Insulin Therapy
Overcoming Resistance

Lucia M. Novak, MSN, ANP-BC, BC-ADM, COTC
Riverside Medical Associates, P. A.
Riverdale, MD

Adjunct Assistant Professor
The Uniformed Services University of the Health Sciences
Bethesda, MD

Conflict of Interest/Disclosures

• None

General Principles for Advancing Treatment of T2DM With Antihyperglycemic Medications1-4

• Antihyperglycemic medications should be:
  – Used in conjunction with lifestyle therapy
  – Selected using a patient-centered approach

• Metformin is generally the first agent—as long as it is safe for and tolerated by the individual patient

• When additional medications are needed, current treatment recommendations emphasize:
  – Avoidance of hypoglycemia and weight gain
  – Use of complementary agents
  – Timely intensification to additional non-insulin agents or insulin

ADA/EASD Position Statement: Approach to Goal Setting

ADA/EASD Position Statement:
Approach to Goal Setting


Current Recommendations Emphasize Avoidance of Hypoglycemia and Weight Gain

Patients rank risk of hypoglycemia and weight impact as important characteristics when choosing antihyperglycemic medications.5,a

Progressive β-Cell Dysfunction in T2DM

Some antihyperglycemic agents (e.g., TZDs, incretin agents) may preserve β-cell function.5 Animal studies suggest possible preservation of β-cell mass.5

Insulin is needed when residual β-cell function is insufficient.5


• Timely treatment intensification is needed to maintain glycemic control;5,7
• Patients with T2DM frequently progress to a need for insulin.5,7
### When to Use Insulin Therapy: General Recommendations

<table>
<thead>
<tr>
<th>Indications(^{1-4})</th>
<th>Insulin May Be Used(^{1-5}):</th>
<th>Preferred Uses/ Potential Benefits(^{1-6}):</th>
</tr>
</thead>
</table>
| • All patients with T1DM  
• Any patient with T2DM  
• Patients with DKA (short-acting insulins only) | • As monotherapy when MET is not tolerated or contraindicated  
• As initial therapy in T2DM if A1C ≥ 9% or patient is symptomatic  
• As part of dual, triple, or more complex therapy\(^{a}\)  
• At any time in the progression of T2DM | • Patients with comorbidities that preclude use of other agents  
• Early initiation in T2DM associated with better long-term control |

\(^{1}\) Examples of more complex regimens include combinations of non-insulin agents and insulin (basal and prandial).  
\(^{2}\) Consider discontinuing or reducing the dose of SUs.  
\(^{4}\) ADA. Diabetes Care. 2016;39(suppl 1):S1-S112.  
\(^{6}\) US FDA. Drugs@FDA. http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA.  

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### Health Care Provider: Roadblocks to Timely Insulin Initiation

<table>
<thead>
<tr>
<th>When Do HCP's Consider Using Insulin Therapy?</th>
<th>HCP: Concerns About Starting Insulin Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple medication failure</td>
<td>Poor patient adherence 92%</td>
</tr>
<tr>
<td>A1C &gt; 8.5%</td>
<td>Hypoglycemia 80%</td>
</tr>
<tr>
<td>Worsening of microvascular complications</td>
<td>Pain from glucose monitoring 54%</td>
</tr>
<tr>
<td>Unintentional weight loss</td>
<td>Pain from insulin injections 48%</td>
</tr>
<tr>
<td>Repeated fasting glucose &gt; 200 mg/dL</td>
<td>Patient is too old 47%</td>
</tr>
</tbody>
</table>


### Patient Roadblocks to Starting Insulin

| Concern\(^{1}\) | Prior to Start  
(n = 92) | On Insulin  
(n = 101) |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>My diabetes is not serious enough</td>
<td>47%</td>
<td>7%</td>
</tr>
<tr>
<td>Insulin addiction</td>
<td>39%</td>
<td>20%</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>12%</td>
<td>4%</td>
</tr>
<tr>
<td>Insulin would not help</td>
<td>11%</td>
<td>4%</td>
</tr>
</tbody>
</table>

"...if the practitioner feels that [a transition to insulin] is important, encouragement and education can usually overcome [patient] reticence."\(^{2}\)

Possible Barriers to the Initiation of Insulin

Patient
- Fear of needles
- Negative misconceptions about insulin
- Inconvenience
- Patient perception as personal failure

Health Care Professional
- Fear of hypoglycemia
- Weight gain
- Complexity of dosing regimen
- Cost
- Lack of available educational tools/resources
- Lack of familiarity/comfort with insulin
- Time constraints

Diabetes Attitudes, Wishes, and Needs Survey* (DAWN2)

“Most people with diabetes are not actively engaged by their healthcare professionals to take control of their condition; education and psychosocial care are often unavailable.”

