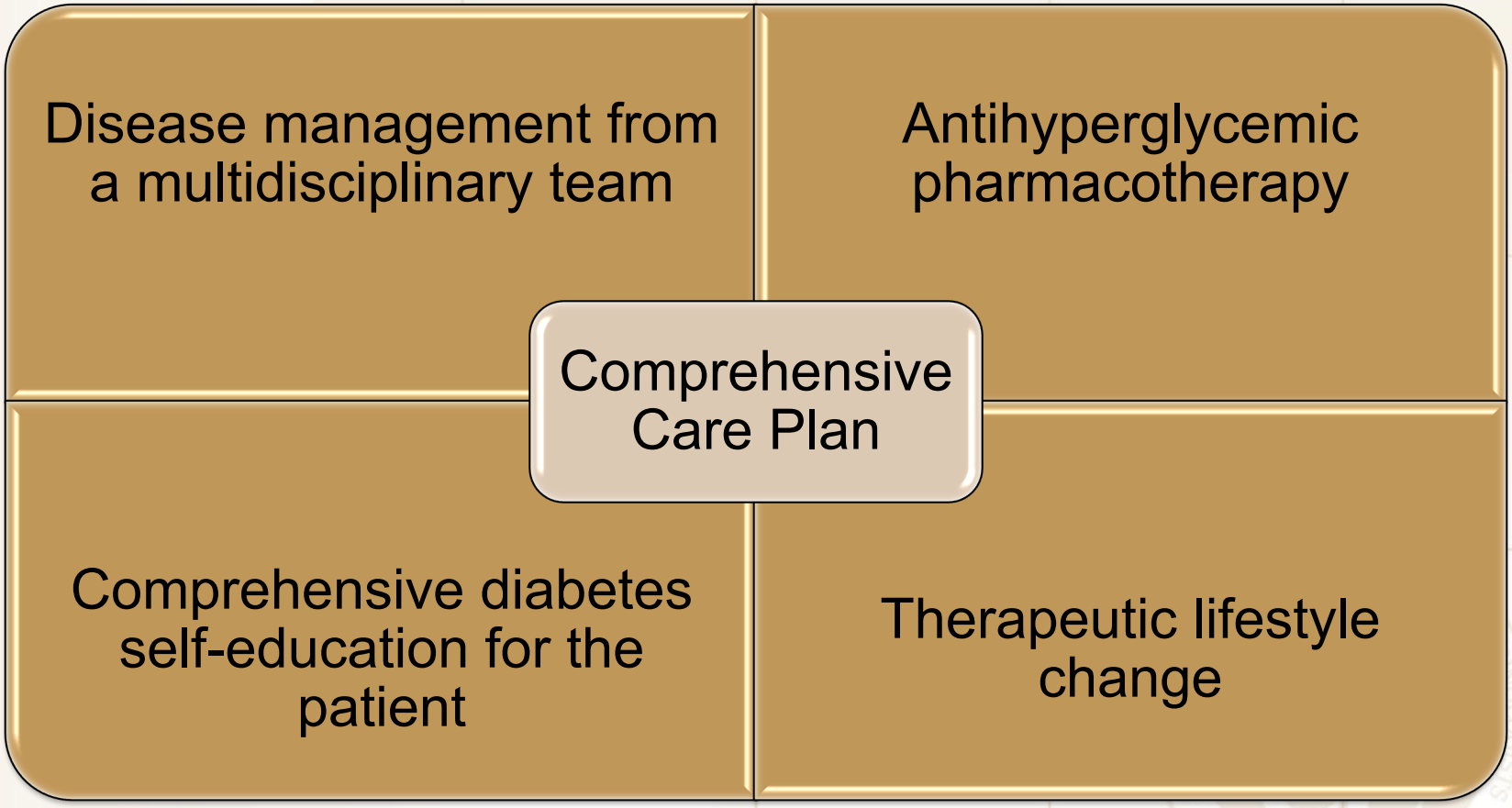
# Glycemic Management of Type 2 Diabetes

# AACE Comprehensive Care Plan




Handelsman YH, et al. *Endocr Pract*. 2015;21(suppl 1):1-87.

Glycemic Management of Type 2 Diabetes

# THERAPEUTIC LIFESTYLE CHANGE

# LIFESTYLE THERAPY

## RISK STRATIFICATION FOR DIABETES COMPLICATIONS

**INTENSITY STRATIFIED BY BURDEN OF OBESITY AND RELATED COMPLICATIONS**

| | | | |
|---|---|---|---|
| **Nutrition** | • Maintain optimal weight<br>• Calorie restriction (if BMI is increased)<br>• Plant-based diet; high polyunsaturated and monounsaturated fatty acids | • Avoid *trans* fatty acids; limit saturated fatty acids | • Structured counseling<br>• Meal replacement |
| **Physical Activity** | • 150 min/week moderate exertion (eg. walking, stair climbing)<br>• Strength training<br>• Increase as tolerated | • Structured program<br>• Wearable technologies | • Medical evaluation/ clearance<br>• Medical supervision |
| **Sleep** | • About 7 hours per night<br>• Basic sleep hygiene | • Screen OSA<br>• Home sleep study | • Referral to sleep lab |
| **Behavioral Support** | • Community engagement<br>• Alcohol moderation | • Discuss mood with HCP | • Formal behavioral therapy |
| **Smoking Cessation** | • No tobacco products | • Nicotine replace-ment therapy | • Referral to structured program |

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# Components of Therapeutic Lifestyle Change

- Healthful eating
- Sufficient physical activity
- Sufficient sleep
- Avoidance of tobacco products
- Limited alcohol consumption
- Stress reduction

Handelsman YH, et al. *Endocr Pract*. 2015;21(suppl 1):1-87.

# AACE Recommendations: Therapeutic Lifestyle Changes

| Parameter | Treatment Goal |
|---|---|
| Weight loss (for overweight and obese patients) | Reduce by 5% to 10% |
| Physical activity | 150 min/week of moderate-intensity exercise (eg, brisk walking) plus flexibility and strength training |
| Diet | • Eat regular meals and snacks; avoid fasting to lose weight<br>• Consume plant-based diet (high in fiber, low calories/glycemic index, and high in phytochemicals/antioxidants)<br>• Understand Nutrition Facts Label information<br>• Incorporate beliefs and culture into discussions<br>• Use mild cooking techniques instead of high-heat cooking<br>• Keep physician-patient discussions informal |

Handelsman YH, et al. *Endocr Pract*. 2015;21(suppl 1):1-87.

# AACE Recommendations: Healthful Eating

| | |
|---|---|
| **Carbohydrate** | Specify healthful carbohydrates (fresh fruits and vegetables, legumes, whole grains); target 7-10 servings per day<br>Preferentially consume lower-glycemic index foods (glycemic index score <55 out of 100: multigrain bread, pumpernickel bread, whole oats, legumes, apple, lentils, chickpeas, mango, yams, brown rice) |
| **Fat** | Specify healthful fats (low mercury/contaminant-containing nuts, avocado, certain plant oils, fish)<br>Limit saturated fats (butter, fatty red meats, tropical plant oils, fast foods) and trans fat; choose fat-free or low-fat dairy products |
| **Protein** | Consume protein in foods with low saturated fats (fish, egg whites, beans); there is no need to avoid animal protein<br>Avoid or limit processed meats |
| **Micronutrients** | Routine supplementation is not necessary; a healthful eating meal plan can generally provide sufficient micronutrients<br>Chromium; vanadium; magnesium; vitamins A, C, and E; and CoQ10 are not recommended for glycemic control<br>Vitamin supplements should be recommended to patients at risk of insufficiency or deficiency |

Handelsman YH, et al. *Endocr Pract*. 2015;21(suppl 1):1-87.

# AACE Recommendations: Medical Nutritional Therapy

- Consistency in day-to-day carbohydrate intake
- Adjusting insulin doses to match carbohydrate intake (eg, use of carbohydrate counting)
- Limitation of sucrose-containing or high-glycemic index foods
- Adequate protein intake
- “Heart-healthy” diets
- Weight management
- Exercise
- Increased glucose monitoring

Handelsman YH, et al. *Endocr Pract*. 2015;21(suppl 1):1-87.

Glycemic Management of Type 2 Diabetes

# ANTIHYPERGLYCEMIC THERAPY

# Noninsulin Agents Available for T2D

| Class | Primary Mechanism of Action | Agent(s) | Available as |
|---|---|---|---|
| α-Glucosidase inhibitors | • Delay carbohydrate absorption from intestine | Acarbose<br>Miglitol | Precose or generic<br>Glyset |
| Amylin analogue | • Decrease glucagon secretion<br>• Slow gastric emptying<br>• Increase satiety | Pramlintide | Symlin |
| Biguanide | • Decrease HGP<br>• Increase glucose uptake in muscle | Metformin | Glucophage or generic |
| Bile acid sequestrant | • Decrease HGP?<br>• Increase incretin levels? | Colesevelam | WelChol |
| DPP4 inhibitors | • Increase glucose-dependent insulin secretion<br>• Decrease glucagon secretion | Alogliptin<br>Linagliptin<br>Saxagliptin<br>Sitagliptin | Nesina<br>Tradjenta<br>Onglyza<br>Januvia |
| Dopamine-2 agonist | • Activates dopaminergic receptors | Bromocriptine | Cycloset |
| Glinides | • Increase insulin secretion | Nateglinide<br>Repaglinide | Starlix or generic<br>Prandin |

DPP4, dipeptidyl peptidase; HGP, hepatic glucose production.

Garber AJ, et al. *Endocr Pract*. 2017;23:207-238.
ADA. *Diabetes Care*. 2017;40:S64-S74.

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# Noninsulin Agents Available for T2D

| Class | Primary Mechanism of Action | Agent(s) | Available as |
|---|---|---|---|
| GLP1 receptor agonists | • Increase glucose-dependent insulin secretion<br>• Decrease glucagon secretion<br>• Slow gastric emptying<br>• Increase satiety | Albiglutide<br>Dulaglutide<br>Exenatide<br>Exenatide XR<br>Liraglutide | Tanzeum<br>Trulicity<br>Byetta<br>Bydureon<br>Victoza |
| SGLT2 inhibitors | • Increase urinary excretion of glucose | Canagliflozin<br>Dapagliflozin<br>Empagliflozin | Invokana<br>Farxiga<br>Jardiance |
| Sulfonylureas | • Increase insulin secretion | Glimepiride<br>Glipizide<br>Glyburide | Amaryl or generic<br>Glucotrol or generic<br>Diaβeta, Glynase, Micronase, or generic |
| Thiazolidinediones | • Increase glucose uptake in muscle and fat<br>• Decrease HGP | Pioglitazone<br>Rosiglitazone | Actos<br>Avandia |

GLP1, glucagon-like peptide; HGP, hepatic glucose production; SGLT2, sodium glucose cotransporter 2.

Garber AJ, et al. *Endocr Pract*. 2017;23:207-238.
ADA. *Diabetes Care*. 2017;40:S64-S74.

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# Current Insulin Options

| Type | Basal Insulins | Prandial Insulins | Premixed Insulins |
|---|---|---|---|
| Human | U-100 NPH | U-100 regular human insulin<br>U-500 regular human insulin<br>Technosphere inhaled insulin | U-100 70/30 RHI |
| Analog | U-100 glargine<br>U-100 glargine equivalent*<br>U-100 detemir<br>U-100 degludec<br>U-200 degludec<br>U-300 glargine | U-100 lispro<br>U-100 aspart<br>U-100 glulisine<br>U-200 lispro | U-100 50/50 lispro<br>U-100 70/30 aspart<br>U-100 75/25 lispro<br>U-100 70/30 degludec/aspart |

- Analogue insulins are associated with less hypoglycemia than human insulins, although these differences are not always statistically significant

*In the US, U-100 glargine equivalent is not approved as a biosimilar product.

Singh SR, et al. *CMAJ*. 2009;180:385-397. Drugs@FDA. http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA. FDA. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm477734.htm.

# Fixed-Dose Oral Combination Agents for Type 2 Diabetes

| Class | Added Agent | Available as |
|---|---|---|
| DPP4 inhibitor + SGLT-2 inhibitor | Linagliptin + empagliflozin | Glyxambi |
| | Saxagliptin + dapagliflozin | Qtern |
| Metformin + DPP4 inhibitor | Alogliptin | Kazano |
| | Linagliptin | Jentadueto |
| | Sitagliptin | Janumet |
| Metformin + glinide | Repaglinide | Prandimet |
| Metformin + SGLT2 inhibitor | Canagliflozin | Invokamet |
| | Dapagliflozin | Xigduo XR |
| Metformin + sulfonylurea | Glipizide | Metaglip and generic |
| | Glyburide | Glucovance and generic |
| Metformin + thiazolidinedione | Pioglitazone | ACTOplus Met |
| | Rosiglitazone* | Avandamet |
| Thiazolidinedione + DPP4 inhibitor | Pioglitazone + alogliptin | Oseni |
| Thiazolidinedione + sulfonylurea | Pioglitazone | Duetact |
| | Rosiglitazone | Avandaryl |

# Fixed-Ratio Injectable Combination Agents Available for Type 2 Diabetes

| GLP1 receptor agonist + | Basal insulin | Available as |
|---|---|---|
| Liraglutide + | Degludec | Xultophy |
| Lixisenatide + | Glargine | Soliqua |

Garber AJ, et al. *Endocr Pract*. 2017;23:207-238.
ADA. *Diabetes Care*. 2017;40:S64-S74.

