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THE PRESENT AND FUTURE

JACC GUIDELINE COMPARISON

Guidelines for Cardiovascular Risk Reduction in Patients With Type 2 Diabetes

JACC Guideline Comparison

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ABSTRACT

Cardiovascular disease is a leading cause of morbidity and mortality in individuals with type 2 diabetes mellitus. These high-risk patients benefit from aggressive risk factor management, with blood pressure and low-density lipoprotein-cholesterol treatment, glycemic control, kidney protection, and lifestyle intervention. There are several recommendation and guideline documents across cardiology, endocrinology, nephrology, and general medicine professional societies from the United States and Europe with recommendations for cardiovascular risk reduction in patients with type 2 diabetes mellitus. Although there are some noteworthy differences, particularly in risk stratification, low-density lipoprotein-cholesterol and blood pressure treatment targets, and the use of sodium-glucose cotransporter-2 inhibitors and glucagon-like peptide-1 receptor agonists, overall there is considerable alignment across recommendations from different professional societies. (J Am Coll Cardiol 2022;79:1849–1857) © 2022 by the American College of Cardiology Foundation.

The landscape of cardiovascular (CV) risk reduction in type 2 diabetes mellitus (T2DM) has changed rapidly over the past decade. Multiple novel agents have been developed, including sodium-glucose cotransporter-2 inhibitors (SGLT2i) and glucagon-like peptide 1 receptor agonists (GLP-1RA), which have led to unexpected, but welcome benefits with regard to reducing CV outcomes. In addition, there have been significant therapeutic advances in low-density lipoprotein cholesterol (LDL-C) and blood pressure management. To incorporate these advances into clinical care, several scientific society recommendation and guideline documents outlining strategies for cardiovascular risk reduction in T2DM have been developed or updated within the past 10 years, by general medical, cardiovascular, kidney, and endocrine societies, in both the United States and Europe (**Central Illustration**).

Here, these society documents are compared, focusing on recommendations and strategies targeting CV risk reduction in T2DM. Recommendations were included from the U.S. Preventive Services Task Force (USPSTF),[1-3] American Diabetes Association (ADA),[4] the American Association of Clinical Endocrinology/American College of Endocrinology (AACE/

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ABBREVIATIONS AND ACRONYMS

AACE = American Association of Clinical Endocrinology

ACC = American College of Cardiology

ACE = American College of Endocrinology

ADA = American Diabetes Association

AHA = American Heart Association

ARB = angiotensin receptor blockers

ASCVD = atherosclerotic cardiovascular disease

CKD = chronic kidney disease

CV = cardiovascular

eGFR = estimated glomerular filtration rate

ESC = European Society of Cardiology

GLP-1RA = glucagon-like peptide 1 receptor agonists

KDIGO = Kidney Disease Improving Global Outcomes

LDL-C = low-density lipoprotein-cholesterol

SGLT2i = sodium-glucose cotransporter-2 inhibitors

T2DM = type 2 diabetes mellitus

USPSTF = US Preventive Services Task Force

ACE),[5,6] the European Society of Cardiology (ESC)/European Association for the Study of Diabetes,[7] the American College of Cardiology (ACC)/American Heart Association (AHA),[8,9] and Kidney Disease Improving Global Outcomes (KDIGO).[10,11] Although there are some notable differences in the details of these recommendations, there is considerable similarity in the guidance that different specialties provide for the care of patients with T2DM (**Table 1**). Continued efforts toward alignment of professional society recommendations across disciplines and around the world would benefit providers and patients alike, to support an integrated, comprehensive management of these patients at high CV risk.

HIGHLIGHTS

- Subspecialty society guidelines in the United States and Europe include similar recommendations for cardiovascular risk reduction in patients with T2DM, but there are a number of clinically important differences.
- The guidelines are generally aligned in recommending lifestyle interventions, aggressive management of blood pressure, LDL-C and blood glucose, and providing renal protection.
- The main differences involve risk stratification criteria, lipid and blood pressure treatment targets, and indications for addition of SGLT2i and GLP-1RA.

