
IN THE NAME OF GOD

Diabetes Mellitus(part 2)

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Objectives

- Comprehensive Medical Evaluation
- Assessment of Comorbidities
  - Microvascular complications
    - Nephropathy
    - Retinopathy
    - Neuropathy
  - Macrovascular complications
  - HTN
  - LIPID
  - ANTIPLATELET AGENTS

Table 4.1 – Components of the comprehensive diabetes medical evaluation at initial, follow-up, and annual visits

		INITIAL VISIT	EVERY FOLLOW-UP VISIT	ANNUAL VISIT
PAST MEDICAL AND FAMILY HISTORY	**Diabetes history**			
	▪ Characteristics at onset (e.g., age, symptoms)	✓		
	▪ Review of previous treatment regimens and response	✓		
	▪ Assess frequency/cause/severity of past hospitalizations	✓		
	Family history			
	▪ Family history of diabetes in a first-degree relative	✓		
	▪ Family history of autoimmune disorder	✓		
	Personal history of complications and common comorbidities			
	▪ Macrovascular and microvascular	✓		✓
	▪ Common comorbidities (e.g., obesity, OSA)	✓		✓
	▪ Hypoglycemia: awareness/frequency/causes/timing of episodes	✓	✓	✓
	▪ Presence of hemoglobinopathies or anemias	✓		✓
	▪ High blood pressure or abnormal lipids	✓		✓
	▪ Last dental visit	✓		✓
	▪ Last dilated eye exam	✓		✓
	▪ Visits to specialists	✓	✓	✓
	Interval history			
	▪ Changes in medical/family history since last visit		✓	✓

Table 4.1 – Components of the comprehensive diabetes medical evaluation at initial, follow-up, and annual visits

		INITIAL VISIT	EVERY FOLLOW-UP VISIT	ANNUAL VISIT
LIFESTYLE FACTORS	▪ Eating patterns and weight history	✓	✓	✓
	▪ Physical activity and sleep behaviors	✓	✓	✓
	▪ Tobacco, alcohol, and substance use	✓		✓
MEDICATIONS AND VACCINATIONS	▪ Current medication regimen	✓	✓	✓
	▪ Medication-taking behavior	✓	✓	✓
	▪ Medication intolerance or side effects	✓	✓	✓
	▪ Complementary and alternative medicine use	✓	✓	✓
	▪ Vaccination history and needs	✓		✓
TECHNOLOGY USE	▪ Assess use of health apps, online education, patient portals, etc.	✓		✓
	▪ Glucose monitoring (meter/CGM): results and data use	✓	✓	✓
	▪ Review insulin pump settings and use	✓	✓	✓

Table 4.1 – Components of the comprehensive diabetes medical evaluation at initial, follow-up, and annual visits

		INITIAL VISIT	EVERY FOLLOW-UP VISIT	ANNUAL VISIT
BEHAVIORAL AND DIABETES SELF-MANAGEMENT SKILLS	**Psychosocial conditions**			
	▪ Screen for depression, anxiety, and disordered eating; refer for further assessment or intervention if warranted	✓		✓
	▪ Identify existing social supports	✓		✓
	▪ Consider assessment for cognitive impairment*	✓		✓
	Diabetes self-management education and support			
	▪ History of dietician/diabetes educator visits/classes	✓	✓	✓
	▪ Assess diabetes self-management skills and barriers	✓		✓
	▪ Assess familiarity with carbohydrate counting (type 1 diabetes)	✓		
	Pregnancy planning			
	▪ For women with childbearing capacity, review contraceptive needs and preconception planning	✓	✓	✓

