Welcome to UVM ECHO: Treatment of Diabetes Mellitus Type II

Facilitators: Mark Pasanen MD, Liz Cote

September 10, 2020

“Introduction” to ZOOM

- Please mute microphone when not speaking
- Please use camera as much as possible
- Test both audio & video before joining
- Communicate clearly during clinic:
  - Can use “raise hand” feature to comment
  - Speak clearly
  - Use chat function for technical issues

CME disclosures

University of Vermont Office of Continuing Medical and Interprofessional Education is approved as a provider of Continuing Medical Education (CME) by the ACCME. UVMCMIE designates this educational activity for a maximum of 1.0 Category 1 Credits towards the AMA Physicians Recognition Award.

Interest Disclosures:

- As an organization accredited by the ACCME to sponsor continuing medical education activities, UVMCMIE is required to disclose any real or apparent conflicts of interest (COI) that any speakers may have related to the content of their presentations.

Disclosures: None or will be resolved

Planners:

- Elizabeth Cote
- Mark Pasanen, MD
- Charles MacLean, MD

Faculty/Guest Faculty:

- Shreya Amin, MD
- Kaitlyn Barrett, DO
- Matthew Gilbert, DO
- Jack Leahy, MD
- Muriel Nathan, MD
- Mark Pasanen, MD
- Joel Schnure, MD
- Amy Shah, DO
- Kelsey Sheahan, MD