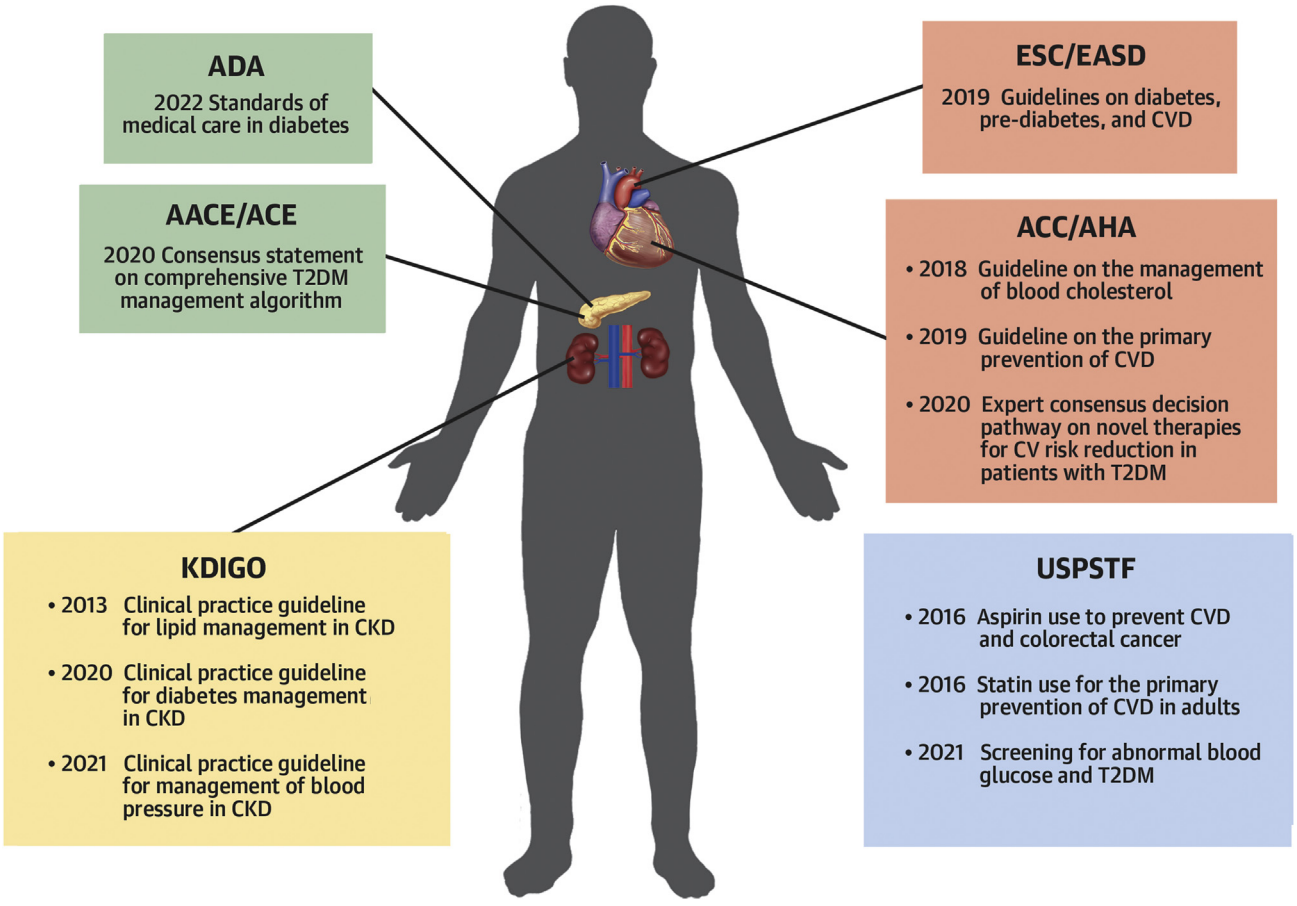
RISK ASSESSMENT

In determining eligibility for primary CV preventive therapies, the ACC/AHA, ADA, and USPSTF each endorse the use of the pooled cohort equations to estimate 10-year atherosclerotic cardiovascular disease (ASCVD) risk.[1,4,8] Introduced in 2013, the pooled cohort equations were derived from multiple, prospective U.S. cohort studies.[12] This calculation includes age, sex, race, blood pressure, total and high-density lipoprotein cholesterol, smoking status, and history of diabetes, the latter of which significantly increases predicted 10-year ASCVD risk for all race-sex groups. The ACC/AHA guidelines also identify diabetes-specific risk enhancers, which increase risk independently of the other factors in the pooled cohort equations.[13] These include the following: prolonged duration of disease (≥10 years); albuminuria ≥30 μg/mg of creatinine; reduced estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2; retinopathy; neuropathy; and reduced ankle-brachial index <0.90. Although the pooled cohort equations are well calibrated for individuals with T2DM, some concerns have been raised about risk discrimination in this model.[14,15] Moreover, the pooled cohort equations are validated for use in individuals aged 40-79 years, leaving as many as 10% of young and very old patients with T2DM outside this age range without a validated method for risk assessment.[16]

The ESC/EASD endorses a different strategy, using similar risk factors, but with 3 distinct risk categories: moderate, high, or very high CV risk.[7] "Moderate risk" includes those with T2DM who are younger than 50 years of age, with T2DM for <10 years. "High risk" includes individuals with >10 years of T2DM, with 1 additional CV risk factor (ie, age, hypertension, dyslipidemia, smoking, or obesity). "Very high risk" includes individuals with T2DM with multiple CV risk factors, target organ damage, or established ASCVD. These categories rely on a similar list of risk factors as the ACC/AHA Guidelines, with the exception of left ventricular hypertrophy included only