48.8% had received formal education; 81.1% found it helpful

Addressing Patient Concerns/Fears Regarding Injectable Therapy

Assessment of Fear
- Identify past experiences with injections
- Acknowledge fears or perceptions regarding injectable therapy

Needle Selection
- Select smaller and thinner needles to improve ease of use
- Discuss how needles have been specifically designed to improve patient comfort

Patient Education
- Show patients the device and needles that they will be using
- Demonstrate proper injection technique and identify unique features of injection device

Behavioral Interventions
- Deep breathing
- Forceful exhale during injection
Patient Education, Resources, and Support Tools for Your Patients With T2DM

- Care and educational support and materials should be specifically contoured for the patient.
- "Pre-injectable" education programs offered before injectable therapy becomes necessary may alleviate some of the anxiety and stress.
- Identify local resources in your area and provide those to your patients with T2DM as needed.

http://www.diabetes.org/in-my-community/local-offices


A common problem with health education content is that providers give too much detail regarding pathophysiology and too little practical information regarding daily disease management.

The Value of DSME/S: Refer When Appropriate

- More frequent DSME/S visits may be needed when a patient is starting a new diabetes medication.
- Some competencies related to the AADE7 Self-Care Behavior "Taking medication" include:
  - Discuss characteristics of medications
  - Reinforce safe use of medications
  - Work with patient and team to individualize regimen
- DSME/S focuses on helping individuals with diabetes to make informed self-management choices.

Approved Insulins: United States, February 2016

- Basal
  - Human Insulins
    - U-100 NPH
    - U-100 detemir
    - U-100 glargine equivalent
  - Analogue Insulins
    - U-100 aspart
    - U-100 glulisine
    - U-100 lispro

- Prandial
  - Human Insulins
    - U-100 RHI
    - U-100 aspart
    - U-100 detemir
    - U-100 glargine
    - U-100 glargine equivalent
    - U-100 detemir equivalent
    - U-100 glulisine
    - U-100 lispro

- Premixed/Biphasic
  - Human Insulins
    - 70/30 RHI
  - Analogue Insulins
    - 70/30 aspart
    - 70/30 glulisine

1. Available only in prefilled pens.

http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA.

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  - Human Insulins
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  - Human Insulins
    - U-100 RHI
    - U-100 aspart
    - U-100 detemir
    - U-100 glargine
    - U-100 glargine equivalent
    - U-100 detemir equivalent
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http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA.
Pharmacokinetic Profiles of Human Insulin and Insulin Analogs

- Rapid-acting
- Regular insulin
- NPH
- Detemir/Glargine U-100
- Glargine U-300
- Degludec U-100 & U-200

Basal Insulins Used in the U.S.

<table>
<thead>
<tr>
<th>Name</th>
<th>Form</th>
<th>Time of Action (h)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate-acting (Basal)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NPH</td>
<td>Humulin N; Novolin N</td>
<td>1-2 4-12 10-16</td>
<td>Increased risk of hypoglycemia when compared to analog insulins. Pregnancy category B - safe.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long-acting (Basal)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detemir U-100</td>
<td>Levemir Analog</td>
<td>1-2 Relatively peakless 24</td>
<td>Glucose-lowering effect of glargine U-300 is lower than equivalent dose of glargine U-100. Pregnancy category (Glargine C; Degludec C; Detemir - B)</td>
</tr>
<tr>
<td>Glargine U-100</td>
<td>Lantus Analog</td>
<td>1-2 Relatively peakless 24</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ultralong-acting (Basal)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glargine U-300</td>
<td>Toujeo Analog</td>
<td>6 Relatively peakless ≥24</td>
<td></td>
</tr>
<tr>
<td>Degludec U-100, U-200</td>
<td>Tresiba Analog</td>
<td>1-2 Relatively peakless ≥42</td>
<td></td>
</tr>
</tbody>
</table>

Ultralong-Acting Basal Insulins

- Have Minimal Glycemic Variability

Prandial Insulins Used in the U.S.

