Current Trends in Management of Blood Glucose in Type 2 Diabetes Mellitus (T2DM)

Susan Cornell, BS, PharmD, CDE, FAPhA, FAADE
Assistant Professor, of Pharmacy Practice
Midwestern University Chicago College of Pharmacy

Presenter Disclosure:

Board Member/Advisory Panel:
Kestrel Diabetes Product Sourcebook, Kestrel Health Information Advisory Board
Advanced Studies in Medicine: Endocrinology Advisory Board, Johns Hopkins

Speaker’s Bureau:
Merck, Abbott Diabetes Care, Novo-Nordisk, Johnson and Johnson Diabetes Institute, Takeda

Board of Directors
Illinois Pharmacists Association, President-Elect
Objectives

• Describe the similarities and differences between the two current treatment algorithms for the management of blood glucose levels in Type 2 diabetes

• Identify the medications that have a positive or negative impact on weight in each of the treatment algorithms

• Identify the medications that may cause hypoglycemia in each of the treatment algorithms

• Recognize the appropriate therapeutic choices in individual patients based on their demographic and clinical characteristics

Patient Case #1
Patient Case # 1 - SR

SR is a 59 y/o Asian American woman

• PMH:
  - Dyslipidemia x 6 yr
  - T2DM x 3 yr
  - Osteoporosis x 2 yr
  - Recurrent DVT
  - Recurrent UTI

• SH:
  (+) tobacco
  (+) alcohol socially

• FH:
  Mother: OP, T2DM, HTN

• VS:
  - BP: 128/78 mm Hg, HR: 68 bpm
  - Wt: 135 lb, Ht: 5’2”
  - A1C: 8.1%, FBG: 320 mg/dL
  - LDL: 118 mg/dL
  - HDL: 32 mg/dL
  - TG: 325 mg/dL
  - INR: 2.4

Case # 1 - SR

• Exercise/daily activities; walks 2-3x/week for 25 minutes
• Nutrition: 2-3 meals daily
• Current medications:
  - Glimepiride 2 mg once daily
  - Metformin 1000 mg twice daily
  - Nateglinide 60 mg three times daily
  - Alendronate 70 mg / week
  - Simvastatin 20 mg once daily
  - Warfarin 2 mg once daily
  - Paroxetine 20 mg once daily
  - Aspirin 81 mg once daily
  - Acetaminophen 500 mg as needed for pain
• SMBG every morning
  - Average FBG: 150-160 mg/dL
Does SR need a change in her diabetes medication regimen?

1. Yes
2. No
3. Not sure

Which of the following diabetes medications, if any, would you discontinue?

A. Glimepiride
B. Metformin
C. Nateglinide
D. No changes
E. Not sure
Which of the following diabetes medications, if any, would you increase?

A. Glimepiride
B. Metformin
C. Nateglinide
D. No changes
E. Not sure

Which of the following diabetes medications, if any, would you add?

A. Basal insulin
B. Thiazolidinedione (glitazone)
C. Incretin agent (glucagon-like peptide 1 agent or dipeptidyl peptidase-4 inhibitor)
D. A and B
E. A and C
F. Not sure
Diabetes Mellitus

- **Type 1**
  - Autoimmune
  - Acute onset

- **Type 2**
  - Insulin resistance and insulin secretory defects
  - Chronic onset

- **Gestational (GDM)**

- **At Risk (formerly known as pre-diabetes)**
  - Insulin resistance and insulin secretory defects
  - Chronic onset

- **Latent Autoimmune Diabetes in Adults (LADA)**
  - a.k.a. Type 1.5
  - Acute onset

---

Does early, aggressive treatment have a long-term effect in preventing diabetes related complications?