in the ESC/EASD document, and neuropathy and reduced ankle-brachial index included only in the ACC/AHA document. The predefined categories of the ESC/EASD Guidelines leave less room for interpretation, as patients with proteinuria, chronic kidney disease, left ventricular hypertrophy, and/or retinopathy are automatically categorized as "very high risk" in the ESC/EASD model, whereas the same individual depending on their age, sex, and race, may not earn an equally elevated 10-year ASCVD risk prediction by the pooled cohort equations alone.[7]

The AACE/ACE Guidelines, on the other hand, recommend risk stratification with either the Framingham Risk Assessment tool, the Multi-Ethnic Study of Atherosclerosis 10-year ASCVD risk with Coronary Artery Calcification Calculator, the Reynolds Risk Score, or the United Kingdom Prospective Diabetes Study risk calculator to estimate ASCVD risk.[5] Individuals with T2DM are then further classified as high, very high, or extreme risk depending on the presence of other comorbidities or prior history of ASCVD. Of note, these guidelines propose the most inclusive list of risk factors, identifying even lifestyle changes (cigarette smoking) and advanced lipid

CENTRAL ILLUSTRATION **Cardiovascular Risk Reduction in Type 2 Diabetes Mellitus Guidelines and Consensus Recommendations**



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Guideline documents and consensus statements across general medical, CV, kidney, and endocrine professional societies with recommendations for CV risk reduction in T2DM. AACE = American Association of Clinical Endocrinology; ACE = American College of Endocrinology; ADA = American Diabetes Association; ACC = American College of Cardiology; AHA = American Heart Association; CKD = chronic kidney disease; CV = cardiovascular; CVD = CV disease; ESC = European Society of Cardiology; EASD = European Association for the Study of Diabetes; KDIGO = Kidney Disease: Improving Global Outcomes; T2DM = type 2 diabetes mellitus; USPSTF = U.S. Preventive Services Task Force.

testing parameters (apolipoprotein B, small dense LDL-C).

