Diabetes Boot Camp – Class 5
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Diabetes Meds for Type 2:
Objectives

1. Describe the main action of the different categories of type 2 diabetes medications.
2. Discuss strategies to determine the right medication for the right patient.
3. List the side effects and clinical considerations of each category of medication.

CDE Exam Outline

They will provide generic and trade name for Meds on Exam
Poll question 1

- When starting patients on medications, what is the most important factor to consider?
  a. Their level of compliance
  b. Their diabetes pathology
  c. Their education level
  d. Their preferences, needs and values

Diabetes Agents Considerations

- Diabetes medications can be used as monotherapy, in combo or with insulin
- Combining agents from different classes has additive effect
- Most reduce A1c 0.5 – 2.0%
- Not to be used during preconception, pregnancy or when breastfeeding

Patient Centered Approach

“...providing care that is respectful of and responsive to individual patient preferences, needs, and values - ensuring that patient values guide all clinical decisions.”

- Gauge patient’s preferred level of involvement.
- Explore, where possible, therapeutic choices.
- Utilize decision aids.
- Shared decision making – final decisions re: lifestyle choices ultimately lie with the patient.
Considerations

- Cost
- Hypoglycemia
- Age
- Weight
- Comorbidities
  - Kidney disease
  - Heart disease — CHF, CAD
  - Liver dysfunction

When goal is to minimize cost

- Go generic. Metformin and Sulfonylureas
- Walmart offers 3 month supply of following meds for ~ $10
  - Metformin and Metformin XR
  - Glipizide, Glyburide, Glimepiride
- Other generics include
  - Actos and Avandia
  - Acarbose
  - Can still cost up to $100 a month

- Meds on a Budget Article

ADA Standards of Care 2015

ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

Diabetes Care 2012;35:1364–1379
Diabetologia 2012;55:1577–1596
Poll question 2

According to the AACE Glycemic Control Algorithm, what is the first step to control hyperglycemia in type 2?
a. Lifestyle modification  
b. Start insulin  
c. Start metformin  
d. Start 2 meds if their A1c is 7.4%

Antihyperglycemic Therapy – 1st Step

Lifestyle Changes
- Weight control
- Healthy eating
- Activity

Action/Classes of Type 2 Meds

1. Suppressor  
   - Biguanide – Metformin
2. Squirter  
   - Sulfonylureas
   - Meglitinides
3. Satiators  
   - AmylinoMimetics
   - Incretin Mimetics
   - DPP-4 Inhibitors
4. Sensitizer  
   - Thiazolidinediones (TZD)
5. Glucoretics  
   - SGLT2 Inhibitors
6. Circadian Switchers  
   - Dopamine Receptor Agonists
7. Slower  
   - Alpha-glucosidase inhibitors
ADA Step Wise Approach to Hyperglycemia 2015

- Start with lifestyle coaching
- When lifestyle alone is not achieving A1c goal – Metformin should be added at, or soon after diagnosis (unless contraindicated).
- Metformin has a long standing evidence base for efficacy and safety, is cheap and may reduce CV risk.
- If A1c target is not achieved after 3 months, consider adding one of 6 treatment options or basal insulin.
- For all patients, consider initiating dual therapy or insulin if A1c ≥ 9%
- A1c still above target? Consider:
  - Basal bolus therapy or add a GLP-1 Agonist.
  - Twice daily premixed biphasic insulin (70/30)
Ideal Diabetes Med -

- No hypoglycemia
- No weight gain
- Affordable
- Lowers CV risk
- Most people can tolerate/use?

Poll question 3

John is started on Metformin 500mg BID. What of the following is true?

a. Hold metformin if your blood glucose is below 90 mg/dl.
b. If you forget to take metformin before the meal, hold the dose.
c. Take metformin with meals
d. Always hold metformin if you are sick

Biguanides – Suppressor
Metformin (Glucophage®)

- Action: suppresses release of glycogen from the liver
- Who?
  - Fasting hyperglycemia
  - Dysmetabolic Syndrome
  - For pediatrics starting age 10
    - (XR age 17)

Glycogen Stopper and GLP Enhancer?
**Biguanides - Metformin**

- **Action:** decrease hepatic glucose (glycogen)
- **Names:**
  - Metformin (Glucophage)
    - Starting dose: 500 BID, max 2500mg daily
  - Metformin extended release (3 different versions)
    - Starting dose 500mg at dinner, max dose 2000 to 2500mg daily
- **Efficacy:**
  - Decrease fasting plasma glucose 60-70 mg/dl
  - Reduce A1C 1.0-2.0%
Metformin – How does it rate?

