AACE/ACE COMPREHENSIVE TYPE 2 DIABETES MANAGEMENT ALGORITHM 2017

TASK FORCE
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## Comprehensive Type 2 Diabetes Management Algorithm

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</tr>
<tr>
<td><strong>1.</strong></td>
<td>Lifestyle therapy, including medically supervised weight loss, is key to managing type 2 diabetes.</td>
</tr>
<tr>
<td><strong>2.</strong></td>
<td>Weight loss should be considered as a lifelong goal in all patients with prediabetes and T2D who also have overweight or obesity, utilizing behavioral interventions and weight loss medications as required to achieve chronic therapeutic goals.</td>
</tr>
<tr>
<td><strong>3.</strong></td>
<td>The A1C target must be individualized.</td>
</tr>
<tr>
<td><strong>4.</strong></td>
<td>Glycemic control targets include fasting and postprandial glucose.</td>
</tr>
<tr>
<td><strong>5.</strong></td>
<td>The choice of therapies must be individualized on the basis of patient characteristics, impact of net cost to patient, formulary restrictions, personal preferences, etc.</td>
</tr>
<tr>
<td><strong>6.</strong></td>
<td>Minimizing risk of hypoglycemia is a priority.</td>
</tr>
<tr>
<td><strong>7.</strong></td>
<td>Minimizing risk of weight gain is a priority.</td>
</tr>
<tr>
<td><strong>8.</strong></td>
<td>Initial acquisition cost of medications is only a part of the total cost of care which includes monitoring requirements, risk of hypoglycemia, weight gain, safety, etc.</td>
</tr>
<tr>
<td><strong>9.</strong></td>
<td>This algorithm stratifies choice of therapies based on initial A1C.</td>
</tr>
<tr>
<td><strong>10.</strong></td>
<td>Combination therapy is usually required and should involve agents with complementary actions.</td>
</tr>
<tr>
<td><strong>11.</strong></td>
<td>Comprehensive management includes lipid and blood pressure therapies and related comorbidities.</td>
</tr>
<tr>
<td><strong>12.</strong></td>
<td>Therapy must be evaluated frequently until stable (e.g., every 3 months) and then less often.</td>
</tr>
<tr>
<td><strong>13.</strong></td>
<td>The therapeutic regimen should be as simple as possible to optimize adherence.</td>
</tr>
<tr>
<td><strong>14.</strong></td>
<td>This algorithm includes every FDA-approved class of medications for diabetes.</td>
</tr>
</tbody>
</table>
## LIFESTYLE THERAPY

### INTENSITY STRATIFIED BY BURDEN OF OBESITY AND RELATED COMPlications

<table>
<thead>
<tr>
<th>Category</th>
<th>Strategies</th>
<th>Strategies</th>
<th>Strategies</th>
</tr>
</thead>
</table>
| **Nutrition**       | • Maintain optimal weight  
                      • Calorie restriction (if BMI is increased)  
                      • Plant-based diet; high polyunsaturated and monounsaturated fatty acids | • Avoid trans fatty acids; limit saturated fatty acids | • Structured counseling  
                      • Meal replacement |
| **Physical Activity**| • 150 min/week moderate exertion (eg. walking, stair climbing)  
                      • Strength training  
                      • Increase as tolerated | • Structured program  
                      • Wearable technologies | • Medical evaluation/clearance  
                      • Medical supervision |
| **Sleep**           | • About 7 hours per night  
                      • Basic sleep hygiene | • Screen OSA  
                      • Home sleep study | • Referral to sleep lab |
| **Behavioral Support** | • Community engagement  
                      • Alcohol moderation | • Discuss mood with HCP | • Formal behavioral therapy |
| **Smoking Cessation** | • No tobacco products | • Nicotine replacement therapy | • Referral to structured program |
Comlications-Centric Model for Care of the Patient with Overweight/Obesity

