NEW GUIDELINES FOR THE MANAGEMENT OF DM2

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DISCLOSURES

I have nothing to disclose
OBJECTIVES

• Review 2019 Guidelines in the Management of Type 2 Diabetes in Adults
• 9.4% of US pop had DM 2015 (30million)
• 12% US pop ≥18yo, 25% ≥65yo have DM
• 34% US pop ≥18yo have pre DM, 48% ≥65
• 90% of diabetes is from DM2, 10% DM1

• DM1 – autoimmune destruction of pancreas results in lack of insulin
  • Treatment - basal/bolus insulin via injections or pumps
• DM2 - Decreased insulin sensitivity due to genetics and obesity
  • 80% of DM2 is attributed to obesity
  • Initially increased insulin levels followed by pancreatic failure and low levels
WHAT IS THE BEST TREATMENT FOR DM2?

- DIET, EXERCISE AND WT LOSS
- YOU CAN PREVENT & CURE DM2 WITH DIET, EXERCISE, AND WT LOSS
- 70.2% of the US pop is overwt or obese – obviously we aren’t succeeding at this

Meds:
- GLP1, DPP4, TZD, SU/glinides – require some pancreatic function
- SGLT2 (doesn’t require insulin but if none, increased DKA risk)
- Bromocriptine, colesevelam, alpha glucosidase inhibitors, pramlintide
- Basal or basal/bolus insulin when pancreas fails
EASD/ADA AND AACE GUIDELINES

Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)


American Diabetes Association Standards of Medical Care in Diabetes 2019
Diabetes Care. Jan 2019; Vol. 42, Supplement 1

Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm – 2019 Executive Summary.
ADHERENCE AND INERTIA

• Patient preferences regarding route of administration, injection devices, side effects, cost may prevent their use by some individuals

• Inconsistent use and discontinuation factors
  • patient perceived lack of medication efficacy
  • fear of hypoglycemia
  • lack of access to medication/cost
  • adverse effects of medication

• Multidisciplinary teams that include pharmacists, nurses, diabetic educators, dietitians, and nurse practitioners may help reduce therapeutic inertia
FACTORS FOR CHOOSING MED

• Current HbA1c and goal
• Obesity
• CVD, CHF, CKD
• Risks of hypoglycemia
• Insurance coverage/cost
• Uncontrolled HTN (on diuretic or not)
• Hx of UTIs, genital fungal infections, circumcised or not
Order not meant to denote any specific preference – Choice dependent on a variety of patient-and disease-specific factors.
WHY DID THE GUIDELINES CHANGE?

- Cardiovascular and Renal outcomes trials
- Major Adverse Cardiac Events [MACE] = composite outcome of cardiovascular death, nonfatal MI, and nonfatal stroke
IMPROVED CVD OUTCOMES – SGLT-2

• EMPA-REG OUTCOME 2015: Empagliflozin (Jardiance), (n = 7,020)
  • 14% decrease in MACE
  • 38% decrease CVD death, 13% decrease in MI, no decrease in stroke
  • 12% decrease in all cause mortality
  • (metformin in UKPDS was 15% decrease in MI)

• CANVAS 2017: Canagliflozin (Invokana) (n= 10,142)
  • 14% decrease in MACE HR 0.86,
  • Increased LE amputations - 6.3 vs 3.4 pts/1000 pt-years

• CREDENCE 2019:Canagliflozin, n= 4401,
  • 20% decrease in MACE, no increased amputations

• DECLAR-TIMI 2018– Dapagliflozin (Farxiga)
  • 17,160pts (10,186 without CVD)
  • noninferior MACE
IMPROVED CVD OUTCOMES – GLP1S: LIRAGLUTIDE, SEMAGLUTIDE

• LEADER 2016: Liraglutide (Victoza) (n=9,340)
  • 13% decrease in MACE
  • 22% decrease in CVD death, 14% decrease in MI, 14% decrease in Stroke,
  • 15% decrease in all cause mortality

• SUSTAIN 6 2016: Semaglutide (Ozempic) (n = 3,297)
  • 26% decrease in MACE
  • 39% decrease in stroke, other’s not significant

• REWIND 2018: Dulaglutide (Trulicity) (n = 9901)
  • 69% of pts did NOT have CVD (other trials 80-100% with CVD)
  • 12% decreased MACE, 24% decrease stroke
NOT ALL HAVE CVD BENEFIT

• Not a Glp-1 class effect
  • Exenatide and lixisenatide non-inferior but no CVD benefit

• DPP-4s: No CVD benefit
  • Saxagliptin (Onglyza)
    • Increased risk of CHF hospitalizations
  • Alogliptin (Nesina)
  • Sitagliptin (Januvia)
CHF BENEFIT WITH SGLT2’S