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<td>(GI, creat)</td>
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Poll Question 4

Mary has newly diagnosed type 2 and is concerned about taking glipizide (Glucotrol). Which of the following are teaching points for pts on sulfonylureas?

- a. Most patients experience some weight loss
- b. 50% of patients have no improvement in BG levels
- c. Do not take with grapefruit juice
- d. Know the signs of hypoglycemia

Sulfonylureas –

- Action: tells pancreas to squirt insulin all day
- Who?
  - Lean type 2
**Sulfonylureas - Squirts**

- **Action:** Increase endogenous insulin secretion
- **Efficacy:**
  - Decrease FPG 60-70 mg/dl
  - Reduce A1C by 1.0-2.0%
- **Secondary failures:** 5-10% shortly after initial response, many more later
  - Usually after 5 or more years of therapy due to natural history of DM 2

**Sulfonylureas: 2nd Generation**

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Duration</th>
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<tbody>
<tr>
<td>Glyburide</td>
<td>Diabeta, Micronase, most likely to cause hypo – last choice</td>
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<tr>
<td>Glipizide*</td>
<td>Glucotrol, Glucotrol XL</td>
<td>12-24 hrs</td>
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<tr>
<td>Glimepiride</td>
<td>Amaryl</td>
<td>16-24 hrs</td>
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**Sulfonylureas**

- **Other Effects**
  - Hypoglycemia
  - Weight gain
  - Cleared by kidney, use caution for pts with kidney problems
  - Generally the least expensive class of medication
  - Amaryl safest for those with CV Disease
Indication for “Fast Acting” Insulin Secretagogues - Meglitinides

- **Action:** tells pancreas to squirt insulin with meals
- **Who?**
  - Targets post-prandial hyperglycemia

Meglitinides - Squirts

- **Action:** stimulate insulin secretion (rapid and short duration) when glucose present
- **Names:**
  - repaglinide (Prandin)
    - **Dosing:** 0.5 to 4 mg a.c. Max dose 16 mg
    - Metabolized by liver and mostly excreted in feces (some renally).
  - nateglinide (Starlix)
    - **Dosing:** 120 mg tid with meals
    - Metabolized by liver, excreted by kidney
- **Efficacy:**
  - Decreases peak postprandial glucose
  - Decreases plasma glucose 60-70 mg/dl
  - Reduce A1C 1.0-2.0%

Squirters – How does they rate?

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What questions?

- Limited Income
- Good insurance

Poll Question 5

- Fred is ready to take medications to get his blood sugar to target. Yet, he is very concerned about avoiding hypoglycemia, since his brother almost died from a hypoglycemic incident. Which medication class would you recommend?
  a. Meglitinides
  b. SGLT-2 Inhibitors
  c. Sulfonylureas
  d. Analog insulins

Older Adults - Considerations

- Reduced life expectancy
- Higher CVD burden
- Reduced GFR
- At risk for adverse events from polypharmacy
- More likely to be compromised from hypoglycemia

- Less ambitious targets
- A1c <7.5–8.0%
- Focus on drug safety
When goal is to avoid Hypoglycemia

- Avoid sulfonylureas
- Careful insulin dosing
- May need to up adjust glucose goals
- Monitor kidney function
- Reinforce for patients on insulin to “TIE”
  - Test
  - Inject
  - Eat

DPP-4 Inhibitors — “Incretin Enhancers”

Januvia (sitagliptin) – Tradjenta (linagliptin)
Onglyza (saxagliptin) Nesina (alogliptin)

- **Action:**
  - Increase insulin release w/ meals
  - Suppress glucagon
- **Dosing:**
  - Januvia – 100mg a day
  - Onglyza – up to 5mg a day
  - Tradjenta – 5mg a day
  - Nesina – up to 25 mg a day
- **Efficacy:** Decreases A1c by 0.6 -0.8%
- **Indication:** For type 2s

- Januvia, Onglyza eliminated via kidney, lower dose needed
- Do not cause wt gain or hypoglycemia
- Side effects – headache, runny nose, sore throat - watch for pancreatitis
- Cost $100 - $150 mo
### DPP-IV Inhibitors – How do they rate?

