A focused review of cardiovascular guideline related recommendations for the primary care physician in the USA

Omar Sheikh^a, Mouhamed Nashawi^a, Ayman Battisha^b and Robert Chilton^a

Primary care physicians in the USA serve the critical role of first contact for undiagnosed or mismanaged pathologies as well as providers of continuous care in multiple communities. Their scope of practice is broad from medication reconciliation to coordinating specialty care and even performing office procedures. Primary care physicians in the USA commonly encounter patients with diabetes and associated comorbidities related to prolonged insulin resistance. Mainly these include heart failure exacerbation or major adverse cardiovascular events. The demanding roles primary care physicians serve may render these providers encumbered to navigate through long, verbose and dynamic guidelines related to managing diabetes and cardiac diabetology sequelae. Our aim is to compose current, prominent evidence-based points from American medical societies such as the American College of Cardiology/American Heart Association and the American Diabetes Association

central to lifestyle modifications, antiplatelet therapy, anti-hyperglycemic and SGLT2-inhibitor utilization, hypertension, dyslipidemia, and heart failure screening in a way that is both succinct and valuable to primary care physicians. *Cardiovasc Endocrinol Metab* 9: 36–41 Copyright © 2020 Wolters Kluwer Health, Inc. All rights reserved.

Cardiovascular Endocrinology & Metabolism 2020, 9:36–41

Keywords: cardiovascular, diabetes, guidelines, hypertension, preventive, primary care physician, SGLT2 inhibitors

^aDivision of Medicine–Cardiology, UT Health San Antonio, San Antonio, Texas and ^bDepartment of Internal Medicine, University of Massachusetts Medical School-Bay State, Springfield, Massachusetts, USA

Correspondence to Mouhamed Nashawi, BS, University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, Mail Code 7872, San Antonio, TX 78229, USA
E-mail: nashawi@livemail.uthscsa.edu

Received 9 November 2019 Accepted 23 December 2019

Introduction

Diabetes mellitus (DM) has a profound financial impact on the US healthcare system and economy, affecting over 30.3 million Americans with a national economic burden of over \$400B according to recent analyses conducted by the Center for Disease Control and the American Diabetes Association (ADA), respectively [1,2]. In the USA, primary care physicians (PCPs) are usually the principal and extended providers who help patients manage their hyperglycemia, with referrals to specialists usually reserved for complex pathophysiological presentations or acute comorbidities. PCPs also generally see patients for a wide array of health problems, providing a critical role for comprehensive patient care. However, there is still a gap in glycemic control of complex patients and the availability of guidelines for management of such cases [3]. This is partially due to the density of specialty specific guidelines in the literature, the burden PCPs face with large patient volumes, and a gap in proclivity due to missed opportunity in practice. We seek in this work to distill the most recent evidence-based guidelines established by the ADA, American Heart Association (AHA), and American College of Cardiology (ACC) regarding multifactorial care for diabetic patients in a palatable form for PCPs to maintain the durability and duration of the PCP to diabetic patient relationship. These areas draw from management of comorbidities, mitigation of adverse health events, and preventive medicine. Specifically, we have chosen to select concise guidelines pertinent to

lifestyle modifications, the use of antiplatelet therapy, pharmacotherapeutic management of diabetes with an emphasis on SGLT2 inhibitor utilization, blood pressure (BP) levels, dyslipidemia, and heart failure (HF) screening (Figs. 1–3).

Cardiovascular diabetology recommendations

Lifestyle changes and risk assessment

- (1) Initiation of an exercise program has been shown to significantly reduce HbA1c by up to 0.7 points in a meta-analysis. Exercise programs comprised of both resistance training and aerobic exercise have been shown to be more effective than either training alone [4].
- (2) Type 2 diabetic patients should perform at least 150 minutes of moderate-intensity exercise per week or 75 minutes of vigorous exercise weekly to lower Atherosclerotic Cardiovascular Disease (ASCVD) risk factor and improve glycemic control [4].
- (3) Per the ACC/AHA guidelines, it is suggested that patients without type 2 DM (T2DM), race and sex specific pooled cohort equation (ASCVD Risk Estimator Plus) to estimate 10-year ASCVD risk for asymptomatic adults aged 40–79 years should be used [4]. Adults should be categorized into low (<5%), borderline (5 to <7.5%), intermediate (≥7.5 to <20%), or high (≥20%) 10-year risk [4].

