Cost-effectiveness of Interventions to Manage Diabetes: Has the Evidence Changed Since 2008?

Karen R. Siegel,[1] Mohammed K. Ali,[1,2] Xilin Zhou,[1] Boon Peng Ng,[1,3] Shawn Jawanda,[1] Krista Proia,[1] Xuanping Zhang,[1] Edward W. Gregg,[1] Ann L. Albright,[1] and Ping Zhang[1]

Diabetes Care 2020;43:1557–1592 | https://doi.org/10.2337/dci20-0017

OBJECTIVE

To synthesize updated evidence on the cost-effectiveness (CE) of interventions to manage diabetes, its complications, and comorbidities.

RESEARCH DESIGN AND METHODS

We conducted a systematic literature review of studies from high-income countries evaluating the CE of diabetes management interventions recommended by the American Diabetes Association (ADA) and published in English between June 2008 and July 2017. We also incorporated studies from a previous CE review from the period 1985–2008. We classified the interventions based on their strength of evidence (strong, supportive, or uncertain) and levels of CE: cost-saving (more health benefit at a lower cost), very cost-effective (≤$25,000 per life year gained [LYG] or quality-adjusted life year [QALY]), cost-effective ($25,001–$50,000 per LYG or QALY), marginally cost-effective ($50,001–$100,000 per LYG or QALY), or not cost-effective (>$100,000 per LYG or QALY). Costs were measured in 2017 U.S. dollars.

RESULTS

Seventy-three new studies met our inclusion criteria. These were combined with 49 studies from the previous review to yield 122 studies over the period 1985–2017. A large majority of the ADA-recommended interventions remain cost-effective. Specifically, we found strong evidence that the following ADA-recommended interventions are cost-saving or very cost-effective: In the cost-saving category are *1*) ACE inhibitor (ACEI)/angiotensin receptor blocker (ARB) therapy for intensive hypertension management compared with standard hypertension management, *2*) ACEI/ARB therapy to prevent chronic kidney disease and/or end-stage renal disease in people with albuminuria compared with no ACEI/ARB therapy, *3*) comprehensive foot care and patient education to prevent and treat foot ulcers among those at moderate/high risk of developing foot ulcers, *4*) telemedicine for diabetic retinopathy screening compared with office screening, and *5*) bariatric surgery compared with no surgery for individuals with type 2 diabetes (T2D) and obesity (BMI ≥30 kg/m^2). In the very cost-effective category are *1*) intensive glycemic management (targeting A1C <7%) compared with conventional glycemic management (targeting an A1C level of 8–10%) for individuals with newly diagnosed T2D, *2*) multicomponent interventions (involving behavior change/education and pharmacological therapy targeting hyperglycemia, hypertension, dyslipidemia, microalbuminuria, nephropathy/retinopathy, secondary prevention of cardiovascular disease with aspirin) compared with usual care, *3*) statin therapy compared with no statin therapy for individuals with T2D and history of cardiovascular disease, *4*) diabetes self-management education and support compared with usual care, *5*) T2D screening every 3 years starting at age 45 years compared with no screening, *6*) integrated, patient-centered care compared with usual care, *7*) smoking cessation compared with no smoking cessation, *8*) daily aspirin use as primary prevention for cardiovascular complications compared with usual care, *9*) self-monitoring of blood glucose three times per day compared with once per day among those using insulin, *10*) intensive glycemic management compared with conventional insulin therapy for

[1]Division of Diabetes Translation, Centers for Disease Control and Prevention, Atlanta, GA
[2]Hubert Department of Global Health and Department of Family and Preventive Medicine, Emory University, Atlanta, GA
[3]College of Nursing and Disability, Aging and Technology Cluster, University of Central Florida, Orlando, FL

Corresponding author: Ping Zhang, paz2@cdc.gov

Received 23 March 2020 and accepted 3 April 2020

This article contains supplementary material online at https://doi.org/10.2337/figshare.12081801.

The findings and conclusions are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

See accompanying article, p. 1593.

T2D among adults aged ≥50 years, and *11*) collaborative care for depression compared with usual care.

CONCLUSIONS

Complementing professional treatment recommendations, our systematic review provides an updated understanding of the potential value of interventions to manage diabetes and its complications and can assist clinicians and payers in prioritizing interventions and health care resources.

Diabetes is a serious, common, and costly disease, affecting 34 million Americans (1) and leading to $327 billion (2) in annual health expenditures in 2017. To better manage and lower the burdens of diabetes, the American Diabetes Association (ADA) annually publishes its *Standards of Medical Care in Diabetes* (SOC) (3), the most comprehensive and up-to-date clinical knowledge regarding diabetes care. Worldwide, the SOC provides clinicians, patients, researchers, and payers with the most current evidence-based screening, diagnostic, prevention, and management recommendations for diabetes. However, the cost-effectiveness (CE) of these strategies—in other words, the value they provide for these investments—varies greatly and should be considered in management or policy decisions.

CE analysis is an analytical framework that weighs the benefits and costs of an intervention by comparing it with standard care or other alternatives to see if the value of the intervention justifies its cost. The CE of different treatment options provides critical information to stakeholders at a variety of levels; this information helps in development of optimal treatment strategies or policies to lower current and future health and economic burdens and help determine use of limited health care resources.

In 2010, Li et al. (4) systematically reviewed all English-language studies published between January 1985 and May 2008 on the CE of diabetes prevention and management interventions recommended by the ADA's SOC 2008 (5). The authors concluded that a large majority of the interventions recommended by ADA at that time were cost-saving or very cost-effective. Since then, however, many new technologies and medications have become available and have been added to updated iterations of the ADA's SOC, leading to important changes in the ways diabetes care is delivered, how complications are managed, and the resulting costs. Recently published CE studies on these new technologies and medications can provide evidence on how to prioritize these novel interventions together with older strategies that remain cost-effective.

To provide up-to-date guidance that aligns with the 2019 SOC (the most up-to-date version at the time of data analysis) (6,7), we aggregated all available data published in English regarding the CE of ADA-recommended interventions to identify diabetes or gestational diabetes mellitus, manage diabetes, screen for diabetes complications, and manage complications and comorbidities. We included data from the previous review by Li et al. and systematically added data from the last decade to provide findings that are relevant to contemporary clinical practice. The result allows us to assess economic implications of changes that have occurred in the way diabetes care is delivered and how complications are managed. As a complement to the ADA's 2019 SOC recommendations, findings from this review could assist clinicians and policy makers in selecting interventions that are not only effective but also deliver value.

RESEARCH DESIGN AND METHODS

Data Sources and Literature Search

We followed the same search strategy that was used in the 2010 review by Li et al. (4). Briefly, we performed a thorough literature search of seven databases (Cumulative Index to Nursing and Allied Health Literature [CINAHL], Cochrane, EMBASE, MEDLINE, PsycINFO, Scopus, and Sociological Abstracts [Soc Abs]) following the Cochrane Collaboration's protocol (8) covering the period of June 2008 to July 2017. Medical subject headings matching the previous review's search protocol were selected to create a search strategy. Our search terms were diabetes (indicating the disease of diabetes: "type 1," "type 2," "gestational," "impaired glucose," and "insulin resistance"), costs ("cost or expenditure," "health care cost," "costs or cost analysis"), effectiveness ("benefit" OR "life year" OR "quality-adjusted life years" OR "disability adjusted life years"), cost-effectiveness (indicating CE analysis, such as "cost-effectiveness analysis" OR "cost-utility analysis" OR "economic"). We also screened reference lists of all included articles and publications from leading medical and diabetes-focused journals during the period for additional articles that may have been missed.

Article Screening and Selection

We included studies from populations in high-income countries (based on World Bank classifications [9]) that assessed the economic value associated with diabetes management interventions included in the ADA's SOC 2019 (7), the most up-to-date version available at the time of our analysis. We included studies of patients with undiagnosed or diagnosed diabetes, including type 1 diabetes (T1D), type 2 diabetes (T2D), and gestational diabetes mellitus.

We included studies that used one of the three major types of economic evaluations: cost-effectiveness analyses, cost-utility analyses, or cost-benefit analyses, with outcomes measured as cost per additional quality-adjusted life year (QALY) gained, cost per additional life year gained (LYG), or cost per additional disability-adjusted life year averted.

We included original research studies published in English and excluded review articles, commentaries or letters, conference abstracts, and dissertations. For this review, we also excluded studies that focused on preventing T2D. Each study was screened for eligibility by two authors (K.R.S., X.Zho., B.P.N., S.J., K.P., and X.Zha. all participated in this stage), with disagreements resolved by group discussion and consensus.

Data Abstraction

For studies from June 2008 through July 2017, we used the same detailed data extraction form used by Li et al. (4) to systematically gather the following information from each included study: publication information (title, first author's name, publication year), study population, intervention and comparison, study method (within trial versus modeled/simulation), analytical time horizon and discounting, perspective used, costs, health outcome measures, survey instruments for measuring utility, incremental cost-effectiveness ratio (ICER), whether a sensitivity analysis was conducted, and study conclusion(s). For studies from January 1985 through May 2008, we used the previously abstracted data from Li et al.

Quality Assessment of Included Studies

To evaluate the quality of the included CE studies, we selected a widely used quality

assessment tool based on *The BMJ* authors' guide for economic studies (10), which was used in the 2010 review by Li et al. We considered four quality score items: source of cost-specific data, categories of costs, source of benefit-specific data, and categories of benefits. We classified studies that did not report all four items as "low quality." Of studies that had all four components, we assessed nine additional items (analytical time horizon, study perspective, description of the CE model, diagram for constructing the decision tree, currency and year of cost, cost discounting, benefit discounting, ICERs, and sensitivity analysis) for further classification. We assigned one point for each item that was reported. We rated each study as "fair" if it scored 3 or less, "good" if it scored 4–6, and "excellent" if it scored 7–9 points. We restricted our analysis to articles rated as "excellent" or "good" quality. Our quality assessment methodology mirrored that used by Li et al. Figure 1 illustrates the complete process for screening articles.

Data Analysis and Synthesis

To synthesize findings, we first grouped articles into four broad categories: *1*) screening for undiagnosed diabetes (including T2D and gestational diabetes mellitus), *2*) managing diabetes and risk factors to prevent diabetes-related complications (comprehensive lifestyle interventions; diabetes self-management education [DSME]; self-monitoring of blood glucose [SMBG]; intensive glycemic, blood pressure, and lipid control; integrated and coordinated care; smoking cessation), *3*) screening for and early treatment of diabetes complications (cardiovascular disease [CVD], eye complications, foot ulcers, end-stage renal disease [ESRD]), or *4*) treating diabetes-related complications and comorbidities (CVD, eye complications, foot ulcers, and comorbidities such as obesity, mental health, and sleep apnea). Within each of the four broader groups, we further classified studies into specific categories corresponding to each ADA-recommended intervention.

To facilitate comparisons across studies, we converted all costs and ICERs to 2017 U.S. dollars using the Consumer Price Index (11). If costs were reported in other currencies, we used the annual exchange rate from the Federal Reserve Bank (12) to convert them into U.S. dollars. If a study did not mention the year used in cost calculations, we assumed cost was for the one year prior to publication. ICERs were expressed as dollars per QALY or dollars per LYG and were rounded to the nearest hundred dollars. We calculated a range and median ICER for each intervention category.

Classifying the Interventions

We classified interventions based on their median levels of CE (five tiers) and strength of evidence (three levels). As there are no universally accepted thresholds to judge whether an intervention is cost-effective, we grouped the CE tiers of the intervention based on conventional norms according to their estimated ICERs: *1*) cost-saving when the intervention generates better health outcomes and costs less than the comparison intervention or is cost neutral (ICER = 0), *2*) very cost-effective if the ICER is greater than zero but less than or equal to $25,000 per QALY or LYG, *3*) cost-effective if the ICER is greater than $25,000 but less than or equal to $50,000 per QALY or LYG, *4*) marginally cost-effective if the ICER is greater than $50,000 but less than or equal to $100,000 per QALY or LYG, and *5*) not cost-effective if the ICER is greater than $100,000 per QALY or LYG. Since there are no conventional norms for thresholds of cost per LYG, we used the same threshold for cost per QALY, which was the same approach used by Li et al. (4).

We classified the evidence level of the CE findings as strong, supportive, or uncertain. Strong evidence included findings from one of the following two categories:

Category 1:

1. The CE of the intervention was evaluated by two or more studies, AND
2. these studies were rated as at least "good" in quality, AND
3. the effectiveness of the interventions was based on either well-conducted, generalizable randomized clinical trials with adequate power or well-conducted meta-analyses or a diabetes disease simulation model that was validated, AND
4. the effectiveness of the intervention was also rated as level A or level B evidence by the ADA's SOC 2019 (13), AND
5. the ICERs of the intervention from different studies consistently fell into the same CE tier.

Category 2:

1. CE assessment meets items 3 and 4 from category 1, but only one study evaluated the intervention, AND
2. the study was rated as "excellent" in quality.

We considered evidence on the CE of an intervention to be supportive if:

1. the CE of the intervention was evaluated by only one study AND this study was rated lower than "excellent" quality, OR

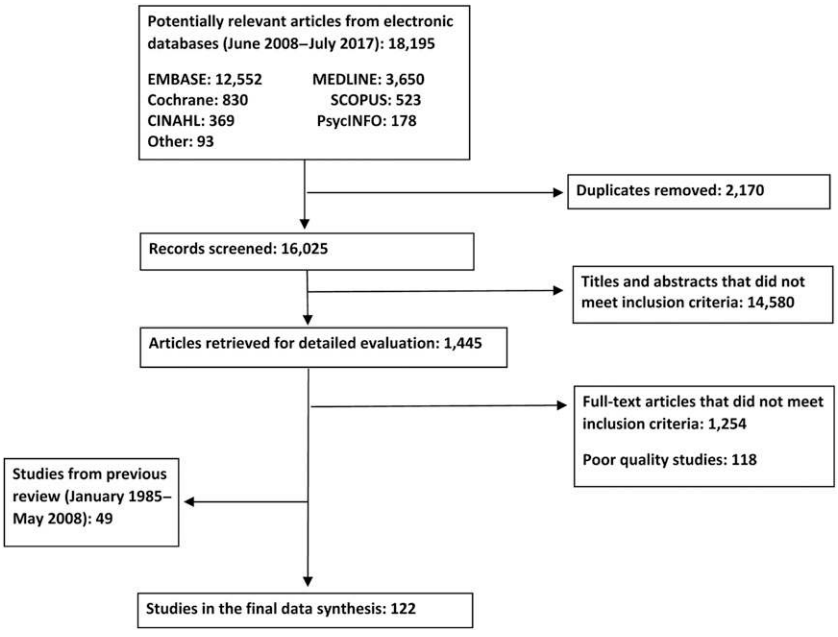

Figure 1—Flowchart for article inclusion.

2. the effectiveness of the intervention was supported by level C evidence according to the ADA's SOC 2019 (13) or by expert consensus only, OR
3. the CE was based on a simulation by a diabetes disease model that was not validated (a model was considered to be validated if it was explicitly stated in the text of the article or if the model was known to be validated based on previous literature).

For each ADA-recommended intervention within each evidence-CE level category, we described its comparison intervention, the study population in which the intervention was implemented, and the ADA's level of evidence rating. We also reported the number of studies that evaluated the CE of this intervention (based on the current evidence and on the previous review), and the median and range of the ICERs across the studies.