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### Poll Question 6

Pt is on Metformin and Sulfonylurea. Her A1c is 8.4. Patient has been trying to lose weight with limited success. Which of the following medications would be indicated to improve BG without increasing weight?

- a. Basal insulin
- b. GLP-1 Agonists
- c. Meglitinides
- d. Bolus insulin

### When goal is to avoid weight gain

- These meds are weight neutral
  - Metformin
  - DPP-IV Inhibitors - Januvia, Onglyza, Tradjenta, Nesina
  - AGIs - Acarbose

- These meds associated with wt loss
  - GLP-1 agonists (Byetta, Bydureon, Victoza, Tanzeum, Trulicity)
  - SGLT-2 Inhibitors (Canagliflozin, Dapagliflozin etc.)
  - Symlin (Pramlintide)
Incretin Mimetics – “Gut Hormone Imitators”
GLP-1 Agonists

- How do they work?

GLP-1 Effects in Humans
Understanding the Natural Role of Incretins

- GLP-1 secreted upon the ingestion of food
- Promotes satiety and reduces appetite
- ↑ Beta-cell response
- Beta cells: Enhances glucose-dependent insulin secretion
- Alpha cells: ↓ Postprandial glucagon secretion
- Liver: ↓ Glucagon reducing hepatic glucose output
- Stomach: Helps regulate gastric emptying
- GLP-1 degraded by DPP-4 within minutes

Weight Considerations

- Majority of T2DM patients overweight / obese
- Intensive lifestyle program
- Metformin
- GLP-1 receptor agonists
- ? Bariatric surgery
- Consider LADA in lean patients
**Poll Question 7**

Alice injects exenatide XR (Bydureon) once a week. Which of the following should she report immediately?

a. Bump at the injection site
b. Nausea
c. Weight loss
d. Sudden abdominal pain

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**Incretin Mimetics**

Exenatide (Byetta), Exenatide XR (Bydureon)

- **Action:**
  - Insulin release in response to meal
  - Slows gastric emptying
  - Causes Satiety
  - Protects Beta Cells
- **Exenatide Dosing:**
  - 5-10 mcg before break, dinner
  - Long acting version - 1x week (available in pens in 2015)
- **Efficacy:** Decreases A1c by 0.7%, wt by 3lbs
- **Indication:** For type 2s only - mono or in combo

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**Incretin Mimetics — Exenatide XR - Bydureon**

- **Once a Week Dosing:** 2mg
- **Efficacy:** Decreases A1c by 1.6%, wt by ~6lbs
- **Indication:** For type 2s only
- **Other:** – Available in pen
- **Caution:**
  - not indicated for pt’s w/ history of medullary thyroid tumor
  - pancreatitis warning
**Incretin Mimetics — Albiglutide - Tanzeum**

- **Once a Week Dosing:** 30 – 50mg
- **Efficacy:**
  - Decreases A1c by ~ 1%, wt by ~2lbs
- **Indication:** For type 2s only
- **Other:** Pen injector
- **Caution:** not indicated for those with history of medullary thyroid tumor - pancreatitis warning

**Incretin Mimetics — dulaglutide — Trulicity**

- **Once a Week Dosing:** 0.75 – 1.5 mg
- **Efficacy:**
  - Decreases A1c by ~ 1%, wt by ~2lbs
- **Indication:** For type 2s only
- **Other:** Premixed Pen injector with retracting needle
- **Caution:** not indicated for those with history of medullary thyroid tumor - pancreatitis warning

**Incretin Mimetics - GLP-1 Analog**

**Liraglutide (Victoza)**

- **Liraglutide Dosing:** 1x daily, time not critical
  - 0.6 x 1 week – if tolerated (nausea), go to >
  - 1.2 x 1 week – if tolerated go to >
  - 1.8 mg daily
- **Efficacy:** lowers; A1c by 1%, body wt by ~ 2.5kg
- **Indication:** Monotherapy or in combo . Type 2 only
- **Other:** In pen

**Black box—thyroid tumor warning (avoid if family hx, notify MD of hoarseness, lump).**
Liraglutide Approved for Weight Loss

- Saxenda and Victoza contain the same active ingredient (liraglutide) at different doses
- Saxenda 3 mg and Victoza 1.8 mg
- Saxenda – as a treatment option for chronic weight management in addition to a reduced calorie diet and physical activity.
- Saxenda is approved for use in adults with a
  - BMI of ≥ 30 or
  - BMI of ≥ 27 or greater who have hypertension, type 2 diabetes, or dyslipidemia.

