Body System: Endocrine		
Session Topic: Customizing Diabetes Intensification Based Upon Cardiovascular Risk		
Educational Format		**Faculty Expertise Required**
REQUIRED	Interactive Lecture	Expertise in the field of study. Experience teaching in the field of study is desired. Preferred experience with audience response systems (ARS). Utilizing polling questions and engaging the learners in Q&A during the final 15 minutes of the session are required.
OPTIONAL	Problem-Based Learning (PBL)	Expertise teaching highly interactive, small group learning environments. Case-based, with experience developing and teaching case scenarios for simulation labs preferred. Other workshop-oriented designs may be accommodated. A typical PBL room is set for 50-100 participants, with 7-8 each per round table. Please describe your interest and plan for teaching a PBL on your proposal form.

Professional Practice Gap	**Learning Objective(s) that will close the gap and meet the need**	**Outcome Being Measured**
• Physicians are often not aware of updated clinical guidelines and results of clinical interventions from retrospective studies that prove such recommendations to be effective. • Physicians do not routinely use clinical guidelines in managing care for patients with diabetes, and often do not provide optimal coordination of care with specialists. • Physicians are often not up to date on the latest Db treatment research.	1. Explore the rationale behind the FDA's guidance on approving new drugs for patients with diabetes. 2. Compare and contrast the outcomes of CVOTs for DPP-4 inhibitors, SGLT2 inhibitors, bromocriptine and GLP-1 receptor agonists. 3. Evaluate the renal effects of SGLT2 inhibitors and GLP-1 RAs in CVOTs. 4. Recognize the importance of reducing weight gain and mitigating the likelihood of hypoglycemia. 5. Recognize why hypoglycemia increases CV risk.	Learners will submit written commitment to change statements on the session evaluation, indicating how they plan to implement presented practice recommendations.

ACGME Core Competencies Addressed (select all that apply)

X	Medical Knowledge		Patient Care
	Interpersonal and Communication Skills		Practice-Based Learning and Improvement
	Professionalism		Systems-Based Practice

Faculty Instructional Goals

Faculty play a vital role in assisting the AAFP to achieve its mission by providing high-quality, innovative education for physicians, residents and medical students that will encompass the art, science, evidence and socio-economics of family medicine and to support the pursuit of lifelong learning. By achieving the instructional goals provided, faculty will

facilitate the application of new knowledge and skills gained by learners to practice, so that they may optimize care provided to their patients.

- Provide up to 3 evidence-based recommended practice changes that can be immediately implemented, at the conclusion of the session; including SORT taxonomy & reference citations
- Facilitate learner engagement during the session
- Address related practice barriers to foster optimal patient management
- Provide recommended journal resources and tools, during the session, from the American Family Physician (AFP), Family Practice Management (FPM), and Familydoctor.org patient resources; those listed in the References section below are a good place to start
    - Visit http://www.aafp.org/journals for additional resources
    - Visit http://familydoctor.org for patient education and resources
- Provide recommendations regarding the rationale behind the FDA's guidance on approving new drugs for patients with diabetes.
- Provide recommendations regarding the implications to practice from the outcomes of CVOTs for DPP-4 inhibitors, SGLT2 inhibitors, bromocriptine and GLP-1 receptor agonists.
- Provide recommendations regarding the renal effects of SGLT2 inhibitors and GLP-1 RAs in CVOTs
- Provide recommendations for patient-centered care that recognize the importance of reducing weight gain and mitigating the likelihood of hypoglycemia
- Provide explanations as to why hypoglycemia increases CV risk.

Needs Assessment

Diabetes mellitus is one of the most common diagnoses made by family physicians. It is estimated that in the United States, 44 million people with have type 2 diabetes mellitus within the next 20 years. Early screening and diagnosis can lead to interventions that have the potential to decrease the degree of associated complications and increase patient quality of life.[1] Treating patients with diabetes mellitus can be complicated, and data from the 2012 American Academy of Family Physicians (AAFP) CME Needs Assessment Survey indicate that family physicians have a statistically significant and meaningful gap in knowledge and skills necessary to manage patients with diabetes.[2] CME outcomes data from the 2016 Chronic Conditions evaluation report validates the need for family physicians to have further education. Over 34% of physician-learners identified the need to pursue additional education on diabetes.[3]

Additionally, CME outcomes data from several 2012-2016 AAFP FMX (formerly Assembly) sessions focused on diabetes topics suggest that physicians have knowledge and practice gaps with regard to utilizing a patient-centered approach to care that involves the entire care team to help make the office visit with the physician more efficient; recognizing latent autoimmune diabetes in adults (LADA); understanding and adhering to current screening and evaluation guidelines; being up to date on current guidelines for medications and therapeutic approaches; improving efforts toward patient education and counseling for prevention in pre-diabetic patients, including effective use of group visits; effective control and maintenance of patients receiving treatment; and having an awareness of current guidelines for gestational diabetes.[4-8]

