LONG-TERM MANAGEMENT OF TYPE 2 DM

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CASE

- M 47Y Married barber
- PH: Appendectomy in 1395
- FH: DM in her mother
- SH: He is living with her wife & 2 daughter, No smoker
- PE: BP: 110/60 mmHg, PR: 68/min, RR: 18/min, T: 36˚c , BMI: 29
- WC :102cm
- Others: Nr

Lab data

Lab	First
WBC	5600
Hgb	16
PLT	198000
FBS mg/dL	114
BUN mg/dL	15
Cr mg/dL	0.9
eGFR ml/min/1.73m^2	101
U/A	Nr

Lab	First
Cho mg/dL	226
TG mg/dL	197
HDL mg/dL	54
LDL mg/dL	129
K mEq/L	4.2
HbA1C	6.1%
ALT	34

DM2 PREVENTION & CVD APPROACH

- In people with prediabetes :
  - DM2 prevention:
    - Life style management:
    - Drugs
  - CVD risk score

(Identify & treat cardiovascular disease risk factors)

LIFESTYLE THERAPY

- Medical nutrition therapy
- Regular physical activity
- Sufficient amounts of sleep
- Behavioral support
- Smoking cessation & avoidance of all tobacco products.

THE ACC/AHA ASCVD RISK CALCULATOR

- **Age***
- **Sex***
- **Race***
- **SBP***
- **DBP***
- **Total cholesterol***
- **HDL***
- **LDL++**
- **History of DM***
- **Smoker *(current, former, never)**
- **On HTN treatment***
- **On statin++**
- **On ASA++**
- Low-risk (<5%)
  Borderline risk (5% to 7.4%)
  Intermediate risk (7.5% to 19.9%)
  High risk (≥20%)

* Indicates a field required to calculate current 10-year ASCVD risk for patients age 40-79 or Lifetime risk for patients age 20-59.

tools.acc.org/ASCVD-Risk-EstimatorPlus

AMERICAN COLLEGE of CARDIOLOGY

ASCVD Risk Estimator Plus

Estimate Risk | **Therapy Impact**

2.2% Low — **Current 10-Year ASCVD Risk****

Lifetime ASCVD Risk: **46%** Optimal ASCVD Risk: **1.5%**

Value must be between 130 - 320

Value must be between 20 - 100

Value must be between 30-300

History of Diabetes? *

Yes | ✔ No

Smoker? *

Current | Former | ✔ Never

On Hypertension Treatment? *

Yes | ✔ No

On a Statin?

Yes | ✔ No

On Aspirin Therapy?

Yes | ✔ No

Do you want to refine current risk estimation using data from a previous visit?

Yes | ✔ No

Insulin Resistance Intervention after Stroke

IRIS Trial

DM prevention and risk of recurrent stroke and MI

IRIS Trial

- In the new analysis, progression to diabetes-a pre specified secondary end point of IRIS -occurred in 3.8% of the 1939 individuals randomized to 45 mg/day of pioglitazone compared with 7.7% of the 1937 receiving placebo, a significant 52% reduction in the time to DM onset ($P < .0001$).

IRIS Trial

- The main IRIS finding- that pioglitazone reduced by a significant **24%** the risk for recurrent stroke or MI in people with insulin resistance, no frank DM, & a recent history of stroke or TIA were presented earlier this year at the International Stroke Conference 2016 & simultaneously published in the *New England Journal of Medicine*.

Pioglitazone Slows Progression to Type 2 Diabetes

نسخه ۱

Rx

1.Tab Pioglitazone 15 mg

روزی 1 عدد **N: 100/---**

OR

1.Tab Metformin 500 mg

روزی 1 عدد با نهار **N: 100/---**

CASE
AFTER 4YS:

51Y, Activity: Moderate

FH CAD: Negative

PE: BP: 125/80 mmHg, PR: 78/min, RR: 18/min, T: 36˚c, BMI: 32 , WC:105 cm

Others & foot exam: Normal

Lab data

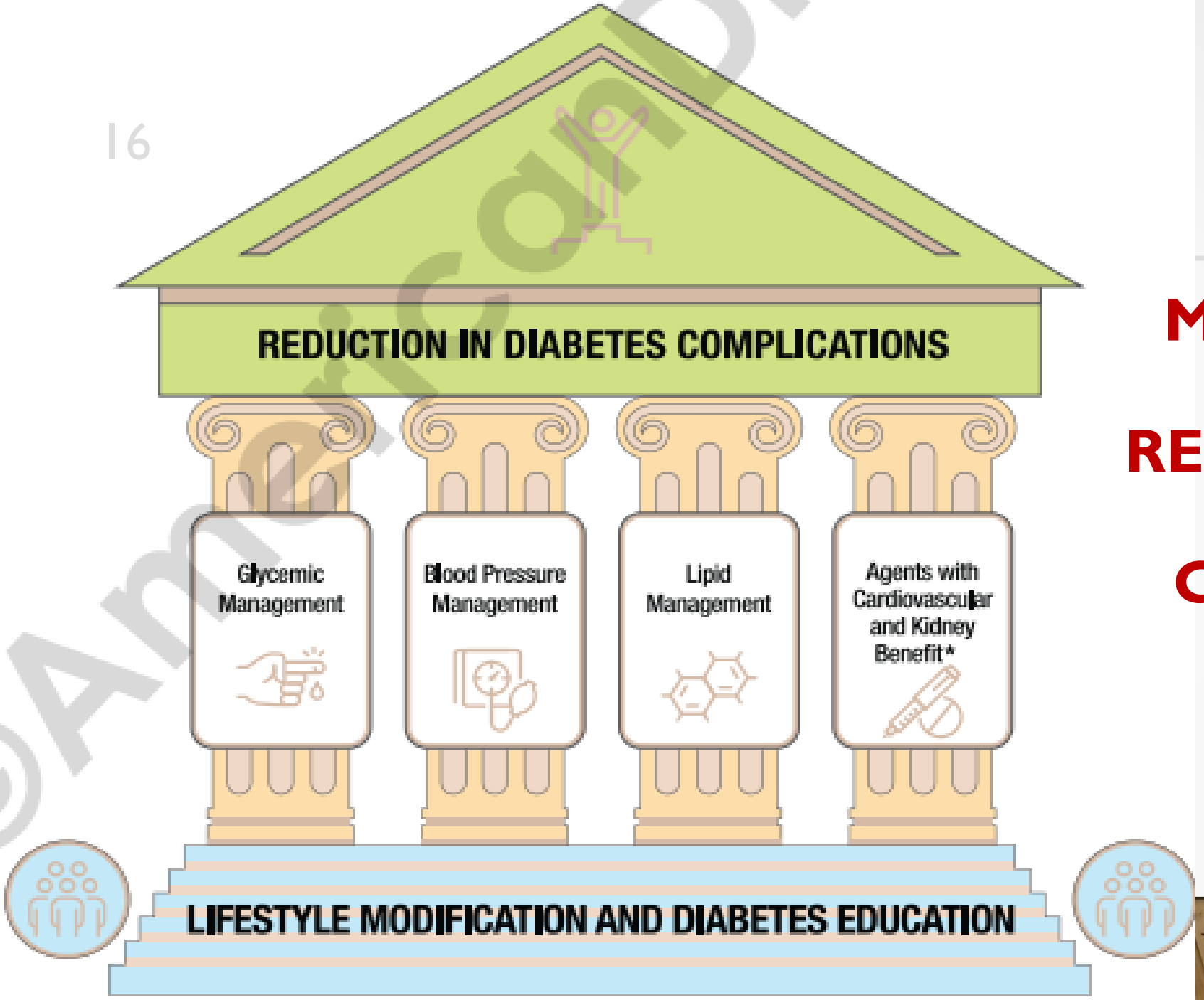
Lab	First	After 4 ys
WBC	5600	6200
Hgb	16	17
PLT	198000	223000
FBS	114	132
BUN	15	17
Cr	0.9	1
eGFR	101	87
ACR	-	23

Lab	First	After 4 ys
Cho	226	234
TG	197	211
HDL	54	45
LDL	129	134
K	4.2	4.1
U/A	Nr	Nr
HbA1C	6.1%	7.2%
ALT	34	35

OUTPATIENT MANAGEMENT:

- **Lifestyle modification**
- **Lipid management**
- **Bp control**
- **No smoking**
- **Glycemic control**
- **ASCVD risk stratification**

MULTIFACTORIAL APPROACH TO REDUCTION IN RISK OF DIABETES COMPLICATIONS



medical evaluation at initial, follow-up, and annual visits

		INITIAL VISIT	FOLLOW-UP VISIT	ANNUAL VISIT
PHYSICAL EXAMINATION	▪ Height, weight, and BMI; growth/pubertal development in children and adolescents	✓	✓	✓
	▪ Blood pressure determination	✓	✓	✓
	▪ Orthostatic blood pressure measures (when indicated)	✓		
	▪ Fundoscopic examination (refer to eye specialist)	✓		✓
	▪ Thyroid palpation	✓		✓
	▪ Skin examination (e.g., acanthosis nigricans, insulin injection or insertion sites, lipodystrophy)	✓	✓	✓
	▪ Comprehensive foot examination			
	• Visual inspection (e.g., skin integrity, callous formation, foot deformity or ulcer, toenails)**	✓		✓
	• Screen for PAD (pedal pulses—refer for ABI if diminished)	✓		✓
	• Determination of temperature, vibration or pinprick sensation, and 10-g monofilament exam	✓		✓
	▪ Screen for depression, anxiety, and disordered eating	✓		✓
	▪ Consider assessment for functional performance*	✓		✓
	▪ Consider assessment for functional performance*	✓		✓

BP CONTROL

- Postural changes in BP & pulse may be evidence of autonomic neuropathy & therefore require adjustment of BP targets.
- Orthostatic BP measurements should be checked on initial visit & as indicated.

