Diabetes Education SERVICES

15 years

Diabetes Boot Camp – Class 4

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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.

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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

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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%

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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

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Poll Question 4

- Which of the following is true about 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. Be aware of signs of hypoglycemia

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Poll Question 5

- When goal is to avoid hypoglycemia, which medication class would you recommend?

a. Meglitinides
b. SGLT-2 Inhibitors
c. Sulfonylureas
d. Analog insulins

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Poll Question 6

- 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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Poll Question 7

- For patients on SGLT-2 Inhibitors, a potential side effect is:

a. Balanitis
b. Hypertension
c. Kidney tenderness
d. Increased uric acid

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Poll Question 8

- George type 2, is losing weight and thirsty with an A1c of 10.3%. Using AACE guidelines, what is appropriate action?

a. Evaluate lifestyle changes for 3 months
b. Start insulin therapy
c. Start metformin immediately
d. Start metformin plus another agent

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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."

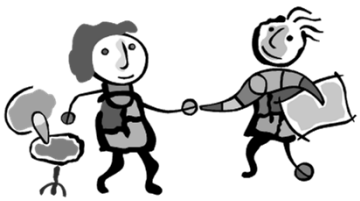
- **Gauge patient's preferred level of involvement.**
- **Explore, where possible, therapeutic choices.**
- **Utilize decision aids.**
- **<u>Shared</u> decision making – final decisions re: lifestyle choices ultimately lie with the patient.**

ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

***Diabetes Care* 2012;35:1364–1379**
***Diabetologia* 2012;55:1577–1596**

Considerations

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



ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

Diabetes Care **2012;35:1364–1379**
Diabetologia **2012;55:1577–1596**

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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

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Resources for Medications

- Partnership for Prescription Assistance
  - www.pparx.org
- NeedyMeds.org
- www.rxassist.org

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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

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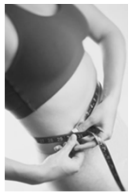
Antihyperglycemic Therapy – 1st Step

- Lifestyle Changes
  - Weight control
  - Healthy eating
  - Activity



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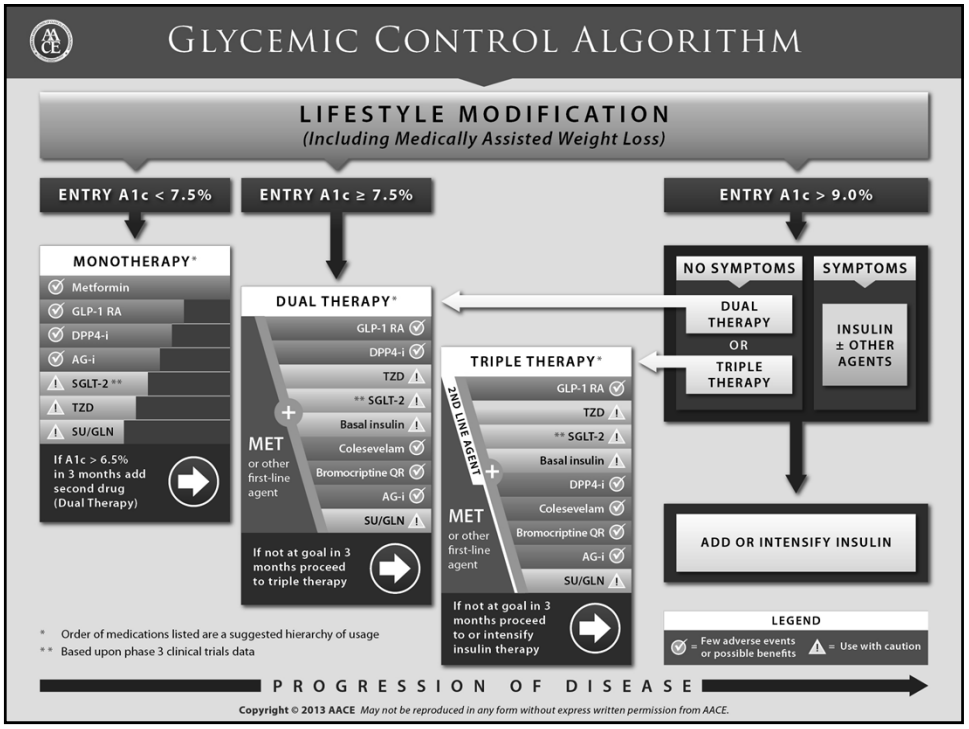
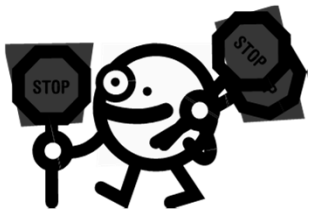


Ideal Diabetes Med -

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

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 2500 mg daily
  - **Efficacy:**
    - Decrease fasting plasma glucose 60-70 mg/dl
    - Reduce A1C 1.0-2.0%

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Biguanides - Metformin

- Benefits
  - Decrease LDL cholesterol and triglycerides
  - No weight gain, possible modest weight loss
  - Cancer protective?
- Concerns
  - Diarrhea and abdominal discomfort – Use XR
  - Lactic acidosis if improperly prescribed
  - Watch for B12 deficiency
  - Hold prior to IV contrast dye studies and use caution during acute illness. Resume when kidney function adequate

Considerations
Biguanide - Metformin (Glucophage®)

- Contraindications due to lactic acidosis:
  - creatinine >1.4 females, >1.5 males
  - liver disease
  - alcohol abuse
  - over 80 years old
  - risk of acidosis
  - during IV dye study
  - CHF requiring meds

Metformin – How does it rate?