For all the Previous GLP-1 Agonists

- Pancreatitis Warning
  - Please tell all patients to report signs right away and discontinue meds
  - Signs include:
  - Sudden abdominal pain, nausea and vomiting

Incretin Mimetics – How do they rate?

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What questions?

- 69 year old male, BMI 28, on Metformin 1000mg BID and Exenatide 10mcg before breakfast and dinner.
- A1c 8.1%. Creat 1.2
- Pt is overweight, 11 yr history of diabetes

Poll Question 8

- For patients on SGLT-2 Inhibitors, a potential side effect is:
  - a. Balanitis
  - b. Hypertension
  - c. Kidney tenderness
  - d. Increased uric acid

SGLT2 Inhibitors- “Glucoretics”

- **Action:** “Glucoretic” decreases renal reabsorption in the proximal tubule of the kidneys (reset renal threshold and increase glucosuria)

  - **Names:**
    - Canagliflozin (Invokana)
      - Dosing: 100 – 300 mg once daily ac first meal
      - If eGFR 45-60: do not exceed 100mg a day
      - If eGFR <45, do not use
    - Empagliflozin - Jardiance
      - 10 – 25 mg daily
      - If GFR < 60, don’t use
    - Dapagliflozin (Farxiga)
      - Dosing: 5 – 10 mg once daily ac first meal
      - If eGFR <60, do not use
      - Don’t use if pt has bladder cancer and report blood in urine

  - **Efficacy:**
    - Weight loss of 1-3 lbs
    - Reduce A1C ~0.7-1.5%
Considerations

- May temporarily lower GFR
- Monitor B/P, K+ & renal function.
- Side effects: hypotension, UTI, increased urination, genital yeast infections.
- Other benefits?
  - Reverses glucose toxicity by increasing GLUT4 transport in muscle
  - Increase liver sensitivity to insulin and decreases gluconeogenesis.

SGLT2 Inhibitors - How do they rate?

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Indications for Insulin Sensitizers

Rosiglitazone (Avandia), Pioglitazone (Actos)

- **Action:** decrease insulin resistance by making muscle and adipose cells more sensitive to insulin. Decrease free fatty acids
- **Names:**
  - pioglitazone (Actos) – bladder cancer warning
  - Dosing: 15-45 mg daily
  - rosiglitazone (Avandia) – restriction relaxed
  - Dosing: 4-8 mg daily
- **Efficacy/Considerations**
  - Reduce A1C ~0.5-1.0%
  - 6 weeks for maximum effect
  - $100 a month
  - Can cause fluid retention, not indicated w/ CHF
TZDs – How do they rate?

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<td>Watch</td>
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<td>Can most tolerate/use?</td>
<td>CHF</td>
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Acarbose—How does it rate?

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Poll Question 9

- George type 2, is losing weight and thirsty with an A1c of 10.3%. Using AACE guidelines, what is appropriate action?
  - Evaluate lifestyle changes for 3 months
  - Start insulin therapy
  - Start metformin immediately
  - Start metformin plus another agent

Critical Points

- Individualize Glycemic targets & BG-lowering
- Diet, exercise, & education: foundation T2DM therapy
- Metformin = optimal 1st-line drug.
- After metformin, data limited. Combo therapy reasonable
- Ultimately, many T2 patients will require insulin therapy
- All treatment decisions should be made in conjunction with the patient (focus on preferences, needs & values.)
- CV risk reduction - a major focus of therapy.

ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

Diabetes Care 2012;35:1364–1379
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Self Study - List the Treatment Options

- 35 yr old, BMI 28, creat 0.8, A1c 6.7%
  Sit 1: Wants to try lifestyle changes before meds
  Sit 2: Started on Januvia, can’t afford it. What alt med?

- 72 yr old, thin, lives alone, A1c 7.3%. History of MI, stroke. On glyburide 10mg a day and beta blocker. Creat 1.4.

- 69 year old male, BMI 25, on Metformin 1000mg BID. AM glucose 120s, A1c 8.1%. Creat 1.3

- 64 yr old on daily; amaryl 4mg, Januvia 100mg, Avandia* 4 mg. A1c 9.2%. Pt c/o of 12 lb wt gain over past month. Creat 1.2, LDL 138

- Pt on Exenatide 10mcg BID, c/o of sudden abd pain.

Thank You