



15 years

Please Download Medication PocketCards for this section – DiabetesEd.net > Resources

Diabetes Boot Camp – Class 5

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Diabetes Education SERVICES

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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Diabetes Education SERVICES

CDE Exam Outline

- value of history, etc.)
- B. Assess Medical/Health/Psychosocial and Economic Status (20)
1. Diabetes-specific health history (duration, symptoms, complications, adherence to standards of care, treatment, etc.)
 2. General health history (family history, allergies, medical history, nutrition history, etc.)
 3. Previous and current medication regimen (medication dosage, prescription and nonprescription drugs, herbals, alternative remedies, adverse reactions, etc.)
 4. Treatment fears and myths (hypoglycemia, hyperglycemia, needles, weight gain, etc.)
 5. Family/Caregiver dynamics and social supports
 6. Substance use (alcohol, tobacco, caffeine, etc.)
 7. Developmental transitions and mental health status (age, life stages, coping ability, adjustment to diagnosis, etc.)
 8. Specific barriers to diabetes self-care regimen (cognitive ability, language, cultural, spiritual, psychosocial, physical, economic, etc.)
- d) Adjustment of monitoring, food, and/or medication
6. Pharmacologic management
- a) ADA/European Association for the Study of Diabetes (EASD), AACE guidelines
 - b) Medications (insulin, oral and injectable medications, administration, side effects, etc.)
 - c) Delivery systems (pump therapy, devices, etc.)
 - d) Medication adjustment
 - e) Interactions (drug-drug, drug-food, etc.)
 - f) Non-prescription preparations
7. Acute complications: causes, prevention and treatment
- Clinical Practice (16)
1. Apply inpatient standards (AACE, ADA, Endocrine Society, etc.)
 2. Apply outpatient standards (AACE, ADA, Endocrine Society, etc.)

They will provide generic and trade name for Meds on Exam



Diabetes Education SERVICES

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 Education SERVICES

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



Diabetes Education SERVICES

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.



ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

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



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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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Antihyperglycemic Therapy – 1st Step

▶ Lifestyle Changes

- ▶ Weight control
- ▶ Healthy eating
- ▶ Activity



ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

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



Diabetes Education SERVICES

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 |



Diabetes Education SERVICES

Ideal Diabetes Med -



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



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Poll question 3

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



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



Diabetes Education SERVICES

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?



Diabetes Education SERVICES

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



Diabetes Education SERVICES

Considerations

Biguanide - Metformin (Glucophage®)

- ▶ **Contraindications due to risk of 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



ADA Stds 2015 suggests GFR may be a more appropriate measure. If GFR <45, max dose is 1000mg a day. If GFR <30, stop metformin.



Diabetes Education SERVICES

Metformin – How does it rate?

Question	Answer
▶ Cause hypoglycemia?	No
▶ Cause weight gain?	No
▶ Affordable?	Yes
▶ Lowers CV risk?	Yes
▶ Can most tolerate /use?	Yes/No (GI, creat)



Diabetes Education SERVICES

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



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Sulfonylureas –

- ▶ Action: tells pancreas to squirt insulin all day
- ▶ Who?
- ▶ Lean type 2



Diabetes Education SERVICES

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



Diabetes Education SERVICES

Sulfonylureas: 2nd Generation

Generic	Trade	Duration
▶ Glyburide	Diabeta, Micronase, <small>most likely to cause hypo – last choice</small>	12-24 hrs
▶ Glipizide*	Glucotrol, Glucotrol XI	12-24 hrs
▶ Glimepiride	Amaryl	16-24 hrs



Diabetes Education SERVICES

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



Diabetes Education SERVICES

Indication for “Fast Acting” Insulin Secretagogues- Meglitinides

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



Diabetes Education SERVICES

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%



Diabetes Education SERVICES

Squirters – How does they rate?

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



Diabetes Education SERVICES

What questions?

- ▶ 72 yr old, thin, lives alone, A1c 7.3%. History of MI, stroke. DM for 12 yrs, “diet controlled”. Creat 1.4.
- ▶ Limited Income
- ▶ Good insurance



Diabetes Education SERVICES

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



Diabetes Education SERVICES

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



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



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Diabetes Education SERVICES

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



Diabetes Education SERVICES

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



Diabetes Education SERVICES

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



Diabetes Education SERVICES

DPP-IV 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



Diabetes Education SERVICES

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



Diabetes Education SERVICES

When goal is to avoid weight gain

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



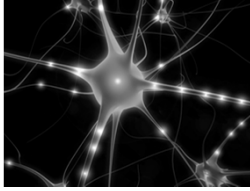
- ▶ These meds associated with wt loss
 - ▶ GLP-1 agonists (Byetta, Bydureon, Victoza, Tanzeum, Trulicity)
 - ▶ SGLT-2 Inhibitors (Canagliflozin, Dapagliflozin etc.)
 - ▶ Symlin (Pramlintide)