RESULTS

Our initial search yielded 18,195 articles over the period of June 2008 to July 2017. After removal of duplicates and screening of all abstracts, 1,445 articles remained, of which we reviewed full texts to identify 73 CE studies that met our inclusion criteria. We added the 49 relevant studies on diabetes management from the 2010 review by Li et al. (encompassing 1985–2008), bringing the total number of studies to 122 over the period 1985–2017 (Fig. 1). Table 1 describes the CE studies included in our final review by intervention category. Studies that evaluated multiple interventions or a single intervention in diverse subgroups were assigned to more than one intervention or population category, respectively.

Supplementary Fig. 1 provides a summary of the numbers of studies across the four broad intervention categories—screening for undiagnosed diabetes (8 studies), managing diabetes and risk factors to prevent diabetes-related complications (71 studies), screening for and early treatment of diabetes complications (33 studies), and treating diabetes-related complications and comorbidities (19 studies)—as well as how the number of articles in each category changed from the previous review (1985–2008) to the current review (1985–2017). Except for smoking cessation, the number of articles in every category increased over time, and five new categories emerged: preventing CVD complications, treating CVD complications, and addressing comorbidities of obesity, mental health, and sleep apnea.

In Table 2, we classified each of the ADA-recommended interventions based on their levels of CE and strength of evidence by intervention category, using all studies over the period 1985–2017. To facilitate use by clinicians and decision makers, we describe the findings across each of the four intervention categories from a health system perspective.

Strong Evidence

Screening for Undiagnosed Diabetes

Screening for T2D every 3 years starting at age 45 years for the U.S. population without diabetes, compared with no screening, had strong evidence of being very cost-effective at $7,898/QALY (every 1 year compared with every 3 years was also very cost-effective at $8,139/QALY). On the other hand, there was strong evidence that universal opportunistic screening for undiagnosed T2D among the U.S. population (whether or not followed by treatment), compared with targeted screening in high-risk individuals, was not cost-effective (>$100,000/QALY).

Managing Diabetes and Risk Factors to Prevent Diabetes-Related Complications

For interventions to manage diabetes and risk factors to prevent complications, the evidence was mixed. We found strong evidence that DSME for individuals with diabetes, compared with usual care, is very cost-effective ($5,047/QALY). Additionally, there were several new studies on the daily frequency of SMBG, which led to the new finding that SMBG three times per day, compared with SMBG once per day, is very cost-effective ($3,719/QALY) among adults with T2D currently taking insulin.

The ICERs for intensively managing glycemia varied according to a patient's age, duration of diabetes, and diabetes type (1 or 2). We found that intensive glycemic management compared with conventional management was very cost-effective among young individuals with newly diagnosed T2D ($4,318/QALY) and older individuals (aged ≥50 years) with T2D ($15,398/QALY) and was cost-effective when given to individuals with T1D regardless of age ($41,339/QALY).

For blood pressure management, ACE inhibitor (ACEI) and angiotensin receptor blocker (ARB) therapies, used either for intensive hypertension management (compared with suboptimal blood pressure management) or to prevent chronic kidney disease and/or ESRD in patients with albuminuria, compared with no ACEI/ARB therapy, emerged with strong evidence of being cost-saving.

Over the period 1985–2017, studies comparing multicomponent interventions (including behavior change and medication adherence to improve glycemia, blood pressure/CVD, lipids, and nephropathy/retinopathy prevention and screening together) with usual care have shown a range of value achieved from cost-effective to cost-saving. Overall, however, we found that these multicomponent interventions were on average very cost-effective ($2,315/QALY) for individuals with T1D and T2D compared with usual care.

Diabetes management interventions that remained consistent with the previous review as very cost-effective were *1*) integrated, patient-centered care based on the Chronic Care Model for individuals with T2D compared with usual care ($11,339/QALY), and *2*) smoking cessation for individuals with diabetes compared with no smoking cessation (<$31,750/QALY).

Screening for and Early Treatment of Diabetes-Related Complications

We found strong evidence for two cost-saving screening and early treatment interventions: *1*) comprehensive foot care and patient education to prevent and treat foot ulcers among individuals with diabetes and at moderate/high risk of developing foot ulcers, compared with usual care, and *2*) telemedicine for diabetic retinopathy screening among individuals with diabetes compared with office screening for diabetic retinopathy. Additionally, we found strong evidence that screening for eye complications every 1–2 years for individuals with diabetes, compared with no screening, is very cost-effective ($8,763/QALY).

Treatment of Diabetes-Related Complications and Comorbidities

Statin therapy for secondary prevention of CVD—i.e., in individuals with T2D and a history of CVD—compared with no statin therapy remained consistent from the previous review as very cost-effective ($4,627/QALY), while among individuals with T2D, hyperlipidemia, and no history of CVD, statin therapy was marginally cost-effective ($67,873/QALY). A new finding in

Table 1—Description of the CE studies for diabetes interventions

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Screening for undiagnosed T2D						
Centers for Disease Control and Prevention, 1998/U.S. (21)	U.S. population aged 25 years and older	Opportunistic screening for undiagnosed T2D starting at age 25 years, then treatment (universal screening)	No screening and treatment until clinical diagnosis of T2D		Lifetime; 3%	$114,046/QALY
Hoerger et al., 2004/U.S. (22)	Individuals with hypertension	Targeted screening for undiagnosed diabetes among persons with hypertension	No screening or treatment until clinical diagnosis of T2D		Lifetime; 3%	$59,436–$165,735/QALY, decreasing with age $89,535/QALY for age 45 years
	U.S. population	One-time opportunistic screening, then treatment (universal screening)	No screening or treatment until clinical diagnosis of T2D			$91,694–$240,157/QALY, decreasing with age $233,045/QALY for age 45 years
	U.S. population	One-time opportunistic screening, then treatment (universal screening)	Targeted screening, then treatment			$273,812–$888,746/QALY increasing with age
Gillett et al., 2015/ U.K. (23)	Adults aged 40–74 years with preDM and undiagnosed T2D	Prescreening with a risk score, then screening with A1C test (cutoff of 6%)	No screening	Computer simulation (Sheffield T2D Model) of LEADER study cohort	Lifetime; 5%	$2,088/QALY
	Adults aged 40–74 years with preDM and undiagnosed T2D	Prescreening with a risk score, then screening with FPG test (cutoff of 5.5 mmol)	No screening	Computer simulation (Sheffield T2D Model) of LEADER study cohort	Lifetime; 1.5%	$4,301/QALY
Kahn et al., 2010/ U.S. (24)	U.S. population without DM, mean age 30 years	T2D screening every 3 years starting at age 30 years	No screening	Computer simulation (Archimedes)	Lifetime; 3%	$14,807/QALY
		T2D screening every 1 year starting at age 45 years	No screening	Computer simulation (Archimedes)	Lifetime; 3%	$21,846/QALY
		T2D screening every 3 years starting at age 45 years	No screening	Computer simulation (Archimedes)	Lifetime; 3%	$13,707/QALY
		T2D screening every 5 years starting at age 45 years	No screening	Computer simulation (Archimedes)	Lifetime; 3%	$13,784/QALY
		T2D screening every 3 years starting at age 60 years	No screening	Computer simulation (Archimedes)	Lifetime; 3%	$36,253/QALY
		T2D screening every 1 year following hypertension diagnosis	No screening	Computer simulation (Archimedes)	Lifetime; 3%	$8,855/QALY
		T2D screening every 5 years following hypertension diagnosis	No screening	Computer simulation (Archimedes)	Lifetime; 3%	$9,141/QALY
		T2D screening every 6 months starting at age 30 years	No screening	Computer simulation (Archimedes)	Lifetime; 3%	$57,438/QALY

Continued on p. 1562

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Screening for and treating GDM						
Nicholson et al., 2005/U.S. (25)	30-year-old pregnant women 24–28 weeks' gestation	Sequential method (50-g GCT + 100-g GTT)	No screening or 75-g GTT	RCT	<1 year; 0%	Cost-saving
		100-g GTT	No screening or 75-g GTT			Cost-saving
		100-g GTT	Sequential method			$44,704/QALY for maternal outcomes, $11,430/QALY for neonatal outcomes
Werner et al., 2012/U.S. (26)	Simulated cohort of 100,000 pregnant women	Sequential method (50-g GCT at 24–28 weeks + 100-g GTT) [current practice]	No screening	Computer simulation (decision tree)	Lifetime; 3%	$19,746/QALY
	Simulated cohort of 100,000 pregnant women	FPG at 1st prenatal visit + 75-g GTT at 24–28 weeks [practice proposed by IADPSG]	Sequential method (50-g GCT at 24–28 weeks + 100-g GTT) [current practice]	Computer simulation (decision tree)	Lifetime; 3%	$24,060/QALY
Chen et al., 2016/ Singapore (27)	Pregnant women at risk for GDM	Universal GDM screening (75-g OGTT) among all pregnant women	Targeted GDM screening among high risk women	Computer simulation (decision tree)	<1 year; 3%	$11,841/QALY
		Targeted GDM screening	No screening	Computer simulation (decision tree)	<1 year; 3%	$10,047/QALY
Danyliv et al., 2016/Ireland (28)	Pregnant women at risk for GDM	75-g OGTT method in primary care setting, then treatment	No screening	Computer simulation (decision tree)	Lifetime; 5%	Cost-saving
		75-g OGTT method in hospital setting, then treatment	No screening	Computer simulation (decision tree)	Lifetime; 5%	Cost-saving
		75-g OGTT method in hospital setting, then treatment	75-g OGTT method in primary care setting, then treatment	Computer simulation (decision tree)	Lifetime; 5%	Cost-saving
Intensive glycemic control						
DCCT Research Group, 1996/ U.S. (29)	T1D	Intensive glycemic control through insulin management, self-monitoring, and outpatient visits. The goal was to achieve A1C level as normal as possible (6%)	Conventional therapy (less intensive)	DCCT multicenter RCT (n = 1,441)	Lifetime; 3%	$64,516/QALY
Eastman et al., 1997/U.S. (30)	Newly diagnosed T2D	Intensive treatment targeting maintenance of A1C level at 7.2%	Standard antidiabetic treatment targeting A1C level at 10%	DCCT (n = 1,441)	Lifetime; 3%	$22,098/QALY
Gray et al., 2000/ U.K. (31)	T2D	Intensive insulin therapy through multiple insulin injections A1C <7%	Conventional management (mainly through diet) aiming at FPG<15 mmol/L	UKPDS multicenter RCT (n = 5,120)	10 years; 6%	Cost-saving
Palmer et al., 2000/ Switzerland (32)	T1D	Intensive insulin therapy	Conventional insulin therapy	Literature review	Lifetime; 3%	$59,182/LYG
Wake et al., 2000/ Japan (33)	T2D	Intensive insulin therapy through multiple insulin injections A1C <7%	Conventional insulin therapy	Kumamoto study RCT (n = 110)	10 years; 3%	Cost-saving

Continued on p. 1563

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Clarke et al., 2001/U.K. (34)	Newly diagnosed T2D + overweight	Intensive blood glucose control with metformin aiming at FPG <6 mmol/L	Conventional treatment primarily with diet	UKPDS (n = 5,120)	Median 10.7 years; 6%	Cost-saving
Centers for Disease Control and Prevention, 2002/U.S. (35)	Newly diagnosed T2D	Intensive glycemic control with insulin or sulfonylurea aiming at FPG of 6 mmol/L	Conventional glucose control (mainly diet)	UKPDS (n = 5,120)	Lifetime; 3%	$78,740/QALY; increasing rapidly with age at diagnosis: $18,288/QALY for age 25–34 years; >$127,000–$3.9 million for age 55–94 years. Cost-saving under UKPDS cost scenario (no case management cost, much less self-testing, slightly fewer physician visits)
Scuffham and Carr, 2003/U.K. (36)	T1D	Continuous subcutaneous insulin intervention for persons using insulin pump	Multiple daily insulin injections	1 systematic review, 1 meta-analysis	8 years; 6%	$12,954/QALY
Roze et al., 2005/U.K. (37)	T1D	Continuous subcutaneous insulin infusion	Multiple daily insulin injections	DCCT (n = 1,441) mainly meta-analysis	60 years; 3%	$23,495/QALY
Clarke et al., 2005/U.K. (38)	Newly diagnosed T2D requiring insulin	Intensive glycemic control with insulin or sulfonylurea at FPG <6 mmol/L	Conventional glucose control therapy (mainly diet)	UKPDS (n = 5,120)	Lifetime; 3.5%	$4,318/QALY
	Newly diagnosed T2D + overweight	Intensive glycemic control with metformin	Conventional glucose control therapy (mainly diet)			Cost-saving
Eddy et al., 2005/U.S. (39)	Newly diagnosed T2D	Intensive DPP lifestyle with FPG >125 mmol/L; target: A1C level of 7%	Dietary advice	DPP (n = 3,234)	30 years; 3%	$42,037/QALY
Cameron and Bennett, 2009/Canada (40)	T1D and T2D	Insulin aspart	Regular human insulin	Computer simulation (Center for Outcomes Research Model)	35 and 60 years; 5%	Among T1D: Cost-saving Among T2D: $28,261/QALY
		Insulin lispro	Regular human insulin	Computer simulation (Center for Outcomes Research Model)	35 and 60 years; 5%	Among T1D: $36,440/QALY Among T2D: $164,460/QALY
		Insulin glargine	Insulin neutral protamine hagedorn	Computer simulation (Center for Outcomes Research Model)	35 and 60 years; 5%	Among T1D: $110,506/QALY Among T2D: $808,061/QALY
		Insulin detemir	Insulin neutral protamine hagedorn	Computer simulation (Center for Outcomes Research Model)	35 and 60 years; 5%	Among T1D: $487,266/QALY Among T2D: dominated (intervention was more costly, less effective)

Continued on p. 1564

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Howard et al., 2010/Australia (41)	T2D aged ≥25 years	Intensive glycemic control	Usual care	Markov computer simulation (AusDiab Study)	Lifetime; 5%	Cost-saving
	Adults aged 50–69 years	Screening for T2D + intensive glycemic control	Usual care	Markov computer simulation (AusDiab Study)	Lifetime; 5%	$15,398/QALY
Klarenbach et al., 2011/Canada (42)	T2D inadequately controlled by metformin	Metformin + sulfonylureas	Metformin alone	Computer simulation (UKPDS Outcomes Model)	Lifetime; 5%	$14,094/QALY
		Metformin + meglitinide	Metformin + sulfonylurea	Computer simulation (UKPDS Outcomes Model)	Lifetime; 5%	Intervention associated with higher cost, worse outcome
		Metformin + α-glucosidase inhibitor	Metformin + sulfonylurea	Computer simulation (UKPDS Outcomes Model)	Lifetime; 5%	$1,037,902/QALY
		Metformin + TZD	Metformin + α-glucosidase inhibitor	Computer simulation (UKPDS Outcomes Model)	Lifetime; 5%	$5,106,028/QALY
		Metformin + DPP-4 inhibitor	Metformin + TZD	Computer simulation (UKPDS Outcomes Model)	Lifetime; 5%	Intervention associated with higher cost, worse outcome
		Metformin + basal insulin	Metformin + TZD	Computer simulation (UKPDS Outcomes Model)	Lifetime; 5%	Intervention associated with higher cost, worse outcome
		Metformin + biphasic insulin	Metformin + TZD	Computer simulation (UKPDS Outcomes Model)	Lifetime; 5%	Intervention associated with higher cost, worse outcome
Gordon et al., 2017/U.K. (43)	Adults with T2D (mean age 73 years)	Metformin + sulfonylurea	Metformin + DPP-4 inhibitor	Program evaluation/ computer simulation (CORE Diabetes Model)	Lifetime; 3.5%	$30,264/QALY
		Metformin + TZD	Metformin + DPP-4 inhibitor	Program evaluation/ computer simulation (CORE Diabetes Model)	Lifetime; 3.5%	$24,857/QALY
SMBG						
Simon et al., 2008/ U.K. (44)	T2D, non–insulin treated	SMBG (less intensive) for 1 year	Standard care	Trial	1 year; no discounting	Intervention associated with higher cost, worse outcome
		SMBG (more intensive) for 1 year	Standard care	Trial	1 year; no discounting	Intervention associated with higher cost, worse outcome

