

# Optimizing Outcomes From Pharmacologic Management of Type 2 Diabetes

## Impact of Type 2 Diabetes on Patient Outcomes and the Health Care System

**THE BURDEN OF TYPE 2 DIABETES** (T2D) is considerable and extends to those individuals living with comorbid conditions and the health care systems that support them. In 2017, the total cost incurred by those with diagnosed diabetes in the United States was \$327 billion compared with \$245 billion in 2012, when the cost was last examined.<sup>1,2</sup> After accounting for inflation, this represents a 26% increase during the 5-year period evaluated, due in part to the increasing prevalence of diabetes.<sup>1,2</sup> The American Diabetes Association (ADA) noted that the largest drivers of the cost of diabetes are higher use of prescription medications beyond antihyperglycemic medications; higher use of inpatient services, medications, and supplies to directly treat T2D; and more office visits to physicians and other health providers, compared with patients without T2D.<sup>1</sup>

Adding to the complexities of diabetes cost and treatment are associated risk factors, as well as comorbidities such as cardiovascular disease (CVD) (**Figure 1**).<sup>3</sup> In 2017, the ADA estimated that \$37.3 billion was spent in cardiovascular-related costs incurred by patients with diabetes.<sup>1</sup> The results of a 2015 retrospective, cross-sectional study of the claims of 1,202,596 patients from the MarketScan database showed that the total health care costs of patients with T2D and concomitant atherosclerotic cardiovascular disease (ASCVD) were more than doubled compared with those of patients with T2D alone. Of that, medical (outpatient, inpatient, and emergency department visits) costs were 3 times higher and pharmacy costs were approximately 40% higher among patients with T2D and ASCVD compared with patients with T2D but not ASCVD.<sup>3</sup>

Further, the presence of at least 1 additional comorbidity, such as CVD, not only adds to the complexity and cost of treating T2D but is also associated with increased health care service utilization.<sup>3,4</sup> The results of a 2006 retrospective health care registration study by Struijs et al demonstrated health care utilization among patients with T2D increased in tandem with the number of comorbidities.<sup>4</sup> It was noted that patients with only T2D had fewer health care specialist consultations, overall hospital admissions, and hospital stay days compared with those individuals with T2D and any vascular or nonvascular-related comorbidity.<sup>4</sup> Similar results were shown by Weng et al in a 2020 retrospective, cross-sectional study of 2015 US claims data, the results of which demonstrated that patients with T2D and ASCVD had visited physicians more frequently and had a higher

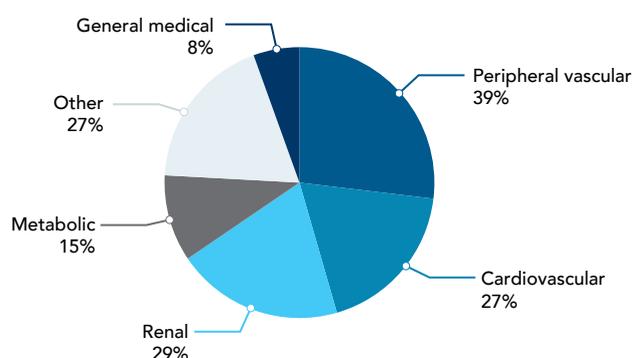
number of annual visits compared with patients with T2D only.<sup>3</sup> The results of this study also demonstrated a 3.5-fold number of hospital inpatient visits in those patients with T2D and ASCVD (15.6%) compared those with T2D only (4.4%).<sup>3</sup>

Further, the results of a 2013 cluster randomized controlled trial by Teljeur et al highlighted an association between the number of chronic conditions a patient has and polypharmacy.<sup>5</sup> This study illustrated a nearly 2-fold increase in polypharmacy in patients with more than 1 chronic condition compared with patients with only 1.<sup>5</sup> Multimorbidity can have implications in an individual's disease management, and awareness of this association could lead to better treatment outcomes.<sup>5</sup>

Lastly, the prevalence of diabetes has increased at a more pronounced rate among certain populations, including racial/ethnic minorities and individuals with a lower level of education.<sup>6</sup> The results of a 2011 prospective, randomized, placebo-controlled study by Lee et al noted an inverse relationship between diabetes incidence and both level of education and income.<sup>7</sup> Additionally, the results of a 2009 community-based epidemiologic survey completed by Link et al demonstrated that the more important indicator when determining rates of diabetes is socioeconomic status (SES), compared with race or ethnicity.<sup>8</sup>

A better understanding of the relationship of these comorbid and SES associations will improve the

**FIGURE 1.** Percent Expenditure Due to Specific Medical Conditions in Patients With Type 2 Diabetes<sup>1</sup>



Adapted from: American Diabetes Association. Economic costs of diabetes in the US in 2017. *Diabetes Care*. 2018;41(5):917-928. doi: 10.2337/dci18-0007.

development of cost-effective, culturally tailored programs for patients with T2D that are sensitive to the needs of the populations being served. It is particularly important to identify areas that providers and health care organizations might focus on to simultaneously lower costs and improve care.