**STEP 1**

**Evaluation for Complications and Staging**

<table>
<thead>
<tr>
<th>CardioMetabolic Disease</th>
<th>Biomechanical Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &lt; 25</td>
<td><strong>No Complications</strong></td>
</tr>
<tr>
<td></td>
<td><strong>BMI ≥ 25</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Overweight or Obesity</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Stage 0</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Stage 1</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Stage 2</strong></td>
</tr>
<tr>
<td>BMI ≥ 25</td>
<td><strong>ComplIcations</strong></td>
</tr>
<tr>
<td></td>
<td><strong>BMI ≥ 25</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Mild to Moderate</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Severe</strong></td>
</tr>
</tbody>
</table>

**STEP 2**

**Select:**

- Therapeutic targets for improvement in complications
- Treatment modality
- Treatment intensity based on staging

**Lifestyle Therapy:**

- Physician/RD counseling, web/remote program, structured multidisciplinary program

**Medical Therapy (BMI ≥ 27):**

- Individualize care by selecting one of the following based on efficacy, safety, and patients’ clinical profile: phentermine, orlistat, lorcaserin, phentermine/topiramate ER, naltrexone/bupropion, liraglutide 3 mg

**Surgical Therapy (BMI ≥ 35):**

- Gastric banding, sleeve, or bypass

**STEP 3**

If therapeutic targets for complications not met, intensify lifestyle, medical, and/or surgical treatment modalities for greater weight loss. Obesity is a chronic progressive disease and requires commitment to long-term therapy and follow-up.

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PREDIABETES ALGORITHM

IFG (100–125)  |  IGT (140–199)  |  METABOLIC SYNDROME (NCEP 2001)

LIFESTYLE THERAPY
(Including Medically Assisted Weight Loss)

TREAT ASCVD RISK FACTORS

WEIGHT LOSS THERAPIES

TREAT HYPERGLYCEMIA
FPG > 100  |  2-hour PG > 140

ASCVD RISK FACTOR MODIFICATIONS ALGORITHM

DYSLIPIDEMIA ROUTE

HYPERTENSION ROUTE

NORMAL GLYCEMIA

Progression

OVERT DIABETES

1 PRE-DM CRITERION

INTENSIFY WEIGHT LOSS THERAPIES

Low-risk Medications
Metformin
Acarbose

MULTIPLE PRE-DM CRITERIA

Consider with Caution
TZD
GLP-1 RA

If glycemia not normalized

LEGEND
Orlistat, lorcaserin, phentermine/topiramate ER, naltrexone/bupropion, liraglutide 3 mg, or bariatric surgery as indicated for obesity treatment
Prediabetes Treatment Algorithm

- Weight-loss agents orlistat, lorcaserin, and phentermine/topiramate can prevent progression to T2DM
  - Improve BP, triglycerides, and insulin sensitivity
- Metformin and acarbose can reduce progression to T2DM by 25% - 30%
  - Use for prediabetes is off-label
  - Both are safe, confer CVD risk benefit; metformin is well tolerated
- TZDs prevented progression to T2DM in 60% - 75% of patients in clinical trials
  - Associated with adverse outcomes
- GLP-1 receptor agonists may be as effective as TZDs
  - Promote weight loss, but inadequate safety data
- TZDs and GLP-1 RAs reserved for patients not responding to conventional therapies or at highest risk for T2DM

T2DM = type 2 diabetes mellitus
BP = blood pressure
CVD = cardiovascular disease
TZD = thiazolidinedione
GLP-1 RA = glucagon-like peptide-1 receptor agonist

Increased risk for both microvascular and macrovascular disease begins early in the prediabetic state

- Insulin resistance is already present in patients with NGT who later develop T2DM
- Patients with prediabetes already have high insulin resistance and significantly decreased beta-cell function
- Both diabetic retinopathy, peripheral neuropathy, and nephropathy occur in patients with prediabetes
- Patients with prediabetes have a 2 to 3-fold increase in CHD risk, similar to patients with diabetes

CHD = coronary heart disease; NGT = normal glucose tolerance; T2DM = type 2 diabetes mellitus

**DYSLIPIDEMIA**

**LIFESTYLE THERAPY** (Including Medically Assisted Weight Loss)

**LIPID PANEL:** Assess ASCVD Risk

**STATIN THERAPY**
If TG > 500 mg/dL, fibrates, Rx-grade omega-3 fatty acids, niacin

If statin-intolerant

Try alternate statin, lower statin dose or frequency, or add nonstatin LDL-C-lowering therapies

