Burden of Illness in Type 2 Diabetes Mellitus

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ABSTRACT

An estimated 30.2 million Americans have diabetes, and this number is expected to increase based on trends over recent decades and compounded by an aging U.S. population. As reviewed in this article, type 2 diabetes mellitus (T2DM) is associated with impaired health-related quality of life (HRQoL) and with a substantial socioeconomic burden. Compared with individuals without T2DM, those with T2DM have worse HRQoL, greater decrements in HRQoL over time, and possibly greater depressive symptomology. Diabetes-related complications and comorbidities (e.g., obesity and cardiovascular disease) are associated with worse HRQoL. Hypoglycemic episodes are associated with reduced HRQoL and greater levels of depression; they can also interfere with social and occupational activities. In turn, low HRQoL can be a driver for poor glycemic control. In 2012, the total estimated cost associated with diagnosed diabetes in the United States was $245 billion. Factors contributing to increased health care resource utilization and costs in patients with T2DM include medical comorbidities, diabetes-related complications, inadequate glycemic control, and hypoglycemic episodes. Readmission is a key driver of hospital-related costs and is more common among elderly patients with T2DM. Elderly patients with T2DM represent a particularly vulnerable population given that these patients may have varying degrees of physical and mental comorbidities that can increase their risk of hypoglycemia, falls, and depression.

This review demonstrates that T2DM imposes a considerable burden on both the individual and society. Treatment strategies should consider the effects of treatment on HRQoL and on outcomes (e.g., complications and hypoglycemia) that affect both HRQoL and costs. Management strategies that maximize HRQoL while minimizing the risk of hypoglycemia and other treatment-related complications are particularly critical in the elderly.

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An estimated 30.3 million Americans have diabetes (9.4% of the population). Of these, 23 million people have diagnosed diabetes and 7.2 million people have undiagnosed disease.[1] The prevalence of diabetes in the U.S. population has increased dramatically over the past half century (Figure 1).[2] Approximately 40% of Americans with diabetes are aged 65 years or older, and 25% of all U.S. adults over age 65 have diabetes.[1] As the U.S. population ages, the number of patients with diabetes is expected to increase; by 2030, the number of people in the United States with diagnosed or undiagnosed diabetes is projected to increase to 55 million.[3]

Type 2 diabetes mellitus (T2DM) accounts for 90%-95% of diabetes cases and is characterized by relative insulin deficiency, peripheral insulin resistance, and high blood glucose levels.[4,5] In patients with T2DM, insulin secretion is insufficient to compensate for insulin resistance. Risk factors for T2DM include older age, obesity, family history of diabetes, a history of gestational diabetes, physical inactivity, impaired glucose metabolism, and race/ethnicity, with African Americans, Hispanics/Latinos, Native Americans, Asian populations (especially Indians and Filipinos), and Native Hawaiians or other Pacific Islanders being at an increased risk.[1,4] Globally, the prevalence of diabetes (percentage of population) in adults aged 20-79 years is highest in Central America and the Middle East/northern Africa.[6]

Diabetes-Related Complications

Uncontrolled diabetes is associated with the development of complications that may compromise health-related quality of life (HRQoL) and may increase mortality risk. These include macrovascular (e.g., coronary artery disease, stroke, and peripheral vascular disease) and microvascular (e.g., retinopathy, nephropathy, and neuropathy) complications.[7] Global data from diverse independent studies have reported increased relative risk of stroke ranging from 1.4 to 5.8 in people with diabetes.[8] After adjustment for population age differences, cardiovascular disease death rates in 2003-2006 were about 1.7 times higher among adults aged 18 and older with diagnosed diabetes than among those without diabetes.[4]

During 2011-2012, the estimated crude prevalence of chronic kidney disease (stages 1-4) was 36.5% among U.S. adults aged 20 years and older with diagnosed diabetes.[9] Diabetes is a key cause of end-stage renal disease and, in 2011, was listed as the primary cause of renal failure in 44% of new cases.[4] In 2011, nearly 50,000 people initiated treatment for renal failure due to diabetes, and 228,924 people with renal failure due to diabetes were receiving chronic dialysis or living with a kidney transplant.[4] In 2014, more than 52,000 U.S. adults developed end-stage renal disease with diabetes as the primary cause.[10]