### Challenges Facing Patients With T2D Leading to Poor Management and Nonadherence

In the United States, societal costs compounded with increasing diabetes prevalence, morbidity, and mortality create immense health care challenges.<sup>9</sup> The ADA recognizes the association between social and environmental factors and diabetes and the necessity of considering these factors when working to prevent, manage, and treat diabetes.<sup>10</sup> Novel strategies are required to address these social and environmental factors when providing care to patients with T2D (Figure 2).<sup>11</sup>

One area of promise involves improving care coordination. Models that incorporate novel education techniques and drug combinations have demonstrated success in improving glycated hemoglobin (A<sub>1c</sub>) control, reducing excess health care utilization, and increasing patients' treatment adherence and access to care.<sup>9,12-15</sup>

### Education

"Diabetes self-management education/training (DSME) is the ongoing process of facilitating the knowledge, skill, and ability necessary for diabetes self-care."<sup>16</sup> It has been shown that the first 6 months to 4 years after diagnosis are crucial to the long-term management of T2D.<sup>17</sup> The specific goals of DSME are as follows: explaining the basic concepts of T2D; illustrating the importance of identifying and counting carbohydrates; describing the benefits of maintaining a healthy body weight and exercising regularly; and monitoring and controlling blood sugar via medication planning, management, and administration.<sup>17-20</sup>

Despite its proven benefits, the number of individuals with T2D who receive DSME is low.<sup>21</sup> Low rates of DSME uptake and utilization are influenced by patient-specific and health system-specific barriers that can affect the attainment of optimal health status (Figure 2).<sup>11</sup> Patient-specific barriers can include financial and logistical access to DSME, such as difficulty accessing transportation to care sessions, which may affect populations that live within rural communities and those without health care coverage.<sup>19</sup>

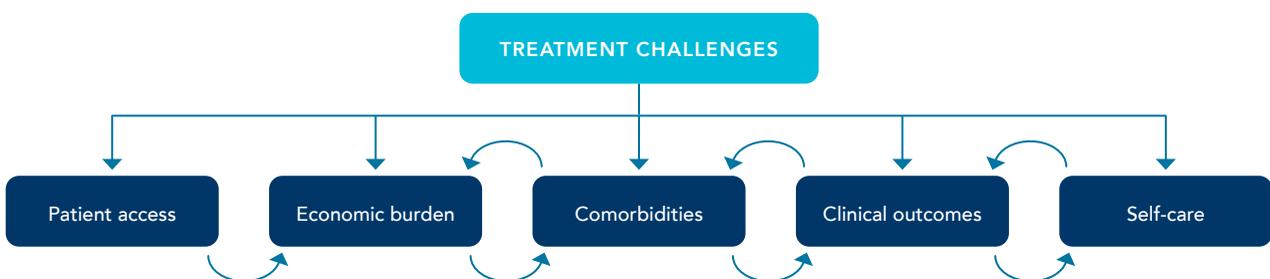
New platforms such as electronic delivery (computer and telephone) and the use of community-based group educational settings offer potential for greater patient access and uptake of DSME.<sup>9,11,14,19</sup> The results of a 2018 cluster randomized trial by Sood et al demonstrated that the use of electronic telecommunication decreased a patient's need for travel and provided an effective means of communication between the patient and their entire care team.<sup>11</sup>

### Cost and Health Care Economics

As mentioned previously, the high cost of managing diabetes presents a growing challenge for health care systems and patients. Out-of-pocket (OOP) costs and health care system utilization costs (eg, those related to inpatient, outpatient, and emergency department visits) can influence the therapies that physicians suggest and patients ultimately use.<sup>22,23</sup>

The cost of medication can be a major deterrent toward achieving treatment goals and patient adherence.<sup>1,10</sup> As such, less costly treatment options which lead to greater health outcomes should be considered in line with drug safety and efficacy, associated comorbidities, and patient lifestyles and preferences. New drug classes of treatments (eg, SGLT2 and DPP4 inhibitors) present an opportunity to overcome these challenges due to the potential to reduce health care costs outside of the medication cost alone. SGLT2 and DPP4 inhibitors and fixed-dose combinations demonstrate reductions in hospitalizations and heightened