Repeat lipid panel; assess adequacy, tolerance of therapy

Intensify therapies to attain goals according to risk levels

---

**RISK LEVELS: HIGH**

<table>
<thead>
<tr>
<th>DESIRABLE LEVELS</th>
<th>VERY HIGH</th>
<th>EXTREME</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C (mg/dL)</td>
<td>&lt;100</td>
<td>&lt;70</td>
</tr>
<tr>
<td>Non-HDL-C (mg/dL)</td>
<td>&lt;130</td>
<td>&lt;100</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>&lt;150</td>
<td>&lt;150</td>
</tr>
<tr>
<td>Apo B (mg/dL)</td>
<td>&lt;90</td>
<td>&lt;80</td>
</tr>
</tbody>
</table>

**IF NOT AT DESIRABLE LEVELS:** Intensify lifestyle therapy (weight loss, physical activity, dietary changes) and glycemic control; consider additional therapy

**TO LOWER LDL-C:**
- Intensify statin, add ezetimibe, PCSK9i, colesve lam, or niacin

**TO LOWER Non-HDL-C, TG:**
- Intensify statin and/or add Rx-grade OM3 fatty acid, fibrate, and/or niacin

**TO LOWER Apo B, LDL-P:**
- Intensify statin and/or add ezetimibe, PCSK9i, colesve lam, and/or niacin

Statin + PCSK9i

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**TO LOWER LDL-C in FH:**

Assess adequacy & tolerance of therapy with focused laboratory evaluations and patient follow-up

* EVEN MORE INTENSIVE THERAPY MIGHT BE WARRANTED  ** FAMILIAL HYPERCHOLESTEROLEMIA

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**HYPTERTENSION**

**GOAL:** SYSTOLIC <130, DIASTOLIC <80 mm Hg

**ACEi or ARB**
For initial blood pressure >150/100 mm Hg: DUAL THERAPY

- Calcium Channel Blocker
- β-blocker
- Thiazide

If not at goal (2–3 months)

Add calcium channel blocker, β-blocker or thiazide diuretic

If not at goal (2–3 months)

Add next agent from the above group, repeat

If not at goal (2–3 months)

Additional choices (β-blockers, central agents, vasodilators, aldosterone antagonist)

Achievement of target blood pressure is critical
INDIVIDUALIZE GOALS

A1C ≤ 6.5%
For patients without concurrent serious illness and at low hypoglycemic risk

A1C > 6.5%
For patients with concurrent serious illness and at risk for hypoglycemia
Risk of Hypoglycemia

- Plays a significant role in choice of agents in AACE algorithm

- For patients at highest risk of hypoglycemia, may consider close evaluation of agents chosen as well as therapeutic goal

- Patients with type 2 diabetes at highest risk of low blood glucose include those with:
  - Diabetes duration >15 years
  - Advanced macrovascular disease
  - Hypoglycemia unawareness
  - Limited life expectancy
  - Severe comorbidities

Clinical Considerations

- Combining therapeutic agents with different modes of action may be advantageous.

- Use insulin sensitizers such as metformin and/or TZDs as part of the therapeutic regimen in most patients (unless contraindicated or intolerance to these agents has been demonstrated).

- Insulin and secretagogues are the only medications that cause significant hypoglycemia.
  
  Therefore, dosage of secretagogues or insulin should be adjusted as blood glucose levels decline, when used in combination with metformin, TZD, DPP-4 inhibitors, and/or incretin mimetics (GLP-1 agonists).

TZD = thiazolidinediones; DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1

**Effect of Glucose-lowering Drugs on Patient Weight**

<table>
<thead>
<tr>
<th>Therapeutic Options</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfonylurea(^1,2)</td>
<td>↑</td>
</tr>
<tr>
<td>TZD(^3,4)</td>
<td>↑</td>
</tr>
<tr>
<td>Insulin(^5,6)</td>
<td>↑</td>
</tr>
<tr>
<td>Metformin(^7)</td>
<td>⇔</td>
</tr>
<tr>
<td>DPP-4 inhibitor(^8)</td>
<td>⇔</td>
</tr>
<tr>
<td>GLP-1 receptor agonist(^9)</td>
<td>↓</td>
</tr>
<tr>
<td>SGLT-2 Inhibitors(^10)</td>
<td>↓</td>
</tr>
</tbody>
</table>

