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Type 2 Meds Management Update

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2020

Type 2 Meds Management Update. Objectives

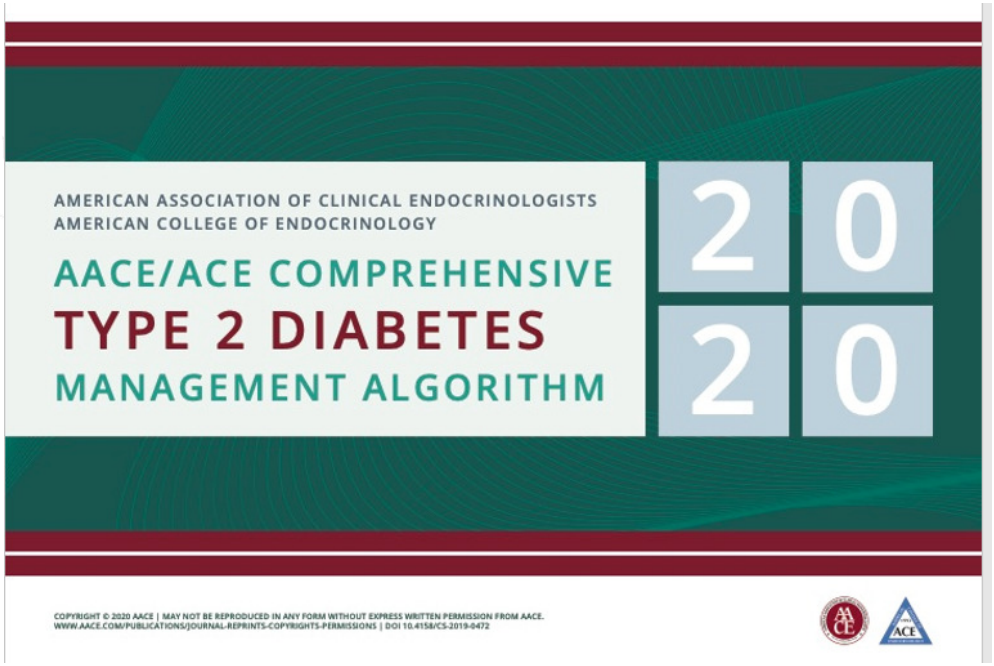
1. Describe the role of Diabetes Care and Education Specialist in Stopping Clinical Inertia
2. Discuss using the latest ADA and AACE Guidelines to determine best therapeutic approach.
3. Using the ADA and AACE Guidelines, describe strategies to initiate and adjust insulin therapy.

Resources for This Presentation

Position Statements

9. Pharmacologic Approaches to Glycemic Treatment: *Standards of Medical Care in Diabetes—2020*

American Diabetes Association
Diabetes Care 2020 Jan; 43(Supplement 1): S98-S110.
https://doi.org/10.2337/dc20-S009



Coach Bev has no conflict of interest

- Not on any speaker's bureau
- Does not invest in pharmaceutical or device companies
- Gathers information from reading package inserts, research and standards
- She does engage in “pill-ow” talk with her husband (who is a PharmD)

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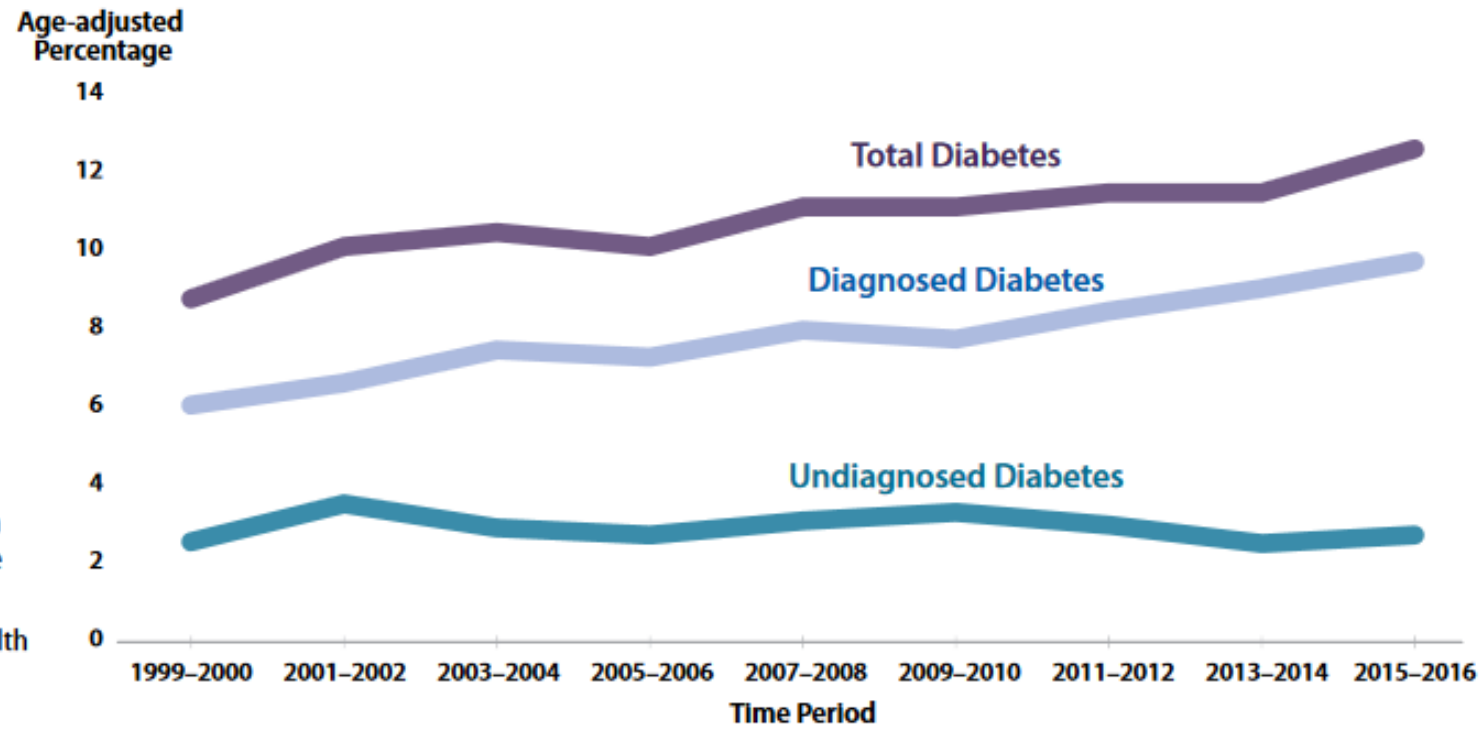
Standards of Care
Meds PocketCards
Question of the Week
Online Course Viewing

Diabetes in America 2020 - CDC

- 13% of adults have diabetes (34 mil)
  - 21% of those don't know they have diabetes
- 35% adults have pre diabetes (88 mil)
  - 85% of those don't know they have prediabetes

Figure 1. Trends in age-adjusted prevalence of diagnosed diabetes, undiagnosed diabetes, and total diabetes among adults aged 18 years or older, United States, 1999–2016.

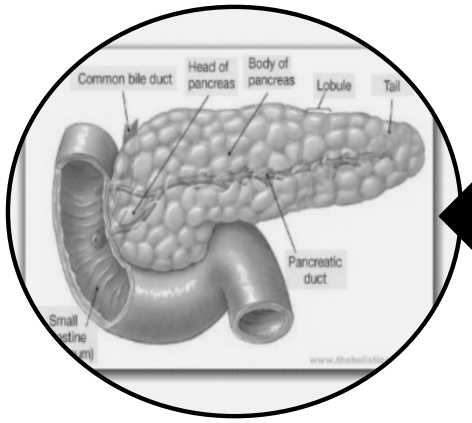


Notes: Diagnosed diabetes was based on self-report. Undiagnosed diabetes was based on fasting plasma glucose and A1C levels among people self-reporting no diabetes.

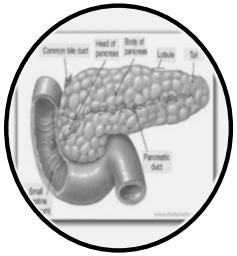
Data source: 1999–2016 National Health and Nutrition Examination Surveys.

CDC 2020 Report www.DiabetesEd.net

Natural History of Diabetes



Yes!



NO

No Diabetes

FBG <100

Random <140

A1c <5.7%

Prediabetes

FBG 100-125

Random 140 - 199

A1c ~ 5.7- 6.4%

50% working pancreas

Diabetes

FBG 126 +

Random 200 +

A1c 6.5% or +

20% working pancreas

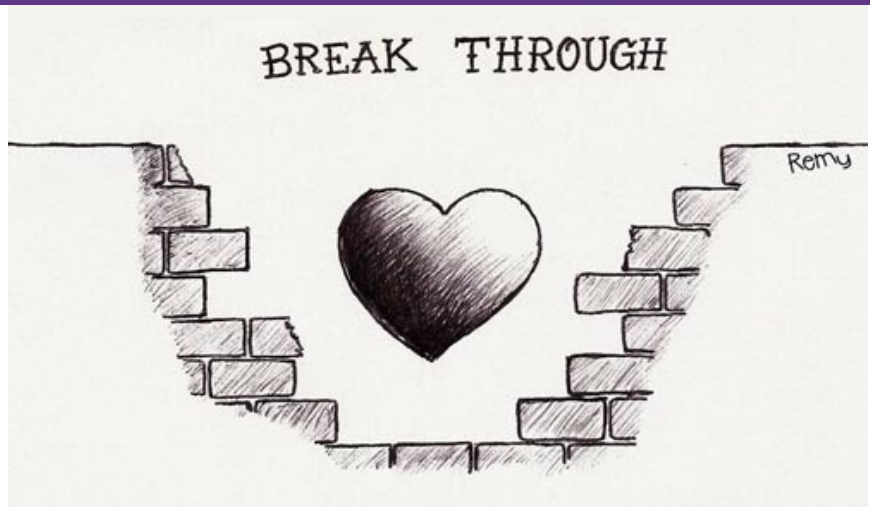
Development of type 2 diabetes happens over years or decades

Breaking Through Clinical Inertia

We have a lot to offer

Evidence Based Guides

- ADA Standards
- AACE Guidelines



- Person Centered Strength based approach
- Pharmacology
- Lifestyle
- Mental health

Case Study - RT

48-year-old with type 2 diabetes on insulin for over 18 years. Most recent A1 8.4, LDL cholesterol 112, HDL 37, triglycerides 324, GFR 110. TSH in 2017 was 4.4

Very upset about her blood sugars and weight, because she says “she is trying to do everything correctly and her blood sugars are always above 200.”