<table>
<thead>
<tr>
<th>Name</th>
<th>Form</th>
<th>Time of Action* (h)</th>
<th>Meal Timing (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Generic</td>
<td>Brand</td>
<td>Onset</td>
</tr>
<tr>
<td>Rapid-acting (‘Bolus’ or ‘Prandial’)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspart</td>
<td>Novolog</td>
<td>Analog</td>
<td>&lt; 0.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt; 0.25</td>
</tr>
<tr>
<td>Glulisine</td>
<td>Apidra</td>
<td>Analog</td>
<td>&lt; 0.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt; 0.25</td>
</tr>
<tr>
<td>Lispro</td>
<td>Humalog</td>
<td>Analog</td>
<td>&lt; 0.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt; 0.25</td>
</tr>
<tr>
<td>Glulisine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspart</td>
<td>Humalog</td>
<td>Analog</td>
<td>&lt; 0.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt; 0.25</td>
</tr>
<tr>
<td>Short-acting (‘Bolus’ or ‘Prandial’)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Humulin</td>
<td>R</td>
<td>Human</td>
<td>&lt; 0.25</td>
</tr>
<tr>
<td></td>
<td>Novolin</td>
<td>R</td>
<td>&lt; 0.25</td>
</tr>
</tbody>
</table>

*Dose dependent

Premixed Insulin Analogs Commonly Used in the U.S.

<table>
<thead>
<tr>
<th>Name</th>
<th>Time of Action (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Generic</td>
</tr>
<tr>
<td>70% aspart protamine/30% aspart</td>
<td>Novolog Mix</td>
</tr>
<tr>
<td>75% lispro protamine/25% lispro</td>
<td>Humalog Mix</td>
</tr>
<tr>
<td>50% lispro protamine/50% lispro</td>
<td>Humalog Mix</td>
</tr>
<tr>
<td>70% degludec/30% aspart</td>
<td>Ryzodeg 70/30</td>
</tr>
<tr>
<td>70% NPH/30% regular</td>
<td>Humulin 70/30</td>
</tr>
<tr>
<td></td>
<td>Novolin 70/30</td>
</tr>
</tbody>
</table>

NR, not reported

Basal Insulin Initiation and Titration

• Once-daily basal insulin is the most convenient way to initiate insulin

| Basal Insulin Titration: ADA/EASD
<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial dose</td>
</tr>
<tr>
<td>Titrating</td>
</tr>
<tr>
<td>Hypoglycemia: determine and address cause; reduce dose by 4 U or 10%-20%</td>
</tr>
</tbody>
</table>

AACE has also published algorithms for basal insulin initiation and titration.

Intensification of Insulin Therapy

### Recognizing When to Add a Therapy That Complements Basal Insulin

- A1C or FPG is above target despite FPG being in target range

Further increases in basal insulin are associated with higher risk of hypoglycemia and/or greater weight gain.

- Basal insulin dose is > 0.5 U/kg/d

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### Options for Intensifying Basal Insulin Therapy

- **Consider trial of GLP-1 RA**
- **Stepwise prandial insulin**
- **GLP-1 RA**
- **SGLT2 inhibitor**
- **DPP-4 inhibitor**
- **Stepwise prandial insulin**

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### Effects of Newer Antihyperglycemic Agents

- **GLP-1 RAs**
  - Glucose dependent (↑ insulin, glucagon)
  - Slow gastric emptying
  - Increase satiety
  - Potential weight loss
  - Low risk of hypoglycemia

- **DPP-4 inhibitors**
  - Glucose dependent (↑ insulin, glucagon)
  - Weight neutral
  - Low risk of hypoglycemia

- **SGLT2 inhibitors**
  - Insulin independent (↑ renal glucose reabsorption, glucosuria)
  - Potential weight loss
  - Low risk of hypoglycemia

- **Newer antihyperglycemic agents may minimize insulin AEs by supporting use of lower insulin doses.**

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*Hypoglycemia risk is increased when used with insulin or insulin secretagogues (eg, sulfonylureas), which are known to cause hypoglycemia.*

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Safety Considerations

<table>
<thead>
<tr>
<th>DPP-4 Inhibitors</th>
<th>GLP-1 RAs</th>
<th>SGLT2 Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute pancreatitis</td>
<td>Severe GI AEs/hypoglycemia (renal impairment risk)</td>
<td>Hypotension (edema and fluid retention)</td>
</tr>
<tr>
<td>Heart failure (observe for signs/symptoms)</td>
<td>Hypoglycemia risk with medicationsa</td>
<td>Renal impairment</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>Potential for medication errors</td>
<td>Ketoacidosis (rarely)</td>
</tr>
</tbody>
</table>

