ADA 2021 REVIEW

DR ROZITA NASERI

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Section 2.

Classification and Diagnosis of Diabetes

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Classification

Diabetes can be classified into the following general categories:

1. Type 1 diabetes (due to autoimmune ß-cell destruction, usually leading to absolute insulin deficiency, including latent autoimmune diabetes of adulthood)
2. Type 2 diabetes (due to a progressive loss of ß-cell insulin secretion frequently on the background of insulin resistance)
3. Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young), diseases of the exocrine pancreas (such as cystic fibrosis and pancreatitis), and drug- or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation)
4. Gestational diabetes mellitus (diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation)

A1C (continued)

2.3 **hemoglobinopathies** including

sickle cell disease

pregnancy (second and third trimesters and the postpartum period)

glucose-6-phosphate dehydrogenase deficiency

HIV

hemodialysis

recent blood loss or transfusion

erythropoietin therapy

only plasma blood glucose criteria should be used to diagnose diabetes. B

Posttransplantation Diabetes Mellitus

2.20 The oral glucose tolerance test is the preferred test to make a diagnosis of posttransplantation diabetes mellitus. B

Gestational Diabetes Mellitus

2.25 Test for undiagnosed prediabetes and diabetes at the first prenatal visit in those with risk factors using standard diagnostic criteria. B

2.26 Test for gestational diabetes mellitus at 24–28 weeks of gestation in pregnant women not previously found to have diabetes. A

2.27 Test women with gestational diabetes mellitus for prediabetes or diabetes at 4–12 weeks postpartum, using the 75-g

Section 4.

Comprehensive Medical Evaluation and Assessment of Comorbidities

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Immunizations

4.6 Provide routinely recommended vaccinations for **children and adults with diabetes** as indicated by age (A

Section 6.

Glycemic Targets

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Glycemic Assessment

6.1 Assess glycemic status (A1C or other glycemic measurement) at least two times a year in patients who are meeting treatment goals (and who have stable glycemic control).E

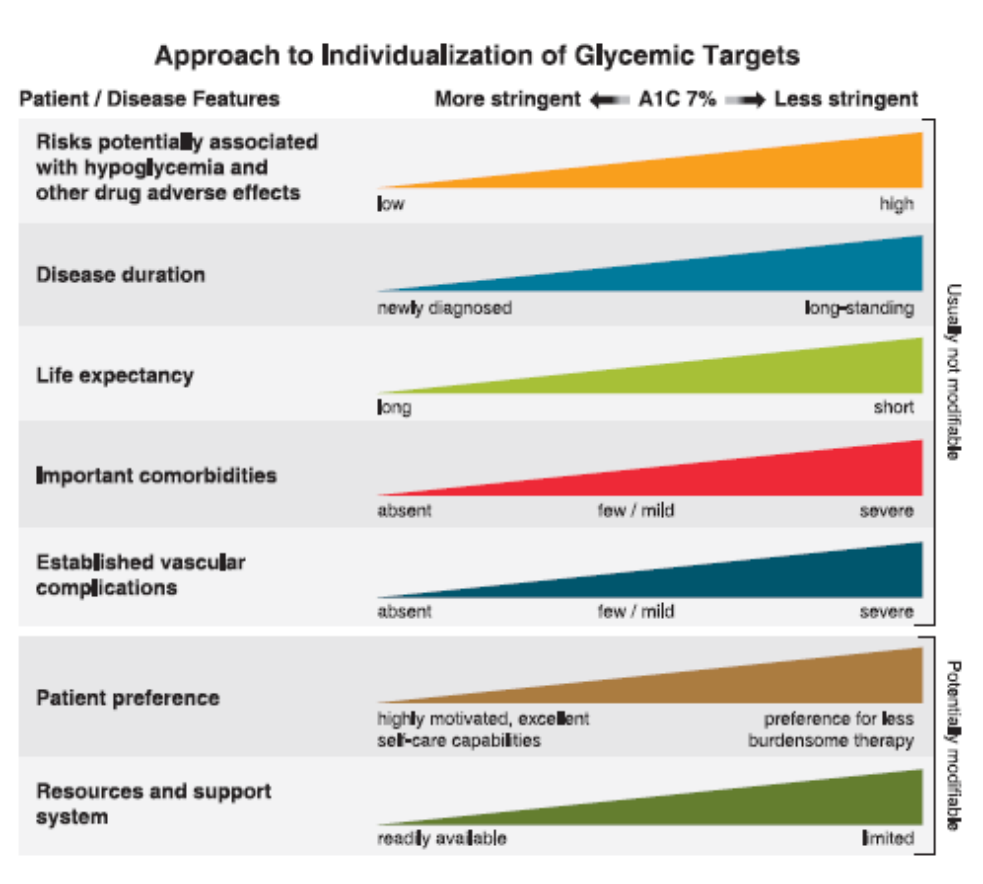
6.2 Assess glycemic status at least quarterly, and as needed, in patients whose therapy has recently changed and/or who are not meeting glycemic goals. E

Glycemic Goals

6.5a An A1C goal for many nonpregnant adults of <7%(53 mmol/mol) without significant hypoglycemia is appropriate. A

6.6 On the basis of provider judgment and patient preference, achievement of lower A1C levels than the goal of 7% may be acceptable, and even beneficial, if it can be achieved safely without significant hypoglycemia or other adverse effects of treatment. C

GLYCEMIC TARGETS



Glycemic Targets:
Standards of Medical Care in Diabetes - 2021. *Diabetes Care* 2021;44(Suppl. 1):S73-S84

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Table 6.3—Summary of glycemic recommendations for many nonpregnant adults with diabetes

A1C	<7.0% (53 mmol/mol)*#
Preprandial capillary plasma glucose	80–130 mg/dL* (4.4–7.2 mmol/L)
Peak postprandial capillary plasma glucose†	<180 mg/dL* (10.0 mmol/L)

*More or less stringent glycemic goals may be appropriate for individual patients. #CGM may be used to assess glycemic target as noted in Recommendation 6.5b and **Fig. 6.1**. Goals should be individualized based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations (as per **Fig. 6.2**). †Postprandial glucose may be targeted if A1C goals are not met despite reaching preprandial glucose goals. Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in patients with diabetes.

Glycemic Targets:
Standards of Medical Care in Diabetes - 2021. *Diabetes Care* 2021;44(Suppl. 1):S73-S84

Hypoglycemia (continued)

6.13 **Insulin-treated patients with hypoglycemia unawareness, one level 3 hypoglycemic event, or a pattern of unexplained level 2 hypoglycemia should be advised to raise their glycemic targets to strictly avoid hypoglycemia for at least several weeks in order to partially reverse hypoglycemia unawareness and reduce risk of future**

Table 6.4—Classification of hypoglycemia

	Glycemic criteria/description
Level 1	Glucose <70 mg/dL (3.9 mmol/L) and ≥54 mg/dL (3.0 mmol/L)
Level 2	Glucose <54 mg/dL (3.0 mmol/L)
Level 3	A severe event characterized by altered mental and/or physical status requiring assistance for treatment of hypoglycemia

Reprinted from Agiostratidou et al. (63).

Glycemic Targets:
Standards of Medical Care in Diabetes - 2021. *Diabetes Care* 2021;44(Suppl. 1):S73-S84

Section 8.

Obesity Management for the Treatment of Type 2 Diabetes

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Assessment

8.2 Measure height and weight and calculate BMI at annual visits or more frequently. Assess weight trajectory to inform treatment considerations. E

Diet, Physical Activity, & Behavioral Therapy

8.5 **Diet**, **physical activity,** and **behavioral therapy** designed to achieve and maintain **≥5% weight loss** is recommended for most patients with type 2 diabetes who have overweight or obesity and are ready to achieve weight loss.

Greater benefits in control of diabetes and cardiovascular risk may be gained from **even greater weight loss**. **B**

8.6 Such interventions should include a high frequency of counseling (≥16 sessions in 6 months) and focus on dietary changes, physical activity, and behavioral strategies to achieve a 500–750 kcal/day energy deficit. A

OBESITY MANAGEMENT FOR THE TREATMENT OF TYPE 2 DIABETES

Table 8.1—Treatment options for overweight and obesity in type 2 diabetes

	BMI category (kg/m^2)		
Treatment	25.0–26.9 (or 23.0–24.9*)	27.0–29.9 (or 25.0–27.4*)	≥30.0 (or ≥27.5*)
Diet, physical activity, and behavioral therapy	†	†	†
Pharmacotherapy		†	†
Metabolic surgery			†

*Recommended cut points for Asian American individuals (expert opinion). †Treatment may be indicated for select motivated patients.

Obesity Management for the Treatment of Type 2 Diabetes:
Standards of Medical Care in Diabetes - 2021. *Diabetes Care* 2021;44(Suppl. 1):S100-S10

Medication name	Typical adult maintenance dose	Average wholesale price (30-day supply) (118)	National Average Drug Acquisition Cost (30-day supply) (119)	Treatment arms	Weight loss (% loss from baseline)	Common side effects (120–124)	Possible safety concerns/ considerations (120–124)
				loss (% loss from baseline)			
Short-term treatment (£12 weeks)							
Sympathomimetic amine anorectic							
Phentermine (125)	8–37.5 mg q.d.*	$5–$46 (37.5 mg dose)	$3 (37.5 mg dose)	15 mg q.d.† 7.5 mg q.d.† PBO	6.1 5.5 1.2	Dry mouth, insomnia, dizziness, irritability, increased blood pressure, elevated heart rate	c Contraindicated for use in combination with monoamine oxidase inhibitors
Long-term treatment (>12 weeks)							
Lipase inhibitor							
Orlistat (3)	60 mg t.i.d. (OTC) 120 mg t.i.d. (Rx)	$412$82 $823	$41 $556	120 mg t.i.d.‡ PBO	9.6 5.6	Abdominal pain, flatulence, fecal urgency	c Potential malabsorption of fat-soluble vitamins (A, D, E, K) and of certain medications (e.g., cyclosporine, thyroid hormone, anticonvulsants, etc.) c Rare cases of severe liver injury reported c Cholelithiasis c Nephrolithiasis
Sympathomimetic amine anorectic/antiepileptic combination							
Phentermine/ topiramate ER (126)	7.5 mg/46 mg q.d.§	$223 (7.5 mg/ 46 mg dose)	$179 (7.5 mg/ 46 mg dose)	15 mg/92 mg q.d.‖ 7.5 mg/46 mg q.d.‖ PBO	9.8 7.8 1.2	Constipation, paresthesia, insomnia, nasopharyngitis, xerostomia, increased blood pressure	c Contraindicated for use in combination with monoamine oxidase inhibitors c Birth defects c Cognitive impairment c Acute angle-closure glaucoma
Opioid antagonist/antidepressant combination							
Naltrexone/ bupropion ER (15)	16 mg/180 mg b.i.d.	$334	$266	16 mg/180 mg b.i.d. PBO	5.0 1.8	Constipation, nausea, headache, xerostomia, insomnia, elevated heart rate and blood pressure	c Contraindicated in patients with uncontrolled hypertension and/or seizure disorders c Contraindicated for use with chronic opioid therapy c Acute angle-closure glaucoma Black box warning: c Risk of suicidal behavior/ideation in persons younger than 24 years old

Medication name	Typical adult maintenance dose	Average wholesale price (30-day supply) (118)	National Average Drug Acquisition Cost (30-day supply) (119)	Treatment arms	Weight loss (% loss from baseline)	Common side effects (120–12
Glucagon-like peptide 1 receptor agonist						
Liraglutide(16)**	3 mg q.d.	$1,557	$1,243	3.0 mg q.d. 1.8 mg q.d. PBO	6.0 4.7 2.0	Gastrointestinal side effect (nausea, vomiting, diarrhea esophagealreflux),injections reactions, elevated heart ra

Metabolic Surgery

8.16 Metabolic surgery should be recommended as an option to treat type 2 diabetes in screened surgical candidates with BMI ≥40 kg/m^2 (BMI ≥37.5 kg/m^2 in Asian Americans) and in adults with BMI 35.0–39.9 kg/m^2 (32.5— 37.4 kg/m^2 in Asian Americans) who do not achieve durable weight loss and improvement in comorbidities (including hyperglycemia) with nonsurgical methods.