Current medications for diabetes include:

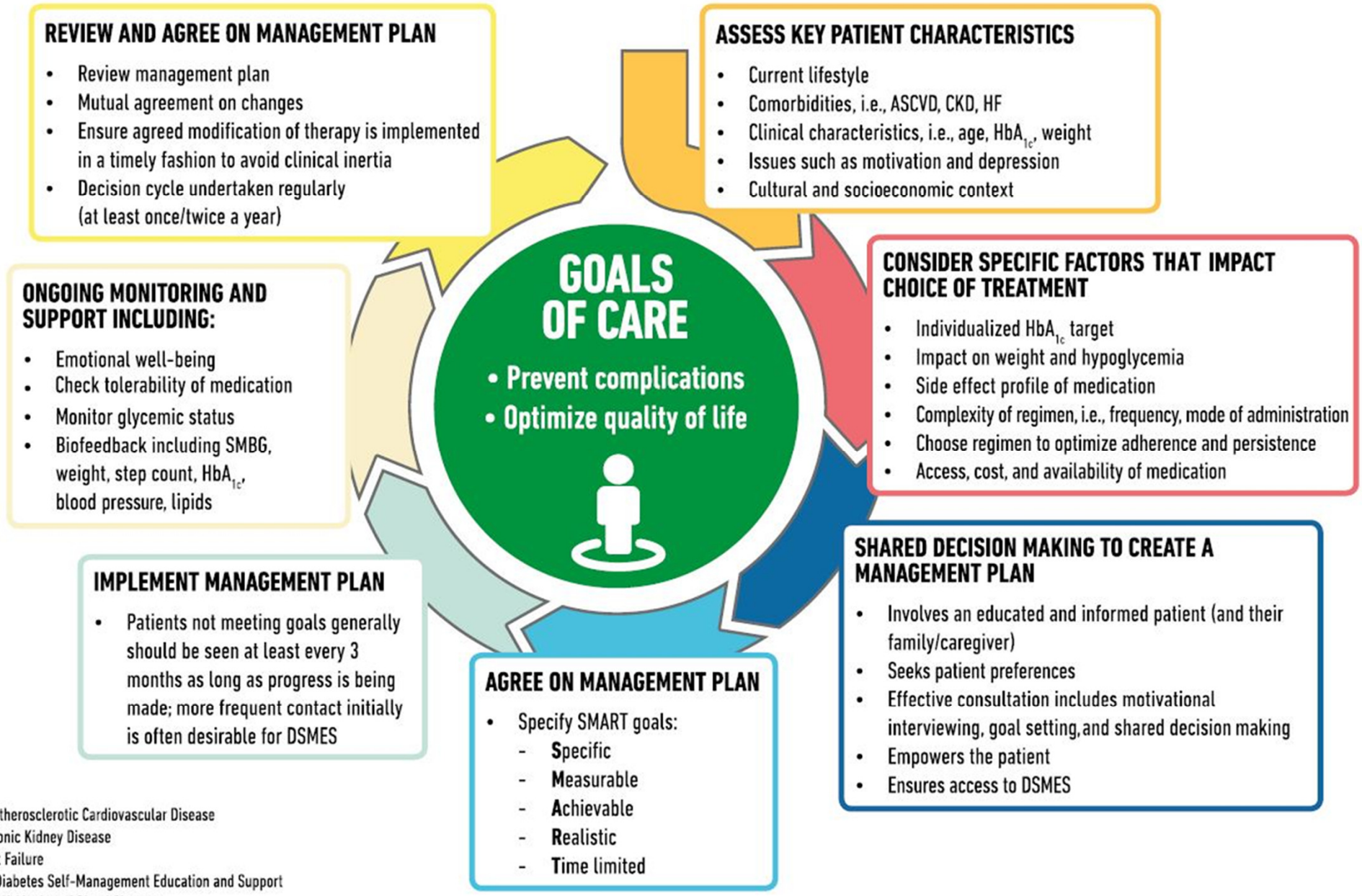
- Detemir (Levemir) 80 units BID and
- Semaglutide (Ozempic) 0.5 mg once a week.
- She is also on atorvastatin (Lipitor) 10 mg daily.

Nutrition, rarely eats at breakfast because she is not hungry, her first meal is usually at noon and she has a subway sandwich. At 3 PM she has a snack bar, around six or seven she eat dinner. Dinner usually includes either rice or beans and six corn tortillas plus meat.

Monitoring: has Freestyle Libre meter, but often doesn't swipe it every eight hours to gather that data.

Plan: RT is very focused on getting blood sugars to target. Will focus first on managing hyperglycemia.

DECISION CYCLE FOR PATIENT-CENTERED GLYCEMIC MANAGEMENT IN TYPE 2 DIABETES



ASCVD = Atherosclerotic Cardiovascular Disease
CKD = Chronic Kidney Disease
HF = Heart Failure
DSMES = Diabetes Self-Management Education and Support
SMBG = Self-Monitored Blood Glucose

Figure 1—Decision cycle for patient-centered glycemic management in type 2 diabetes.

ADA Standards of Care

Next Steps

What Diabetes Med(s) are missing?

Current medications for diabetes include:

- Detemir (Levemir) 80 units BID and
- Semaglutide (Ozempic) 0.5 mg once a week.
- She is also on atorvastatin (Lipitor) 10 mg daily.

Common Oral Diabetes Meds

Diabetes Education SERVICES

Class/Main Action	Name(s)	Daily Dose Range	Considerations
Biguanides • Decreases hepatic glucose output • First line med at diagnosis of type 2	metformin (Glucophage) Riomet (liquid metformin)	500 - 2500 mg (usually BID w/ meal) 500 - 2500mg 500mg/5mL	**Side effects:** nausea, bloating, diarrhea, B12 deficiency. To minimize GI Side effects, use XR and take w/ meals. **Obtain GFR before starting.** • If GFR <30, do not use. • If GFR <45, don't start Meformin • If pt on Metformin and GFR falls to 30-45, eval risk vs. benefit; consider decreasing dose. **For dye study,** if GFR <60, liver disease, alcoholism or heart failure, restart metformin after 48 hours if renal function stable. **Benefits:** lowers cholesterol, no hypo or weight gain, cheap. Approved for pediatrics, 10 yrs + Lowers A1c 1.0%-2.0%.
	Extended Release-XR (Glucophage XR) (Glumetza) (Fortamet)	(1x daily w/dinner) 500 – 2000 mg 500 – 2000 mg 500 – 2500 mg	

Biguanide derived from:
Goat's Rue *Galega officinalis*,
French Lilac
Does NOT harm kidneys
$10 for 3-month supply from
Walmart & other pharmacies

Common Oral Diabetes Meds

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Class/Main Action	Name(s)	Daily Dose Range	Considerations
Sulfonylureas • Stimulates sustained insulin release	glyburide: (Diabeta) (Glynase PresTabs)	 1.25 – 20 mg 0.75 – 12 mg	Can take once or twice daily before meals. Low cost generic. **Side effects**: hypoglycemia and weight gain. Eliminated via kidney. **Caution**: Glyburide most likely to cause hypoglycemia. Lowers A1c 1.0% – 2.0%.
	glipizide: (Glucotrol) (Glucotrol XL)	2.5 – 40 mg 2.5 – 20 mg	
	glimepiride (Amaryl)	1.0 – 8 mg	

Sulfonylureas not our first choice, since RT is already on basal insulin.
A consideration if affordability is an issue.

$10 for 3-month supply from Walmart and other pharmacies

Common Oral Diabetes Meds

Class/Main Action	Name(s)	Daily Dose Range	Considerations
SGLT2 Inhibitors "Glucoretic" • Decreases glucose reabsorption in kidneys	Canagliflozin* (Invokana)	100 - 300 mg 1x daily Don't start if GFR <45.	**Side effects:** hypotension, UTIs, increased urination, genital infections, ketoacidosis. **Monitor GFR and other considerations:** See package insert for dosing based on GFR. *Empagliflozin, Dapagliflozin, & Canagliflozin: - Reduce risk of CV death, heart failure and preserve long-term kidney function. **Benefits:** no hypo or weight gain. Lowers A1c 0.6%-1.5%. Lowers wt 1-3 lbs.
	Dapagliflozin* (Farxiga)	5 - 10 mg 1x daily Don't start if GFR<45.	
	Empagliflozin* (Jardiance)	10 - 25 mg 1x daily Don't start if GFR <45.	
	Ertugliflozin (Steglatro)	5 – 15 mg 1x daily Don't start if GFR <60.	
DPP – 4 Inhibitors "Incretin Enhancers" • Prolongs action of gut hormones • Increases insulin secretion • Delays gastric emptying	sitagliptin (Januvia)	25 - 100 mg daily – eliminated via kidney*	*If creat elevated, see med insert for dosing. **Side effects:** headache and flu-like symptoms. **Can cause severe, disabling joint pain.** Contact MD, stop med. Report signs of pancreatitis. †Saxagliptin and alogliptin can increase risk of heart failure. Notify MD for shortness of breath, edema, weakness, etc. No wt gain or hypoglycemia. Lowers A1c 0.6%-0.8%.
	saxagliptin (Onglyza)†	2.5 - 5 mg daily – eliminated via kidney*, feces	
	linagliptin (Tradjenta)	5 mg daily – eliminated via feces	
	alogliptin (Nesina)†	6.25 - 25 mg daily – eliminated via kidney*	

New Triple Diabetes Pill Combo

- **Trijardy XR = SGLT-2 + DPP-4 + metformin**
  - 5 mg empagliflozin/2.5 mg linagliptin/1,000 mg metformin ER
  - 10 mg empagliflozin/5 mg linagliptin/1,000 mg metformin ER
  - 12.5 mg empagliflozin/2.5 mg linagliptin/1,000 mg metformin ER
  - 25 mg empagliflozin/5 mg linagliptin/1,000 mg metformin ER.