**FIGURE 2.** Treatment Challenges Associated With the Management of Type 2 Diabetes<sup>11</sup>



Arrows indicate compounding associations between factors relating to treatment challenges in type 2 diabetes.

health benefits relating to weight reduction,  $A_{1C}$  levels, and CVD risk.<sup>24</sup>

A 2018 retrospective observational study examining de-identified patient data from 4 observational databases compared the risk of hospitalization due to heart failure (HHF) between new SGLT2 inhibitors and other anti-hyperglycemic agents (AHA) users.<sup>25</sup> The use of SGLT2 inhibitors versus other available AHAs lead to an overall lower risk of HHF for patients with T2D (95% CI, 0.39 [0.26-0.60]) and reached significance for those patients with established CVD.<sup>25</sup> These health care utilization reductions were demonstrated to lead to a significant decrease in all-cause health care costs ( $P < .0001$ ).<sup>26</sup>

DPP4 inhibitors, listed as a second line treatment by the ADA, may be a cost-effective treatment option for those patients with low CVD risk and who attain their  $A_{1C}$  and weight loss goals.<sup>27</sup> DPP4 inhibitors are weight neutral, show benefits in hypoglycemia, and carry low adverse reactions.<sup>27</sup> If treatment goals remain uncontrolled on DPP4 inhibitors, the escalation or addition of alternate therapies (eg, SGLT2 inhibitors or fixed-dose combinations) can further mitigate cost and enhance patient health outcomes by decreasing prescription costs and greater attainment of treatment goals.

In 2018, the ADA estimated the total costs of the treatment of diagnosed diabetes in the United States. The majority (67%) of these costs are covered by government-provided insurance (ie, Medicare, Medicaid, and military). Private insurance (31%) and the uninsured (2%) make up the rest of the costs.<sup>2</sup>

Research has revealed substantial disparities in health and access to health care services across SES groups in the United States.<sup>7,28-30</sup>

A 2007 cross-sectional study by Nwasuruba et al utilized data collected via a telephone-based survey and demonstrated racial differences in self-care behaviors in patients with T2D. Self-care behaviors, such as attaining the recommended number of physical activity minutes or engaging in at home self-monitoring of blood glucose, were diminished in black and Hispanic populations compared with white populations.<sup>29</sup>

Health care insurance type and access were also demonstrated to affect  $A_{1C}$  levels based on the results of a 2019 cross-sectional study in which Liese et al evaluated surveillance data from 481 youth and young adults with a diagnosis of diabetes. The results illustrated a protective effect of private insurance on  $A_{1C}$  levels when compared with individuals with state or federal insurance ( $P = .0025$ ) or no insurance ( $P < .0001$ ).<sup>31</sup>

Further, the results of 2017 cross-sectional study by Assari et al demonstrated that SES and governmental insurance may be predictors of  $A_{1C}$  control and may be influenced by characteristics such as age, race, and gender, although

the study lacks generalizability due to sample size.<sup>30</sup> For example, for black men, age ( $P = .040$ ) and having governmental insurance ( $P = .042$ ), were correlated with  $A_{1C}$ .<sup>30</sup> In another study of SES in relation to diabetes care, Arpey et al (2017) conducted patient interviews to evaluate patients' perceptions to care in relation to their SES status. They noted that most subjects felt their SES status influenced the type and amount of care they received. Individuals also felt that their SES altered the amount, type, and ability to schedule needed tests and obtain medications.<sup>32</sup>

SES is a potentially modifiable risk factor for disease that should be targeted for early implementation of public health strategies aimed at improving SES disparities for vulnerable populations.<sup>7</sup> Public health policies and guidelines created with community based initiatives can ensure clinical benefits are achieved across SES groups.

Effective partnerships among medical care, social services, public health, and community-based organizations could improve population health outcomes by addressing the social determinants of health. A retrospective evaluation of a 12-month pilot diabetes care program in a rural setting by McLendon et al noted that DSME was successful due to strong partnerships with a community advisory network, health care leadership representatives, and 2 primary care host sites within the rural community, allowing for the successful execution of their pilot care model program.<sup>9</sup> Quinoñes et al (2015) noted that community health workers can bolster and build personal connections between health care systems and patients to ease the difficulty of navigating these complex systems. These workers can increase access to care by illuminating pathways to limited community resources, helping patients understand their care options, and helping to tailor treatment interventions to encompass social and cultural needs.<sup>28</sup>