1. Yes
2. No
3. Not sure
Lowering A1c Reduces Complications

<table>
<thead>
<tr>
<th></th>
<th>DCCT**</th>
<th>Kumamoto†</th>
<th>UKPDS§</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1c</td>
<td>9 → 7%</td>
<td>9 → 7%</td>
<td>8 → 7%</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>↓ 63%</td>
<td>↓ 69%</td>
<td>↓ 17-21%</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>↓ 54%</td>
<td>↓ 70%</td>
<td>↓ 24-33%</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>↓ 60%</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Macrovascular</td>
<td>↓ 41%</td>
<td>—</td>
<td>↓ 16%</td>
</tr>
<tr>
<td>Disease</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Distribution of A1c in the Former DCCT Intensive & Conventional Groups During EDIC

Mean A1c During EDIC
Conventional 8.2% Intensive 8.0%

Conventional
Intensive

Fasting vs. Postprandial Glucose Relationship to Complications

• Fasting Glucose
  – Microvascular complications
    • Retinopathy
    • Neuropathy
    • Nephropathy

• Postprandial Glucose
  – Macrovascular complications
    • Dyslipidemia
    • Hypertension

The American Diabetes Association Estimates That By The Time A Patient Is Finally Diagnosed With Type 2 Diabetes They Have Actually Had Diabetes For About 9 Years!
Natural History of Type 2 Diabetes: Disease Progression

IFG=Impaired fasting glucose; IGT=Impaired glucose tolerance.


Insulin Resistance

Hyperinsulinemia

Genetics
Weight Gain
Dyslipidemia
Hypertension

Hyperglycemia

IGT
IFG
Early Diabetes
Late Diabetes

Macrovascular Complications
Advancing Age

Microvascular Complications

How many dysfunctional (broken) organs are currently identified in T2DM?

1. 1-2
2. 3-5
3. 6-7

IFG:Impaired fasting glucose; IGT:Impaired glucose tolerance.
Organ Defects in Diabetes

Type 2
- Chronic onset
  - 9-12 years

- **1) Pancreas**
  - Increased α-cell secretion
  - B-cell impairment
    - incorrect insulin secretion
    - Incorrect amylin secretion
  - **2) Brain**
    - impaired satiety
    - ↓ dopamine
    - impaired circadian rhythm

- **3) Liver**
  - Increased gluconeogenesis
    - Due to ↑ α-cell secretion

- **4) Peripheral tissue**
  - ↓ GLUT-4 transporters

- **5) GI tract**
  - ↓ GLP-1

- **6) Adipose tissue (fat)**
  - ↓ adiponectin
  - ↑ cytokines, IL-6, TN

Possible 7) Kidney ???

Sites of Action of Diabetes Medications

- **Dopamine agonists** (brain)
- **Insulin secretagogues** (sulfonylureas, meglitinides) (pancreas)
- **Biguanides** (liver)
- **Alpha-glucosidase inhibitors** (GI tract)
- **Amylinomimetics** (GI tract, liver, pancreas, brain)
- **Incretins** (GLP-1 enhancers, DPP-4 inhibitors) (GI tract, liver, pancreas, brain)
- **Insulin** (pancreas, peripheral tissue)
- **Muscle/tissue**
- **Thiazolidinediones (TZDs)** (peripheral tissue, fat)

Key to Optimal Control is Early Diagnosis and Treatment with Agents That Address the Underlying Pathophysiologic Abnormalities

Pharmacotherapy Options

- Insulin
  - Bolus insulin
    - Insulin lispro
    - Insulin aspart
    - Insulin glulisine
    - Regular human insulin
  - Basal insulin
    - Insulin NPH
    - Insulin detemir
    - Insulin glargine

- Oral Medications
  - α-glucosidase inhibitors (AGI)
  - Dipeptidyl peptidase-4 (DPP-4) inhibitors (gliptins)
  - Dopamine agonists
  - Glitnides
  - Biguanides
  - Sulfonylureas
  - Thiazolidinediones (TZDs or glitazones)

- Non-insulin injectable agents
  - Glucagon-like peptide-1 (GLP-1) mimetic (GLP-1 agonists)
  - Amylinomimetic
Key Points to Consider when Selecting Pharmacotherapy for T2DM

- How long the patient has had diabetes (duration of disease).
  - Quality of β-cell function & quantity of β-cell mass
- How many dysfunctional organs are targeted (fixed)
- Which blood glucose level is not at target (e.g., fasting, postprandial, or both).
- Patient preference for route of administration (e.g., oral, inhaled, injectable)
- The degree of A1C-lowering effect required to achieve goal.
- The side effect profile and the patient’s tolerability.
- Co-existing conditions (e.g. CVD, depression, osteoporosis, etc)