medical evaluation at initial, follow-up, and annual visits		INITIAL VISIT	FOLLOW-UP VISIT	ANNUAL VISIT
LABORATORY EVALUATION	▪ A1C, if the results are not available within the past 3 months	✓	✓	✓
	▪ If not performed/available within the past year	✓		✓
	• Lipid profile, including total, LDL, and HDL cholesterol and triglycerides#	✓		✓^
	• Liver function tests#	✓		✓
	• Spot urinary albumin-to-creatinine ratio	✓		✓
	• Serum creatinine and estimated glomerular filtration rate+	✓		✓
	• Thyroid-stimulating hormone in patients with type 1 diabetes#	✓		✓
	• Vitamin B12 if on metformin	✓		✓
	• Serum potassium levels in patients on ACE inhibitors, ARBs, or diuretics+	✓		✓

Table 4.2—Assessment and treatment plan*

Assessing risk of diabetes complications

- ASCVD and heart failure history
- ASCVD risk factors and 10-year ASCVD risk assessment
- Staging of chronic kidney disease (see **Table 11.1**)
- Hypoglycemia risk (see **Table 4.3**)
- Assessment for retinopathy
- Assessment for neuropathy

Table 4.3—Assessment of hypoglycemia risk

Factors that increase risk of treatment-associated hypoglycemia

- Use of insulin or insulin secretagogues (i.e., sulfonylureas, meglitinides)
- Impaired kidney or hepatic function
- Longer duration of diabetes
- Frailty and older age
- Cognitive impairment
- Impaired counterregulatory response, hypoglycemia unawareness
- Physical or intellectual disability that may impair behavioral response to hypoglycemia
- Alcohol use
- Polypharmacy (especially ACE inhibitors, angiotensin receptor blockers, nonselective β-blockers)

REFERRALS FOR INITIAL CARE MANAGEMENT

- Eye care professional for annual dilated eye exam
- Family planning for women of reproductive age
- Registered dietitian nutritionist for medical nutrition therapy
- Diabetes self-management education and support
- Dentist for comprehensive dental and periodontal examination
- Mental health professional, if indicated
- Audiology, if indicated
- Social worker/community resources, if indicated

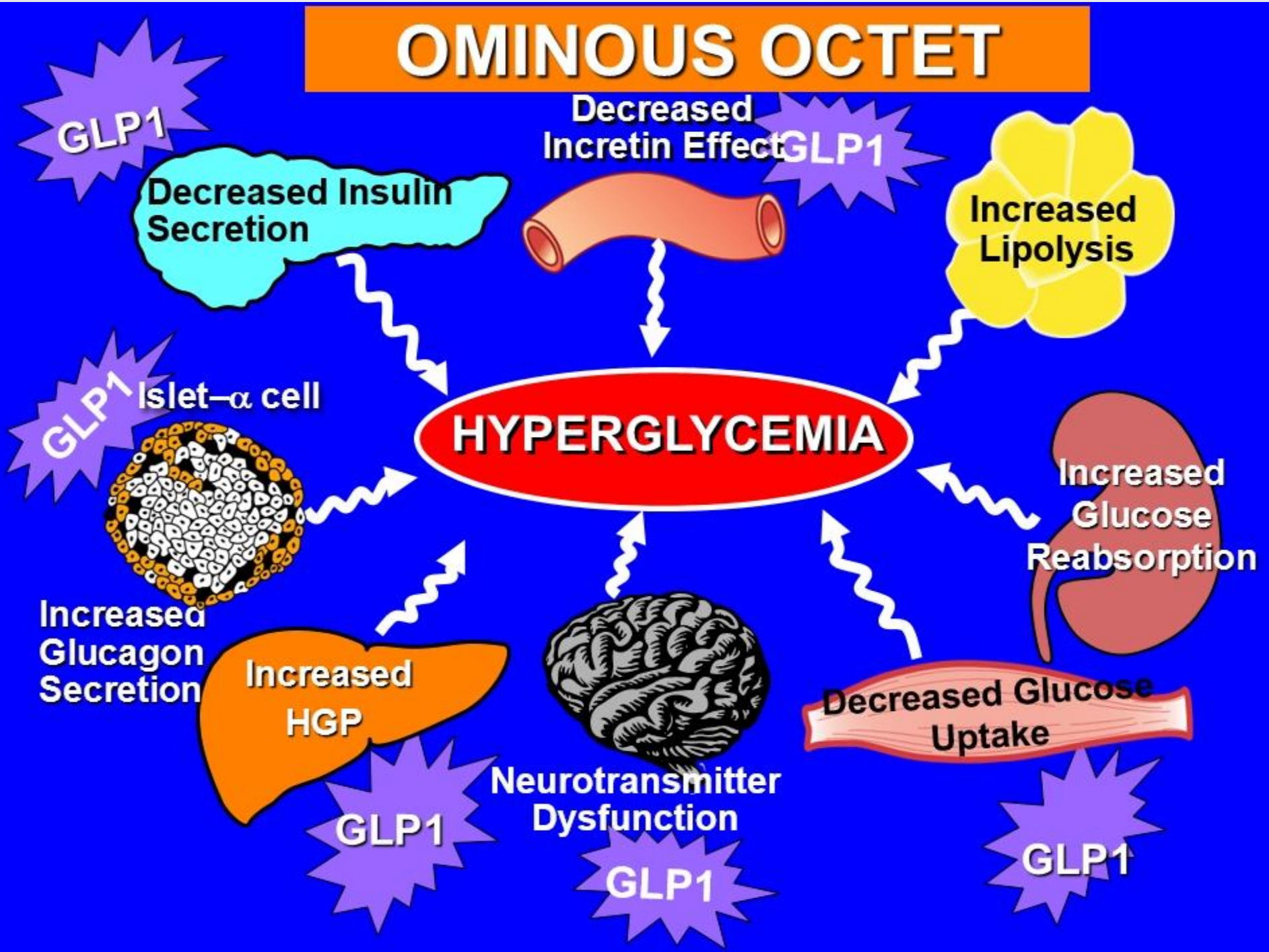
GLYCEMIC CONTROL

Key factors for Selection of Hypoglycemic Agent:

Comorbidities:

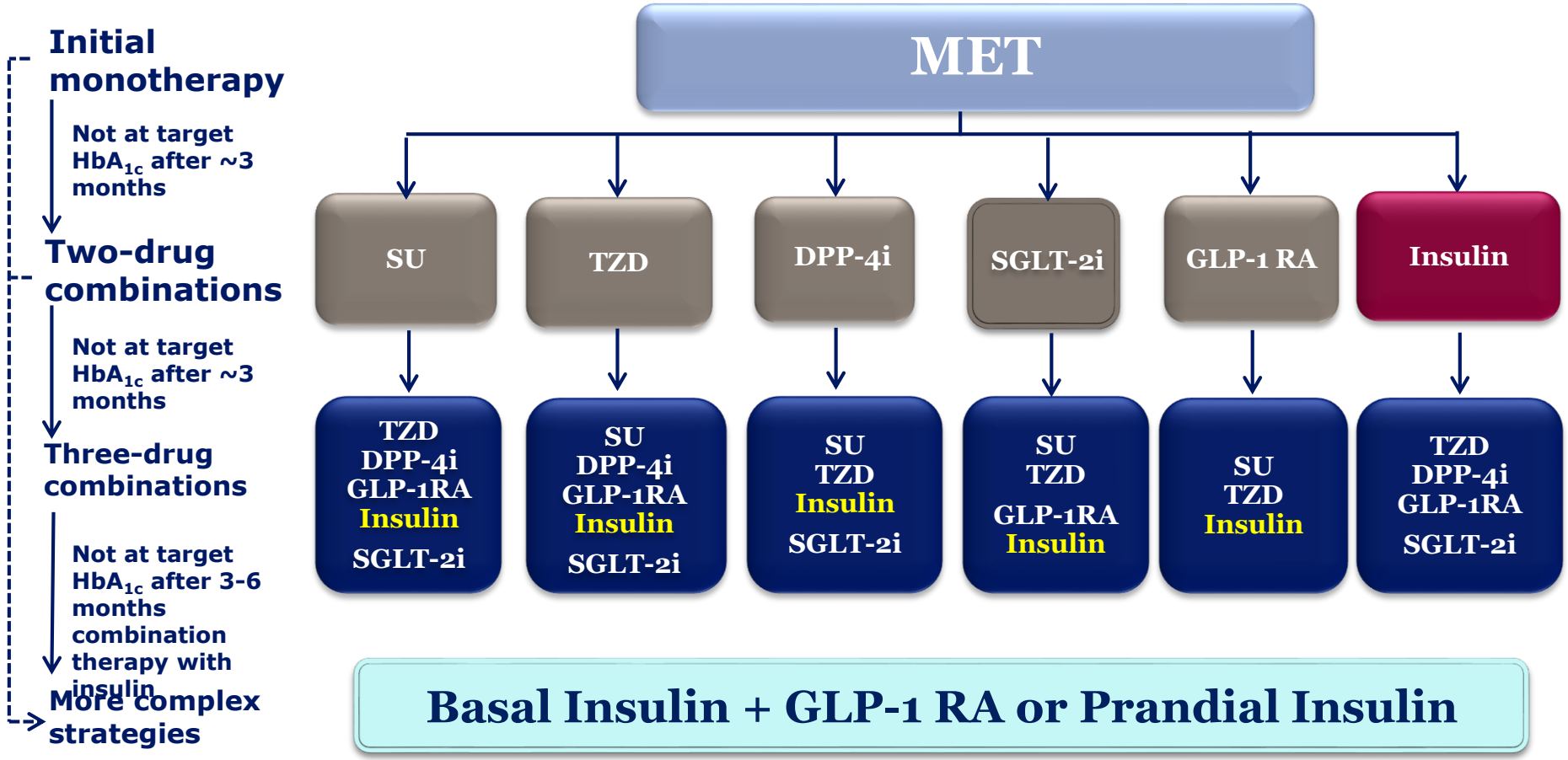
- ASCVD
- CKD
- High risk of HF
- Hypoglycemia risk