Fig. 1

Recommendations for treatment based on blood pressure stratified by CV risk, adapted from the 2019 ACC/AHA HTN guidelines [15]. ^αThe presence of CKD or T2DM automatically places patients in the high-risk category. If RAAS inhibitors or diuretic pharmacotherapy is deemed to be a viable option for these patients, laboratory workup within 4 weeks of therapy initiation is recommended (basic metabolic panel or functional equivalent) [18]. ^βStage 2 hypertension preferably should be managed with 2 medications of different classes [18,19]. ACC, American College of Cardiology, AHA, American Heart Association, CKD, Chronic Kidney Disease, CV, Cardiovascular, HTN, hypertension.

Fig. 2

Management of Dyslipidemia Stratified by Age, Risk, and Lipid Profile

Assessment guides for the primary prevention of ASCVD risk factors, adapted from the ACC/AHA [15]. *Class IIA scoring for evidence-based recommendations are based on data compiled from multiple randomized clinical trials and the weight of evidence or opinion is in favor of therapeutic efficacy. It is assumed to be a reasonable pursuit to perform these procedures or treatments [20]. ACC, American College of Cardiology, AHA, American Heart Association, ASCVD, Atherosclerotic Cardiovascular Disease.

- (4) Preventive therapy is uncertain for individuals with borderline or intermediate estimated 10-year risk. These patients may benefit from stratification of coronary artery calcium, with shared decision-making as the central role in primary prevention strategies between providers and patients [4].
- (5) Younger adults aged 20–59 may benefit from classification of health status based on estimated lifetime risk [4].
- (6) Mediterranean diets have been linked with reductions in stroke, but no significant improvements over control for mortality or lifetime myocardial infarction prevalence [5].

Fig. 3

Assessment guides for the workup of HF in patients, adapted from the ACC/AHA/Heart Failure Society of America (HFSA) 2017 Guidelines on the Management of HF [17]. ^ψStage A HF is defined by the ACC/AHA as patients who are at risk for HF but have not yet developed cardiovascular remodeling, whereas stage B HF is defined by the presence of structural heart disease such as left ventricular hypertrophy, but do not show clinical symptoms of HF. Stages C and D encompass patients who have developed clinical HF and patients with refractory HF necessitating invasive interventions, such as pacemaker implantation [21,22]. ^φAcute decompensated HF. ^λNew York Heart Failure Association classification deems stage II as HF with slight limitation of physical activity and stable at rest, stage III as marked limitation of physical activity and stable at rest, and stage IV as unable to carry physical activity without symptomatic discomfort [23]. [†]Class of recommendation. *Markers include galectin-3 and ST2 receptor, among others [24,25]. Multiple biomarkers may be more useful than single biomarkers [26]. ACC, American College of Cardiology, AHA, American Heart Association, HF, heart failure, HFSA, Heart Failure Society of America.

Aspirin use

- (1) Low-dose aspirin (75–100 mg orally daily) might be considered for the primary prevention of ASCVD among select adults 40–70 years of age who are at higher ASCVD risk but do not exhibit an increased risk of bleeding (class IIb) [4].
- (2) Class III (HARM): low-dose aspirin (75–100 mg orally daily) should not be administered on a routine basis for the primary prevention of ASCVD among adults >70 years of age [4].
- (3) Aspirin therapy (75–162 mg/d) in patients with T2DM and a history of atherosclerotic CV disease

is recommended as a secondary prevention factor of adverse cardiac events per the ADA. Patients allergic to aspirin should receive Clopidogrel (75 mg/d) instead [6].

- (4) Per the ADA, Aspirin is recommended as a primary prevention strategy of adverse cardiac events in patients with diabetes who are ≥50 years but without established atherosclerotic disease and at least one of the following [6]:
 - (a) Family history of premature ASCVD
 - (b) Hypertension
 - (c) Dyslipidemia
 - (d) Smoking
 - (e) CKD with or without albuminuria

Providers should exercise caution in using aspirin as a primary prevention strategy of preventing adverse cardiac events in the latter population if they have a diagnosis of anemia or renal disease due to the increased risk of increased bleeding and analgesic nephropathy, respectively.

- (1) The ACC/AHA 2019 guidelines recommend against the frequent use of aspirin in the routine use of primary prevention of ASCVD due to the lack of shown benefit-clinical judgment on a patient by patient basis should be used by PCPs when considering antiplatelet therapy in patients [4].