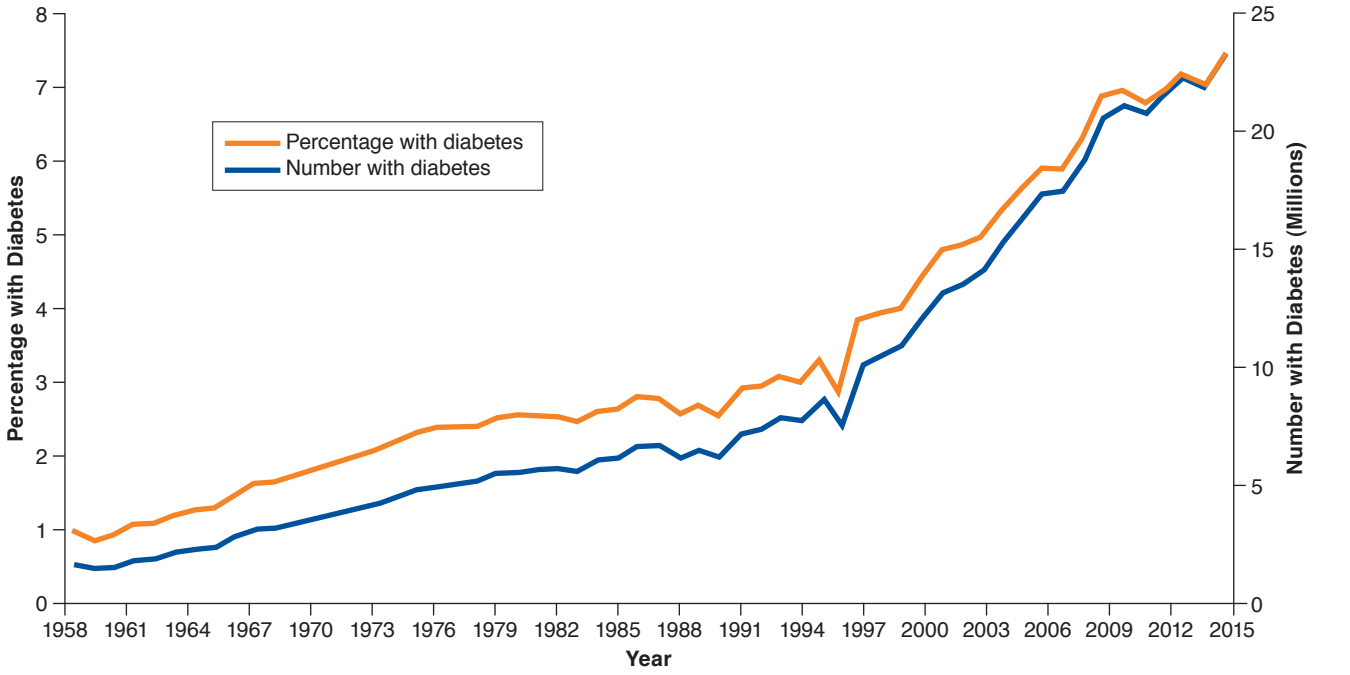
Diabetes complications such as peripheral neuropathy and retinopathy lead to potentially disabling sequelae. Diabetes accounts for approximately 60% of non-traumatic lower-limb amputations among people aged 20 and older.[4] Retinopathy affects an estimated 28.5% of adults with diabetes aged 40 years and older.[4] About 4% of adults aged ≥40 years with diabetes have advanced diabetic retinopathy, with associated conditions (e.g., macular edema and proliferative diabetic retinopathy) that result in severe vision loss. Notably, diabetic retinopathy is the leading cause of blindness among U.S. adults.[11]

This review provides an overview of the burden of T2DM, including the effects on HRQoL and economic impact, with a focus on the U.S. market.

Studies Evaluating the Impact of T2DM on Quality of Life

The association between diabetes and impaired HRQoL has long been recognized.[12-14] The large, multinational Diabetes Attitudes, Wishes and Needs (DAWN) study evaluated psychosocial issues and experiences relating to diabetes management from the perspective of both patients and providers.[15] Among

FIGURE 1 Number and Percentage of U.S. Population with Diagnosed Diabetes, 1958-2015[2]



From Centers for Disease Control and Prevention, Division of Diabetes Translation. United States Diabetes Surveillance System, available at: http://www.cdc.gov/diabetes/data.

those with T2DM, 41% of patients reported that they experienced poor psychological well-being. Additionally, providers (including nurses, primary care physicians, and specialists) estimated that 62%-72% of their patients with T2DM had psychological problems, including depression, anxiety, stress, and burnout.