Clinical Guidelines / Algorithms: ADA vs. AACE/ACE
ADA Medical Management of Type 2 Diabetes

At diagnosis:
- lifestyle + metformin

Step 1

Step 2
- lifestyle + metformin and basal insulin
- lifestyle + metformin and sulfonylurea

Tier 1: well-validated core therapies

Step 3
- lifestyle + metformin and intensive insulin
- lifestyle + metformin and pioglitazone and sulfonylurea
- lifestyle + metformin and GLP-1 agonist

Tier 2: less well-validated therapies


AACE/ACE Diabetes Algorithm

- Recommends the use of specific combinations based on:
  - Current A1C
  - A1C-lowering potential
  - Drug naïve or under treatment status
  - Safety, with emphasis on avoiding hypoglycemia
  - Targeted glucose action of the combination

ACE/AACE Diabetes Road Map Task Force. Road maps to achieve glycemic control in type 2 diabetes mellitus (2009 update). Available at: http://www.aace.com
AACE/ACE 2009 Algorithm

- Algorithm is stratified by HbA1c level
  - HbA1c \( \leq 7.5\% \)
    - Start with monotherapy to achieve a goal HbA1c of 6.5%. If monotherapy fails, progress to dual and then to triple therapy. Finally, insulin therapy should be initiated, with or without additional agents
  - HbA1c 7.6%–9.0%
    - Begin dual therapy because no single agent is likely to achieve the goal of 6.5%. If dual therapy fails, progress to triple therapy and then to insulin therapy, with or without additional orally administered agents
  - HbA1c > 9.0%
    - If the patient is asymptomatic, begin with triple therapy. If, however, the patient is symptomatic, or therapy with similar medications has failed, it is appropriate to initiate insulin therapy, either with or without additional orally administered agents


**A1C 6.5 – 7.5%**
- Monotherapy
  - MET + GLP-1 or DPP4
  - TZD
  - GLP-1 or DPP4
  - Metformin
  - Colesevelam

**A1C 7.6 – 9.0%**
- Dual Therapy
  - MET + GLP-1 or DPP4
  - TZD
  - GLP-1 or DPP4

- Triple Therapy
  - MET + GLP-1 or DPP4
  - TZD

**A1C > 9.0%**
- If drug-naive
  - Insulin ± Other Agent(s)
- If under treatment
  - Insulin ± Other Agent(s)

- May not be appropriate for all patients
- For patients with diabetes and A1C < 6.5%, pharmacologic Rx may be considered
- If A1C goal not achieved safely
- Preferred initial agent
  - DPP4 if \( \uparrow \) PPG and \( \uparrow \) FPG or GLP-1 or DPP4
  - TZD if metabolic syndrome and/or nonalcoholic fatty liver disease (NAFLD)
  - AGI if \( \uparrow \) PPG
  - Glinide if \( \uparrow \) PPG or SU if \( \uparrow \) FPG
  - Low-dose secretagogue recommended

- May not be reproduced in any form without express written permission from AACE
### Type 2 Diabetes Oral Medications