Various interventions, such as reducing patient cost sharing, have been suggested to decrease SES disparities in health care, and studies looking at cost sharing in patients with T2D have demonstrated an inverse relationship between cost and attainment of treatment goals and medication adherence.<sup>33,34</sup> Henk et al noted that for patients enrolled in fixed tiered plans, a 10% higher medication copayment led to a significant reduction ( $P < .001$ ) in medication adherence.<sup>33</sup>

A 2016 retrospective cohort study of medical and pharmacy claims data from 2004 to 2012 from 92,410 patients with T2D enrolled in 1514 health care plans evaluated the associations among cost sharing, medication adherence, and per-patient all-cause hospital days. Results of this study showed a 1.6% point decrease in adherence (2.4%;  $P < .01$ ) with a \$10 increase in patient OOP cost. A 10% reduction in adherence was associated with 15% more per-patient hospital days.<sup>34</sup>

Comprehensive care models should account for costs, value, and clinical outcomes to the patient to be the most cost and clinically beneficial.<sup>34</sup> Given that health care-related costs in the United States have continued to rise, many stakeholders are looking to novel means to optimize the value of health care. Programs focusing on incentivizing optimal clinical outcomes for patients are being explored (eg, consumer-driven health plans, wellness and prevention programs, pay-for-performance initiatives, and health information technology tracking). Programs may prove most successful to the patient and health care ecosystem when they are able to both benefit health-related behaviors and mitigate costs.<sup>35</sup>

Strategies to move toward value-based care, a system that provides incentives for the attainment of treatment goals, may prove helpful to reducing cost and treatment burden. Value-based packages are created to motivate positive clinical outcomes by providing financial incentives to patients and clinicians to use certain treatments by employing lower OOP costs and higher reimbursement, respectively (Figure 3).<sup>36</sup> In patients with T2D, these value-based systems need to go beyond A<sub>1C</sub> levels and encompass

comorbidities like CVD and heart failure. The ADA has included treatment agents with protective effects against CVD (eg, sodium-glucose cotransporter 2 inhibitors) into their guidelines in tandem with other first-line agents for patients with comorbid CVD and T2D, based on their potential to decrease cardiovascular events.<sup>27</sup> Value-based partnerships that capitalize on these ADA recommendations have the potential to decrease the cost of T2D care and improve patient outcomes.

### Access to T2D Care

Care coordination by both patient and their health care provider are required to elicit optimal care.<sup>37</sup> In order to be inclusive patient centered care programs cannot assume a standardized level of access to care.<sup>37</sup> According to Nash et al, 3 unique steps are key to obtain appropriate access to care: “gaining entry into the health care system; (2) getting access to care settings where the patient can receive needed services; and (3) finding providers who meet the needs of individual patients and with whom patients can develop a relationship based on mutual communication and trust.”<sup>37</sup>

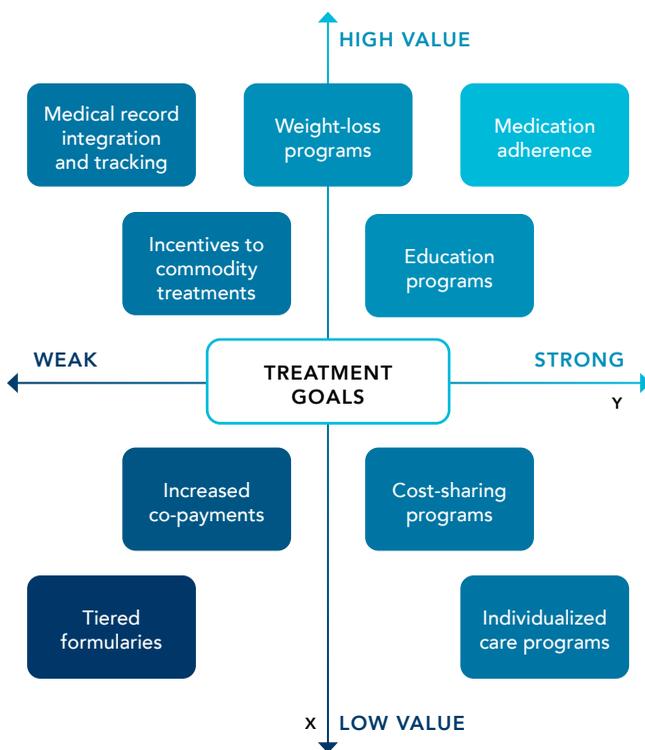
Access to treatment can further be compounded by a lack of knowledge or understanding of treatment option by both patient and provider.<sup>37</sup> The establishment of T2D treatment guidelines and care centers through public or private policy should be accessible to patients regardless of income, self-care ability, or living situation.<sup>37</sup>