ECHO Series
Overview of Diabetes Care:
Metformin, Sulfonylureas and CGMs

Amy Shah, DO, MPH

September 10, 2020

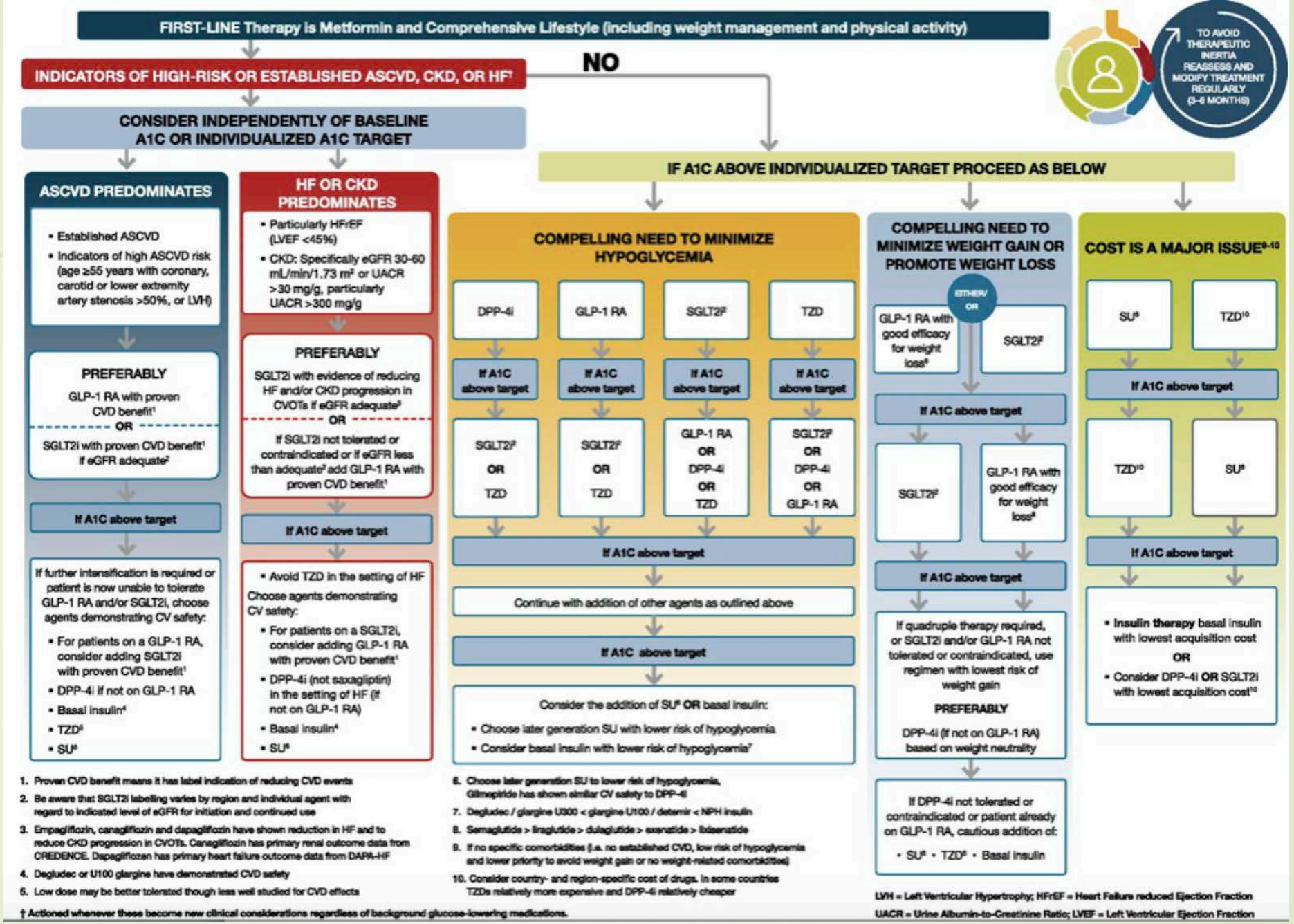
METFORMIN, SULFONYLUREAS, CGMs

Amy Shah, DO, MPH, Endocrinology Fellow

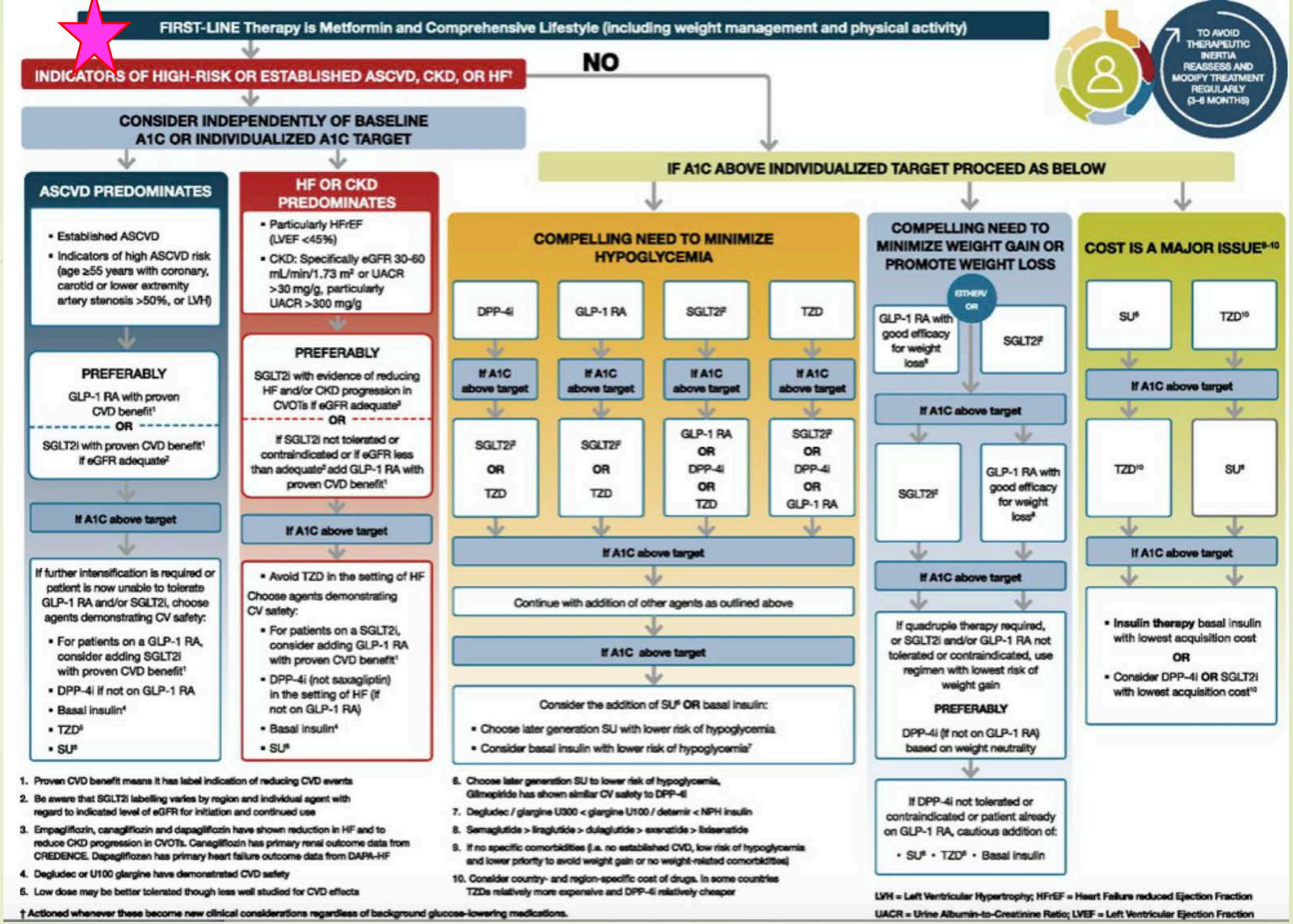
OBJECTIVES

- Metformin
  - MOA
  - Benefits
  - Cautions
- Sulfonylureas
  - MOA
  - Benefits
  - Cautions
- Continuous Glucose Monitors
  - What are they?
  - Who would benefit?
  - Insurance Coverage