<table>
<thead>
<tr>
<th>Class</th>
<th>Medication</th>
<th>Target Organ/ MOA</th>
<th>Blood Glucose Affected/ Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-Glucosidase inhibitors</td>
<td>Acarbose</td>
<td>Small intestine/ Slows breakdown of glucose in the GI tract</td>
<td>Postprandial/ Gas, diarrhea, abdominal discomfort</td>
</tr>
<tr>
<td></td>
<td>Miglitol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biguanides</td>
<td>Metformin</td>
<td>Liver/ ↓ hepatic glucose output</td>
<td>Fasting/ GI distress, gas, metallic taste</td>
</tr>
<tr>
<td>DPP-4 Inhibitors (Gliptins)</td>
<td>Sitagliptin</td>
<td>GI tract/ Inhibits GLP-1 breakdown</td>
<td>Postprandial (some fasting)/ Runny nose, sore throat, headache</td>
</tr>
<tr>
<td></td>
<td>Saxagliptin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glitinites</td>
<td>Repaglinide</td>
<td>↑ Pancreas/ endogenous insulin secretion (fast)</td>
<td>Postprandial/ Hypoglycemia, GI distress, weight gain</td>
</tr>
<tr>
<td></td>
<td>Nateglinide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulfonylureas (second- generation)</td>
<td>Glimipiride</td>
<td>↑ Pancreas/ endogenous insulin secretion (slow)</td>
<td>Fasting &amp; postprandial/ Hypoglycemia, GI distress, weight gain, skin rash</td>
</tr>
<tr>
<td></td>
<td>Glyburide</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Glipizide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thiazolidine-diones</td>
<td>Pioglitazone</td>
<td>Peripheral tissues/ ↑ glucose uptake in peripheral tissues</td>
<td>Fasting &amp; postprandial/ Weight gain, headache, edema</td>
</tr>
<tr>
<td></td>
<td>Rosiglitazone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dopmaine agonists</td>
<td>Bromocriptine</td>
<td>↑ Brain/ dopamine; regulate circadian rhythm; ↑ adipose tissue</td>
<td>Postprandial/ Nausea, Headache, fatigue, ↓ TG, hypotension</td>
</tr>
</tbody>
</table>


### Type 2 Diabetes Injectable Medications

<table>
<thead>
<tr>
<th>Class</th>
<th>Medication</th>
<th>Target Organ / MOA</th>
<th>Blood Glucose Affected/ Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLP-1 agents</td>
<td>Exenatide</td>
<td>GI tract/ Exogenous GLP-1</td>
<td>Postprandial/(some fasting) Nausea, vomiting, satiety, weight loss, headache</td>
</tr>
<tr>
<td></td>
<td>Exenatide LAR</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Liraglutide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amylinomimetic</td>
<td>Pramlintide</td>
<td>(Pancreas) &amp; Brain/ Exogenous amylin</td>
<td>Postprandial/ GI upset, headache, anorexia, cough, fatigue, hypoglycemia with insulin</td>
</tr>
<tr>
<td>Insulin</td>
<td>Various</td>
<td>(Pancreas)/ Exogenous insulin</td>
<td>Basal: fasting (some postprandial) Bolus: postprandial Hypoglycemia, weight gain</td>
</tr>
</tbody>
</table>

# A1c Lowering & β-Cell Function Comparison

<table>
<thead>
<tr>
<th>Monotherapy</th>
<th>A1C (%) Reduction</th>
<th>Save β-Cell Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfonylurea</td>
<td>1.5–2.0</td>
<td>no</td>
</tr>
<tr>
<td>Metformin</td>
<td>1.5</td>
<td>maybe</td>
</tr>
<tr>
<td>Glitazones (TZD’s)</td>
<td>1.0–1.5</td>
<td>yes</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>0.5–1.0</td>
<td>no</td>
</tr>
<tr>
<td>α-Glucosidase Inhibitors (AGI’s)</td>
<td>maybe</td>
<td>Not sure</td>
</tr>
<tr>
<td>GLP-1 agonists</td>
<td>0.8 – 1.9</td>
<td>yes</td>
</tr>
<tr>
<td>DDP-4 Inhibitors (Glitins)</td>
<td>0.5 - 1.1</td>
<td>yes</td>
</tr>
<tr>
<td>Insulin</td>
<td>Open to target</td>
<td>yes</td>
</tr>
</tbody>
</table>

## Fasting or Postprandial Blood Glucose Help?

### Fasting
- **Metformin**
- **Exenatide**, **Liraglutide**
- **Sitagliptin**, **Saxagliptin**
- **TZDs**
  - Pioglitazone
  - Rosiglitazone
- Sulfonylureas
  - Multiple
  - Basal Insulin
  - Glargine
  - Detemir
  - NPH @ bedtime