$500-600 for a month's supply – Good Rx Website

What Diabetes Med Add-on or Adjustments?

Current medications for diabetes include:

- Detemir (Levemir) 80 units BID and
- Semaglutide (Ozempic) 0.5 mg once a week.
- She is also on atorvastatin (Lipitor) 10 mg daily.

We add empagliflozin (Jardiance) 25mg daily

GLP-1 Receptor Agonists & Injectables

Class/Main Action	Name	Dose Range	Considerations
GLP-1 Receptor Agonist (GLP-1 RA) **"Incretin Mimetic"** • Increases insulin release with food • Slows gastric emptying • Promotes satiety • Suppresses glucagon	exenatide (Byetta)	5 and 10 mcg BID	**Side effects for all:** Nausea, vomiting, weight loss, injection site reaction. Report signs of acute pancreatitis (severe abdominal pain, vomiting), stop med. Renally excreted. **Black box warning:** Thyroid C-cell tumor warning for exenatide XR, liraglutide, dulaglutide, and semaglutide (avoid if family history of medullary thyroid tumor). *Significantly reduces risk of CV death, heart attack, and stroke. Lowers A1c 0.5 – 1.6% Weight loss of 1.6 to 6.0kg†
	exenatide XR (Bydureon)	2 mg 1x a week Pen injector - Bydureon BCise	
	liraglutide (Victoza)*	0.6, 1.2 and 1.8 mg daily Approved for pediatrics 10 yrs +	
	dulaglutide (Trulicity)*	0.75, 1.5, 3.0 and 4.5 mg 1x a week pen injector	
	lixisenatide (Adlyxin)	10 mcg 1x a day for 14 days 20 mcg 1x day starting day 15	
	semaglutide (Ozempic)*†	0.5 and 1.0 mg 1x a week pen injector	
	(Rybelsus) Oral tablet	3, 7, and 14 mg daily in a.m. Take on empty stomach w/H2O sip	
Amylin Mimetic • Slows gastric emptying • Supress glucagon	pramlintide (Symlin)	Type 1: 15 - 60 mcg; Type 2: 60 - 120 mcg immediately before major meals	For Type 1 or 2 on insulin. Severe hypoglycemic risk, decrease insulin dose when starting. **Side effects:** nausea, weight loss. Lowers A1c 0.5 – 1%

Oral Semaglutide (Rybelsus)

- Dose: 3, 7 and 14 mg daily
- Take daily at least 30 mins before first food, beverage, or other oral meds
- Take with no more than 4 ounces of plain water
- Swallow tablets whole (don't cut or crush)
- Dosing:
  - Start with 3 mg once daily for 30 days
  - Then increase to 7mg once daily for 30 days
  - If A1c at target, maintain at 7mg daily
  - If A1c not at target, increase to 14 mg once daily

What Diabetes Med is missing?

Current medications for diabetes include:

- Detemir (Levemir) 80 units BID and
- Semaglutide (Ozempic) 0.5 mg once a week.
- She is also on atorvastatin (Lipitor) 10 mg daily.

- We add empagliflozin (Jardiance) 25mg daily
- Increase semaglutide to 1.0 mg

WAIT – What about Insulin Dose

48-year-old with type 2 diabetes on insulin for over 18 years. Most recent A1 8.4, LDL cholesterol 112, HDL 37, triglycerides 324, GFR 110. TSH in 2017 was 4.4

Very upset about her blood sugars because she says “she is trying to do everything correctly and her blood sugars are always above 200.”

Updated medications for diabetes include:

- Detemir (Levemir) 80 units BID
- Semaglutide (Ozempic) 1.0 mg once a week.
- Empagliflozin 25mg a day

Decrease morning insulin to 40 units in the morning

Plan of care recommendations

1. Add empagliflozin 25 mg daily - instructed on potential side effects.
2. Increase semaglutide to 1.0 mg once weekly
3. Once start these two medications,
   decrease detemir in morning to 40 units and continue 80 units of detemir at bedtime.

Eventual goal is to get her on one injection of detemir at night.

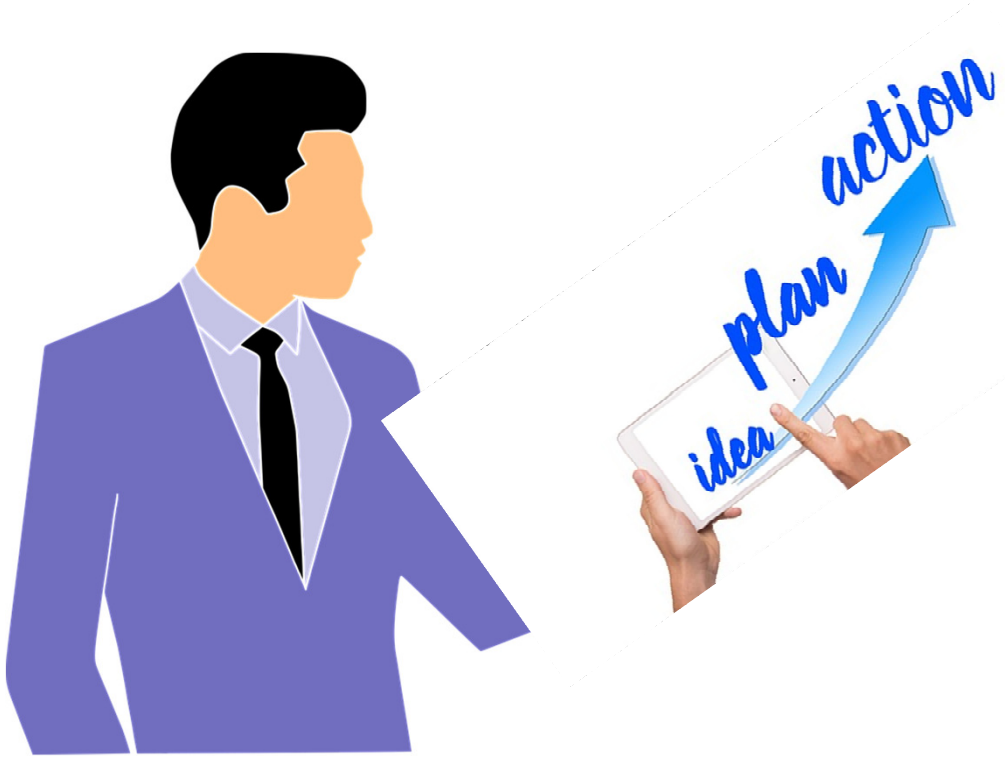
4. Consider increasing atorvastatin if LDL continues to be elevated.
5. Keep on eye on carbs per meal
6. Check TSH with next lab draw.
7. Return in one week for evaluation and coaching.

2 weeks Later

- Since making changes in her medications last week, she is feeling a lot better about her diabetes. Blood sugars in the 80 -130 range and she is happy she is taking less insulin.
- Current medications for diabetes include Detemir 40 units, in am and 80 units in pm, plus semaglutide 1.0 mg once a week and empagliflozin 25mg daily. She is also on atorvastatin 10 mg daily.
- Nutrition: due to semaglutide increased dose, she experienced some nausea and decreased appetite, especially the first few days after injection. She has been eating less. However, she is not able to weigh herself since she does not have a scale.
- Monitoring: has a freestyle libre meter and is swiping it regularly to evaluate her blood sugar management. She stated last night she noticed her blood sugar was running in the 60s, but she did not feel it. Reviewed signs and symptoms of hypoglycemia and the importance of having a 15 g snack on her person at all times.