Continued on p. 1565

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Tunis and Minshall, 2008/ U.S. (45)	T2D treated with oral agents in a large HMO	SBMG 1×/day	No SMBG	Kaiser Permanente longitudinal study of cohort of "new antidiabetic drug users"	40 years; 3%	$10,414/QALY
		SMBG 3×/day	No SMBG		40 years; 3%	$8,763/QALY
		SBMG 1×/day	No SMBG		5 years	$30,734/QALY
					10 years	$12,319/QALY
		SMBG 3×/day	No SMBG		5 years	$38,481/QALY
					10 years	$686/QALY
Cameron et al., 2010/Canada (46)	T1D	SMBG	Standard care	Simulation (UKPDS Outcomes Model)	Lifetime; 5%	$138,669/QALY
Pollock et al., 2010/ Switzerland (47)	T2D adults (mean age 63 years) on oral antidiabetics	SMBG 1×/day	Usual care	Computer simulation (CORE Diabetes Model)	30 years; 3%	$10,341/QALY
		SMBG 2×/day	Usual care	Computer simulation (CORE Diabetes Model)	30 years; 3%	$14,568/QALY
		SMBG 3×/day	Usual care	Computer simulation (CORE Diabetes Model)	30 years; 3%	$19,542/QALY
Tunis and Minshall, 2010/ U.S. (48)	T2D adults (mean age 60 years) on oral treatment	SMBG 1×/day	No intervention	Computer simulation model	40 years; 3%	$36,916/QALY
		SMBG 2×/day	No intervention	Computer simulation model	40 years; 3%	$26,160/QALY
		SMBG 3×/day	No intervention	Computer simulation model	40 years; 3%	$35,828/QALY

Continued on p. 1566

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Tunis et al., 2010/ France, Germany, Italy, Spain (49)	T2D adults in France (mean age 63 years) on oral treatment	SMBG 1×/day	No intervention	Computer simulation model	40 years; 3%	$22,405/QALY
		SMBG 2×/day	No intervention	Computer simulation model	40 years; 3%	$11,619/QALY
		SMBG 3×/day	No intervention	Computer simulation model	40 years; 3%	$14,719/QALY
	T2D adults in Germany (mean age 63 years) on oral treatment	SMBG 1×/day	No intervention	Computer simulation model	40 years; 3%	$3,020/QALY
		SMBG 2×/day	No intervention	Computer simulation model	40 years; 3%	$3,651/QALY
		SMBG 3×/day	No intervention	Computer simulation model	40 years; 3%	$9,331/QALY
	T2D adults in Italy (mean age 63 years) on oral treatment	SMBG 1×/day	No intervention	Computer simulation model	40 years; 3%	$23,478/QALY
		SMBG 2×/day	No intervention	Computer simulation model	40 years; 3%	$22,072/QALY
		SMBG 3×/day	No intervention	Computer simulation model	40 years; 3%	$28,424/QALY
	T2D adults in Spain (mean age 63 years) on oral treatment	SMBG 1×/day	No intervention	Computer simulation model	40 years; 6%	$6,771/QALY
		SMBG 2×/day	No intervention	Computer simulation model	40 years; 6%	$5,736/QALY
		SMBG 3×/day	No intervention	Computer simulation model	40 years; 6%	$10,637/QALY
Tunis, 2011/ Canada (50)	T2D adults (mean age 60 years) not on insulin	Canadian Optimal Prescribing and Utilization Service (1.29 strips per day of self-monitored blood glucose)	No intervention	Computer simulation model	40 years; 5%	$77,684/QALY
McQueen et al., 2015/Canada (51)	T1D adults (mean age 50 years) with baseline A1C 7.6%	Provision of SMBG device with strip price Can$0.73 and a 10% error (exceeding accuracy requirements by ISO)	Provision of SMBG device with strip price Can$0.60 and 15% error (accuracy meeting ISO)	Markov computer simulation model	Lifetime and 3 years; 5%	Lifetime: $130,820/QALY 3-year: cost-saving
Intensive hypertension control						
UKPDS Group, 1998/U.K. (52)	T2D + hypertension	Tight control of hypertension, BP <150/80 mmHg, ACEI, β-blocker, and other agents	Less tight control of BP (mmHg), initially <200/105, later 180/105	UKPDS (n = 5,120)	Lifetime; 6%	Cost-saving

Continued on p. 1567

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Elliot et al., 2000/U.S. (53)	T2D, hypertension, initially free of CVD or ESRD	Reduction of BP to 130/85 mmHg	Reduction of BP to 140/90 mmHg	Meta-analysis of data from epidemiological studies and clinical trials	Lifetime; 3%	
	Treatment started at age 50 years					$1,524/LYG
	Treatment started at age 60 years					Cost-saving
	Treatment started at age 70 years					Cost-saving
Centers for Disease Control and Prevention, 2002/U.S. (35)	T2D + hypertension	Intensified hypertension control (ACEI, β-blocker), average BP 144/82 mmHg	Moderate hypertension control, average BP 154/86 mmHg	UKPDS (n = 5,120)	Lifetime; 3%	Cost-saving
Clarke et al., 2005/U.K. (38)	T2D + hypertension	Tight BP control BP <150/85 mmHg, ACEI (captopril) or β-blocker (atenolol)	Less tight control of BP (mmHg), initial <200/105, later <180/105	UKPDS (n = 5,120)	Lifetime; 3.5%	$254/QALY
Ly et al., 2009/U.S. (54)	Newly diagnosed T2D and existing hypertension	Hypertension management program for 1 year	Standard care	Markov computer simulation model	1 year; costs discounted 3%	Cost-saving
		Hypertension management program for 3 years	Standard care	Markov computer simulation model	3 years; 3%	Cost-saving
		Hypertension management program for 5 years	Standard care	Markov computer simulation model	5 years; 3%	Cost-saving
Howard et al., 2010/Australia (41)	T2D (AusDiab)	ACEI treatment	Usual care	Markov computer simulation model	Lifetime; 5%	Cost-saving
Cholesterol control						
Herman et al., 1999/U.S. (55)	T2D + dyslipidemia + previous myocardial infarction or angina	Simvastatin	Placebo	RCT	5 years; 3% for cost, 0% for benefit	Cost-saving
Jönsson et al., 1999/European countries (56)	T2D + dyslipidemia + previous myocardial infarction or angina	Simvastatin	Placebo	RCT	Lifetime; 3%	Cost-saving–$11,938/LYG in different countries. Median: $3,556/LYG
Grover et al., 2000/Canada (57)	T2D + dyslipidemia + CVD history, adults aged ≥60 years	Simvastatin	Placebo	RCT	Lifetime; 5%	$7,747–$15,621/LYG increasing with pretreatment of LDL cholesterol level. More cost-effective for men than women

Continued on p. 1568

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Centers for Disease Control and Prevention, 2002/U.S. (35)	T2D + dyslipidemia, no CVD history	Pravastatin	Placebo	RCT	Lifetime; 3%	$98,806/QALY
Raikou et al., 2007/ U.K. and Ireland (58)	T2D, no CVD history, no elevated LDL cholesterol, ≥1 CVD risk factor (retinopathy, microalbuminuria or macroalbuminuria, current smoking, or hypertension)	Atorvastatin	Placebo	RCT	Lifetime; 3%	$4,445/QALY
Sorensen et al., 2009/U.S. (59)	T2D adults (mean age 60 years) with T2D and mixed dyslipidemia	Maintaining lipid levels without particular targets, including through combination therapy as recommended by National Cholesterol Education Program Adult Treatment Panel III guidelines	Usual care	Computer simulation model	Lifetime; 3%	$67,873/QALY $70,291/CHD event avoided
de Vries et al., 2014/the Netherlands (60)	T2D (mean age 61.3 years)	Statin treatment started at time of T2D diagnosis	No lipid-regulating treatment	Markov computer simulation model	10 years; costs discounted 4%, benefits discounted 1.5%	$3,294/QALY (<45 years: $84,012/QALY; ages 45–55: $12,174/QALY; 55–65 years: $3,640/QALY)
Smoking cessation						
Earnshaw et al., 2002/U.S. (61)	Newly diagnosed T2D + smoker, aged 25–84 years Aged 85–94 years	Smoking cessation, standard antidiabetic care	Standard antidiabetic care		Lifetime; 3%	<$31,750/QALY $114,046/QALY
Educational/DSME program						
Gozzoli et al., 2001/ Switzerland (62)	T2D	Standard antidiabetic care plus educational program, self-monitoring, recommendations on diet and exercise, self-management of diabetes and complications, general health education	Standard antidiabetic care	Literature review	Lifetime; 3%	$5,080/LYG
Shearer et al., 2004/Germany (63)	T1D	Structured treatment and teaching program: educational course of training to self-manage diabetes and enjoy dietary freedom	Usual care (daily insulin injection)	RCT	Lifetime; 6%	Cost-saving

Continued on p. 1569

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Brownson et al., 2009/U.S. (64)	Hispanic and African American adults with T2D; insured and uninsured	DM self-management program (DSME classes, walking clubs, group visits/ classes, weekly phone follow-up, one-on-one self-management sessions, mental health services) provided by health care providers, community health educators, nurses in real-world setting for 3–4 years	No intervention (baseline treatment)	Simulation model using the CDC-RTI Diabetes Cost-Effectiveness Model	Lifetime (100 years max); 3%	$55,726/QALY
Gillett et al., 2010/ U.K. (65)	Newly diagnosed T2D	DSME focused on lifestyle factors (diet + physical activity), facilitated by registered health care professionals trained as educators, 1 year	Standard care	Trial and computer simulation	Lifetime; 3.5%	Real-world cost data: $5,047/QALY Trial data: $12,994/QALY
Gillespie et al., 2014/Ireland (66)	T1D	Dose Adjustment for Normal Eating (DAFNE) program for 18 months; group-based structured education sessions on insulin dose adjustment, carbohydrate estimation, and hypoglycemia management	Usual care	Cluster randomized trial	18 months; no discounting	Cost-saving
Kruger et al., 2013/ U.K. (67)	Simulated cohort of patients with existing T1D (mean age 40 years)	Dose Adjustment for Normal Eating (DAFNE), a 5-day structured education program (flexible insulin therapy and insulin doses to match carbohydrate intake), delivered in groups of 6–8	No intervention	Trial/Sheffield T1D Policy Simulation Model	Lifetime; 3.5%	$26,054/QALY
Gordon et al., 2014/Australia (68)	T2D adults	24-week educational advice and feedback on DM self-management provided via weekly telephone calls + DM kit with handbook, glucose meter, test strips, cell phone	Standard care	Markov computer simulation model	5 years; 5%	Cost-saving
Prezio et al., 2014/ U.S. (69)	Uninsured Mexican American adults with T2D	One-to-one culturally tailored diabetes education and management program	Usual care	Computer simulation model	20 years; 3%	5-year duration: $114,354/QALY 10-year duration: $44,199/QALY 20-year duration: $405/QALY

Continued on p. 1570

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Ryabov, 2014/U.S. (70)	Mexican American adults with T2D	Educational program following the National DPP and led by community health workers (monthly 40–60-min visits for 2 years)	Usual care	Computer simulation model	5, 10, 20 years and lifetime; 3%	$17,964/QALY
Varney et al., 2016/Australia (71)	Adults (mean age 60 years) with poorly controlled T2D	Monthly tele-coaching by dietitian to address lifestyle modification, treatment adherence, goal setting, barriers to change	Usual care	Computer simulation model (UKPDS Outcomes Model)	10 years; 5%	Cost-saving
Odnoletkova et al., 2016/Belgium (72)	T2D on glucose-lowering medication therapy	Telephone counseling intervention (SMBG, lifestyle, medications) delivered by diabetes nurse educators and consisting of five 30-min phone sessions over 6 months	Usual care	Markov computer simulation model	40 years; costs discounted 3%, benefits discounted 1.5%	$8,238/QALY
Screening for and preventing diabetes complications						
Cardiovascular disease						
Li et al., 2010/U.S. (73)	T2D	Daily use of aspirin (80 mg)	No aspirin use	Computer simulation model	Lifetime; 3%	$7,646/LYG $2,395/QALY
van Giessen et al., 2016/the Netherlands (74)	T2D on oral drugs only and without previous diagnosis of heart failure	Screening for heart failure via EMR symptoms	No screening	Markov computer simulation model	Lifetime; costs discounted 4%, benefits discounted 1.5%	Men: $10,078/QALY Women: $10,413/QALY
		Screening for heart failure via EMR symptoms and physical exam	Screening for heart failure via EMR symptoms	Markov computer simulation model	Lifetime; costs discounted 4%, benefits discounted 1.5%	Intervention associated with higher cost and worse outcome

Continued on p. 1571

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
		Screening for heart failure via EMR symptoms and physical exam and natriuretic peptide	Screening for heart failure via EMR symptoms	Markov computer simulation model	Lifetime; costs discounted 4%, benefits discounted 1.5%	Intervention associated with higher cost and worse outcome
		Screening for heart failure via EMR symptoms and physical exam and natriuretic peptide and ECG	Screening for heart failure via EMR symptoms	Markov computer simulation model	Lifetime; costs discounted 4%, benefits discounted 1.5%	Intervention associated with higher cost and worse outcome
		Screening for heart failure via ECG	Screening for heart failure via EMR symptoms	Markov computer simulation model	Lifetime; costs discounted 4%, benefits discounted 1.5%	Men: $47,963/QALY Women: $64,818/QALY
Eye complications						
Javitt et al., 1994/ U.S. (75)	Newly diagnosed T2D	Eight strategies for eye screening with dilation: screening every 1, 2, 3, or 4 years and more frequent follow-up screening for diabetes patients with background retinopathy	No screening	Cross-sectional/ longitudinal studies	Lifetime; 5%	Cost-saving (all 8 strategies)
Javitt and Aiello, 1996/U.S. (76)	Newly diagnosed T1D and T2D	Annual eye screening with dilation for all patients with diabetes but no retinopathy	Eye screening in 60% of diabetes patients	Cross-sectional/ longitudinal studies	Lifetime; 5%	$8,763/QALY
	T1D					$5,461/QALY
	T2D	Examination every 6 months for those with retinopathy				$8,763/QALY
Palmer et al., 2000/ Switzerland (32)	T1D	Annual eye screening and treatment, conventional insulin therapy	Conventional insulin therapy	Literature review	Lifetime; 3%	Cost-saving

Continued on p. 1572

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Vijan et al., 2000/ U.S. (77)	T2D	Eye screening for diabetes patients every 5 years; subsequent annual screening for those with background retinopathy	No screening	Epidemiological studies	Lifetime; 3%	$29,845/QALY
		Eye screening for diabetes patients every 3 years; subsequent annual screening for those with background retinopathy	No screening			$34,290/QALY
		Eye screening for diabetes patients every 2 years; subsequent annual screening for those with background retinopathy	No screening			$38,989/QALY
		Eye screening for diabetes patients annually; subsequent annual screening for those with background retinopathy	No screening			$50,165/QALY
		Eye screening for diabetes patients every 3 years	5-year screening intervals			$41,656/QALY
		Eye screening for diabetes patients every 2 years	3-year screening intervals			$68,580/QALY
		Annual eye screening for diabetes patients	2-year screening intervals			$148,336/QALY
Maberley et al., 2003/Canada (78)	T1D and T2D	Screening using digital camera, with immediate assessment of quality or electronically transferred to a remote reading center	Retina specialists visit Moose Factory every 6 months to examine people with diabetes, and patients in outlying communities are flown to Moose Factory, Canada		10 years; 5%	Cost-saving