For individuals with renal or hepatic impairment:
- Increased risk with multiple medications, such as insulin secretagogues

Contraindications:
- SGLT2 inhibitors: severe renal impairment, ESRD, dialysis
- GLP-1 RAs (except EXN BID and LXN): history of MTCa,b or MEN2a,b
- C/Top drug or nursing
- Oldera: consider renal function (if drug absorption)
- Hepaticd: use with caution/monitor (ALO)

Use in Specific Populations

<table>
<thead>
<tr>
<th>DPP-4 Inhibitors</th>
<th>GLP-1 RAs</th>
<th>SGLT2 Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy: B or C (agent specific)</td>
<td>Renal: use with caution; risk with hypoglycemia; EXN should not be used if CrCl &lt; 30mL/min; LXN recommended in ESRD</td>
<td>Pregnancy: C/stop drug or nursing</td>
</tr>
<tr>
<td>Oldera: consider renal function</td>
<td>Renal: dose adjustment (except LXN)</td>
<td>Elder: consider renal function, volume status</td>
</tr>
<tr>
<td>Hepaticd: use with caution/monitor (ALO)</td>
<td>Renal: Cr in severe RI, ESRD, dialysis; risk with hypokalemia</td>
<td>Elder: higher hypoglycemia risk; may need dose adjustment</td>
</tr>
<tr>
<td>Gastrointestinal disease: not recommended in severe cases</td>
<td>Elder: higher hypoglycemia risk; may need dose adjustment</td>
<td>Elder: CANA, DAPA not studied in severe hepatic insufficiency</td>
</tr>
</tbody>
</table>

Initiate GLP-1 RA or Basal Insulin?1-3

<table>
<thead>
<tr>
<th>GLP-1 RA</th>
<th>Basal Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advantages</td>
<td>Advantages</td>
</tr>
<tr>
<td>- Reduced A1C change</td>
<td>- Theoretically unlimited efficacy</td>
</tr>
<tr>
<td>- Low hypoglycemia risk—glucose-dependent action</td>
<td>- Universally effective</td>
</tr>
<tr>
<td>- Weight reduction</td>
<td>-</td>
</tr>
<tr>
<td>- Multiple dosing options (eg, QW)</td>
<td>-</td>
</tr>
<tr>
<td>- Less need for BG monitoring</td>
<td>-</td>
</tr>
</tbody>
</table>

Limitations
- Injected—training required
- GI adverse effects
- Contraindicated/not recommended in some populations:

1. DeFronzo RA. Diabetes Care 2016;39(suppl 1):S1-S112.
2. AHA. Diabetes Care 2016;39(suppl 1):S1-S112.
3. Drugs@FDA. http://www.accessdata.fda.gov/scripts/cder/DrugsatFDA.
GLP-1 RAs With Insulin

<table>
<thead>
<tr>
<th>Insulin Type</th>
<th>Approval Status for Use With Identified Insulin Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal</td>
<td>• Approved: ALBI, EXN BID, LIRA, LIXI</td>
</tr>
<tr>
<td></td>
<td>• Not studied/cannot be recommended: DULA, EXN QW</td>
</tr>
<tr>
<td>Prandial</td>
<td>• Approved: DULA</td>
</tr>
<tr>
<td></td>
<td>• Not studied/cannot be recommended: ALBI, EXN BID, EXN QW, LIRA, LIXI</td>
</tr>
</tbody>
</table>


Clinical Considerations:
Combination Injectable Therapy with Basal Insulin

<table>
<thead>
<tr>
<th>Consideration</th>
<th>Short-Acting GLP-1 RAs</th>
<th>Long-Acting GLP-1 RAs</th>
<th>Prandial Insulin</th>
<th>Fixed-Ratio Combination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improves PPG</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Weight change</td>
<td>Potential loss</td>
<td>Potential loss</td>
<td>Potential gain</td>
<td>Loss vs basal insulin</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>Higher with insulin, lower vs prandial + basal</td>
<td>✓</td>
<td>Lower vs prandial + basal</td>
<td></td>
</tr>
<tr>
<td>Common adverse effects</td>
<td>Gastrointestinal AEs</td>
<td>Weight gain, hypoglycemia</td>
<td>Severe GI AEs vs GLP-1 RA</td>
<td></td>
</tr>
<tr>
<td>Administration</td>
<td>Once or twice daily</td>
<td>Once daily or weekly</td>
<td>Twice daily</td>
<td>Once daily</td>
</tr>
<tr>
<td>SMBG</td>
<td>Recommended with insulin</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