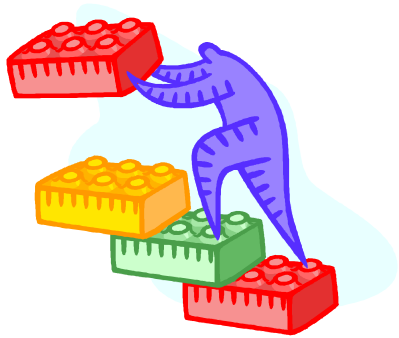
Updated Plan

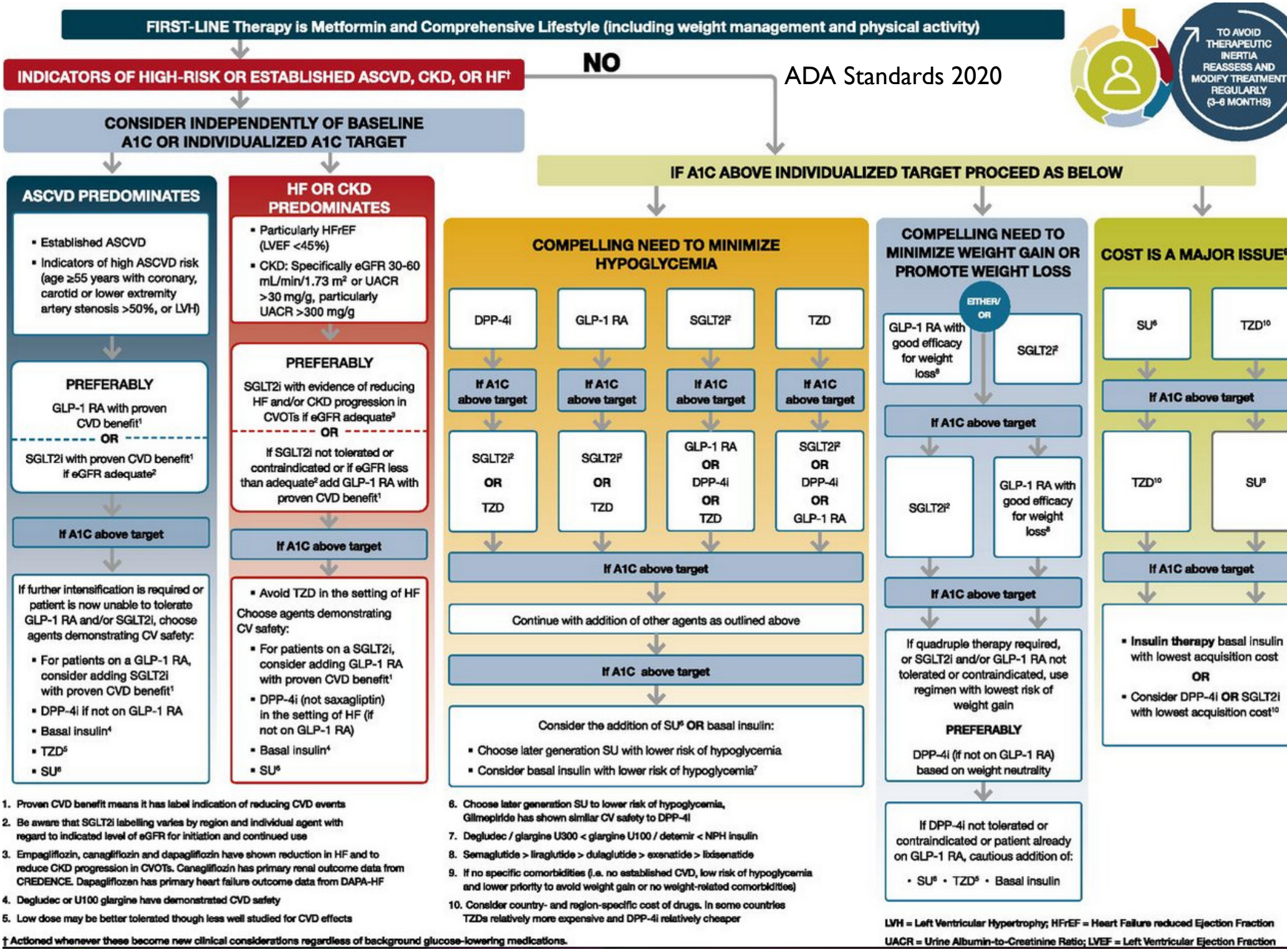
- 1. Keep semaglutide at 1.0 mg once weekly. Inject on Fridays, so that the nausea doesn't cause her to miss work.
- 2. Decrease detemir in morning to 40 units and 40 units of detemir at bedtime to prevent nighttime lows.



ADA Step Wise Approach

- **Step 1** – Metformin + Lifestyle
- **Step 2** - If A1c target not achieved in 3 months, add another med
  - If CVD, CHF, or CKD, consider second agent that reduces risk (based on drug effects and risk factors).
- **Step 3** - If A1c target still not achieved after 3 months, combine metformin plus two other (3 drugs)
- **Step 4** - If A1c target not achieved in 3 mo's, add injectable therapy (GLP-1 RA or basal insulin)





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

Cardiovascular Disease is the Leading Cause of Death in Diabetes

Heart Disease & DM = 3-5xs Risk

- CHF
  - 7.9 % w/ diabetes vs.
  - 1.1 % no diabetes
- Heart attack
  - 9.8 % w/ diabetes vs.
  - 1.8 % no diabetes
- Coronary heart disease
  - 9.1 % w/ diabetes vs.
  - 2.1 % no diabetes
- Stroke
  - 6.6 % w/ diabetes vs.
  - 1.8 % no diabetes

- 2007 AACE

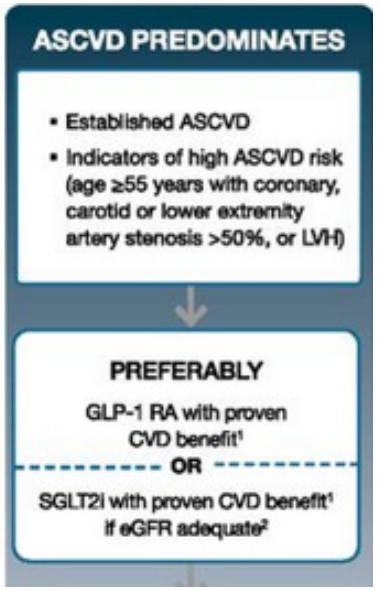
Diabetes Meds that do more than lower BG

- When adding meds, consider presence or absence of
  - ASCVD
  - HF (Heart Failure) and
  - CKD (Chronic Kidney Disease)

- Approved SGLT2 and GLP-1s
  - Improve CV outcomes
  - Decrease heart failure
  - Improve kidney function.

Atherosclerotic Cardiovascular Disease

- ASCVD risk – how is that defined?
  - Established heart disease
  - 55+ with coronary, carotid or lower extremity artery stenosis > 50% or Left Ventricular Hypertrophy (LVH)
  - Preferred Meds:
    - GLP-1 RA with proven CVD benefit
    - SGLT-2s that reduce heart failure, CKD progression, Cardiovascular Outcomes Trial (CVOT)



ADA Stds – Injectables Algorithm small print

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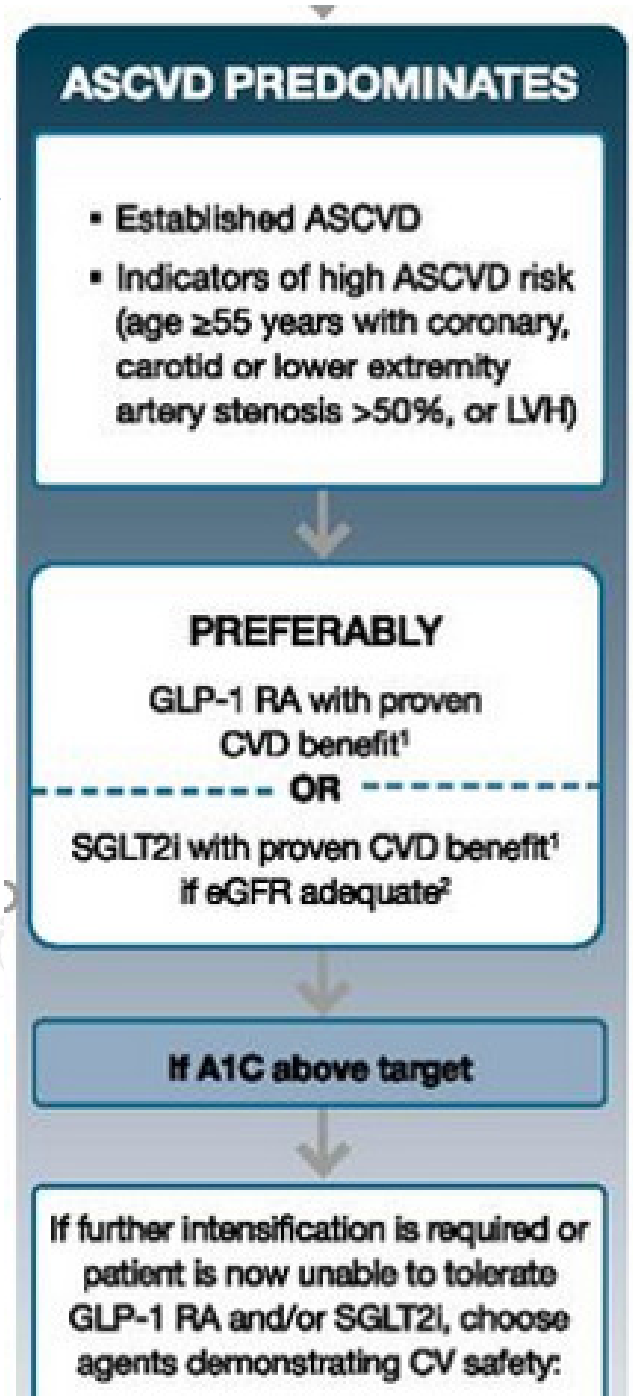
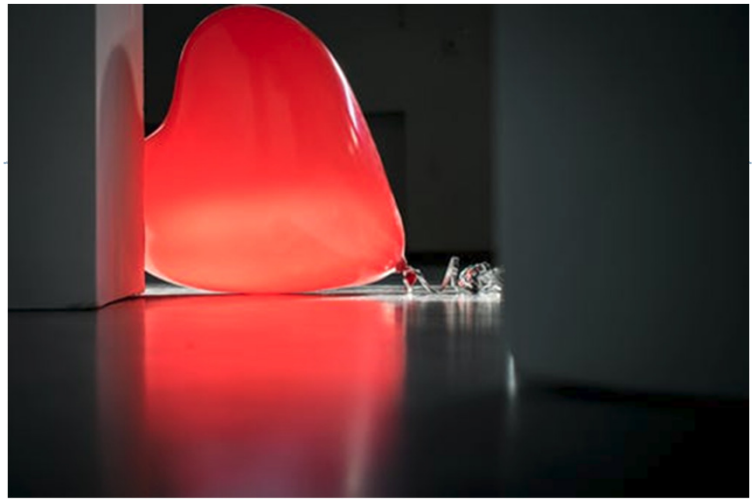
9. If no specific comorbidities (i.e. no established CVD, low risk of hypoglycemia and lower priority to avoid weight gain or no weight-related comorbidities)
10. Consider country- and region-specific cost of drugs. In some countries TZDs relatively more expensive and DPP-4i relatively cheaper

If DPP-4i not tolerated or contraindicated or patient already on GLP-1 RA, cautious addition of:
• SU[6] • TZD[5] • Basal insulin

tioned 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





If ASCVD Predominates Consider:

Try GLP-1 RA

- Semaglutide
- Liraglutide
- Dulaglutide

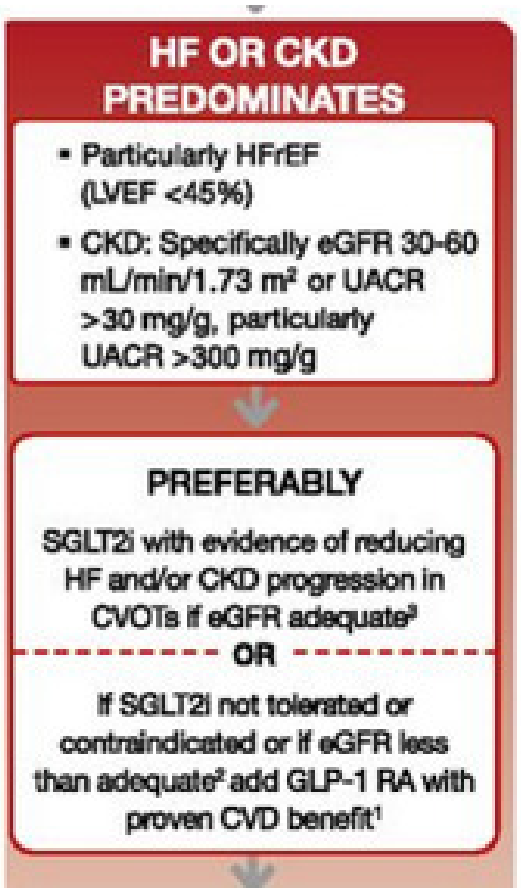
or

SGLT2i

- Canagliflozin
- Empagliflozin
- Dapagliflozin

Heart Failure (HF) or Chronic Kidney Disease Predominate

- If HF or reduced Ejection Fraction (rEF) and Left Ventricular Ejection Fraction (LVEF) <45%
- Kidney disease
  - CKD: If eGFR 30-60 or
  - Urine Albumin to Creatinine Ratio (UACR) > 30 mg/g especially if UACR > 300
- Use SGLT2i if eGFR is adequate
  - Empagliflozin (Jardiance), canagliflozin (Invokana), dapagliflozin (Farxiga)
- If can't tolerate, use GLP-1 RA
  - Semaglutide > liraglutide > dulaglitide > exenatide > lixisenatide
- Insulin Basal next - Risk of hypoglycemia; least to most
  - Degludec /glargine U300 < glargine U100 < detemir < NPH



Diabetes + CKD – Consider SGLT2

- Diabetes + CKD = increase CVD Risk
  - In several studies, participants on SGLT2 with GFRs of 30-60 (stage 3) reduced ASCVD risk
  - In addition to reducing ASCVD risk, those on SGLT2 and GLP-1s had improved renal function
    - Slowed kidney disease or death
    - Most consistent improvement with SGLT2s

CKD = Chronic Kidney Disease

Bottom Line – Diabetes and CVD

- If not meeting A1c target on metformin
- Add SGLT2 or GLP-1 RA to treatment regimen if affordable and best choice based on individual

- There is no evidence to date of CV protective benefit of using these meds in people with A1c <7 and no history of ASCVD.

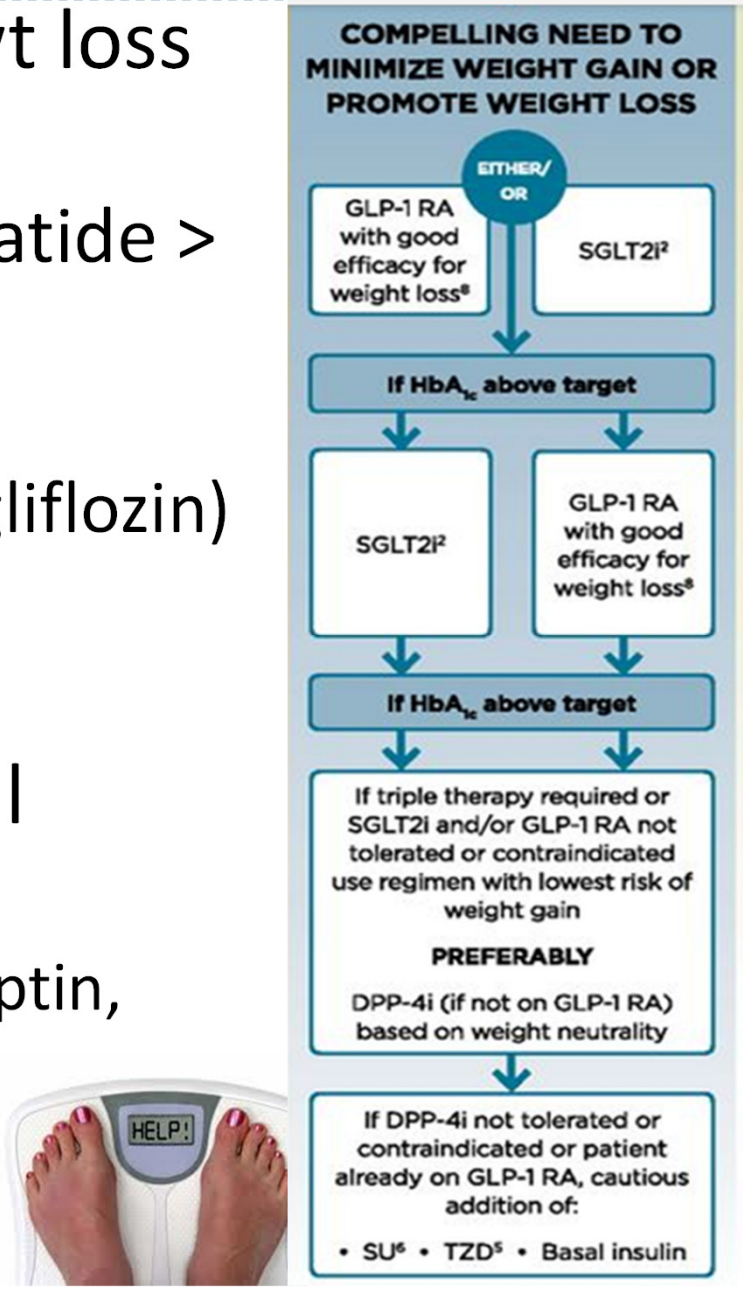
ADA Step Wise Approach to Hyperglycemia 2020

- ***For all steps, consider* these additional factors**
  - Minimize wt gain or promote wt loss
  - Minimize Hypoglycemia
  - Consider Cost