Continued on p. 1573

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Kirkizlar et al., 2013/U.S. (79)	DM and diabetic retinopathy	Telemedicine for the screening of diabetic retinopathy	Usual care (diabetic retinopathy screening by an eye care professional)	Markov computer simulation model	Lifetime; 3%	Patient pool size: 3,000: $61,124/QALY 3,500: $53,013/QALY 4,000: $46,929/QALY 6,000: $32,735/QALY 9,000: $23,273/QALY Age (years): <30: −$16,313 (cost-saving) 30–39: −$12,599 (cost-saving) 40–49: −$7,320 (cost-saving) 50–59: $8,248 60–69: $16,800 70–79: $39,395 80–89: $87,975 90–99: $105,371 Race: Black or African American: $20,322 Native American: −$5,550 White: $24,779 Unanswered: $25,751
Chan et al., 2015/ Hong Kong (80)	Adults with DM	Annual screening and treatment for intermediate age-related macular degeneration	No screening	Markov computer simulation model	Lifetime (100 years max); 3%	$16,027/QALY
Kawasaki et al., 2015/Japan (81)	Adults with DM	Screening for diabetic retinopathy by ophthalmologists using dilated fundus examinations	No screening	Markov computer simulation model	50 year; 3%	$13,533/QALY
Scanlon et al., 2015/U.K. (82)	DM	DR screening every 6 months	Annual DR screening	Decision-analytic model	Lifetime; 3.5%	$502,666/QALY
		Annual DR screening	DR screening every 2 years	Decision-analytic model	Lifetime; 3.5%	$170,900/QALY
		DR screening every 2 years	DR screening every 3 years	Decision-analytic model	Lifetime; 3.5%	$79,599/QALY
		DR screening every 3 years	DR screening every 5 years	Decision-analytic model	Lifetime; 3.5%	$45,574/QALY
Nguyen et al., 2017/Singapore (83)	T2D and diabetic retinopathy	Telemedicine-based DR screening program, with real-time assessment of DR photographs by a centralized team supported by tele-ophthalmology IT infrastructure	Usual care (family physician assessment of DR)	Computer simulation model (decision tree and Markov)	Lifetime; 3%	Cost-saving

Continued on p. 1574

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Scotland et al., 2016/Scotland (84)	T1D and T2D	Annual DR screening for those with no or mild retinopathy and biannual screening for observable retinopathy/maculopathy	Screening at 2-year intervals for those with no DR at two consecutive screening episodes	Markov computer simulation model (continuous-time hidden)	30 years; 3.5%	$404,733/QALY
		Screening at 2-year interval for those observed with no DR at two consecutive screening episodes	Screening at 2-year interval for those with no DR and no DR previously recorded	Markov computer simulation model (continuous-time hidden)	30 years; 3.5%	$836,344/QALY
		Screening at 2-year interval for those with no DR and no DR previously recorded	Screening at 2-year interval for those with no DR	Markov computer simulation model (continuous-time hidden)	30 years; 3.5%	$128,865/QALY
van Katwyk et al., 2017/Canada (85)	Existing DM	DR screening by optometrists are publicly insured	Usual care (DR screening by primary care physician or referral to ophthalmologists are publicly insured)	Computer simulation probabilistic decision-analytic model	30 years; 5%	$1,399/QALY
Foot ulcers						
Ragnarson Tennvall and Apelqvist, 2001/ Sweden (86)	T1D and T2D, moderate to high risk (previous foot ulcer/ amputation, neuropathy)	Optimal prevention of foot ulcer including foot inspection, appropriate footwear, treatment, and education	Usual care	Clinical and epidemiological data	5 years; 0%	Cost-saving
	Low risk (no specific risk factor)					>$127,000/QALY
Ortegon et al., 2004/the Netherlands (87)	Newly diagnosed T2D + foot ulcer	Intensive glycemic control + optimal foot care	Standard care	Trial	Lifetime; 3%	$57,023/QALY
End-stage renal disease						
Borch-Johnsen et al., 1993/ Germany (88)	T1D	Annual screening for microalbuminuria at 5 years after diabetes onset + ACEI treatment	Treatment of macroalbuminuria	Cohort	30 years; 6%	Cost-saving
Kiberd and Jindal, 1995/Canada (89)	T1D	Screening for microalbuminuria + ACEI treatment	Treatment of hypertension and/or macroproteinuria	Clinical trial	Lifetime; 5%	$74,168/QALY
Golan et al., 1999/ U.S. (90)	Newly diagnosed T2D	Treat patients with new diagnosis with ACEI	Screening for macroalbuminuria and treatment with ACEI	RCT	Lifetime; 3%	Cost-saving
		Screening for microalbuminuria and treatment with ACEI	Screening for macroalbuminuria and treatment with ACEI			Cost-saving
		Treat patients with new diagnosis with ACEI	Screening for microalbuminuria and treatment with ACEI			$13,843/QALY

Continued on p. 1575

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Clark et al., 2000/ Canada (91)	T1D	Province or territory paying for ACEI	Pay from out of pocket	Collaborative observational study using admin data base	21 years; 5%	Cost-saving
Palmer et al., 2000/ Switzerland (32)	T1D, high cholesterol, high systolic BP	Microalbuminuria monitoring, ACE treatment, conventional insulin therapy	Conventional insulin therapy	Literature review	Lifetime; 3%	Cost-saving
Palmer et al., 2003/Belgium, France (92)	T2D + macroalbuminuria + hypertension	Irbesartan	Standard therapy for hypertension	RCT	Lifetime; 3%	Cost-saving
Souchet et al., 2003/France (93)	T2D + nephropathy	Losartan	Placebo	Trial	4 years; costs discounted 8%, benefits not discounted	Cost-saving
Dong et al., 2004/ U.S. (94)	T1D	ACEI treatment starting at 1 year after diagnosis	Annual screening for microalbuminuria ACE treatment	Trial	Lifetime; 3%	$48,260/QALY, increased with lowering A1C level, at A1C level 9%, <$31,750/QALY
Palmer et al., 2004/U.K. (95)	T2D + hypertension + nephropathy	Irbesartan	Standard therapy for hypertension	RCT	10 years; 6% for costs, 1.5% for benefits	Cost-saving
Palmer et al., 2004/U.S. (96)	T2D + hypertension + microalbuminuria	Irbesartan	Standard therapy for hypertension	RCT	25 years; 3%	Cost-saving
Szucs et al., 2004/ Switzerland (97)	T2D + nephropathy	Losartan	Placebo	Trial	3.5 years; 0%	Cost-saving
Palmer et al., 2005/Spain (98)	T2D + microalbuminuria + hypertension	Irbesartan	Standard therapy for hypertension, no ACEI, AIIRA, or β-blockers	RCT	25 years; 3%	Cost-saving
Rosen et al., 2005/ U.S. (99)	Medicare population (T1D and T2D)	Medicare full payment for ACEI (target: ACEI use increased by at least 7.2%)	Pay from out of pocket	RCT	Lifetime; 3%	Cost-saving
Coyle et al., 2007/ Canada (100)	T2D + hypertension + macronephropathy + micronephropathy	Irbesartan added at stage of microalbuminuria	Conventional treatment for diabetes and hypertension, no ACEI or AIIRAs	RCT	Lifetime; 5%	Cost-saving
Palmer et al., 2007/ Hungary (101)	T2D + microalbuminuria	Adding irbesartan	Placebo + standard therapy for hypertension	RCT	25 years; 5%	Cost-saving

Continued on p. 1576

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Palmer et al., 2007/ U.K. (102)	T2D + hypertension + microalbuminuria	Irbesartan	Standard therapy for hypertension	RCT	25 years; 3.5%	Cost-saving
		Irbesartan added at stage of overt nephropathy	Conventional treatment for diabetes and hypertension			Cost-saving
		Irbesartan added at stage of microalbuminuria	Irbesartan added at stage of overt nephropathy			Cost-saving
Howard et al., 2010/ Australia (41)	Individuals aged 50–69 years with T2D from the AusDiab study	Screening for proteinuria + addition of an ACEI	Usual care	Markov computer simulation model	Lifetime; 5%	$5,310/QALY
Comprehensive interventions						
Palmer et al., 2000/ Switzerland (32)	T1D	Conventional glycemic control + ACEI therapy + eye screening and treatment	Conventional glycemic control		Lifetime; 3%	Cost-saving
		Intensive insulin therapy + ACEI therapy	Intensive insulin therapy			$59,055/LYG
		Intensive insulin therapy + eye screening	Intensive insulin therapy			$64,262/LYG
		Intensive insulin therapy + ACEI therapy + eye screening	Intensive insulin therapy			$63,246/LYG
Gozzoli et al., 2001/ Switzerland (62)	T2D	Added education program, nephropathy screening, and ACEI therapy to standard antidiabetic care	Standard antidiabetic care		Lifetime; 0%, 3%	Cost-saving
		Added education program, nephropathy screening, ACEI therapy, and retinopathy screening and laser therapy to standard antidiabetic care	Standard antidiabetic care			Cost-saving
		Multifactorial intervention included educational program, screening for nephropathy and retinopathy, control of CVD risk factors, early diagnosis and treatment of complications, and health education	Standard antidiabetic care			Cost-saving

Continued on p. 1577

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Gaede et al., 2008/ Denmark (103)	T2D and microalbuminuria (mean age 55 years)	Intensive treatment for 7.8 years (stepwise implementation of behavior modification and pharmacologic therapy targeting hyperglycemia, hypertension, dyslipidemia, and microalbuminuria, and 2° prevention of CVD with aspirin)	Standard care	Markov computer simulation model	Lifetime; 3%	$4,629/QALY $7,162/LYG
Tasosa et al., 2010/ U.S. (104)	Newly diagnosed T2D, African American adults	Aggressive hypertension control with ACEI or β-blocker, glycemic control with insulin or sulfonylurea, hyperlipidemia treatment based on pravastatin and four physician visits with blood/lipid/biochemical profiles	Usual care	Markov computer simulation model	Lifetime; 3%	$33,912/QALY
	Newly diagnosed T2D	Aggressive hypertension control with ACEI or β-blocker, glycemic control with insulin or sulfonylurea, hyperlipidemia treatment based on pravastatin and four physician visits with blood/lipid/biochemical profiles	Usual care	Markov computer simulation model	Lifetime; 3%	$51,587/QALY
Giorda et al., 2014/ Italy (105)	T2D	Physician-led 5-year quality-of-care scheme to improve A1C, BP, lipids, and BMI	Standard care	Computer simulation model	50 years; 3%	Cost-saving
Laxy et al., 2017/ U.K. (106)	Newly diagnosed T2D (mean age 61.5 years) from ADDITION-UK	Intensive lifestyle changes and medication adherence, delivered by a specialist team of doctors, nurses, dietitians (2 years)	Usual care	Trial/UKPDS Outcomes model	10, 20, and 30 years; 3.5%	10-year: $98,613/QALY 20-year: $39,378/QALY 30-year: $38,139/QALY
Integrated and coordinated care						
Coordinated care						
Mason et al., 2005/ England (107)	T2D + hypertension	Policy to implement clinics led by specialist nurses to treat and control hypertension through consultation, medication review, condition assessment, and lifestyle advice	Usual care	RCT	Lifetime; 5%	$6,096/QALY
	Diagnosed diabetes + dyslipidemia	Policy to implement clinics led by specialist nurses to treat and control hyperlipidemia by usual care	Usual care			$29,972/QALY

Continued on p. 1578

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Gilmer et al., 2007/ U.S. (108)	Diabetes, 48% Latinos, uninsured population	Culturally sensitive case management and self-management training program led by bilingual/bicultural medical assistant and registered dietitian stepped-care pharmacologic management of glucose and lipid levels and hypertension	Standard care	Cohort study	40 years; 3%	$15,240/QALY
McRae et al., 2008/Australia (109)	T2D	Integrated care program whereby GPs serve as case manager and program facilitates case management via provision of info and education to GPs (5 years)	Usual care	Computer simulation model	40 years; 5%	$9,058/LYG $10,871/QALE
Schouten et al., 2010/the Netherlands (110)	Existing T2D	Integrated diabetes care with teams of 5–6 providers that attended learning sessions in quality-improvement techniques and diabetes care, and access to endocrinologists and diabetes educators for patients unresponsive to treatment or with difficult-to-manage diabetes.	Usual care	Computer simulation model (Dutch diabetes model)	Lifetime; costs discounted at 4.5%, benefits discounted at 1.5%	Men: $11,806/QALY Women: $13,474/QALY
Kuo et al., 2011/ U.S. (111)	T2D patients at U.S. Air Force base	Diabetes management using the Chronic Care Model for 3 years	Usual care	Markov computer simulation model	20 years; 3%	$55,465/QALY
Haji et al., 2013/ Australia (112)	T2D	High level of practice nurse involvement in T2D management in primary care setting	Low level of practice nurse involvement in T2D management in primary care setting	Computer simulation model (UKPDS Outcomes Model)	40 years; 5%	Cost-saving
Slingerland et al., 2013/the Netherlands (113)	T2D + A1C <7%	Patient-centered medical care in which patients receive detailed "diabetes passports" based on national guidelines for 1 year	Usual care	Trial	Lifetime; costs discounted 3%	Intervention was associated with higher costs and fewer QALYs
	T2D + A1C 7–8.5%	Patient-centered medical care in which patients receive detailed "diabetes passports" based on national guidelines for 1 year	Usual care	Trial	Lifetime	$23,764/QALY
	T2D + A1C >8.5%	Patient-centered medical care in which patients receive detailed "diabetes passports" based on national guidelines for 1 year	Usual care	Trial	Lifetime; costs discounted 3%	$7,622/QALY

Continued on p. 1579

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Yu et al., 2013/U.S. (114)	Existing T2D + A1C >7%	Addition of a pharmacist to patient's care (prescribed/adjusted medications, ordered laboratory work, ordered/administered immunizations, provided DM self-management education, and worked to optimize overall glycemic and cardiovascular care of patients)	Usual care (primary care physician only)	Markov computer simulation model	10 years; costs discounted 3%, benefits discounted 5%	Cost-saving
Tsiachristas et al., 2014/the Netherlands (115)	T2D and Charlson comorbidity index 2.22	DM management program consisting of personal coaching and motivational interviewing	DM management program consisting of lifestyle interventions, periodic discussion sessions between providers and patients	Program evaluation	Not reported	Cost-saving
Wilson et al., 2014/U.K. (116)	T2D	Intermediate care clinics for diabetes, in which diabetes specialist nurses worked closely with hospital-based specialist teams and community services (podiatry and dietetic services) to manage patients until risk factor control was achieved (18 months max)	Usual care	Trial	18 months; no discounting	$13,552/QALY
Tao et al., 2015/ U.K. (117)	Adults with screen-detected T2D	Intensive DM care (more frequent provider contact, interactive audit and feedback sessions, theory-based education materials, dietitian referrals, group programs)	Usual care	Computer simulation model	30 years; 3.5%	$70,649/QALY
Hirsch et al., 2017/ U.S. (118)	T2D + complications (average of 8 comorbidities)	Obtaining care in an endocrinologist-pharmacist collaborative practice (3 personalized 60-min visits over 6 months)	Usual PCP visits	Program evaluation; Archimedes computer simulation model (VA Health System)	2, 5, and 10 years; 3%	Cost-saving
Cobden et al., 2010/U.S. (119)	Medicare adults with T2D and preexisting complications	Injectable insulin (human or analog), without adherence	Oral medications (metformin +/− sulfonylurea or TZD) without adherence	Markov computer simulation model	Lifetime (35 years max); 3%	$15,251/QALY
		Injectable insulin (human or analog insulin), with adjustments for adherence	Oral medications (metformin +/− sulfonylurea or TZD), with adjustments for adherence	Markov computer simulation model	Lifetime (35 years max); 3%	$20,476/QALY