• All SGLT2s had showed decreased CHF hospitalizations
  • Empagliflozin, decreased 35%
  • Canagliflozin, decreased 33-39%
  • Dapagliflozin, decreased 27%

• Now being studied in CHF, WITHOUT DM due to significant improvement

• For GLP-1 studies, there was no significant effect on hospitalization for HF.
Studied composite outcome of new or worsening nephropathy (progression to urine albumin/creatinine ratio 0.3 mg/g, doubling of serum creatinine, ESRD, or death by ESRD)

GLP-1
• Liraglutide, 22% decrease
• Semaglutide, 36% decrease
• Dulaglutide, 15% decrease
• Lixisenatide also had decreased renal outcomes

SGLT2s
• Empagliflozin 39% decrease
• Canagliflozin 40% decrease
• Dapagliflozin 23% decrease

DPP4 studies suggest may decrease albuminuria.
MEDS WITH IMPROVED CVD, HF, CKD OUTCOMES

• Improved CVD outcomes
  • GLP-1: Liraglutide, Semaglutide, Dulaglutide
  • SGLT-2: Empagliflozen, Canagliflozen
  • Metformin

• Improved CHF hospitalizations
  • SGLT-2: Empagliflozen, Canagliflozen, Dapagliflozen

• Improved CKD
  • GLP-1: Liraglutide, Semaglutide, Dulaglutide, Lixisenatide
  • SGLT-2: Empagliflozen, Canagliflozen, Dapagliflozen
GLYCEMIC CONTROL ALGORITHM

INDIVIDUALIZE GOALS

A1C ≤6.5% For patients without concurrent serious illness and at low hypoglycemic risk

A1C >6.5% For patients with concurrent serious illness and at risk for hypoglycemia

LIFESTYLE THERAPY (Including Medically Assisted Weight Loss)

Entry A1C <7.5%

Entry A1C ≥7.5%

Entry A1C >9.0%

MONOTHERAPY¹

- Metformin
- GLP1-RA²,³
- SGLT2i²,³
- DPP4i
- TZD
- AGI
- SU/GLN

If not at goal in 3 months proceed to Dual Therapy

DUAL THERAPY¹

- GLP1-RA²,³
- SGLT2i²,³
- DPP4i
- TZD
- Basal Insulin
- Colesvelam
- Bromocriptine QR
- AGI
- SU/GLN

If not at goal in 3 months proceed to Triple Therapy

TRIPLE THERAPY¹

- GLP1-RA²,³
- SGLT2i²,³
- TZD
- Basal Insulin
- DPP4i
- Colesvelam
- Bromocriptine QR
- AGI
- SU/GLN

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

SYMPTOMS

NO

DUAL Therapy

OR

TRIPLE Therapy

YES

INSULIN ± Other Agents

ADD OR INTENSIFY INSULIN

Refer to Insulin Algorithm

LEGEND

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

PROGRESSION OF DISEASE

2019 AACE Guidelines
• Felt benefit is in pts with established CVD because guidelines published prior to REWIND showing primary prevention data.
• Their recommendations were for pts with CVD risk, if not on SGLT2 or GLP-1, add one, and if Hba1c <7% need to adjust other meds or d/c and add SGLT2/GLP-1 with improved CVD outcomes to improve CVD risk
• Statements may change with release of REWIND data for use of GLP-1 for non-CVD pts.
DIFFERENCES

• AACE target ≤6.5, ADA <7 but both modify based on individual
• AACE differentiates meds based on how high Hba1c is not comorbidities. Cardiac and renal benefits then noted by footnotes and through length of “green line”. Hypoglycemia and wt gain are discussed in text and noted with caution sign.
• AACE says start 2 or 3 meds at once ADA/EASD give sequentially to avoid SE
• AACE stops at 3 meds and moves on to insulin whereas EASD says can add 4, but assumes efficacy of 3rd and 4th meds will be generally less than expected and adds side effects.
DIFFERENCES

• ADA/EASD doesn’t have pramlintide, bromocriptine, acarbose, colesevelam, or glyminides on their algorithm but do acknowledge possible use in limited populations due to minimal efficacy, side effects, and cost.

• ADA/EASD gives order of meds for best wt loss and least hypoglycemia.

