevant, given the substantial impact this disease imposes on healthcare systems and patients' quality of life. Comparative analyses across countries reveal considerable variability in cost estimation methods and resulting figures. Key challenges in cross-country comparisons include methodological heterogeneity, differences in costing perspectives, healthcare system structures, financing models, and variability in drug and service pricing. These findings underscore the substantial variability in direct T2DM-related expenditures across countries, which may reflect differences in healthcare system structure, service utilization patterns, and the inclusion or exclusion of complication-related costs. Understanding these differences is essential for benchmarking and for informing cross-country economic comparisons. The evidence on indirect costs highlights important socioeconomic and occupational disparities in how T2DM affects productivity and income. Regional variations in reporting methods and cost components further complicate cross-country comparisons, underscoring the need for standardized approaches to assess the broader societal burden of diabetes.

A central gap across the evidence base is the underreporting of indirect costs: only one-third of included studies quantified productivity losses, disability, informal care, or premature mortality. This undermeasurement likely biases total burden downward and limits the ability of payers to evaluate cost-saving preventive and adherence interventions.

A) Heterogeneity among cost studies of T2DM

The standardized societal COI framework and PPP-adjusted 2024 USD reporting used here mitigate, though cannot fully eliminate, cross-country heterogeneity in methods, currencies, and perspectives.

1. Differences in calculation methods and analytical perspective

Due to methodological heterogeneity (perspectives, cost categories, currencies, price years), we did not conduct a formal meta-analysis. Instead, we provided a structured narrative synthesis using standardized costs to enhance comparability. Although subgroup or meta-regression analyses could in principle explore cost variability drivers (e.g., region, healthcare system type, adherence), they were not performed because study subgroups were small and outcomes were not sufficiently comparable across perspectives and cost components.

Most studies in this review focused primarily on direct costs, with indirect costs remaining underreported despite their significant long-term impact [13]. Only five studies addressed indirect cost components [20, 32, 34, 46, 59, 60]. This underrepresentation of indirect costs reflects not only the limited number of available studies, but also substantial methodological heterogeneity in how productivity losses are defined and valued. In particular, the choice between the human capital and friction cost approaches strongly influences the magnitude of estimated indirect costs. The friction cost approach restricts productivity losses to the labor replacement period and often excludes components such as informal care, non-medical costs, and premature mortality, leading to lower estimates, whereas the human capital approach captures productivity losses over a longer time horizon. In the included studies, methodological choices were frequently implicit or insufficiently reported, contributing to variability and limited comparability of indirect cost estimates, especially for a chronic condition such as T2DM and in settings with heterogeneous labor market structures.

Afroz et al. [2] previously noted this omission in low- and middle-income countries, where out-of-pocket spending dominates. Our findings echo this, particularly in Pakistan, where a 30.3% prevalence coexists with extremely low per capita healthcare spending (USD 17.74), limiting access to diagnosis, treatment, and prevention [20]. More comprehensive cost evaluations that include household and productivity impacts are urgently needed.

The analytical perspective also shapes outcomes. Evaluations adopting a societal perspective tend to report higher total costs, as they consider broader psychosocial and economic dimensions [53]. Investment in prevention, self-care education, and therapeutic programs can significantly alter long-term costs, even if these benefits are not immediately captured (Spanish Society of Primary Care Physicians et al. [55].

Demographics such as age and gender also influence cost projections. Jiménez-González et al. [28] observed rising prevalence among younger individuals, which may increase lifetime healthcare expenditures. Despite their importance, such variables are often overlooked in cost analyses, though some studies reported basic sociodemographic data [32, 34, 36, 44, 59, 67].

2. Variability in health systems and financing models

Healthcare system design and financing models strongly shape patients' financial burden, particularly in managing chronic diseases like T2DM. Countries with universal coverage -such as Spain, the UK, Scandinavian nations, and to some extent China- typically reduce patient expenditures through strong public financing. In contrast, many middle-income countries rely heavily on private spending, leading to substantial out-of-pocket payments [69].

China operates a near-universal mixed system, moderating private expenditures. Indonesia's National Health Insurance Program (JKN) covers around 95% of the population, emphasizing primary care and yielding relatively low per capita costs [45, 63]. In stark contrast, Pakistan exhibits regional disparities in access and relies predominantly on out-of-pocket spending, with public health expenditure below 1% of GDP [50].

In Europe, Spain's tax-funded system offers broad coverage with minimal copayments. Germany and the Netherlands, however, rely more on private insurance schemes and cost-sharing models, which promote efficiency but may affect access. These systems also invest more effectively in prevention, unlike Spain, where strategies have been insufficient to control T2DM growth [54].