Practice Gaps

Although multiple therapies are currently available for patients with T2DM, only 52 % of patients are able to achieve their targeted A1C of < 7 %. Family physicians require guidance on the current best practice methods to approach disease prevention, screening and management for their patients. They also require updates on the recent evidence surrounding the use of pharmacologic and non-pharmacologic treatments of the disease and its complications – including reducing cardiovascular risk, and management of diabetic peripheral neuropathy. An overview of the literature review is as follows:

- Currently available medications have many drawbacks including inducing weight gain, treatment emergent hypoglycemia and loss of efficacy over time. These adverse events can affect adherence. Fewer than 60 % of patients taking oral agents continue use of these prescribed medications for over 6 months. Adherence to insulin use in some studies is less than 20 %.[9]
- Reduced adherence is associated with a rise in A1C, increase in hospitalizations, higher rates of ER and clinician visits. Poor medical adherence increase all-cause mortality by 1.6 %.[10,11]
- The correlation between poor glycemic control and cardiovascular risk is clear. However, proving the causal relationship between improved diabetes control and reduced CV risk has proven difficult.
- The FDA mission statement suggests a dual role: 1) Protect the public by ensuring safety and efficacy of new products and devices and 2) advance the public health by speeding innovative drugs to market which are more effective, safer and more affordable than drugs currently available. Providing clinicians with evidence based assessments related to a drug's risks and benefits is expensive and challenging.
- Prior to 2008 the FDA mandated that drugs could be approved solely on improvements in A1C and safety. Patients with existing CVD were often excluded from clinical trials. A new drug's impact on CV safety was assessed through investigator initiated trials or post marketing adverse event reporting. In 2007 Rosiglitazone (a TZD) was reported to demonstrate a 43 % increase risk of myocardial infarction and a 64 % increase risk of CV death. A controversial publication (Nissen SE, et al. N Engl J Med. 2007; 356: 2457-2471)[12] accused the FDA of abdicating its duty to protect public safety. In 7/08 the FDA voted in favor or recommending a long-ter CV safety trial to rule out unacceptable CV risk for all new glucose-lowering agents. In 12/2008 the FDA released guidance for evaluating the CV safety of these therapies. The FDA advised that pre-marketing interim outcome data should rule out a hazard ratio of 1.8 (based on the upper bound of a two-sided 95 % confidence interval) for CV death, nonfatal MI and nonfatal stroke). If the pre-marketing data had not already ruled out a hazard ratio of 1.3, a drug approved based on interim outcomes data would be required to perform a CV outcomes trial.
- Every antidiabetetic agent approved since 2008 has undergone a dedicated cVOT involving 5000-15,000 people with T2DM and high CV risk. These trials are expensive and last typically between 3-5 years. By June 2017, 7 CVOT trials will have reported with at least 9 others ongoing. Some trials have shown CV benefit with glucose lowering agents; others have not.

Practicing physicians need to understand the implications to practice, that multiple CVOT studies have reported:

- CVOT are complex and often difficult to interpret. For example, DPP4 inhibitors neither benefit or worsen CV events. However, alogliptin has been shown to slightly increase the risk of hospitalizations due to CHF.[13] EMPA-REG evaluated the safety and efficacy of empagliflozin in a high-risk population of patients with T2DM and noted early and significant improvement in CV death (38 %) as well as a 35 % reduction in CHF hospitalizations.[14] The LEADER CV OUTCOMES study demonstrated a 13 % reduction in 3-Point MACE independent of glycemic control.[15] Semaglutide, a once weekly GLP-1 RA demonstrated a robust 26 % reduction inn 3-point MACE in high risk T2DM patients.[16] The Canagliflozin CVOT, CANVAS, is reporting in June 2017.
    - 90 % of patients with T2DM are managed within the primary care setting. Therefore, education PCPs, NP and PA regarding CVOTs is imperative to reduce the burden and expense of diabetes management in the US.
    - Currently only metformin, sulfonylureas and thiazolodinediones are available in generic and inexpensive formulations. Some managed care organizations have formularies which ONLY approve these drug therapies, implying that reducing CV risk in patients with diabetes may not be a primary objective of 3rd party payors.
    - Drugs which have proven to be beneficial in providing improvement in primary and secondary outcomes should be discussed in detail with PCP learners.
    - The exact mechanism of CV risk improvement is open to scientific speculation. Additional studies are needed to elucidate the mechanistic and CV protective nature of glucose lowering therapies.

References

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