+ low risk of hypoglycemia

### Postprandial Control
- **Exenatide**, **Liraglutide**
- **Sitagliptin**, **Saxagliptin**
- Nateglinide, Repaglinide
- Acarbose, Miglitol
- **TZDs**
  - Pioglitazone
  - Rosiglitazone
- Sulfonylureas
  - Multiple
- Prandial insulins
  - Aspart
  - Lispro
  - Glulisine
  - Regular
## Considerations in Pharmacotherapy in Diabetes Patients

<table>
<thead>
<tr>
<th>Medication</th>
<th>Potential benefits</th>
<th>Caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha-glucosidase inhibitors</td>
<td>Postprandial glucose lowering (delays digestion of carbohydrates)</td>
<td>Gi side effects (flatulence, diarrhea)</td>
</tr>
<tr>
<td>Amylinomimetics (pramlintide)</td>
<td>Weight loss, used with insulin to enhance postprandial glucose lowering</td>
<td>Gi side effects, hypoglycemia</td>
</tr>
<tr>
<td>Biguanides (Metformin)</td>
<td>Weight loss, improved lipids</td>
<td>Avoid in patients with renal or hepatic insufficiency</td>
</tr>
<tr>
<td>Bile acid sequestrant (colesevelam)</td>
<td>Lowers cholesterol</td>
<td>Gi obstruction, hypertriglyceridemia</td>
</tr>
<tr>
<td>DPP-4 inhibitors (sitagliptin, saxagliptin)</td>
<td>Weight neutral, minimal risk of hypoglycemia, minimal side effects</td>
<td>Nasopharyngitis, URI, headache</td>
</tr>
<tr>
<td>Glitinides (nateglinide, repaglinide)</td>
<td>Patients with irregular eating habits</td>
<td>Hypoglycemia, weight gain</td>
</tr>
<tr>
<td>GLP-1 agonists (exenatide, liraglutide*)</td>
<td>Minimal risk of hypoglycemia, weight loss</td>
<td>Gi side effects, pancreatitis, *thyroid tumors</td>
</tr>
<tr>
<td>Insulin</td>
<td>Patients with high A1Cs; most effective glucose lowering</td>
<td>Hypoglycemia, weight gain</td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td>Inexpensive</td>
<td>Hypoglycemia, weight gain</td>
</tr>
<tr>
<td>TZDs (pioglitazone, rosiglitazone)</td>
<td>Improve insulin sensitivity</td>
<td>Weight gain, edema/congestive heart failure, bone loss</td>
</tr>
</tbody>
</table>


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## Early aggressive treatment with insulin can result in remission of type 2 diabetes

A. Yes  
B. No  
C. Maybe
Early insulinization with intensive insulin management

“Remissions” in New Onset Patients with type 2 diabetes

- 126 Chinese patients with new onset type 2 diabetes: mean A1C 10.1%, FPG 245 mg/dL, BMI 25 kg/m²
- Treated with CSII for 2 wks
- Followed for 2 yrs on diet only
- Relapse defined as FPG > 126 mg/dL or 2 h PPG > 180 mg/dL

Remission Rate (%) over time:

- 3mo
- 6mo
- 12mo
- 24mo


Early Insulin Replacement

- Induce beta-cell “rest”
- Preserve beta-cell function
- Reduce CVD risk
- Better blood glucose control
- Risk reduction in complication

Rosenstock J. Clinical Update: Type 2 Diabetes Management. 2006 1(1):1-4
Shaefer C. Insulin 2006 1(2):61-64
### Characteristics of Insulin

<table>
<thead>
<tr>
<th>Insulin Type</th>
<th>Onset (hr)</th>
<th>Peak (hr)</th>
<th>Duration (hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rapid Acting (Bolus)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin aspart</td>
<td>0.25</td>
<td>1-2</td>
<td>3-5</td>
</tr>
<tr>
<td>Insulin lispro</td>
<td>0.25</td>
<td>0.5-1.5</td>
<td>3-5</td>
</tr>
<tr>
<td>Insulin glulisine</td>
<td>0.25</td>
<td>0.5-1.5</td>
<td>3-5</td>
</tr>
<tr>
<td><strong>Short Acting (Bolus)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular</td>
<td>0.5-1.0</td>
<td>2-4</td>
<td>5-8</td>
</tr>
<tr>
<td><strong>Intermediate Acting (Basal)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NPH</td>
<td>1-2</td>
<td>4-12</td>
<td>16-20</td>
</tr>
<tr>
<td><strong>Long Acting (Basal)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin detemir</td>
<td>1</td>
<td>No peak</td>
<td>20-24</td>
</tr>
<tr>
<td>Insulin glargine</td>
<td>1-2</td>
<td>No peak</td>
<td>20-24</td>
</tr>
</tbody>
</table>

### Tips for Medication Adherence

- **Education**
  - What is the importance of this medication?
    - How does it work to help lower blood glucose level?