Basal Insulin–GLP-1 RA Fixed-Ratio Coformulations
Patients Not Controlled on Basal Insulin

<table>
<thead>
<tr>
<th></th>
<th>□IDeg,Lira</th>
<th>□IDeg</th>
<th>□IGlar,Lixi</th>
<th>□IGlar</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔA1C, %</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ΔA1C, %</td>
<td>-2.3</td>
<td>-0.9</td>
<td>-3.1</td>
<td>-3.3</td>
</tr>
<tr>
<td>P</td>
<td>&lt; .0001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ΔBW, kg</td>
<td>0</td>
<td>0.0</td>
<td>-0.7</td>
<td>0.7</td>
</tr>
<tr>
<td>P</td>
<td>&lt; .0001</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a Insulin dose capped at 50 U/d; final insulin doses, 45 U in both groups; b Most participants had a final insulin dose of 40-60 U.

2. Lixisenatide and IGlarLixi FDA briefing document.
3. IDegLira FDA briefing document.
4. IDeg1,aIGlar2,bIDeg,Lira1,aIGlarLixi2,bIDeg1,aIGlar1,b
Basal Insulin–GLP-1 RA Fixed-Ratio Coformulations in
Individuals Not Controlled on Oral Agents

<table>
<thead>
<tr>
<th>A1C &lt; 7%</th>
<th>Basal Insulin–GLP-1 RA -1.6</th>
<th>Basal Insulin–GLP-1 RA -1.4</th>
<th>Basal Insulin–GLP-1 RA -1.3</th>
<th>Basal Insulin–GLP-1 RA -1.3</th>
<th>Basal Insulin–GLP-1 RA -0.9</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1C &lt; 7%</td>
<td>81</td>
<td>65</td>
<td>60</td>
<td>74</td>
<td>59</td>
</tr>
</tbody>
</table>

- Hypoglycemia (IDegLira, IDeg, LIRA, IGLarLixi, IGLar, and LIXI, respectively)
  - Severe hypoglycemic episodes, %: 0.5, 0.3, 0, 0, 0, 0
  - Documented symptomatic hypoglycemia, %: 36, 46, 9, 26, 24, 6

* P < 0.05 vs fixed-ratio combination.

2. Lixisenatide and IGlarLixi FDA briefing document.
3. IDegLira FDA briefing document.

Dosing of Fixed-Ratio GLP-1 RA–Insulin Coformulations in Clinical Trials

**IDegLira**
- Within 1 hour before breakfast
- Started at IGLar 10 U/LIXI 5 µg
- Titrated based on IGLar according to FPG
- LIXI dose follows IGLar dose—IGlar 2 U/LIXI 1 µg
- Maximum daily dose: 60 U/30 µg

**IGlarLixi**
- Any time of day, but consistently at that time of day
- Started at IDeg 10 U/LIRA 0.36 mg
- Titrated based on prebreakfast PG using algorithm
  - Each dose step has IDeg 1 U and LIRA 0.036 mg
  - Maximum daily dose: 50 U/1.8 mg

* FPG  7.2 mg/dL: decrease by 2 dose steps. If FPG < 7.2 mg/dL, no change; FPG > 9. mg/dL, increase by 2 dose steps.


Individualizing Therapy

Discuss as part of shared decision-making

- Bias/personal experiences (eg, with injectable therapies)
- A1C change or glycemic efficacy
- Weight change
- Risk of hypoglycemia
- Ease of use (eg, daily routine, administration, glucose monitoring)
- Common adverse effects
- Accessibility/resources

Additional clinical considerations

- Abilities/adherence/ motivation
- Age
- Disease duration
- Safety
- Comorbidities (eg, ASCVD, renal impairment, hepatic impairment)

References
3. ADA. Diabetes Care. 2016;39(suppl 1):S1-S112
Guidelines for Preventing Hypoglycemia

AACE1-4
- Address in each patient contact
- If problematic, adjust regimen by:
  - Reviewing/applying diabetes self-management
  - Frequent SMBG
  - Flexible, appropriate insulin regimens
  - Individualized glycemic goals
  - Ongoing professional guidance and support
  - Consider each of the known risk factors for hypoglycemia