Continued on p. 1580

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Decision support						
Cleveringa et al., 2010/the Netherlands (120)	T2D	Diabetes care protocol, consisting of a diabetes consultation hour run by a practice nurse, a CDSS diagnostic and treatment algorithm based on Dutch T2D guidelines, a recall system, and a feedback at both practice and patient level every 3 months	Usual care	Computer microsimulation model	Lifetime; costs discounted 4%, benefits discounted 1.5%	$73,253/QALY $19,360/LYG
O'Reilly et al., 2012/Canada (121)	T2D	Computerized decision support system linked to EMR, shared between patients and physicians	Usual care	Computer simulation model (Ontario Diabetes Economic Model)	40 years; 5%	$190,417/QALY $185,831/LYG
Olvey, 2014/U.S. (122)	DM and hypertension or high cholesterol	Patients spoke by phone to a Medication Management Center pharmacist who discussed ACEI/ARB and statin guidelines, and potential addition of those treatments based on final recommendation by the patient's physician	Patients received a letter listing current prescription info and advising to discuss treatments with their physician	Computer simulation model (decision tree and Monte Carlo)	5 years; costs discounted 5%, benefits discounted 2.5%	$5,710/5-year treatment success
Peer support						
Gillespie et al., 2012/Ireland (123)	T2D	Group-based peer support in addition to standardized diabetes care for 2 years	Standard care	Computer simulation model	Lifetime; 3.5%	Cost-saving
Treatment of diabetes-related complications						
Cardiovascular disease						
Hlatky et al., 2009/U.S., Canada, Brazil, Mexico, Czech Republic, Austria (124)	T2D and CHD	Prompt coronary revascularization combined with intensive medical management for 4 years	Intensive medical management, with coronary revascularization at a later date if clinically indicated	Trial	Lifetime; costs discounted 3%	Within trial: control dominant (Lifetime: $810/LYG)
		CABG with intensive medical management	Intensive medical management, with coronary revascularization at a later date if clinically indicated	Trial	Lifetime; costs discounted 3%	Within trial: control dominant Lifetime: $63,401/LYG
		Patients taking metformin or rosiglitazone or both for 4 years	Patients on insulin or sulfonylurea or both	Trial	Lifetime; costs discounted 3%	Within trial: $395,245/QALY Lifetime: $70,146/LYG

Continued on p. 1581

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Eye complications						
Sharma et al., 2001/U.S. (125)	Diabetic retinopathy (HMO)	Immediate vitrectomy for management of vitreous hemorrhage secondary to diabetic retinopathy	Deferral of vitrectomy	DRVS	Lifetime; 6%	$3,683/QALY
Mitchell et al., 2012/U.K. (126)	Existing DM and DME	Ranibizumab monotherapy	Laser photocoagulation	Markov computer simulation model (RESTORE Study)	15 years; 3.5%	$45,264/QALY
		Ranibizumab combined with laser therapy	Laser photocoagulation	Markov computer simulation model (RESTORE Study)	15 years; 3.5%	$68,017/QALY
Hutton et al., 2017/U.S. (127)	DM and proliferative diabetic retinopathy, with and without DME	Ranibizumab (0.5 mg)	Laser photocoagulation	Trial	2 years; no discounting	With DME: $56,752/QALY Without DME: $677,108/QALY
Foot ulcers						
Habacher et al., 2007/Austria (128)	Newly diagnosed diabetic food ulcer	Intensified treatment by international consensus on diabetic foot care	Standard treatment	Retrospective of patient records	15 years; 0–8%	Cost-saving
O'Connor et al., 2008/U.S. (129)	DM and painful diabetic peripheral neuropathy	Duloxetine 60 mg 1×/day	Desipramine 100 mg 1×/day	Computer simulation model (decision tree)	3 months; no discounting	$67,188/QALY
		Pregabalin 100 mg 1×/day	Desipramine 100 mg 1×/day	Computer simulation model (decision tree)	3 months; no discounting	Intervention associated with higher cost, worse outcome
		Gabapentin 800 mg 1×/day	Desipramine 100 mg 1×/day	Computer simulation model (decision tree)	3 months; no discounting	Intervention associated with higher cost, worse outcome
Cheng et al., 2017/ Australia (130)	Simulated cohort of existing DM and at high risk of developing foot ulcers	Optimal care for foot ulcers and patient education	Usual care	Markov computer simulation model	5 years; 5%	Cost-saving
Addressing diabetes comorbidities						
Obesity						
Anselmino et al., 2009/Austria, Italy, Spain (131)	T2D and BMI >35 kg/m^2	Gastric banding surgery	Usual care	Computer simulation model (deterministic linear algorithm)	5 years; 3.5%	Austria: (−$5,027)/QALY, cost-saving Italy: (−$1,945)/QALY cost-saving Spain: $2,558/QALY
		Gastric bypass surgery	Usual care	Computer simulation model (deterministic linear algorithm)	5 years; 3.5%	Austria: (−$2,542)/QALY, cost-saving Italy: (−$2,189)/QALY, cost-saving Spain: $4,680/QALY

Continued on p. 1582

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Ikramuddin et al., 2009/U.S. (132)	T2D and obesity	Gastric bypass surgery	Standard medical management	Computer simulation model (CORE Diabetes Model)	35 years; 3%	$29,641/QALY $40,032/LYG
Keating et al., 2009/Australia (133)	T2D and obesity (class I and II)	Gastric band surgery + conventional therapy for 2 years	Conventional therapy for 2 years	Computer simulation model	Lifetime; 3%	Cost-saving
Hoerger et al., 2010/U.S. (134)	Newly diagnosed or existing T2D and BMI ≥35 kg/m^2	Gastric bypass/gastric banding surgery	Standard care	Computer simulation model	Lifetime; 3%	For newly diagnosed DM: $10,254/QALY for gastric bypass $16,115/QALY for gastric banding For existing DM: $17,580/QALY for gastric bypass $19,045/QALY for gastric banding
Pollock et al., 2013/U.K. (135)	T2D and obesity	Gastric banding surgery	Standard care	Computer simulation model (CORE Diabetes Model)	40 years; 3.5%	$6,785/QALY
Borisenko et al., 2015/Sweden (136)	T2D and obesity	Bariatric surgery	No surgery	Decision-analytic model using Markov processes	Lifetime; 3%	Bariatric surgery becomes cost-effective after 2 years ($39,604/QALY) and cost-saving after 17 years
James et al., 2017/Australia (137)	Simulated cohort of 30-year-old Australian females with T2D and obesity	Gastric banding surgery	Usual care (pharmacotherapy, diet, exercise management)	Markov computer simulation model	Lifetime; 5%	Cost-saving
		Gastric bypass surgery	Usual care (pharmacotherapy, diet, exercise management)	Markov computer simulation model	Lifetime; 5%	Cost-saving
		Sleeve gastrectomy surgery	Usual care (pharmacotherapy, diet, exercise management)	Markov computer simulation model	Lifetime; 5%	Cost-saving
Wentworth et al., 2017/U.S. (138)	T2D and overweight	Gastric banding surgery	Usual care	Computer simulation model (UKPDS Outcomes Model)	2 and 10 years; 3%	Within 2-year trial: $100,050/QALY 5-year simulation: $55,120/QALY 10-year simulation: $30,747/QALY 15-year simulation: $23,320/QALY
Mental health						
Katon et al., 2006/U.S. (139)	Depression + poorly controlled DM or CHD	Multicondition collaborative treatment program led by a physician-supervised registered nurse and including patient education to promote self-care for 2 years (TEAMCare)	Usual care	Trial	NA	Cost-saving

Continued on p. 1583

Table 1—Continued

Source (author, year/country)	Study population	Intervention	Comparison	Study method	Time horizon; discount rate	ICER (in 2017 US$)
Johnson et al., 2016/Canada (140)	T2D + depressive symptoms (PHQ ≥10)	Screening for depression + enhanced care (follow-up with family physician)	Usual care	Trial	1 year; no discounting	$91,270/QALY
		Screening for depression + coordinated, collaborative care led by a nurse care manager, in consultation with psychiatrists/ endocrinologists (adapted TEAMCare)	Usual care	Trial	1 year; no discounting	$29,160/QALY
		Screening for depression + coordinated, collaborative care led by a nurse care manager, in consultation with psychiatrists/ endocrinologists (adapted TEAMCare)	Screening for depression + enhanced care (follow-up with family physician)	Trial	1 year; no discounting	$18,980/QALY
Kearns et al., 2017/ U.K. (141)	Simulated cohort of existing T2D	Collaborative care	Usual care	Computer simulation (discrete event)	Lifetime; 3.5%	$18,814/QALY
		Improved opportunistic screening for depression	Usual care	Computer simulation (discrete event)	Lifetime; 3.5%	$111,180/QALY
		Collaborative care + improved opportunistic screening for depression	Usual care	Computer simulation (discrete event)	Lifetime; 3.5%	$65,201/QALY
Sleep apnea						
Guest et al., 2014/ U.K. (142)	T2D with obstructive sleep apnea	Treatment with CPAP for 5 years	Standard care	Program evaluation/ trial	5 years; no discounting	$27,750/QALY

A1C, hemoglobin A_{1c} test; AIIRA, angiotensin II receptor antagonist; AusDiab, Australian Diabetes, Obesity, and Lifestyle Study; BP, blood pressure; CABG, coronary artery bypass graft; CDSS, clinical decision support system; CHD, coronary heart disease; DCCT, Diabetes Control and Complications Trial; DRVS, Diabetic Retinopathy Vitrectomy Study; ECG, electrocardiogram; EMR, electronic medical record; FPG, fasting plasma glucose; DM, diabetes; DME, diabetic macular edema; DPP, Diabetes Prevention Program; DPP-4, dipeptidyl peptidase 4; DR, diabetic retinopathy; GCT, glucose challenge test; GDM, gestational diabetes mellitus; GP, general practitioner; GTT, glucose tolerance test; HMO, health maintenance organization; IADPSB, International Association of the Diabetes and Pregnancy Study Groups; ISO, International Organization for Standardization; IT, information technology; LEADER, Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results; max, maximum; OGTT, oral glucose tolerance test; PHQ, patient health questionnaire; preDM, prediabetes; QALE, quality-adjusted life expectancy; RCT, randomized controlled trial; TZD, thiazolidinedione; UKPDS, UK Prospective Diabetes Study.

Table 2—Summary of the CE studies by intervention (U.S. and non-U.S. high-income country studies)

Intervention	Comparison	Intervention population	Level of recommendation by ADA	Range of the CE ratios	Median of the CE ratios (no. of studies)	CE based on previous review (no. of studies)
Strong evidence						
Cost-saving						
ACEI/ARB therapy for intensive hypertension control	Standard hypertension control	T2D with hypertension	A	Cost-saving–$254/QALY	Cost-saving (6)	Cost-saving (4)
ACEI/ARB therapy to prevent CKD and/or ESRD	No ACEI/ARB therapy	T2D	A	Cost-saving–$5,310/QALY	Cost-saving (11)	Cost-saving (11)
Comprehensive foot care and patient education to prevent and treat foot ulcers	Usual care	DM and moderate/high risk of developing foot ulcers	B	Cost-saving	Cost-saving (3)	Cost-saving (2)
Telemedicine for DR screening	Office screening for DR	DM	B	Cost-saving–$7,781/QALY	Cost-saving (4)	***New finding*** (previously only supportive evidence)
Bariatric surgery	No bariatric surgery	T2D and obesity	A	Cost-saving–$29,641/QALY	Cost-saving (7)	***New finding***
Very cost-effective						
Intensive glycemic control	Conventional glycemic control	T2D, newly diagnosed and young age	A	Cost-saving–$78,740	$4,318/QALY (6)	$4,318/QALY (6)
Multicomponent interventions (behavior change/education and pharma therapy targeting hyperglycemia, hypertension, dyslipidemia, microalbuminuria, nephropathy/retinopathy, 2° prevention of CVD with aspirin)	Usual care	T1D/T2D	A: behavior modification A: aspirin A: risk factor control B: pharma therapy B: education	Cost-saving–$58,587/QALY	$2,315/QALY (6)	Cost-saving (2)
Statin therapy	No statin therapy	T2D with hyperlipidemia + CVD history	A	Cost-saving–$15,621/LYG	$4,627/LYG (4)	Very cost-effective (3)
Diabetes self-management education	Usual care	T1D/T2D	B	Cost-saving–$55,726/QALY	$5,047/QALY (11)	Cost-saving, supportive evidence (2)
T2D screening every 3 years starting at age 45 years (as recommended by ADA)	No screening	U.S. population without DM	B	$2,088–$13,707/QALY	$7,898/QALY (2)	Very cost-effective (1)
T2D screening every 1 year starting at age 45 years	T2D screening every 3 years starting at age 45 years	U.S. population without DM	B	$8,139/QALY	$8,139/QALY (2)	Very cost-effective (1)
Screening for eye complications every 1–2 years (as recommended by ADA)	No screening	T1D/T2D	B	Cost-saving–$50,165/QALY	$8,763/QALY (7)	Very cost-effective (5)
Integrated, patient-centered care (high level of nurse/pharmacist involvement) and based on Chronic Care Model	Usual care	T2D	B	Cost-saving–$55,465/QALY	$11,339/QALY (8)	Very cost-effective, supportive evidence

Continued on p. 1585

Table 2—Continued

Intervention	Comparison	Intervention population	Level of recommendation by ADA	Range of the CE ratios	Median of the CE ratios (no. of studies)	CE based on previous review (no. of studies)
Smoking cessation	No smoking cessation	T2D	A, B	<$31,750–$114,046/QALY	<$31,750/QALY(1)	Very cost-effective (1)
Daily aspirin use as primary prevention for cardiovascular complications	Usual care	T2D	B	$2,395/QALY	$2,395/QALY (1)	***New finding***
SMBG 3×/day	SMBG 1×/day	T2D adults	B	Cost-saving–$9,201/QALY	$3,719 (4)	***New finding***
Intensive glycemic control	Conventional insulin therapy	T2D aged ≥50 years	A	$15,398/QALY	$15,398/QALY (1)	***New finding***
Collaborative care for depression (TEAMCare)	Usual care	T2D + depression	B	Cost-saving–$29,160/QALY	$18,814/QALY (3)	***New finding***
Cost-effective						
Intensive glycemic control	Usual care	T1D	A	$12,954–$64,516/QALY	$41,339/QALY (4)	Cost-effective (4)
Marginally cost-effective						
Statin therapy	No statin therapy	T2D with hyperlipidemia without CVD history	A	$4,445–$98,906/QALY	$67,873/QALY (3)	Cost-effective (3)
Ranibizumab treatment	Panretinal photocoagulation	DM and DR, with DME	A	$45,264–$56,752/QALY	$51,008/QALY (2)	***New finding***
Duloxetine for the treatment of PDPN	Desipramine	DM and PDPN	A	$67,188/QALY	$67,188/QALY (1)	***New finding***
Not cost-effective						
Universal opportunistic screening for undiagnosed T2D	Targeted screening in persons with hypertension	U.S. population ≥45 years	B	$89,535–$888,746/QALY	>$100,000/QALY (1)	Not cost-effective (1)
Universal opportunistic screening for undiagnosed T2D and ensuing treatment	No screening	U.S. population ≥45 years	B	$89,027–$1,178,560/QALY	>$100,000/QALY (2)	Not cost-effective (2)
Supportive evidence						
Cost-saving						
Reimbursement for ACEI by public insurance	Paying out of pocket	T1D/T2D	B/E	Cost-saving	Cost-saving (1)	Cost-saving (1)
Group-based peer support (9 group meetings led by peer supporters in general practice)	Usual care	T2D	B	Cost-saving	Cost-saving (1)	Supportive—recommendation updated in new ADA
Very cost-effective						
Statin treatment at T2D diagnosis (as primary prevention)	No lipid-regulating treatment	T2D adults	No recommendation level	$3,294/QALY; $3,640–$84,012/QALY for different age-groups	$3,294/QALY (1)	***New finding***