METFORMIN

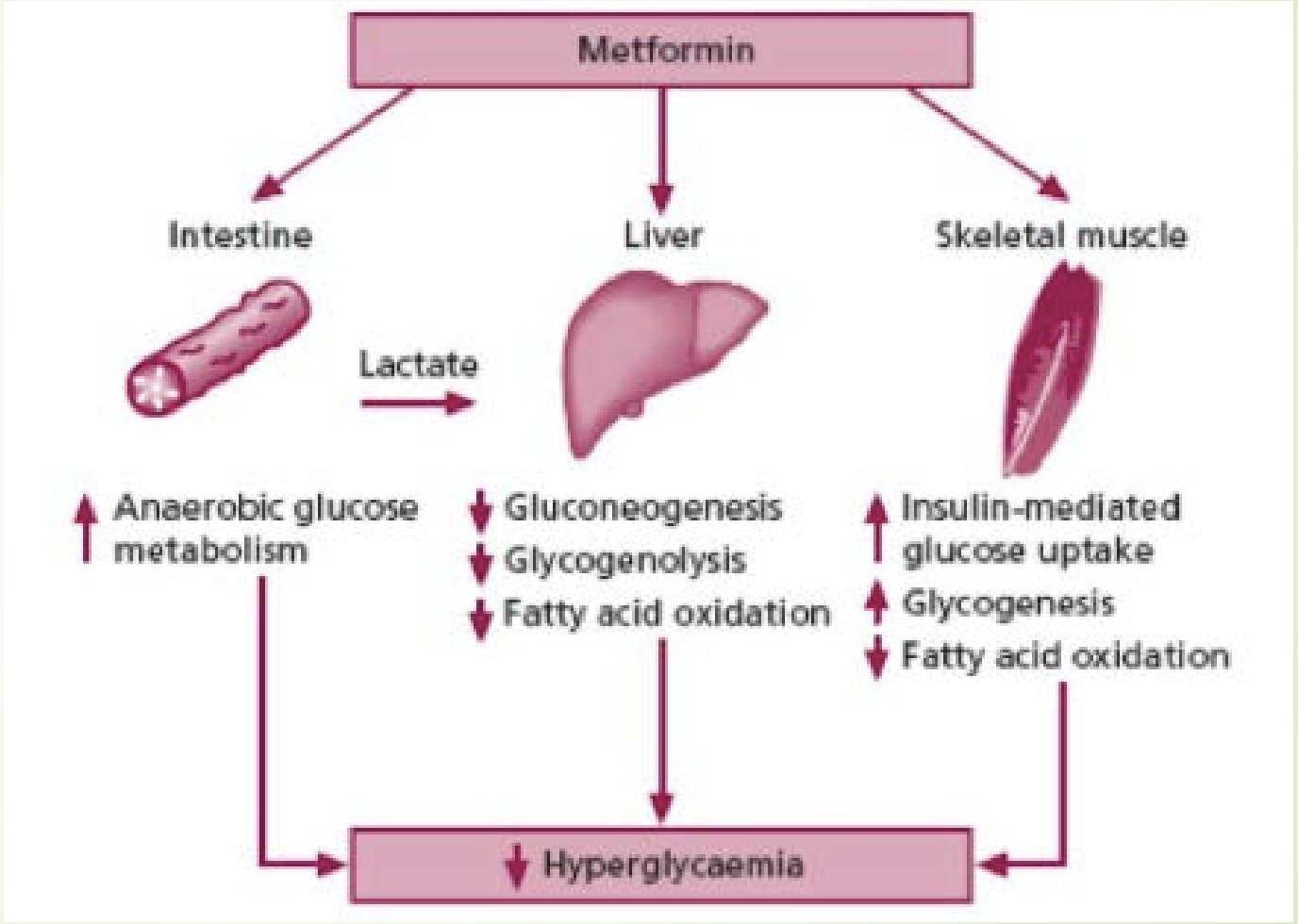


American Diabetes Association. Diabetes Care 2020 Jan; 43(Supplement 1): S98-S110



American Diabetes Association. Diabetes Care 2020 Jan; 43(Supplement 1): S98-S110

MOA


Metformin
Intestine
Liver
Skeletal muscle
Lactate
Anaerobic glucose metabolism
Gluconeogenesis
Glycogenolysis
Fatty acid oxidation
Insulin-mediated glucose uptake
Glycogenesis
Fatty acid oxidation
Hyperglycaemia