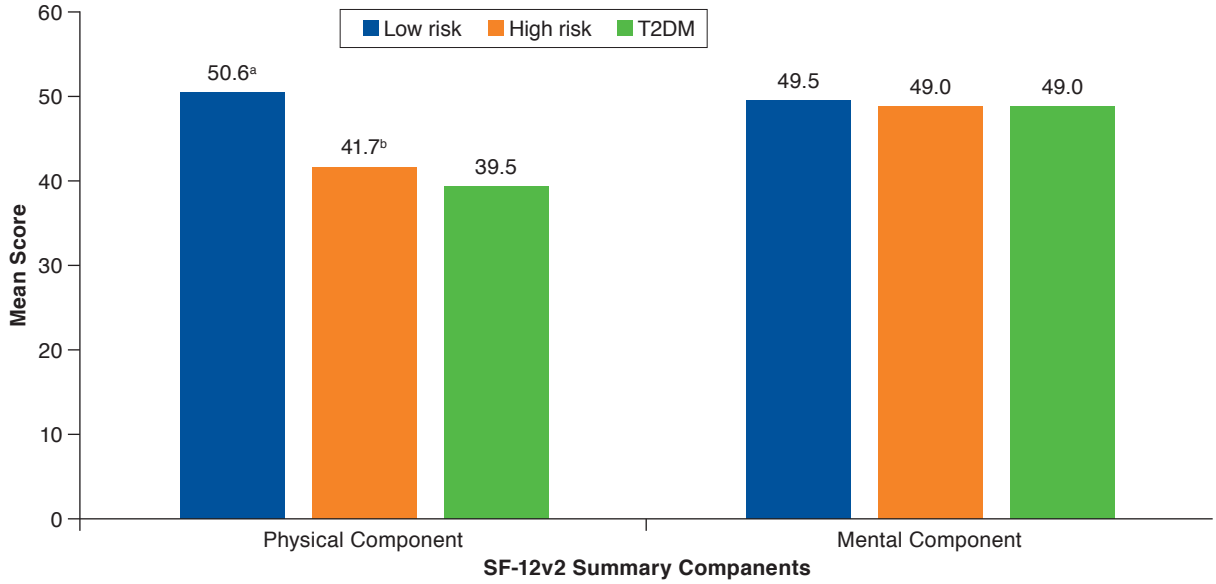
The Study to Help Improve Early evaluation and management of risk factors Leading to Diabetes (SHIELD) was a 5-year, U.S.-based survey study initiated in 2004 that was designed to enhance understanding of patterns of attitudes, knowledge, and health behavior of individuals with T2DM and those with varying levels of cardiometabolic risk.[16] This study included the Short-Form 12-item Health Survey (SF-12), a brief measure of overall health status, and the 9-item Patient Health Questionnaire (PHQ-9), an assessment of depression. The SF-12 was completed by adults across the United States with T2DM (n = 3,530) and by those determined to be at high risk (n = 5,051) or low risk (n = 5,335) for T2DM based on the presence of recognized risk factors. Compared with low-risk respondents, those with T2DM were found to have significantly reduced physical, but not mental, HRQoL (Figure 2) and also had greater depressive symptomology and higher rates of moderate to severe depression (19.6% vs. 11.3%).

The SHIELD study also longitudinally assessed changes in health status and HRQoL in patients with T2DM using the EuroQol-5D (EQ-5D) instrument for measuring quality of life. This was completed at baseline and 5 years later by 1,741 patients with T2DM and 4,543 respondents without diabetes.[17] Patients with T2DM had impaired HRQoL compared with those without diabetes at baseline and at 5 years ($P < 0.0001$ for both index and visual analog scale [VAS] scores). Among patients with T2DM followed for 5 years, HRQoL worsened over time to a significantly greater degree ($P = 0.001$) compared with adults without diabetes, indicating a long-term adverse impact on HRQoL. An international study of patients with T2DM (the Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation [ADVANCE] trial) found that HRQoL among patients with T2DM declined over a 5-year follow-up period based on EQ-5D scores.[18] Similarly, a German study demonstrated that patients with T2DM demonstrated large decrements in both mental and physical HRQoL over time compared with individuals without diabetes.[19]

Impact of Diabetes-Related Complications and Comorbidities on Quality of Life

Diabetes-related complications and comorbidities (e.g., obesity and cardiovascular disease) reduce HRQoL in patients with

FIGURE 2 Mean SF-12 Physical Component Summary and Mental Component Summary Scores in Patients with Low Risk for T2DM, High Risk for T2DM, or T2DM in the SHIELD Study[16]



From Grandy S, Chapman RH, Fox KM; SHIELD Study Group. Quality of life and depression of people living with type 2 diabetes mellitus and those at low and high risk for type 2 diabetes: findings from the Study to Help Improve Early evaluation and management of risk factors Leading to Diabetes (SHIELD). Int J Clin Pract. 2008;62(4):562-68. Copyright © 2008. Reproduced with permission.

[a]P < 0.001, T2DM vs. low risk.

[b]P < 0.001, T2DM vs. high risk.