LIFESTYLE RECOMMENDATIONS

Societies are generally in agreement about the importance of lifestyle modification, both to prevent T2DM and to decrease risk for cardiovascular complications. However, it is of note that almost all of the data supporting these recommendations derive from observational analyses of associations with little support from intervention trials. The ACC/AHA, AACE/ACE, ESC/EASD, ADA, and KDIGO specifically recommend >150 minutes per week of moderate intensity physical activity for adults with T2DM.[6-8,10,17] Dietary guidance is also similar among these 4 groups, each emphasizing individualized nutritional assessment. The ADA, AACE/ACE, ESC/EASD, and the ACC/AHA support the Mediterranean diet to affect intermediate markers of glycemic control and weight loss, and (as a Class IIa recommendation for the ESC/EASD and Class B for the ADA), CV risk reduction, although data specifically in individuals with T2DM are limited.[6,7,17-19] The ESC/EASD specifically does not support vitamin supplementation to reduce the risk of T2DM, or reduce CV risk in those with T2DM.[7] This

TABLE 1 Comparison of Type 2 Diabetes Guideline Recommendations

	ACC/AHA[8,13,39]	ADA[4,17,38,43]
Risk assessment		
Method	Pooled Cohort Equation and diabetes-specific risk enhancers	Pooled Cohort Equation and diabetes-specific risk enhancers
Lifestyle recommendations		
Exercise	150 min of moderate-intensity activity per week	150 min of moderate-intensity activity per week
Diet	Individualized nutrition assessment; Mediterranean Diet	Individualized nutrition assessment; Mediterranean Diet
Vitamin use	No recommendation	No recommendation
Blood pressure management		
BP target	<130/80 mm Hg	<130/80 mm Hg if 10-y ASCVD risk ≥15%; <140/90 if 10-y ASCVD risk <15%
First-line treatment of hypertension	Angiotensin-converting enzyme/ARB if albuminuria	Angiotensin-converting enzyme/ARB if albuminuria
Indication for combination therapy	If BP >140/90 mm Hg	Dual therapy first line regardless of BP
LDL-C management		
Primary prevention treatment targets	50% LDL-C lowering for those at high risk	50% LDL-C lowering for those at high risk
Primary prevention in young patients	Treat if longstanding disease, end-organ damage, risk factors	Treat if longstanding disease, end-organ damage, risk factors
Secondary prevention treatment targets	Goal 50% LDL-C reduction, start meds LDL-C <70 mg/dL	Goal 50% LDL-C reduction, start meds at LDL-C <70 mg/dL
Secondary prevention second-line therapy	Ezetimibe	Ezetimibe or PCSK9i
Hyperglycemia treatment and novel agents		
First line	SGLT2i/GLP-1RA may be beneficial regardless of background metformin	SGLT2i/GLP-1RA may be beneficial regardless of background metformin
Relative priority of SGLT2/GLP-1RA	SLGT2i >GLP-1RA for HF, renal disease, weight loss	SLGT2i >GLP-1RA for HF and renal disease
Aspirin recommendations		
Primary prevention	May be considered if elevated ASCVD risk without increased bleeding risk	May be considered if elevated ASCVD risk without increased bleeding risk
CKD		
Type 2 diabetes treatment	SGLT2i	SGLT2i, specifically canagliflozin

AACE = American Association of Clinical Endocrinology; ACC = American College of Cardiology; ACE = American College of Endocrinology; ADA = American Diabetes Association; AHA = American Heart Association; ARB = angiotensin receptor blocker; ASCVD = atherosclerotic cardiovascular disease; BP = blood pressure; CKD = chronic kidney disease; EASD = European Association for the Study of Diabetes; ESC = European Society of Cardiology; GLP-1RA = glucagon-like peptide-1 receptor agonist; HF = heart failure; KDIGO = Kidney Disease Improving Global Outcomes; LDL-C = calculated low density lipoprotein cholesterol; LVH = left ventricular hypertrophy; N/A = not applicable; SGLT2i = sodium-glucose cotransporter-2 inhibitor; T2DM = type 2 diabetes mellitus; USPSTF = US Preventive Services Task Force.