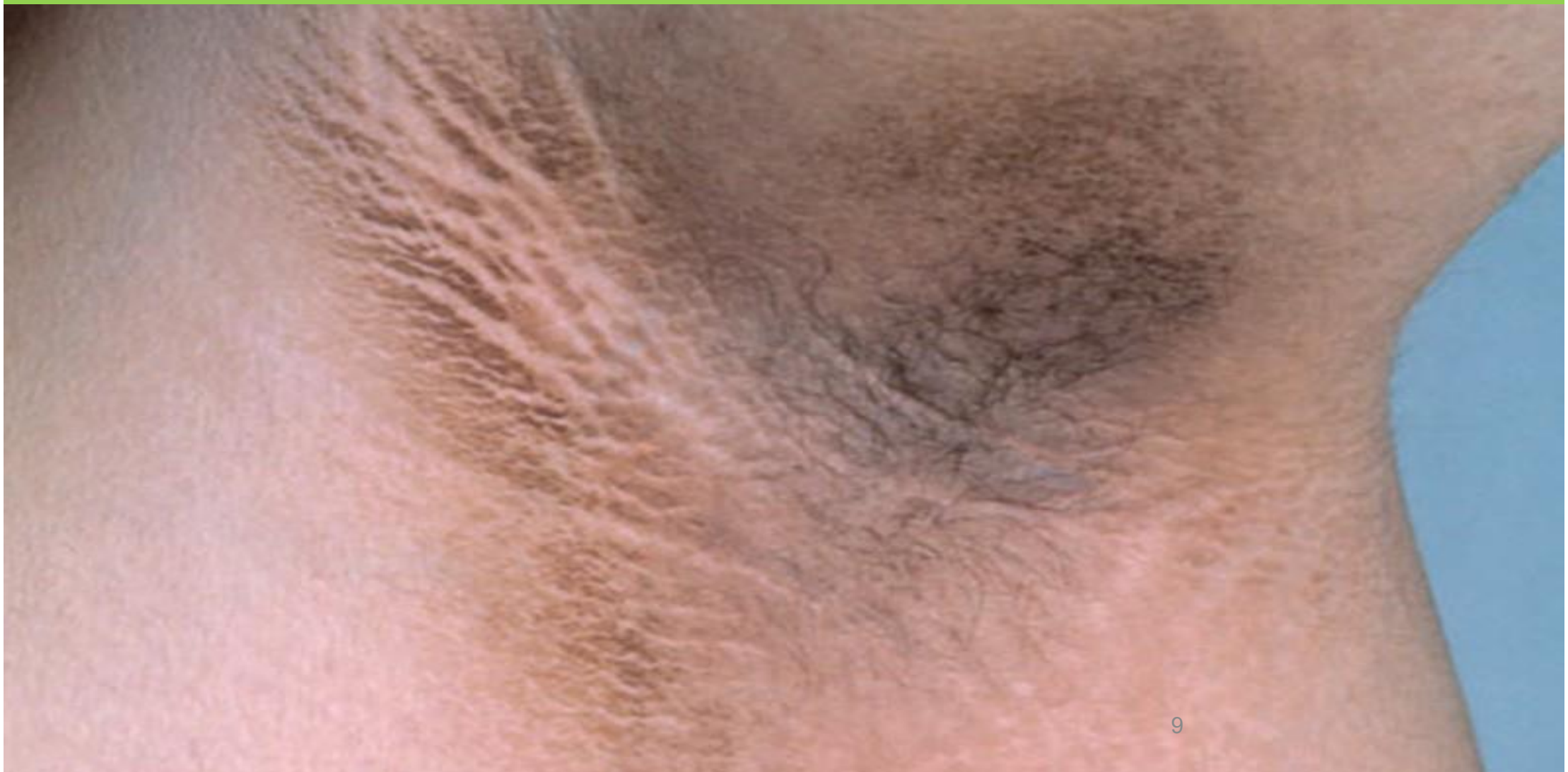
Table 4.1 (cont.)– Components of the comprehensive diabetes medical evaluation at initial, follow-up, and annual visits

		INITIAL VISIT	EVERY 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	✓		✓

Table 4.1 – Components of the comprehensive diabetes medical evaluation at initial, follow-up, and annual visits

		INITIAL VISIT	EVERY 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 (when indicated)	✓		✓
	• Serum potassium levels in patients on ACE inhibitors, ARBs, or diuretics+	✓		✓

Acanthosis Nigricance




Cushing syndrome


Acromegaly

Aerobic Activity

- Most adults with type 1 and type 2 B diabetes should engage in **150 min or more** of moderate-to vigorous intensity aerobic activity per week, spread over at least **3 days/week**, with no more than 2 consecutive days without activity.