A1C = glycated hemoglobin; DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1; SGLT-2 = sodium glucose co-transporter-2; TZD = thiazolidinedione

**LIFESTYLE THERAPY**
(Including Medically Assisted Weight Loss)

**Entry A1C < 7.5%**
- MONOTHERAPY*
  - Metformin
  - GLP-1 RA
  - SGLT-2i
  - DPP-4i
  - TZD
  - AGi
  - SU/GLN

**Entry A1C ≥ 7.5%**
- DUAL THERAPY*
  - GLP-1 RA
  - SGLT-2i
  - DPP-4i
  - TZD
  - Basal Insulin
  - Colesevelam
  - Bromocriptine QR
  - AGi
  - SU/GLN

**Entry A1C > 9.0%**
- TRIPLE THERAPY*
  - GLP-1 RA
  - SGLT-2i
  - TZD
  - Basal insulin
  - DPP-4i
  - Colesevelam
  - Bromocriptine QR
  - AGi
  - SU/GLN

**SYMPTOMS**
- NO
  - DUAL Therapy
- YES
  - INSULIN ± Other Agents

**ADD OR INTENSIFY INSULIN**
Refer to Insulin Algorithm

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* Order of medications represents a suggested hierarchy of usage; length of line reflects strength of recommendation

---

**PROGRESSION OF DISEASE**

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GLYCEMIC CONTROL ALGORITHM

LIFESTYLE THERAPY
(Including Medically Assisted Weight Loss)

**MONOTHERAPY***
- Metformin - 1st choice (if no contraindication)
- Consider drugs in the order suggested
- Order of medications represents a suggested hierarchy of usage
- Length of line reflects strength of recommendation
- SFU’s are lowest on the list (Short-lived effect, strong risk of hypoglycemia that may increase hospitalizations in elderly patients, may increase MI risk, contraindicated for patients with renal failure)

- If unsuccessful, move to dual oral rx
  Metformin still cornerstone of therapy
  (If contraindicated, consider TZD as foundation of rx)

* Order of medications represents a suggested hierarchy. Length of line reflects strength of recommendation.

If not at goal in 3 months proceed to Dual Therapy

**Road Map to Achieve Glycemic Goals A1c < 7.5%**
Dual therapy with metformin provides superior glycemic control over metformin alone.

A1c 7.5-9% Road Map to Achieve Glycemic Goals
If patient is asymptomatic with recent onset of disease and drug naïve, may consider starting with dual or triple oral regimens.

Once A1C has improved to <7.5%, consider initiation of dual oral therapy with tapering and possible discontinuation of insulin rx.

If symptomatic, start insulin.
**Algorithm for Adding/Intensifying Insulin**

### START BASAL (Long-Acting Insulin)

- **A1C < 8%**
  - TDD: 0.1–0.2 U/kg

- **A1C > 8%**
  - TDD: 0.2–0.3 U/kg

**Insulin titration every 2–3 days to reach glycemic goal:**

- Fixed regimen: Increase TDD by 2 U
- Adjustable regimen:
  - FBG > 180 mg/dL: add 20% of TDD
  - FBG 140–180 mg/dL: add 10% of TDD
  - FBG 110–139 mg/dL: add 1 unit
- If hypoglycemia, reduce TDD by:
  - BG < 70 mg/dL: 10% – 20%
  - BG < 40 mg/dL: 20% – 40%

Consider discontinuing or reducing sulfonylurea after starting basal insulin (basal analogs preferred to NPH)

**Glycemic Goal:**

- <7% for most patients with T2D; fasting and premeal BG < 110 mg/dL; absence of hypoglycemia
- A1C and FBG targets may be adjusted based on patient’s age, duration of diabetes, presence of comorbidities, diabetic complications, and hypoglycemia risk

### INTENSIFY (Prandial Control)

#### Add GLP-1 RA
- Or SGLT-2i
- Or DPP-4i

#### Add Prandial Insulin

- **Basal Plus 1, Plus 2, Plus 3**
  - Begin prandial insulin before largest meal
  - If not at goal, progress to injections before 2 or 3 meals
  - Start: 10% of basal dose or 5 units