8.17 Metabolic surgery may be considered as an option to treat type 2 diabetes in adults with BMI 30.0–34.9 kg/m2 (27.5–32.4 kg/m2 in Asian Americans) who do not achieve durable weight loss and improvement in comorbidities (including hyperglycemia) with nonsurgical methods. A

Section 9.

Pharmacologic Approaches to Glycemic Treatment

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Pharmacologic Therapy for Type 1 Diabetes

9.1 Most people with type 1 diabetes should be treated with multiple daily injections of prandial and basal insulin, or continuous subcutaneous insulin infusion. A

9.2 Most individuals with type 1 diabetes should use rapid-acting insulin analogs to reduce hypoglycemia risk. A

Pharmacologic Therapy for Type 2 Diabetes

9.4 **Metformin** is the **preferred initial** pharmacologic agent for the treatment of type 2 diabetes. A

9.5 Once initiated, metformin should be continued as long as it is tolerated and not contraindicated; other agents, including insulin, should be added to metformin. A

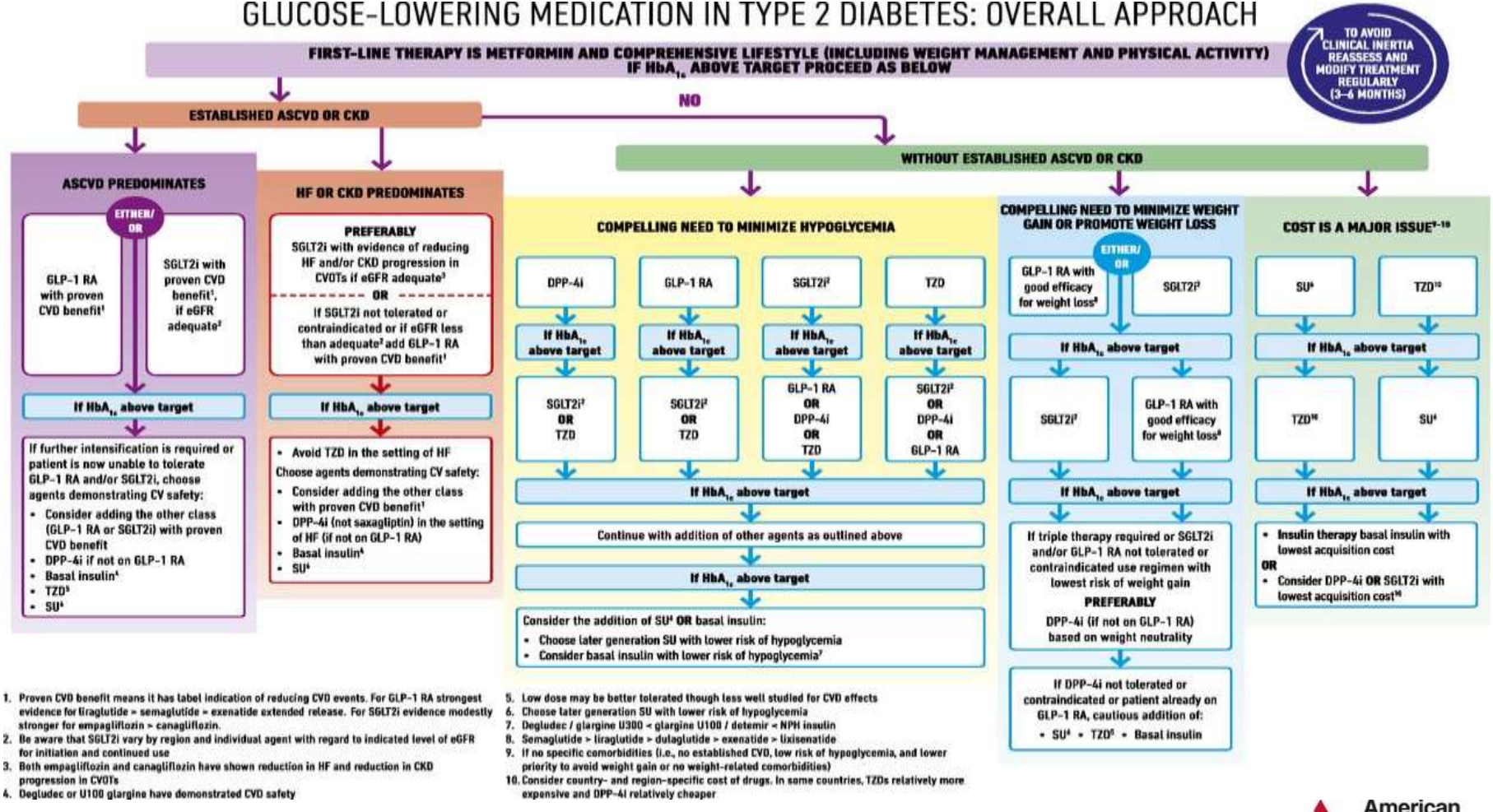
9.7 The early introduction of insulin should be considered if there is evidence of ongoing catabolism (weight loss), if symptoms of hyperglycemia are present, **or** when A1C levels (>10% [86 mmol/mol]) or blood glucose levels (≥300 mg/dL [16.7 mmol/L]) are very high. E

Pharmacologic Therapy for Type 2 Diabetes (continued)

9.8 Considerations include effect on **cardiovascular** and **renal comorbidities**, **efficacy, hypoglycemia risk**, impact on **weight, cost,** risk for **side effects**, and **patient preferences**E

9.9 Among patients with type 2 diabetes who have established atherosclerotic cardiovascular disease or indicators of high risk, established kidney disease, or heart failure, a **sodium–glucose cotransporter 2** inhibitor or glucagon-like peptide 1 receptor agonist with demonstrated cardiovascular disease benefit is recommended as part of the glucose-lowering regimen independent of A1C and in consideration of patient-specific factors.

GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH



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

Melanie J. Davies et al. Dia Care 2018;41:2669-2701

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CHOOSING GLUCOSE-LOWERING MEDICATION IN THOSE WITH ESTABLISHED ATHEROSCLEROTIC CARDIOVASCULAR DISEASE (ASCVD) OR CHRONIC KIDNEY DISEASE (CKD)

Use metformin unless contraindicated or not tolerated

If not at HbA_{1c} target:

- Continue metformin unless contraindicated (remember to adjust dose/stop metformin with declining eGFR)
- Add SGLT2i or GLP-1 RA with proven cardiovascular benefit[1] (see below)

If at HbA_{1c} target:

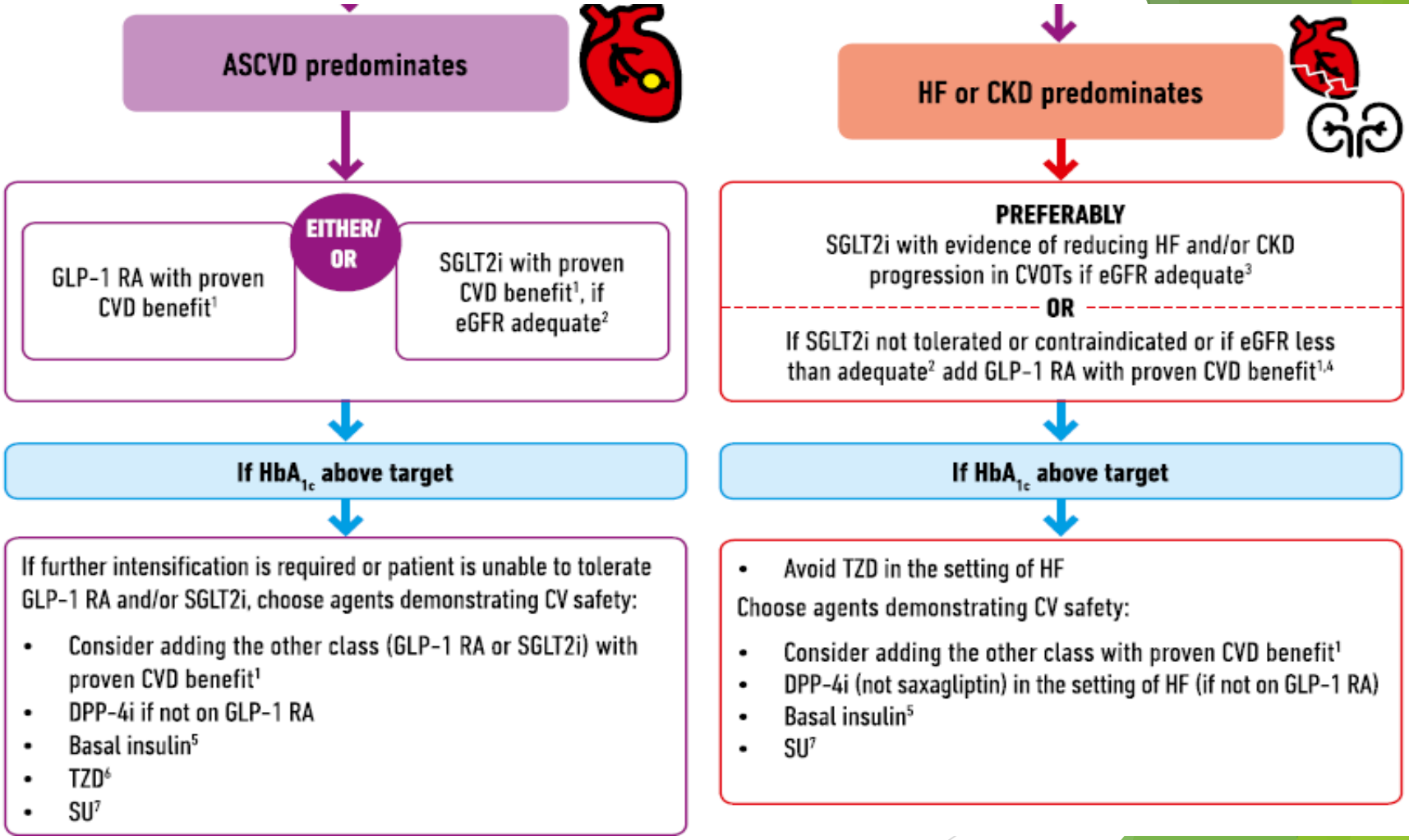
- If already on dual therapy, or multiple glucose-lowering therapies and not on an SGLT2i or GLP-1 RA, consider switching to one of these agents with proven cardiovascular benefit[1] (see below)

OR reconsider/lower individualized target and introduce SGLT2i or GLP-1 RA

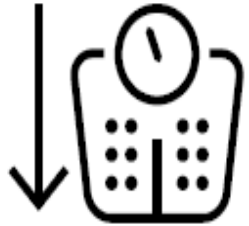
OR reassess HbA_{1c} at 3-month intervals and add SGLT2i or GLP-1 RA if HbA_{1c} goes above target