SMOKING CESSATION: TOBACCO AND E-CIGARETTES

- Advise all patients not to use cigarettes and other tobacco products A or e-cigarettes. B

Arvand Pharmed

CASE # 2

Mozhgan Karimifar, MD.

Endocrinologist

Orchid Pharmed
Sky's the Limit

Arvand Pharmed

OBJECTIVE

ASCVD Risk Management in Diabetes Type 2

Case # 2

Arvand Pharmed

Case Scenario

Case # 2

- A 58 years old gentleman.
- 12 years history of diabetes.
- He is a smoker.
- Current treatment:

  Metformin 2000 mg/day

  Gliclazide 30 mg BID

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Physical examinations

BP 135/93 mmHg

BMI:24 kg/m^2

Case # 2

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Lab Data

HbA1c 7.3%

FBS 136 mg/dl

eGFR 68

Total Cholesterol: 243 mg/dl

HDL: 38 mg/dl

LDL: 153 mg/dl

Case # 2

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Questions

- ASCVD Risk Calculation
- Best HbA1c target
- Best therapeutic approach

Case # 2

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Questions

- Discontinue Gliclazide and Continue Metformin
- Discontinue Gliclazide and add empagliflozin (Paglimet/ Paglimet ER)
- Discontinue Gliclazide, add fixed dose of Empagliflozin and Linagliptin (Avano or AVANOMET ER).
- Discontinue Gliclazide, Add Melitide

Case # 2

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HbA1c Target

Case # 2

BEST TARGET?

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Diabetes Increases Risk of CVD

Global estimate of association and impact of diabetes on CVD

Outcome	Impact	Data systems / study	Reference
Prevalence of cardiovascular diseases	Any cardiovascular disease: 32% Coronary heart disease: 21% Myocardial infarction: 10% Stroke: 7.6%	57 cross-sectional studies	Einarson et al., 2018[14]
Coronary heart disease	160% increased risk	102 prospective studies	Emerging Risk Factors Collaboration, 2010[12]
Ischaemic heart disease	127% increased risk	102 prospective studies	Emerging Risk Factors Collaboration, 2011[13]
Haemorrhagic stroke	56% increases risk	102 prospective studies	
Cardiovascular diseases death	132% increased risk	97 prospective studies	
Years of life lost	5.8 years for men age 50 6.4 years for women age 50	97 prospective studies	

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ASCVD Risk Assessment

American Diabetes Association®

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

Goal setting

- Set A1C/blood glucose/time in range target
- If hypertension is present, establish blood pressure target
- Diabetes self-management goals

Therapeutic treatment plans

- Lifestyle management
- Pharmacologic therapy: glucose lowering
- Pharmacologic therapy: cardiovascular and renal disease risk factors
- Use of glucose monitoring and insulin delivery devices
- Referral to diabetes education and medical specialists (as needed)

ASCVD, atherosclerotic cardiovascular disease. *Assessment and treatment planning are essential components of initial and all follow-up visits.