METFORMIN

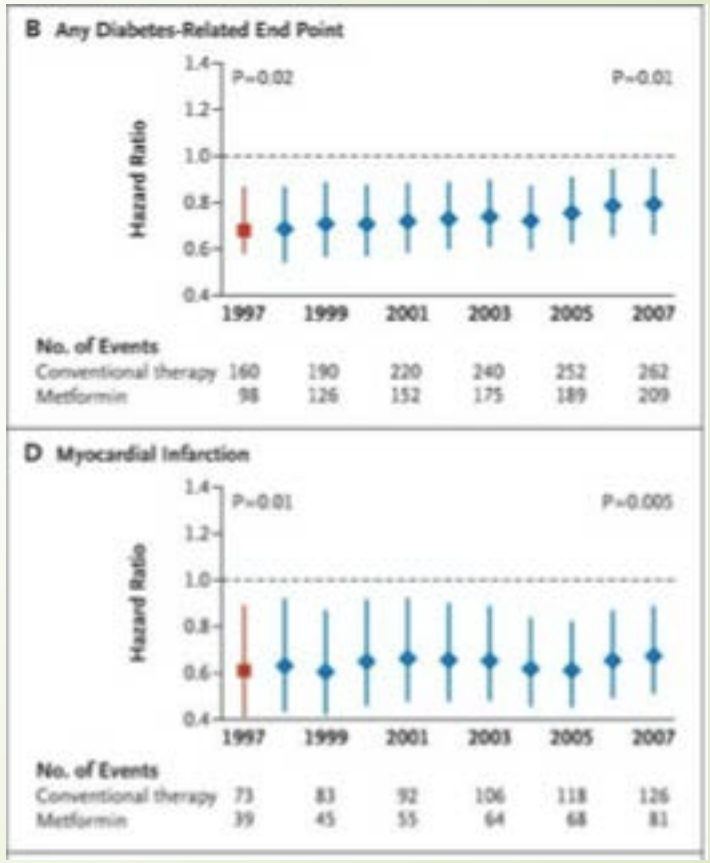
- Extended release vs immediate release
- Max therapeutic dose = 2000mg/day
- Decrease A1c by ~1.5%
- Side Effects
  - GI upset = abdominal bloating, abdominal pain, diarrhea
  - Lactic acidosis (rare)
- Renal Dosing
  - GFR 30-45 = max dose of 1000mg/day
  - GFR <30 = contraindicated
- Take with meals to minimize GI upset

Benefits

- Generally safe and well tolerated
- Effective (up to 1.5% reduction in A1c)
- Can reduce risk of cardiovascular death and events
- Cheap
- Weight neutral

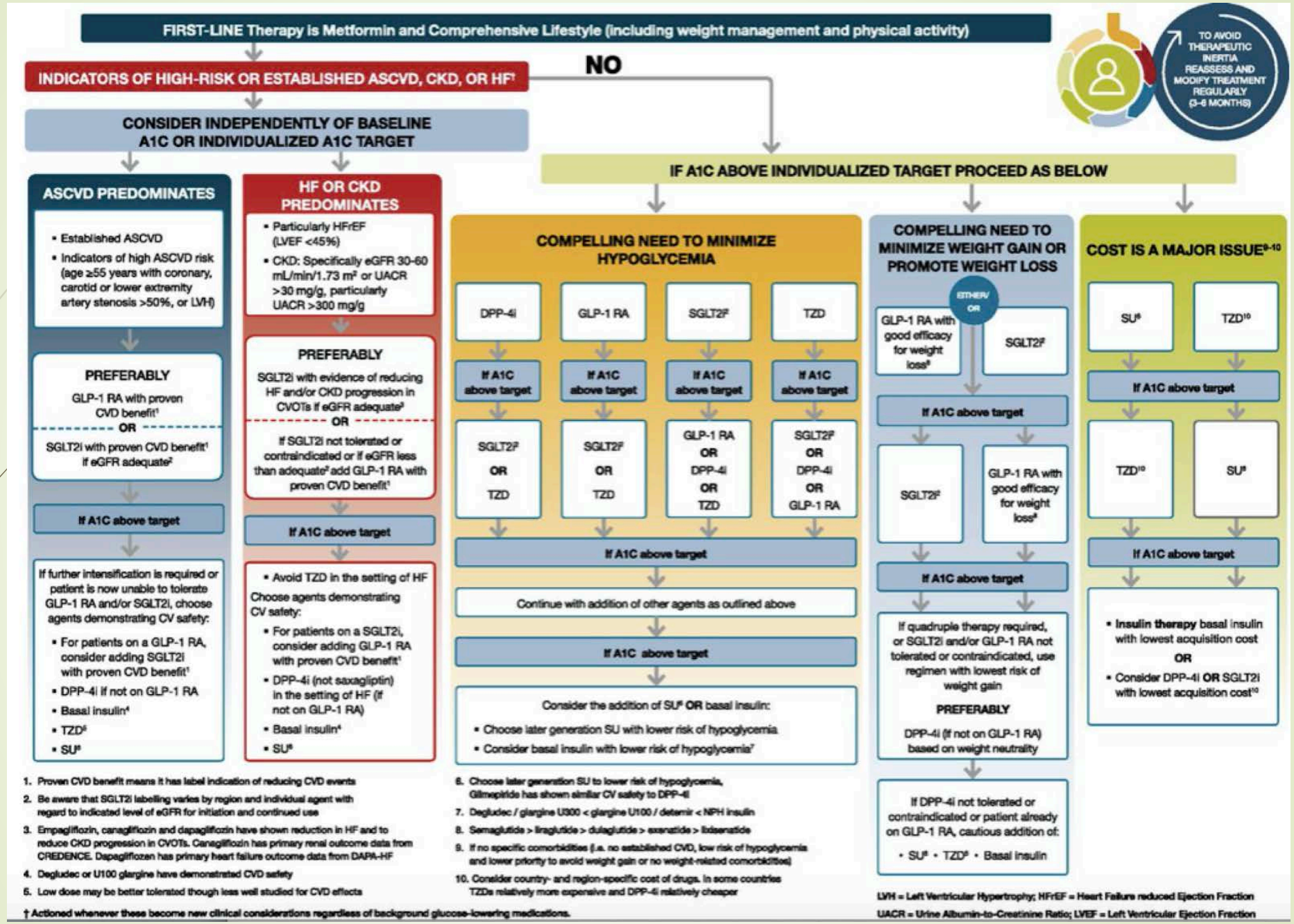
UK Prospective Diabetes Study (UKPDS)