- Body weight
- Costs
- Patient Preferences
- Side effects


OMINOUS OCTET
GLP1
Decreased Insulin Secretion
Decreased Incretin Effect
GLP1
Increased Lipolysis
GLP1
Islet–α cell
HYPERGLYCEMIA
Increased Glucose Reabsorption
Increased Glucagon Secretion
Increased HGP
Neurotransmitter Dysfunction
Decreased Glucose Uptake
GLP1
GLP1
GLP1

ADA Guideline, Diabetes Care:

Healthy eating, weight control, increased physical activity



ASCVD predominates

GLP-1 RA with proven CVD benefit[1]

EITHER/ OR

SGLT2i with proven CVD benefit[1], if eGFR adequate[2]

If HbA_{1c} 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 HbA_{1c} 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]

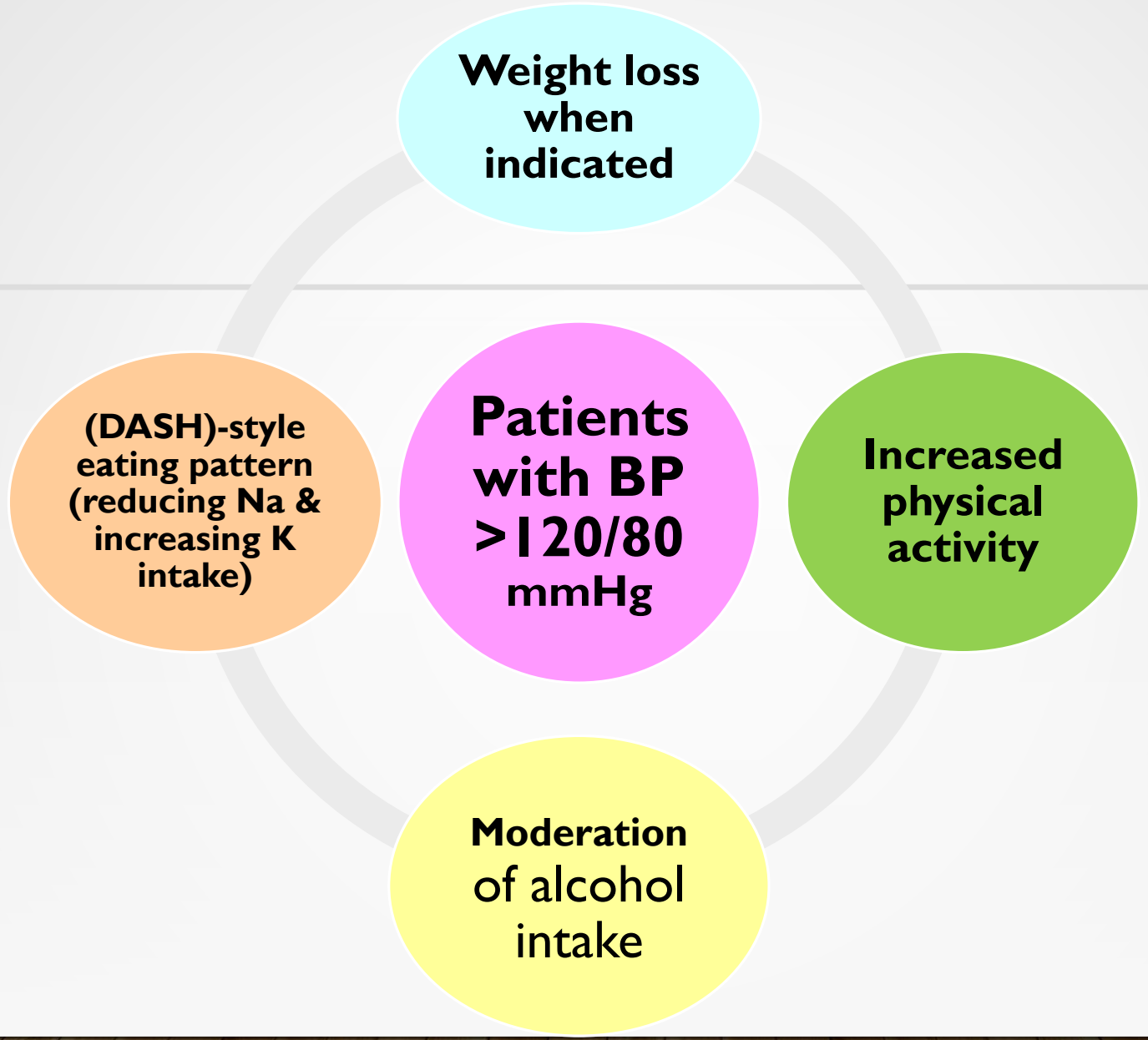
CVD APPROACH

For prevention & management of both ASCVD & heart failure, CV risk factors should be systematically assessed at least annually in all patients with DM.

BP CONTROL

For individuals with DM & HTN at higher CV risk (existing ASCVD or 10-year ASCVD risk ≥15%), a BP target of **<130/80** mmHg may be appropriate, if it can be safely attained.

For individuals with **DM & HTN** at lower risk for CVD (10-year atherosclerotic CV disease risk <15%), treat to a BP target of **<140/90** mmHg**.**


Weight loss when indicated
(DASH)-style eating pattern (reducing Na & increasing K intake)
Patients with BP >120/80 mmHg
Increased physical activity
Moderation of alcohol intake

Lipid Management

Lipid Management Lifestyle Modification

Weight loss

Application of a Mediterranean style or Dietary Approaches to Stop Hypertension (DASH) eating pattern

Reduction of saturated fat & trans fat

Increase of dietary n-3 fatty acids, viscous fiber, & plant stanols/sterols intake

Increased physical activity

LIPID MANAGEMENT (CON….)

- **Intensify lifestyle therapy & optimize glycemic control for patients with:**
  - **Elevated TG levels ≥150 mg/dL &/or low**
  - **HDL cholesterol <40 mg/dL for men**
  - **HDL cholesterol <50 mg/dL for women**

Ongoing Therapy & Monitoring With Lipid Panel

- In adults it is reasonable to obtain a lipid profile:
  - A**t the time of DM diagnosis**
  - At **an initial medical evaluation**
  - **Every 5 years thereafter if under the age of 40 years,** or more frequently if indicated.
  - At initiation of statins or other lipid lowering therapy
  - **4–12 weeks after initiation** or a change in dose, & **annually** thereafter

LIPID MANAGEMENT (CON….)

- **Statins** are the drugs of choice for LDL cholesterol lowering & cardioprotection.
- High-intensity statin therapy will achieve approximately a ≥ **50%** reduction in LDL cholesterol,
- Moderate-intensity statin regimens achieve **30–49%** reductions in LDL cholesterol.
- Low-dose statin therapy is generally not recommended in patients with DM but is sometimes the only dose of statin that a patient can **tolerate**.
- For patients who do not tolerate the intended intensity of statin, the maximally tolerated statin dose should be used.

Table 10.2—High-intensity and moderate-intensity statin therapy*

High-intensity statin therapy (lowers LDL cholesterol by ≥50%)	Moderate-intensity statin therapy (lowers LDL cholesterol by 30–49%)
Atorvastatin 40–80 mg	Atorvastatin 10–20 mg
Rosuvastatin 20–40 mg	Rosuvastatin 5–10 mg
	Simvastatin 20–40 mg
	Pravastatin 40–80 mg
	Lovastatin 40 mg
	Fluvastatin XL 80 mg
	Pitavastatin 1–4 mg

Intensity of lipid lowering treatment

Treatment	Average LDL-C reduction
Moderate intensity statin	≈ 30%
High intensity statin	≈ 50%
High intensity statin plus ezetimibe	≈ 65%
PCSK9 inhibitor	≈ 60%
PCSK9 inhibitor plus high intensity statin	≈ 75%
PCSK9 inhibitor plus high intensity statin plus ezetimibe	≈ 85%