One crucial potential barrier to accessing T2D treatment is a patient’s geographic location. For instance, in rural areas, distance to treatment centers, inclement weather, a lack of public transportation, and health care provider shortages can all affect one’s ability to obtain proper and efficient treatment.<sup>13</sup> Rural areas may have a decreased availability of care services and providers compared with urban areas.<sup>20</sup> Conversely, urban inner cities are faced with their own barriers to access. In urban cities, minority populations may face language barriers, a lack of cultural understanding, low educational attainment, a lack of social reinforcement for health-related behaviors and activities, and provider shortages which can limit appropriate access to treatment.<sup>13</sup>

### Improving Patient Adherence in T2D

There is relatively broad agreement across scientific literature that medication adherence and/or persistence is far from uncommon in patients with T2D and may affect half this population at minimum.<sup>38,39</sup> A magnitude of schemes, such as educational programs, disease management programs, intensive behavioral support, medication reminders, and special packaging, have been utilized to combat the lack of medication adherence across T2D; however, long-term, sustained improvements in rates of adherence have been difficult to achieve.<sup>38</sup> The available

**FIGURE 3.** Framework and Factors Relevant in Value-Based Care Design Models<sup>36,a</sup>



\*X indicates value to patient and health care system; Y indicates evidence for efficacy.

body of data points to 6 key factors leading to nonadherence in T2D treatment: perceived treatment efficacy, hypoglycemia, treatment complexity and convenience, cost of treatment, medication beliefs, and physician trust.<sup>38</sup>

Poor medication adherence in T2D has been linked to negative health consequences, including increased mortality.<sup>38</sup> A 2012 study examining managed care medical records by Jha et al noted that increased treatment adherence was associated a lower rate of hospital visits. The authors noted an approximately 13% lower probability of hospitalization for a patient adherent to treatment.<sup>15</sup> A loss of adherence, however, lead to a nearly 15% increase in hospitalization in the following year.<sup>15</sup> Additionally, greater medication adherence and improvements in measurable T2D treatment outcomes, such as A<sub>1c</sub> levels are linked.<sup>15</sup>

Drug combinations, such as a fixed-dose treatment, ease treatment burden by decreasing pill load which may have beneficial impacts on medication adherence.<sup>38,40</sup> Currently, there are several fixed-dose combinations of agents available for the treatment of hyperglycemia in T2D.

Further, there is data to support initial combination therapy elicits more rapid attainment of glycemic goals.<sup>41,42</sup> Matthews et al noted in their 2019 randomized, double-blind, parallel-group study of newly diagnosed patients with T2D that early combination therapy lead to a significant reduction in time to treatment failure as defined by A<sub>1c</sub> measurements and control ( $P < .0001$ ).<sup>42</sup>

Further, a 2012 retrospective claims database analysis by Williams et al illustrated that patients on a fixed-dose combination had higher rates of achieving their A<sub>1c</sub> goals (61%) compared with step therapy (48%) ( $P < .001$ ) or loose-dose combination (52%) ( $P = .015$ ).<sup>43</sup> This earlier attainment of optimal A<sub>1c</sub> levels due to combination therapy may facilitate decreased AEs due to lower dosing of individual drug components and curb dose intensifications.<sup>41</sup>

A collaboration between clinicians, diabetes educators, and pharmacists should center around optimizing the adherence of patients with T2D through clear communication and the incorporation of DSME and self-care behaviors while being mindful of patients' treatment concerns and preferences.<sup>38,44</sup>

## Summary

Clinicians should personalize goals for A<sub>1c</sub> control in patients with T2D based on a discussion of benefits and harms of drug therapy, patients' preferences, impact of treatment burden, and associated costs of care. Over the past 2 decades, a greater proportion of individuals with T2D and their families have dealt with an increasing cost burden due to rising insurance premiums, drug prices, and health care costs.<sup>27</sup>

As health care systems and providers strive to provide optimal care and improve the health of their patients'

treatments must look outside of traditional clinical measurements but factor social and cultural norms.<sup>28</sup> Novel treatment strategies bearing in mind social and economic factors impacting health should be integrated into patient care plans at all levels of the health care ecosystem.<sup>28</sup> A greater utilization of pharmacists and electronic medical records and a decrease in associated treatment costs can increase patient medication adherence and in turn decrease patient burden.<sup>15</sup> ♦

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