- 10 year follow up of intensive glucose control in Type 2 Diabetes
- Evaluated patients from UKPDS who had been assigned to either conventional therapy (diet and exercise), metformin, or Insulin/sulfonylurea combo
- Post-trial monitoring to see whether glycemic control had persisted and whether there were long-term effects on macrovascular outcomes.

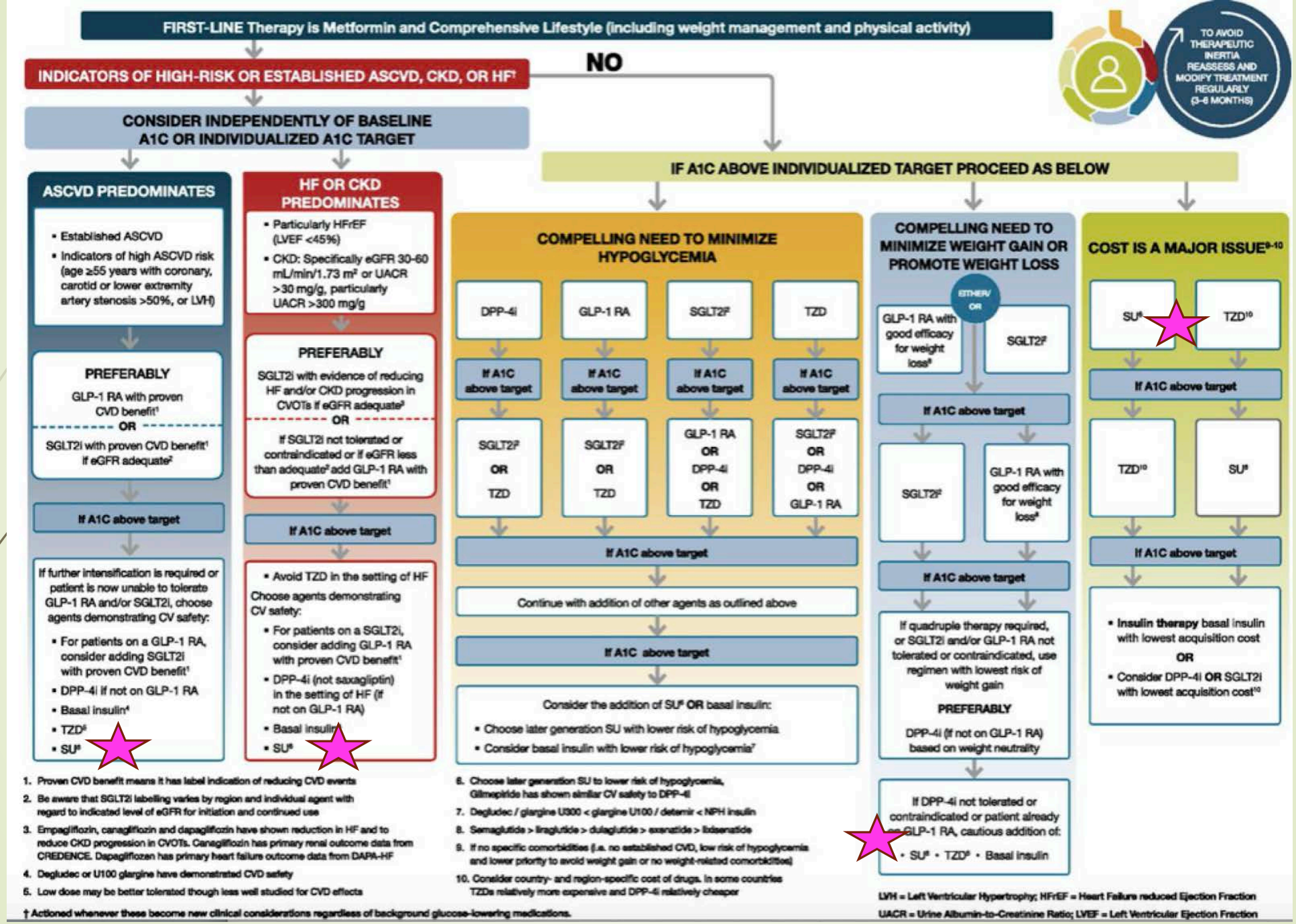


UKPDS. Br J Clin Pharmacol. 1990. Nov; 48(5): 643-648.

SULFONYLUREAS



American Diabetes Association. Diabetes Care 2020 Jan; 43(Supplement 1): S98-S110



1. Proven CVD benefit means it has label indication of reducing CVD events
2. Be aware that SGLT2i labelling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use
3. Empagliflozin, canagliflozin and dapagliflozin have shown reduction in HF and to reduce CKD progression in CVOTs. Canagliflozin has primary renal outcome data from CREDENCE. Dapagliflozen has primary heart failure outcome data from DAPA-HF