ADA3
- Reevaluate SMBG skills periodically
- Avoid aggressive targets in advanced disease
- Limit alcohol intake
  - ≤ 1 drink/day in adult women
  - ≤ 2 drinks/day in adult men
- Add carbohydrate before exercising if BG < 100 mg/dL
- Strict avoidance of hypoglycemia for several weeks partly resolves repeated severe hypoglycemia, hypoglycemia unawareness

SMBG, self-monitoring of blood glucose


CASE STUDIES
**Case Study 1: Maria**

- 38-yr Latina woman
- T2DM for 4 years
  - GDM 8 yrs ago, PreDM 6 yrs ago
- DM-related complications: DPN
- Co-Morbid Conditions
  - HTN
  - Dyslipidemia
  - Obesity
- Denies CAD/MI/PVD/CVA
- Medications
  - Metformin XR 1000 mg/d (max tolerated)
  - Statin, ACE-i + HCTZ
- Dental, own practice, 50+ hours/week
- Mother of 2 (12 and 8) “very busy”
- Never smoked, 1 glass wine 2x week
- Drinking “smoothies” to be more healthy

<table>
<thead>
<tr>
<th>Measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height</td>
</tr>
<tr>
<td>Weight</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
</tr>
<tr>
<td>BP, mm Hg</td>
</tr>
<tr>
<td>FPG, mg/dL</td>
</tr>
<tr>
<td>A1C, %</td>
</tr>
<tr>
<td>eGFR, mL/min/1.73 m²</td>
</tr>
<tr>
<td>UACR &lt; 30 mcg/mg Cr</td>
</tr>
</tbody>
</table>

Preferences/values/QOL

- Wants to avoid GI side effects, impacts her ability to work.
- Would like to lose weight
- Afraid of low blood sugars
- Was on SU in the past

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**Case Study 2: George**

- 69-yr black man
- T2DM for 15 years
- DM-Related complications: DR, DPN
- Co-Morbid conditions
  - CAD: MI 11 yrs ago, stent 2 yrs ago
  - CHF
  - HTN
  - Dyslipidemia
- overweight
- Medications
  - Metformin 2000 mg/d
  - Glyburide 5 mg/d
  - Statin, BB, ACE-I, HCTZ, ASA
- Retired Military and USPS
- Divorced, lives alone, family nearby
- Quit smoking and drinking 11 yrs ago

<table>
<thead>
<tr>
<th>Measurements/Preferances</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height</td>
</tr>
<tr>
<td>Weight</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
</tr>
<tr>
<td>BP, mm Hg</td>
</tr>
<tr>
<td>FPG, mg/dL</td>
</tr>
<tr>
<td>A1C, %</td>
</tr>
<tr>
<td>eGFR, mL/min/1.73 m²</td>
</tr>
<tr>
<td>UACR 45 mcg/mg Cr</td>
</tr>
</tbody>
</table>

Preferences/values/QOL

- Unhappy about needing so many medications
- Concerned about his heart, had to stop pioglitazone because it “hurt him”
- Problems with low blood sugar at least 2x weekly
- Concerned he now needs insulin
Individualizing Glycemic Control for George

<table>
<thead>
<tr>
<th>Most Intensive</th>
<th>Less Intensive</th>
<th>Least Intensive</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Moderate</td>
<td>Low</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>Insulin</td>
<td>None</td>
</tr>
<tr>
<td>Risk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.0%</td>
<td>7.0%</td>
<td>8.0%</td>
</tr>
<tr>
<td>Low</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40</td>
<td>45</td>
<td>50</td>
</tr>
<tr>
<td>55</td>
<td>60</td>
<td>65</td>
</tr>
<tr>
<td>70</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>Disease duration, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>Other comorbid conditions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td></td>
<td>Early microvascular</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td></td>
<td>Advanced microvascular</td>
</tr>
</tbody>
</table>

Considerations based on UKPDS, ACCORD, ADVANCE, and VADT.


Discussion with George

- Your concerns:
  - DM Not well controlled and with microvascular complications
  - Hypoglycemia
  - Heart Disease
- Goal A1C?
- TLC?
- Which are viable options given his concerns/preferences?
  - DPP-4-i
  - GLP-1RA
  - SGLT-2-I
  - Insulin
- What change to existing medication regimen needed?