Metformin, then consider SGLT-2 inhibitors and GLP-1s

- (1) SGLT2 inhibitors are recommended as a treatment option in patients with T2DM (defined as HbA1c >6.5%) and an established increased ASCVD per the 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease, with Empagliflozin showing reduction in CV death [4,7]. Other SGLT2 inhibitors have shown significant reduction in three-point major adverse cardiovascular events (MACE). DAPA-HF found a significant reduction in a composite of worsening HF (hospitalization or an urgent visit resulting in intravenous therapy for HF) or cardiovascular death in diabetes and non-diabetes patients with EF <40% [8].
- (2) SGLT-2 inhibitors and GLP-1 agonists both have been demonstrated to reduce CVD events in adults with T2DM and high ASCVD risk [6].
- (3) The Glucagon-like peptide-1 receptor (GLP-1R) agonists increase insulin while decreasing glucagon production, increase peripheral glucose uptake, and decrease hepatic glucose production. GLP-1R agonists have been found to significantly reduce the risk of ASCVD events in adults with T2DM at high ASCVD risk. In patients with T2DM and additional risk factors for CVD, it may be reasonable to initiate these two classes (SGLT2 inhibitor/GLP-1R) of medications for primary prevention of CVD [4].
- (4) The ADA recommends the use of the SGLT2 inhibitors in patients who are at risk for HF or currently have HF [7].
- (5) The ADA has suggested that SGLT2 inhibitors are appropriate next options for pharmacotherapy in patients who experience CV disease in the context of T2DM and an inadequate clinical response to GLP-1 agonists [7].
- (6) The American Association of Clinical Endocrinologists (AACE) supports the use of SGLT2 inhibitors for further reduction in systolic BP in hypertensive T2DM patients [9].
- (7) Per the AACE/American College of Endocrinology (ACE), it is recommended that PCPs counsel patients on stopping SGLT-2 inhibitors 24–48 hours before surgical procedures and metabolically demanding activities such as marathons to prevent euglycemic diabetic ketoacidosis [9–11].

- (8) An updated position from the ADA in 2019 proposes the consideration of SGLT-2 inhibitors in patients with diabetic kidney disease with an eGFR ≥ 30 ml/min/1.73 m² [12], however the FDA has a higher eGFR cutoff.
- (9) Patients who took GLP-1 in clinical trials mostly had established CVD at baseline, however the reduction in HF hospitalization in general was NS.
- (10) As opposed to reduction in HF with SGLT-2 inhibitors, the benefit of the GLP-1R agonists has been a reduction in ASCVD events though the majority of patients studied had established CVD.

Hypertension

- (1) Per the ADA, patients with T2DM and HTN should be treated to a BP target of <140/90 mmHg [6], however lower targets have been suggested in very high risk factor patients, such as diabetics.
- (2) Per the ADA, patients T2DM and HTN should be treated with agents proven to reduce cardiovascular events (ACE-I, ARBs, thiazide-like diuretics, or dihydropyridine CCBs) [13].
- (3) Per the ACC/AHA, patients with T2DM and HTN should be treated to a BP target of <130/80 mmHg [4]. In adults with T2DM and hypertension, antihypertensive drug treatment should be initiated at a BP of 130/80 mmHg or higher, with a treatment goal of less than 130/80 mmHg.
- (4) Lowering SBP <120 mmHg has not been shown to reduce the rate of fatal and non-fatal MACE, and has been associated with a greater risk of adverse events, such as self-reported hypotension, and a reduction in eGFR [14].
- (5) The only ACC/AHA recommendation for race specific pharmacotherapy is for African Americans without HF or CKD and do not meet criteria for two-drug therapy, and they should be started either on a thiazide-like diuretic or calcium agonist. ACE-Inhibitors or ARBs should be initially prescribed in African Americans with HF or CKD [15].

Lipids

- (1) Patients with T2DM under the age of 40 with an increased ASCVD risk who have persistent low-density lipoprotein (LDL) ≥ 70 mg/dl (1.8 mmol/L) despite maximal statin dose should be considered for alternative LDL lowering therapy (ezetimibe or PCSK-9 inhibitors) [13].
- (2) In adults with T2DM who have multiple ASCVD risk factors, it is reasonable to prescribe high-intensity statin therapy with the aim to reduce LDL-C levels by 50% or more [16].
- (3) In adults 40–75 years of age with diabetes, regardless of estimated 10-year ASCVD risk, moderate- intensity statin therapy is indicated [16].