SF-12v2 = Short-Form 12-item Health Survey Version 2; T2DM = type 2 diabetes mellitus.

T2DM.[20-22] The UK Prospective Diabetes Study (UKPDS) was a landmark, multicenter, randomized controlled trial of glycemic therapies in more than 5,000 patients with newly diagnosed T2DM. It demonstrated conclusively that improving blood glucose levels and/or blood pressure control reduced the risk of microvascular complications of T2DM.[23] Two cross-sectional UKPDS studies evaluated the effects of intensive policies aimed at improving glycemic or blood pressure control on HRQoL.[24] While these substudies did not observe an impact of the interventions on HRQoL, an important finding was that complications of T2DM were associated with impairments in HRQoL: patients with a macrovascular complication within the last year had worse general health, more problems with mobility and usual activities, and reduced vigor. Those patients with microvascular complications in the last year reported elevated levels of tension and mood disturbance.

Longitudinal assessment of the impact of diabetes complications on HRQoL in the UKPDS found that myocardial infarction (MI) caused acute/short-lived impairment of HRQoL (i.e., within 1 year of event), whereas other complications (stroke, heart failure, and amputation) resulted in longer-lasting impairment.[25] Importantly, amputation, stroke, and heart failure had the greatest impact on HRQoL, whereas blindness in 1 eye and ischemic heart disease did not impact HRQoL. In the ADVANCE trial, complications of T2DM reduced HRQoL, with the greatest impact observed for amputation, followed by stroke, blindness, renal failure, heart failure, and MI.[18]

Secondary Quality of Life Impact from Diabetes Treatment

Diabetes treatments can pose risks of dangerously low blood glucose levels, or hypoglycemic events, which are particularly feared by patients and can negatively impact HRQoL.[26,27] Patients with T2DM worry about passing out in public or injuring themselves due to a hypoglycemic episode.[28] In the SHIELD study, respondents with T2DM reporting at least 1 hypoglycemic episode in the past 12 months had significantly worse physical and mental health on the SF-12 than respondents without hypoglycemia; mean PHQ-9 scores were also higher among those with hypoglycemia, indicating greater levels of depression.[29] Similar results were observed when comparing respondents with hypoglycemia versus those without hypoglycemia over the past 4 weeks. In addition, among respondents reporting hypoglycemia over the past 4 weeks, mean SF-12 physical component summary scale scores decreased, and

mean PHQ-9 scores increased as the number of reported hypoglycemic episodes increased.

The U.S. National Health and Wellness Survey (NHWS), a large internet-based study of adults aged ≥ 18 years, found that hypoglycemia negatively impacted HRQoL in patients with T2DM and, in addition to interfering with social activities, was associated with absenteeism (missed work), presenteeism (impairment while at work), and decreased overall work productivity.[30] Further, a European survey of 5,817 patients aged 40 years and older with T2DM duration of at least 1 year found that patients experiencing any hypoglycemic episode over the past year reported greater diabetes-related impairment on multiple measures of HRQoL and health status compared with those with no hypoglycemia episodes.[27]

Hypoglycemia in T2DM patients treated with oral antihyperglycemic drugs is associated with impaired HRQoL, with increases in severity and frequency of hypoglycemia associated with greater decreases in HRQoL.[31,32] In a European multicenter observational study (the Real-Life Effectiveness and Care Pattern of Diabetes Management study) that enrolled patients with T2DM on oral antihyperglycemic agents metformin plus a sulfonylurea or thiazolidinedione, 38% of 1,709 patients reported hypoglycemic symptoms in the 12 months before enrollment. Of patients with hypoglycemic symptoms, the most severe symptoms were mild for 68% of patients, moderate for 27%, and severe for 5%. Adjusted linear regression analyses indicated that patients reporting hypoglycemic symptoms had significantly worse HRQoL (based on EQ-5D VAS) scores and that impairment in HRQoL increased with greater hypoglycemic symptom severity. Similarly, a follow-up survey (the 2007 U.S. NHWS) of patients with self-reported T2DM treated with oral antihyperglycemic drugs (with half of patients taking a treatment regimen that included a sulfonylurea) found that 63% of patients reported hypoglycemic episodes (46% mild, 37% moderate, 13% severe, and 4% very severe) and that patients reporting any hypoglycemic symptoms had significantly worse HRQoL based on EQ-5D utility scores than patients without hypoglycemic symptoms.[32] Adjusted linear regression analysis revealed that decrements in HRQoL (based on EQ-5D utility scores) increased with increasing severity of hypoglycemic episodes.