Continued on p. 1586

Table 2—Continued

Intervention	Comparison	Intervention population	Level of recommendation by ADA	Range of the CE ratios	Median of the CE ratios (no. of studies)	CE based on previous review (no. of studies)
Bariatric surgery – gastric bypass/gastric banding	No surgery	T2D and overweight	A	$23,320/QALY	$23,320/QALY (1)	***New finding***
Cost-effective						
CPAP for the treatment of obstructive sleep apnea	Usual care	T2D with obstructive sleep apnea	E	$27,750/QALY	$27,750/QALY (1)	***New finding***
Marginally cost-effective						
Adhering to National Cholesterol Education Program Adult Treatment Panel III guidelines	Usual care	T2D adults with mixed dyslipidemia	A	$67,873/QALY	$67,873/QALY (1)	***New finding***
Uncertain evidence						
Screening for GDM	No screening	30-year-old pregnant women between 24–28 weeks	C	Cost-saving–$19,746/QALY	Cost-saving (6)	Cost-saving (5)
SMBG 1×/day, provision of device and 1.29 strips per day	Usual care	T1D/T2D patients not using insulin	B: SMBG E: providing device and strips	$77,684–$130,820/QALY	>$100,000/QALY (2)	***New finding***
Computerized decision support system linked to EHR, shared between patients and physicians	Usual care	T2D	B	$190,417/QALY	$190,417/QALY (1)	***New finding***

ADA, American Diabetes Association Standards of Care 2018; DM, diabetes; DME, diabetic macular edema; DR, diabetic retinopathy; EHR, electronic health record; PDPN, painful diabetic peripheral neuropathy. *Cost-saving* is defined as an intervention that generates a better health outcome and costs less than the comparison intervention or is cost neutral (ICER = 0); *very cost-effective*, 0 < ICER ≤ $25,000 per QALY or LYG; *cost-effective*, $25,000 < ICER ≤ $50,000 per QALY or LYG; *marginally cost-effective*, $50,000 < ICER ≤ $100,000 per QALY or LYG; or *not cost-effective*, >$100,000 per QALY or LYG. *A*, as defined in Standards of Care 2018: clear evidence from well-conducted, generalizable, randomized controlled trials that are adequately powered; compelling nonexperimental evidence, i.e., "all or none" rule developed by the Centre for Evidence-Based Medicine at Oxford; supportive evidence from well-conducted randomized controlled trials that are adequately powered. *B*, as defined in Standards of Care 2018: supportive evidence from well-conducted cohort studies; supportive evidence from a well-conducted case-control study. *C*, as defined in Standards Care 2018: supportive evidence from poorly controlled or uncontrolled studies; conflicting evidence with the weight of evidence supporting the recommendation. *E*, as defined in Standards of Care 2018: expert consensus or clinical experience.

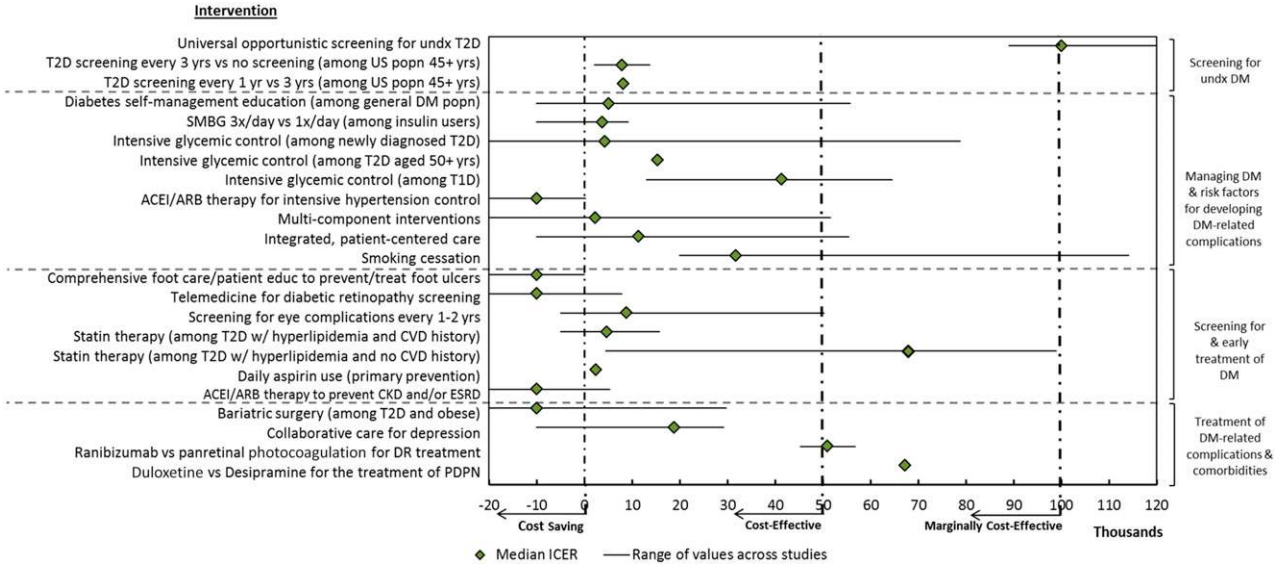

Figure 2—Summary of the CE of interventions (strong evidence only). CKD, chronic kidney disease; DM, diabetes; DR, diabetic retinopathy; PDPN, painful diabetic peripheral neuropathy; undx, undiagnosed.

this review was that daily aspirin use for primary prevention of CVD among individuals with T2D, compared with usual care, was very cost-effective ($2,395/QALY).

There were eight studies evaluating the CE of bariatric surgery in individuals with T2D and obesity (BMI ≥30 kg/m^2) compared with no bariatric surgery. All eight studies found this intervention to be cost-saving. Additionally, three studies evaluated the CE of collaborative care models to comanage depression in individuals with T2D and depression compared with usual care and found such treatment to be very cost-effective ($18,814/QALY).

Studies on two new ADA-recommended drugs (ranibizumab for diabetic retinopathy and duloxetine for painful diabetic peripheral neuropathy) were also included in this review. Both—ranibizumab compared with panretinal photocoagulation and duloxetine compared with desipramine—were found to be marginally cost-effective ($51,008/QALY and $67,188/QALY, respectively).

Supportive and Uncertain Evidence

There were nine specific interventions for which the level of CE was based on supportive evidence. Among these, cost-saving interventions are *1*) reimbursement for ACEI by public insurance for individuals with diabetes compared with paying out of pocket and *2*) group-based peer support for individuals with T2D compared with usual care. Very cost-effective interventions, based on supportive evidence, were both new findings in this updated review: *1*) statin treatment at T2D diagnosis compared with no lipid-regulating treatment ($3,294/QALY) and *2*) bariatric surgery for individuals with T2D and overweight compared with no surgery ($23,320/QALY). Continuous positive airway pressure (CPAP) therapy for individuals with T2D and obstructive sleep apnea compared with usual care was also cost-effective ($27,750/QALY). Adhering to the National Cholesterol Education Program Adult Treatment Panel III guidelines for adults with T2D and mixed dyslipidemia compared with usual care was marginally cost-effective ($67,873/QALY).

There were three specific interventions in the "uncertain evidence" category: *1*) screening a 30-year-old pregnant woman between 24–28 weeks' gestation (base case) for gestational diabetes mellitus compared with no screening (cost-saving); *2*) SMBG once per day and provision of monitoring devices and strips for individuals with T1D and for those with T2D not using insulin compared with usual care (SMBG once per day without provision of devices and strips), at >$100,000/QALY; and *3*) computerized decision-support systems linked to electronic health records and shared between patients and physicians ($190,417/QALY).

CONCLUSIONS

Our systematic review provides an updated understanding of the potential value of interventions to manage and treat diabetes from a health system perspective. Since the last review in 2010, the evidence that interventions to manage diabetes are cost-effective has grown in terms of additional evaluations to bolster existing evidence, as well as new economic evaluations of novel interventions and methods of care delivery. ACEI/ARB therapy compared with standard hypertension management, comprehensive foot care compared with usual care, and intensive glycemic management compared with conventional therapy are confirmed as very cost-effective interventions, while multicomponent interventions compared with usual care, statin therapy for secondary prevention compared with no statin therapy, T2D screening every 3 years compared with no screening, and screening for eye complications compared with no screening are confirmed as very cost-effective interventions. New findings include telemedicine for diabetic retinopathy screening and bariatric surgery for type 2 diabetes and BMI ≥30 kg/m^2 as cost-saving interventions and aspirin use for primary prevention of cardiovascular complications, SMBG three times per day for insulin-treated patients (compared with once per day), intensive glycemic management among those aged ≥50 years, and collaborative care for depression as very cost-effective interventions. This review complements professional treatment recommendations and can assist clinicians and payers in prioritizing interventions in an evidence-based manner that may

lead to better allocation of health care resources.

Figure 2 is a comprehensive guide to our findings. Overall, the ADA-recommended interventions included in the previously published review remain cost-saving, very cost-effective, or cost-effective. The strength of the evidence improved from supportive to strong for both DSME (compared with usual care) and integrated, patient-centered care based on the Chronic Care Model (compared with usual care) due to additional studies on these topics during the 2008–2017 time period. Interventions that are cost-saving should be implemented, and those that are very cost-effective or cost-effective based on strong evidence warrant consideration for implementation. ADA-recommended interventions rated as cost-saving, very cost-effective, or cost-effective with supportive evidence should be adopted if extra resources are available or if similar interventions with strong evidence are unavailable or infeasible in a specific setting.

Our review highlighted the value associated with new and innovative interventions to manage and treat diabetes, including technology-related innovations and those focused on addressing diabetes-related comorbidities. The focus on technological innovations and diabetes-related comorbidities is well-aligned with the ADA SOC 2019 (14) (as well as the recently updated ADA SOC 2020 [3,14]). In addition, the inclusion of collaborative care models for depression is a big step toward acknowledging and addressing the comorbid conditions of diabetes and depression, which is increasingly being seen as an important consideration in the care of people with diabetes (15).

Multicomponent interventions are also featured prominently in the current review and may have implications for delivery system design, especially in the context of persistent gaps in achievement of diabetes care goals (16,17). Among individuals with diabetes, interventions that included a combination of practice change, behavior change and education, pharmacologic therapy targeting hyperglycemia, hypertension, dyslipidemia, microalbuminuria, or nephropathy/retinopathy, and secondary prevention of CVD with aspirin were very cost-effective compared with usual care, based on strong evidence. Of note, our review predates the ASCEND (A Study of Cardiovascular Events in Diabetes) trial, which showed that the primary CVD prevention benefits of aspirin were offset by the increased risk of major bleeding events (18).

In some cases, CE evaluations may help to provide more insight into how ADA-recommended interventions might be prioritized for specific populations receiving the intervention. For example, bariatric surgery was cost-saving among individuals with T2D and obesity but only very cost-effective among individuals with T2D and overweight, likely due to larger health risks posed by obesity. We also noted differences in the CE of statin therapy for individuals with diabetes with and without CVD; when used as secondary prevention, there is clear value to statin use (cost-saving). However, for primary prevention, statin use has been found to be less cost-effective. We found that the CE of intensive glycemic management (with a goal of reducing A1C values) depends on age and duration since diabetes diagnosis. Among young individuals with newly diagnosed T2D, intensive glycemic management, compared with conventional insulin therapy, is cost-saving; indeed, recent research shows that earlier intensive management is associated with lower long-term risk of complications (19). For older individuals (aged $\geq$50 years) with T2D and shorter life expectancy, the ability to see benefits of intensive glycemic management is limited, in part because cardiovascular or mortality benefits may not be seen for at least 10 years (20). In individuals with T1D, intensive glycemic management compared with conventional insulin therapy remains cost-effective.

There are a few key areas that future economic evaluations of diabetes should consider. First, more studies are needed to evaluate the CE of interventions that fell in the "supportive" or "uncertain" evidence categories. In cases where interventions have uncertain value due to a small number of studies (i.e., incomplete knowledge), adding to the evidence base could help to clarify their value. There are also a number of new, efficacious medications and treatments for the management of glycemia (glucagon-like peptide 1 receptor agonists, sodium–glucose cotransporter 2 inhibitors), lipids (PSK9 inhibitors), and heart failure (sacubitril/valsartan [Entresto]) that were not included in this review because there are no published CE studies. For studies with weaker efficacy data, further efficacy studies are needed.

Second, more studies are needed that address interventions in real-world settings, as our current review is predominantly based on randomized controlled trials or computer simulation models. In real life, however, there are many factors to consider in addition to the CE of an intervention, such as *1*) coverage for the intervention in question (determine access), *2*) motivation (side effects or mode of delivery [e.g., injectable versus oral] may deter patients from taking specific medications), and *3*) whether the risk reduction in real life is similar to what was observed in trials and models (i.e., effectiveness versus efficacy). These are many of the unknowns that clinicians and policy makers must consider as they attempt to use the data from this review in practice.

Third, there may be additional cost-effective interventions that exist but have not been studied or about which the right questions are not being asked. For example, the 2010 review included one article regarding the CE of smoking cessation, which was found to be very cost-effective. There were no additional articles in this category from 2008–2017, likely because it is universally understood that smoking cessation is good and thus no one would be compelled to argue its value; a more interesting contemporary economic question might be to inquire how often a smoking cessation intervention should be implemented for it to be most cost-effective and most adoptable by clinicians and their patients.

The CE of an intervention in decision-making is important, but it is not the only factor to consider. CE analysis does not address equity in the distribution of costs and the benefits of an intervention, societal or personal willingness to pay, social and legal aspects, or ethical issues associated with each intervention. However, with an eye toward finding diabetes management and treatment interventions that can best increase the value of our health care dollars, this review of the most up-to-date available evidence can help to guide clinicians and policy makers toward the most cost-effective use of their prescriptions and health care dollars.

Acknowledgments. This work is a collaboration between the Centers for Disease Control and

Prevention and the ADA. The authors thank the external and internal reviewers for their valuable comments during the review process. The authors thank Rui Li for generously sharing materials from her previous review and William Thomas for his timely help with the literature search (both from Centers for Disease Control and Prevention).

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

Author Contributions. K.R.S., X.Zho., B.P.N., S.J., K.P., and X.Zha. reviewed the abstracts and full text of all articles for inclusion and abstracted the data. X.Zho. and B.P.N. performed the literature search and rated the quality of the studies for inclusion. K.R.S., M.K.A., X.Zho., E.W.G., A.L.A., and P.Z. interpreted the data and results. K.R.S. drafted the manuscript. All authors reviewed and edited the manuscript.