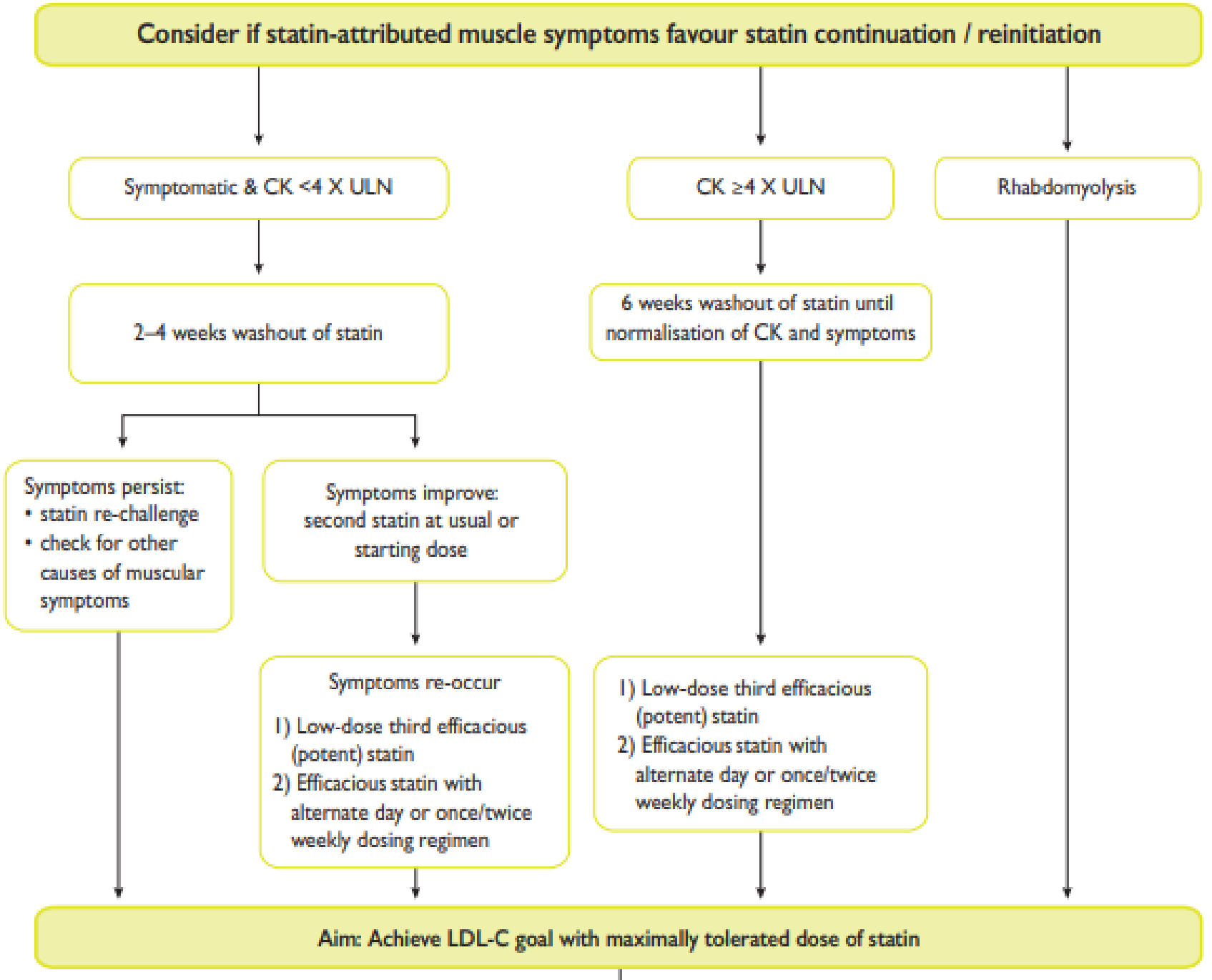
Primary Prevention:

- **There are 3 approaches:**
  1. **Based on ADA Diabetic care 2022**
  2. **Based on 2019 ESC/EAS Guidelines**
  3. **2019 ACC/AHA Guideline on the Primary Prevention of CVD**

Table 1
AACE Lipid Targets for Patients with T2D (188,189,197,200,240-251)

Risk category	Risk factors[a]/10-year risk[b]	Treatment goals	
		LDL-C (mg/dL)	Non-HDL-C (mg/dL)
Extreme risk	– Progressive ASCVD including unstable angina in patients after achieving an LDL-C <70 mg/dL – Established clinical cardiovascular disease in patients with DM, CKD 3/4, or HeFH – History of premature ASCVD (<55 male, <65 female)	<55	<80
Very high risk	– Established or recent hospitalization for ACS, coronary, carotid or peripheral vascular disease – Diabetes or CKD 3/4 with 1 or more risk factor(s) – HeFH	<70	<100
High risk	≥2 risk factors and 10-year risk >10% or CHD risk equivalent[c], including diabetes or CKD 3, 4 with no other risk factors	<100	<130
Moderate risk	≥2 risk factors and 10-year risk <10%	<130	<160
Low risk	≤1 risk factor	<160	<190

SOME POINTS ABOUT STATINS IT IS BETTER TO KNOW


Consider if statin-attributed muscle symptoms favour statin continuation / reinitiation
Symptomatic & CK <4 X ULN
CK ≥4 X ULN
Rhabdomyolysis
2–4 weeks washout of statin
6 weeks washout of statin until normalisation of CK and symptoms
Symptoms persist:
• statin re-challenge
• check for other causes of muscular symptoms
Symptoms improve: second statin at usual or starting dose
Symptoms re-occur
1) Low-dose third efficacious (potent) statin
2) Efficacious statin with alternate day or once/twice weekly dosing regimen
1) Low-dose third efficacious (potent) statin
2) Efficacious statin with alternate day or once/twice weekly dosing regimen
Aim: Achieve LDL-C goal with maximally tolerated dose of statin

If a statin-based regimen is not tolerated at any dosage (even after rechallenge), ezetimibe should be considered.[197,265,353]	IIa
If a statin-based regimen is not tolerated at any dosage (even after rechallenge), a PCSK9 inhibitor added to ezetimibe may also be considered.[197,265,353]	IIb
If the goal[c] is not achieved, statin combination with a bile acid sequestrant may be considered.	IIb

Adverse Effects Of Statins On Kidney Function.

- There is no clear evidence that statins have a clinically significant beneficial or adverse effect on renal function.
- An increased frequency of proteinuria has been reported for all statins, but has been analyzed in more detail for **rosuvastatin**. With a dose of 80 mg, a frequency of 12% was reported.
- With the approved doses of <40 mg, the frequency is much lower & in line with the frequency for other statins.
- The proteinuria induced by statins is of tubular origin, usually transitory, & is believed to be due to reduced tubular reabsorption & not to glomerular dysfunction.

Drugs Potentially Interacting With Statins Metabolized By Cytochrome P450 3A4 Leading To Increased Risk Of Myopathy & Rhabdomyolysis

Anti-infective agents	Calcium antagonists	Other
Itraconazole	Verapamil	Ciclosporin
Ketoconazole	Diltiazem	Danazol
Posaconazole	Amlodipine	Amiodarone
Erythromycin		Ranolazine
Clarithromycin		Grapefruit juice
Telithromycin		Nefazodone
HIV protease inhibitors		Gemfibrozil

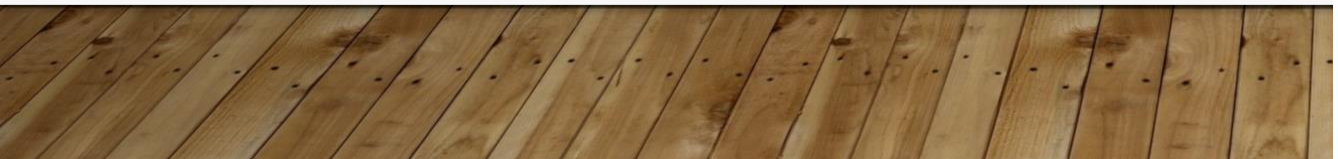
Diabetes Risk With Statin Use

- On average treatment of 255 patients with statins for 4 years resulted in one additional case of DM while simultaneously preventing 5.4 vascular events among those 255 patients.
- A concern that statins or other lipid-lowering agents might cause cognitive dysfunction or dementia is not currently supported by evidence & should not deter their use in individuals with DM at high risk for ASCVD.

ASA Therapy

Aspirin As Primary Prevention

- Include both men & women aged ≥ 50 ys with DM & at least one additional major risk factor (**FH of premature ASCVD, HTN, dyslipidemia, smoking, or CKD/albuminuria**) who are not at increased risk of bleeding (e.g., older age, anemia, renal disease).
- Aspirin therapy for primary prevention may be considered in the context of shared decision-making, which carefully weighs the cardiovascular benefits with the fairly comparable increase in risk of bleeding.



Aspirin As Primary Prevention

- For patients > 70 ys (with or without DM), the balance appears to have greater risk than benefit.
- Thus, for primary prevention, the use of aspirin needs to be carefully considered & may generally not be recommended.
- Aspirin may be considered in the context of high cardiovascular risk with low bleeding risk, but generally not in older adults.

ADA 2022

Increased Risk Of Bleeding Including:

1. A history of GI bleeding or peptic ulcer disease
2. Bleeding from other sites
3. Age >70 years
4. Thrombocytopenia
5. Coagulopathy
6. CKD
7. Concurrent use of NSAIDs, steroids, & anticoagulants.

SCREENING FOR CORONARY ARTERY DISEASE

- In asymptomatic patients, routine screening for CAD is **not** recommended as it does not improve outcomes as long as ASCVD risk factors are treated.
- **A 12 lead ECG** is recommended as part of the routine assessment for screening for conduction abnormalities, LVH, & arrhythmias.
- Consider investigations for CAD in the presence of any of the following:
  1. Typical & atypical cardiac symptoms (e.g., unexplained dyspnea, chest discomfort)
  2. Signs or symptoms of associated vascular disease including carotid bruits, TIA, stroke, claudication, or peripheral arterial disease
  3. ECG abnormalities (e g., Q waves)

SCREENING FOR CAD BY CARDIOLOGIST

- **Exercise ECG** testing without or with echocardiographymay be used as the initial test.
- In adults with DM > 40 years of age, measurement of **coronary artery calcium** is also reasonable for cardiovascular risk assessment.