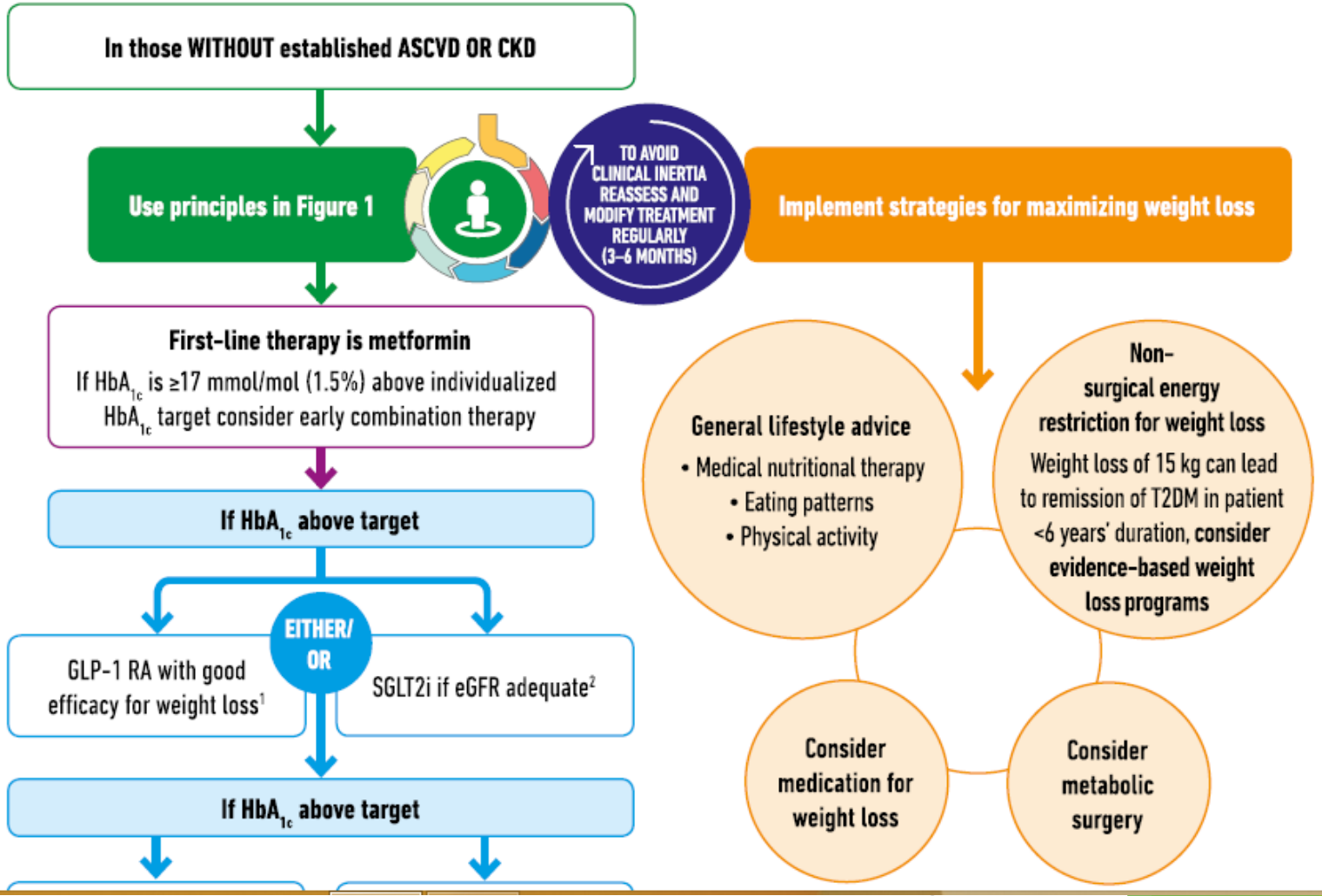
ASCVD predominates

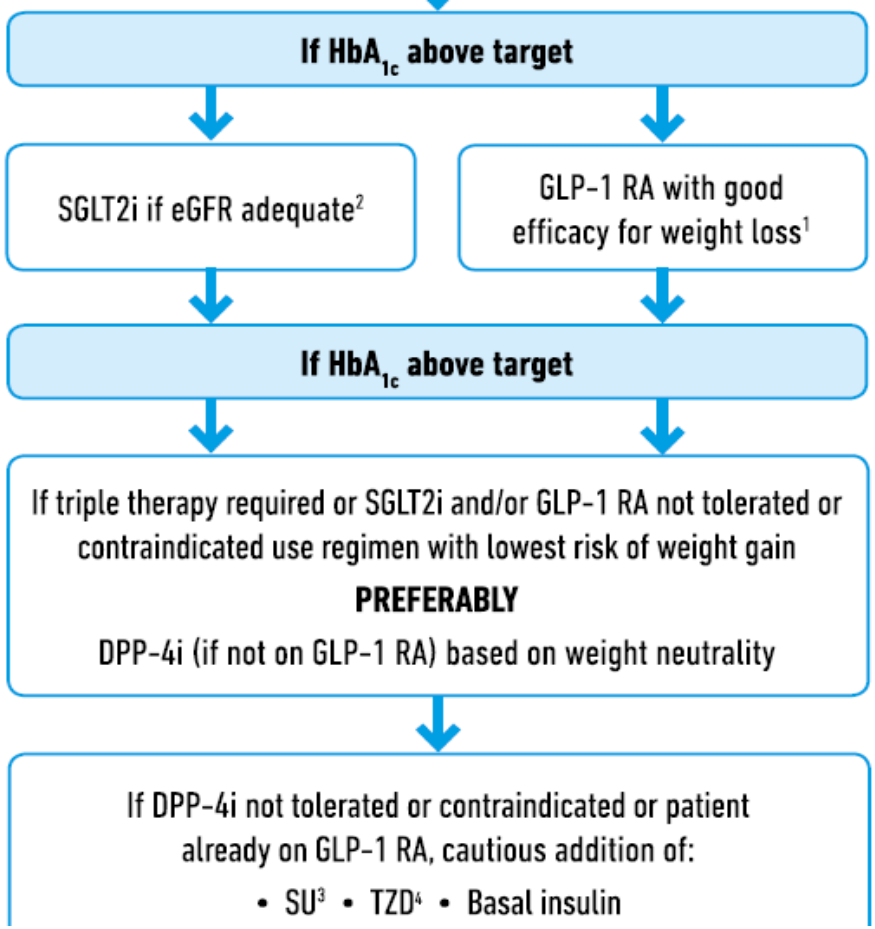
HF or CKD predominates


ASCVD predominates
GLP-1 RA with proven CVD benefit[1]
EITHER/ OR
SGLT2i with proven CVD benefit[1], if eGFR adequate[2]
If HbA1c above target
If further intensification is required or patient is unable to tolerate GLP-1 RA and/or SGLT2i, choose agents demonstrating CV safety:
• Consider adding the other class (GLP-1 RA or SGLT2i) with proven CVD benefit[1]
• DPP-4i if not on GLP-1 RA
• Basal insulin[5]
• TZD[6]
• SU[7]
HF or CKD predominates
PREFERABLY
SGLT2i with evidence of reducing HF and/or CKD progression in CVOTs if eGFR adequate[3]
OR
If SGLT2i not tolerated or contraindicated or if eGFR less than adequate[2] add GLP-1 RA with proven CVD benefit[1,4]
If HbA1c above target
• Avoid TZD in the setting of HF
Choose agents demonstrating CV safety:
• Consider adding the other class with proven CVD benefit[1]
• DPP-4i (not saxagliptin) in the setting of HF (if not on GLP-1 RA)
• Basal insulin[5]
• SU[7]