- **Basal Bolus**
  - Begin prandial insulin before each meal
  - 50% Basal / 50% Prandial
  - TDD 0.3–0.5 U/kg
  - Start: 50% of TDD in three doses before meals

**Insulin titration every 2–3 days to reach glycemic goal:**

- Increase prandial dose by 10% or 1–2 units if 2-h postprandial or next premeal glucose consistently > 140 mg/dL
- If hypoglycemia, reduce TDD basal and/or prandial insulin by:
  - BG consistently < 70 mg/dL: 10% – 20%
  - Severe hypoglycemia (requiring assistance from another person) or BG < 40 mg/dL: 20% – 40%
# Profiles of Antidiabetic Medications

<table>
<thead>
<tr>
<th></th>
<th>MET</th>
<th>GLP-1 RA</th>
<th>SGLT-2i</th>
<th>DPP-4i</th>
<th>AGi</th>
<th>TZD (moderate dose)</th>
<th>SU</th>
<th>GLN</th>
<th>COLSVEL</th>
<th>BCR-QR</th>
<th>INSULIN</th>
<th>PRAML</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HYPO</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate/Severe</td>
<td>Mild</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate to Severe</td>
<td>Neutral</td>
</tr>
<tr>
<td><strong>WEIGHT</strong></td>
<td>Slight Loss</td>
<td>Loss</td>
<td>Loss</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Gain</td>
<td>Gain</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Gain</td>
<td>Loss</td>
</tr>
<tr>
<td><strong>RENAL / GU</strong></td>
<td>Contraindicated if eGFR &lt; 30 mL/min/1.73 m²</td>
<td>Exenatide Not Indicated CrCl &lt; 30</td>
<td>Genital Mycotic Infections</td>
<td>Dose Adjustment Necessary (Except Linagliptin)</td>
<td>Effective in Reducing Albuminuria</td>
<td>Neutral</td>
<td>Neutral</td>
<td>More Hypo Risk</td>
<td>Neutral</td>
<td>Neutral</td>
<td>More Hypo Risk</td>
<td>Neutral</td>
</tr>
<tr>
<td><strong>GI Sx</strong></td>
<td>Moderate</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Mild</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td><strong>CHF</strong></td>
<td>Neutral</td>
<td>Possible Benefit of Liraglutide</td>
<td>Possible Benefit of Empagliflozin</td>
<td>Possible Risk for Saxagliptin and Alogliptin</td>
<td>Neutral</td>
<td>Moderate</td>
<td>More CHF Risk</td>
<td>Neutral</td>
<td>Neutral</td>
<td>More CHF Risk</td>
<td>Neutral</td>
<td></td>
</tr>
<tr>
<td><strong>CARDIAC</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>Possible Benefit of Empagliflozin</td>
<td>Possible CV Benefit</td>
<td>Neutral</td>
<td>May Reduce Stroke Risk</td>
<td>?</td>
<td>Benefit</td>
<td>Safe</td>
<td>Neutral</td>
<td>Neutral</td>
<td></td>
</tr>
<tr>
<td><strong>ASCVD</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>Possible CV Benefit</td>
<td>Neutral</td>
<td>Moderate Fracture Risk</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td></td>
</tr>
<tr>
<td><strong>BONE</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>Canagliflozin Warning</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate Fracture Risk</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
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</tr>
<tr>
<td><strong>KETOACIDOSIS</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>DKA Occurring in T2D in Various Stress Settings</td>
<td>Neutral</td>
<td>Neutral</td>
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<td>Neutral</td>
<td>Neutral</td>
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<td>Neutral</td>
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</tr>
</tbody>
</table>

- Green: Few adverse events or possible benefits
- Yellow: Use with caution
- Orange: Likelihood of adverse effects
- Question mark: Uncertain effect

* FDA indication to prevent CVD death in diabetes plus prior CVD events

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UKPDS: Benefits of Glycemic Control

Every 1% decrease in A1C led to significant reductions in diabetes-related complications

- 14% decrease in risk of myocardial infarction
- 21% decrease in risk of diabetes-related death
- 37% decrease in risk of microvascular complications
- 43% decrease in risk of amputation or PVD Death