نسخه ۲

Rx

1.Tab Atorvastatin 20 mg

روزی 1 عدد N: 60/---

2.Tab Metformin 500 mg

1 عدد با صبحانه و 1 عدد با شام میل شود N:120/---

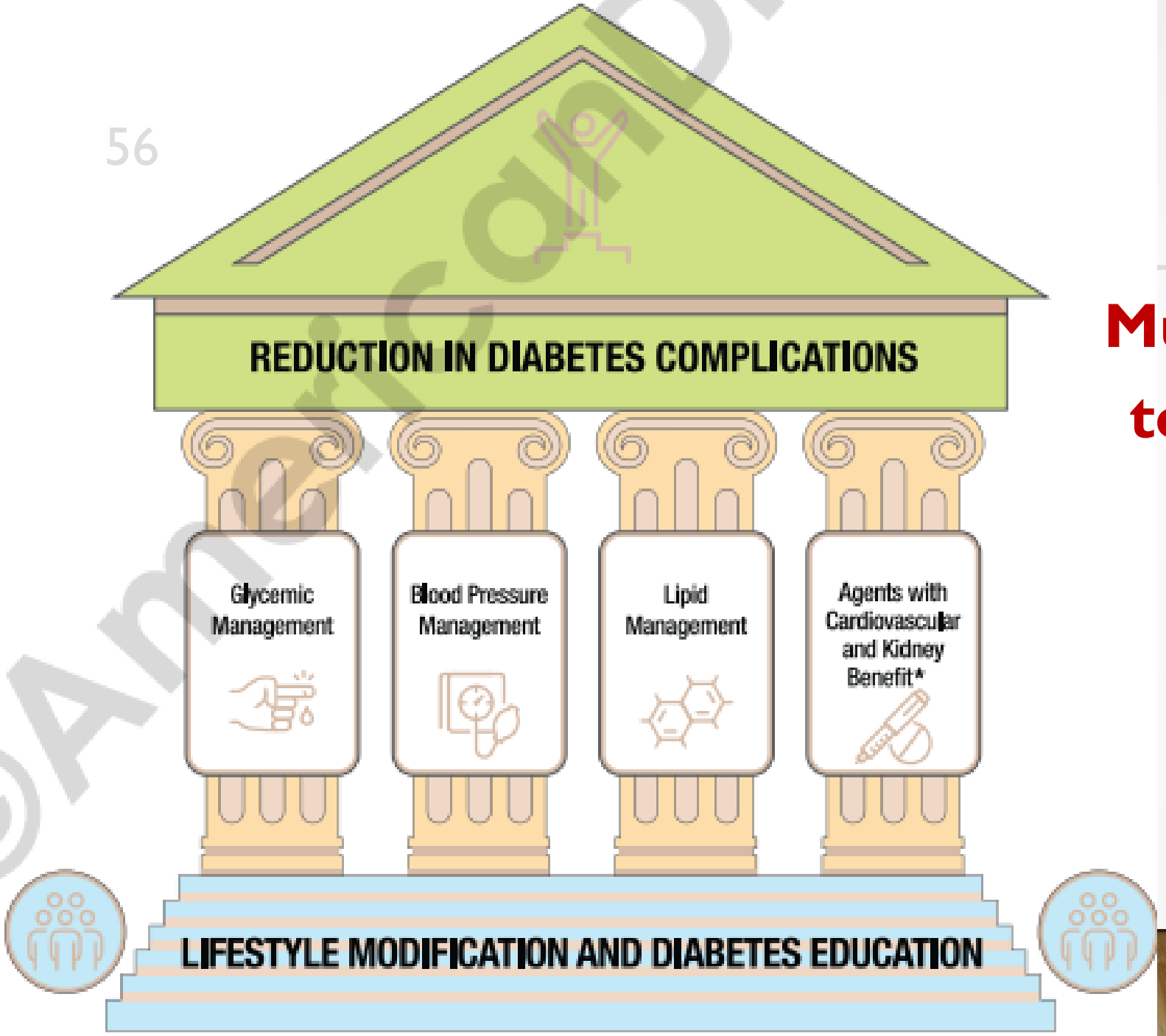
CASE
AFTER 9YS

- PE: BP: 145/80 mmHg, PR: 78/min, RR: 18/min, T: 36 , BMI: 33 WC: 110
- Others: Normal
- Foot Exam: Small fiber disease
- ECG: Nr

Lab data

Lab	First	After 4 ys	After 9 ys
WBC	5600	6200	6000
Hgb	16	17	15
PLT	198000	223000	210000
FBS	114	132	185
BUN	15	17	19
Cr	0.9	1	1.1
eGFR	101	87	75
ACR mg/g cr	-	23	65

Lab	First	After 4 ys	After 9 ys
Cho	226	234	201
TG	197	211	198
HDL	54	45	42
LDL	129	133	113
TSH	4	-	3
U/A	Nr	Nr	Nr
HbA1C	6.1%	7.2%	8.9%
K	4.2	4.1	4.6



Multifactorial approach to reduction in risk of DM complications

Medical Therapy in HTN:

- ARB
- ACE inhibitors
- Ca blockers
- Thiazid like

Bp control

- Should, in addition to lifestyle therapy, have prompt initiation & timely titration of pharmacologic therapy to achieve BP goals

Patients with confirmed office based BP **≥140/90**

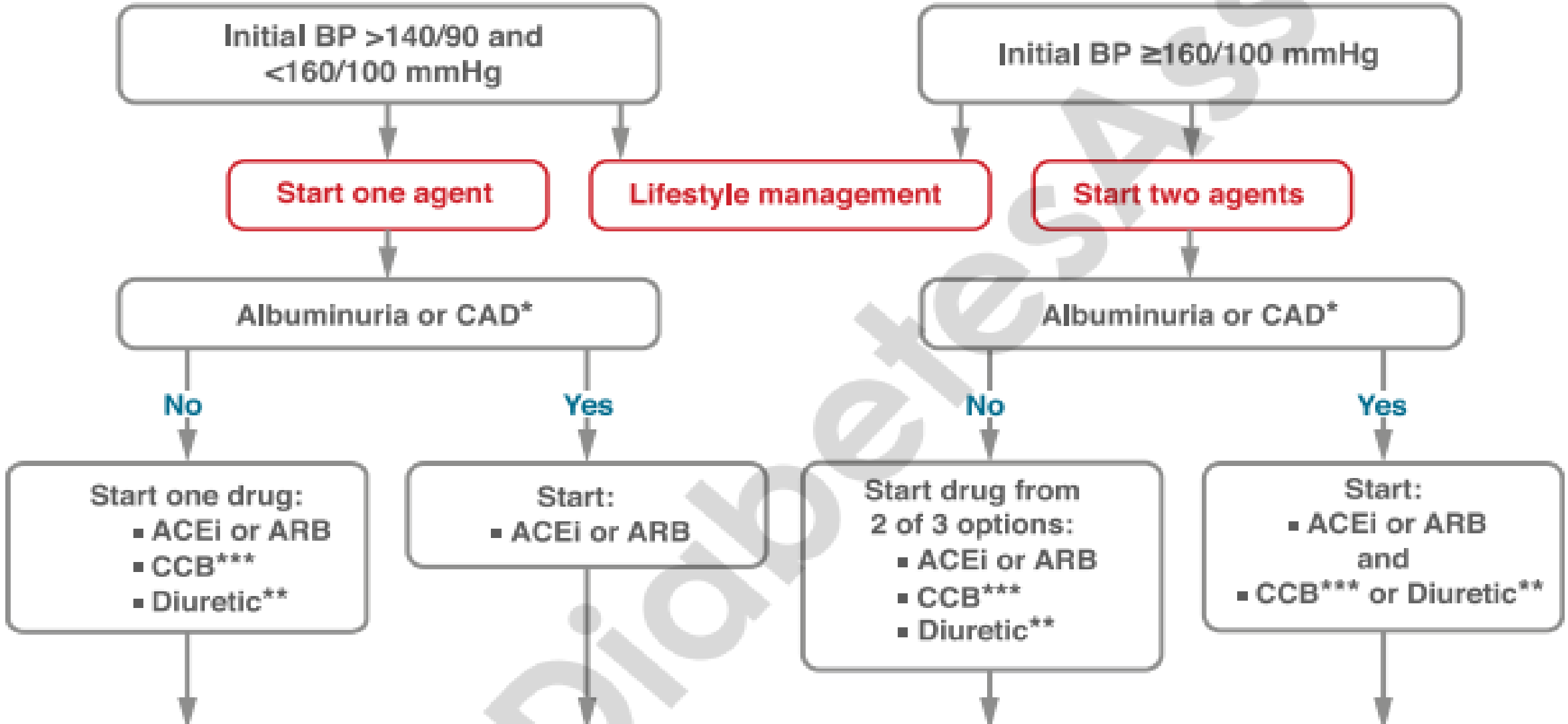
- Should, in addition to lifestyle therapy, have prompt initiation & timely titration of 2 drugs or a single-pill combination of drugs demonstrated to reduce CV events in patients with DM