4. Degludec or U100 glargine have demonstrated CVD safety
5. Low dose may be better tolerated though less well studied for CVD effects
6. Choose later generation SU to lower risk of hypoglycemia, Glimepiride has shown similar CV safety to DPP-4i
7. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin
8. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
9. If no specific comorbidities (i.e. no established CVD, low risk of hypoglycemia and lower priority to avoid weight gain or no weight-related comorbidities)
10. Consider country- and region-specific cost of drugs. In some countries TZDs relatively more expensive and DPP-4i relatively cheaper

† Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.

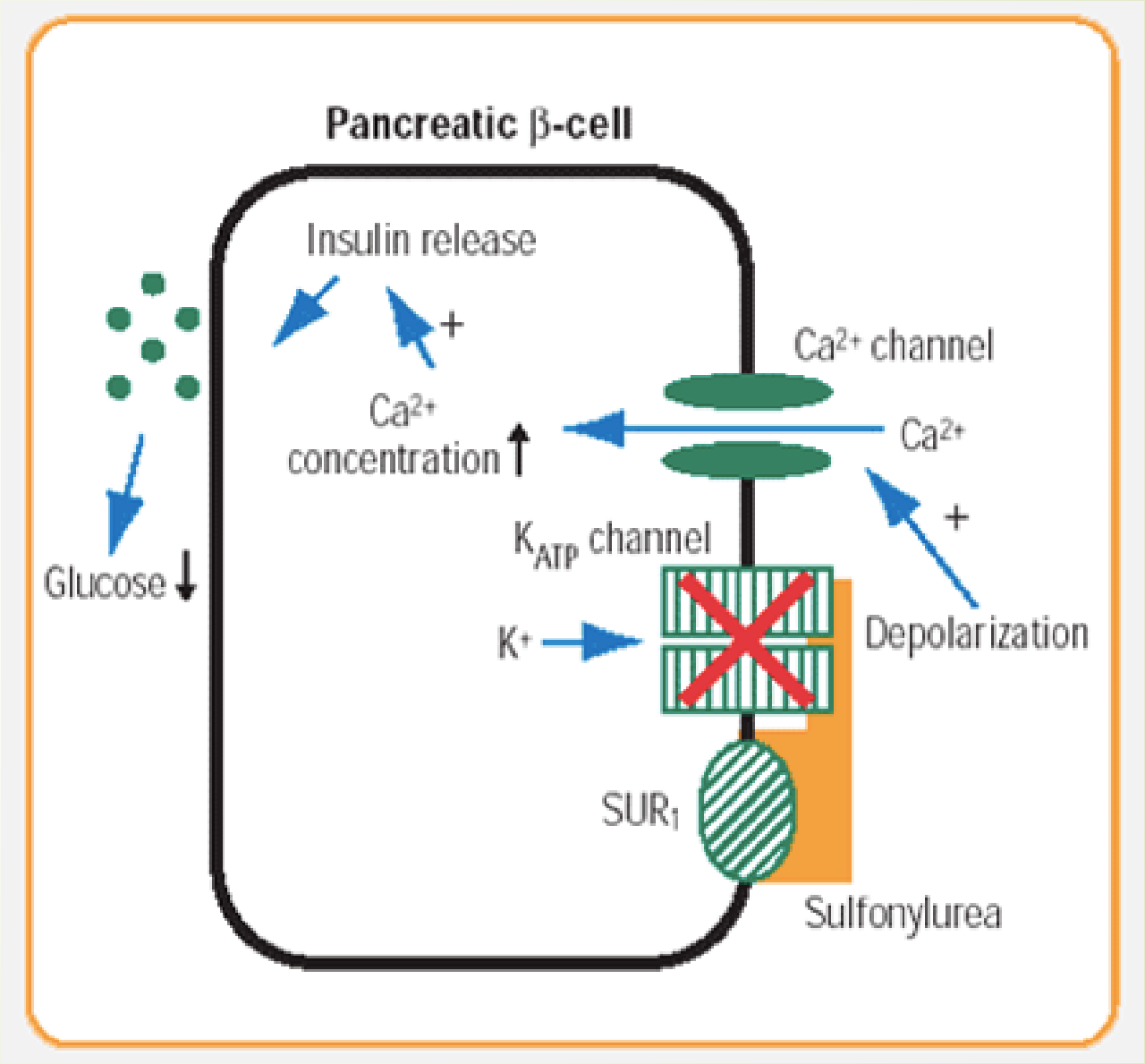
LVH = Left Ventricular Hypertrophy; HFrEF = Heart Failure reduced Ejection Fraction
UACR = Urine Albumin-to-Creatinine Ratio; LVEF = Left Ventricular Ejection Fraction