CHOOSING GLUCOSE-LOWERING MEDICATION IF COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS

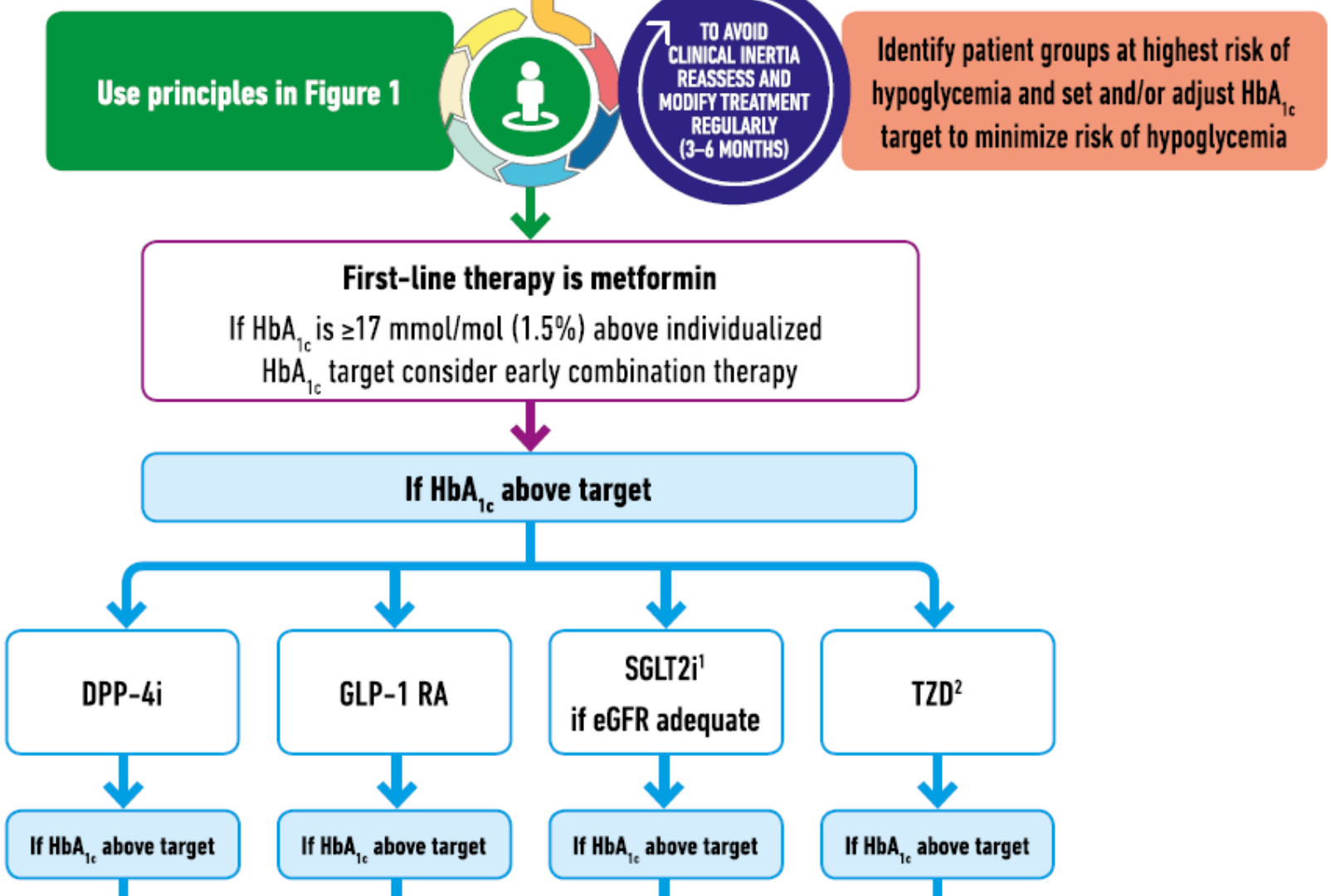


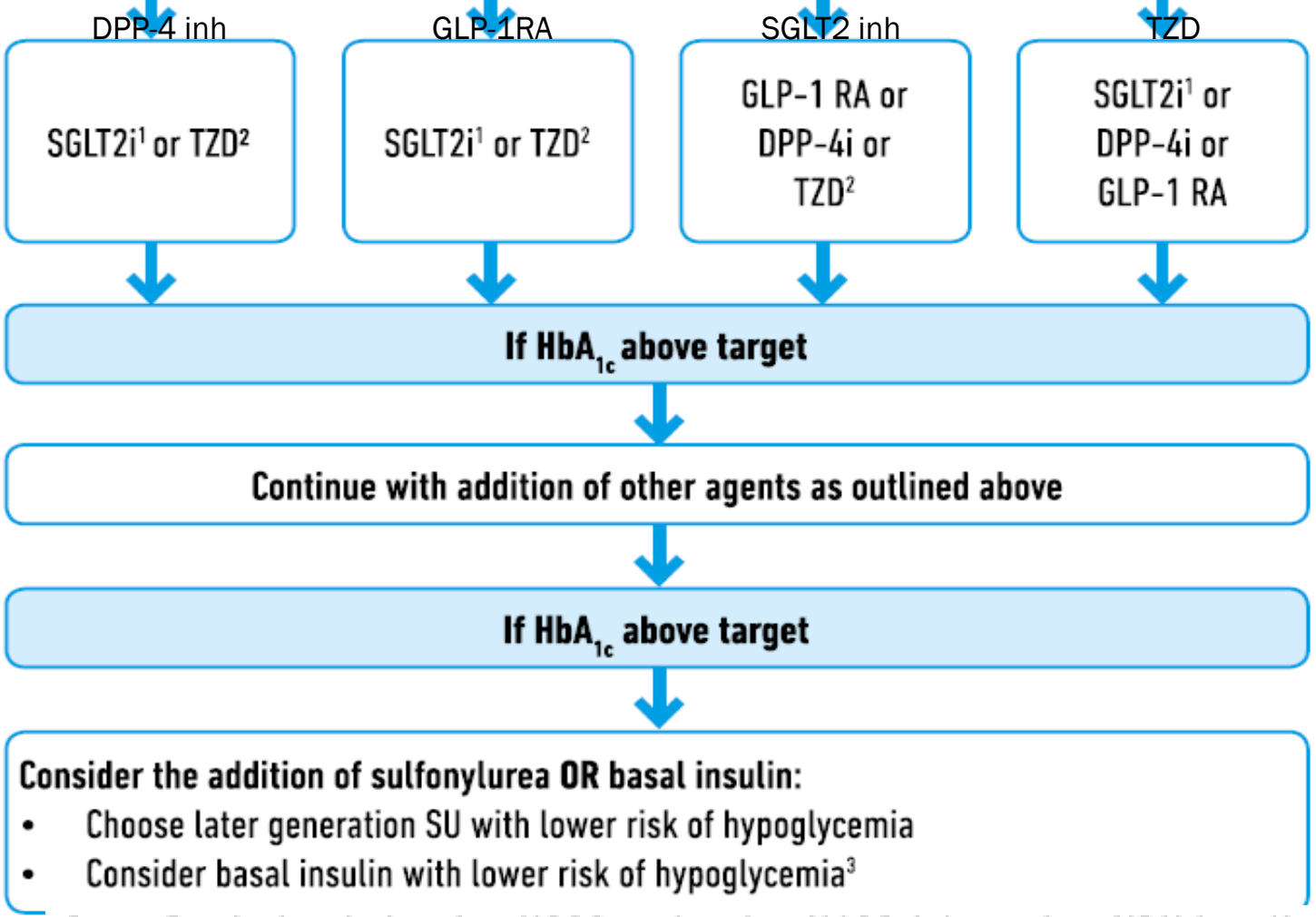

In those WITHOUT established ASCVD OR CKD
Use principles in Figure 1
TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)
Implement strategies for maximizing weight loss
First-line therapy is metformin
If HbA1c is ≥17 mmol/mol (1.5%) above individualized HbA1c target consider early combination therapy
If HbA1c above target
EITHER/ OR
GLP-1 RA with good efficacy for weight loss[1]
SGLT2i if eGFR adequate[2]
If HbA1c above target
General lifestyle advice
• Medical nutritional therapy
• Eating patterns
• Physical activity
Non-surgical energy restriction for weight loss
Weight loss of 15 kg can lead to remission of T2DM in patient <6 years' duration, consider evidence-based weight loss programs
Consider medication for weight loss
Consider metabolic surgery



1. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
2. Be aware that SGLT2i vary by region and individual agent with regard to indicated level of eGFR for initiation and continued use
3. Choose later generation SU with lower risk of hypoglycemia
4. Low dose may be better tolerated though less well studied for CVD effects

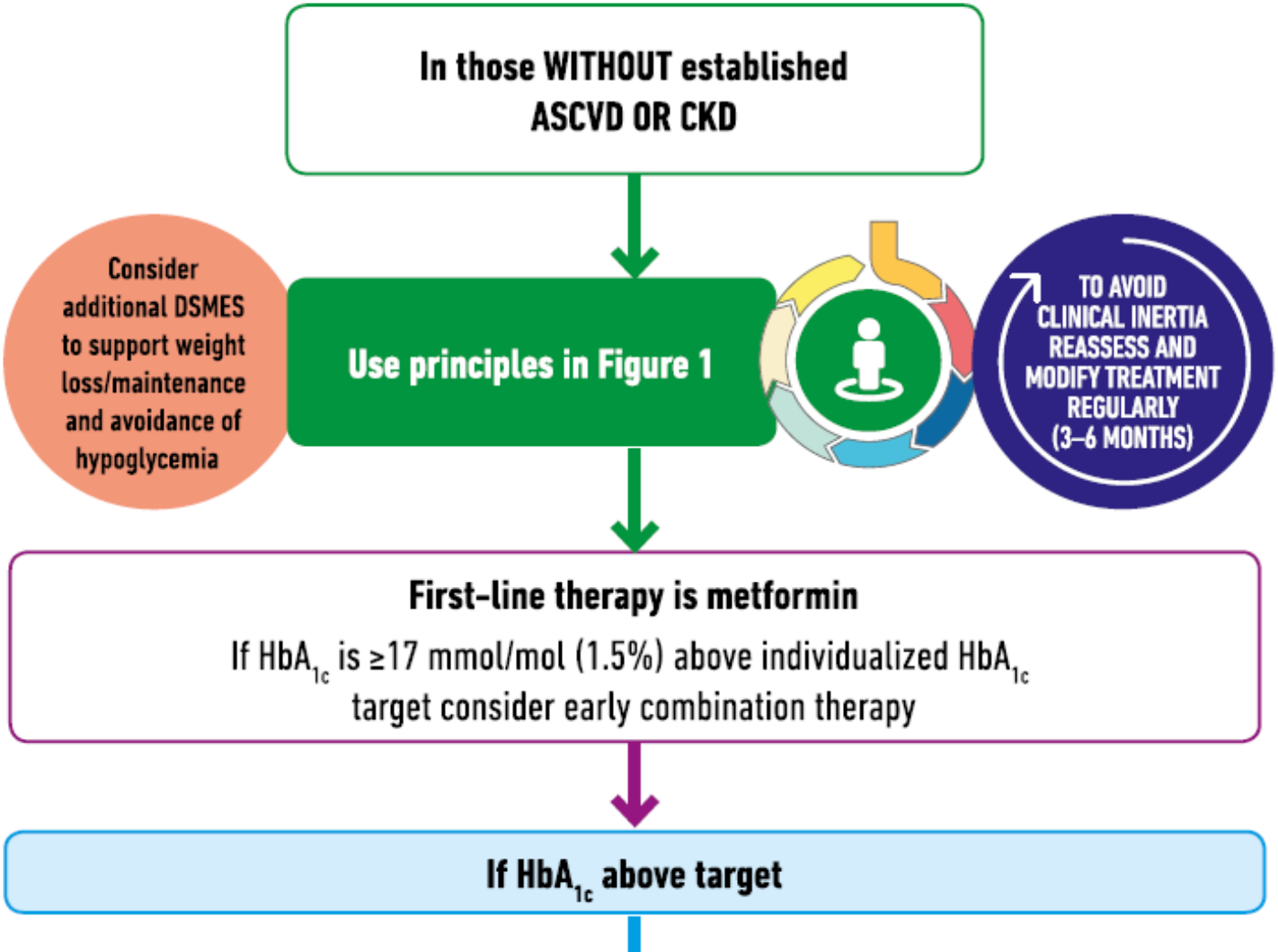
CHOOSING GLUCOSE-LOWERING MEDICATION IF COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA

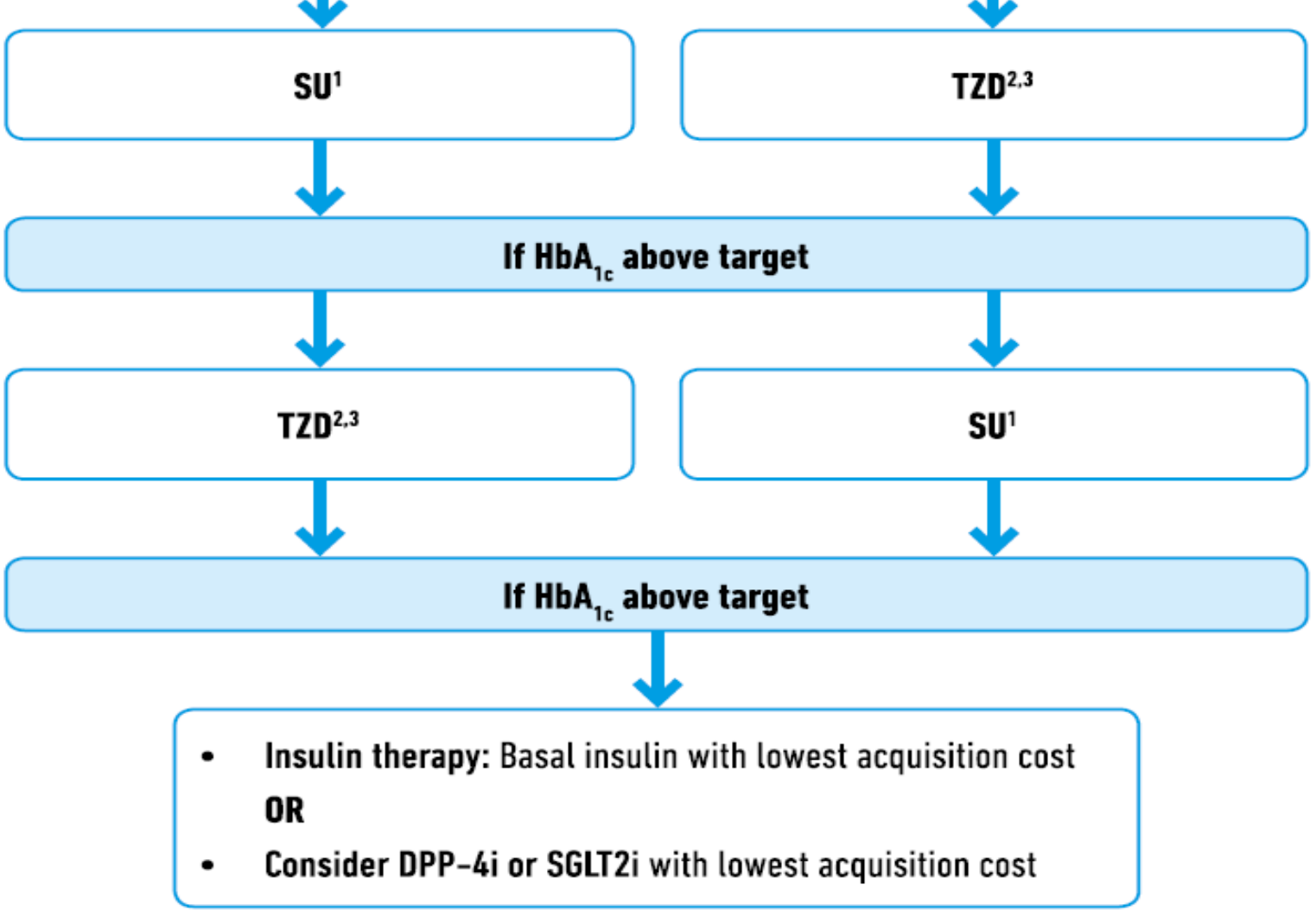

Use principles in Figure 1
TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)
Identify patient groups at highest risk of hypoglycemia and set and/or adjust HbA1c target to minimize risk of hypoglycemia
First-line therapy is metformin
If HbA1c is ≥17 mmol/mol (1.5%) above individualized HbA1c target consider early combination therapy
If HbA1c above target
DPP-4i
GLP-1 RA
SGLT2i[1] if eGFR adequate
TZD[2]
If HbA1c above target
If HbA1c above target
If HbA1c above target
If HbA1c above target