Ultimately, differences in per capita health expenditure reflect broader structural disparities. While China, Indonesia, and most European countries maintain relatively high coverage for T2DM care, Pakistan allocates minimal public resources to health (< 1% of GDP), shifting the burden of treatment directly onto patients. This is compounded by a lack of preventive interventions and early diagnosis strategies [8]. Such structural differences are also evident at the regional level within countries. Research conducted in rural areas or in regions with limited access to specialized care has shown a higher economic burden on patients with T2DM (Spanish

Society of Primary Care Physicians et al. (SEMERGEN), [55]. Furthermore, in countries with substantial investment in medical technologies, total healthcare costs may be higher due to the adoption of advanced therapies, even when such technologies lead to improved clinical outcomes.

3. Differences in drug prices and healthcare services

Medication pricing introduces substantial variation in cost estimates. The cost of essential drugs such as insulin varies widely across countries, influenced by factors such as pricing regulations, subsidies, generic availability, and the purchasing power of the population. According to the International Diabetes Federation (IDF) [58], differences in treatment accessibility and affordability can directly affect medication adherence and, consequently, overall healthcare costs. For example, in Germany and the Netherlands, specific regulatory frameworks help contain drug prices. In contrast, in Spain -until the COVID-19 pandemic- pharmaceutical procurement was decentralized to the regional level, complicating price negotiations. In response, the "Compra Pública Sanitaria Basada en Valor" (Value-Based Public Health Procurement) initiative was introduced in 2022 as a long-term sustainability strategy [52].

4. Variation in study duration and data sources

The data sources used in cost studies are diverse and can affect the comparability of results, ranging from hospital records to national surveys and insurance claims databases. This variation in data origin and quality can introduce significant heterogeneity in cost estimates, even within the same country. As noted by Catalá-López & García-Altés [11], the lack of standardization in methodologies and data sources complicates direct comparison across studies, highlighting the need to harmonize approaches in order to produce more robust and comparable cost estimates.

B) Costs from the perspective of treatment adherence

Across all studies, treatment adherence was associated with higher pharmaceutical spending but lower hospitalization and complication-related costs, suggesting potential long-term economic benefits. These findings reinforce the importance of investing in adherence strategies, especially in contexts where healthcare systems aim to reduce preventable expenditures. The studies reviewed consistently indicate that treatment adherence among individuals with T2DM has a dual effect on healthcare costs. On the one hand, it is associated with increased short-term expenditures, primarily due to higher medication use and more frequent utilization of outpatient services. On the other hand, adherence leads to significant long-term cost reductions, particularly related to hospitalizations, emergency care, and the management of severe complications [12, 15].

In a sample of 23,000 patients, Eby et al. [15] demonstrated that while adherent patients incurred higher pharmacy and outpatient costs, they avoided substantial hospitalization costs. This aligns with other studies showing that adherence improves outcomes and optimizes resource use [12, 41].

Alomar et al. [5] illustrated how better patient knowledge, healthier behaviors, and positive attitudes toward treatment reduced medication costs. These findings support the role of education and self-care in promoting both health and system efficiency. This perspective is supported by prior studies showing that self-care and healthy lifestyles -particularly dietary control and physical activity- contribute to improved glycemic control, which in turn reduces the need for costly medical interventions [25, 27, 39].

Lum et al. [37] emphasized the influence of diabetes-related distress, identifying an inverse relationship between emotional distress and treatment adherence. This psychosocial dimension -rarely explored in cost studies- may help explain why some patients fail to achieve adequate glycemic control despite access to effective medical interventions [23, 57]. These findings underscore the importance of integrating psychosocial support into treatment programs.

Finally, although some studies have explored the role of sociodemographic variables in adherence [38, 40], most did not examine their relationship to economic costs, leaving a significant gap for future research.

C) Per capita expenditure and disease prevalence

Per capita cost is a useful proxy for economic burden, especially when adjusted for disease prevalence. According to the World Health Organization (WHO) and the IDF, the rising prevalence of T2DM -particularly in countries experiencing rapid population ageing and lifestyle changes- partly explains the increase in both direct and indirect costs observed in this review [58, 64].

In countries like China [32, 34, 36], Indonesia [60] and Pakistan [20], demographic shifts and nutritional transitions have driven prevalence upward. According to the IDF Atlas, the prevalence of T2DM was 8.8% in China and 5.1% in Indonesia [58], with projections indicating continued growth. In Indonesia, this increase has been linked to dietary changes and longer life expectancy. However, these differences can also be explained by variations in healthcare coverage, public investment, and care models, as discussed in the previous section

[64]. In Pakistan, adult T2DM prevalence rose from 7.9% to 30.3% over the past decade, largely attributed to rapid urbanization, sedentary lifestyles, and high consumption of ultra-processed foods. Low public health expenditure contributes to limited access to early diagnosis, affordable treatments, and essential medications such as insulin [54]. Many patients are not diagnosed until severe complications have already developed. The combination of these factors -along with population growth and the absence of effective government policies-has led to an alarming T2DM burden in the country [8].