- **Timing**
  - When is the best time to take the medication to get the maximum benefit?

- **Monitoring**
  - When should the patient perform self-monitoring of blood glucose level in order to know the medication is effective?
  - What are common adverse effects?
Tips for Medication Adherence

• Regular medication “checkup”
  – Review (at least every 6 months; preferably at each visit)
    • Appropriateness of drug therapy for each agent
    • Potential for drug–drug interactions
    • Potential for drug–disease interactions
    • Occurrence of adverse effect(s)

• Medication dosing schedules or regimens
  – Can assist in
    • “Best” timing for taking medicine(s)
    • Decreasing some adverse effects
    • Remembering to take medicine(s)


Blood Glucose–Lowering Agents and the “Best” Time to Take Them

• Agents to be taken before meals
  – α-glucosidase inhibitors
  – Dopamine agonists
  – Glinides
  – Exenatide
  – Pramlintide
  – Bolus insulin

• Agents to be taken with or after meals
  – Sulfonylureas
  – Metformin

• Agents that can be taken with or without food
  – TZDs
  – DPP-4 inhibitors
  – Liraglutide
  – Basal insulin

Back to Patient 1: SR

Current medications:
- Glimepiride 2 mg once daily
- Metformin 1000 mg twice daily
- Nateglinide 60 mg three times daily
- Alendronate 70 mg / week
- Simvastatin 20 mg once daily
- Warfarin 2 mg once daily
- Paroxetine 20 mg once daily
- Aspirin 81 mg once daily
- Acetaminophen 500 mg as needed for pain

VS/Labs:
- BP: 128/78 mm Hg
- HR: 68 bpm
- Wt: 135 lb
- Ht: 5’2”
- A1C: 8.1%
- FBG: 320 mg/dL
- LDL: 118 mg/dL
- HDL: 32 mg/dL
- TG: 325 mg/dL
- INR: 2.4

Which of the following medications should be discontinued in patient SR and Why?

A. Glimepiride - may increase risk of myocardial infarction
B. Metformin - due to renal dysfunction
C. Nateglinide - therapeutic duplication
D. Not sure

0% 0% 0% 0%
Which of the following diabetes medications, if any, would you increase?

- A. Glimepiride
- B. Metformin
- C. Nateglinide
- D. No changes
- E. Not sure

Which of the following diabetes medications, if any, would you add?

- A. Basal insulin
- B. Thiazolidinedione (glitazone)
- C. Incretin agent (glucagon-like peptide 1 agent or dipeptidyl peptidase-4 inhibitor)
- D. A and B
- E. A and C
- F. Not sure
Possible Pharmacotherapeutic Changes for SR

<table>
<thead>
<tr>
<th>Weight Effect</th>
<th>Hypoglycemia</th>
<th>β-cell protection</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase gliimepiride to 4 mg daily</td>
<td>gain</td>
<td>+ risk</td>
<td>no</td>
</tr>
<tr>
<td>Start pioglitazone 15 mg daily</td>
<td>gain</td>
<td>low risk</td>
<td>possible</td>
</tr>
<tr>
<td>Increase gliimepiride to 4 mg daily and add pioglitazone 15 mg daily</td>
<td>gain</td>
<td>+ risk</td>
<td>possible (from pio)</td>
</tr>
<tr>
<td>Start insulin detemir or glargine 10 units at bedtime</td>
<td>gain</td>
<td>low risk</td>
<td>possible</td>
</tr>
<tr>
<td>Start exenatide 5 mcg twice daily before meals or liraglutide 0.6 mg daily</td>
<td>loss</td>
<td>low risk</td>
<td>possible</td>
</tr>
<tr>
<td>Start sitagliptin 100 mg or saxagliptin 5 mg daily</td>
<td>neutral</td>
<td>low risk</td>
<td>possible</td>
</tr>
</tbody>
</table>