Another potential treatment-related burden pertains to changes in body weight. Obesity is a common comorbidity of diabetes, and obesity contributes independently to lower HRQoL.[21,33] Weight gain secondary to diabetes treatment can potentially add to the HRQoL burden of the disease. A number of diabetes treatments are well known for their potential to cause weight gain, including insulin, sulfonylureas, and thiazolidinediones.[34]

Clinical Consequences of Quality of Life Burdens

The phenomenon of "diabetes-related distress" refers to the negative emotional reactions to a diabetes diagnosis, demands of self-management, risk of complications, inadequate provider care, and unsupportive interpersonal relationships.[35] One author has termed this phenomenon "diabetes overwhelmus."[36] Ironically, poor HRQoL can, in turn, be a driver leading to poor glycemic control, which can increase risks for greater comorbidity and added HRQoL burden, thus creating a vicious cycle.[37] Evaluating diabetes-related distress and addressing underlying factors may potentially improve patients' HRQoL and self-care capacity.

Another potential contributor to diabetes-related distress is the logistical characteristics of diabetes management, such as the pill/injection burden, along with the glucose testing burden. Patients with diabetes often feel overwhelmed and frustrated by the daily hassles of disease management.[38] Such feelings may contribute not just to reduced HRQoL, but could have broad negative impacts on diabetes self-management, possibly leading to poor clinical outcomes.

The Economic Impact of Diabetes

In 2012, the total estimated cost of diagnosed diabetes in the United States was $245 billion, comprising $176 billion in direct medical costs and $69 billion in lost productivity due to work-related absenteeism, reduced productivity at work and at home, unemployment attributable to chronic disability, and premature mortality.[39] Hospital inpatient care accounted for 43% of total medical costs. Diabetes-related costs in the United States are projected to reach $622.3 billion in 2030, including $472 billion in annual medical costs.[3] The estimated additional lifetime cost of treating T2DM and associated complications in U.S. patients differs based on gender and age at diagnosis.[40] For men, lifetime costs range from $54,700 for those diagnosed at age ≥ 65 years to $124,700 for those diagnosed between age 25 and 44 years. For women, lifetime costs range from $56,600 for patients diagnosed at age ≥ 65 years to $130,800 for those diagnosed between age 25 and 44 years.

In California, about one third of hospitalizations in patients aged 35 years and older occur in people with diabetes.[41] Regardless of primary diagnosis, the average hospital stay costs almost $2,200 more for a patient with diabetes versus a patient without diabetes ($18,691 vs. $16,492). A retrospective study examined health care resource utilization (HCRU) and costs for patients with T2DM and matched case controls in a Medicare Advantage Prescription Drug plan.[42] Compared with controls without T2DM, patients with T2DM had significantly higher mean annual all-cause health care costs per patient associated with inpatient hospitalizations; outpatient, office, and emergency department (ED) visits; pharmacy expenditures; and total health care costs. The excess total annual cost for patients with T2DM was $3,120, and the excess total medical cost was $2,689. Patients with T2DM also had significantly greater HCRU with respect to inpatient hospitalization, average number of inpatient days, outpatient visits, office visits, ED visits, and pharmacy claims.

Managed care administrative claims data were used to identify high-cost patients with T2DM, defined as those patients with costs in the top 10% of the overall cost distribution.[43] Annual per-patient costs were $56,468 for high-cost patients compared with $4,674 for non-high-cost patients. Logistic regression was used to assess predictors of being a high-cost T2DM patient. High underlying comorbidity burden (Charlson Comorbidity Index ≥ 2) was the strongest predictor of being a high-cost patient (odds ratio [OR] = 4.896), followed by renal impairment (OR = 2.368), obesity (OR = 2.106), and insulin use (OR = 2.098).

Readmission is a key driver of costs in hospitalized patients with T2DM. In a retrospective cohort analysis of data from patients with T2DM enrolled in Humana Medicare Advantage with Prescription Drug Insurance and commercial insurance plans, mean 12-month all-cause medical costs were highest for patients with an inpatient admission and 30-day readmission ($76,806), followed by patients with an inpatient admission without a 30-day readmission ($42,011), and lowest for matched patients without an inpatient admission ($9,624; $P < 0.001$).[44] Similar patterns were observed for all-cause medical costs, all-cause pharmacy costs, DM-related total costs, DM-related medical costs, and DM-related pharmacy costs. Notably, the risk of 30-day hospital readmission is significantly higher among individuals aged 75 years and older with T2DM relative to patients younger than 65 years of age.[45] Ravel et al. (2015) examined all-cause 30-day hospital readmissions among Medicare beneficiaries aged ≥ 65 years with T2DM.[46] Overall, 13.2% of hospitalized patients were readmitted within 30 days of initial hospitalization. Age ≥ 75 years was associated with a greater risk of readmission, as was cognitive impairment, depression, falls and fall risk, polypharmacy, and urinary incontinence; depression was not significant in multivariate analysis.