In Europe, prevalence rates also vary significantly. For example, Germany has roughly twice the population of Spain but shows a lower prevalence of T2DM (10%) compared to Spain's estimated 10—15%, which affects approximately one in every seven adults [54]. Within Germany, prevalence rates also vary regionally [17]. When comparing China, Indonesia, Germany, and the Netherlands, similar T2DM prevalence levels were reported (~10%), while Spain reported a notably higher rate (~15%) [54]. This disparity may be partly attributed to factors such as population ageing, increasing obesity and sedentary behavior, and the limited effectiveness of diabetes prevention strategies implemented in Spain in recent years [31].

D) The case of the United States

A notable finding was the limited number of recent cost studies from the United States, despite high T2DM prevalence. This may be partly explained by the current emphasis on primary prevention. Programs such as the Diabetes Prevention Program (DPP) and the National DPP have been shown to reduce the risk of developing T2DM by 58% [6, 10], which may have shifted research priorities toward the cost-effectiveness of preventive interventions rather than curative treatment.

E) Policy recommendations (12—24 months)

In middle- and high-income settings, near-term actions to reduce the economic burden of T2DM should focus on improving adherence through adherence-supportive benefit design (lower copayments for essential antidiabetics and supplies), regimen simplification with routine medication reviews in primary care, pharmacist-led follow-up, and scalable low-cost digital tools targeted to patients at highest risk of hospitalization. Health services should align incentives across integrated care pathways (primary care–pharmacy–endocrinology–community) to prevent complications, which is likely to be budget-neutral or cost-saving via fewer acute events and admissions. To strengthen decision-making and cross-country consistency, health systems should capture both direct medical and indirect/productivity costs, supported by routine dashboards that track adherence, complications, and cost outcomes at population level [18, 26].

Limitations

Our scope intentionally excludes low-income countries, where financing structures, coverage gaps, and informal labor markets differ substantially. External validity is therefore constrained: the relative weight of indirect costs may be higher in low-income settings due to greater productivity losses, care-giving burdens, and out-of-pocket financing. Dedicated syntheses using the same harmonization protocol are warranted.

In addition, although costs were converted to USD using year-specific exchange rates to enhance cross-country comparability, this approach is subject to exchange rate volatility, which may influence cost estimates independently of real changes in healthcare expenditure. Currency fluctuations across study years may therefore introduce variability in international comparisons. Alternative methods, such as purchasing power parity (PPP) adjustments, may improve comparability by accounting for differences in overall price levels; however, PPP-based conversions also have limitations in health economic analyses, as they rely on general consumption baskets that may not accurately reflect healthcare-specific costs or structural differences between health systems. These considerations should be considered when interpreting cross-country differences in the reported costs of type 2 diabetes.

Conclusions

This systematic review shows that the economic burden of T2DM is substantial but unevenly measured across settings. Direct costs (medications, hospitalizations, outpatient services) are most frequently reported and vary widely by region and health-system design, while indirect costs remain underreported and inconsistently assessed.

Standardizing costing methods and strengthening treatment adherence, through education, clinical pharmacy/telepharmacy, and supportive care, can reduce avoidable hospitalizations and improve equity and efficiency. Future work should expand consistent reporting of indirect costs and explore how socioeconomic factors shape both adherence and costs.

Standardizing methods and strengthening adherence are cost-effective levers to reduce complications and hospitalizations, improving long-term system efficiency. Adopting standardized societal-perspective costing and routine reporting of indirect costs would materially improve comparability, sharpen policy targeting, and help redirect resources from avoidable hospitalizations to effective long-term adherence support.

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Authors' contributions
Conceptualization: MTF-R and MLL-H; Data curation and methodology: PG-T, IRB-O, ES-DC, EF-L, SP-C, MTF-R; MG-B; Project administration: PG-T, IRB-O, ES-DC, EF-L, SP-C, MTF-R; Supervision: MTF-R and MLL-H, ER-A, MG-B; Validation: PG-T, IRB-O, ES-DC, EF-L, SP-C, MTF-R; MG-B, ER-A, MLL-H; Writing-original draft: PG-T, IRB-O, ES-DC, EF-L, SP-C, MTF-R; Writing -review and editing: PG-T, IRB-O, ES-DC, EF-L, SP-C, MTF-R; MG-B, ER-A, MLL-H. All authors have approved the submitted version.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This study is a systematic review and did not involve the collection of original human data. Therefore, ethical approval was not required. The methodology followed PRISMA guidelines, and all data included were extracted from previously published, peer-reviewed sources.

Competing interests
The authors declare no competing interests.

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