- (4) Adults with T2DM with multiple ASCVD risk factors, should be considered for high-intensity statin therapy with the aim to reduce LDL-C levels by 50% or more [16].
- (5) Patients with diabetes have a higher lifetime risk than those without diabetes, and would benefit from high-intensity statin therapy as they develop risk modifiers (i.e. duration of T2DM for >10 years, albuminuria, retinopathy) [4].
- (6) The occurrence of a first ASCVD event in patients 40–75 years of age with diabetes is associated with increased morbidity and mortality compared with those without diabetes, which places a particularly high premium on primary prevention in individuals with diabetes in that age range [16].
- (7) Combination therapy of statins and niacin has not shown to be beneficial in providing additional cardiovascular protection in patients with T2DM relative to statins alone, and may increase the risk of stroke per ADA [13].
- (8) Patients who are between the ages of 40–75 with T2DM and an LDL ≥ 70 mg/dl (1.8 mmol/L), should be treated with statins without calculating 10-year ASCVD risk [16].

Brain Natriuretic Peptide

- (1) Patients with an HgbA1c >6.5% and shortness of breath of unknown etiology may benefit from brain natriuretic peptide (BNP) screening due to increased risk for HF. Patients with BNP ≥ 50 ng/L should seek referrals to cardiovascular specialists for potential echocardiography [17]. Patients who are screened with BNP measurements and receive subsequent personal education on preventive measures have better long-term outcomes relative to those without BNP screening and education.

Exercising clinical prudence

The following figures are meant to give concise outlines for general recommendations on managing cardiovascular status within patients, based on recent clinical and evidence-based guidelines (Table 1). However, judgement by physicians is encouraged in patients whose clinical picture does not fit concisely into a delineated category, or if patient intrinsic factors call for modulation of therapy (cost, compliance, etc.).

Table 1 Risk-factors of cardiovascular disease) and diabetic exacerbation given mutually exclusive risk factors, adapted from Grundy et al. [16]

Retinopathy or nephropathy secondary to prolonged insulin resistance
Ankle to brachial index <0.9 (warrants consult for vascular disease)
Chronic T2DM (≥ 10 years for T2DM, ≥ 20 years for T1DM)
eGFR <60 ml/min/1.73 m ²
Albuminuria (defined as loss of protein in the urine set at ≥ 30 μ g albuminuria per mg of creatine)

Discussion

The role of the PCP in maintaining the figurative lattice of health care access in the US is paramount. These providers serve as the initial provider for millions of individuals and subsequently serve as conduits to channel patients with more complex presentations to specialized health care systems to receive cases which may be more demanding or require more resources when they are transiently more ill than baseline. However, the PCP is also equipped with the capacity to manage a broad spectrum of clinical problems independently, while also sometimes serving an auxiliary role in guiding patients through social barriers. This burden may have the unintended consequence of acting as a rift between PCPs and access to the dense architecture of ever-changing evidence-based clinical guidelines. A common pathology PCPs encounter is diabetes with accompanying clinical sequelae related to cardiac diabetology. In this work, we sought to distill salient points of cardiac diabetology and the management of diabetic sequelae with cardiovascular considerations derived from current American guidelines recommended by the AHA, ACC, ADA, and collaborations with the latter institutions. Topics included in this compilation included lifestyle modifications, antiplatelet therapy usage, anti-hyperglycemic and SGLT2 inhibitor utilization, management of ASCVD risk factors such as hypertension and dyslipidemia, and the clinical work-up of HF. It should be noted that these are merely recommendations used to guide and supplement clinical judgement and reason, and that the astute PCP who is knowledgeable about their individual patients, community, or institutions on a more familiar basis may modulate them to better serve their patient populations. These include, but are not limited to, awareness of compliance capability, insurance status, and the patient’s right to play a role in the clinical decision-making process. Nevertheless, it is our anticipation that this focused review has familiarized providers with recent cardiovascular guideline related recommendations with an emphasis on the hyperglycemic patient.

References

1 Control CfD, Prevention %J Atlanta GCfDC, Prevention UDoH, Services H. National diabetes statistics report, 2017. 2017.

2 Dall TM, Yang W, Gillespie K, Mocarski M, Byrne E, Cintina I, et al. The economic burden of elevated blood glucose levels in 2017: diagnosed and undiagnosed diabetes, gestational diabetes, and prediabetes. *Diabetes Care* 2019; **42**:1661–1668.

3 Rushforth B, McCrorie C, Glidewell L, Midgley E, Foy R. Barriers to effective management of type 2 diabetes in primary care: qualitative systematic review. *Br J Gen Pract* 2016; **66**:e114–e127.

4 Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease. *Circulation* 2019; **140**:e596–e646.

5 Agarwal A, Ioannidis JPA. PREDIMED trial of mediterranean diet: retracted, republished, still trusted? *BMJ* 2019; **364**:i341.