References

1. Centers for Disease Control and Prevention. *National Diabetes Statistics Report, 2017*. Atlanta, GA, Centers for Disease Control and Prevention, U.S. Department of Health and Human Services, 2017
2. American Diabetes Association. Economic costs of diabetes in the U.S. in 2017. Diabetes Care 2018; 41:917–928
3. American Diabetes Association. *Standards of Medical Care in Diabetes—2020* abridged for primary care providers. Clin Diabetes 2020;38:10–38
4. Li R, Zhang P, Barker LE, Chowdhury FM, Zhang X. Cost-effectiveness of interventions to prevent and control diabetes mellitus: a systematic review. Diabetes Care 2010;33:1872–1894
5. American Diabetes Association. Standards of medical care in diabetes—2008. Diabetes Care 2008;31(Suppl. 1):S12–S54
6. Association American Diabetes. Updates to the *Standards of Medical Care in Diabetes—2018*. Diabetes Care 2018;41:2045–2047
7. American Diabetes Association. *Standards of Medical Care in Diabetes—2019* abridged for primary care providers. Clin Diabetes 2019;37:11–34
8. Clarke M, Oxman A., Eds. Cochrane Reviewers' Handbook 4.2.0. [updated March 2003]. The Cochrane Libr 2003;(2)
9. The World Bank. *World Bank Country and Lending Groups*. The World Bank Group, 2017
10. Drummond MF, Jefferson TO; The BMJ Economic Evaluation Working Party. Guidelines for authors and peer reviewers of economic submissions to the BMJ. BMJ 1996;313:275–283
11. U.S. Bureau of Labor Statistics. Consumer Price Index, 2017. Available from https://www.bls.gov/cpi/. Accessed 20 March 2018
12. The Federal Reserve. Foreign exchange rates (annual). Available from http://www.federalreserve.gov/releases/g5a/. Accessed 28 August 2017
13. American Diabetes Association. Introduction: *Standards of Medical Care in Diabetes—2019*. Diabetes Care 2019;42(Suppl. 1):S1–S2
14. American Diabetes Association. Summary of revisions: *Standards of Medical Care in Diabetes—2019*. Diabetes Care 2019;42(Suppl. 1):S4–S6
15. Owens-Gary MD, Zhang X, Jawanda S, Bullard KM, Allweiss P, Smith BD. The importance of addressing depression and diabetes distress in adults with type 2 diabetes. J Gen Intern Med 2019;34:320–324
16. Ali MK, Bullard KM, Gregg EW. Achievement of goals in U.S. diabetes care, 1999-2010. N Engl J Med 2013;369:287–288
17. Ali MK, Bullard KM, Gregg EW, Del Rio C. A cascade of care for diabetes in the United States: visualizing the gaps. Ann Intern Med 2014;161: 681–689
18. Bowman L, Mafham M, Wallendszus K, et al.; ASCEND Study Collaborative Group. Effects of aspirin for primary prevention in persons with diabetes mellitus. N Engl J Med 2018;379:1529–1539
19. Laiteerapong N, Ham SA, Gao Y, et al. The legacy effect in type 2 diabetes: impact of early glycemic control on future complications (the Diabetes & Aging Study). Diabetes Care 2019;42:416–426
20. Tung EL, Davis AM, Laiteerapong N. Glycemic control in nonpregnant adults with type 2 diabetes. JAMA 2018;319:2430–2431
21. CDC Diabetes Cost-Effectiveness Study Group. The cost-effectiveness of screening for type 2 diabetes. JAMA 1998;280:1757–1763
22. Hoerger TJ, Harris R, Hicks KA, Donahue K, Sorensen S, Engelgau M. Screening for type 2 diabetes mellitus: a cost-effectiveness analysis. Ann Intern Med 2004;140:689–699
23. Gillett M, Brennan A, Watson P, et al. The cost-effectiveness of testing strategies for type 2 diabetes: a modelling study. Health Technol Assess 2015;19:1–80
24. Kahn R, Alperin P, Eddy D, et al. Age at initiation and frequency of screening to detect type 2 diabetes: a cost-effectiveness analysis. Lancet 2010;375:1365–1374
25. Nicholson WK, Fleisher LA, Fox HE, Powe NR. Screening for gestational diabetes mellitus: a decision and cost-effectiveness analysis of four screening strategies. Diabetes Care 2005;28:1482–1484
26. Werner EF, Pettker CM, Zuckerwise L, et al. Screening for gestational diabetes mellitus: are the criteria proposed by the International Association of the Diabetes and Pregnancy Study Groups cost-effective? Diabetes Care 2012;35:529–535
27. Chen PY, Finkelstein EA, Ng MJ, et al. Incremental cost-effectiveness analysis of gestational diabetes mellitus screening strategies in Singapore. Asia Pac J Public Health 2016;28:15–25
28. Danyliv A, Gillespie P, O'Neill C, et al. The cost-effectiveness of screening for gestational diabetes mellitus in primary and secondary care in the Republic of Ireland. Diabetologia 2016;59:436–444
29. The Diabetes Control and Complications Trial Research Group. Lifetime benefits and costs of intensive therapy as practiced in the Diabetes Control and Complications Trial. JAMA 1996;276:1409–1415
30. Eastman RC, Javitt JC, Herman WH, et al. Model of complications of NIDDM. II. Analysis of the health benefits and cost-effectiveness of treating NIDDM with the goal of normoglycemia. Diabetes Care 1997;20:735–744
31. Gray A, Raikou M, McGuire A, et al.; United Kingdom Prospective Diabetes Study Group. Cost effectiveness of an intensive blood glucose control policy in patients with type 2 diabetes: economic analysis alongside randomised controlled trial (UKPDS 41). BMJ 2000;320:1373–1378
32. Palmer AJ, Weiss C, Sendi PP, et al. The cost-effectiveness of different management strategies for type I diabetes: a Swiss perspective. Diabetologia 2000;43:13–26
33. Wake N, Hisashige A, Katayama T, et al. Cost-effectiveness of intensive insulin therapy for type 2 diabetes: a 10-year follow-up of the Kumamoto study. Diabetes Res Clin Pract 2000;48:201–210
34. Clarke P, Gray A, Adler A, et al.; UKPDS Group. Cost-effectiveness analysis of intensive blood-glucose control with metformin in overweight patients with type II diabetes (UKPDS No. 51). Diabetologia 2001;44:298–304
35. CDC Diabetes Cost-effectiveness Group. Cost-effectiveness of intensive glycemic control, intensified hypertension control, and serum cholesterol level reduction for type 2 diabetes. JAMA 2002;287:2542–2551
36. Scuffham P, Carr L. The cost-effectiveness of continuous subcutaneous insulin infusion compared with multiple daily injections for the management of diabetes. Diabet Med 2003;20:586–593
37. Roze S, Valentine WJ, Zakrzewska KE, Palmer AJ. Health-economic comparison of continuous subcutaneous insulin infusion with multiple daily injection for the treatment of type 1 diabetes in the UK. Diabet Med 2005;22:1239–1245
38. Clarke PM, Gray AM, Briggs A, Stevens RJ, Matthews DR, Holman RR; UKPDS 72 United Kingdom Prospective Diabetes Study. Cost-utility analyses of intensive blood glucose and tight blood pressure control in type 2 diabetes (UKPDS 72). Diabetologia 2005;48:868–877
39. Eddy DM, Schlessinger L, Kahn R. Clinical outcomes and cost-effectiveness of strategies for managing people at high risk for diabetes. Ann Intern Med 2005;143:251–264
40. Cameron CG, Bennett HA. Cost-effectiveness of insulin analogues for diabetes mellitus. CMAJ 2009;180:400–407
41. Howard K, White S, Salkeld G, et al. Cost-effectiveness of screening and optimal management for diabetes, hypertension, and chronic kidney disease: a modeled analysis. Value Health 2010;13:196–208
42. Klarenbach S, Cameron C, Singh S, Ur E. Cost-effectiveness of second-line antihyperglycemic therapy in patients with type 2 diabetes mellitus inadequately controlled on metformin. CMAJ 2011;183:E1213–E1220
43. Gordon J, McEwan P, Evans M, Puelles J, Sinclair A. Managing glycaemia in older people with type 2 diabetes: a retrospective, primary care-based cohort study, with economic assessment of patient outcomes. Diabetes Obes Metab 2017;19:644–653
44. Simon J, Gray A, Clarke P, Wade A, Neil A, Farmer A; Diabetes Glycaemic Education and Monitoring Trial Group. Cost effectiveness of self monitoring of blood glucose in patients with non-insulin treated type 2 diabetes: economic evaluation of data from the DiGEM trial. BMJ 2008; 336:1177–1180
45. Tunis SL, Minshall ME. Self-monitoring of blood glucose in type 2 diabetes: cost-effectiveness in the united states. Am J Manag Care 2008;14:131–140
46. Cameron C, Coyle D, Ur E, Klarenbach S. Cost-effectiveness of self-monitoring of blood glucose in patients with type 2 diabetes mellitus managed without insulin. CMAJ 2010;182:28–34
47. Pollock RF, Valentine WJ, Goodall G, Brändle M. Evaluating the cost-effectiveness of self-monitoring of blood glucose in type 2 diabetes patients on oral anti-diabetic agents. Swiss Med Wkly 2010; 140:w13103
48. Tunis SL, Minshall ME. Self-monitoring of blood glucose (SMBG) for type 2 diabetes patients treated with oral anti-diabetes drugs and with a recent history of monitoring: cost-effectiveness in the US. Curr Med Res Opin 2010;26:151–162
49. Tunis SL, Willis WD, Foos V. Self-monitoring of blood glucose (SMBG) in patients with type

2 diabetes on oral anti-diabetes drugs: cost-effectiveness in France, Germany, Italy, and Spain. Curr Med Res Opin 2010;26:163–175
50. Tunis SL. Cost effectiveness of self-monitoring of blood glucose (SMBG) for patients with type 2 diabetes and not on insulin: impact of modelling assumptions on recent Canadian findings. Appl Health Econ Health Policy 2011;9:351–365
51. McQueen RB, Breton MD, Ott M, Koa H, Beamer B, Campbell JD. Economic value of improved accuracy for self-monitoring of blood glucose devices for type 1 diabetes in Canada. J Diabetes Sci Technol 2015;10:366–377
52. UK Prospective Diabetes Study Group. Cost effectiveness analysis of improved blood pressure control in hypertensive patients with type 2 diabetes: UKPDS 40. BMJ 1998;317:720–726
53. Elliott WJ, Weir DR, Black HR. Cost-effectiveness of the lower treatment goal (of JNC VI) for diabetic hypertensive patients. Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Arch Intern Med 2000;160:1277–1283
54. Ly D, Fu AZ, Hebert C. Cost effectiveness analysis of a hypertension management program in patients with type 2 diabetes. J Clin Hypertens (Greenwich) 2009;11:116–124
55. Herman WH, Alexander CM, Cook JR, et al. Effect of simvastatin treatment on cardiovascular resource utilization in impaired fasting glucose and diabetes. Findings from the Scandinavian Simvastatin Survival Study. Diabetes Care 1999; 22:1771–1778
56. Jönsson B, Cook JR, Pedersen TR. The cost-effectiveness of lipid lowering in patients with diabetes: results from the 4S trial. Diabetologia 1999;42:1293–1301
57. Grover SA, Coupal L, Zowall H, Dorais M. Cost-effectiveness of treating hyperlipidemia in the presence of diabetes: who should be treated? Circulation 2000;102:722–727
58. Raikou M, McGuire A, Colhoun HM, et al.; CARDS Investigators. Cost-effectiveness of primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes: results from the Collaborative Atorvastatin Diabetes Study (CARDS). Diabetologia 2007;50:733–740
59. Sorensen SV, Frick KD, Wade A, Simko R, Burge R. Model-based simulation to explore the cost-effectiveness of following practice guidelines for triglyceride and low-density lipoprotein cholesterol control among patients with diabetes mellitus and mixed dyslipidemia. Clin Ther 2009;31:862–879
60. de Vries FM, Denig P, Visser ST, Hak E, Postma MJ. Cost-effectiveness of statins for primary prevention in patients newly diagnosed with type 2 diabetes in the Netherlands. Value Health 2014; 17:223–230
61. Earnshaw SR, Richter A, Sorensen SW, et al. Optimal allocation of resources across four interventions for type 2 diabetes. Med Decis Making 2002;22(Suppl):S80–S91
62. Gozzoli V, Palmer AJ, Brandt A, Spinas GA. Economic and clinical impact of alternative disease management strategies for secondary prevention in type 2 diabetes in the Swiss setting. Swiss Med Wkly 2001;131:303–310
63. Shearer A, Bagust A, Sanderson D, Heller S, Roberts S. Cost-effectiveness of flexible intensive insulin management to enable dietary freedom in people with type 1 diabetes in the UK. Diabet Med 2004;21:460–467
64. Brownson CA, Hoerger TJ, Fisher EB, Kilpatrick KE. Cost-effectiveness of diabetes self-management programs in community primary care settings. Diabetes Educ 2009;35:761–769
65. Gillett M, Dallosso HM, Dixon S, et al. Delivering the diabetes education and self management for ongoing and newly diagnosed (DESMOND) programme for people with newly diagnosed type 2 diabetes: cost effectiveness analysis. BMJ 2010; 341:c4093
66. Gillespie P, O'Shea E, O'Hara MC, Dinneen SF, Irish DAFNE Study Group. Cost effectiveness of group follow-up after structured education for type 1 diabetes: a cluster randomised controlled trial. Trials 2014;15:227
67. Kruger J, Brennan A, Thokala P, et al. The cost-effectiveness of the Dose Adjustment for Normal Eating (DAFNE) structured education programme: an update using the Sheffield Type 1 Diabetes Policy Model. Diabet Med 2013;30: 1236–1244
68. Gordon LG, Bird D, Oldenburg B, Friedman RH, Russell AW, Scuffham PA. A cost-effectiveness analysis of a telephone-linked care intervention for individuals with type 2 diabetes. Diabetes Res Clin Pract 2014;104:103–111
69. Prezio EA, Pagán JA, Shuval K, Culica D. The Community Diabetes Education (CoDE) program: cost-effectiveness and health outcomes. Am J Prev Med 2014;47:771–779
70. Ryabov I. Cost-effectiveness of community health workers in controlling diabetes epidemic on the U.S.-Mexico border. Public Health 2014; 128:636–642
71. Varney JE, Liew D, Weiland TJ, Inder WJ, Jelinek GA. The cost-effectiveness of hospital-based telephone coaching for people with type 2 diabetes: a 10 year modelling analysis. BMC Health Serv Res 2016;16:521
72. Odnoletkova I, Ramaekers D, Nobels F, Goderis G, Aertgeerts B, Annemans L. Delivering diabetes education through nurse-led telecoaching. cost-effectiveness analysis. PLoS One 2016;11:e0163997
73. Li R, Zhang P, Barker LE, Hoerger TJ. Cost-effectiveness of aspirin use among persons with newly diagnosed type 2 diabetes. Diabetes Care 2010;33:1193–1199
74. van Giessen A, Boonman-de Winter LJ, Rutten FH, et al. Cost-effectiveness of screening strategies to detect heart failure in patients with type 2 diabetes. Cardiovasc Diabetol 2016;15:48
75. Javitt JC, Aiello LP, Chiang Y, Ferris FL III, Canner JK, Greenfield S. Preventive eye care in people with diabetes is cost-saving to the federal government. Implications for health-care reform. Diabetes Care 1994;17:909–917
76. Javitt JC, Aiello LP. Cost-effectiveness of detecting and treating diabetic retinopathy. Ann Intern Med 1996;124:164–169
77. Vijan S, Hofer TP, Hayward RA. Cost-utility analysis of screening intervals for diabetic retinopathy in patients with type 2 diabetes mellitus. JAMA 2000;283:889–896
78. Maberley D, Walker H, Koushik A, Cruess A. Screening for diabetic retinopathy in James Bay, Ontario: a cost-effectiveness analysis. CMAJ 2003; 168:160–164
79. Kirkizlar E, Serban N, Sisson JA, Swann JL, Barnes CS, Williams MD. Evaluation of telemedicine for screening of diabetic retinopathy in the Veterans Health Administration. Ophthalmology 2013;120:2604–2610
80. Chan CK, Gangwani RA, McGhee SM, Lian J, Wong DS. Cost-effectiveness of screening for intermediate age-related macular degeneration during diabetic retinopathy screening. Ophthalmology 2015;122:2278–2285
81. Kawasaki R, Akune Y, Hiratsuka Y, Fukuhara S, Yamada M. Cost-utility analysis of screening for diabetic retinopathy in Japan: a probabilistic Markov modeling study. Ophthalmic Epidemiol 2015;22:4–12
82. Scanlon PH, Aldington SJ, Leal J, et al. Development of a cost-effectiveness model for optimisation of the screening interval in diabetic retinopathy screening. Health Technol Assess 2015;19:1–116
83. Nguyen HV, Finkelstein EA, Mital S, Gardner DS. Incremental cost-effectiveness of algorithm-driven genetic testing versus no testing for maturity onset diabetes of the young (MODY) in Singapore. J Med Genet 2017;54:747–753
84. Scotland G, McKeigue P, Philip S, et al. Modelling the cost-effectiveness of adopting risk-stratified approaches to extended screening intervals in the national diabetic retinopathy screening programme in Scotland. Diabet Med 2016;33:886–895
85. van Katwyk S, Jin YP, Trope GE, et al. Cost-utility analysis of extending public health insurance coverage to include diabetic retinopathy screening by optometrists. Value Health 2017; 20:1034–1040
86. Ragnarson Tennvall G, Apelqvist J. Prevention of diabetes-related foot ulcers and amputations: a cost-utility analysis based on Markov model simulations. Diabetologia 2001;44:2077–2087
87. Ortegon MM, Redekop WK, Niessen LW. Cost-effectiveness of prevention and treatment of the diabetic foot: a Markov analysis. Diabetes Care 2004;27:901–907
88. Borch-Johnsen K, Wenzel H, Viberti GC, Mogensen CE. Is screening and intervention for microalbuminuria worthwhile in patients with insulin dependent diabetes? BMJ 1993; 306:1722–1725
89. Kiberd BA, Jindal KK. Screening to prevent renal failure in insulin dependent diabetic patients: an economic evaluation. BMJ 1995;311: 1595–1599
90. Golan L, Birkmeyer JD, Welch HG. The cost-effectiveness of treating all patients with type 2 diabetes with angiotensin-converting enzyme inhibitors. Ann Intern Med 1999;131: 660–667
91. Clark WF, Churchill DN, Forwell L, Macdonald G, Foster S. To pay or not to pay? A decision and cost-utility analysis of angiotensin-converting-enzyme inhibitor therapy for diabetic nephropathy. CMAJ 2000;162:195–198
92. Palmer AJ, Annemans L, Roze S, Lamotte M, Rodby RA, Cordonnier DJ. An economic evaluation of irbesartan in the treatment of patients with type 2 diabetes, hypertension and nephropathy: cost-effectiveness of Irbesartan in Diabetic Nephropathy Trial (IDNT) in the Belgian and French settings. Nephrol Dial Transplant 2003; 18:2059–2066
93. Souchet T, Durand Zaleski I, Hannedouche T, Rodier M, Gaugris S, Passa P; RENAAL study. An economic evaluation of Losartan therapy in type 2 diabetic patients with nephropathy: an analysis of the RENAAL study adapted to France. Diabetes Metab 2003;29:29–35