Decrease was statistically significant for all comparisons shown

Landmark Glycemia Trials

- Action to Control Cardiovascular Risk in Diabetes (ACCORD)
- Action in Diabetes and Vascular Disease Preterax and Diamicron MR Controlled Evaluation (ADVANCE)
- Veterans Affairs Diabetes Trial (VADT)
- All conducted in:
  - “Older” patients (≥60 years of age)
  - Patients with cardiovascular disease (CVD; 1/3 to 1/2 of cohorts)
    or
  - ≥1 CVD risk factors

Probability of All-cause Mortality with Intensive Glucose-lowering vs. Standard Treatment

<table>
<thead>
<tr>
<th>Intensive treatment/standard treatment</th>
<th>Weight of study size</th>
<th>Odds ratio (95% CI)</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Participants</td>
<td>Events</td>
<td></td>
</tr>
<tr>
<td>UKPDS\textsuperscript{4,7}</td>
<td>3071/1549</td>
<td>539/302</td>
<td>10.1%</td>
</tr>
<tr>
<td>PROactive\textsuperscript{18-20*}</td>
<td>2605/2633</td>
<td>177/186</td>
<td>21.5%</td>
</tr>
<tr>
<td>ADVANCE\textsuperscript{5}</td>
<td>5571/5569</td>
<td>498/533</td>
<td>29.4%</td>
</tr>
<tr>
<td>VADT\textsuperscript{21,22}</td>
<td>892/899</td>
<td>102/95</td>
<td>15.5%</td>
</tr>
<tr>
<td>ACCORD\textsuperscript{8}</td>
<td>5128/5123</td>
<td>257/203</td>
<td>23.6%</td>
</tr>
<tr>
<td>Overall</td>
<td>17267/15773</td>
<td>1573/1319</td>
<td>100%</td>
</tr>
</tbody>
</table>

All-cause mortality

Empagliflozin is the first SGLT2 inhibitor to report CV benefit

- 14% reduction in the hazard of MACE in over 7000 patients with T2DM + CVD
- 38% reduction in CV mortality
- Heart failure hospitalization was reduced by 38%
- Also shown to have renal benefits: 39% decrease in pre specified end points (progression to macroalbuminuria, doubling of serum Cr, worsening nephropathy, initiation of renal replacement therapy).
LEADER-Trial (Liraglutide)

- Liraglutide is the second Drug to show CV benefits
- 13% lower risk of primary composite MACE outcome
- 22% lower risk of CV mortality
- 15% lower risk of all cause mortality
- 15% lower risk of microvascular (renal events-driven mainly by reduction in macroalbuminuria)
CVOT’s-Summary

- Empagliflozin has an FDA indication to reduce the risk of cardiovascular death in adult patients with type 2 diabetes mellitus and cardiovascular disease.

- On 8/25/17, FDA approved a new indication for Victoza® (liraglutide) to reduce the risk of major adverse cardiovascular (CV) events, heart attack, stroke and CV death, in adults with type 2 diabetes and established CV disease.

- Weigh the risk vs benefits of all antihyperglycemic agents before prescribing.

- ADA 2017 and AACE/ACE 2017 guidelines now include recommendations for considerations of empagliflozin or liraglutide in patients with T2 DM not at goal and established atherosclerotic CVD.
CVOT’s and Diabetes in 2017—some takeaways...

- Based on recent CVOT’s, the manner in which glucose is lowered is more important than the degree of glucose lowering.
- Should we be using therapies proven to reduce CV events in those with pre-existing CVD?
- In those without CVD and mild hyperglycemia, DPP-4 inhibitors may be reasonable options.
- Pioglitazone has limited use but can be considered in the very insulin resistant patient with no major risks of HF.
CVOTs and Diabetes in 2017- any takeaways?

- Sulfonylureas could be used selectively in those with intact renal function possibly third line in those not able to use the other agents (avoid in elderly)
- If the HbA1c is very high, insulin therapy remains the most efficacious therapy as long as the dose is appropriately titrated.
- COST remains the major issue with branded medications and of course this aspect must be taken into account.
“It’s a pacemaker for your heart. Plus, you can download apps for your liver, kidneys, lungs, and pancreas!”