Diabetes Education SERVICES

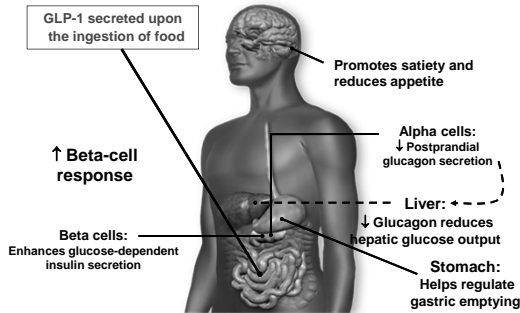
Incretin Mimetics – “Gut Hormone Imitators” GLP-1 Agonists

▶ How do they work?



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



Adapted from Flint A, et al. J Clin Invest. 1998;101:515-520
Adapted from Larsson H, et al. Acta Physiol Scand. 1997;160:413-422
Adapted from Nauck MA, et al. Diabetologia. 1998;39:1546-1553
Adapted from Drucker DJ. Diabetes. 1998;47:159-169

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



Diabetes Education
SERVICES

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
Diabetologia
2012;55:1577-1596

ADA-EASD Position Statement: Management of Hyperglycemia in T2DM



Diabetes Education
SERVICES

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



Diabetes Education SERVICES

Incretin Mimetics

Exenatide (Byetta), Exenatide XR (Bydureon)

▶ Action:

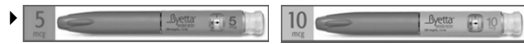
- ▶ Insulin release in response to meal
- ▶ Slows gastric emptying
- ▶ Causes Satiety
- ▶ Protects Beta Cells

▶ 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



Diabetes Education SERVICES

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



Diabetes Education SERVICES

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.



Diabetes Education SERVICES

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
-



Diabetes Education SERVICES

Incretin Mimetics – How do they rate?

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



Diabetes Education SERVICES

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



Diabetes Education SERVICES

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



Diabetes Education SERVICES

SGLT2 Inhibitors- "Glucoretics"

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

▶ **Names:**

- ▶ Canagliflozin (Invokana) Empagliflozin - Jardiance
- ▶ Dosing: 100 – 300 mg once daily ac first meal 10 – 25 mg daily
- ▶ If eGFR 45-60: do not exceed 100mg a day If GFR < 60, don't use
- ▶ If eGFR <45, do not 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%



Diabetes Education SERVICES

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.



Diabetes Education SERVICES

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?



Diabetes Education SERVICES

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



Diabetes Education SERVICES

TZDs – How do they rate?

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



Diabetes Education SERVICES

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

Action: Slower

- ▶ Target post-prandial blood glucose
- ▶ Minimal systemic absorption



Diabetes Education SERVICES

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))



Diabetes Education SERVICES

Acarbose– How does it rate?

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



Diabetes Education SERVICES

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



Diabetes Education SERVICES

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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PROFILES OF ANTIDIABETIC MEDICATIONS


	MET	DPP-4i	GLP-1 RA	TZD	AGI	COLSVL	BCR-QR	SU GLN	INSULIN	SGLT-2	PRAML
HYP0	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate/ Severe Mild	Moderate to Severe	Neutral	Neutral
WEIGHT	Slight Loss	Neutral	Loss	Gain	Neutral	Neutral	Neutral	Gain	Gain	Loss	Loss
RENAL/ GU	Contra- indicated Stage 3B,4,5	Dose Adjustment May be Necessary (Except Linagliptin)	Exenatide Contra- indicated CrCl < 30	May Worsen Fluid Retention	Neutral	Neutral	Neutral	More Hypo Risk	More Hypo Risk & Fluid Retention	Infections	Neutral
GI 5x	Moderate	Neutral	Moderate	Neutral	Moderate	Mild	Moderate	Neutral	Neutral	Neutral	Moderate
CHF	Neutral	Neutral	Neutral	Moderate	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral
CVD	Benefit	Neutral	Neutral	Neutral	Neutral	Neutral	Safe	?	Neutral	Neutral	Neutral
BONE	Neutral	Neutral	Neutral	Moderate Bone Loss	Neutral	Neutral	Neutral	Neutral	Neutral	? Bone Loss	Neutral

Few adverse events or possible benefits
 Use with caution
 Likelihood of adverse effects

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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