6 Diabetes ADAJC. Standards of medical care in diabetes–2019 abridged for primary care providers. *Clin Diabetes* 2019; **37**:11–34.

7 Das SR, Everett BM, Birtcher KK, Brown JM, Cefalu WT, Januzzi JL Jr, et al. 2018 ACC expert consensus decision pathway on novel therapies

- for cardiovascular risk reduction in patients with type 2 diabetes and atherosclerotic cardiovascular disease. A report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways. *J Am Coll Cardiol* 2018; **72**:3200–3223.
- 8 McMurray JJ, Solomon SD, Inzucchi SE, Køber L, Kosiborod MN, Martinez FA, *et al.* Dapagliflozin in patients with heart failure and reduced ejection fraction. *N Engl J Med* 2019; **381**:1995–2008.
 - 9 Garber AJ, Abrahamson MJ, Barzilay JI, Blonde L, Bloomgarden ZT, Bush MA, *et al.* Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the comprehensive type 2 diabetes management algorithm—2019 executive summary. *Endocr Pract* 2019; **25**:69–100.
 - 10 Umpierrez GE. Diabetes: SGLT2 inhibitors and diabetic ketoacidosis—a growing concern. *Nat Rev Endocrinol* 2017; **13**:441–442.
 - 11 Erondy N, Desai M, Ways K, Meininger G. Diabetic ketoacidosis and related events in the canagliflozin type 2 diabetes clinical program. *Diabetes Care* 2015; **38**:1680–1686.
 - 12 Care ADAJD. 11. Microvascular complications and foot care: standards of medical care in diabetes—2019. *Diabetes Care* 2019; **42**:S124–S138.
 - 13 Care ADAJD. 10. Cardiovascular disease and risk management: standards of medical care in diabetes—2019. *Diabetes Care* 2019; **42**:S103–S123.
 - 14 O'Connor EC, Wang J, Gibney KD, Yu X, Young GR, Jones T, *et al.* Lowering systolic blood pressure does not increase stroke risk: an analysis of the SPRINT and ACCORD trial data. *Ann Clin Transl Neurol* 2019; **6**:144–153.
 - 15 Flack JM, Adekola B. Blood pressure and the new ACC/AHA hypertension guidelines. 2019; pii:S1050–1738.
 - 16 Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, *et al.* 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2019; **73**:e285–e350.
 - 17 Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Colvin MM, *et al.* 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. *Circulation* 2017; **70**:776–803.
 - 18 Carey RM, Whelton PK; 2017 ACC/AHA Hypertension Guideline Writing Committee. Prevention, detection, evaluation, and management of high blood pressure in adults: synopsis of the 2017 american college of cardiology/american heart association hypertension guideline. *Ann Intern Med* 2018; **168**:351–358.
 - 19 Rutecki GWJH. Combination hypertension Rx: why wait? *Drugs context* 2018; **7**:212531.
 - 20 Gibbons RJ, Smith S, Antman E; American College of Cardiology; American Heart Association. American college of cardiology/american heart association clinical practice guidelines: part I: where do they come from? *Circulation* 2003; **107**:2979–2986.
 - 21 Daniels LB, Clopton P, Jiang K, Greenberg B, Maisel AS. Prognosis of stage A or B heart failure patients with elevated B-type natriuretic peptide levels. *J Card Fail* 2010; **16**:93–98.
 - 22 Kemp CD, Conte JV. The pathophysiology of heart failure. *Cardiovasc Pathol* 2012; **21**:365–371.
 - 23 Fisher JD. New York heart association classification. *Arch Intern Med* 1972; **129**:836.
 - 24 de Boer RA, Lok DJ, Jaarsma T, van der Meer P, Voors AA, Hillege HL, van Veldhuisen DJ. Predictive value of plasma galectin-3 levels in heart failure with reduced and preserved ejection fraction. *Ann Med* 2011; **43**:60–68.
 - 25 Manzano-Fernández S, Mueller T, Pascual-Figal D, Truong QA, Januzzi JL. Usefulness of soluble concentrations of interleukin family member ST2 as predictor of mortality in patients with acutely decompensated heart failure relative to left ventricular ejection fraction. *Am J Cardiol* 2011; **107**:259–267.
 - 26 Lassus J, Gayat E, Mueller C, Peacock WF, Spinar J, Harjola VP, *et al.*; GREAT-Network. Incremental value of biomarkers to clinical variables for mortality prediction in acutely decompensated heart failure: the multinational observational cohort on acute heart failure (MOCA) study. *Int J Cardiol* 2013; **168**:2186–2194.