- Once start insulin, stop sulfonylurea and DPP-IV Inhibitors

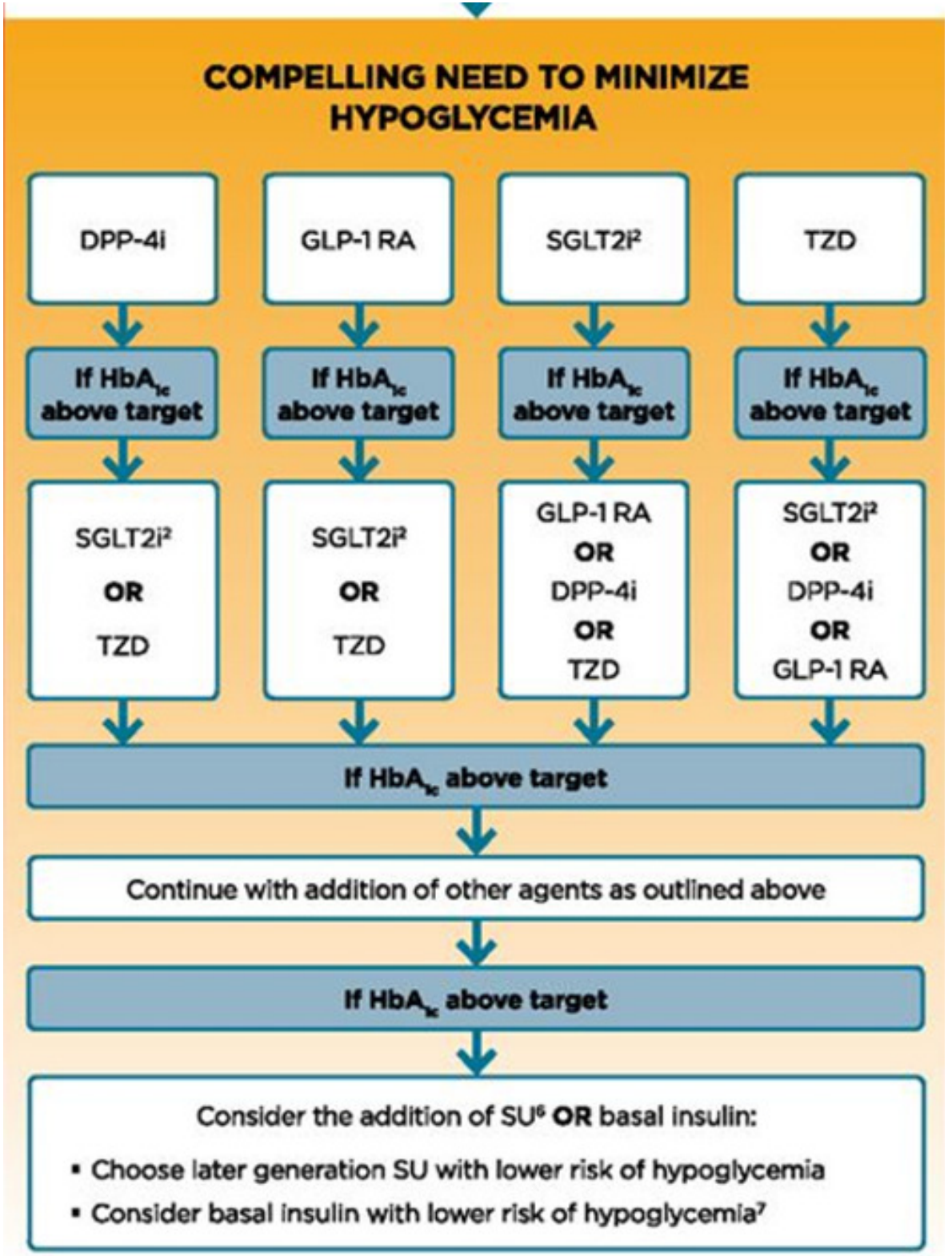
When goal is to avoid weight gain

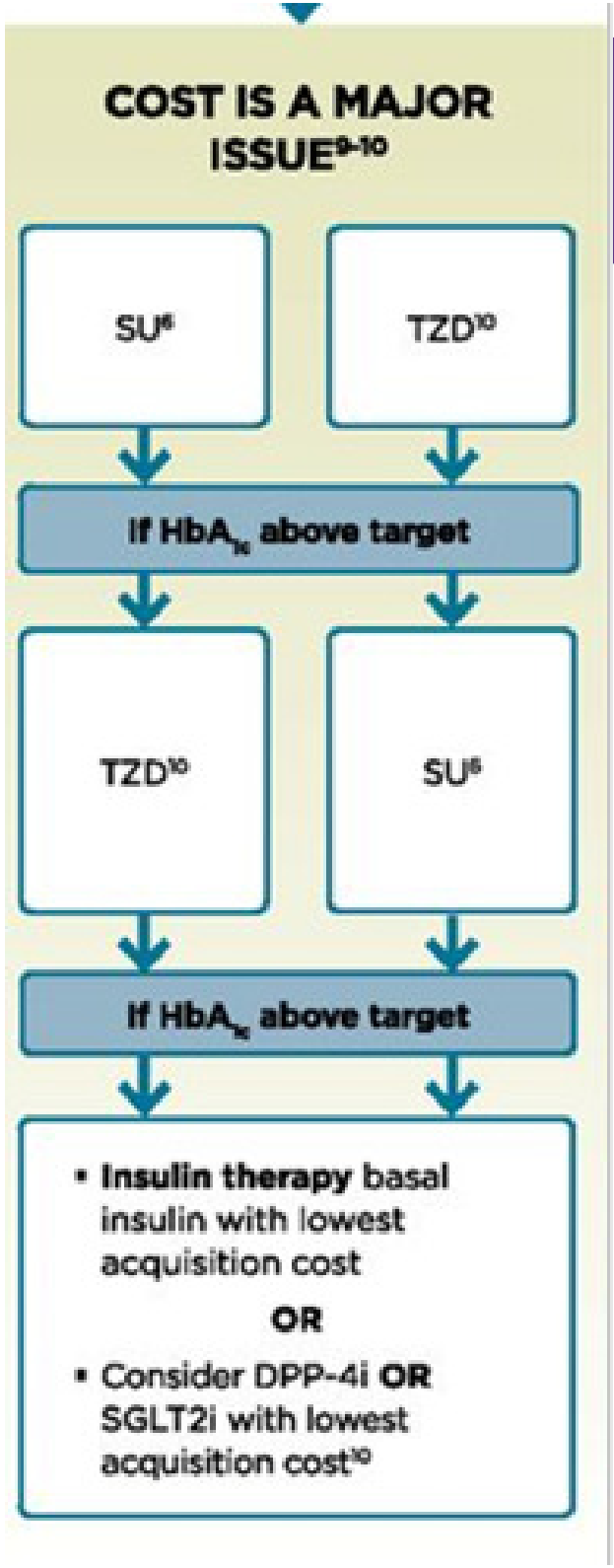
- These meds associated with wt loss
  - GLP-1 agonists (Semaglutide > liraglutide > dulaglitide > exenatide > lixisenatide
  - SGLT-2 Inhibitors (empagliflozin, dapagliflozin, canagliflozin, ertugliflozin)
  - Symlin (Pramlintide)
- These meds are weight neutral
  - Metformin
  - DPP-IV Inhibitors: sitagliptin, saxgliptin, linagliptin, alogliptin
  - Acarbose



When goal is to avoid Hypoglycemia

- Caution with sulfonylureas
- Careful insulin dosing
- May need to up adjust glucose goals
- Monitor kidney function


COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA
DPP-4i
GLP-1 RA
SGLT2i[2]
TZD
If HbA1c above target
If HbA1c above target
If HbA1c above target
If HbA1c above target
SGLT2i[2] OR TZD
SGLT2i[2] OR TZD
GLP-1 RA OR DPP-4i OR TZD
SGLT2i[2] OR DPP-4i OR GLP-1 RA
If HbA1c above target
Continue with addition of other agents as outlined above
If HbA1c above target
Consider the addition of SU[6] OR basal insulin:
• Choose later generation SU with lower risk of hypoglycemia
• Consider basal insulin with lower risk of hypoglycemia[7]



Goal to minimize cost

- Go generic.
- Oral Meds -Metformin and Sulfonylureas
  - Walmart, Target and others
  - 3 mo supply of following meds for ~ $10
    - Metformin and Metformin XR (500 & 750mg)
    - Glipizide, Glyburide, Glimepiride
- Insulins – Oldies but Goodies
  - NPH, Regular, 70/30 mix
    - $25 a vial at Walmart – ReliOn
  - Also have ReliOn
    - Syringes, meters, strips

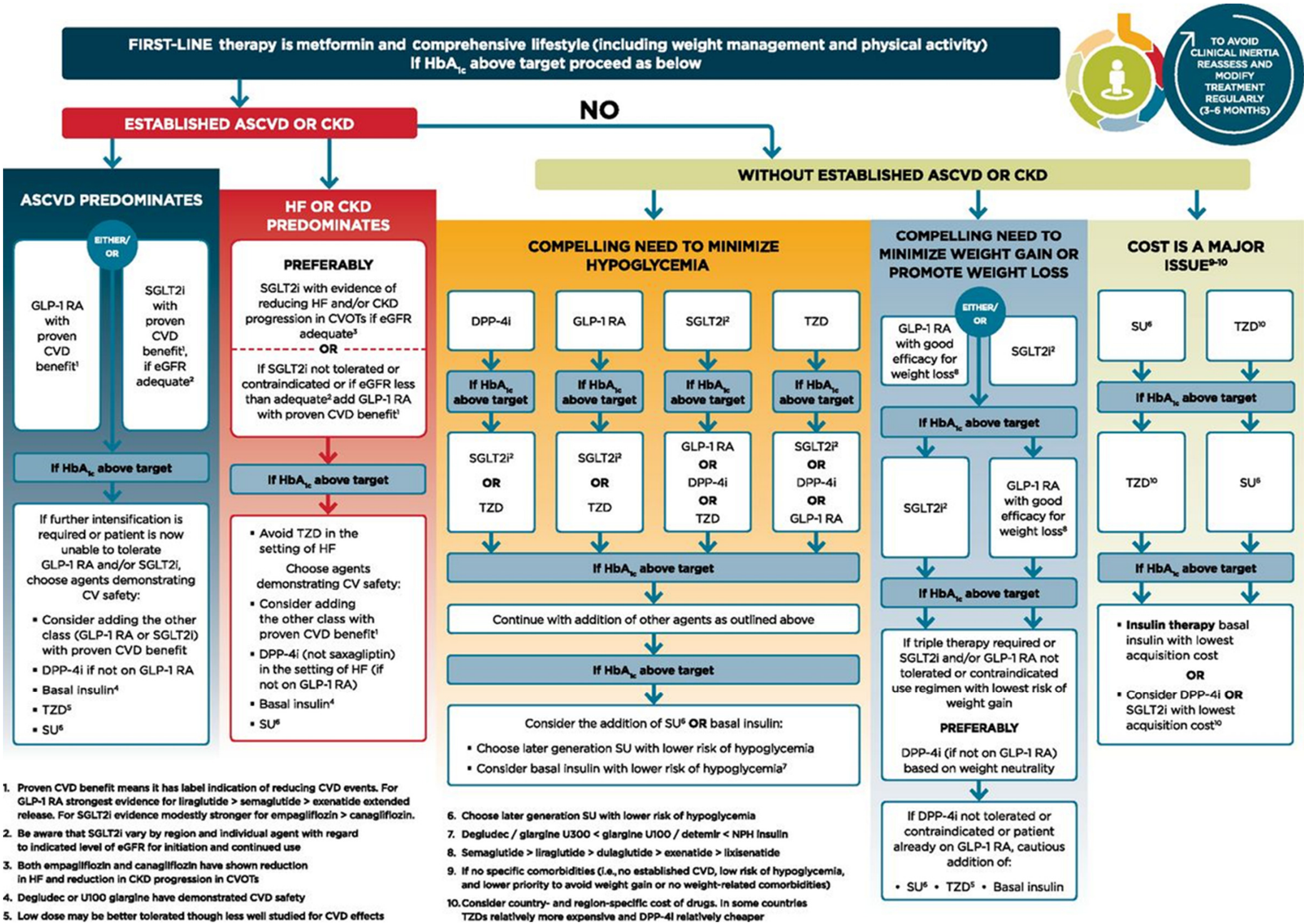
Insulin Cost-Saving Resource Guide

Manufacturer	Manufacturer Patient Assistance Program	Product	Copay Card Link	Copay as low as	Additional Information
Eli Lilly	**Lilly Cares Program** • **Products:** Humalog U100®, Humalog U200®, Humalog Mix 75/25®, Humalog Mix 50/50®, Humulin 70/30®, Humulin R®, Humulin R U500®, Basaglar® • For people with no prescription coverage, not enrolled in Medicaid or VA benefits, and must meet the household income guidelines • Must be U.S. citizen, household income ≤400% of federal poverty • Exceptions include people who entered the coverage gap (donut hole) in Medicare Part D and applied for and were denied Medicare Extra Help/Low Income Subsidy (LIS) and spent over $1,100 on prescription medications within the calendar year • For more information visit www.lillycares.com/	Humalog U200®	www.humalog.com/u-200-kwikpen/humalog-savings-card/	$25 per month	– Maximum savings $100 per month – Must be enrolled in commercial plan
		Basaglar®	www.basaglar.com/savings-support	$5 per month	– Maximum savings $150 per month – Must be enrolled in commercial plan
		Humulin R U500®	www.humulin.com/savings-support	$25 per month	– Must be enrolled in commercial plan – No cap – In most cases, total cost is no more than $25/month
		Insulin lispro U100, insulin 75/25, insulin junior kwikpen	Generic, no copay card needed	NA	– Interchangeable with brand name product – Approximately 50% off brand name price
Novo Nordisk	**Novo Nordisk Patient Assistance Program (PAP) NovoCare** • **Products:** Tresiba®, Levemir®, Fiasp®, Novolog®, Novolog Mix 70/30®, Novolin R®. Novolin N®, Novolin 70/30®, Xultophy® • People also qualify for a glucagon pen, and NovoFine®, NovoTwist® pen needles • For people with no prescription coverage, not enrolled in Medicaid, Medicare or VA benefits	Novolog®	www.novocare.com/novolog/savings-card.html	$25 per month	– Maximum savings $100 per month – Must be enrolled in commercial plan – Free box of Novo Nordisk needles
		Novolog® Mix 70/30,	www.novocare.com/novologmix70-30/savings-card.html		
		Fiasp®	www.novocare.com/fiasp/savings-card.html		
		Tresiba®	www.novocare.com/tresiba/savings-card.html	$5 per month	