• ADA/EASD advocates combo meds for better compliance

• EASD/ADA does not recommend premixed insulin, AACDE notes that premixed insulin may help compliance in selected pts
• All reduce weight and blood pressure and do not increase hypoglycemia risk
• Cardiac and renal benefits have been demonstrated down to a GFR of 30 mL/min/1.73m² but none approved for use for GFR below 45
• Dehydration may lead to renal impairment, hypotension, syncope, and falls
• Increased risk of mycotic genital infections and UTI
• Increased bone fractures with canagliflozin and dapagliflozin
EUGLYCEMIC DKA AND SGLT2

• DM2, the incidence was 0.16 to 0.76 events per 1,000 patient-years
• AACE recommended stopping SGLT2 inhibitors 24 hours prior to scheduled surgeries and anticipated metabolically stressful activities (e.g., extreme sports) and if taking SGLT2 inhibitors with insulin should avoid very low carbohydrate meal plans and excess alcohol intake
GLP-1 RISKS

• All reduce weight and no increase the risk for hypoglycemia
• DO NOT substantially increase risk for pancreatitis, pancreatic cancer, or bone disease (meta-analysis of 9347 GLP-1 and 9353 placebo DM patients)
• Increased risk of gallbladder events, nausea, vomiting
• Semaglutide had increased retinopathy in SUSTAIN 6 (HR1.76), mainly in pts with baseline retinopathy with rapid improvement of glycemic control. Also a recognized effect of rapid glycemic control with insulin.
• Contraindicated in Medullary Thyroid CA, MEN2, or Family Hx
• GLP1 contraindicated in stages 4 and 5 CKD (GFR <30 mL/min), gastroparesis
If CVD, GLP1 or SGLT2 then add the other.

If CKD or CHF, SGLT2 first then add the other.
METHOD TO THE MADNESS

Always start with Metformin then add:
• If CVD alone without HF or CKD - Semaglutide HR .74, Empagliflozin .86, Canagliflozin .86(80), Liraglutide .87, Dulaglutide .88
• If CVD with HF give Empagliflozin .65 or Canagliflozin .67 (.61)
• If need third med in CVD, give Empagliflozin or Canagliflozin with Liraglutide/Semaglutide/Dulaglutide
• If just CKD without CVD then Canagliflozin .60 (.70), Empagliflozin .61, Semaglutide .64, Liraglutide .78, Dulaglutide .85. (give 1 or both classes)
Don’t give a sulfa or insulin. Give metformin, GLP-1, (DPP4), SGLT2, and TZD. (Can use acarbose, bromocriptine, colesevelam)
"I think diabetes is affecting my eyesight. I have trouble seeing the consequences of poor food choices."
For wt loss use: Metformin, GLP1, SGLT2.

Avoid sulfa, TZD, insulin

*15kg wt loss if <6yrs duration DM can resolve DM

Best wt loss: semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
Only cheap meds are metformin Sulfas, and TZD for orals then NPH and Regular.
• Pioneer Trials 1-10: Oral Semaglutide (Rybelsus)
• FDA approved 9/20/19, adults, not first line
• 3mg titration dose, then 7 and 14mg po daily, decreased Hba1c 0.9 and 1.1%
• Wt decreased 0.9 and 2.3 kg
• More efficacious than empagliflozin at 14mg dose 1.3 vs 0.9% Hba1c lowering
• Given with basal insulin, can decrease insulin dose and have wt reduction 2.4-3.7kg
• Noninferior CVD safety – stopped before reached superiority
ORAL SEMAGLUTIDE

• Side effects nausea, abd pain, diarrhea, vomiting, constipation
• Same medullary thyroid cancer black box

• 3mg x 30 days, then 7mg x 30 days, then 14 mg if needed.
• Take fasting with no more than 4 oz water and wait 30 min before eat/meds.

• Don’t break tabs and don’t give two of the 7mg to =14mg
• Semaglutide sc (Ozempic) 0.5mg = Semaglutide oral (Rybelsus) 14mg
Intensifying to injectable therapies

Start insulin if HbA1c >11%. Suggest basal followed by bolus at the largest meal. AACE >9% for insulin
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

INTENSIFY (Prandial Control)

Add GLP1-RA
- Or SGLT2i
- Or DPP4i

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

Glycemic Control Not at Goal*

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%
HYPOGLYCEMIA AND INSULIN

- Degludec and Glargine U300 have lower risk of severe hypoglycemia compared with Glargine U100
- Basal insulin analogs have less hypoglycemia than NPH, particularly nocturnal hypoglycemia
- No insulin has been shown to reduce risk for CVD, but glargine U100 and degludec do not increase risk for MACE
A meta-analysis showed that the Mediterranean diet reduced HbA1c more than Low-carbohydrate, low glycemic index, and high-protein diets, and the DASH diet.
• Calories in – calories burned = weight gained or lost
• Each pound = 3500 calories
• To lose ½ lb/wk, decrease 250 cals/day, for 1 lb/wk, decrease 500 cals/day
• You MUST count calories!
“Resistance training is just as important as cardio. Train yourself to resist chocolate, pastries, fried foods, beer, pizza....”
Pumps and CGMs
CGMS

4 injections/day or pump
4 finger sticks/day
Must say this in clinic note
Daily Log
September 7, 2019 - September 20, 2019 (14 Days)

THU Sep 12
Glucose mg/dL

FRI Sep 13
Glucose mg/dL

SAT Sep 14
Glucose mg/dL

SUN Sep 15

Report Settings
THANK YOU!

Questions?

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