# PROFILES OF ANTIDIABETIC MEDICATIONS

| | MET | GLP-1 RA | SGLT-2i | DPP-4i | AGi | TZD (moderate dose) | SU / GLN | COLSVL | BCR-QR | INSULIN | PRAML |
|---|---|---|---|---|---|---|---|---|---|---|---|
| HYPO | Neutral | Neutral | Neutral | Neutral | Neutral | Neutral | Moderate/Severe / Mild | Neutral | Neutral | Moderate to Severe | Neutral |
| WEIGHT | Slight Loss | Loss | Loss | Neutral | Neutral | Gain | Gain | Neutral | Neutral | Gain | Loss |
| RENAL / GU | Contrain-dicated if eGFR < 30 mL/min/1.73 $m^2$ | Exenatide Not Indicated CrCl < 30<br>Possible Benefit of Liraglutide | Not Indicated for eGFR < 45 mL/min/1.73 $m^2$<br>Genital Mycotic Infections<br>Possible Benefit of Empagliflozin | Dose Adjustment Necessary (Except Linagliptin)<br>Effective in Reducing Albuminuria | Neutral | Neutral | More Hypo Risk | Neutral | Neutral | More Hypo Risk | Neutral |
| GI Sx | Moderate | Moderate | Neutral | Neutral | Moderate | Neutral | Neutral | Mild | Moderate | Neutral | Moderate |
| CHF | Neutral | Possible Benefit of Liraglutide | Possible Benefit of Empagliflozin | Possible Risk for Saxagliptin and Alogliptin | Neutral | Moderate | More CHF Risk | Neutral | Neutral | More CHF Risk | Neutral |
| CARDIAC* / ASCVD | | Possible CV Benefit | Possible CV Benefit | Neutral | | May Reduce Stroke Risk | ? | Benefit | Safe | Neutral | |
| BONE | Neutral | Neutral | Canagliflozin Warning | Neutral | Neutral | Moderate Fracture Risk | Neutral | Neutral | Neutral | Neutral | Neutral |
| KETOACIDOSIS | Neutral | Neutral | DKA Occurring in T2D in Various Stress Settings | Neutral | Neutral | Neutral | Neutral | Neutral | Neutral | Neutral | Neutral |

Few adverse events or possible benefits | Use with caution | Likelihood of adverse effects | ? Uncertain effect | * FDA indication to prevent CVD death in diabetes plus prior CVD events

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# Metformin

**Recommended for All Patients, Unless Contraindicated or Not Tolerated**

| | |
|---|---|
| Hypoglycemia | Neutral |
| Weight | Slight loss |
| Renal / Genitourinary | Contraindicated if eGFR <30 mL/min/1.73 $m^2$ |
| Gastrointestinal adverse effects | Moderate |
| Cardiac | Neutral |
| Bone | Neutral |
| Ketoacidosis | Neutral |

Few adverse events or possible benefits | Use with caution | Likelihood of adverse effects | ? Uncertain effect

eGFR = estimated glomerular filtration rate.

Garber AJ, et al. *Endocr Pract*. 2017;23:207-238.

# Glucagon-like Peptide 1 Receptor Agonists (GLP1 RAs)

| | |
|---|---|
| Hypoglycemia | Neutral |
| Weight | Loss |
| Renal / Genitourinary | Exenatide not indicated if CrCl <30 mL/min |
| | Possible benefit of liraglutide |
| Gastrointestinal adverse effects | Moderate |
| Cardiac—CHF | Possible benefit of liraglutide |
| Cardiac--ASCVD | Possible cardiovascular benefit |
| Bone | Neutral |
| Ketoacidosis | Neutral |

Few adverse events or possible benefits | Use with caution | Likelihood of adverse effects | ? Uncertain effect

ASCVD = atherosclerotic cardiovascular disease; CHF = congestive heart failure; CrCl = creatinine clearance.

Garber AJ, et al. *Endocr Pract*. 2017;23:207-238.

# Sodium Glucose Cotransporter 2 Inhibitors (SGLT2is)

| | |
|---|---|
| Hypoglycemia | Neutral |
| Weight | Loss |
| Renal / Genitourinary | Not indicated for eGFR <45 mL/min/1.73 $m^2$<br>Genital mycotic infections |
| | Possible benefit of empagliflozin |
| Gastrointestinal adverse effects | Neutral |
| Cardiac—CHF | Possible benefit of empagliflozin |
| Cardiac--ASCVD | Possible cardiovascular benefit |
| Bone | Canagliflozin warning |
| Ketoacidosis | DKA occurring in T2D in various stress settings |

Few adverse events or possible benefits | Use with caution | Likelihood of adverse effects | ? Uncertain effect

ASCVD = atherosclerotic cardiovascular disease; CHF = congestive heart failure; DKA = diabetic ketoacidosis; eGFR = estimated glomerular filtration rate; T2D = type 2 diabetes.

Garber AJ, et al. *Endocr Pract*. 2017;23:207-238.

# AACE/ACE Position Statement on Association of SGLT2 Inhibitors With DKA

- DKA occurs infrequently
- Risk-benefit ratio favors continued use of SGLT2 inhibitors with no changes in current recommendations
- DKA diagnosis may be missed or delayed due to atypical presentation involving lower-than-anticipated glucose levels or other misleading laboratory values
  - This atypical presentation has been seen with other antihyperglycemic agents long before the introduction of SGLT2 inhibitors

DKA = diabetic ketoacidosis; SGLT2 = sodium glucose cotransporter 2.

Handelsman Y, et al. *Endocr Pract*. 2016;22:753-762.

# Dipeptidyl Peptidase 4 Inhibitors (DPP4is)

| | |
|---|---|
| Hypoglycemia | Neutral |
| Weight | Neutral |
| Renal / Genitourinary | Dose adjustment necessary (except linagliptin)<br>Effective in reducing albuminuria |
| Gastrointestinal adverse effects | Neutral |
| Cardiac—CHF | Possible risk for saxagliptin and alogliptin |
| Cardiac--ASCVD | Neutral |
| Bone | Neutral |
| Ketoacidosis | Neutral |

Few adverse events or possible benefits | Use with caution | Likelihood of adverse effects | ? Uncertain effect

ASCVD = atherosclerotic cardiovascular disease; CHF = congestive heart failure.

Garber AJ, et al. *Endocr Pract*. 2017;23:207-238.

# Alpha Glucosidase Inhibitors (AGis)

| | |
|---|---|
| Hypoglycemia | Neutral |
| Weight | Neutral |
| Renal / Genitourinary | Neutral |
| Gastrointestinal adverse effects | Moderate |
| Cardiac | Neutral |
| Bone | Neutral |
| Ketoacidosis | Neutral |

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

ASCVD = atherosclerotic cardiovascular disease; CHF = congestive heart failure.

Garber AJ, et al. *Endocr Pract*. 2017;23:207-238.

# Thiazolidinediones (TZDs)*

| | |
|---|---|
| Hypoglycemia | Neutral |
| Weight | Gain |
| Renal / Genitourinary | Neutral |
| Gastrointestinal adverse effects | Neutral |
| Cardiac—CHF | Moderate |
| Cardiac--ASCVD | May reduce stroke risk |
| Bone | Moderate fracture risk |
| Ketoacidosis | Neutral |

Few adverse events or possible benefits | Use with caution | Likelihood of adverse effects | ? Uncertain effect

*Moderate dose (pioglitazone 30 mg).

ASCVD = atherosclerotic cardiovascular disease; CHF = congestive heart failure.

Garber AJ, et al. *Endocr Pract*. 2017;23:207-238.

# Secretagogues

| | SU | GLN |
|---|---|---|
| Hypoglycemia | Moderate / severe | Mild |
| Weight | Gain | |
| Renal / Genitourinary | More hypoglycemia risk | |
| Gastrointestinal adverse effects | Neutral | |
| Cardiac—CHF | More CHF risk | |
| Cardiac--ASCVD | ? | |
| Bone | Neutral | |
| Ketoacidosis | Neutral | |

Few adverse events or possible benefits | Use with caution | Likelihood of adverse effects | ? Uncertain effect

ASCVD = atherosclerotic cardiovascular disease; CHF = congestive heart failure; GLN = glinide; SU = sulfonylurea.

Garber AJ, et al. *Endocr Pract*. 2017;23:207-238.

# Colesevelam and Bromocriptine Mesylate

| | Colesevelam | BCR-QR |
|---|---|---|
| Hypoglycemia | Neutral | Neutral |
| Weight | Neutral | Neutral |
| Renal / Genitourinary | Neutral | Neutral |
| Gastrointestinal adverse effects | Mild | Moderate |
| Cardiac—CHF | Neutral | Neutral |
| Cardiac--ASCVD | Benefit | Safe |
| Bone | Neutral | Neutral |
| Ketoacidosis | Neutral | Neutral |

Few adverse events or possible benefits | Use with caution | Likelihood of adverse effects | ? Uncertain effect

ASCVD = atherosclerotic cardiovascular disease; BCR-QR = bromocriptine mesylate quick release; CHF = congestive heart failure.

Garber AJ, et al. *Endocr Pract*. 2017;23:207-238.

# Insulin

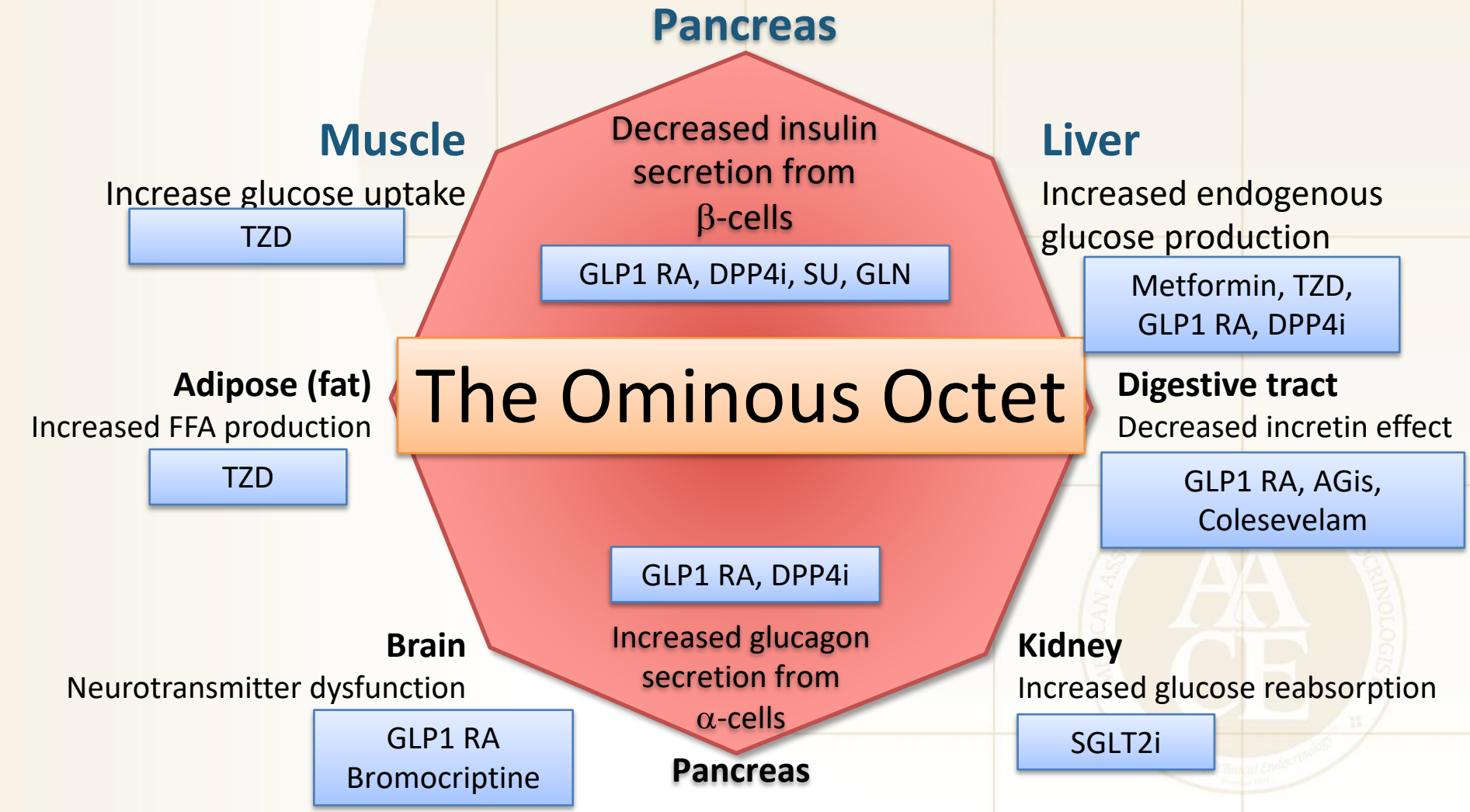
| | |
|---|---|
| Hypoglycemia | Moderate to severe |
| Weight | Gain |
| Renal / Genitourinary | More hypoglycemia risk |
| Gastrointestinal adverse effects | Neutral |
| Cardiac—CHF | More CHF risk |
| Cardiac—ASCVD | Neutral |
| Bone | Neutral |
| Ketoacidosis | Neutral |

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

ASCVD = atherosclerotic cardiovascular disease; CHF = congestive heart failure.

Garber AJ, et al. *Endocr Pract*. 2017;23:207-238.

# Mechanism of Action of Antihyperglycemic Agents




DeFronzo RA. *Diabetes*. 2009;58:773-795

# Effects of Agents Available for T2D

| | Met | GLP1RA | SGLT2I | DPP4I | TZD | AGI | Coles | BCR-QR | SU/ Glinide | Insulin | Pram |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **FPG lowering** | Mod | Mild to mod* | Mod | Mild | Mod | Neutral | Mild | Neutral | SU: mod Glinide: mild | Mod to marked (basal insulin or premixed) | Mild |
| **PPG lowering** | Mild | Mod to marked | Mild | Mod | Mild | Mod | Mild | Mild | Mod | Mod to marked (short/ rapid-acting insulin or premixed) | Mod to marked |

AGI = α-glucosidase inhibitors; BCR-QR = bromocriptine quick release; Coles = colesevelam; DPP4I = dipeptidyl peptidase 4 inhibitors; FPG = fasting plasma glucose; GLP1RA = glucagon-like peptide 1 receptor agonists; Met = metformin; Mod = moderate; PPG = postprandial glucose; SGLT2I = sodium-glucose cotransporter 2 inhibitors; SU = sulfonylureas; TZD = thiazolidinediones.

*Mild: albiglutide and exenatide; moderate: dulaglutide, exenatide extended release, and liraglutide.

Handelsman YH, et al. *Endocr Pract*. 2015;21(suppl 1):1-87.