Last updated 4/26/2020

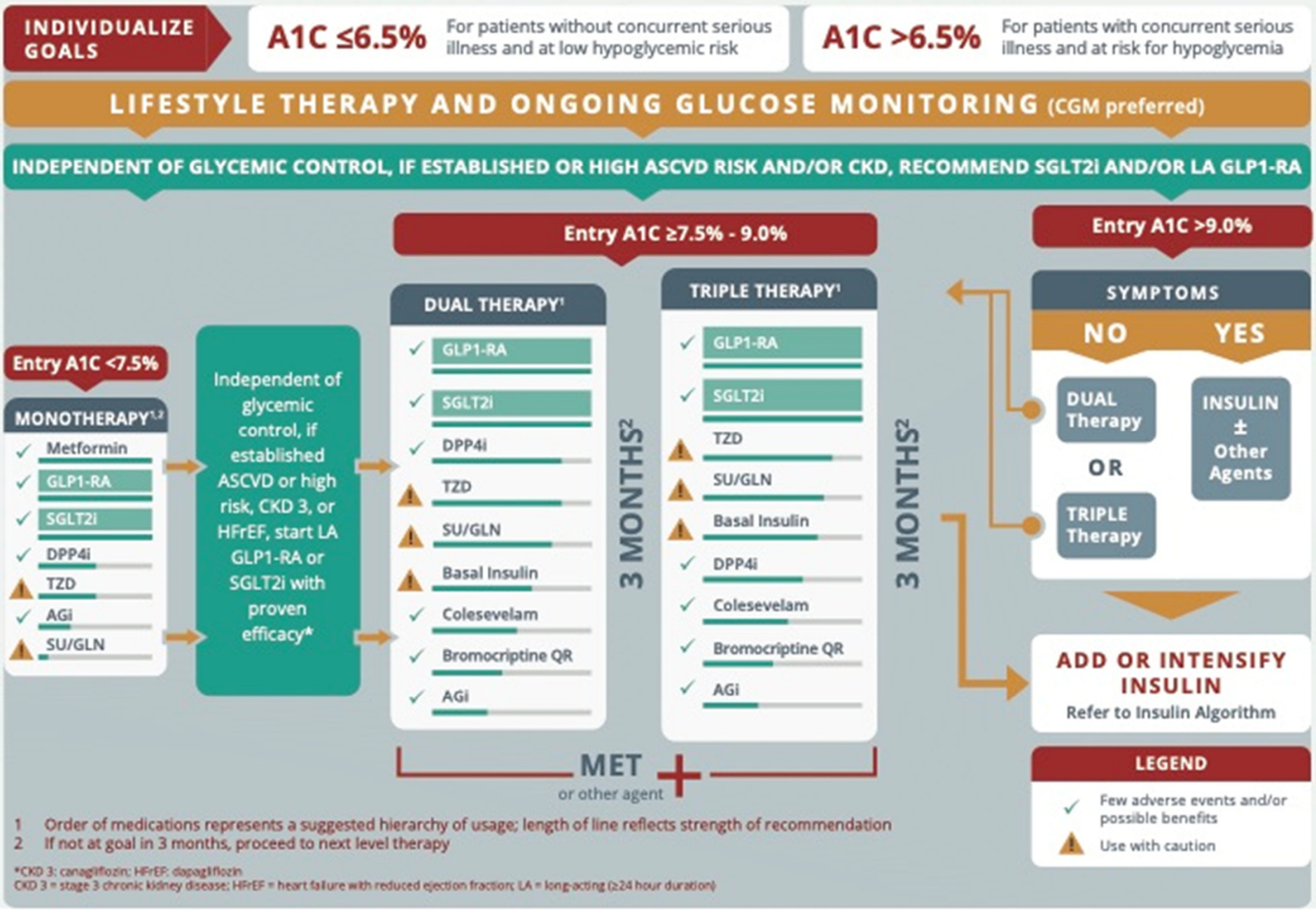
Life Study

- 61 year old woman with BMI of 28 and type 2 diabetes 3 months. Has been trying to manage diabetes with diet and exercise. GFR in 90s. Worried about weight gain.
- Most recent A1c 7.2%
  - ADA
  - AACE
  - Cash pay



1. Proven CVD benefit means it has label indication of reducing CVD events. For GLP-1 RA strongest evidence for liraglutide > semaglutide > exenatide extended release. For SGLT2i evidence modestly stronger for empagliflozin > canagliflozin.
2. Be aware that SGLT2i vary by region and individual agent with regard to indicated level of eGFR for initiation and continued use
3. Both empagliflozin and canagliflozin have shown reduction in HF and reduction in CKD progression in CVOTs
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 with lower risk of hypoglycemia
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

GLYCEMIC CONTROL ALGORITHM



Life Study - Answer

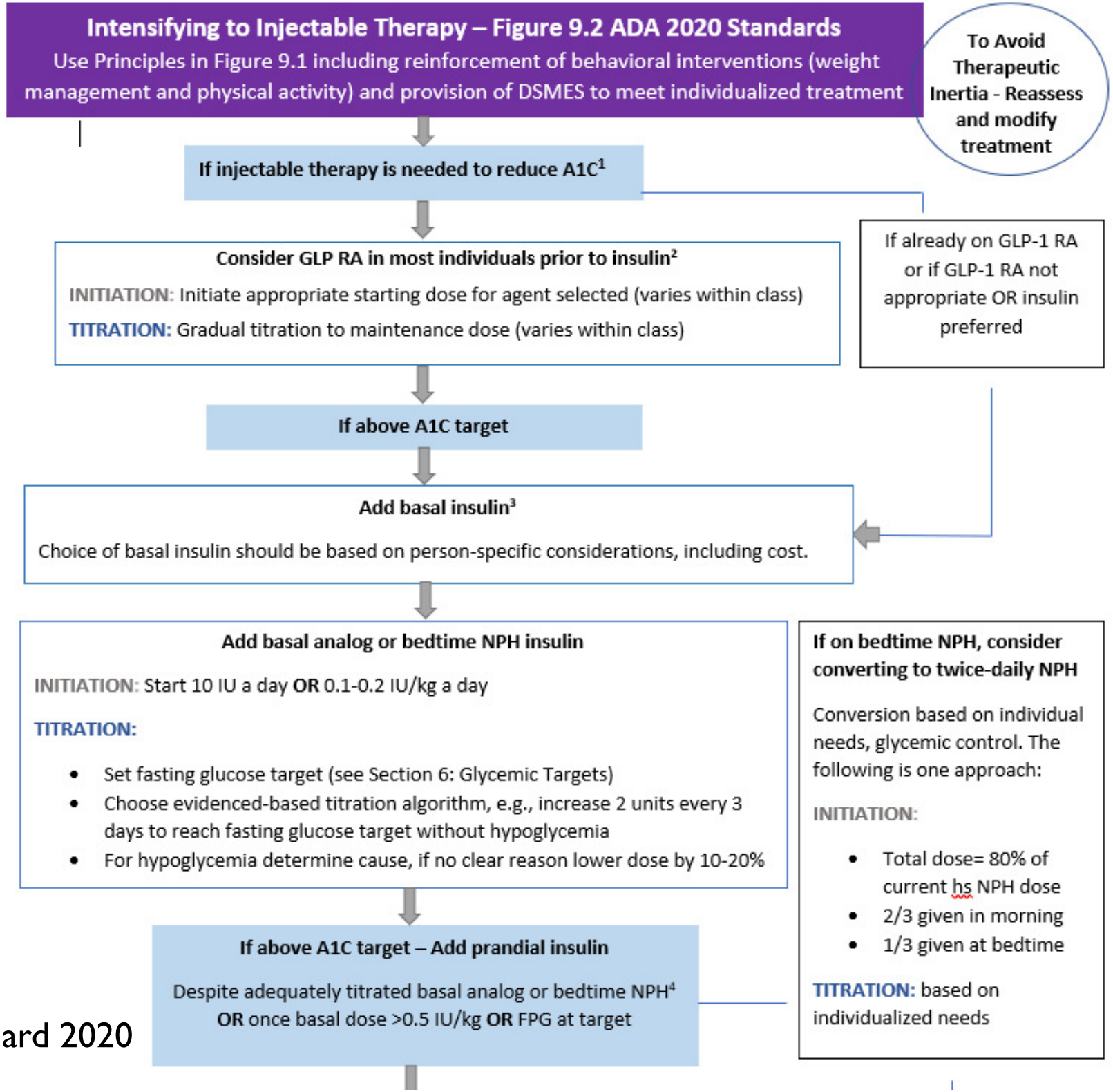
- 61 year old woman with BMI of 28 and type 2 diabetes 3 months. Has been trying to manage diabetes with diet and exercise. GFR in 90s. Worried about weight gain.
- Most recent A1c 7.2%
  - ADA - Metformin
  - AACE - Metformin
  - Cash pay - Metformin

What next?