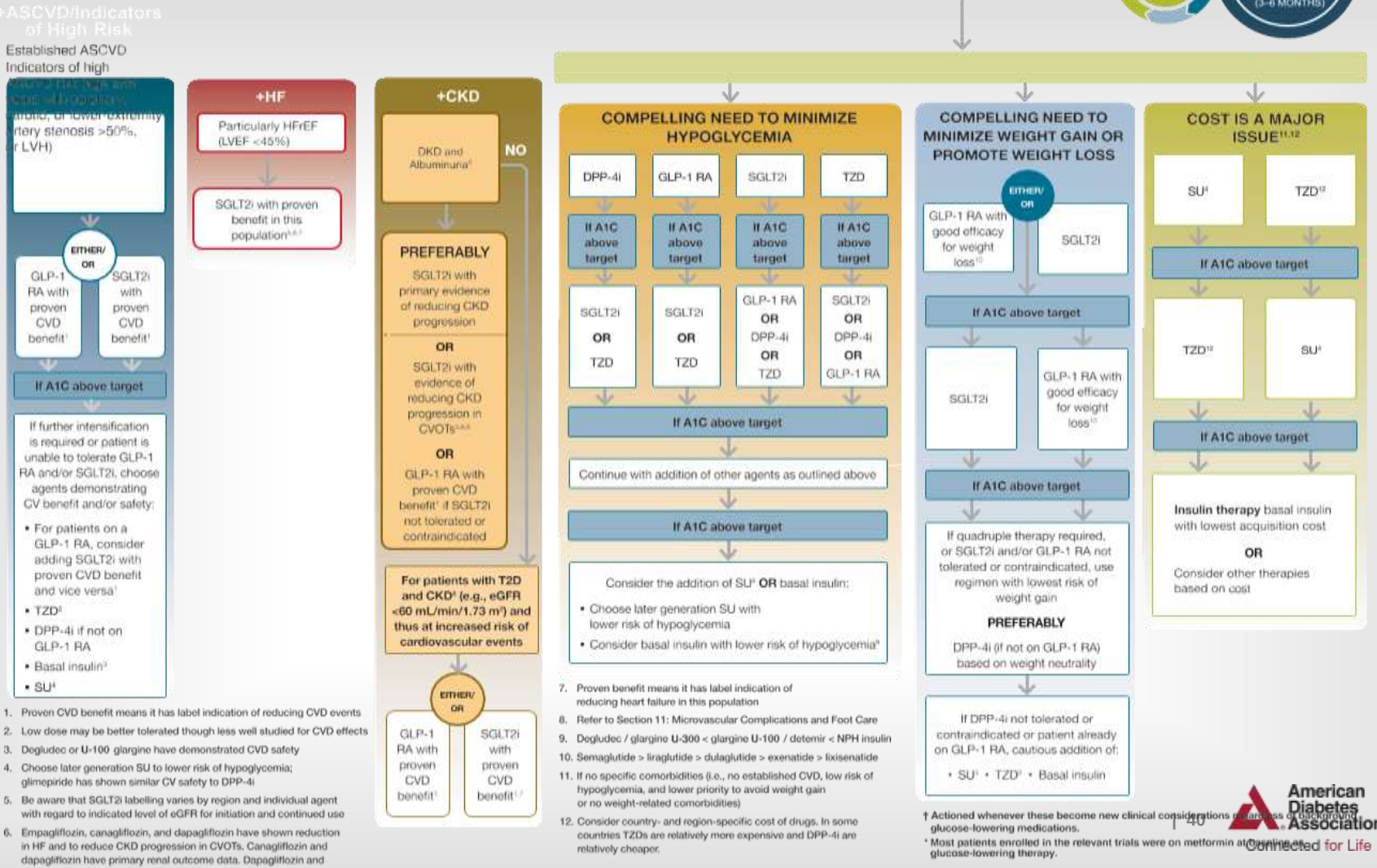


3. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin

CHOOSING GLUCOSE-LOWERING MEDICATION IF COST IS A MAJOR ISSUE


In those WITHOUT established ASCVD OR CKD
Consider additional DSMES to support weight loss/maintenance and avoidance of hypoglycemia
Use principles in Figure 1
TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)
First-line therapy is metformin
If HbA1c is ≥17 mmol/mol (1.5%) above individualized HbA1c target consider early combination therapy
If HbA1c above target

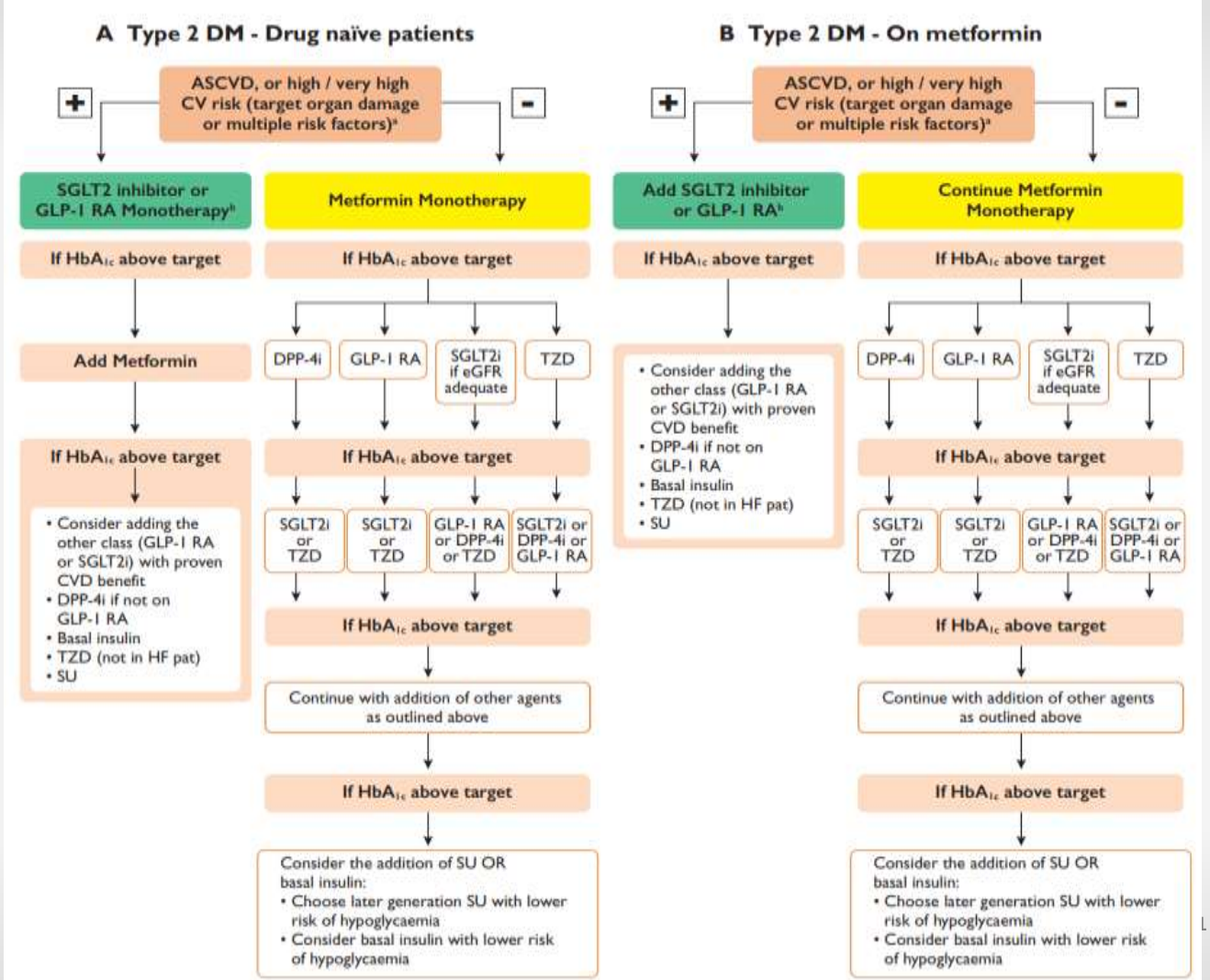

SU[1]
TZD[2,3]
If HbA1c above target
TZD[2,3]
SU[1]
If HbA1c above target
• Insulin therapy: Basal insulin with lowest acquisition cost
OR
• Consider DPP-4i or SGLT2i with lowest acquisition cost



1. Proven CVD benefit means it has label indication of reducing CVD events
2. Low dose may be better tolerated though less well studied for CVD effects
3. Degludec or U-100 glargine have demonstrated CVD safety
4. Choose later generation SU to lower risk of hypoglycemia; glimepiride has shown similar CV safety to DPP-4i
5. Be aware that SGLT2i labelling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use
6. Empagliflozin, canagliflozin, and dapagliflozin have shown reduction in HF and to reduce CKD progression in CVOTs. Canagliflozin and dapagliflozin have primary renal outcome data. Dapagliflozin and empagliflozin have primary heart failure outcome data.
7. Proven benefit means it has label indication of reducing heart failure in this population
8. Refer to Section 11: Microvascular Complications and Foot Care
9. Degludec / glargine U-300 < glargine U-100 / detemir < NPH insulin
10. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
11. 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)
12. Consider country- and region-specific cost of drugs. In some countries TZDs are relatively more expensive and DPP-4i are relatively cheaper.

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

* Most patients enrolled in the relevant trials were on metformin at baseline as glucose-lowering therapy.