Continued on the next page

is based on the Scottish Intercollegiate Guidelines Network and the ADA Lifestyle Guidelines, which likewise describe a lack of evidence for this practice.[20,21] There is no such recommendation from ACC/AHA, AACE/ACE, or KDIGO given lack of randomized control trial evidence for this practice.

The USPSTF recommends a healthy diet (left undefined) and physical activity for individuals with, or at risk for T2DM, but unlike other societies, does not provide specific guidance on types of food or duration of activity, as individuals with T2DM were excluded from their behavioral counseling intervention document.[3,22] The USPSTF Guidelines do reference the Guide to Community Preventive Services, which provides some advice for implementation of lifestyle change across a population.[23,24]

BLOOD PRESSURE MANAGEMENT

There are some notable differences in recommendations across societies for blood pressure targets and treatment strategies in individuals with T2DM, reflecting inconsistent evidence as to optimal management. The ACC/AHA, AACE/ACE, and ESC/EASD recommend a blood pressure goal of <130/80 mm Hg for all-comers with T2DM.[6-8] The ADA recommends

TABLE 1 Continued

AACE/ACE[5,6]	ESC/EASD[7]	USPSTF[1-3]	KDIGO[10,11,33]
Framingham Risk Assessment Tool and risk factors	Moderate, high, very high risk	Pooled Cohort Equation	No recommendation
150 min of moderate-intensity activity per week	150 min of moderate-intensity activity per week	No specific recommendation	150 min of moderate-intensity activity per week
Individualized nutrition assessment; Mediterranean Diet	Individualized nutrition assessment; Mediterranean Diet	No specific recommendation	Individualized nutrition assessment; Mediterranean Diet, 0.8 g protein/day if CKD
No recommendation	Avoid vitamin supplementation to reduce ASCVD risk in T2DM	No recommendation	No recommendation
<130/80 mm Hg	<130/80 mm Hg, (but not <120/70 mm Hg), and 130-139 mm Hg in those older than 65 y	<120/80 mm Hg only for stroke risk reduction	<120/80 mm Hg if concurrent CKD
Angiotensin-converting enzyme/ARB	Angiotensin-converting enzyme/ARB if albuminuria or LVH	No recommendation	Angiotensin-converting enzyme/ARB if albuminuria
If BP >150/100 mm Hg	If BP >160/100 mm Hg	No recommendation	No recommendation
Numeric goal (LDL-C <55, 70, or 100 mg/dL)	Numeric goal (LDL-C <55, 70, or 100 mg/dL)	N/A	N/A
No recommendation	Treat if LDL-C > 100 mg/dL	N/A	N/A
LDL-C <55 mg/dL	LDL-C < 55mg/dL	N/A	N/A
No recommendation	Ezetimibe	N/A	N/A
SGLT2i/GLP-1RA may be beneficial regardless of background metformin	SGLT2i/GLP-1RA first line	No recommendation	Metformin and SGLT2i in combination for those with CKD
SLGT2i >GLP-1RA for HF and renal disease	No specific recommendation	No recommendation	SGLT2 inhibitor first, GLP-1RA second line
No recommendation	Not in moderate risk, but can be considered in high or very high risk	No significant risk reduction with aspirin in individuals with T2DM	May be considered if elevated ASCVD risk without increased bleeding risk
SGLT2i	SGLT2i	No recommendation	SGLT2i

risk-based treatment, targeting a blood pressure goal <130/80 mm Hg if 10-year ASCVD risk ≥15% and a goal of <140/90 mm Hg if 10-year ASCVD risk <15%.[4] The USPSTF does not provide a specific target, but suggests there is limited evidence for intensive control (<120/80 mm Hg) with the exception of reduced risk of incident stroke.[3] The KDIGO Guidelines do not offer a target for individuals with T2DM generally, but do support a blood pressure goal of <120/80 mm Hg for those with concurrent chronic kidney disease (CKD).[11] The ESC/EASD includes 1 notable caveat to their blood pressure targets, which is not explicitly listed in other recommendations.[4,7,8] The ESC/EASD recommends a more liberal systolic blood pressure target of 130-139 mm Hg in those with T2DM who are older than 65 years.

