A Conversation among AACE, ACP, Endocrine Society and ADA Regarding Diabetes Guidelines

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AACE: Member of the National Board of Directors, Chair of Diabetes Disease State Network, Chair of Diabetes Clinical Practice Guideline Committee
2018 - 2019
Dr. Guillermo Umpierrez, MD, CDE, FACE, FACP
Personal/Professional Financial Relationships with Industry/publishers

<table>
<thead>
<tr>
<th>External Industry Relationships *</th>
<th>Company Name(s)</th>
<th>Role</th>
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<tr>
<td>Equity, stock, or options in biomedical industry companies or publishers</td>
<td>BMJ Open Diabetes Research &amp; Care</td>
<td>Editor-in-Chief</td>
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<tr>
<td>Industry funds to Emory University for my research</td>
<td>Merck, Sanofi, Novo Nordisk Astra Zeneca Insulcloud, Dexcom</td>
<td>Principal Investigator - Initiated Research Projects</td>
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<td>Industry Advisory/Consultant activities</td>
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2009 AACE/ACE Algorithm:

- A1C Goal and glucose monitoring recommendations
- Treatment: mono- dual - triple therapy of 8 major FDA approved antidiabetic agents with complementary mechanisms of action
- Prioritized choices of medications according to:
  - safety,
  - risk of hypoglycemia,
  - efficacy,
  - simplicity,
  - anticipated degree of patient adherence,
  - cost of medications.
Effects of intensive glucose control on microvascular outcomes in patients with diabetes

DCCT: Type 1 Diabetes

UKPDS: Type 2 Diabetes

A1C and Microvascular Complications: DCCT

UKPDS: Risk Reductions With Intensive Therapy (Median HbA1c = 7.0%)


A1C (%)

-50 -46 -12 -25 -29 -24 -33 -16

Effects of intensive glucose control on microvascular outcomes in patients with type 2 diabetes

Meta-analysis: ACCORD, ADVANCE, UKPDS, and VADT with 27049 participants.

The relative risk was reduced by 20% for kidney events (hazard ratio 0.80, 95% CI 0.72 to 0.88; p<0.0001) and by 13% for eye events (0.87, 0.76 to 1.00; p=0.04), but was not reduced for nerve events (0.98, 0.87 to 1.09; p=0.68)

Intensive glucose control, if safely achieved (avoiding hypoglycemia and adverse events) reduces microvascular complications

2019 Algorithm

Medications with higher hypoglycemia risk and adverse events

P R O G R E S S I O N O F D I S E A S E
Glycemic Control Declines Over Time With Monotherapy

Most patients on traditional therapies will fail to monotherapy and require another agent(s) to maintain glycemic control

UKPDS: 4075 patients with newly diagnosed T2D, age 25-65 years, average BG 11.5 mmol/L (9.0-14.4 mmol/l), HbA1c 9.1% (7.5-10.7%) and BMI 29 (6) kg/m2. Follow up at 3, 6 and 9 years after enrollment

Turner RC et al. JAMA. 1999;281:2005
Traditional Management vs Early Combination Therapy in T2D

When Cost Is a Major Issue

- Metformin
- Sulfonylureas
- Thiazolidinedione
- Human insulin
### Individualized Treatment

#### Profiles of Antidiabetic Medications

<table>
<thead>
<tr>
<th></th>
<th>MET</th>
<th>GLP1-RA</th>
<th>SGLT2I</th>
<th>DPP4I</th>
<th>AGI</th>
<th>TZD (moderate dose)</th>
<th>SU</th>
<th>COLSVL</th>
<th>BCR:QR</th>
<th>INSULIN</th>
<th>PRAML</th>
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<tr>
<td>HYPO</td>
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<td>Neutral</td>
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<td>Moderate to Severe</td>
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<tr>
<td>WEIGHT</td>
<td>Slight Loss</td>
<td>Loss</td>
<td>Loss</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Gain</td>
<td>Gain</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Gain</td>
<td>Loss</td>
</tr>
<tr>
<td>RENAL / GU</td>
<td>Creatinine Indicated if sCr &lt; 1.5 mg/dL or Ccr &lt; 90 mL/min</td>
<td>Elevation Not Indicated if Ccr &gt; 90 mL/min</td>
<td>Genital Mycotic Infections</td>
<td>Dose Adjustment Necessary (Except Lisinopril)</td>
<td>Neutral</td>
<td>Neutral</td>
<td>More Hypo Risk</td>
<td>Neutral</td>
<td>Neutral</td>
<td>More Hypo Risk</td>
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<tr>
<td>GI Sx</td>
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<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
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<td>Moderate to Severe</td>
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<td>Mild Fracture Risk</td>
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<td>Moderate Fracture Risk</td>
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<tr>
<td>BONE</td>
<td>Neutral</td>
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<td>DKA Can Occur in Various Stress Settings</td>
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1. Liraglutide: FDA approved for prevention of MACE events.
2. Empagliflozin: FDA approved for reduction in TV mortality. Canagliflozin: FDA approved to reduce MACE events.
3. Possible increased hospitalizations for heart failure with angiotensin and sodium-gluco.
4. Only empagliflozin and canagliflozin show CV and CVD benefits.
5. Liraglutide only shows CV and CVD benefits.

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**Use with caution:**
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Thank you!
Evolution of Clinical Recommendations for the Management of Type 2 Diabetes

- **EFFICACY**
  - Lowering HgA1c

- **SAFETY**
  - Hypoglycemia Prevention

- Cardiovascular Disease Prevention
2009 Algorithm