elsewhere. Evolocumab has recently been approved by the FDA for children aged 10 years and older. The reader is referred to Wiegman et al[77] and Goldberg et al[74] for excellent guidance on this important topic.

5.3. Adults With Diabetes and Without ASCVD and Baseline LDL-C <190 mg/dL on Statin Therapy for Primary Prevention (Figure 4)

Because primary prevention trials in large cohorts of individuals with diabetes demonstrate that moderate-intensity statin therapy provides significant cardiovascular outcomes benefit, the 2018 AHA/ACC/multisociety cholesterol guideline recommends that all adults aged 40-75 years with diabetes benefit from at least a moderate-intensity statin. Higher-risk subgroups of patients with diabetes (older patients, patients with additional ASCVD risk factors, albuminuria, retinopathy, long duration of diabetes, reduced eGFR <60 ml/min/1.73 m^2, neuropathy, ankle brachial index <0.9) are potential candidates for high-intensity statin therapy. Thus, all patients aged 40-75 years with diabetes should undergo assessment of 10-year ASCVD risk and comprehensive risk factor evaluation. Patients with diabetes have increased morbidity and mortality associated with a first cardiovascular event, making intensive prevention efforts even more critical.

5.3.1. Adults Aged 40-75 Years With Diabetes and Without Clinical ASCVD and Baseline LDL-C <190 mg/dL, on Statin Therapy for Primary Prevention (Figure 4)

For the small proportion of patients aged 40-75 years with diabetes who have 10-year predicted ASCVD risk <7.5% and no additional high-risk features, a high level of evidence supports the use of moderate-intensity statin therapy (anticipated LDL-C reduction 30%-49%).[79] In addition to adherence to appropriate lifestyle interventions, the use of soluble dietary fiber and phytosterols may also be considered.

If patients with diabetes and 10-year ASCVD risk <7.5% achieve inadequate lowering of LDL-C or non-HDL-C despite adherence to lifestyle recommendations and moderate-intensity statin therapy and have <30% to 49% reduction in LDL-C or LDL-C ≥100 mg/dL (or non-HDL-C ≥130 mg/dL), consideration of intensification of therapy is indicated. Due to the frequency of elevated non-HDL-C despite lower levels of LDL-C in patients with diabetes, non-HDL-C thresholds are important to consider in this high-risk patient population.

As a first step, routine clinical assessment and interventions are warranted (see **Section 3.3**). If the patient has now achieved the anticipated response to therapy, with a 30% to 49% reduction in LDL-C and LDL-C <100 mg/dL (or non-HDL-C <130 mg/dL), it is reasonable to continue current therapy and continue to monitor adherence to medications and lifestyle modifications and ongoing LDL-C response to therapy.

If, after these interventions, the patient still has <30% to 49% reduction in LDL-C or LDL-C ≥100 mg/dL (or non-HDL-C ≥130 mg/dL), the patient and clinician may consider increasing the statin dose to a high-intensity statin. If the patient has now achieved the anticipated response to therapy, it is reasonable to continue current therapy and continue to monitor adherence to medications and lifestyle modifications and ongoing LDL-C response to therapy.

If escalation to high-intensity statin therapy results in inadequate percent LDL-C reduction or LDL-C ≥100 mg/dL (or non-HDL-C ≥130 mg/dL), the clinician and patient should enter a discussion focused on shared decision-making regarding the addition of a nonstatin medication to the current regimen (see **Table 5**). If a decision is made to pursue no additional medication at this point, it is reasonable to continue current therapy and continue to monitor adherence to medications and lifestyle modifications and ongoing LDL-C response to therapy.

If escalation to high-intensity statin therapy results in inadequate percent LDL-C reduction or LDL-C ≥100 mg/dL (or non-HDL-C ≥130 mg/dL), ezetimibe 10 mg daily may be considered as the initial nonstatin agent for most patients when additional LDL-C lowering is desired. Although there is a gap in RCT evidence demonstrating outcomes benefits of using ezetimibe plus statin in primary prevention with diabetes, the writing committee supports ezetimibe as the preferred initial

FIGURE 4 Continued

*Diabetes-specific high-risk features include long duration (≥10 years for type 2 diabetes or ≥20 years for type 1 diabetes, albuminuria ≥30 mcg of albumin/mg creatinine, eGFR <60 mL/min/1.73 m^2, retinopathy, neuropathy, ankle-brachial index <0.9. †The writing committee emphasizes that these are not firm triggers for adding medication, but factors that may be considered within the broader context of an individual patient's clinical situation. ‡May consider a bile acid sequestrant as optional alternative agent if ezetimibe-intolerant and triglycerides <300 mg/dL. §Fasting triglycerides ≥150 mg/dL following a minimum of 4-12 weeks of lifestyle intervention, a stable dose of maximally tolerated statin therapy when indicated, as well as evaluation and management of secondary causes of hypertriglyceridemia. ‖Refer to 2021 ACC expert consensus decision pathway on the management of ASCVD risk reduction in patients with persistent hypertriglyceridemia: a report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol.* 2021;78(9):960-993.

ASCVD = atherosclerotic cardiovascular disease; ECDP = Expert Consensus Decision Pathway; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; RD/RDN = registered dietician/registered dietician nutritionist; SASE = statin-associated side effect