Differences in blood pressure treatment goals for patients with T2DM have arisen as a result of conflicting evidence and variation in trial design. Results of meta-analyses of randomized clinical trial data have suggested optimal benefit with blood pressure targets <130/80 mm Hg,[25-27] particularly for stroke risk reduction in individuals with T2DM.[28] The ACC/AHA and ESC/EASD base their recommendations on this evidence.[7,8] The ADA, on the other hand, uses an individualized approach for blood pressure targets, with the rationale that those at highest risk can derive more benefit from tighter control.[29,30]

With regard to blood pressure treatment strategies, the ADA, ACC/AHA, AACE/ACE, EASC/EASD, and KDIGO recommend lifestyle modification for individuals with T2DM and hypertension.[4,6-8,31] This includes weight loss, increasing physical activity,

reducing sodium intake, avoiding excess alcohol, and increasing consumption of fruits and vegetables. All of these societies support the use of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers (ARBs), calcium-channel blockers, and diuretics for the treatment of hypertension to their respective targets. Similarly, all of these societies recommend angiotensin-converting enzyme inhibitors and ARBs as first-line therapy for individuals with T2DM, hypertension, and albuminuria. The ESC/EASD notably includes left ventricular hypertrophy in addition to albuminuria as an indication for angiotensin-converting enzyme inhibitor or ARB as a first-line blood pressure agent,[7] and the ADA specifically includes history of coronary disease as an indication for angiotensin-converting enzyme inhibitor or ARB.[4] The USPSTF does not make any specific treatment recommendations for blood pressure management in individuals with T2DM.

There are some differences between society guidelines regarding the need for combination therapy. Although the ACC/AHA, AACE/ACE, EASD/ESC, and ADA acknowledge that many patients with T2DM and hypertension will require >1 medication for optimal blood pressure control, there are some differences in the threshold to initiate a second agent. The ADA recommends 2 agents if baseline blood pressure is >160/100 mm Hg.[4] The ACC/AHA recommends 2 agents for stage 2 hypertension, defined as blood pressure >140/90 mm Hg.[31] The AACE/ACE recommends 2 agents for blood pressure >150/100 mm Hg.[6] The ESC/EASD, on the other hand, recommends dual therapy as first line regardless of blood pressure.[7] All of these societies recommend an angiotensin-converting enzyme inhibitor or ARB with a calcium-channel blocker or a diuretic when combination therapy is indicated, and all recommend against using angiotensin-converting enzyme inhibitor and ARB simultaneously.[4,7,31] Neither the KDIGO nor USPSTF Guidelines make specific recommendations about combination therapy.

RECOMMENDATIONS FOR LDL-C MANAGEMENT

Although LDL-C management recommendations are mostly consistent among guidelines, there are some important differences in treatment targets and chosen therapies for both primary and secondary prevention. The ADA recommendations are generally aligned with the ACC/AHA, as their 2018 cholesterol management guidelines are specifically referenced in the ADA document.[4,32] The ESC/EASD and AACE/ACE Guidelines favor lower LDL-C targets. The KDIGO lipid guidelines, published in 2013, and the USPSTF Guidelines, published in 2016, were excluded from this comparison, as they rely on a different body of evidence.[1,33]