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# GLYCEMIC CONTROL ALGORITHM

## LIFESTYLE THERAPY
(Including Medically Assisted Weight Loss)

### Entry A1C < 7.5%

**MONOTHERAPY***

- ✓ Metformin
- ✓ GLP-1 RA
- ✓ SGLT-2i
- ✓ DPP-4i
- ! TZD
- ✓ AGi
- ! SU/GLN

If not at goal in 3 months proceed to Dual Therapy

### Entry A1C ≥ 7.5%

**DUAL THERAPY***

MET or other 1st-line agent +

- ✓ GLP-1 RA
- ✓ SGLT-2i
- ✓ DPP-4i
- ! TZD
- ! Basal Insulin
- ✓ Colesevelam
- ✓ Bromocriptine QR
- ✓ AGi
- ! SU/GLN

If not at goal in 3 months proceed to Triple Therapy

**TRIPLE THERAPY***

MET or other 1st-line agent + 2nd-line agent +

- ✓ GLP-1 RA
- ✓ SGLT-2i
- ! TZD
- ! Basal insulin
- ✓ DPP-4i
- ✓ Colesevelam
- ✓ Bromocriptine QR
- ✓ AGi
- ! SU/GLN

If not at goal in 3 months proceed to or intensify insulin therapy

### Entry A1C > 9.0%

**SYMPTOMS**

| NO | YES |
|---|---|
| DUAL Therapy OR TRIPLE Therapy | INSULIN ± Other Agents |

**ADD OR INTENSIFY INSULIN**

Refer to Insulin Algorithm

**LEGEND**

- ✓ Few adverse events and/or possible benefits
- ! Use with caution

* Order of medications represents a suggested hierarchy of usage; length of line reflects strength of recommendation

## PROGRESSION OF DISEASE

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# INSULIN THERAPY

# ALGORITHM FOR ADDING/INTENSIFYING INSULIN

## START BASAL (Long-Acting Insulin)

**A1C < 8%**

**TDD** 0.1–0.2 U/kg

**A1C > 8%**

**TDD** 0.2–0.3 U/kg

**Insulin titration every 2–3 days to reach glycemic goal:**

- Fixed regimen: Increase TDD by 2 U
- Adjustable regimen:
  - **FBG** > 180 mg/dL: add 20% of TDD
  - **FBG** 140–180 mg/dL: add 10% of TDD
  - **FBG** 110–139 mg/dL: add 1 unit
- If hypoglycemia, reduce TDD by:
  - **BG** < 70 mg/dL: 10% – 20%
  - **BG** < 40 mg/dL: 20% – 40%

**Consider discontinuing or reducing sulfonylurea after starting basal insulin (basal analogs preferred to NPH)**

***Glycemic Goal:**

- <7% for most patients with T2D; fasting and premeal BG < 110 mg/dL; absence of hypoglycemia
- A1C and FBG targets may be adjusted based on patient's age, duration of diabetes, presence of comorbidities, diabetic complications, and hypoglycemia risk

**Glycemic Control Not at Goal***

## INTENSIFY (Prandial Control)

**Add GLP-1 RA**

Or SGLT-2i
Or DPP-4i

**Add Prandial Insulin**

**Basal Plus 1, Plus 2, Plus 3**

- Begin prandial insulin before largest meal
- If not at goal, progress to injections before 2 or 3 meals
- Start: 10% of basal dose or 5 units

**Basal Bolus**

- Begin prandial insulin before each meal
- 50% Basal / 50% Prandial TDD 0.3–0.5 U/kg
- Start: 50% of TDD in three doses before meals

**Insulin titration every 2–3 days to reach glycemic goal:**

- Increase prandial dose by 10% or 1-2 units if 2-h postprandial or next premeal glucose consistently > 140 mg/dL
- If hypoglycemia, reduce TDD basal and/or prandial insulin by:
  - BG consistently < 70 mg/dL: 10% - 20%
  - Severe hypoglycemia (requiring assistance from another person) or BG < 40 mg/dL: 20% - 40%

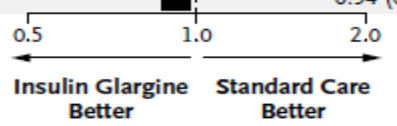
 DOI 10.4158/EP161682.CS

# Early Insulin Use in Type 2 Diabetes

## ORIGIN

### (N=12,537 patients with CV risk factors + prediabetes or T2D)

| Outcome | Insulin Glargine (N=6264) | | Standard Care (N=6273) | | Hazard Ratio (95% CI) | P Value |
|---|---|---|---|---|---|---|
| | *no. (%)* | *no./100 patient-yr* | *no. (%)* | *no./100 patient-yr* | | |
| First coprimary outcome | 1041 (16.6) | 2.94 | 1013 (16.1) | 2.85 | 1.02 (0.94–1.11) | 0.63 |
| Second coprimary outcome | 1792 (28.6) | 5.52 | 1727 (27.5) | 5.28 | 1.04 (0.97–1.11) | 0.27 |
| Microvascular outcomes | 1323 (21.1) | 3.87 | 1363 (21.7) | 3.99 | 0.97 (0.90–1.05) | 0.43 |
| Total mortality | 951 (15.2) | 2.57 | 965 (15.4) | 2.60 | 0.98 (0.90–1.08) | 0.70 |
| Total myocardial infarctions | 336 (5.4) | 0.93 | 326 (5.2) | 0.90 | 1.02 (0.88–1.19) | 0.75 |
| Total strokes | 331 (5.3) | 0.91 | 319 (5.1) | 0.88 | 1.03 (0.89–1.21) | 0.69 |
| Death from cardiovascular causes | 580 (9.3) | 1.57 | 576 (9.2) | 1.55 | 1.00 (0.89–1.13) | 0.98 |
| Hospitalization for congestive heart failure | 310 (4.9) | 0.85 | 343 (5.5) | 0.95 | 0.90 (0.77–1.05) | 0.16 |
| Revascularization | 908 (14.5) | 2.69 | 860 (13.7) | 2.52 | 1.06 (0.96–1.16) | 0.24 |
| Angina | 709 (11.3) | 2.07 | 743 (11.8) | 2.17 | 0.95 (0.85–1.05) | 0.29 |
| Unstable | 238 (3.8) | 0.66 | 261 (4.2) | 0.72 | 0.91 (0.76–1.08) | 0.28 |
| New | 100 (1.6) | 0.27 | 138 (2.2) | 0.38 | 0.72 (0.56–0.93) | 0.01 |
| Worsening | 455 (7.3) | 1.29 | 446 (7.1) | 1.26 | 1.02 (0.89–1.16) | 0.80 |
| Limb or digit amputation | 47 (0.8) | 0.13 | 53 (0.8) | 0.14 | 0.89 (0.60–1.31) | 0.55 |
| Cardiovascular hospitalization | 2081 (33.2) | 6.98 | 2071 (33.0) | 6.91 | 1.00 (0.94–1.07) | 0.90 |
| Noncardiovascular hospitalization | 2339 (37.3) | 7.90 | 2349 (37.4) | 7.93 | 0.99 (0.94–1.05) | 0.85 |
| Any cancer | 476 (7.6) | 1.32 | 477 (7.6) | 1.32 | 1.00 (0.88–1.13) | 0.97 |
| Death from cancer | 189 (3.0) | 0.51 | 201 (3.2) | 0.54 | 0.94 (0.77–1.15) | 0.52 |




ORIGIN, Outcome Reduction With an Initial Glargine Interventionl T2D, type 2 diabetes.

ORIGIN Trial Investigators. *N Engl J Med*. 2012;367:319-328.

# Pharmacokinetics of Available Insulins

| | Agent | Onset (h) | Peak (h) | Duration (h) | Considerations |
|---|---|---|---|---|---|
| Basal | NPH | 2-4 | 4-10 | 10-16 | Greater risk of nocturnal hypoglycemia compared to insulin analogs |
| Basal | Glargine<br>Detemir<br>Degludec | ~1-4 | No pronounced peak* | Up to 24† | Less nocturnal hypoglycemia compared to NPH |
| Basal-Prandial | Regular U-500 | ≤0.5 | ~2-3 | 12-24 | • Inject 30 min before a meal<br>• Indicated for highly insulin resistant individuals<br>• Use caution when measuring dosage to avoid inadvertent overdose |
| Prandial | Regular | ~0.5-1 | ~2-3 | Up to 8 | • Must be injected 30-45 min before a meal<br>• Injection with or after a meal could increase risk for hypoglycemia |
| Prandial | Aspart<br>Glulisine<br>Lispro<br>Inhaled insulin | <0.5 | ~0.5-2.5 | ~3-5 | • Can be administered 0-15 min before a meal<br>• Less risk of postprandial hypoglycemia compared to regular insulin |

* Exhibits a peak at higher dosages.

† Dose-dependent.

NPH, Neutral Protamine Hagedorn.

Moghissi E et al. *Endocr Pract*. 2013;19:526-535. Humulin R U-500 (concentrated) insulin prescribing information. Indianapolis: Lilly USA, LLC.

# Insulin Concentrations

| Concentration | Units/mL | Units/vial | Units/pen |
|---|---|---|---|
| U-100 | 100 | 1000<br>(10 units per vial) | 300<br>(3 mL/pen) |
| U-200 | 200 | Not available in vials | 600<br>(3 mL/pen) |
| U-300 | 300 | Not available in vials | 450<br>(1.5 mL/pen) |
| U-500 | 500 | 10,000<br>(20 units/vial) | 1500<br>(1.5 mL/pen) |

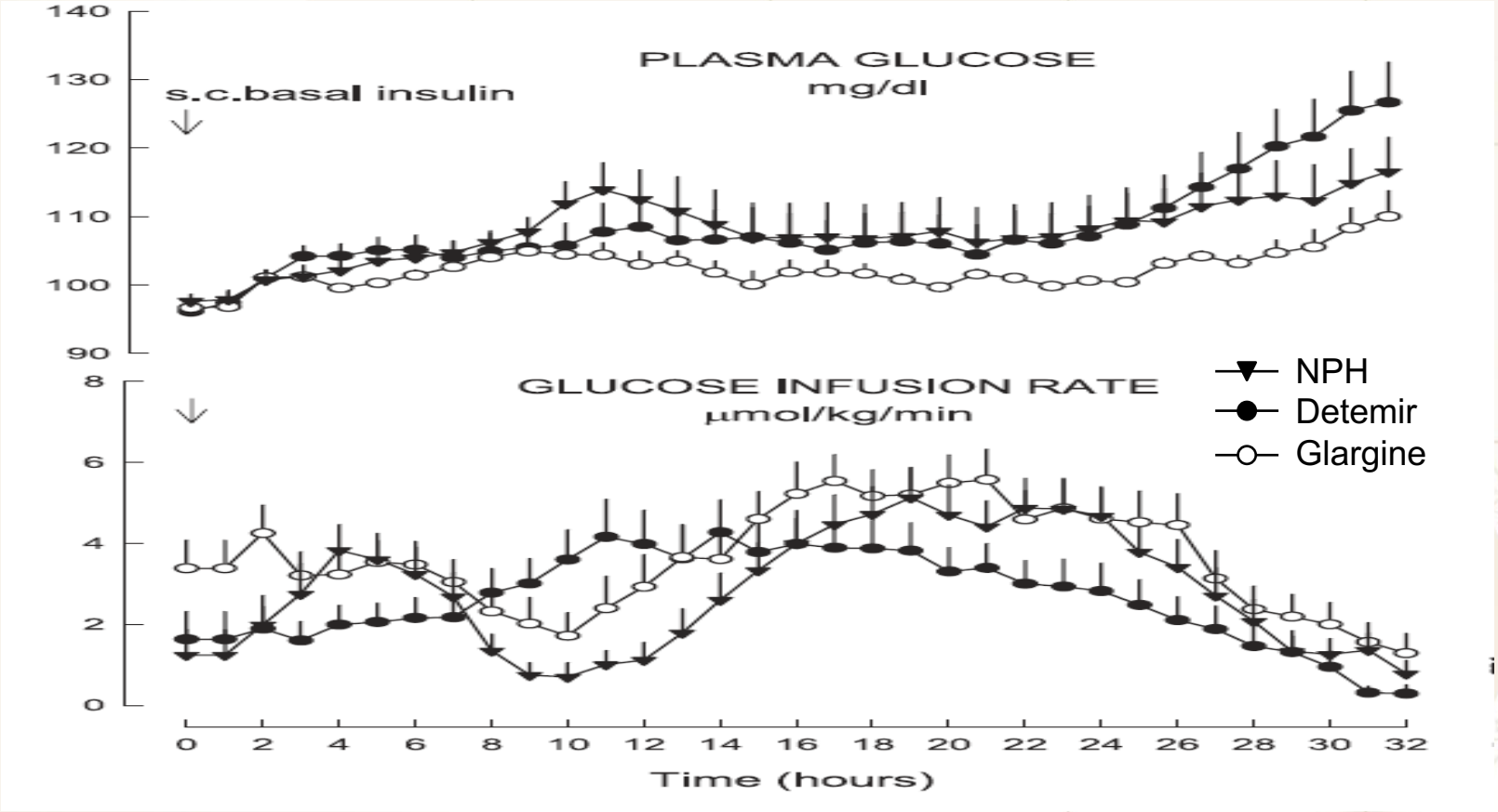
- Insulin pens significantly reduce the risk of dosing errors and hypoglycemic events
- Pens completely eliminate the need for converting doses based on the volume of insulin injected
- Dosing errors with U-500 insulin vials are common and dangerous but can be avoided with newly available pens
  - 5-fold higher insulin dose relative to the same volume of a U-100 insulin

Drugs@FDA. http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA. Newton C, et al. AACE Annual Meeting. 2013 [abstract 271]. Segal AR, et al. Am J Health Syst Pharm. 2010;67:1526-1535.