- 69 year old male, BMI 28, on Metformin 2000mg a day, Glipizide 40mg a day and Dapagliflozin 10mg a day.
- A1c 10.1%. GFR 50s.
- Complains of foot pain, polyuria, 11 yr diabetes
  - ADA What next?
  - Insurance
  - No insurance

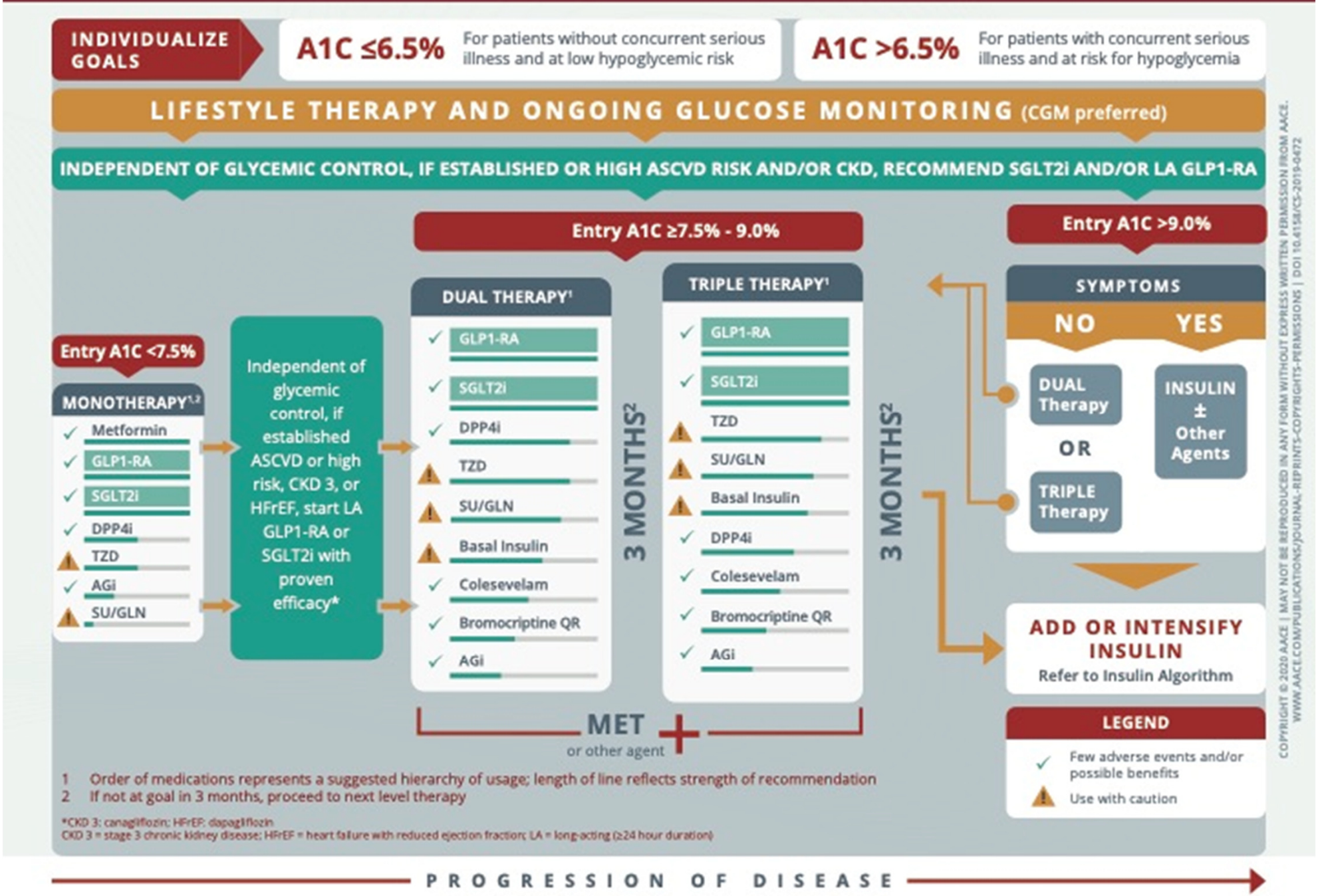
Intensifying Injectable Therapy – Type 2

- Consider GLP-1 RA first
- Start basal insulin 10 units or 0.1 to 0.2 units/kg day
- Titrate up 2 units every 3 days, until FBG at goal
- If hypo, decrease insulin 20% or 4 units
- If basal insulin is >0.5 unit/kg day, add bolus insulin
- Adding bolus
  - Start with 4 units bolus at largest meal or
  - Start 1-2 injections with 10% of basal or
  - Switch to 70/30 twice or three times daily.



ADA Standard 2020

GLYCEMIC CONTROL ALGORITHM



What next?

- 69 year old male, BMI 28, on Metformin 2000mg a day, Glipizide 40mg a day and Dapgliflozin 10mg a day.
- A1c 10.1%. GFR 50s.
- Solutions
  - Insurance – Add Basal + GLP-1 combo or
  - Start basal insulin, then add GLP-1, then bolus insulin (stop glipizide)
  - No insurance – Stop Glipizide, keep metformin, add 70/30 insulin
    - Add 70/30 insulin 1-2 times a day
    - 100kg x 0.5 = 50 units daily (30units am/ 20units dinner)

Insulin/Injectable Combos

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Name	Combines	Considerations
IDegLira* Xultophy 100/3.6	Insulin degludec (IDeg or Tresiba) Ultra long insulin + Liraglutide (Victoza) GLP-1 Receptor Agonist (GLP-1 RA)	**Xultophy 100/3.6 pre-filled pen** = 100 units IDeg / 3.6 mg liraglutide per mL Once daily injection – Dose range 10 to 50 = 10 – 50 units IDeg + 0.36 -1.8 mg liraglutide **Recommended starting dose:** • 16 IDegLira (= 16 units IDeg + 0.58 mg liraglutide) Titrate dose up or down by 2 units every 3-4 days to reach target. Supplied in package of five single-use 3mL pens. Once opened, good for 21 days.
iGlarLixi* Soliqua 100/33	Insulin glargine (Lantus) Basal Insulin + Lixisenatide (Adlyxin) GLP-1 Receptor Agonist	**Soliqua 100/33 Solostar Pen** = 100 units glargine / 33 µg lixisenatide per mL Once daily injection an hour prior to first meal of day. Dose range 15 – 60 = 15-60 units glargine + 5 – 20µg lixisenatide **Recommended starting dose:** • 15 units for pts not controlled on 30 units basal insulin or GLP-1 RA • 30 units for pts not controlled on 30 -60 units basal insulin or GLP-1 RA Titrate dose up or down by 2-4 units every week to reach target. Supplied in package of five single-use 3mL pens. Once opened, good for 14 days.

***Discontinue basal insulin /GLP-1 RA therapy before starting. If dose missed, resume with next usual scheduled dose.**

New Insulin **LYUMJEV™** (LOOM-jehv)

FDA Approved June 2020

Lyumjev is insulin lispro-aabc injection.

- Two strengths:
  - U-100 (100 units per milliliter)
    U-200 (200 units per milliliter).
- In studies, lispro-aabc appeared in circulation approximately 1 minute after injection.
- Time to 50% maximum and maximum insulin lispro-aabc concentration was observed to be 13 and 57 minutes, respectively.

Insulin PocketCard™

Diabetes Education Services

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Action		Insulin Name	Onset	Peak	Effective Duration	Considerations
Bolus	Very Rapid Acting Analogs	Aspart (Fiasp)	2.5 min	~60 min	3-5 hours	Bolus insulin lowers after-meal glucose. Post meal BG reflects efficacy. Basal insulin controls BG between meals and nighttime. Fasting BG reflects efficacy. Side effects: hypoglycemia, weight gain. Typical dosing range: 0.5-1.0 units/ kg body wt/day. Discard open vials after 28 days. For pen storage guidelines, see package insert.
		Lispro-aabc (Lyumjev)	1 min	~60 min	4-5 hours	
	Rapid Acting Analogs	Aspart (Fiasp)	2.5 min	~ 60 min	3 - 5 hrs	
		Aspart (Novolog)	5 - 15 min	30 - 90 min	< 5 hrs	
		Lispro (Humalog*/ Admelog)				
		Glulisine (Apidra)				
	Short Acting	Regular*	30 - 60 min	2 - 3 hrs	5 - 8 hrs	
Basal	Intermediate	NPH	2 - 4 hrs	4 - 10 hrs	10 - 16 hrs	
	Long Acting	Detemir (Levemir)	3 - 8 hrs	No peak	6 - 24 hrs	
		Glargine (Lantus*/ Basaglar/Semglee)	2 - 4 hrs		20 - 24 hrs	
		Degludec (Tresiba)*	~ 1 hr		< 42 hrs	
Basal + Bolus	Intermediate + short	Combo of NPH + Reg 70/30 = 70% NPH + 30% Reg 50/50 = 50% NPH + 50% Reg	30 - 60 min	Dual peaks	10 - 16 hrs	
	Intermediate + rapid	Novolog® Mix - 70/30 Humalog® Mix - 75/25 or 50/50	5 - 15 min		24 hrs	

Concentrated insulins available - see Concentrated Insulin Card for details. Insulin action times vary; time periods are general guidelines only.

Critical Points

- Individualize Glycemic targets & BG-lowering
- Metformin = optimal 1st-line med.
- MNT, exercise, & education: foundation T2DM therapy
- CVD and CKD risk reduction - a major focus of therapy.
- Most important, all treatment decisions should be made in conjunction with the person's preferences, needs & values.
- Diabetes Specialists can break the cycle of clinical inertia and improve Quality of Life

Thank You

- Thanks for joining us!
- Please let us know if we can be of more service
- www.DiabetesEd.net

Diabetes Education SERVICES