Gap #1: Statin medications are underutilized and often discontinued due to side effects. This results in residual risk of adverse cardiovascular events.
What is the evidence that this gap exists?
Although the clinical benefits of lowering LDL-C using statins have been repeatedly demonstrated, just over 50% of those in the US who would benefit from lipid lowering agents are on one. [CDC October 24, 2022] The results of an internet-based survey in 2012 showed that muscle related side effects were experienced by 60% and 25% of former and current statin users, respectively. [Cohen 2012] The same study showed that 62% of former statin users discontinued the medication due to side effects. [Cohen 2012] A study in the journal of clinical lipidology compared over 5,000 patients with statin intolerance to risk-matched patients who did not have statin intolerance. They found that patients with statin intolerance were less likely to meet LDL-C goals and more likely to require a revascularization procedure. [Graham 2017] The consensus statements of more than one professional society on the management of statin intolerance suggest that best practices include patient education, working up alternative causes of myalgia, as well as a regimen of discontinuing statin therapy and then re-challenging with the same medication. [Guyton 2014; Stroes 2015] If statin re-challenge is unsuccessful, the authors recommend trying at least two different statins. [Stroes 2015] While the above algorithm is cost effective and evidence-based, it presents a significant patient education hurdle.
What is the learning objective designed to address this gap?
IDENTIFY factors that lead to poor statin adherence and relevant management strategies.

Gap #2: Clinicians may be unaware of residual ASCVD risk in patients on maximally tolerated statin therapy, or of the importance of lowering LDL-C as much as is possible.
What is the evidence that this gap exists?
Several randomized controlled trials and meta-analyses have shown that the more a patient's LDL-C can be lowered, the less likely they are to have major cardiovascular adverse events. A 2010 meta-analysis by the Cholesterol Treatment Trialists (CTT) found that patients on more intensive statin regimens with correspondingly lower LDL-C levels had a significantly decreased risk of cardiovascular events compared to those on less intensive statin therapy. [CTT Collaboration 2010] These results were replicated by subsequent large meta-analyses that showed each mmol/L reduction in LDL-C results in a significant decrease in cardiac risk. [CTT Collaboration 2015; Silverman 2016] Combined with the evidence regarding underutilization and discontinuation of statin medications, it is not surprising that treatment with statins alone often inadequately reduces cardiac risk. A 2014 meta-analysis in the JACC found that >40% of patients on high-dose statin therapy were unable to reach guideline-recommended LDL-C targets of <70mg/dL. [Boekholdt 2014] RCTs of PCSK9 mAb medications alirocumab and evolocumab in 2018 and 2017 respectively both demonstrated the ability of those medications to significantly reduce LDL-C (by more than 50%) in the setting of maximally tolerated statin therapy. [Schwartz 2018; Sabatine 2017] Moreover, those trials showed lower rates of composite adverse outcomes including cardiac death, stroke, and MI.
What is the learning objective designed to address this gap?
SUMMARIZE data supporting residual ASCVD risk in statin patients unable to reach LDL-C goals.

Gap #3: Clinicians may be unfamiliar with recently updated 2022 guidelines on the role of nonstatin therapies in patients unable to achieve adequate risk reduction on statins alone

What is the evidence that this gap exists?
Clinicians may struggle to keep up with the results of recently published and ongoing clinical trials in order to guide their decision-making. In light of this, the ACC writing committee published an expert consensus update to the 2018 ACC/AHA guidelines focused on the use of nonstatin medications. [Writing Committee 2022] In considering the type of nonstatin treatment for patients unable to tolerate statins or achieve LDL-C goals on statins alone, the guidelines recommend a patient-focused approach with shared decision-making. [Writing Committee 2022] In discussing the addition of a PCSK9 mAb, inclisiran or bempedoic acid, clinicians and their patients are urged to consider the high costs of these newer medications. However, a notable difference between the 2018 and 2022 guidelines is that the 2018 guidelines recommended adding ezetimibe before considering any of the biologic medications, whereas the 2022 update state the following: "if patients [not reaching LDL-C goals for their group] require >25% additional lowering of LDL-C, a PCSK9 mAb may be preferred as the initial nonstatin agent. It is reasonable to engage in a clinician-patient discussion with consideration of net risk reduction benefits of a PCSK9 inhibitor, cost, administration by subcutaneous injection, every 14-day or monthly dosing schedule, and storage requirements (eg, refrigeration)." [Writing Committee 2022] The updated guidelines recommend including inclisiran and bempedoic acid in the shared decision-making discussion, but also recommend adding either ezetimibe or a PCSK9 mAb first if all other things are equal. This is due to the fact that RCTs have shown improvements in survival and cardiovascular event risks with the PCSK9 mAbs, whereas clinical outcome trials for inclisiran and bempedoic acid are still ongoing. [Schwartz 2018; Sabatine 2017; NCT03705234; NCT05030428; NCT02993406] However, reasons to consider inclisiran include less frequent dosing (every 6 months) as well as no need to self-inject (doses are clinician-administered). A reason to consider bempedoic acid, or the bempedoic acid/ezetimibe combination drug, is intolerance of injectable medications in patients with high LDL-C levels on maximally tolerated statins. [Writing Committee 2022]
What is the learning objective designed to address this gap?
APPLY evidence-based guidelines for the use of nonstatin treatments in patients with ASCVD and HeFH

Gap #4: There is a lack of consensus on when to select a PCSK9 inhibitor or bempedoic acid. Clinicians may be unaware of the factors to consider in shared decision-making discussions.
What is the evidence that this gap exists?
Despite the addition of the 2022 ACC expert consensus recommendations, there is not a clear-cut algorithm for when to select a particular PCSK9 inhibitor, ezetimibe, or bempedoic acid as an adjuvant to maximally tolerated statin therapy. For all the PCSK9 inhibitors and bempedoic acid, cost to the patient is an important consideration, as there are not generic alternatives available. [Hlatky 2017; Kazi 2016; Cannon 2017] For the PCSK9 mAbs and inclisiran, the patient's ability to tolerate treatment with subcutaneous injections is an important consideration. However, this is less so with inclisiran, which is dosed once every 6 months and is administered by a clinician, rather than dosing every two weeks with self-administration for the mAb medications. Another consideration is that there are not yet published results showing reduced cardiovascular risk with inclisiran and bempedoic acid, though clinical trials are underway. [NCT03705234; NCT05030428; NCT02993406] Two phase 3 clinical trials have clearly demonstrated the efficacy of bempedoic acid in patients with