# Glycemic Variability With NPH, Glargine, and Detemir

## 3-Period Crossover Euglycemic Clamp Study

## (N=18 patients with T2D)

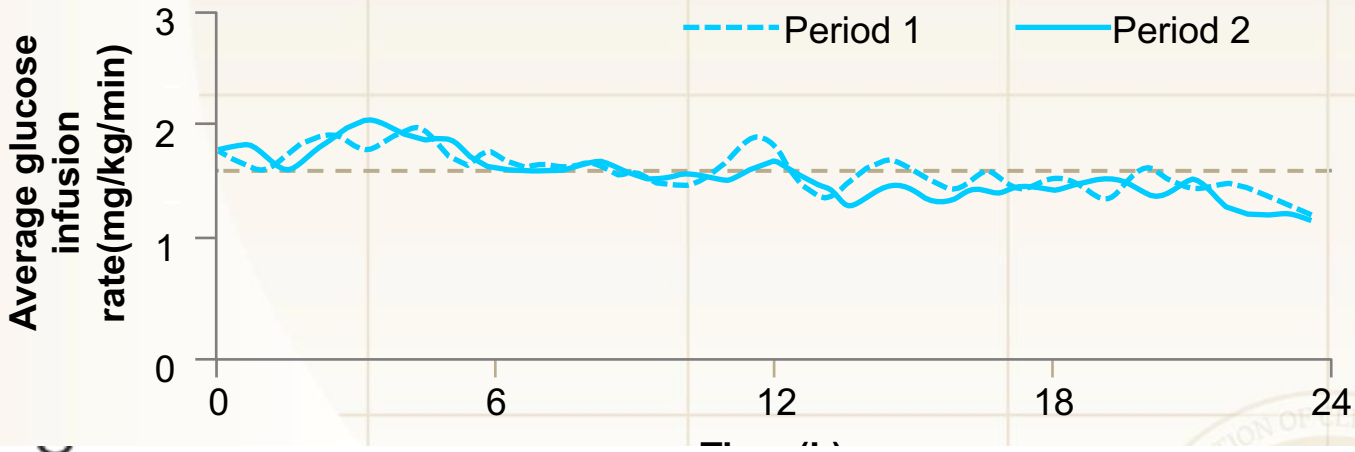


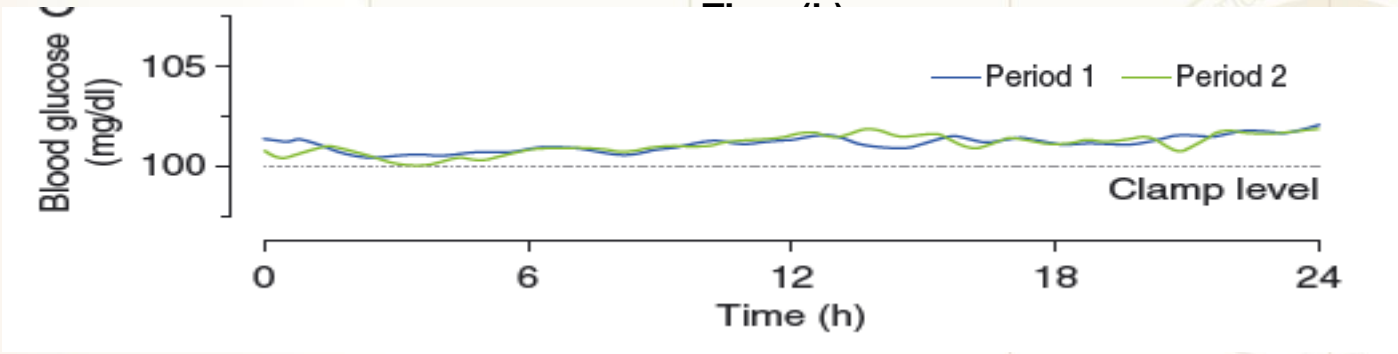

Lucidi P, et al. *Diabetes Care*. 2011;34:1312-1314.

# Glycemic Variability of Glargine U300

**2-Period Crossover Study**

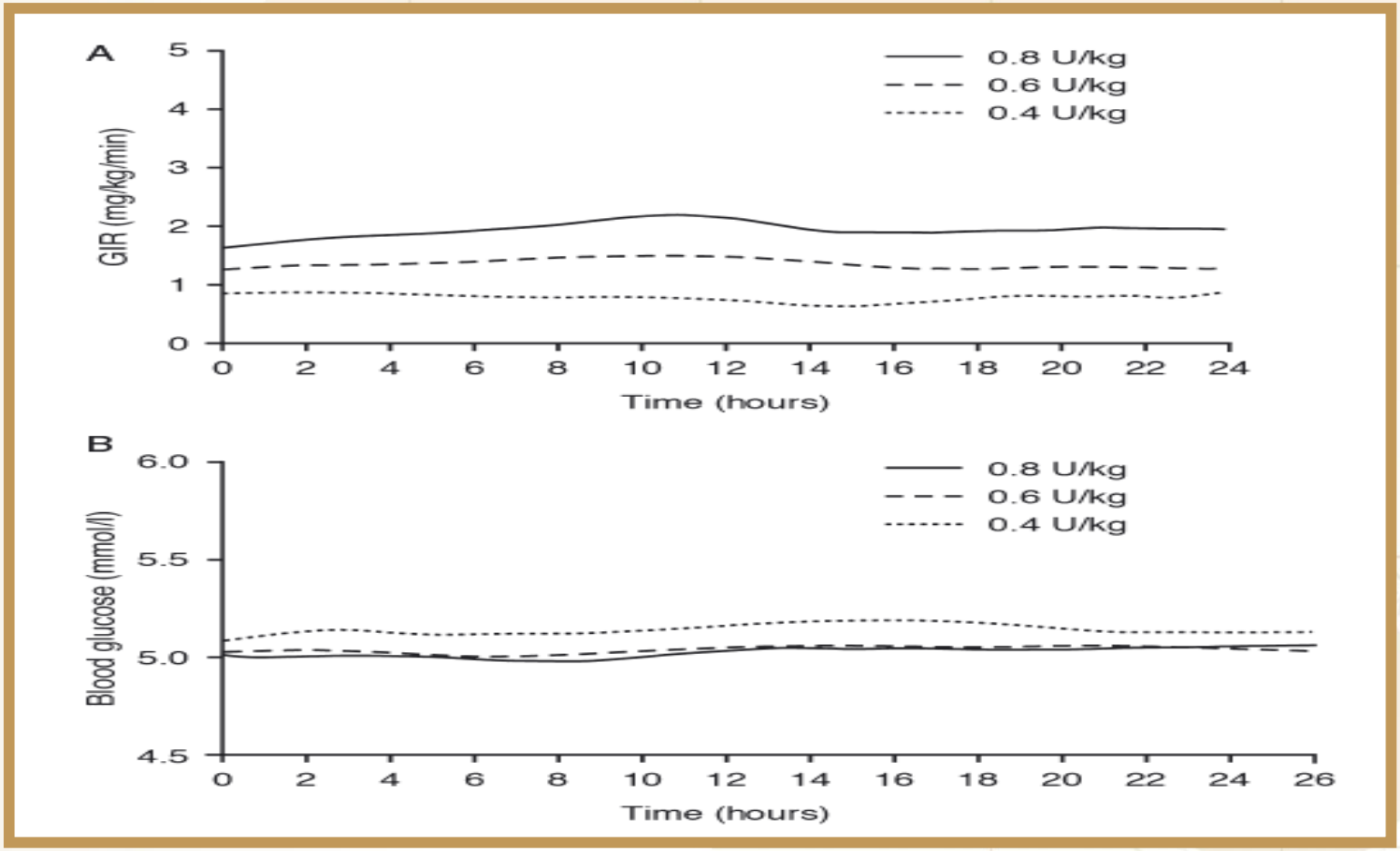
**(N=50 patients with T1D)**




Becker RH, et al. *Diabetes Obes Metab*. 2015;17:261-267.

# Glycemic Variability of Degludec

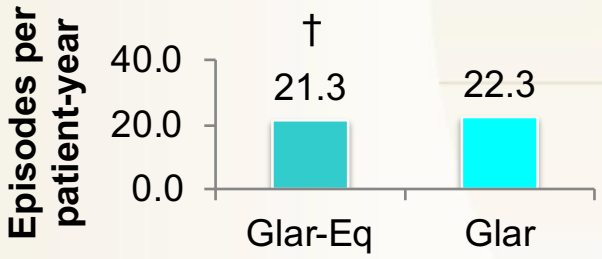



Heise T, et al. *Diabetes Obes Metab*. 2012;14:944-950.

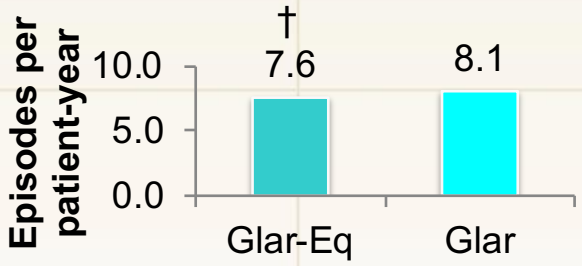
# Efficacy and Safety of U-100 Glargine Equivalent

## Patients With T2D* (N=756)

### Overall
(BG <70 mg/dL or S/S)

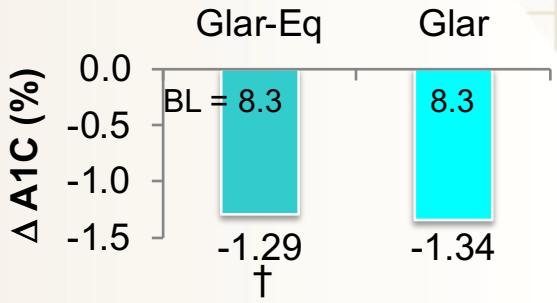



### Nocturnal
(between bedtime and waking)

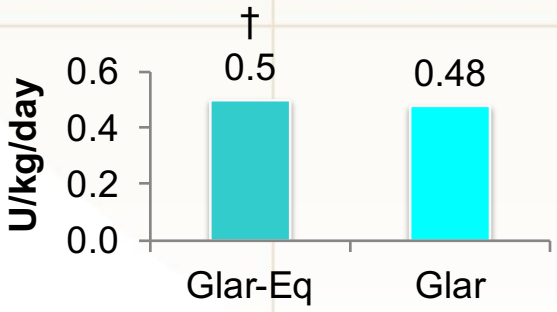



### Severe
(Requiring assistance)

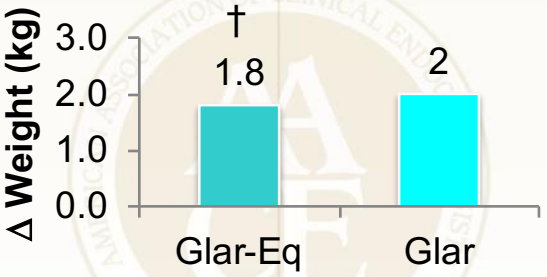

### A1C




### Insulin Dose




### Weight




*Mean age = 59 y; duration of diabetes = 11-12 y; baseline BMI = 32 kg/m$^2$. †Not significant vs glargine.

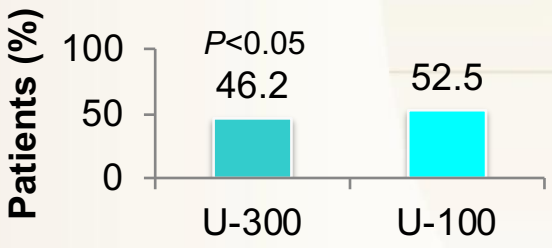
BMI = body mass index; Glar-Eq = glargine equivalent (n=376); Glar = insulin glargine (n=380); S/S = signs and symptoms; T2D = type 2 diabetes.

Rosenstock J, et al. *Diabetes Obes Metab*. 2015;17:734-741.

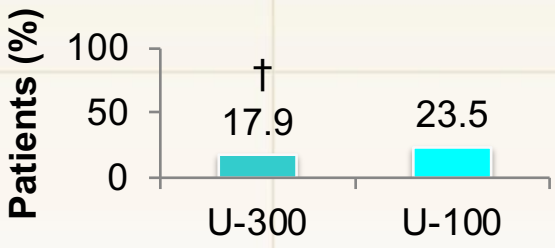
# Efficacy and Safety of Glargine U-300

## Insulin-Naive T2D Patients* (N=878)

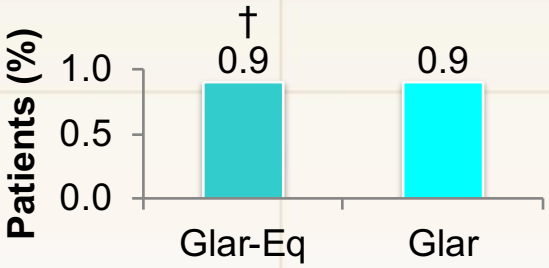
### Overall
(BG <70 mg/dL)



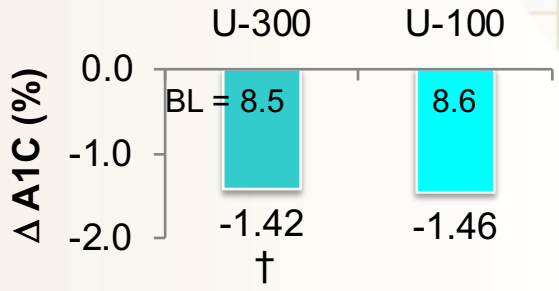

### Nocturnal
(between midnight and 6:00 am)



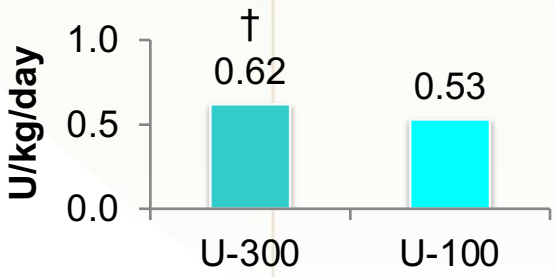

### Severe
(Requiring assistance)



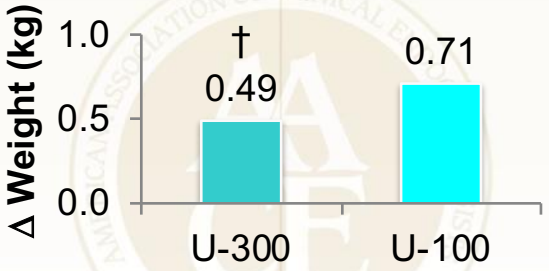

### A1C




### Insulin Dose




### Weight




*Mean age = 58 y; duration of diabetes = 9.8 y; baseline BMI = 33 kg/m$^2$. †Not significant vs glargine U-100.

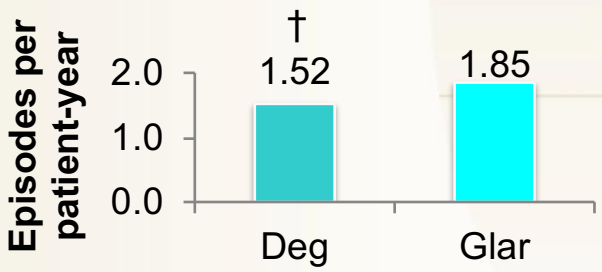
BMI = body mass index; NS = not significant; T2D = type 2 diabetes.

Bolli GB, et al. *Diabetes Obes Metab*. 2015;17:386-394.