ESC European Society of Cardiology

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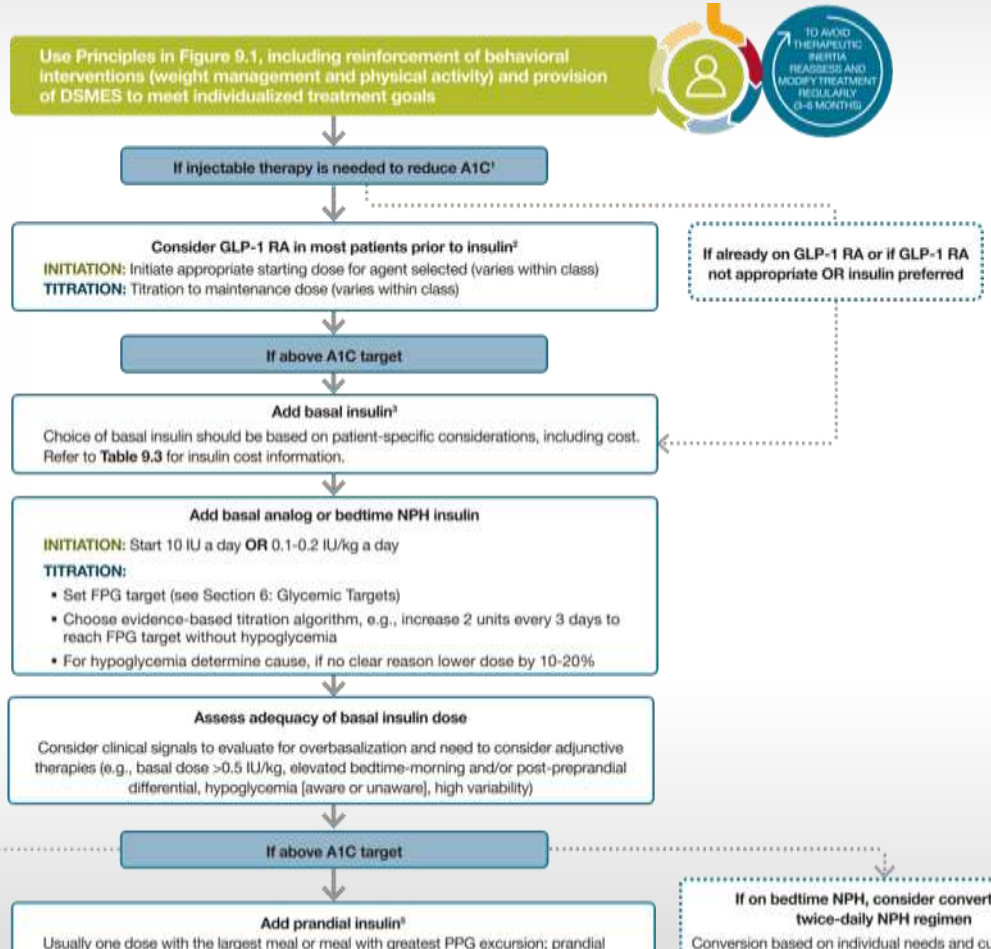

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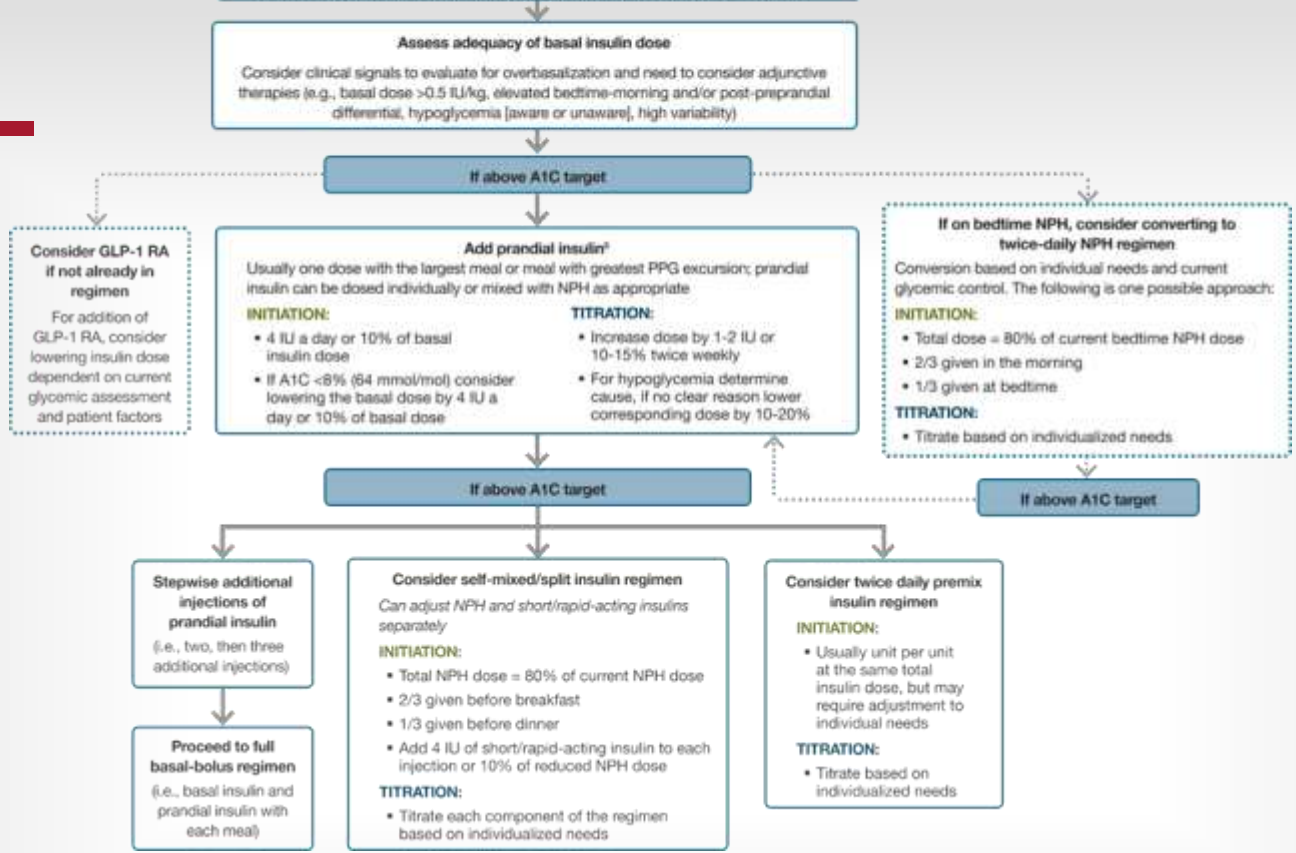

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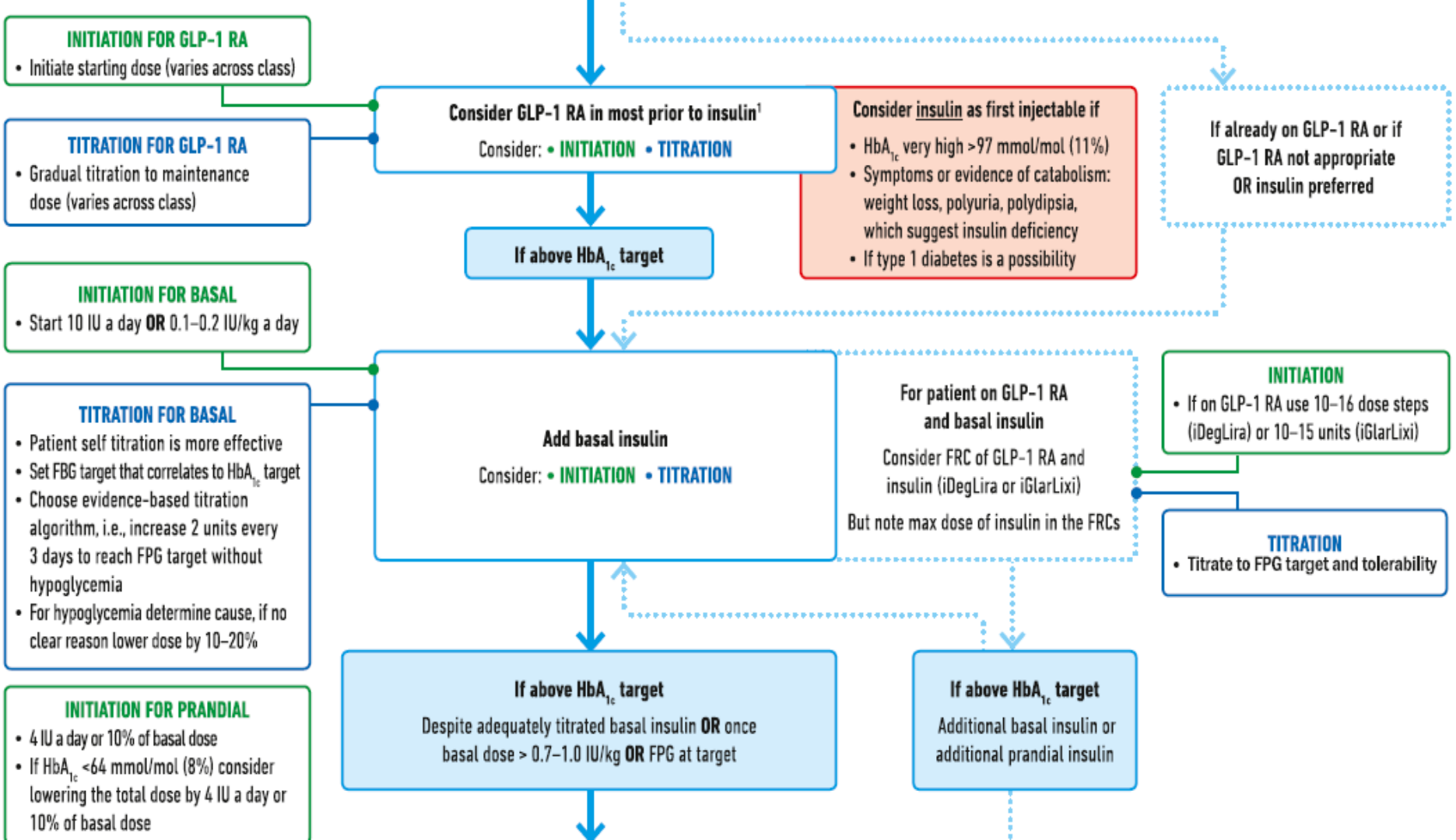
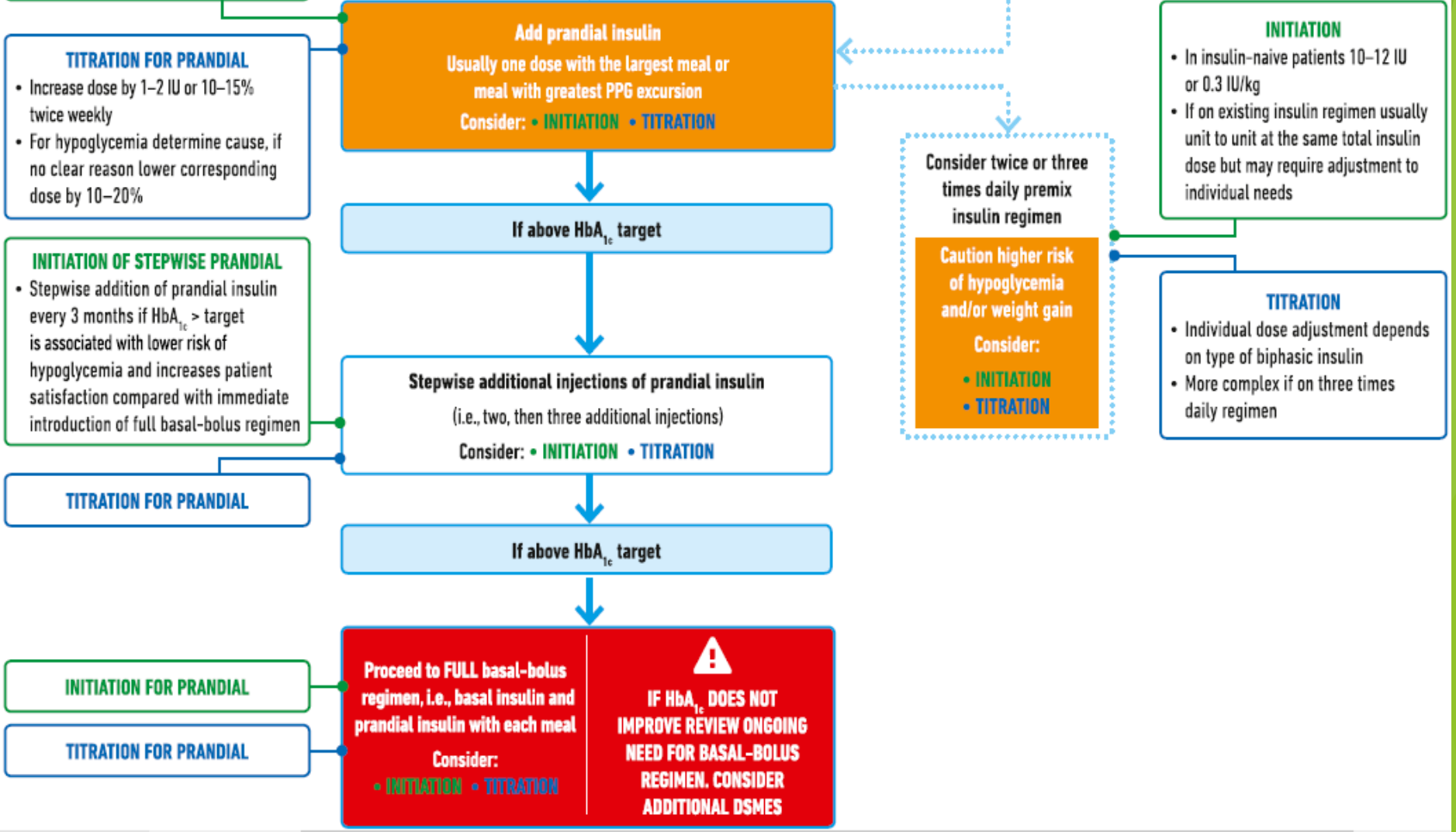
INTENSIFYING TO INJECTABLE THERAPIES