Diabetes-related complications contribute to the economic burden of T2DM. Approximately 20% of commercial insurance or Medicare costs in patients with T2DM are attributable to diabetes-related complications.[47] Among Medicare beneficiaries with T2DM, an increase in complications burden (representing the number and severity of complications) was associated with increased total costs.[48] Every 1-point increase in complications burden on the Diabetes Complications Severity Index was associated with a $2,744 increase in total costs over 24 months, including a $2,480 increase in medical costs and a $264 increase in pharmacy costs.

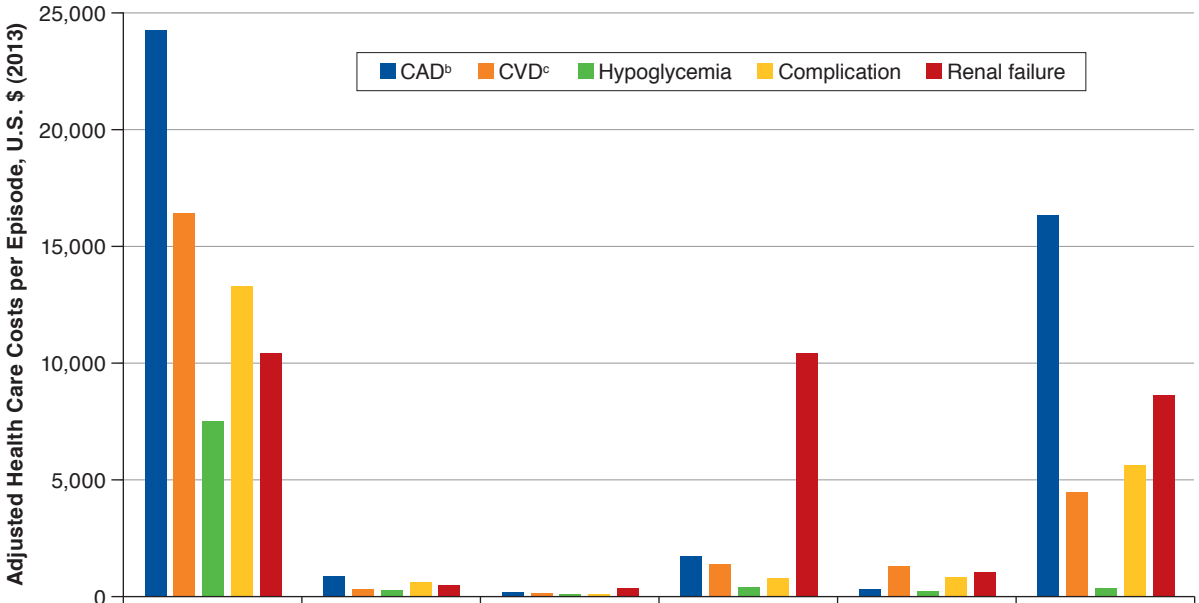
An analysis of data from the MarketScan Commercial Claims and Encounters Database estimated HCRU and costs per episode of care for complications of T2DM.[49] More than 34.7 million episodes of care were identified among 1,846,287 patients. The mean adjusted costs per episode were $16,435 for coronary artery disease (CAD) with acute MI, ventricular fibrillation, shock, and/or cardiac arrest; $4,558 for cerebrovascular disease (CVD) with stroke; $445 for hypoglycemia; $5,675 for complications of diabetes (including cellulitis, pyelonephritis, gangrenous infection, osteomyelitis, hyperosmolar state, ketoacidosis, acute MI, acute cerebrovascular accident, sepsis, coma, hyperosmolar coma, and shock); and $8,765 for renal failure (Figure 3). For each category of care (e.g., inpatient and ED), the cost was determined for the patients who had at least 1 visit related to that category of care (i.e., cost of inpatient care among patients with inpatient care, cost of ED visits among patients with at least 1 ED visit). Inpatient visits represented the largest component of costs for CAD, CVD, and complication episodes, whereas other ancillary care accounted for the largest cost component for hypoglycemia and renal failure.

Ward et al. (2014) estimated the direct medical costs per patient for complications of T2DM, including costs of managing the acute episode and subsequent care within the first year following the event.[50] Highest costs were observed for end-stage renal disease ($71,714), acute MI ($56,445), and ischemic stroke ($42,119). Based on an analysis of U.S. administrative claims data, total initial cost for MI ranged from $28,014 for Medicare to $41,505 for Medicaid, and total cost for follow-up care within 1 year ranged from $2,036 for commercial insurance to $4,799 for Medicaid[51]; for stroke, total initial cost ranged from $22,657 for Medicare to $40,370 for Medicaid, and total cost for follow-up care within 1 year ranged from $2,488 for Medicare to $4,584 for Medicaid.