American Diabetes Association. Diabetes Care 2020 Jan; 43(Supplement 1): S98-S110

SULFONYLUREAS

- Glipizide
- Glimepiride
- Glyburide
- Chlorpropamide
- Glibenclamide

MOA


Pancreatic β-cell
Insulin release
+
Ca2+ channel
Ca2+
concentration
Ca2+
KATP channel
+
Glucose
K+
Depolarization
SUR1
Sulfonylurea

When to use?

- Cost
- Intolerant of other medicines
- A1c reduction ~1.5%
- Use in CKD
  - Should avoid but if needed, preferable to use short acting glipizide or glimepiride vs glyburide (higher risk of hypoglycemia)

RISKS/SIDE EFFECTS

- Hypoglycemia is the major risk in using SU.
- Later generation SU, such as glimepiride, has lower risk of hypoglycemia
- Higher risk of hypoglycemia in patients on insulin or the elderly
- Weight gain

Diabetes Medications as Monotherapy or Metformin-Based Combination Therapy for Type 2 Diabetes

A Systematic Review and Meta-analysis

- 179 trials and 25 observational studies were identified of head-to-head monotherapy or metformin-based combinations (studied all classes of oral antihyperglycemics and GLP1-RA)
- Cardiovascular mortality was lower for metformin vs sulfonylurea
- A1c reduction was about the same between both groups
- Patients on metformin had reduced or maintenance of body weight while patients on sulfonylureas gained weight
- Hypoglycemia was seen more frequently with sulfonylurea
- GI adverse effects, however, seen more frequently with metformin

CONTINOUS GLUCOSE MONITORS (CGM)

What is continuous glucose monitoring?

- Continuous glucose monitoring is a sensor with a catheter that is inserted just underneath the skin that measures the interstitial blood glucose levels continuously

Real-time CGM	CGM systems that measure glucose levels continuously and provide the user automated alarms and alerts at specific glucose levels and/or for changing glucose levels.
Intermittently scanned CGM	CGM systems that measure glucose levels continuously but only display glucose values when swiped by a reader or a smart phone that reveals the glucose levels.
Blinded (professional) CGM	CGM devices that measure glucose levels that are not displayed to the patient in real time. These devices are generally initiated in a clinic, using a reader that is owned by the clinic. They are removed after a period of time (generally 10–14 days) and analyzed by the patient and provider to assess glycemic patterns and trends.
Unblinded CGM	CGM devices that measure glucose levels that are displayed to the patient.

American Diabetes Association. Diabetes Care 2020 Jan; 43(Supplement 1): S77-S88

Who should be on a CGM?

- Children/adolescents and Type 1 diabetics should be considered for CGM
- Type 2 diabetics on MDI with difficulty achieving optimal glycemic control or having frequent hypoglycemia
- Data does support use of CGM in Type 1 diabetics, both on MDI and on insulin pump for optimal A1c reduction
  - **DIAMOND Study Group**: 158 Type 1 diabetic adults who were using MDI and had A1c between 7.5-9.9%. Assigned 2:1 CGM vs routine care. At 24 weeks, the adjusted treatment-group difference in mean change of A1c level from baseline was -0.6%. (Beck et. al., 2017)
  - **The Gold Randomized Clinical Trial**: 161 Type 1 diabetics on MDI with A1c at least 7.5%. Assigned to CGM vs routine care. At 26 weeks, adjusted treatment group difference in mean reduction of A1c from baseline was -0.4% (Lind et. Al., 2017)