94. Dong FB, Sorensen SW, Manninen DL, et al. Cost effectiveness of ACE inhibitor treatment for patients with type 1 diabetes mellitus. Pharmacoeconomics 2004;22:1015–1027
95. Palmer AJ, Annemans L, Roze S, Lamotte M, Rodby RA, Bilous RW. An economic evaluation of the Irbesartan in Diabetic Nephropathy Trial (IDNT) in a UK setting. J Hum Hypertens 2004;18: 733–738
96. Palmer AJ, Annemans L, Roze S, et al. Cost-effectiveness of early irbesartan treatment versus control (standard antihypertensive medications excluding ACE inhibitors, other angiotensin-2 receptor antagonists, and dihydropyridine calcium channel blockers) or late irbesartan treatment in patients with type 2 diabetes, hypertension, and renal disease. Diabetes Care 2004;27:1897–1903
97. Szucs TD, Sandoz MS, Keusch GW. The cost-effectiveness of losartan in type 2 diabetics with nephropathy in Switzerland—an analysis of the RENAAL study. Swiss Med Wkly 2004;134:440–447
98. Palmer AJ, Annemans L, Roze S, et al. Irbesartan is projected to be cost and life saving in a Spanish setting for treatment of patients with type 2 diabetes, hypertension, and microalbuminuria. Kidney Int Suppl 2005;67(Suppl. 93): S52–S54
99. Rosen AB, Hamel MB, Weinstein MC, Cutler DM, Fendrick AM, Vijan S. Cost-effectiveness of full medicare coverage of angiotensin-converting enzyme inhibitors for beneficiaries with diabetes. Ann Intern Med 2005;143:89–99
100. Coyle D, Rodby R, Soroka S, et al. Cost-effectiveness of irbesartan 300 mg given early versus late in patients with hypertension and a history of type 2 diabetes and renal disease: a Canadian perspective. Clin Ther 2007;29: 1508–1523
101. Palmer AJ, Valentine WJ, Ray JA, Roze S, Muszbek N. Health economic implications of irbesartan treatment versus standard blood pressure control in patients with type 2 diabetes, hypertension and renal disease: a Hungarian analysis. Eur J Health Econ 2007;8:161–168
102. Palmer AJ, Valentine WJ, Ray JA. Irbesartan treatment of patients with type 2 diabetes, hypertension and renal disease: a UK health economics analysis. Int J Clin Pract 2007;61:1626–1633
103. Gaede P, Valentine WJ, Palmer AJ, et al. Cost-effectiveness of intensified versus conventional multifactorial intervention in type 2 diabetes: results and projections from the Steno-2 study. Diabetes Care 2008;31:1510–1515
104. Tasosa J, Schuster R, McAlearney JS. Cost-effectiveness of treating hypertension, hyperglycemia, and hyperlipidemia in African Americans and the general population with type 2 diabetes. J Health Care Poor Underserved 2010;21:161–176
105. Giorda CB, Nicolucci A, Pellegrini F, et al. Improving quality of care in people with type 2 diabetes through the Associazione Medici Diabetologi-annals initiative: a long-term cost-effectiveness analysis. Diabet Med 2014;31: 615–623
106. Laxy M, Wilson ECF, Boothby CE, Griffin SJ. Incremental costs and cost effectiveness of intensive treatment in individuals with type 2 diabetes detected by screening in the ADDITION-UK trial: an update with empirical trial-based cost data. Value Health 2017;20:1288–1298
107. Mason JM, Freemantle N, Gibson JM, New JP; SPLINT trial. Specialist nurse-led clinics to improve control of hypertension and hyperlipidemia in diabetes: economic analysis of the SPLINT trial. Diabetes Care 2005;28:40–46
108. Gilmer TP, Roze S, Valentine WJ, et al. Cost-effectiveness of diabetes case management for low-income populations. Health Serv Res 2007; 42:1943–1959
109. McRae IS, Butler JR, Sibthorpe BM, et al. A cost effectiveness study of integrated care in health services delivery: a diabetes program in Australia. BMC Health Serv Res 2008;8:205
110. Schouten LM, Niessen LW, van de Pas JW, Grol RP, Hulscher ME. Cost-effectiveness of a quality improvement collaborative focusing on patients with diabetes. Med Care 2010;48:884–891
111. Kuo S, Bryce CL, Zgibor JC, Wolf DL, Roberts MS, Smith KJ. Cost-effectiveness of implementing the chronic care model for diabetes care in a military population. J Diabetes Sci Technol 2011; 5:501–513
112. Haji Ali Afzali H, Gray J, Beilby J, Holton C, Karnon J. A model-based economic evaluation of improved primary care management of patients with type 2 diabetes in Australia. Appl Health Econ Health Policy 2013;11:661–670
113. Slingerland AS, Herman WH, Redekop WK, Dijkstra RF, Jukema JW, Niessen LW. Stratified patient-centered care in type 2 diabetes: a cluster-randomized, controlled clinical trial of effectiveness and cost-effectiveness. Diabetes Care 2013;36:3054–3061
114. Yu J, Shah BM, Ip EJ, Chan J. A Markov model of the cost-effectiveness of pharmacist care for diabetes in prevention of cardiovascular diseases: evidence from Kaiser Permanente Northern California. J Manag Care Pharm 2013;19:102–114
115. Tsiachristas A, Cramm JM, Nieboer AP, Rutten-van Mölken MP. Changes in costs and effects after the implementation of disease management programs in the Netherlands: variability and determinants. Cost Eff Resour Alloc 2014;12:17
116. Wilson A, O'Hare JP, Hardy A, et al.; ICCD trial group. Evaluation of the clinical and cost effectiveness of intermediate care clinics for diabetes (ICCD): a multicentre cluster randomised controlled trial. PLoS One 2014;9:e93964
117. Tao L, Wilson EC, Wareham NJ, et al. Cost-effectiveness of intensive multifactorial treatment compared with routine care for individuals with screen-detected type 2 diabetes: analysis of the ADDITION-UK cluster-randomized controlled trial. Diabet Med 2015;32:907–919
118. Hirsch JD, Bounthavong M, Arjmand A, et al. Estimated cost-effectiveness, cost benefit, and risk reduction associated with an endocrinologist-pharmacist Diabetes Intense Medical Management "Tune-Up" clinic. J Manag Care Spec Pharm 2017;23:318–326
119. Cobden DS, Niessen LW, Rutten FF, Redekop WK. Modeling the economic impact of medication adherence in type 2 diabetes: a theoretical approach. Patient Prefer Adherence 2010;4:283–290
120. Cleveringa FG, Welsing PM, van den Donk M, et al. Cost-effectiveness of the diabetes care protocol, a multifaceted computerized decision support diabetes management intervention that reduces cardiovascular risk. Diabetes Care 2010; 33:258–263
121. O'Reilly D, Holbrook A, Blackhouse G, Troyan S, Goeree R. Cost-effectiveness of a shared computerized decision support system for diabetes linked to electronic medical records. J Am Med Inform Assoc 2012;19:341–345
122. Olvey E, Guy MC, Chang J, Skrepnek GH Cost-effectiveness of medication therapy management in Part D diabetic enrollees. Am J Pharm Benefits 2014;6:e147–e156
123. Gillespie P, O'Shea E, Paul G, O'Dowd T, Smith SM. Cost effectiveness of peer support for type 2 diabetes. Int J Technol Assess Health Care 2012;28:3–11
124. Hlatky MA, Boothroyd DB, Melsop KA, et al.; Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) Study Group. Economic outcomes of treatment strategies for type 2 diabetes mellitus and coronary artery disease in the Bypass Angioplasty Revascularization Investigation 2 Diabetes trial. Circulation 2009;120: 2550–2558
125. Sharma S, Hollands H, Brown GC, Brown MM, Shah GK, Sharma SM. The cost-effectiveness of early vitrectomy for the treatment of vitreous hemorrhage in diabetic retinopathy. Curr Opin Ophthalmol 2001;12:230–234
126. Mitchell P, Annemans L, Gallagher M, et al. Cost-effectiveness of ranibizumab in treatment of diabetic macular oedema (DME) causing visual impairment: evidence from the RESTORE trial. Br J Ophthalmol 2012;96:688–693
127. Hutton DW, Stein JD, Bressler NM, Jampol LM, Browning D, Glassman AR; Diabetic Retinopathy Clinical Research Network. Cost-effectiveness of intravitreous ranibizumab compared with panretinal photocoagulation for proliferative diabetic retinopathy: secondary analysis from a Diabetic Retinopathy Clinical Research Network randomized clinical trial. JAMA Ophthalmol 2017;135: 576–584
128. Habacher W, Rakovac I, Görzer E, et al. A model to analyse costs and benefit of intensified diabetic foot care in Austria. J Eval Clin Pract 2007;13:906–912
129. O'Connor AB, Noyes K, Holloway RG. A cost-utility comparison of four first-line medications in painful diabetic neuropathy. Pharmacoeconomics 2008;26:1045–1064
130. Cheng Q, Lazzarini PA, Gibb M, et al. A cost-effectiveness analysis of optimal care for diabetic foot ulcers in Australia. Int Wound J 2017;14:616–628
131. Anselmino M, Bammer T, Fernández Cebrián JM, Daoud F, Romagnoli G, Torres A. Cost-effectiveness and budget impact of obesity surgery in patients with type 2 diabetes in three European countries(II). Obes Surg 2009;19:1542–1549
132. Ikramuddin S, Klingman D, Swan T, Minshall ME. Cost-effectiveness of Roux-en-Y gastric bypass in type 2 diabetes patients. Am J Manag Care 2009;15:607–615
133. Keating CL, Dixon JB, Moodie ML, et al. Cost-effectiveness of surgically induced weight loss for the management of type 2 diabetes: modeled lifetime analysis. Diabetes Care 2009; 32:567–574
134. Hoerger TJ, Zhang P, Segel JE, Kahn HS, Barker LE, Couper S. Cost-effectiveness of bariatric surgery for severely obese adults with diabetes. Diabetes Care 2010;33:1933–1939
135. Pollock RF, Muduma G, Valentine WJ. Evaluating the cost-effectiveness of laparoscopic adjustable gastric banding versus standard medical management in obese patients with type 2 diabetes in the UK. Diabetes Obes Metab 2013;15:121–129

136. Borisenko O, Adam D, Funch-Jensen P, et al. Bariatric surgery can lead to net cost savings to health care systems: results from a comprehensive European decision analytic model. Obes Surg 2015;25:1559–1568
137. James R, Salton RI, Byrnes JM, Scuffham PA. Cost-utility analysis for bariatric surgery compared with usual care for the treatment of obesity in Australia. Surg Obes Relat Dis 2017;13:2012–2020
138. Wentworth JM, Dalziel KM, O'Brien PE, et al. Cost-effectiveness of gastric band surgery for overweight but not obese adults with type 2 diabetes in the U.S. J Diabetes Complications 2017;31:1139–1144
139. Katon W, Unützer J, Fan MY, et al. Cost-effectiveness and net benefit of enhanced treatment of depression for older adults with diabetes and depression. Diabetes Care 2006;29:265–270
140. Johnson JA, Lier DA, Soprovich A, Al Sayah F, Qiu W, Majumdar SR. Cost-effectiveness evaluation of collaborative care for diabetes and depression in primary care. Am J Prev Med 2016;51:e13–e20
141. Kearns B, Rafia R, Leaviss J, et al. The cost-effectiveness of changes to the care pathway used to identify depression and provide treatment amongst people with diabetes in England: a model-based economic evaluation. BMC Health Serv Res 2017;17:78
142. Guest JF, Panca M, Sladkevicius E, Taheri S, Stradling J. Clinical outcomes and cost-effectiveness of continuous positive airway pressure to manage obstructive sleep apnea in patients with type 2 diabetes in the U.K. Diabetes Care 2014;37:1263–1271