Inadequate glycemic control may contribute to the economic burden of T2DM. Achieving and sustaining glycemic targets is recommended to reduce the risk of complications in patients with T2DM.[5,52] Despite the broad spectrum of treatment options for T2DM, many patients still have poor glycemic control. One estimate found that, in 2012, about 7.4 million (57%) insured adults with T2DM had controlled diabetes, and 5.6 million (43%) had uncontrolled diabetes based on *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis codes (any ICD-9-CM code indicating uncontrolled diabetes during the year).[53] In another analysis, the percentage of patients represented in a database of privately insured and Medicare Advantage patients with uncontrolled T2DM (defined as A1c ≥ 9%) increased from 9.9% in 2006 to 12.2% in 2013.[54]

A retrospective database analysis of medical and pharmacy claims and laboratory data from a large U.S. managed care health plan reported that, after controlling for confounding factors, the predicted total diabetes-related costs over a 1-year follow-up period were 32% higher for patients with T2DM whose A1c was above 7% relative to patients with A1c ≤ 7% ($1,540 vs. $1,171 per patient; $P < 0.001$).[55] Multivariate analysis of medical and pharmacy administrative claims data from a large managed care organization showed that A1c correlated significantly with diabetes-related medical costs for patients with T2DM, with each 1% increase in A1c corresponding to a

FIGURE 3 Adjusted Health Care Costs per Episode by Episode Type, Patients with Utilization in Each Care Setting[a]



Patients with visits by health care setting	Inpatient	ED	Office Visits	Other Ancillary Care	Pharmacy	Total
CAD, n	25,921	2,452	13,589	24,867	472	45,350
CVD, n	18,822	5,150	44,305	48,390	1,577	85,287
Hypoglycemia, n	281	4,605	14,678	15,314	4,860	29,886
Complication,n	15,055	1,761	18,251	15,821	904	40,339
Renal failure, n	15,376	12,539	167,052	128,654	98,671	211,673

[a]*Data from Candrilli et al. (2015).*[49]
[b]*CAD episodes include coronary artery disease with acute myocardial infarction, ventricular fibrillation, shock, and/or cardiac arrest.*
[c]*CVD episodes include cerebrovascular disease with stroke.*
CAD = coronary artery disease; CVD = cerebrovascular disease; ED = emergency department.

4.4% increase in diabetes-related medical costs (translating to an annual cost increase of $250 per year).[56]

Costs associated with hypoglycemia are considerable. A literature review that combined T1DM and T2DM concluded that both severe and nonsevere hypoglycemia episodes were associated with substantial costs related to HCRU and lost productivity.[57] For older adults with T2DM obtaining tight glycemic control (A1c < 6.5%) with insulin or sulfonylureas, the annual costs of hypoglycemia in the United States exceed $509 million.[58] Notably, retrospective analysis of a pharmacy administrative claims database found that age- and sex-standardized rates of severe hypoglycemia resulting in hospital admission, observation stay, or ED visit did not improve between 2006 and 2013.[54]

Interestingly, the economic impact of T2DM is a further contributor to the overall HRQoL burden. As medical expenditures associated with diabetes increase, HRQoL in patients with diabetes decreases.[59] Campbell et al. (2017) used data from the 2002-2011 Medical Expenditure Panel Survey Household Component to examine the relationship between medical expenditures and HRQoL among U.S. adults with diabetes (type not specified).[59] Quality of life (QoL) was measured using the Physical Component Summary (PCS) and Mental Component Summary (MCS) derived from the SF-12v2, and scores were converted into quartiles, with lower quartiles reflecting worse QoL. After adjusting for covariates (including, among others, age, sex, health insurance status, and comorbidities), increasing mental and physical HRQoL were associated with both lower total expenditures and lower out-of-pocket costs.