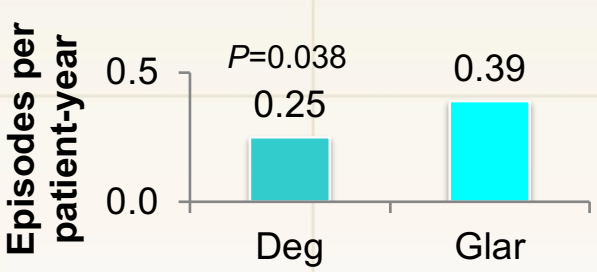
# Efficacy and Safety of Degludec and Glargine U-100

## Insulin-Naive T2D Patients* (N=1030)

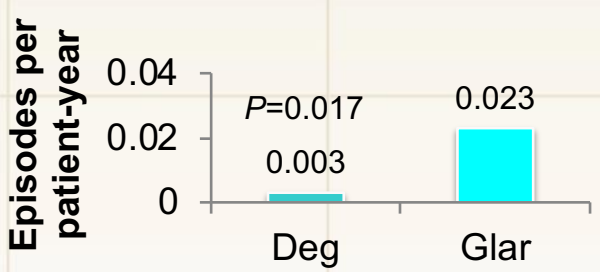
### Overall
(BG <70 mg/dL or S/S)



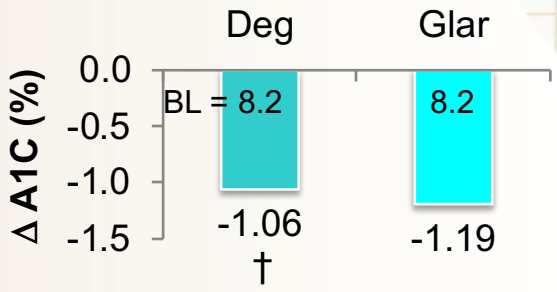

### Nocturnal
(between bedtime and waking)



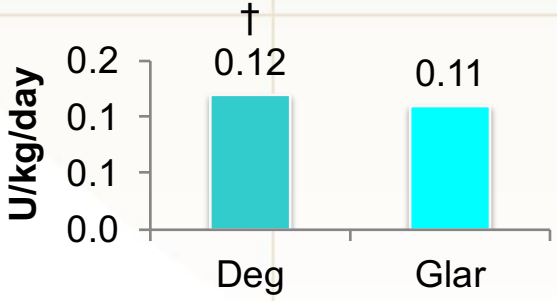

### Severe
(Requiring assistance)



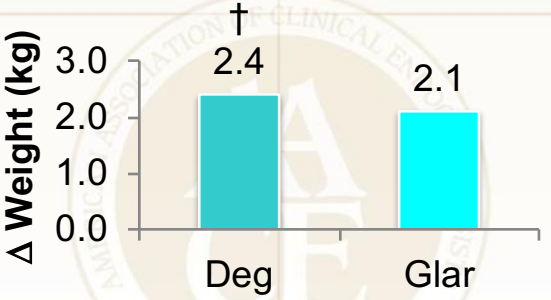

### A1C




### Insulin Dose




### Weight




*Mean age = 59 y; duration of diabetes = 9 y; baseline BMI = 31-32 kg/m$^2$; degludec (n=773); glargine (n=257). †Not significant vs glargine.

BMI = body mass index; Deg = degludec; Glar = glargine; NS = not significant; T2D = type 2 diabetes.

Zinman B, et al. *Diabetes Care*. 2012;35:2464-2471.

Glycemic Management of Type 2 Diabetes

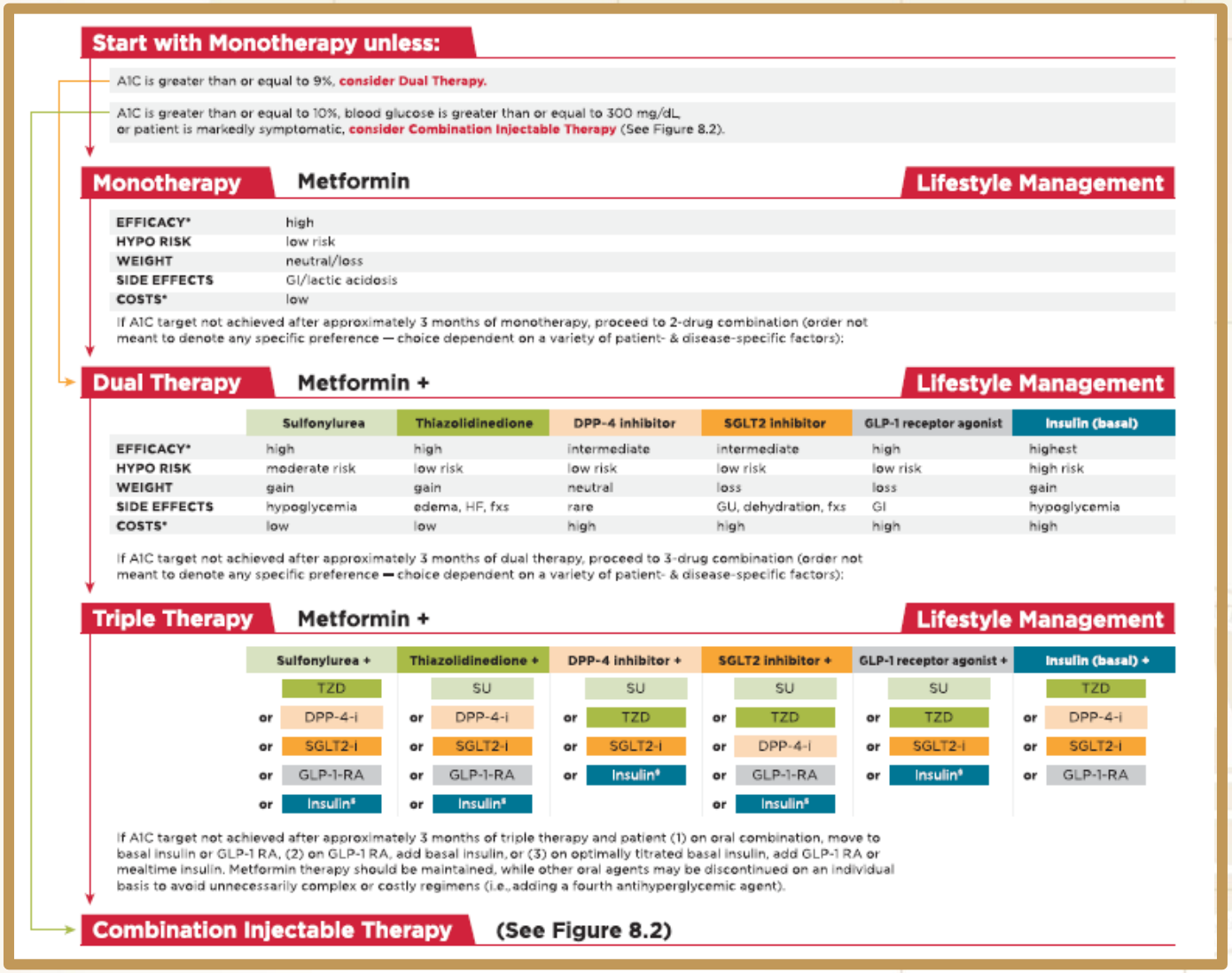
# ADA RECOMMENDATIONS

# Common Principles in AACE/ACE and ADA/EASD T2D Treatment Algorithms

- Individualize glycemic goals based on patient characteristics
- Promptly intensify antihyperglycemic therapy to maintain blood glucose at individual targets
  - Combination therapy necessary for most patients
  - Base choice of agent(s) on individual patient medical history, behaviors and risk factors, ethno-cultural background, and environment
- Insulin eventually necessary for many patients
- SMBG vital for day-to-day management of blood sugar
  - All patients using insulin
  - Many patients not using insulin

Garber AJ, et al. *Endocr Pract*. 2017;23:207-238.
ADA. *Diabetes Care*. 2017;40:S64-S74.

# ADA Treatment Algorithm



**Start with Monotherapy unless:**

A1C is greater than or equal to 9%, **consider Dual Therapy.**

A1C is greater than or equal to 10%, blood glucose is greater than or equal to 300 mg/dL, or patient is markedly symptomatic, **consider Combination Injectable Therapy** (See Figure 8.2).

**Monotherapy** **Metformin** **Lifestyle Management**

| | |
|---|---|
| EFFICACY* | high |
| HYPO RISK | low risk |
| WEIGHT | neutral/loss |
| SIDE EFFECTS | GI/lactic acidosis |
| COSTS* | low |

If A1C target not achieved after approximately 3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

**Dual Therapy** **Metformin +** **Lifestyle Management**

| | Sulfonylurea | Thiazolidinedione | DPP-4 inhibitor | SGLT2 inhibitor | GLP-1 receptor agonist | Insulin (basal) |
|---|---|---|---|---|---|---|
| EFFICACY* | high | high | intermediate | intermediate | high | highest |
| HYPO RISK | moderate risk | low risk | low risk | low risk | low risk | high risk |
| WEIGHT | gain | gain | neutral | loss | loss | gain |
| SIDE EFFECTS | hypoglycemia | edema, HF, fxs | rare | GU, dehydration, fxs | GI | hypoglycemia |
| COSTS* | low | low | high | high | high | high |

If A1C target not achieved after approximately 3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

**Triple Therapy** **Metformin +** **Lifestyle Management**

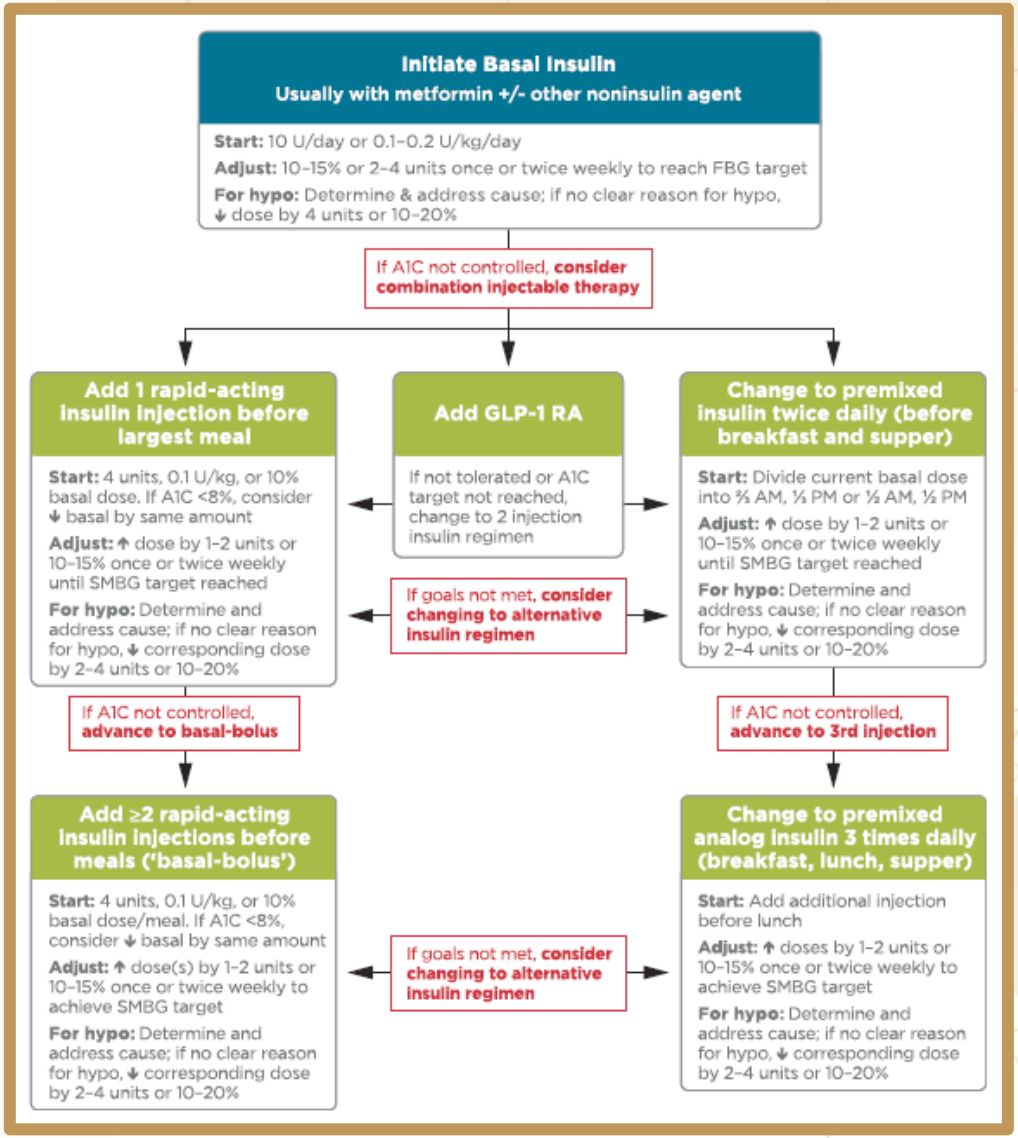
| Sulfonylurea + | Thiazolidinedione + | DPP-4 inhibitor + | SGLT2 inhibitor + | GLP-1 receptor agonist + | Insulin (basal) + |
|---|---|---|---|---|---|
| TZD | SU | SU | SU | SU | TZD |
| or DPP-4-i | or DPP-4-i | or TZD | or TZD | or TZD | or DPP-4-i |
| or SGLT2-i | or SGLT2-i | or SGLT2-i | or DPP-4-i | or SGLT2-i | or SGLT2-i |
| or GLP-1-RA | or GLP-1-RA | or Insulin§ | or GLP-1-RA | or Insulin§ | or GLP-1-RA |
| or Insulin§ | or Insulin§ | | or Insulin§ | | |

If A1C target not achieved after approximately 3 months of triple therapy and patient (1) on oral combination, move to basal insulin or GLP-1 RA, (2) on GLP-1 RA, add basal insulin, or (3) on optimally titrated basal insulin, add GLP-1 RA or mealtime insulin. Metformin therapy should be maintained, while other oral agents may be discontinued on an individual basis to avoid unnecessarily complex or costly regimens (i.e., adding a fourth antihyperglycemic agent).

**Combination Injectable Therapy** **(See Figure 8.2)**

ADA. *Diabetes Care*. 2017;40:S64-S74.

# ADA Treatment Algorithm: Combination Injectable Therapy




ADA. *Diabetes Care*. 2017;40:S64-S74.