A1c Reduction in T2DM

- The Multiple Daily Injections and Continuous Glucose Monitoring in Diabetes (DIAMOND) study randomized 158 adults with T2DM to CGM vs routine care. Followed for 24 weeks with A1c check between 7.5-9.9%. Showed a statistically significant reduction in A1c by -0.3% at the end of 24 weeks. (Beck et. al., 2017)

DEXCOM

- Switch sensor every 10 days
- Alarms for low and high blood sugar
- Do not have to swipe over the sensor for blood sugar reading
- Continually records BG every 5 minutes
- Can communicate with Tandem insulin pump

FREESTYLE LIBRE

- Switch sensor every 10 days or every 14 days
- Do have to swipe over the sensor for a BG reading
- Will stop recording BG every 5 minutes if patient has not swiped over sensor in 8 hours
- No alarms for low BG or high BG
- Freestyle Libre 2
  - Now has optional alarms to set for high and low

DEXCOM

- Must prescribe to a Walgreens
- Or diabetes medical supplier

Medicare Coverage Criteria

Medicare patients with type 1 and type 2 diabetes on intensive insulin therapy may be able to obtain reimbursement if the following Medicare coverage criteria are met:

- The patient has diabetes;
- The patient has been using a home blood glucose monitor (BGM) and performing frequent (four or more times a day) BGM testing;
- The patient is insulin-treated with three or more daily injections (MDI) of insulin or a continuous subcutaneous insulin infusion (CSII) pump;
- The patient's insulin treatment regimen requires frequent adjustments based on therapeutic CGM testing results;
- Within six months prior to ordering the CGM, the patient had an in-person visit with the treating practitioner to evaluate their diabetes control and determine that the above criteria have been met; and Every six months following the initial prescription of the CGM, the patient has an in-person visit with the treating practitioner to assess adherence to their CGM regimen and diabetes treatment plan.

In order to qualify for Medicare coverage of your Dexcom G6 supplies, Medicare requires that you have a receiver that is compatible with Dexcom G6 and that you use that receiver with your supplies, even if you also use a compatible smart device.* Medicare does not cover Dexcom G6 supplies that are only used with a smartphone or other mobile device.

FREESTYLE LIBRE

Medicare Coverage Criteria[1]

Check the criteria for coverage:

Therapeutic CGMs and related supplies are covered by Medicare when all the following coverage criteria are met:

- The beneficiary has diabetes mellitus; and
- The beneficiary has been using a blood glucose monitor (BGM) and performing frequent (4 or more times a day) testing; and
- The beneficiary is insulin-treated with multiple (3 or more) daily injections of insulin or a Medicare covered continuous subcutaneous insulin infusion (CSII) pump; and
- The beneficiary's insulin treatment regimen requires frequent adjustment by the beneficiary on the basis of BGM or CGM testing results; and
- Within six (6) months prior to ordering the CGM, the treating practitioner has an in-person visit with the beneficiary to evaluate their diabetes control and determined that criteria (1-4) above are met; and
- Every six (6) months following the initial prescription of the CGM, the treating practitioner has an in-person visit with the beneficiary to assess adherence to their CGM regimen and diabetes treatment plan.

QUESTIONS?

2020/2021 PROGRAM SCHEDULE

DATES (All Thursdays, 12pm to 1pm)	SESSION	DIDACTIC TOPICS (in addition to case review)
August 13	TeleECHO Session #1	• Project ECHO Orientation • Anatomy of an ECHO session • Newly diagnosed DM2 • Types of diabetes
August 27	TeleECHO Session #2	• Overview of Diabetic Care • ADA guidelines

September 10	TeleECHO Session #3	• Approach to glycemic control
		  • Sulfonylureas, metformin
		  • Continuous Glucose Monitors (CGM)

September 24	TeleECHO Session #4	• GLP1 agonists/DPP4 inhibitors
October 8	TeleECHO Session #5	• SGLT 2 inhibitors
October 22	TeleECHO Session #6	• Insulin 101
November 12	TeleECHO Session #7	• Advanced insulin
December 10	TeleECHO Session #8	• ASCVD prevention: • Lipids, HTN, ASA

January 14	TeleECHO Session #9	• Complications:
		  • Screening
		  • Prevention

January 28	TeleECHO Session #10	• Special Populations:
		  • Elderly, pregnancy
		  • Adherence

ECHO Reminders

- Volunteers to present cases
  - Use the case presentation form template
- Please complete evaluation forms for each session
  - CME will be processed once session evaluation form is received at UVM
- UVM Project ECHO materials available at www.vtahec.org
- Please contact us with any questions/suggestions
  - Mark.Pasanen@uvmhealth.org
  - Elizabeth.Cote@uvm.edu
  - ahec@uvm.edu