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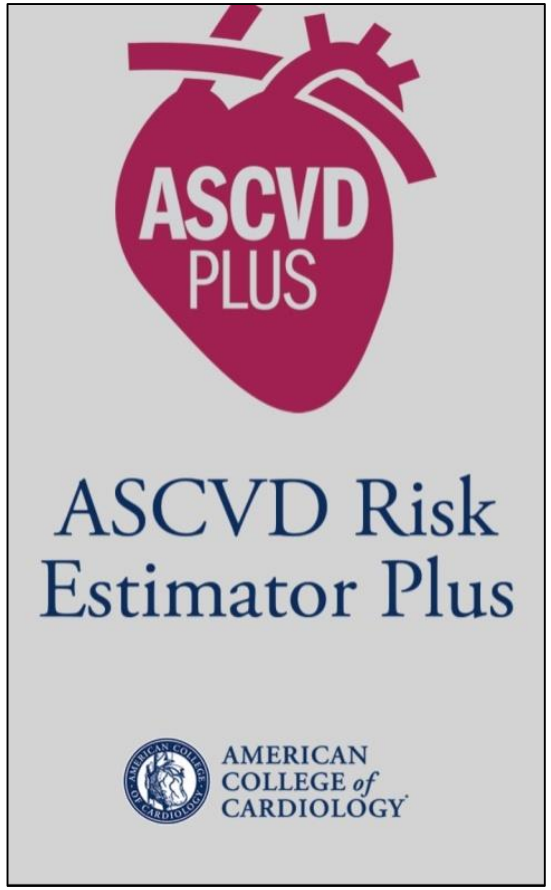
ASCVD Risk Assessment



1. Age
2. Sex
3. Race
4. Systolic Blood Pressure
5. Diastolic Blood Pressure
6. Total Cholesterol
7. HDL Cholesterol
8. LDL Cholesterol
9. History of Diabetes
10. Smoker
11. How long ago did the patient quit smoking
12. On Hypertension treatment
13. On statin
14. On Aspirin Therapy

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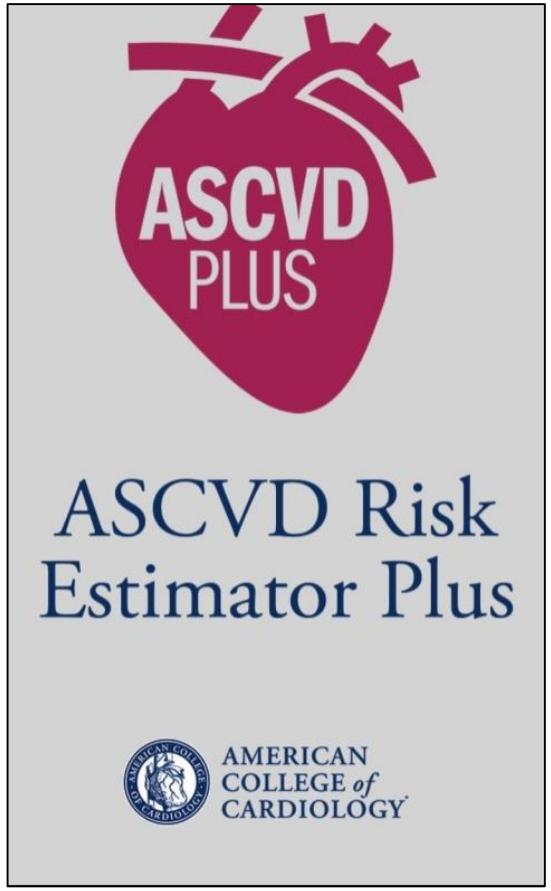
ASCVD Risk Assessment



10-year risk for ASCVD is categorized as:

< 5%	low risk
5% - 7.4%	Borderline risk
7.5%- 19.9%	intermediate risk
≥ 20%	High risk