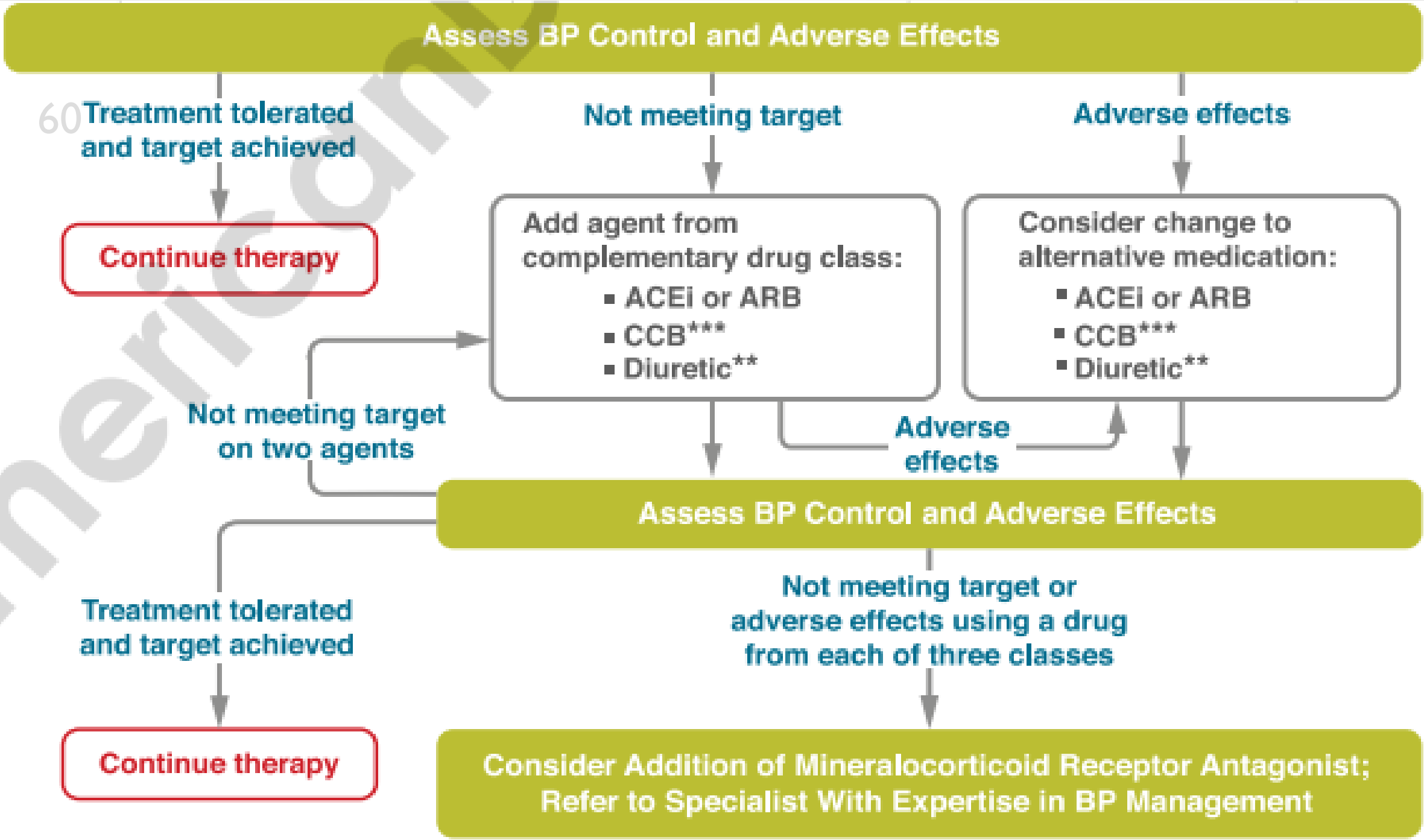
Patients with confirmed office based BP ≥160/100

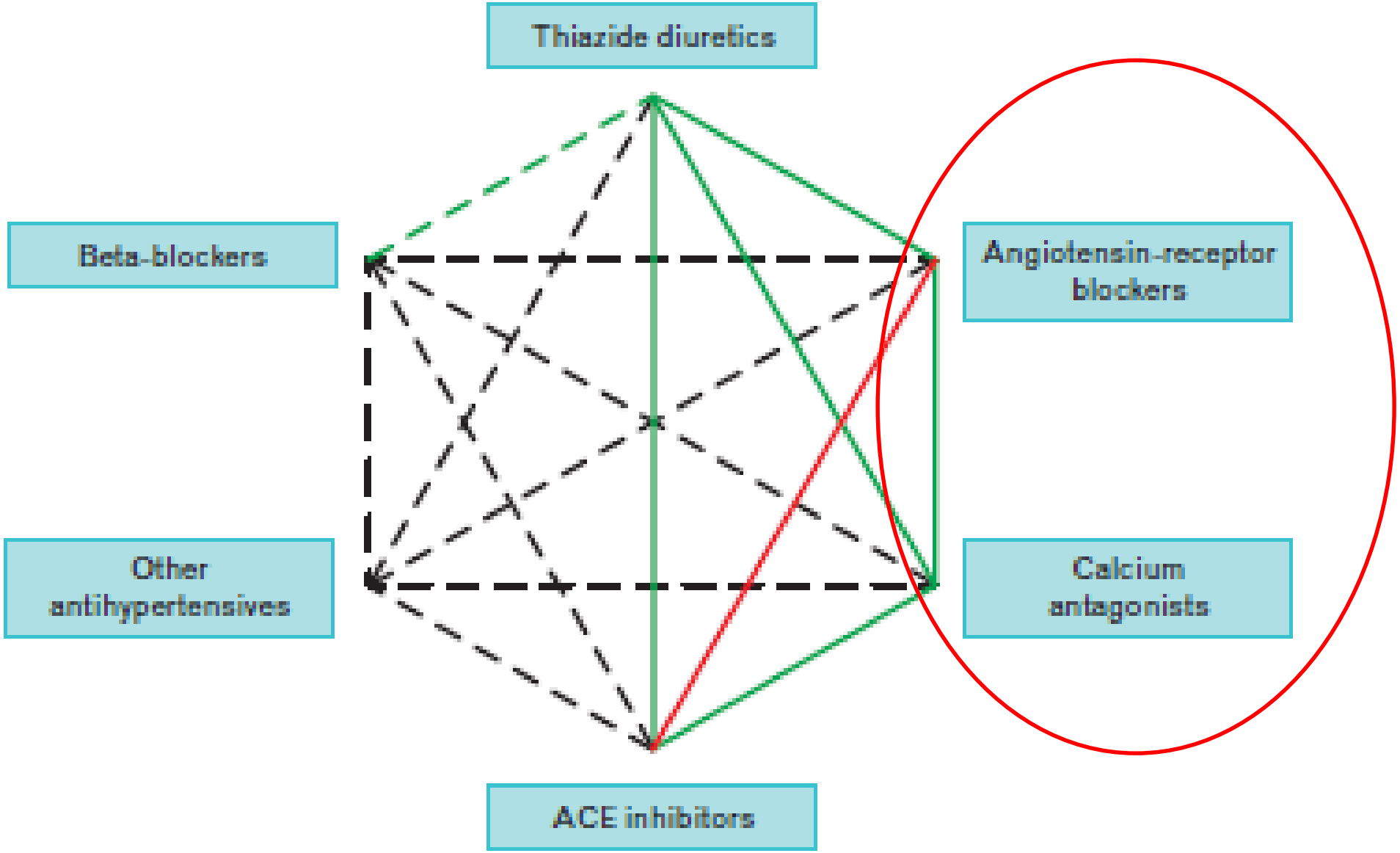
- Treatment for HTN should include drug classes demonstrated to reduce CV events in patients with DM

ACEI or ARB are recommended first line therapy for HTN in people with DM & CAD

Recommendations for the Treatment of Confirmed Hypertension in People With Diabetes




Assess BP Control and Adverse Effects
Treatment tolerated and target achieved
Not meeting target
Adverse effects
Continue therapy
Add agent from complementary drug class:
ACEi or ARB
CCB***
Diuretic**
Consider change to alternative medication:
ACEi or ARB
CCB***
Diuretic**
Not meeting target on two agents
Adverse effects
Assess BP Control and Adverse Effects
Treatment tolerated and target achieved
Not meeting target or adverse effects using a drug from each of three classes
Continue therapy
Consider Addition of Mineralocorticoid Receptor Antagonist; Refer to Specialist With Expertise in BP Management



2013 ESH/ESC Guidelines for the management of arterial hypertension

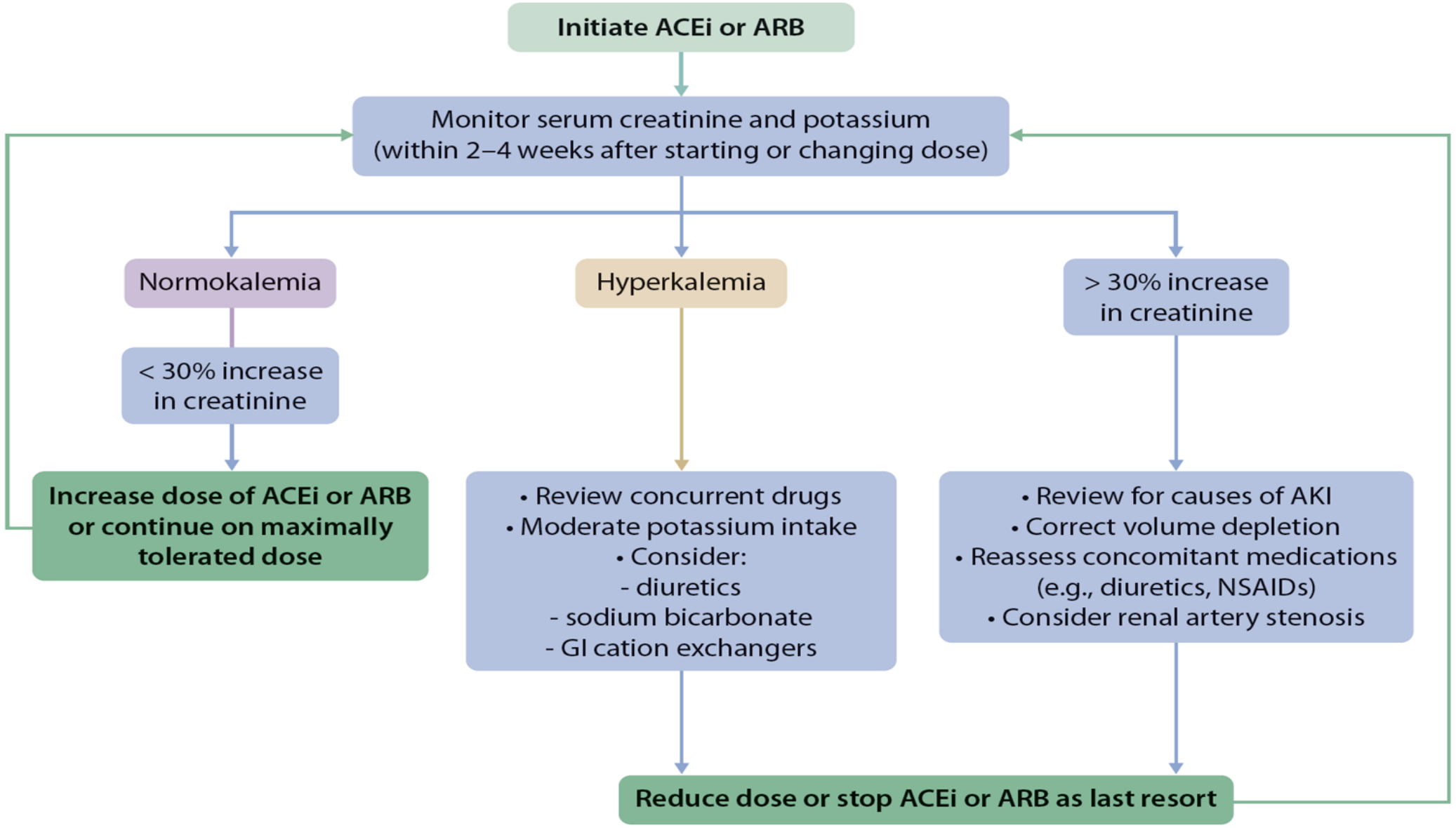
Treatment Strategies:

- ACEi & ARB in combination is not recommended given the lack of added ASCVD benefit & increased rate of adverse events – namely hyperkalemia ,syncope ,& acute kidney injury.