Case Study 3: Terry

- 57-yr black woman
- T2DM for 8 years
- DM-related Complications: DKD, DPN
- Comorbid conditions
  - HTN
  - Dyslipidemia
  - Obesity
  - Renal CDA/IV/PVD/CVA
- Medications
  - Metformin 1000 mg/d
  - Insulin glargine 22 U/d (evening)
- Apart 7 units before meals
  - Misses lunch almost always
  - Misses dinner dose few times a week
  - ACE-I, LCR, statin, ASA
  - Manager at a fast food restaurant
  - Divorced, mother of two (13 and 11)

<table>
<thead>
<tr>
<th>Height</th>
<th>Weight</th>
<th>BMI, kg/m²</th>
<th>BP, mm Hg</th>
<th>FPG, mg/dL</th>
<th>A1C, %</th>
<th>Cholesterol</th>
<th>UAICR</th>
</tr>
</thead>
<tbody>
<tr>
<td>67 in</td>
<td>198 lb</td>
<td>31</td>
<td>142/81</td>
<td>112</td>
<td>8.3</td>
<td>At therapeutic goal</td>
<td>&gt;300 mcg/mg Cr</td>
</tr>
</tbody>
</table>

Preferences/values/QOL
- Gaining weight and unhappy
- Does not like to “do her diabetes” at work
- Afraid of low blood sugar while at work—it happened once, afraid will lose job
- Hoping she doesn’t need more medications—already hard to remember them all
Discussion with Terry

- Your concerns:
  - DM Not well controlled and with microvascular complications
  - Hypoglycemia
  - Not taking her insulin
- Goal A1C?
- TLC?
- Which are viable options given her concerns/preferences?
  - DPP-4-i
  - GLP-1RA
  - SGLT-2-I
  - GLP-1RA + insulin
- What change to existing medication regimen needed?

Thomas: 67-Year-Old Asian Man
Retired University Professor

<table>
<thead>
<tr>
<th>Personal History</th>
<th>Vital Statistics and Lab Values</th>
<th>Current Medications</th>
</tr>
</thead>
</table>
| Diagnosed with T2DM 6 years ago | **Height:** 68 in  
**Weight:** 184 lb (83 kg)  
**BMI:** 28 kg/m²  
**HbA1c:** 8.8%  
**FPG:** 122 mg/dL  
**PPG:** 260 mg/dL  
**eGFR:** 50 ml/min/1.73 m² | Metformin XR 1000 mg  
Piglitazone 30 mg  
Basal insulin 40 U  
Statin  
ACE-I/HCTZ  
Aspirin 81 mg |
| Myocardial infarction 2 years ago  
HTN and dyslipidemia: controlled with medication | |

Camila: 51-Year-Old Hispanic Woman
Human Resources Professional

<table>
<thead>
<tr>
<th>Personal History</th>
<th>Vital Statistics and Lab Values</th>
<th>Current Medications</th>
</tr>
</thead>
</table>
| Diagnosed with T2DM 2 years ago | **Height:** 63 in  
**Weight:** 159 lb (72 kg)  
**BMI:** 28 kg/m²  
**HbA1c:** 9.2%  
**FPG:** 148 mg/dL  
**PPG:** 255 mg/dL  
**eGFR:** 82 ml/min/1.73 m² | Metformin XR 2000 mg  
Basal insulin 64 U  
Statin  
ACE-I/CCB  
Aspirin 81 mg |
| HTN: controlled with medication  
No history of ASCVD events  
Would like to avoid more injections and BG checks - has watched her mother struggle with these | |
**Helen: 72-Year-Old Black Woman**  
*Retired Middle School Teacher*

<table>
<thead>
<tr>
<th>Personal History</th>
<th>Vital Statistics and Lab Values</th>
<th>Current Medications</th>
</tr>
</thead>
</table>
| • Diagnosed with T2DM 8 years ago  
• No history of ASCVD events  
• Lives alone | • Height: 59 in  
• Weight: 149 lb (68 kg)  
• BMI: 30 kg/m²  
• A1C: 8.5%  
• FPG: 135 mg/dL  
• PPG: 190 mg/dL  
• eGFR: 47 ml/min/1.73 m² | • Metformin XR 2000 mg  
• Linagliptin 5 mg  
• Basal insulin 34 U  
• Statin |

**SPECIAL ACKNOWLEDGEMENT**

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