Question	Answer
Cause hypoglycemia?	
Cause weight gain?	
Affordable?	
Lowers CV risk?	
Can most tolerate /use?	

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

Generic	Trade	Duration
Glyburide	Diabeta, Micronase, most likely to cause hypo – last choice	12-24 hrs
Glipizide*	Glucotrol, Glucotrol Xl	12-24 hrs
Glimepiride	Amaryl	16-24 hrs

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

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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 16mg
    - 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%

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Meglitinides

- Other Effects
  - Hypoglycemia (less than with sulfonylureas if patient has a variable eating schedule)
  - Minimal weight gain
  - No significant effect on plasma lipid levels
  - Safe at higher levels of serum Cr than sulfonylureas

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Squirters – How does they rate?

Question	Answer

- Cause hypoglycemia?
- Cause weight gain?
- Affordable?
- Lowers CV risk?
- Can most tolerate /use?

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What questions?

- 72 yr old, thin, lives alone, A1c 7.3%. History of MI, stroke. DM for 12 yrs, "diet controlled". Limited income. Creat 1.4.

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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

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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

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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

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DPP-4 Inhibitors – "Incretin Enhancers"

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

- 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

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DPP-IV Inhibitors – How do they rate?

Question	Answer

- Cause hypoglycemia?
- Cause weight gain?
- Affordable?
- Lowers CV risk?
- Can most tolerate /use?

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If on Metformin and Sulfonylurea – A1c 8.4 - Pt struggling with weight

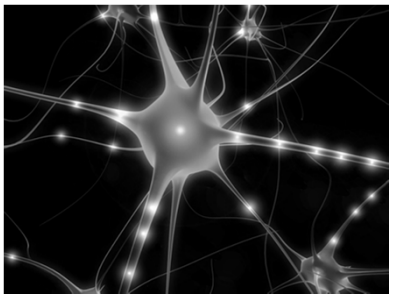
When goal is to avoid weight gain

- These meds are weight neutral
  - Metformin
  - DPP-IV Janvia, Onglyza, Tradjenta, Nesina
  - Acarbose

- These meds associated with wt loss
  - GLP-1 agonists (Byetta, Bydureon, Victoza, Tanzeum)
  - SGLT-2 Inhibitors (Canagliflozin, Dapagliflozin)
  - Symlin (Pramlintide)

Incretin Mimetics – "Gut Hormone Imitators" GLP-1 Agonists

- How do they work?



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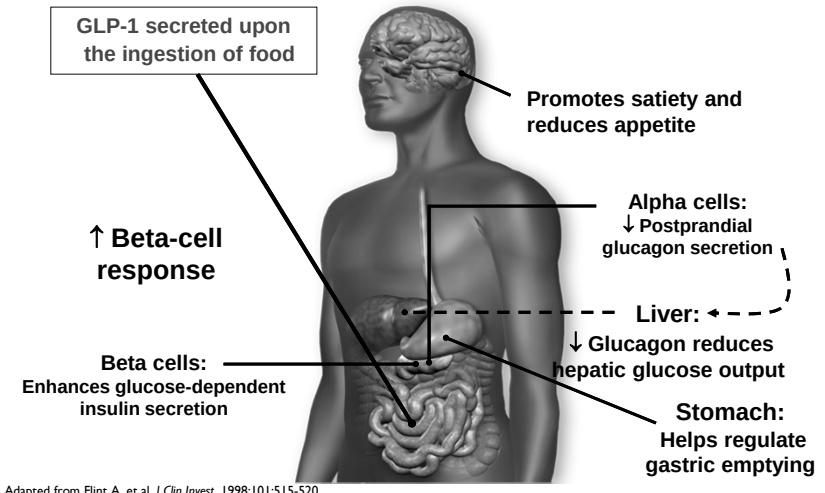
GLP-1 Effects in Humans
Understanding the Natural Role of Incretins



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Adapted from Larsson H, et al. *Acta Physiol Scand.* 1997;160:413-422
Adapted from Nauck MA, et al. *Diabetologia.* 1996;39:1546-1553
Adapted from Drucker DJ. *Diabetes.* 1998;47:159-169

GLP-1 degraded by DPP-4 w/in minutes

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Weight Considerations

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

Diabetes Care 2012;35:1364–1379
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ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

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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 - 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

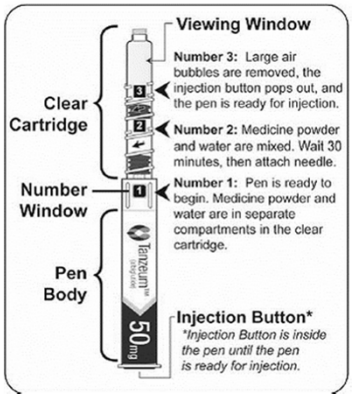
- **Efficacy:** lowers; A1c by 1%, body wt by ~ 2.5kg
- **Indication**: Monotherapy or in combo . Type 2 only
- **Other**: In pen, with preset dosing
- **Black box**–thyroid tumor warning (avoid if family hx, notify MD of hoarseness, lump).