In both the ACC/AHA and ADA documents, the recommendations for statin therapy for primary prevention is driven by 10-year ASCVD risk score, and the goal of treatment, when noted for those at higher risk, is percent LDL-C lowering, rather than a specific numeric target.[4,32] Both the ACC/AHA Guidelines and the ADA Guidelines recommend moderate-intensity statin therapy for all individuals with T2DM, with high-intensity statin for those with multiple ASCVD risk factors. The ESC/EASD and AACE/ACE, on the other hand, outline specific LDL-C treatment goals for those at moderate, high, or very high CV risk (LDL-C <100 mg/dL, LDL-C <70 mg/dL, and LDL-C <55 mg/dL, respectively), with statins as first-line agents for lipid lowering.[6,7] Age-specific recommendations for primary prevention are also different between societies. The ACC/AHA and ADA recommend LDL-C lowering therapy in younger patients aged 20-39 years at high risk, specifically those with longstanding disease, evidence of end-organ damage, or additional ASCVD risk factors. In contrast, the ESD/EASD has a much lower threshold for treatment of younger patients, as they are included within the moderate-risk category (younger than 50 years) even without longstanding disease or additional risk factors. The AACE/ACE does not specify age cutoffs for use of lipid-lowering therapy.[6]

All societies recommend high-intensity statin therapy for secondary prevention in individuals with T2DM, although the treatment goals and medication recommendations differ. Although each recommends at least 50% LDL-C lowering for secondary prevention, the ACC/AHA and ADA target an LDL-C <70 mg/dL, whereas the ESC/EASD and the AACE/ACE target an LDL-C <55 mg/dL.[4,6,7,32] Though all guidelines recommend escalation of therapy if their respective LDL-C targets are not met, there are some differences in the stepwise approach. The ACC/AHA and the ESC/EASD clearly recommend addition of ezetimibe first if LDL-C treatment goals are not met on maximally tolerated statin therapy. The ADA recommends either ezetimibe or PCSK-9 inhibitors for this clinical scenario, although acknowledges ezetimibe may be preferred due to lower cost. The AACE/ACE does not offer a specific recommendation on which agent to prioritize. The variability in the recommendations likely reflects the lack of evidence, as no randomized trial has specifically compared one strategy over another nor randomized patients to different LDL-C targets.[32]

CARDIOVASCULAR EFFECTS OF NOVEL AGENTS

The advent of SGLT2i and selected GLP-1RA has changed the landscape of CV risk reduction in patients with T2DM.[3,4] These agents receive strong recommendations in the ADA, ACC/AHA, AACE/ACE, and ESC/EASD, especially in those at high risk of CV disease for their CV benefits, independent of effects on glucose control. The USPSTF, despite a recent guideline update in 2021, does not make a specific recommendation about either of these classes of medication.[3] The KDIGO guidelines strongly support use of SGLT2i and certain GLP-1RAs for cardiovascular and kidney risk mitigation independent of glucose control considerations; however, their recommendations are limited to patients with underlying CKD and are addressed later in this article in the section "T2DM and CV Risk in Patients With CKD."

The ADA, ACC/AHA, AACE/ACE, and ESC/EASD recommend SGLT2i or GLP-1RA for CV risk reduction in those with T2DM and CVD or at high CV risk, based on the results of multiple clinical trials showing CV benefit with these medications.[4,6,7,9] All of these societies allow for use of SGLT2i and GLP-1RA independent of background metformin for individuals at increased CV risk. This reflects evolving evidence surrounding these novel agents and metformin use. The cardioprotective effects of SGLT2i and GLP-1RA in the completed CV outcomes trials were independent of changes in HbA1c and background medication use, underpinning recommendations for these agents regardless of need for additional glycemic control and background antihyperglycemic medication use.[35,36]

The guidelines differ, however, in the relative priority of SGLT2i and GLP-1RA. Both the ACC/AHA and ADA recommend SGLT2i over GLP-1RA for those with heart failure and those with kidney disease.[37-39] The ACC/AHA also emphasizes GLP-1RA over SGLT2i for those prioritizing weight loss. The ESC/EASD does not give specific guidance about which agent with proven CV efficacy to start first, but simply notes that selected members of both classes reduce CV events for those with CV disease or those at high risk.[7] All 3 societies allow for SGLT2i and GLP-1RA to be used in combination if needed for additional HbA1c lowering. Because the ESC/EASD recommends either SGLT2i or GLP-1RA as first-line therapy, these guidelines recommend the addition of metformin second, with the remaining novel agent third if needed. The optimal sequence of medication addition has not yet been studied.