COMPREHENSIVE CARE IN PATIENTS WITH DM & CKD

- For patients with **DM, albuminuria, & normal BP**, treatment with an ACEi or ARB may be considered.
- Monitor for changes in BP, serum cr, & K within **2-4 weeks** of initiation or increase in the dose of an ACEi or ARB.
- Continue ACEi or ARB therapy unless serum cr rises by **> 30%** within 4 weeks following initiation of treatment or an increase in dose.
- Advise **contraception** in women who are receiving ACEi or ARB therapy & discontinue these agents in women who are considering pregnancy or who become pregnant.

MONITORING OF SERUM CR & K DURING ACEI OR ARB TREATMENT - DOSE ADJUSTMENT & MONITORING OF SIDE EFFECTS



Rx نسخه

1.Tab Atorvastatin 40 mg

روزی 1 عدد N: 30/---

2.Tab Metformin 500 mg

1 عدد با صبحانه و 1 عدد با شام میل شود N:60/---

3.Tab Enalapril 5 mg

روزی 1 عدد صبح و1 عدد شب N:60/---

4.Tab ASA 80 mg

روزی 1 عدد N:30/---

5.Tab Empagliflozin 10 mg

روزی 1 عدد N:30/---

6. Tab vitamin B1 100 mg

روزی 1 عدد N:30/---

CASE
AFTER 14YS

- PE: BP: 145/90 mmHg, PR: 76/min, RR: 18/min, T: 36.5˚c , BMI: 33.5 Wc: 121
- EF: 50% Mild LVH
- 1+ lower limb edema

Lab data

Lab	After 4 ys	After 9 ys	After 14 ys
WBC	6200	6000	4600
Hgb	17	15	14.5
PLT	223000	210000	190000
FBS	132	165	190
BUN	17	19	21
Cr	1	1.1	1.2
eGFR	87	75	65
K	4.1	4.6	5.8

Lab	After 4 ys	After 9 ys	After 14 ys
Cho	234	201	195
TG	211	198	240
HDL	45	42	32
LDL	134	119	110
TSH	-	3	4.5
U/A	Nr	Nr	Pr+
HbA1C	7.2%	7.9%	8.9%
ACR mg/g cr	23	65	-

HYPERTG TREATMENT

- 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.
- In adults with moderate hypertriglyceridemia (fasting or non–fasting 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.

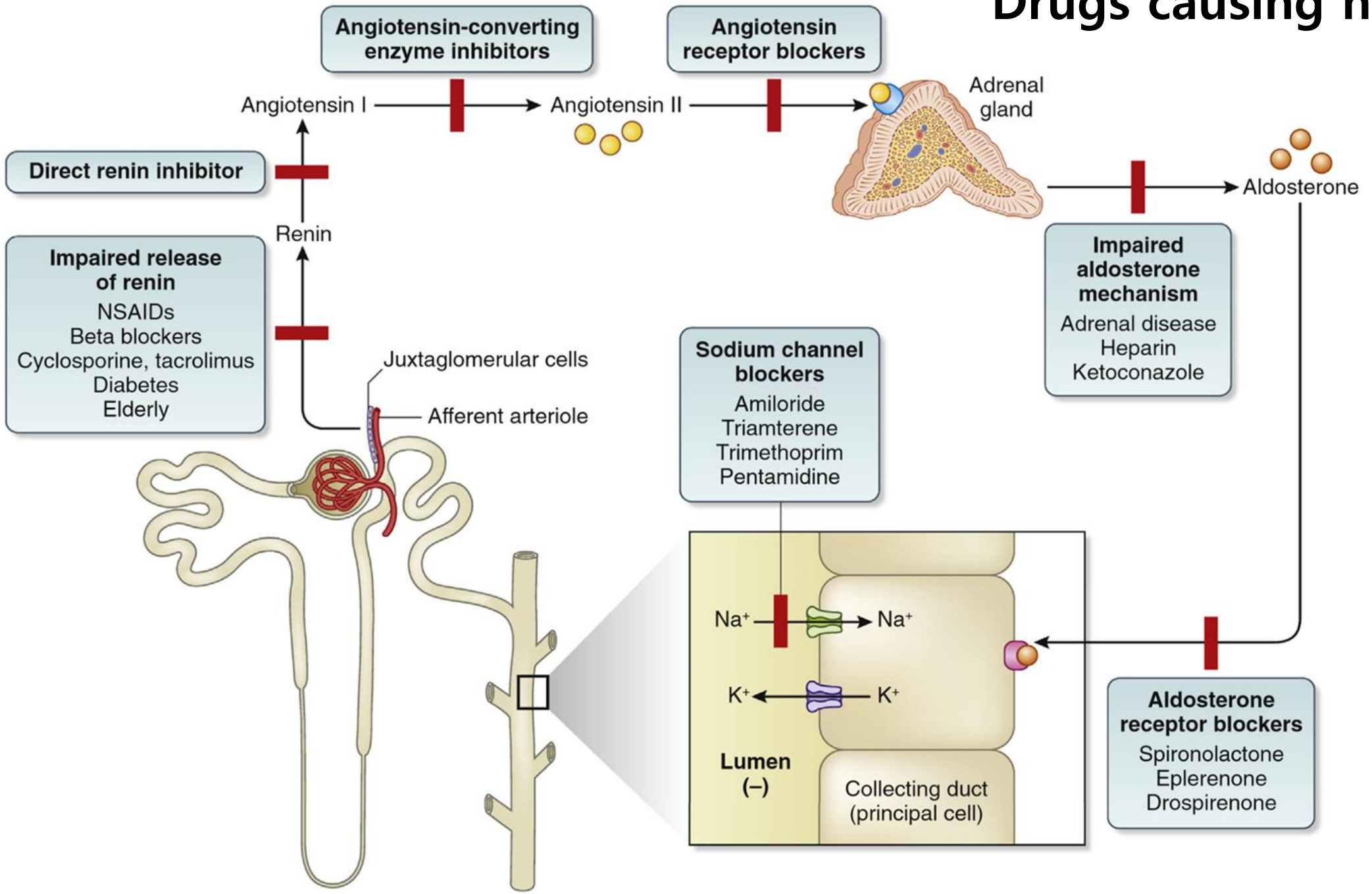
HYPERTG TREATMENT

- In patients with atherosclerotic cardiovascular disease or other CVD 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.
- tatin plus fibrate combination therapy has not been shown to improve atherosclerotic cardiovascular disease outcomes and is generally not recommended.
- 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

Comprehensive Care in Patients with DM & CKD

- **Hyperkalemia** associated with the use of an ACEi or ARB can often be managed by measures to reduce serum K levels rather than decreasing the dose or stopping ACEi or ARB immediately.
- **Reduce the dose or discontinue ACEi or ARB** in the setting of either symptomatic hypotension or uncontrolled hyperK despite medical treatment, or to reduce uremic symptoms while treating kidney failure (eGFR <15 ml/min/1.73 m^2).
- Use only one agent at a time to block the RAS. The combination of an ACEi with an ARB, or the combination of an ACEi or ARB with a direct renin inhibitor, is potentially **harmful**.
- **Mineralocorticoid receptor antagonists** are effective for management of refractory HTN but may cause hyperK or a reversible decline in GFR, particularly among patients with a low eGFR.

Drugs causing hyperkalemia



نسخه

Rx 1.Tab Atorvastatin 40 mg

روزی 1 عدد N: 30/---

2.Tab Metformin 500 mg

1 عدد با صبحانه و 1 عدد با شام میل شود N:60/---

3.Tab Enalapril 5 mg

روزی 1 عدد صبح و1 عدد شب N:60/---

4.Tab ASA 80 mg

روزی 1 عدد N:30/---

5.Tab Empagliflozin 10 mg

روزی 1 عدد N:30/---

6. Tab vitamin B1 100 mg

روزی 1 عدد N:30/---

7. Tab Hydrochlorothiazide 25 mg

روزی نصف عدد N:15/-

8. Tab Linagliptine 5 mg

روزی 1 عدد N:30/---

CASE
AFTER 19YS

- PE: BP: 150/95 mmHg, PR: 76/min, RR: 16/min, T: 36.2˚c , BMI: 32
- Pallor, 3+ lower limb edema

Lab data

Lab	After 9 ys	After 14 ys	After 19 ys
WBC	6000	4600	5000
Hgb	15	14.5	12.5
PLT	210000	190000	175000
FBS	165	145	136
BUN	19	21	31
Cr	1.1	1.2	1.8
eGFR	75	65	38
TSH	3	4.5	4

Lab	After 9 ys	After 14 ys	After 19 ys
Cho	201	195	184
TG	198	190	195
HDL	42	40	39
LDL	119	105	100
U/A	Nr	Pr+	Pr^{2+}
HbA1C	7.9%	8.9%	7.6%
ACR mg/g cr	65	-	-
K	4.6	5.8	6