Considerations in Older Patients

The prevalence of diabetes and complications is increasing in older patients, leading to increasing burdens related to medical

care and HRQoL impairment.[60] In 2012, individuals aged 65 years and older accounted for 59% of U.S. health care expenditures attributable to diabetes, and diabetes-related nursing/residential care costs among those aged ≥65 years were approximately $11.8 billion.[39] T2DM affects 6.1% of commercially insured individuals aged between 20 and 64 years and 19.4% of Medicare beneficiaries aged 65 years and older.[47] Diabetes is particularly problematic in the long-term care (LTC) setting: The estimated prevalence of diabetes is 32.8% among elderly nursing home residents.[61]

In older patients with diabetes, cognitive impairment and dementia may further compromise HRQoL.[62] A survey of U.S. adults found that older age, especially aged ≥75 years, was associated with a greater risk of self-rated fair or poor health.[14] In the ADVANCE trial, described above, greater decrements in HRQoL over time were observed with increasing age among patients with diabetes.[18]

Older patients may have varying degrees of physical and mental comorbidities, such as cognitive impairment, chronic pain, and renal impairment, that can increase their risk of hypoglycemia, falls, and depression. These comorbidities, and the polypharmacy that is often used to treat multiple conditions, can lead to impairment of glycemic control and HRQoL.[63] In particular, older patients are at an increased risk of hypoglycemia, which may lead to falls.[63,64] An analysis of a U.S. commercial database that included more than 1 million patients with T2DM demonstrated that the risk of fall-related events over 1 year increased 2-fold among patients aged ≥65 years who experienced hypoglycemia compared with patients in the same age category without hypoglycemic events.[64] Older patients with hypoglycemia also had an elevated risk of fall-related outcomes of fractures, head injuries, hospital admissions, and LTC placement.

A retrospective analysis of data from a nationally representative insurance claim database found that, among patients with T2DM, age ≥65 years was a significant predictor of hospitalization (hazard ratio = 1.85).[65] Significant clinical predictors of hospitalization were prior diagnosis of cancer and cardiovascular, renal, arterial, and liver disease. Compared with younger patients with T2DM, those aged ≥65 years also have a significantly higher proportion of hypoglycemia-related hospitalizations (38.3% vs. 11.4%).[65] Between 1999 and 2011, rates of hospital admissions among Medicare beneficiaries aged ≥65 years for hyperglycemia decreased, while those for hypoglycemia increased; among older adults, hospital admissions for hypoglycemia now exceed those for hyperglycemia.[62] As described above, hospitalized patients with T2DM aged 75 years and older have an elevated risk of 30-day hospital readmission.[45,46]

According to the American Diabetes Association (ADA), overall health, medical comorbidities, functional status, and cognitive status should be carefully considered when setting glycemic goals and selecting a treatment regimen in older patients with T2DM.[5] An A1c goal of less than 7.5% is reasonable in a healthy older adult with few comorbid illnesses and intact cognitive and functional status, whereas a less stringent target (<8.0%) should be considered for patients with multiple comorbidities or functional or mild to moderate cognitive impairment; an A1c target of <8.5% is reasonable for older patients with very complex/poor health.[5] Risk of hypoglycemia is perhaps the most important factor in determining glycemic goals, especially in the LTC setting.[5,66] As older adults tend to be on many medications, simplified treatment regimens are recommended whenever possible, and the cost of treatment should also be taken into consideration. Additional medication-specific factors that are of particular importance when managing T2DM in older patients include risk of hypoglycemia, safety in patients with renal impairment, effects on comorbidities and diabetic complications, ease/route of administration, and vigilance for drug interactions.[66,67]

A comprehensive approach to managing T2DM in older patients should consider the special vulnerabilities of this patient population and their clinical and functional heterogeneity.[60] Such an approach should carefully evaluate the interrelationship between medical, functional, social, and psychological domains and the impact of different management strategies on these domains. For example, while a healthy older person with excellent self-management and self-efficacy skills and access to care and social support may be able to tolerate more intensive interventions, pharmacologic management becomes more challenging in the older patient as diabetes progresses, medical comorbidities develop or worsen, and factors such as functional impairment and cognitive decline limit the patient's self-management and self-efficacy capacities. It is important to review and adjust diabetes targets accordingly as patients age and to focus on goals, such as prevention of hyperglycemic emergencies, severe hypoglycemia, diabetic polyuria, and dehydration in order to preserve HRQoL. The ADA has published specific treatment guidelines for older adults.[68]

Conclusions

T2DM imposes a considerable burden, in particular with regard to effects on HRQoL and economic costs. Diabetes-related and treatment-related complications contribute substantially to the adverse impact of T2DM on HRQoL and health care costs. Elderly patients with T2DM are a particularly vulnerable population, and management strategies that maximize HRQoL while minimizing the risk of hypoglycemia and other treatment-related complications are warranted. Treatment strategies for T2DM should take into account the effects of treatment on HRQoL, as well as on outcomes such as microvascular and macrovascular complications and hypoglycemia that have

pronounced effects on HRQoL and on HCRU. Recommendations to alleviate the QoL burden of patients with T2DM include selecting effective medications with lower burden of hypoglycemia, addressing complications and comorbidities that may adversely affect HRQoL, and considering factors such as cost and frequency of administration that may impact QoL.

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