Glycemic Management of Type 2 Diabetes

# TECHNOLOGY FOR TYPE 2 DIABETES MANAGEMENT

# SMBG in Type 2 Diabetes: AACE/ACE Recommendations

## Noninsulin Users

- Introduce at diagnosis
- Personalize frequency of testing
- Use SMBG results to inform decisions about whether to target FPG or PPG for any individual patient

Testing positively affects glycemia in T2D when the results are <u>used</u> to:

- Modify behavior
- Modify pharmacologic treatment

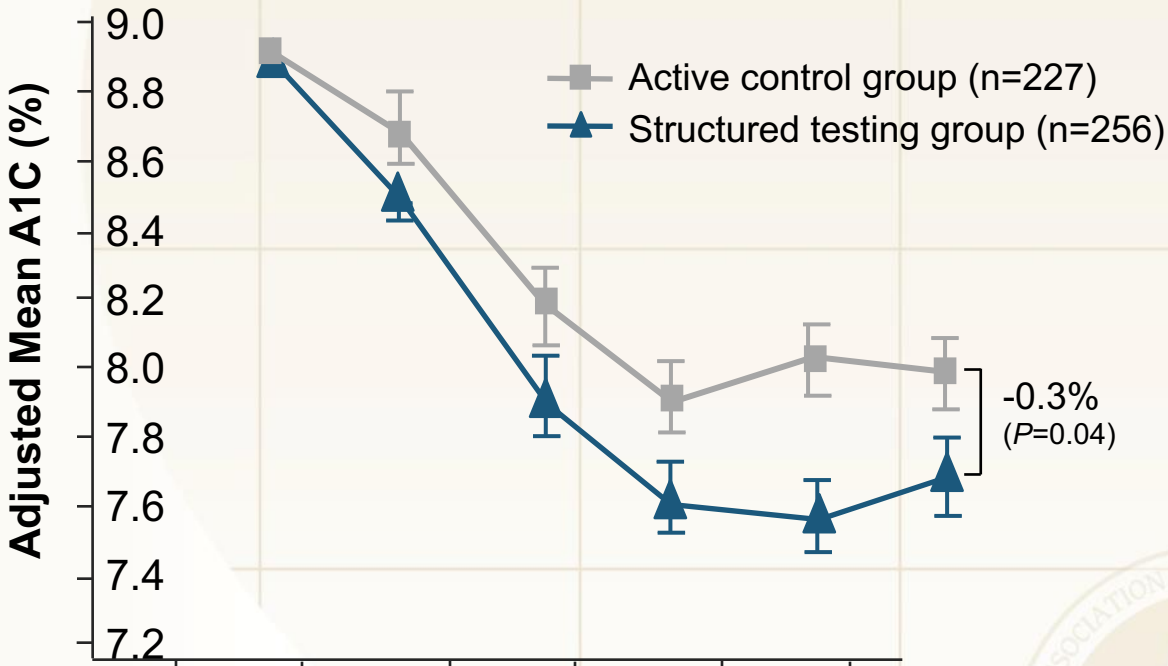
## Insulin Users

- All patients using insulin should test glucose
  - ≥2 times daily
  - Before any injection of insulin
- More frequent SMBG (after meals or in the middle of the night) may be required
  - Frequent hypoglycemia
  - Not at A1C target

FPG, fasting plasma glucose; PPG, postprandial glucose; SMBG, self-monitoring of blood glucose; T2D, type 2 diabetes.

Handelsman YH, et al. *Endocr Pract*. 2015;21(suppl 1):1-87.

# SMBG in Patients With T2D Not Using Insulin




ACG, active control group; SMBG, self-monitoring of blood glucose; STG, structured testing group; T2D, type 2 diabetes.

Polonsky WH, et al. *Diabetes Care*. 2011;34:262-267.

# CSII in Type 2 Diabetes: Patient Candidates

- Absolutely insulin-deficient
- Take 4 or more insulin injections a day
- Assess blood glucose levels 4 or more times daily
- Motivated to achieve tighter glucose control
- Mastery of carbohydrate counting, insulin correction, and adjustment formulas
- Ability to troubleshoot problems related to pump operation and plasma glucose levels
- Stable life situation
- Frequent contact with members of their healthcare team, in particular their pump-supervising physician

CSII, continuous subcutaneous insulin infusion.

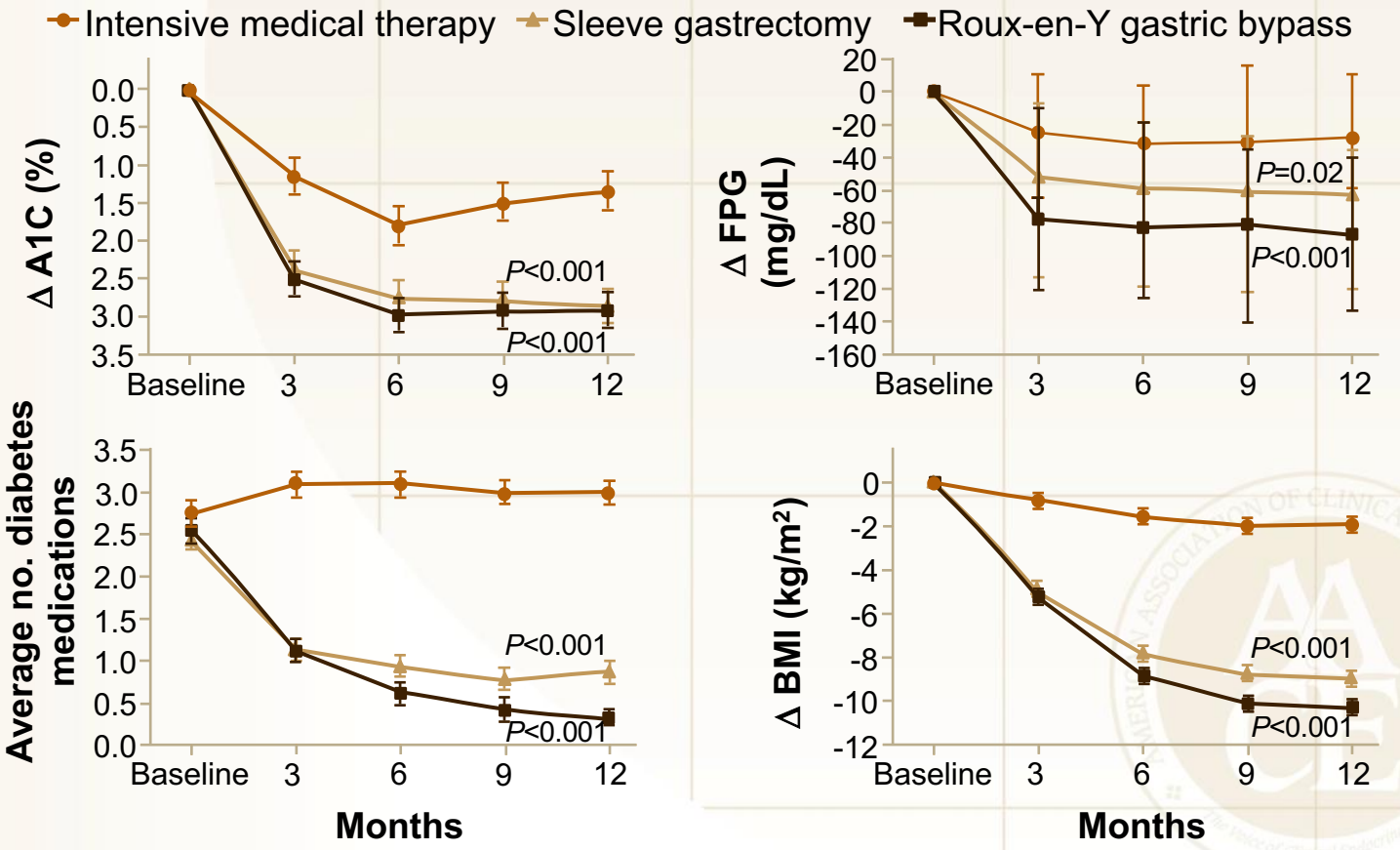
Handelsman YH, et al. *Endocr Pract*. 2015;21(suppl 1):1-87.

Glycemic Management of Type 2 Diabetes

# SURGICAL INTERVENTION

# Surgical Intervention in Type 2 Diabetes

## STAMPEDE Trial (n=150)




STAMPEDE, Surgical Treatment and Medications Potentially Eradicate Diabetes Efficiently.

Schauer PR, et al. *N Engl J Med*. 2012;366:1567-1576.

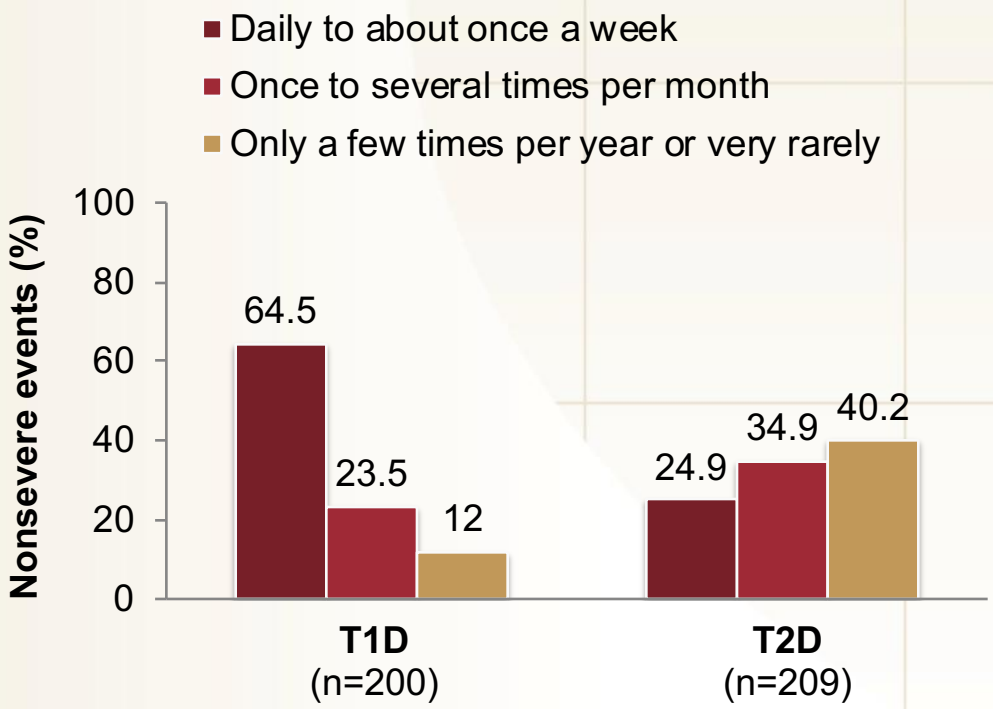
Glycemic Management of Type 2 Diabetes

# SAFETY CONCERNS: HYPOGLYCEMIA

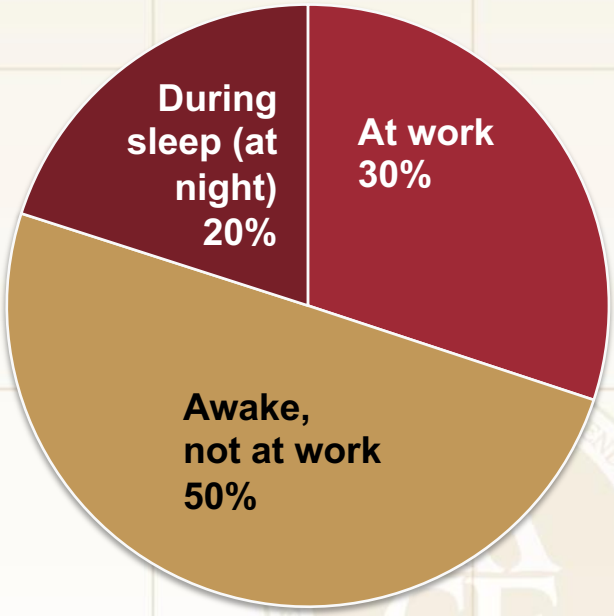
# How Often and When Does Nonsevere Hypoglycemia Occur in Diabetes?

## Internet-Based Patient Survey

### Event Frequency




### Time of Event




T1D, type 1 diabetes; T2D, type 2 diabetes.

Brod M, et al. *Value Health*. 2011;14:665-671.

# Type 2 Diabetes Pathophysiology: Origins of Hypoglycemia

| | Defect |
|---|---|
| β-cells | Increased insulin availability due to use of secretagogues or exogenous insulin |
| Liver | Suppressed hepatic glucose production due to impaired counter-regulatory response |
| Skeletal muscle | Increased glucose uptake due to exercise |
| α-cells | Suppressed glucagon due to impaired counter-regulatory response |
| Brain | Hypoglycemia unawareness |

Cryer PE. *Am J Physiol.* 1993; 264(2 Pt 1):E149-E155.

# Hypoglycemia: Risk Factors

## Patient Characteristics

- Older age
- Female gender
- African American ethnicity
- Longer duration of diabetes
- Neuropathy
- Renal impairment
- Previous hypoglycemia

## Behavioral and Treatment Factors

- Missed meals
- Elevated A1C

Miller ME, et al. *BMJ*. 2010 Jan 8;340:b5444. doi: 10.1136/bmj.b5444.

# Consequences of Hypoglycemia

- Cognitive, psychological changes (eg, confusion, irritability)
- Accidents
- Falls
- Recurrent hypoglycemia and hypoglycemia unawareness
- Refractory diabetes
- Dementia (elderly)
- CV events
  - Cardiac autonomic neuropathy
  - Cardiac ischemia
  - Angina
  - Fatal arrhythmia

Handelsman YH, et al. *Endocr Pract*. 2015;21(suppl 1):1-87.

# Symptoms of Hypoglycemia

| Classification | Blood Glucose Level (mg/dL) | Typical Signs and Symptoms |
|---|---|---|
| Mild hypoglycemia | ~50-70 | • Neurogenic: palpitations, tremor, hunger, sweating, anxiety, paresthesia |
| Moderate hypoglycemia | ~50-70 | • Neuroglycopenic: behavioral changes, emotional lability, difficulty thinking, confusion |
| Severe hypoglycemia | <50* | • Severe confusion, unconsciousness, seizure, coma, death<br>• Requires help from another individual |
| *Severe hypoglycemia symptoms should be treated regardless of blood glucose level. | | |

Handelsman YH, et al. *Endocr Pract*. 2015;21(suppl 1):1-87.