Other Lab data

	After 19 ys
Ca	8.5
Ph	6
Alb	3
Vit D3 ng/ml	18
iPTH (15-65)	65
Fe	79
TIBC	260
TSAT	30.4%
Ferritin	580

Other Lab data

	After 19 ys
Ca	8.5
Ph	6
Alb	3
Vit D3 ng/ml	18
iPTH (15-65)	65

Corrected Ca = Ca + (4 – Alb) 0.8 = 9.3

STRATEGIC PLAN:

- Life style strategies
- Metformin maximum dose 1000 mg (if in previous treatment)
- GLP1 agonist ?
- Empagliflozin 10 mg /day
- Statin : Atorvastatin 40 mg/day
- ACEi or ARB
- ASA 80mg/day (no contraindications)
- CKD management

DM Evaluation:

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- DM complications screening and cv risk reduction
- Vaccination
- Cancer screening: FIT - IDA
- OSA
- Periodontal
- Eating disorder- NAFLD/NASH
- Hearing loss
- Frx risk & BMD
- Cognition & Psychological disorder
- Autonom neuropathy: R/O secondary causes:

Sevelamer Hydrochloride: dose

Serum Ph	Renagel or Renvela 800 mg
> 5.5 and < 7.5 mg/dL	1 tablet 3 times daily with meals
≥ 7.5 and < 9.0 mg/dL	2 tablet 3 times daily with meals
≥ 9.0 mg/dL	3 tablet 3 times daily with meals

https://reference.medscape.com/dru

نسخه

Rx

1. Cap Sevelamer carbonate 800 mg

با هر وعده غذا 1 عدد میل شود N: 90/---

2. Pearl Vit D3 50000 IU

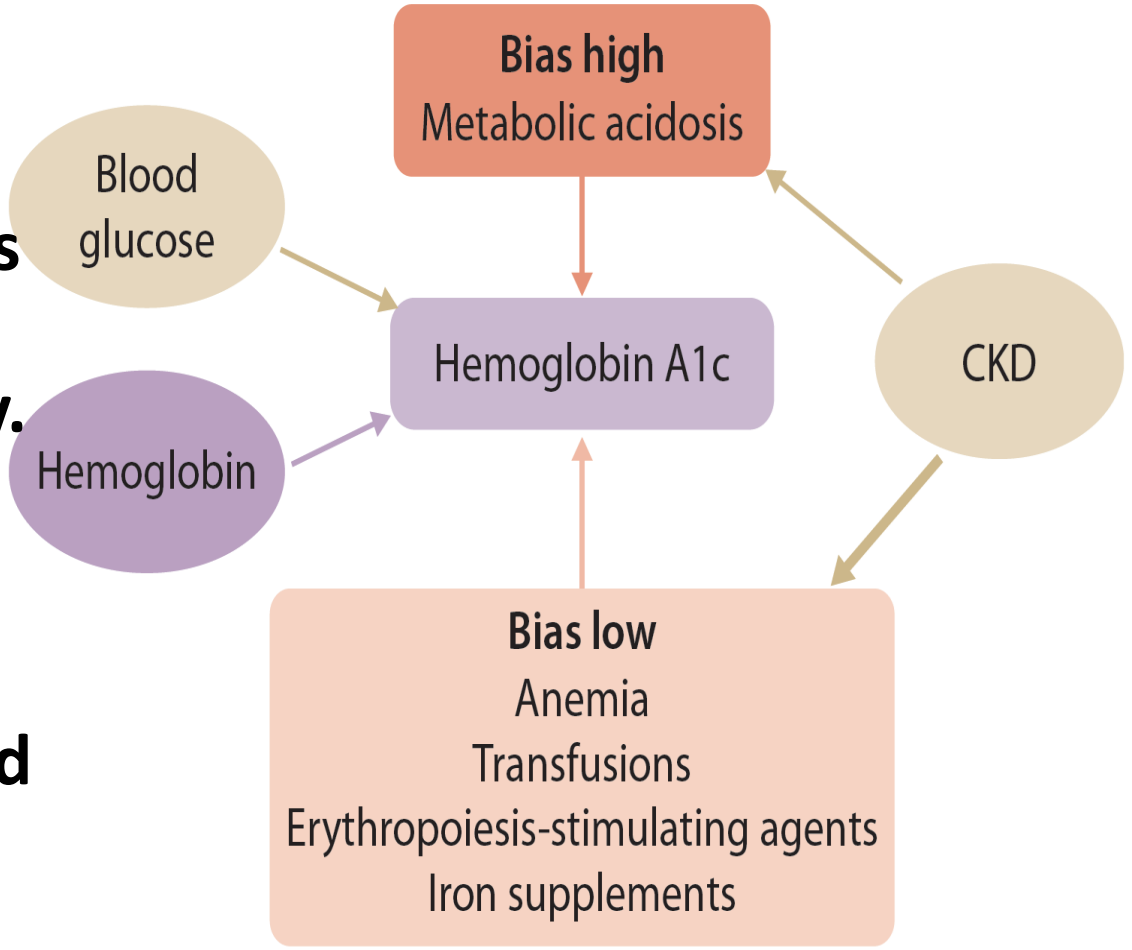
هفته ای 1 عدد برای 8 هفته سپس هر 3 هفته 1 عدد N: 10/--

3. Powder Kayexalate

5 گرم در یک استکان اب با نهار میل شود N: 150/-- gr

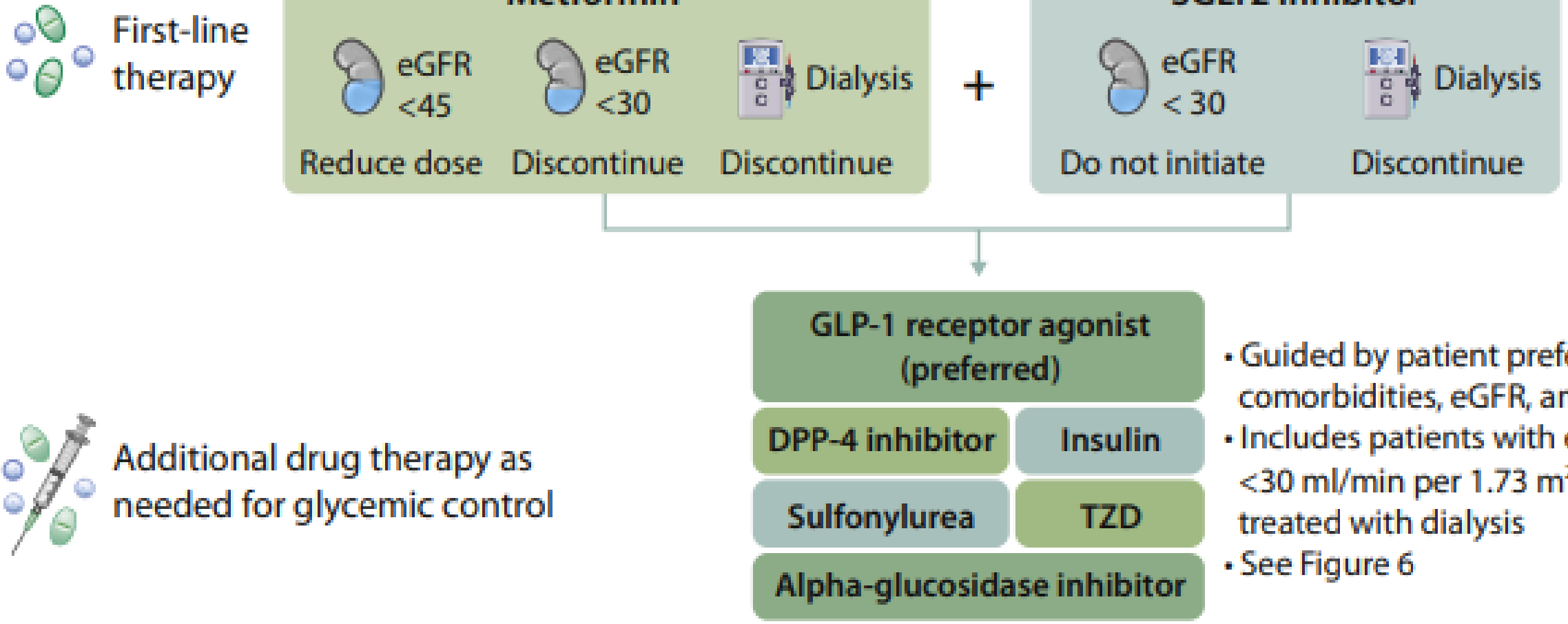
Glycemic Monitoring & Targets in Patients with DM & CKD

PP 2.1.1: Monitoring long-term glycemic control by HbA1c twice per year is reasonable for patients with DN. HbA1c may be measured as often as 4 times per year if the glycemic target is not met or after a change in antihyperglycemic therapy.



PP 2.1.2: Accuracy & precision of HbA1c measurement declines with advanced CKD (G4-G5), particularly among patients treated by dialysis, in whom HbA1c measurements have low reliability.

Treatment algorithm for selecting antihyperglycemic drugs for patients with type 2 DM & CKD



Lifestyle therapy

Physical activity
Nutrition
Weight loss

First-line therapy

Metformin

eGFR <45 — Reduce dose

eGFR <30 — Discontinue

Dialysis — Discontinue

+

SGLT2 inhibitor

eGFR < 30 — Do not initiate

Dialysis — Discontinue

Additional drug therapy as needed for glycemic control

GLP-1 receptor agonist (preferred)

DPP-4 inhibitor | **Insulin**

Sulfonylurea | **TZD**

Alpha-glucosidase inhibitor

- Guided by patient preferences, comorbidities, eGFR, and cost
- Includes patients with eGFR <30 ml/min per 1.73 m^2 or treated with dialysis
- See Figure 6

با تشکر از توجه شما