INITIATION FOR GLP-1 RA
• Initiate starting dose (varies across class)
TITRATION FOR GLP-1 RA
• Gradual titration to maintenance dose (varies across class)
Consider GLP-1 RA in most prior to insulin[1]
Consider: • INITIATION • TITRATION
Consider insulin as first injectable if
• HbA1c very high >97 mmol/mol (11%)
• Symptoms or evidence of catabolism: weight loss, polyuria, polydipsia, which suggest insulin deficiency
• If type 1 diabetes is a possibility
If already on GLP-1 RA or if GLP-1 RA not appropriate OR insulin preferred
If above HbA1c target
INITIATION FOR BASAL
• Start 10 IU a day OR 0.1–0.2 IU/kg a day
TITRATION FOR BASAL
• Patient self titration is more effective
• Set FBG target that correlates to HbA1c target
• Choose evidence-based titration algorithm, i.e., increase 2 units every 3 days to reach FPG target without hypoglycemia
• For hypoglycemia determine cause, if no clear reason lower dose by 10–20%
Add basal insulin
Consider: • INITIATION • TITRATION
For patient on GLP-1 RA and basal insulin
Consider FRC of GLP-1 RA and insulin (iDegLira or iGlarLixi)
But note max dose of insulin in the FRCs
INITIATION
• If on GLP-1 RA use 10–16 dose steps (iDegLira) or 10–15 units (iGlarLixi)
TITRATION
• Titrate to FPG target and tolerability
INITIATION FOR PRANDIAL
• 4 IU a day or 10% of basal dose
• If HbA1c <64 mmol/mol (8%) consider lowering the total dose by 4 IU a day or 10% of basal dose
If above HbA1c target
Despite adequately titrated basal insulin OR once basal dose > 0.7–1.0 IU/kg OR FPG at target
If above HbA1c target
Additional basal insulin or additional prandial insulin


Add prandial insulin
Usually one dose with the largest meal or meal with greatest PPG excursion
Consider: • INITIATION • TITRATION
TITRATION FOR PRANDIAL
• Increase dose by 1–2 IU or 10–15% twice weekly
• For hypoglycemia determine cause, if no clear reason lower corresponding dose by 10–20%
If above HbA1c target
INITIATION OF STEPWISE PRANDIAL
• Stepwise addition of prandial insulin every 3 months if HbA1c > target is associated with lower risk of hypoglycemia and increases patient satisfaction compared with immediate introduction of full basal-bolus regimen
Stepwise additional injections of prandial insulin
(i.e., two, then three additional injections)
Consider: • INITIATION • TITRATION
TITRATION FOR PRANDIAL
If above HbA1c target
INITIATION FOR PRANDIAL
TITRATION FOR PRANDIAL
Proceed to FULL basal-bolus regimen, i.e., basal insulin and prandial insulin with each meal
Consider:
• INITIATION • TITRATION
IF HbA1c DOES NOT IMPROVE REVIEW ONGOING NEED FOR BASAL-BOLUS REGIMEN. CONSIDER ADDITIONAL DSMES
Consider twice or three times daily premix insulin regimen
Caution higher risk of hypoglycemia and/or weight gain
Consider:
• INITIATION
• TITRATION
INITIATION
• In insulin-naive patients 10–12 IU or 0.3 IU/kg
• If on existing insulin regimen usually unit to unit at the same total insulin dose but may require adjustment to individual needs
TITRATION
• Individual dose adjustment depends on type of biphasic insulin
• More complex if on three times daily regimen

Section 10.

Cardiovascular Disease and Risk Management

American Diabetes Association.
Connected for Life

Screening and Diagnosis

10.1 Blood pressure should be measured at every routine clinical visit.

Patients found to have elevated blood pressure (≥140/90 mmHg) should have blood pressure confirmed using multiple readings, including measurements on a separate day, to diagnose hypertension. B

10.2 All hypertensive patients with diabetes should monitor their

2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD

Very high risk	Patients with DM **and** established CVD **or** other target organ damage[b] **or** three or more major risk factors[c] **or** early onset T1DM of long duration (>20 years)
High risk	Patients with DM duration ≥10 years without target organ damage plus any other additional risk factor
Moderate risk	Young patients (T1DM aged <35 years or T2DM aged <50 years) with DM duration <10 years, without other risk factors

CV = cardiovascular; CVD = cardiovascular disease; DM = diabetes mellitus; T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus.

[a]Modified from the 2016 European Guidelines on cardiovascular disease prevention in clinical practice.[27]

[b]Proteinuria, renal impairment defined as eGFR <30 mL/min/1.73 m^2, left ventricular hypertrophy, or retinopathy.

[c]Age, hypertension, dyslipidemia, smoking, obesity.

Treatment Goals

10.4 For individuals with diabetes and hypertension at higher cardiovascular risk (existing atherosclerotic cardiovascular disease [ASCVD] or 10-year ASCVD risk ≥15%), a blood pressure target of, 130/80 mmHg may be appropriate, if it can be safely attained. C

10.5 For individuals with diabetes and hypertension at lower risk for cardiovascular disease (10-year atherosclerotic cardiovascular disease risk <15%), treat to a blood pressure target of <140/90 mmHg. A

Treatment Goals (continued)

10.6 In pregnant patients with diabetes and preexisting hypertension, a blood pressure target of 110–135/85mmHgis suggested in the interest of reducing the risk for accelerated maternal hypertension **A** and minimizing impaired fetal growth. E

- It may be reasonable to target blood pressure ,130/80 mmHg among patients with diabetes and either clinically diagnosed cardiovascular disease (particularly stroke, which was significantly reduced in ACCORD BP) or 10-year ASCVD risk >15%, if it can be attained safely.

- This approach is consistent with guidelines from the American College of Cardiology/American Heart Association, which advocate a blood pressure target ,130/80 mmHg for all patients, with or without diabetes

- older age
- chronic kidney disease
- higher risk of adverse effects of intensive blood pressure control.
- orthostatic hypotension
- substantial comorbidity
- polypharmacy
- some patients may prefer higher blood pressure targets to enhance quality of life.
- Patients with low absolute cardiovascular risk (10- year ASCVD risk <15%)
- a history of adverse effects of intensive blood pressure control

Treatment Strategies—Lifestyle Intervention

10.7 For patients with **blood pressure >120/80** mmHg, lifestyle intervention **consists of weight loss** when indicated, a **Dietary Approaches** to Stop Hypertension (DASH)-style eating pattern including **reducing sodium and increasing potassium** intake, **moderation of alcohol intake**, and **increased physical activity**. A

Treatment Strategies—Pharmacologic Interventions

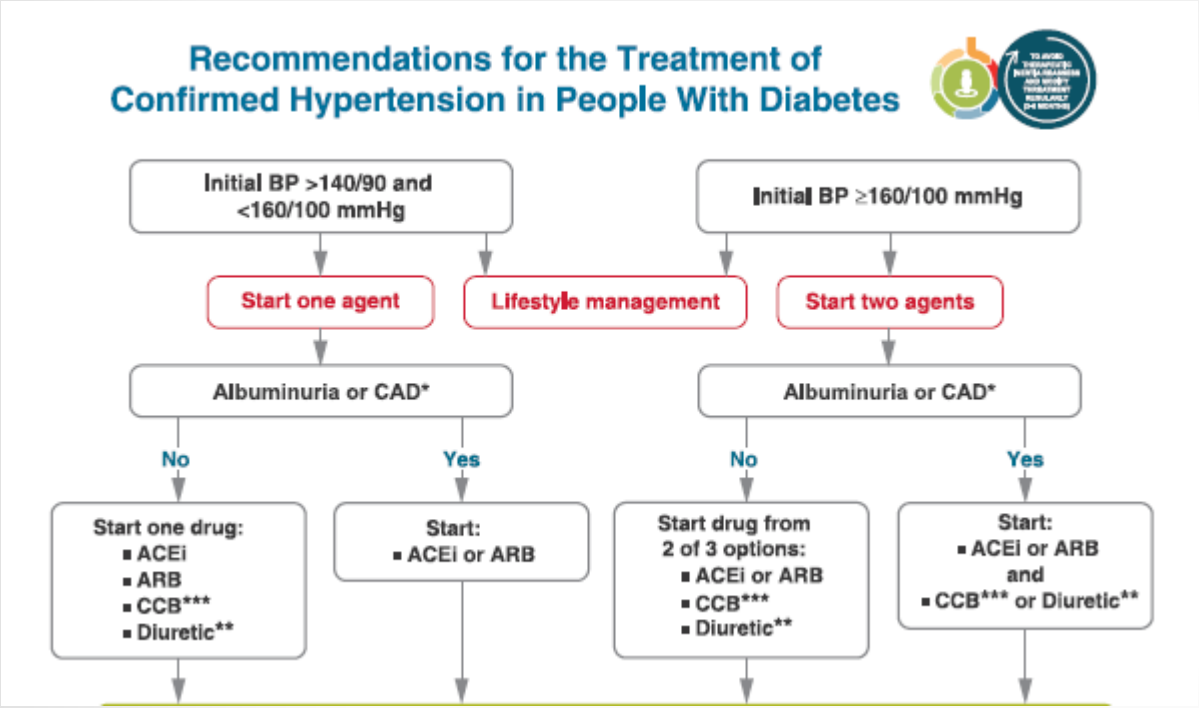
10.8 Patients with confirmed office-based blood pressure ≥140/90 mmHg should, in addition to lifestyle therapy, have prompt initiation and timely titration of pharmacologic therapy to achieve blood pressure goals. A

10.9 Patients with confirmed office based blood pressure ≥160/100 mmHg should, in addition to lifestyle therapy, have prompt initiation and timely titration of two drugs or a single-pill combination of drugs demonstrated to reduce cardiovascular events in patients with diabetes. A

10.10 **A** ACE inhibitors or angiotensin receptor blockers are recommended **first-line** therapy for **hypertension** in people **with diabetes** and **coronary artery disease**. A