# Hypoglycemia: Clinical Consequences

## Acute

- Symptoms (sweating, irritability, confusion)
- Accidents
- Falls

## Long-term

- Recurrent hypoglycemia and hypoglycemia unawareness
- Refractory diabetes
- Dementia (elderly)
- CV events
  - Cardiac autonomic neuropathy
  - Cardiac ischemia
  - Fatal arrhythmia
  - Angina

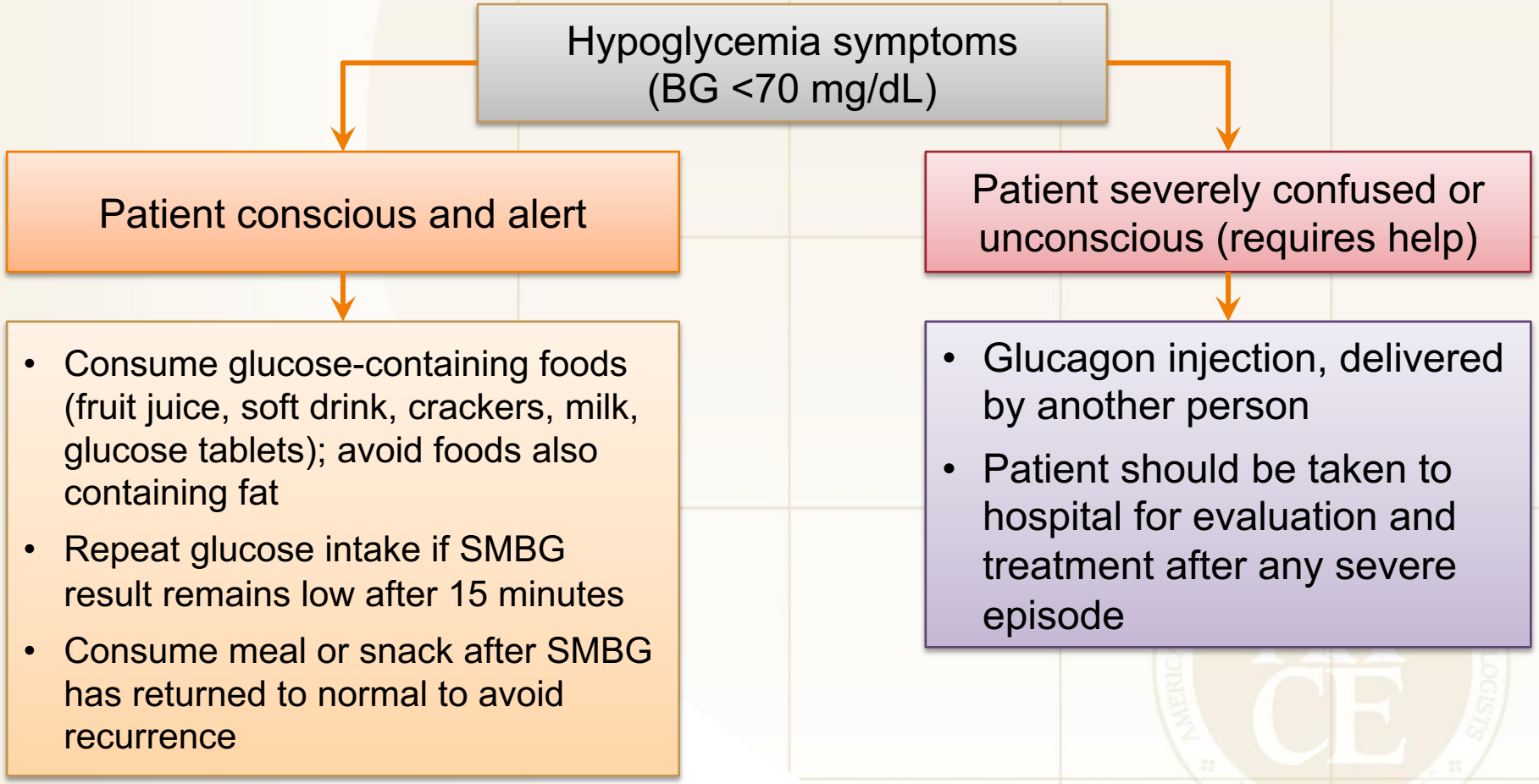
Handelsman YH, et al. *Endocr Pract*. 2015;21(suppl 1):1-87.

# Elements of Hypoglycemia Prevention

| | |
|---|---|
| **Set appropriate glycemic targets for individual patients** | • More stringent goals: young, newly diagnosed, no comorbidities, no micro- or macrovascular disease, strong and effective self-care skills<br>• Less stringent goals: older, limited life expectancy, history of hypoglycemia, longer disease duration, established comorbidities, established vascular disease, limited self-care skills |
| **Educate patients** | • Signs and symptoms of hypoglycemia<br>• Dietary education for improved glycemic control and appreciation of triggers for hypoglycemia<br>• Avoiding missed or delayed meals<br>• Appropriate self-treatment<br>• Understanding of hypoglycemia unawareness<br>• Importance of reporting hypoglycemia |
| **Use self-monitoring of blood glucose** | • Patient education: technique and action<br>• Observation of patient's procedure and reaction<br>• Patient access to providers for purposes of reporting results and for providing guidance<br>• Provider reaction to results increases effectiveness of SMBG |
| **Hold a high index of suspicion for hypoglycemia** | • Understand patients may not report "typical" symptoms<br>• When hypoglycemia is suspected, adjust therapy<br>• Consider use of continuous glucose monitoring to detect unrecognized hypoglycemia |
| **Choose appropriate therapy** | • Use agents with a low risk of hypoglycemia<br>• Be aware of additive effects of combination therapies on hypoglycemia risk<br>• Recognize that long-term costs of hypoglycemia may offset the cost of using older, less physiologic medications |

Moghissi E, et al. *Endocr Pract*. 2013;19:526-535.

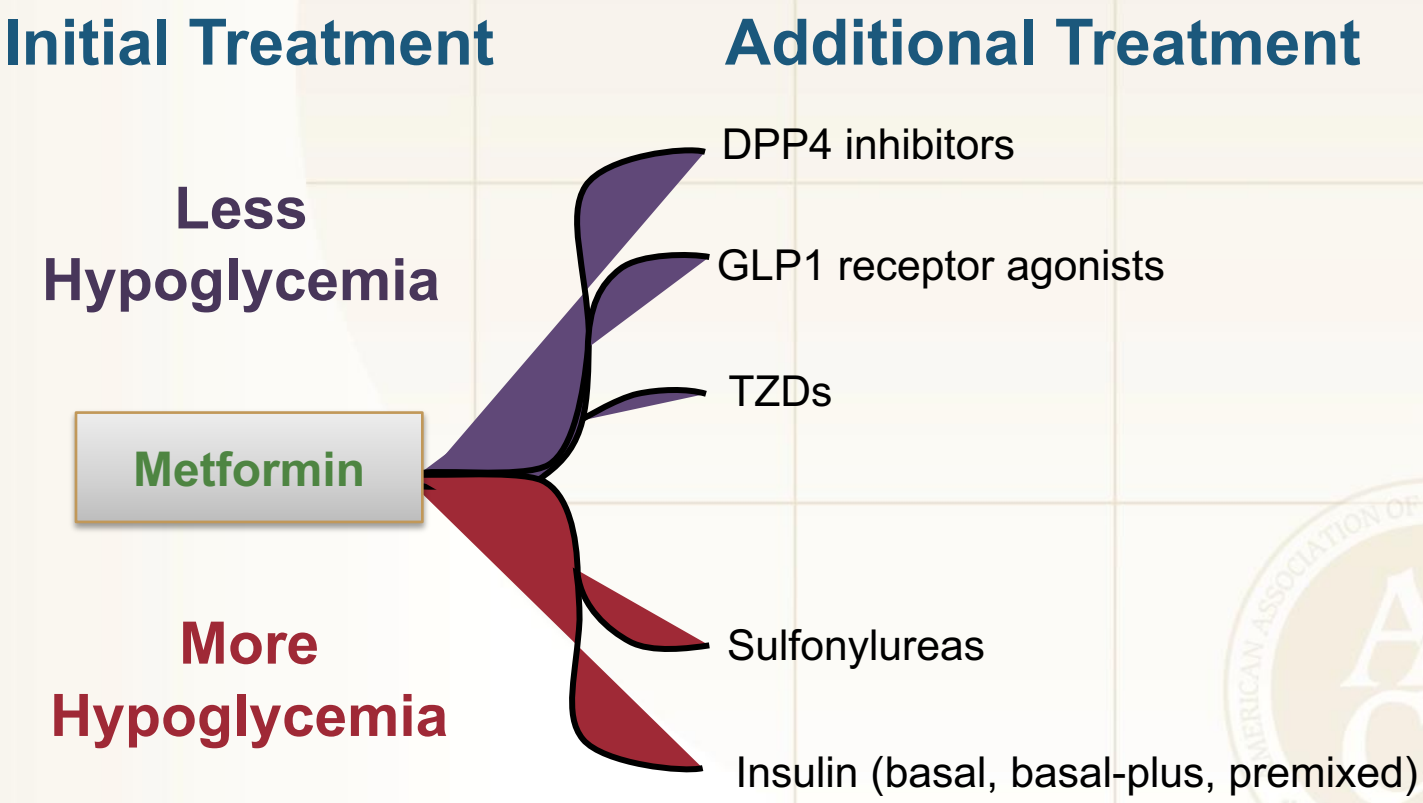
# Treatment of Hypoglycemia




BG = blood glucose; SMBG = self-monitoring of blood glucose.

Handelsman YH, et al. *Endocr Pract*. 2015;21(suppl 1):1-87.

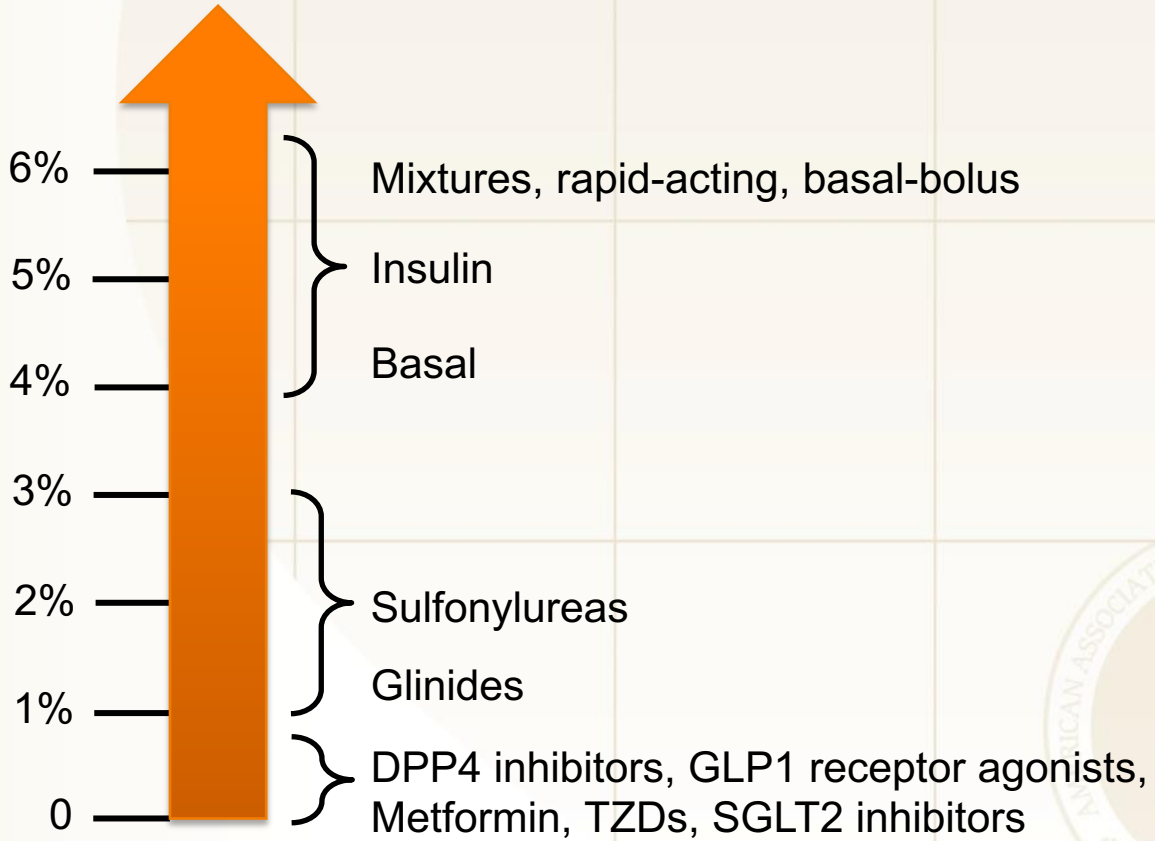
# Hypoglycemia Risk With Antihyperglycemic Agents Added to Metformin




Moghissi E, et al. *Endocr Pract*. 2013;19:526-535.