ASPIRIN

All societies support the use of aspirin for secondary prevention of ASCVD in patients with T2DM.[4,6-8,40] The recommendations for aspirin for primary prevention are more controversial. Although most societies recommend against routine use of aspirin in primary prevention, each delineates a small population in which it may be considered. The ACC/AHA, ADA, and KDIGO guidelines suggest that low-dose aspirin may be considered for those at elevated ASCVD risk, who are not at increased risk of bleeding. Both the ACC/AHA and ADA provide a similar list of risk factors to identify those who may derive the most benefit, specifically individuals older than 50 years, with a strong family history of ASCVD, or with uncontrolled comorbidities, such as hypertension, hyperlipidemia, tobacco use, or CKD. The ACC/AHA and the ADA also mention the use of coronary artery calcium scoring to inform this decision.[41] The ESC/EASD guidelines, on the other hand, use their risk categories (moderate, high, or very high risk) to define the population for which primary prevention aspirin can be considered. The ESC/EASD specifically does not recommend aspirin for those at "moderate" risk. Low-dose aspirin can be considered for those at "high" or "very high" risk, meaning, those with longstanding T2DM (≥10 years' duration), those with target organ damage, or those with 3 or more CV risk factors (age, hypertension, dyslipidemia, smoking, obesity). Although all 3 of these societies are cautious to endorse aspirin only for those at increased ASCVD risk, this population definition varies according to the method of risk stratification. The AACE/ACE does not offer guidance regarding the use of aspirin in individuals with T2DM.[6] The USPSTF guidelines do not specifically reference use of aspirin in individuals with T2DM.[3] Their recommendations for aspirin in general support its use in adults of 50-59 years with a 10-year ASCVD risk >10%.[2]

T2DM AND CV RISK IN PATIENTS WITH CKD

Individuals with T2DM and comorbid CKD represent a unique and high-risk population. The ESC/EASD, ADA, and KDIGO guidelines highlight the increased CV risk in those with CKD (persistent eGFR <60 mL/min/1.73 m^2 and/or albuminuria >30 mg/g creatinine) and T2DM.[42] As such, each society recommends at least yearly screening of eGFR and urinary albumin for individuals with T2DM.[6,7,10,43] All society recommendations endorse SGLT2i for both kidney and CV benefit in those with T2DM and CKD provided

eGFR ≥30 mL/min/1.73 m^2. The ADA and AACE/ACE guidelines recommend use of specific SGLT2i with definitive evidence for kidney outcomes benefit in this population.[6,43-45] GLP-1RAs are recommended as second-line therapy by all societies, with the ESC/EASD providing only a Class IIa recommendation for these agents.[6,7,10,39,43] Although GLP-1RAs have demonstrated some benefit on intermediate markers of kidney risk and disease in CV outcomes trials, specifically reduction in albuminuria,[46,47] dedicated randomized trials of GLP-1RAs for kidney outcomes are forthcoming.[48]

CONCLUSIONS

Guidelines and consensus recommendations for cardiovascular risk reduction in T2DM are generally aligned across professional societies. There remain some notable differences with regard to risk stratification, LDL-C, and blood pressure treatment targets, and optimal use of SGLT2i and GLP-1RA; however, these are minor, reflecting variation in interpretation of the evidence and rapidly progressing updates in clinical research. As the field of CV risk reduction in T2DM has grown exponentially over the past decade, professional societies have generally remained aligned as to how to provide optimal care of these high-risk individuals.

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