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**: Pt will need to mix powdered form and inject – Pen in future
- **Caution**:
  - not indicated for those with 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



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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

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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
-

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Incretin Mimetics – How do they rate?

Question	Answer
Cause hypoglycemia?	
Cause weight gain?	
Affordable?	
Lowers CV risk?	
Can most tolerate /use?	

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What questions?

- 69 year old male, BMI 25, 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

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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%

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Considerations

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

SGLT2 Inhibitors- How do they rate?

Question	Answer
Cause hypoglycemia?	No
Cause weight gain?	No
Affordable?	No
Lowers CV risk?	No
Can most tolerate /use?	Yes?

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

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TZDs – How do they rate?

Question	Answer
Cause hypoglycemia?	
Cause weight gain?	
Affordable?	
Lowers CV risk?	
Can most tolerate /use?	

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Indications for Glucosidase Inhibitors Acarbose (Precose®), Miglitol (Glyset®)

Action: Slower

- Target post-prandial blood glucose
- Minimal systemic absorption

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Alpha-glucosidase Inhibitors

- **Action**: blocks enzymes that digest starches in the small intestine
- **Name**: acarbose (Precose)
  - Dosing: 75-300mg based on weight
- Efficacy
  - Decrease postprandial glucose 40-50 mg/dl
  - Decrease A1C 0.5-1.0%
- Other Effects
  - Flatulence or abdominal discomfort
  - Contraindicated in patients with inflammatory bowel disease or cirrhosis
- Special Consideration
  - In case of hypoglycemia, treat with glucose tabs or milk
  - (other starches are blocked by medication))

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Acarbose– How does it rate?

Question	Answer

- Cause hypoglycemia?
- Cause weight gain?
- Affordable?
- Lowers CV risk?
- Can most tolerate /use?

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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

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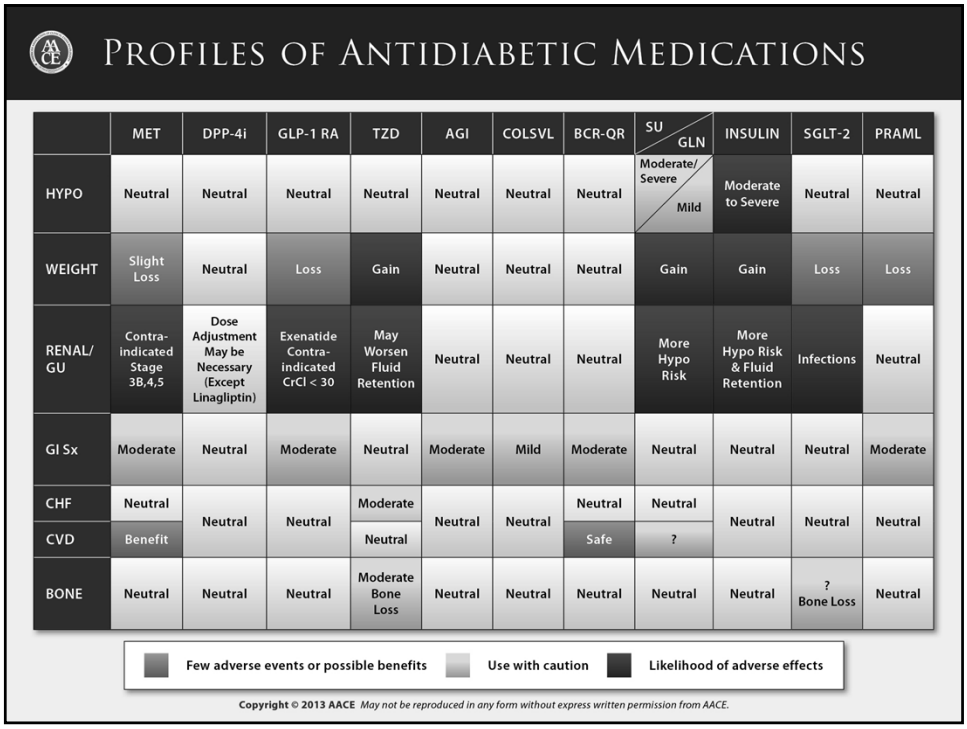

Self Sudy - List the Treatment Options

- 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.

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Thank You

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