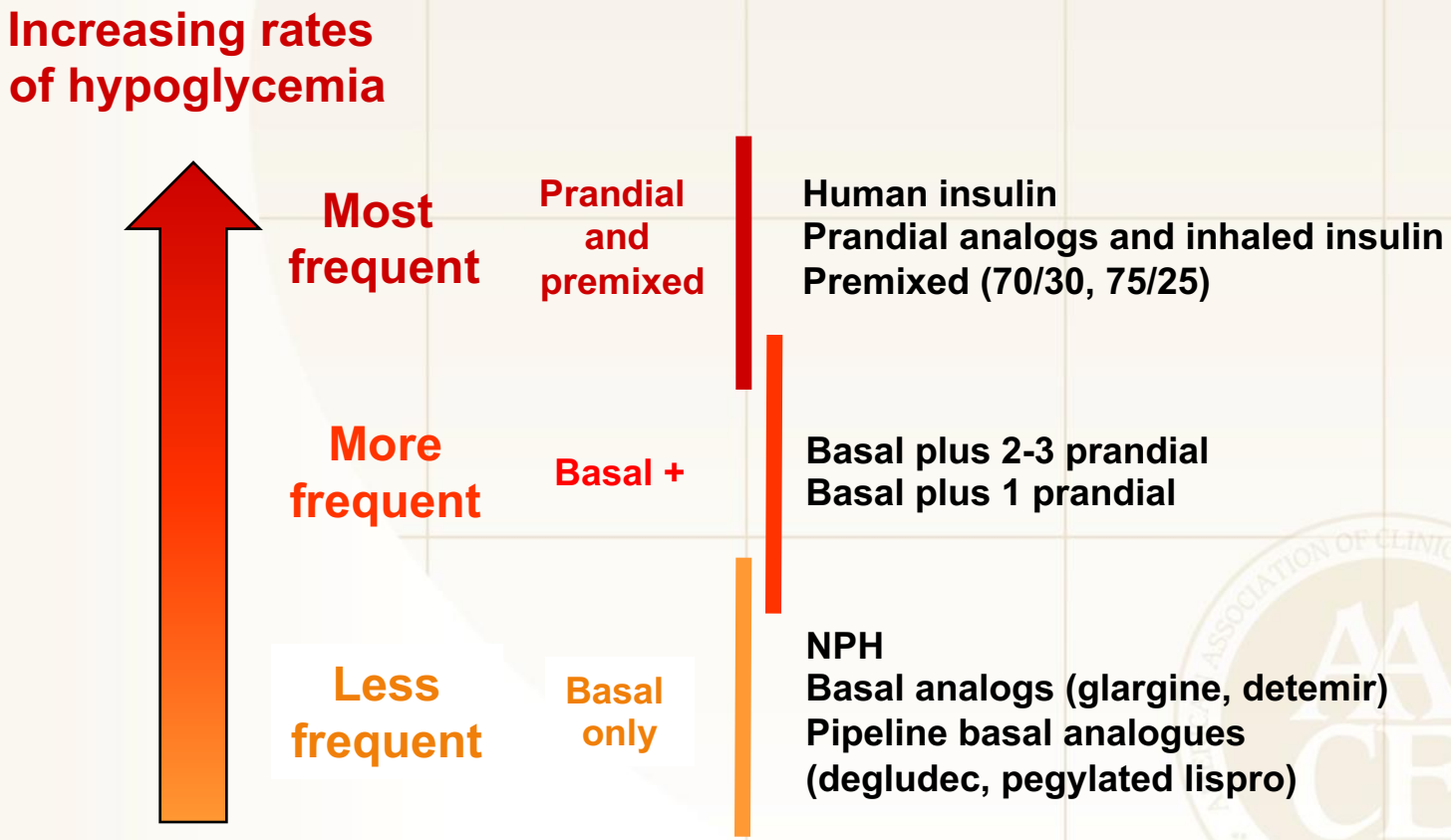
# Frequency of Severe Hypoglycemia With Antihyperglycemic Agents

## Percentage of Patients Treated in 1 Year




Moghissi E, et al. *Endocr Pract*. 2013;19:526-535.

# Relative Rates of Severe Hypoglycemia with Insulin




Moghissi E, et al. *Endocr Pract*. 2013;19:526-535.

Glycemic Management of Type 2 Diabetes

# SAFETY CONCERNS: WEIGHT

# Antidiabetic Agents and Weight

| Class | Agent(s) | Weight Effect |
|---|---|---|
| Amylin analog | Pramlintide | ↓ |
| Biguanide | Metformin | ↓ |
| GLP1 receptor agonists | Albiglutide, dulaglutide, exenatide, exenatide XR, liraglutide | ↓ |
| SGLT-2 inhibitors | Canagliflozin, dapagliflozin, empagliflozin | ↓ |
| α-Glucosidase inhibitors | Acarbose, miglitol | ↔ |
| Bile acid sequestrant | Colesevelam | ↔ |
| DPP4 inhibitors | Alogliptin, linagliptin, saxagliptin, sitagliptin | ↔ |
| Dopamine-2 agonist | Bromocriptine | ↔ |
| Glinides | Nateglinide, repaglinide | ↑ |
| Sulfonylureas | Glimepiride, glipizide, glyburide | ↑ |
| Insulin | Aspart, detemir, glargine, glulisine, lispro, NPH, regular, inhaled | ↑↑ |
| Thiazolidinediones | Pioglitazone, rosiglitazone | ↑↑ |

- Risk of additional weight gain must be balanced against the benefits of the agent
  - Sulfonylureas may negate weight loss benefits of GLP1 receptor agonists or metformin
  - Insulin should not be withheld because of the risk of weight gain

Garber AJ, et al. *Endocr Pract*. 2017;23:207-238.
ADA. *Diabetes Care*. 2017;40:S64-S74.
Handelsman YH, et al. *Endocr Pract*. 2015;21(suppl 1):1-87.

Glycemic Management of Type 2 Diabetes

# SAFETY CONCERNS: CANCER RISK

# Diabetes and Cancer

- Screen obese individuals with DM more frequently and rigorously for certain cancers
  - Endometrial, breast, hepatic, bladder, pancreatic, colorectal cancers
- Increased BMI (≥25 kg/m$^2$) also increases risk of some cancers
  - Strong associations: endometrial, gall bladder, esophageal , renal, thyroid, ovarian, breast, and colorectal cancer
  - Weaker associations: leukemia, malignant and multiple melanoma, pancreatic cancer, non-Hodgkin lymphoma
- To date, no definitive relationship has been established between specific hyperglycemic agents and increased risk of cancer or cancer-related mortality
  - Consider avoiding medications considered disadvantageous to specific cancers in individuals at risk for or with a history of that cancer

Handelsman YH, et al. *Endocr Pract*. 2015;21(suppl 1):1-87.

# Insulin and Cancer Risk

| Study | Hazard Ratio (95% CI) |
|---|---|
| Outcome Reduction With an Initial Glargine Intervention (ORIGIN)<br>N=12,537; prospective RCT<br>Median follow-up: 6.2 years | Any cancer: 1.00 (0.88-1.13); P=0.97<br>Death from cancer: 0.94 (0.77-1.15); P=0.52 |
| Northern European Database Study<br>N=447,821; observational<br>Mean follow-up:<br>Glargine users: 3.1 years<br>Other insulin users: 3.5 years | Breast cancer (women): 1.12 (0.99-1.27)<br>Prostate cancer (men): 1.11 (1.00-1.24)<br>Colorectal cancer (men and women): 0.86 (0.76-0.98) |
| Kaiser-Permanente Collaboration<br>N=115,000; observational<br>Median follow-up:<br>Glargine users: 1.2 years<br>NPH users: 1.4 years | Breast cancer (women): 1.0 (0.9-1.3)<br>Prostate cancer (men): 0.7 (0.6-0.9)<br>Colorectal cancer (men and women): 1.00 (0.8-1.2)<br>All cancers (men and women): 0.9 (0.9-1.0) |
| MedAssurant Database Study<br>N=52,453; observational<br>Mean follow-up:<br>Glargine users: 1.2 years<br>NPH users: 1.1 years | No increased risk for breast cancer |

ORIGIN Trial Investigators. *N Engl J Med*. 2012;367:319-328. Kirkman MS, et al. Presented at the American Diabetes Association 72nd Scientific Sessions. June 11, 2012. Session CT-SY13. Philadelphia, PA.

Glycemic Management of Type 2 Diabetes

# VACCINATIONS

# Vaccinations for Patients with Diabetes

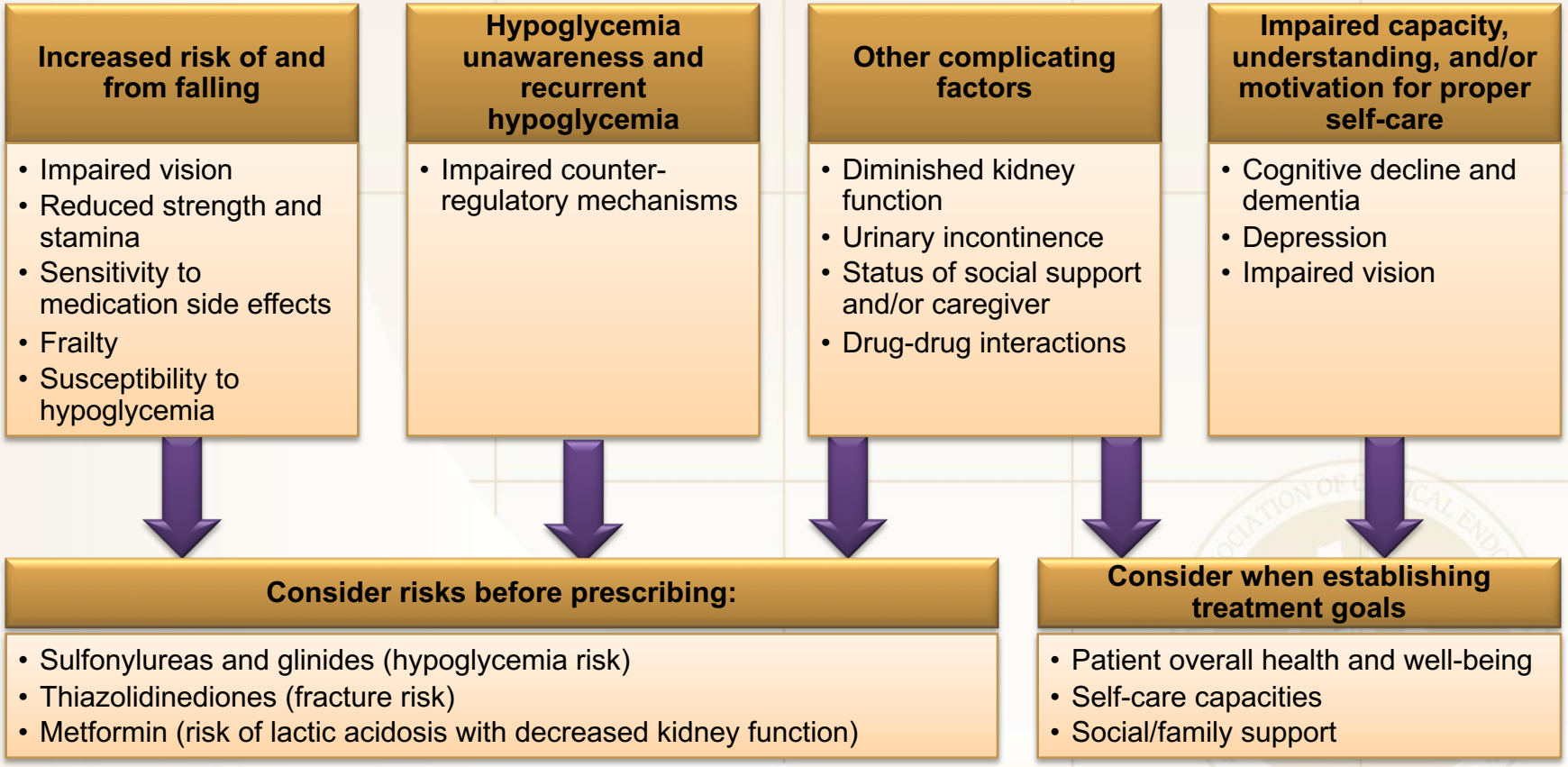
| Vaccine, frequency of administration | Patient age |
|---|---|
| Routine childhood immunizations, according to standard schedule (eg, measles, mumps, rubella, varicella, polio, tetanus-diphtheria) | 6 months to 18 years |
| Influenza, annually | ≥6 months |
| Pneumococcal polysaccharide vaccine | ≥2 years |
| PVC13, 1-2 injections | 2-18 years |
| PPSV23, 1 injection | 19-64 years |
| PVC13 plus PPSV23, 1 injection each, in series | ≥65 years |
| Hepatitis B, 1 injection | 20-59 years* |
| Tetanus-diphtheria booster, every 10 years in adults | ≥19 years |
| Individuals not already immunized for childhood diseases and those requiring vaccines for endemic diseases should be immunized as required by individual patient needs | Any age |
| *Consider for patients ≥60 based on assessment of risk and likelihood of adequate immune response. | |

Handelsman YH, et al. *Endocr Pract*. 2015;21(suppl 1):1-87.

Glycemic Management of Type 2 Diabetes

# SPECIAL SITUATIONS

# Management Considerations for Elderly Patients with Diabetes




Bourdel Marchasson I, et al. *J Nutr Health Aging*. 2009;13:685-691. Handelsman Y, et al. *Endocr Pract*. 2011;17(suppl 2):1-53. Schwartz AV, et al. *Diabetes Care*. 2008;31:391-396. Zammitt NN, Frier BM. *Diabetes Care*. 2005;28:2948-2961.

# Diabetes and Occupational Hazards

- Commercial drivers at high risk for developing T2D
  - Screen as appropriate
  - Encourage healthy lifestyle change
- Be aware of management requirements and use agents with reduced risk of hypoglycemia in patients with occupations that could put others at risk, such as (not inclusive):
  - Commercial drivers
  - Pilots
  - Anesthesiologists
  - Commercial or recreational divers

Handelsman YH, et al. *Endocr Pract*. 2015;21(suppl 1):1-87.

# Risk Considerations for Religious/Cultural Fasting

| Main Risks of Fasting |
|---|
| • Hypoglycemia<br>• Hyperglycemia<br>• Diabetic ketoacidosis<br>• Dehydration and thrombosis |

| Risk Category | Features |
|---|---|
| Low | • Glycemia well-controlled with antihyperglycemic agent that does not cause hypoglycemia (eg, metformin, thiazolidinedione, DPP4 inhibitor, GLP1 receptor agonist)<br>• Otherwise healthy |
| Moderate | • Glycemia well-controlled with glinides |
| High | • Moderate hyperglycemia (A1C 7.5-9.0%), renal insufficiency, cardiovascular complications, and/or other comorbid conditions<br>• Living alone, especially if taking sulfonylureas, insulin, or drugs that affect mentation<br>• Elderly, especially with poor health |
| Very high | • History of recurrent hypoglycemia, hypoglycemia unawareness, or episode of severe hypoglycemia within 3 months prior to Ramadan<br>• Poor glycemic control<br>• Ketoacidosis or hyperosmotic hyperglycemic coma within 3 months prior to Ramadan<br>• Acute illness or chronic dialysis<br>• Intense physical labor<br>• Pregnancy |

Al-Arouj M, et al. *Diabetes Care*. 2005;28:2305-2311.

# Glycemic Management During Religious/Cultural Fasting

- Frequent glucose monitoring—break fast immediately if patient has:
  - Hypoglycemia
    - SMBG <70 mg/dL while taking insulin or sulfonylureas
    - SMBG <60 mg/dL while on other therapies
  - Hyperglycemia: >300 mg/dL
- Healthful eating before and after each fasting period
  - Complex carbohydrates prior to fast
  - Avoid ingesting high-carbohydrate, high-fat foods when breaking fast
- Avoid excessive physical activity but maintain normal exercise routines
- Avoid fasting while ill

Al-Arouj M, et al. *Diabetes Care*. 2005;28:2305-2311.