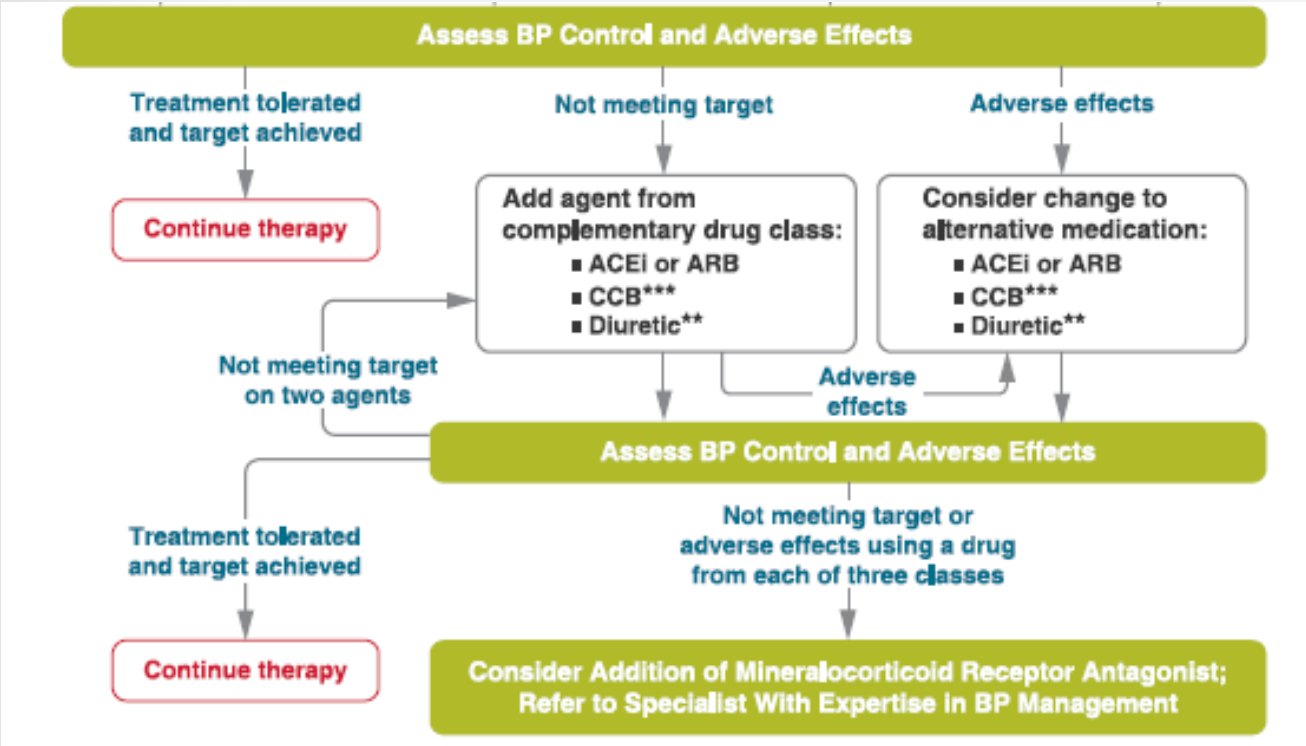
Treatment Strategies—Resistant Hypertension

10.14 Patients with hypertension who are not meeting blood pressure targets on three classes of antihypertensive medications (including a diuretic) should be considered for mineralocorticoid receptor antagonist therapy. B



Recommendations for the Treatment of Confirmed Hypertension in People with Diabetes (1 of 2)

Cardiovascular Disease and Risk Management:
Standards of Medical Care in Diabetes - 2021. *Diabetes Care* 2021;44(Suppl. 1):S111-S150



Recommendations for the Treatment of Confirmed Hypertension in People with Diabetes (2 of 2)

Cardiovascular Disease and Risk Management:
Standards of Medical Care in Diabetes - 2021. *Diabetes Care* 2021;44(Suppl. 1):S111-S150

Lipid Management—Lifestyle Intervention

10.15 Lifestyle modification focusing on weight loss (if indicated); application of a Mediterranean style or Dietary Approaches to Stop Hypertension (DASH) eating pattern; reduction of saturated fat and trans fat; increase of dietary viscous fiber, and increased physical activity should be recommended to improve the lipid profile and reduce the risk of developing atherosclerotic cardiovascular disease in patients with diabetes. A

10.16 Intensify **lifestyle therapy** and optimize **glycemic control** for patients with elevated triglyceride levels (≥150 mg/dL [1.7 mmol/L]) and/or low HDL cholesterol (<40 mg/dL [1.0 mmol/L] for men, <50 mg/dL [1.3 mmol/L] for women) C

Statin Treatment—Primary Prevention

10.19 For patients with diabetes aged 40–75 years **without atherosclerotic cardiovascular disease**, use moderate-intensity statin therapy in addition to lifestyle therapy. A

10.20 For patients with diabetes aged 20–39 years with **additional atherosclerotic** cardiovascular disease risk factors, it maybe reasonable to initiate statin therapy in addition to lifestyle therapy. C

10.21 In patients with diabetes at higher risk, especially those with multiple atherosclerotic cardiovascular disease risk factors or aged 50–70 years, it is reasonable to use high-intensity statin therapy. B

10.22 In adults with diabetes and **10-year ASCVD risk of 20%** or higher, it may be reasonable to add **ezetimibe to maximally tolerated statin** therapy to reduce **LDL cholesterol levels by 50% or more.** C

Statin Treatment—Secondary Prevention

10.23 For patients of all ages with diabetes and atherosclerotic cardiovascular disease, high intensity statin therapy should be added to lifestyle therapy. A

10.24 For patients with diabetes and atherosclerotic cardiovascular disease considered very high risk using specific criteria, if LDL cholesterol is ≥70 mg/dL on maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor). A Ezetimibe may be preferred due to lower cost.

10.25 For patients who do not tolerate the intended intensity, the maximally tolerated statin dose should be used. E

Statin Treatment—Secondary Prevention (continued)

10.26 In adults with diabetes aged >75 years already on statin therapy, it is reasonable to continue statin treatment. B

10.27 In adults with diabetes aged >75 years, it may be reasonable to initiate statin therapy after discussion of potential benefits and risks. C

10.28 Statin therapy is contraindicated in pregnancy. B

Treatment of Other Lipoprotein Fractions or Targets

10.29 For patients with **fasting triglyceride levels ≥500 mg/dL**, evaluate for secondary causes of hypertriglyceridemia and consider medical therapy to reduce the risk of pancreatitis. C

10.30 In adults with moderate hypertriglyceridemia (fasting or nonfasting triglycerides **175–499** mg/dL),clinicians should address and treat lifestyle factors (obesity and metabolic syndrome), secondary factors (diabetes, chronic liver or kidney disease and/or nephrotic syndrome, hypothyroidism), and medications that raise triglycerides. C

10.31 In patients with atherosclerotic cardiovascular disease or other cardiovascular risk factors on a statin with controlled LDL cholesterol but elevated triglycerides (135–499 mg/dL), the addition of **icosapent ethyl** can be considered to reduce cardiovascular risk . A

Other Combination Therapy

10.32 Statin plus fibrate combination therapy has not been shown to improve atherosclerotic cardiovascular disease outcomes and is generally not recommended. A

10.33 Statin plus niacin combination therapy has not been shown to provide additional cardiovascular benefit above statin therapy alone, may increase the risk of stroke with additional side effects, and is generally not recommended. A

Antiplatelet Agents

10.34 Use aspirin therapy (75–162 mg/day) as a **secondary prevention** strategy in those with diabetes and a history of atherosclerotic cardiovascular disease. A

10.35 For patients with atherosclerotic cardiovascular disease and documented **aspirin allergy**, clopidogrel (75 mg/day) should be used. B

10.36 Dual antiplatelet therapy (with low-dose aspirin and a P2Y12 inhibitor) is reasonable for a year after an acute coronary syndrome and may have benefits beyond this period. A

10.37 **Long-term** treatment with dual antiplatelet therapy should be considered for patients with **prior coronary intervention**, high ischemic risk, and **low bleeding risk** to prevent major adverse cardiovascular events. A

Antiplatelet Agents (continued)

10.38 Combination therapy with **aspirin plus low-dose rivaroxaban** should be considered for patients with **stable coronary** and/or **peripheral artery disease** and **low bleeding risk** to prevent **major adverse limb and cardiovascular** events. A

10.39 Aspirin therapy (75–162 mg/day) may be considered as a **primary prevention** strategy in those with diabetes who are at increased cardiovascular risk, after a comprehensive discussion with the patient on the benefits versus the comparable increased risk of

Recommendations for using aspirin as primary prevention include both men and women aged >50 years with diabetes and at least one additional major risk factor (family history of premature ASCVD, hypertension, dyslipidemia, smoking, or chronic kidney disease/ albuminuria) who are not at increased risk of bleeding (e.g., older age, anemia, renal disease) .

Noninvasive imaging techniques such as coronary calcium scoring may potentially help further tailor aspirin therapy, particularly in those at low risk

For patients over the age of 70 years (with or without diabetes), the balance appears to have greater risk than benefit.

Thus, for primary prevention, the use of aspirin needs to be carefully considered and may generally not be recommended

Cardiovascular Disease—Screening

10.40 In asymptomatic patients, routine screening for coronary artery disease is not recommended as it does not improve outcomes as long as atherosclerotic cardiovascular disease risk factors are treated. A

10.41 Consider **investigations for coronary artery disease** in the presence of any of the following:

atypical cardiac symptoms (e.g., unexplained dyspnea, chest discomfort);

signs or symptoms of associated vascular disease including carotid bruits,

transient ischemic attack,

stroke,

claudication,

or peripheral arterial disease; or

electrocardiogram abnormalities (e.g., Q waves).E

Cardiovascular Disease—Treatment

10.42a In patients with type 2 diabetes and established atherosclerotic cardiovascular disease, multiple atherosclerotic cardiovascular disease risk factors, or diabetic kidney disease, a sodium–glucose cotransporter 2 inhibitor with demonstrated cardiovascular benefit is recommended to reduce the risk of major adverse cardiovascular events and/or heart failure

10.42b In patients with type 2 diabetes and established atherosclerotic cardiovascular disease or multiple risk factors for atherosclerotic cardiovascular disease, a glucagon-like peptide 1 receptor agonist with demonstrated cardiovascular benefit is recommended to reduce the risk of major adverse cardiovascular events. A

Cardiovascular Disease—Treatment (continued)

10.43 In patients with type 2 diabetes and established heart failure with reduced ejection fraction, a sodium–glucose cotransporter 2 inhibitor with proven benefit in this patient population is recommended to reduce risk of worsening heart failure and cardiovascular death. A

10.44 In patients with known atherosclerotic cardiovascular disease, particularly coronary artery disease**, ACE inhibitor or angiotensin receptor** blocker therapy is recommended to reduce the risk of cardiovascular events. A

10.45 In patients with prior myocardial infarction, b-blockers should be continued for 3 years after the event. A

Cardiovascular Disease—Treatment (continued)

10.46 Treatment of patients with heart failure with reduced ejection fraction should include a b-blocker with proven cardiovascular outcomes benefit, unless otherwise contraindicated. A

10.47 In patients with type 2 diabetes with stable heart failure, metformin may be continued for glucose lowering if estimated glomerular filtration rate remains .30 mL/min/1.73m2 but should be avoided in unstable or hospitalized patients with heart failure. B

Clinical Scenario

- A 50 year old male comes to see you for diabetes review. He has had type 2 diabetes for 5 years and hypertension for 2 years. He is also smoker (20 packs/year). There is no report of typical or atypical cardiovascular symptoms.

- He is taking MFN 2g /daily , Sitagliptin 100 mg/daily, Atorvastatin 20 mg /daily, Captopril 50 mg/daily,

- BMI = 31 Kg/m^2

- BP= 135/80 mmHg

Clinical Scenario…

- HbA1c 7.8 %, eGFR= 65 ml/min/1.73 m^2, TG= 210 mg/dl, HDL=38 mg/dl, LDL= 65 mg/dl

- 24 uriary albumin excretion= 75 mg

- No retinopathy was detected

Impact of glucose-lowering drugs on heart failure

Drugs that can worsen HF
Insulin
SUs
Thiazolidinediones
DPP-4 inhibitors
Drugs that have no effect on HF
α-Glucosidase inhibitors
GLP-1 receptor agonists
Drugs that may prevent or ameliorate HF
Metformin
SGLT2 inhibitors

Abbreviations: DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide-1; HF, heart failure; SGLT2, sodium-glucose co-transporter-2; SU, sulphonylurea; TZD, thiazolidinedione.