Patient Case: TC

- TC is a 38 y/o Hispanic male
  - Past Medical History
    - Type 2 DM x 1 yr
    - Dyslipidemia x 2 yrs
    - Hypertension x 2 yrs
  - Social History
    - Construction worker
    - Wife does all the cooking
    - Denies smoking, illicit drug use
    - 1-2 beers on weekends
  - Current Medications
    - Metformin 1000mg twice daily
    - Aspirin 81mg daily
    - Atorvastatin 20 mg daily
    - Lisinopril 10mg daily
  - He is adherent to his medication, medical nutrition therapy, and exercise regimen (30 min walking 3-4 days/wk)
Patient Case: TC (cont’d)

Objective Data

BP = 134/78 mm Hg
Pulse = 68 bpm, regular
Weight = 225 lb. Height = 5’ 5”
Physical Exam - WNL

Labs:

Na = 139    K = 4.3    Cl = 99    CO₂ = 23
BUN = 11    SCR = 0.9  AST = 22  ALT = 44
FBG = 148   A1C = 7.6
TChol = 178 LDL = 112 HDL = 29 TG = 217

Does TC need a change in his diabetes medication regimen?

1. Yes
2. No
3. Not sure
Which of the following diabetes medications, if any, would you add?

A. Sulfonylurea  
B. Basal insulin  
C. Thiazolidinedione (glitazone)  
D. GLP-1 agent  
E. DDP-4 inhibitor (gliptin)  
F. Not sure

### Possible Pharmacotherapeutic Changes for TC

<table>
<thead>
<tr>
<th></th>
<th>Weight Effect</th>
<th>Hypoglycemia</th>
<th>β-cell protection</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start glimepiride 2 mg daily</td>
<td>gain</td>
<td>+ risk</td>
<td>no</td>
<td>immediate short-term response, inexpensive</td>
</tr>
<tr>
<td>Start pioglitazone 15 mg daily</td>
<td>gain</td>
<td>low risk</td>
<td>possible</td>
<td>4-8 weeks for response, redistribution of subcutaneous/visceral fat, adverse effects: edema, bone loss</td>
</tr>
<tr>
<td>Start insulin detemir or glargine 10 units at bedtime</td>
<td>gain</td>
<td>low risk</td>
<td>possible</td>
<td>best A1C lowering, injectable</td>
</tr>
<tr>
<td>Start exenatide 5 mcg twice daily before meals or liraglutide 0.6 mg daily</td>
<td>loss</td>
<td>low risk</td>
<td>possible</td>
<td>GI adverse effects (nausea), cost, injectable</td>
</tr>
<tr>
<td>Start sitagliptin 100 mg or saxagliptin 5 mg daily</td>
<td>neutral</td>
<td>low risk</td>
<td>possible</td>
<td>minimal adverse effects, cost</td>
</tr>
</tbody>
</table>
Take-Home Message

• Diabetes is constantly evolving.
  – Reviewing and understanding the literature is pertinent for optimal care
  – Early judgments often require further investigation

• Control to goal
  – Need to diagnose type 2 diabetes early.
    • Need early and intensive management
    • A1C <7% (or <6.5%, if appropriate).
    • If not at goal after 3 months, adjust therapy.
    • Most likely will need combination pharmacotherapy
      – Use combination therapy that targets the different dysfunctional organs.
  – Treat the patient as well as the number.

Take-Home Message

• Taking medication is a self-care behavior
  – Polypharmacy or taking multiple medications at various times can increase nonadherence

• Knowledge is power
  – Educate your patients on the medications they are taking and the reasons WHY they are taking specific medications
  – Inform them of the “best” time to take their medication to get the best effect and least side effects
Thank You For Your Participation.

What Questions Can I Answer For You?

scorne@midwestern.edu