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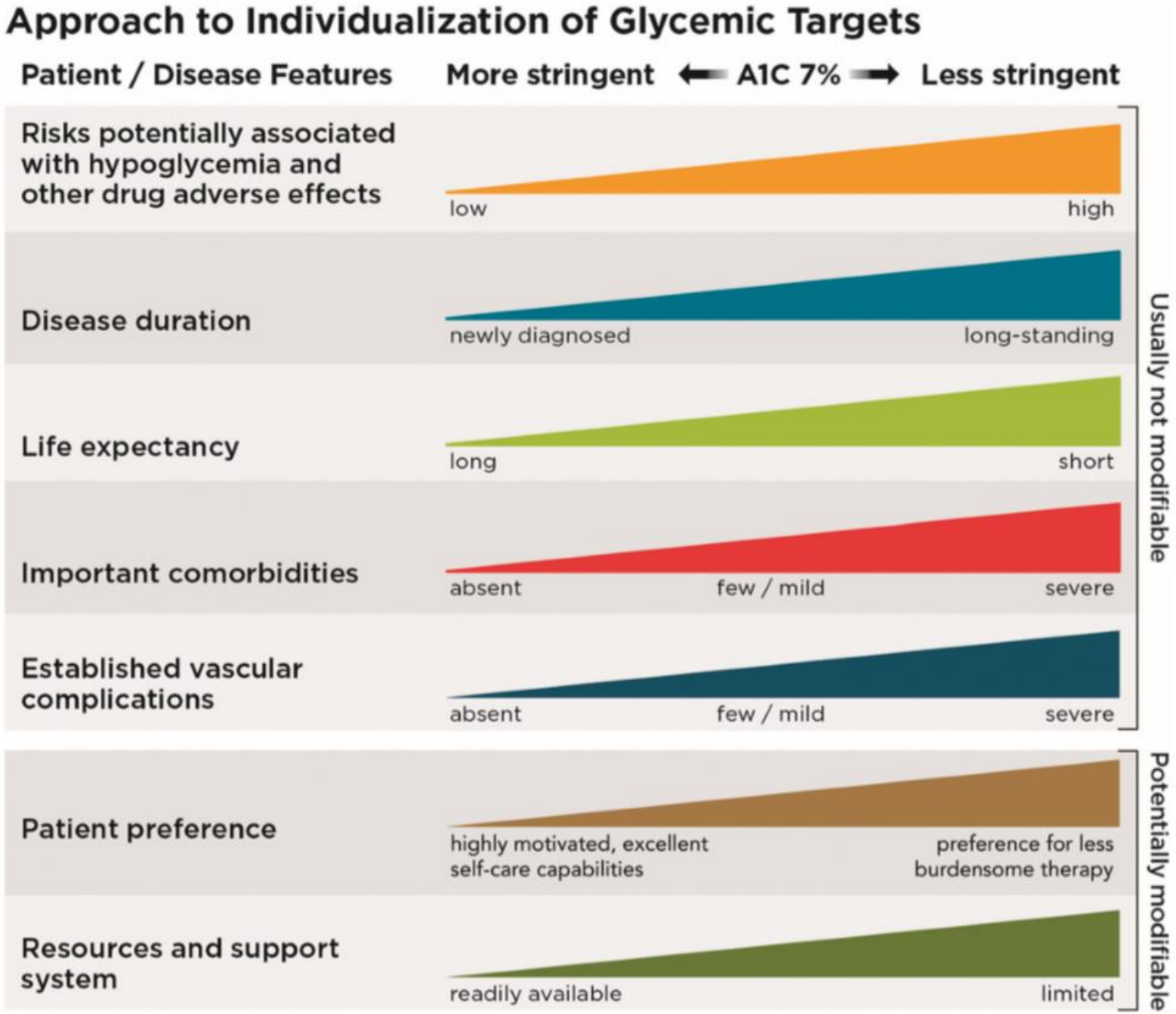
Best HbA1c Target



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A1C Target Individualization

1. What is the risk of hypoglycemia and adverse drug events?
2. What is the disease duration?
3. What is life expectancy?
4. Are there important comorbidities and/or established vascular complications?
5. What is the patient preference?
6. Dose the patient have resources and a support system?

American Diabetes Association®

Blood pressure

- Blood pressure should be measured at every routine clinical visit. When possible, 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.
- A Patients with blood pressure ≥ 180/110 mmHg and cardiovascular disease could be diagnosed with hypertension at a single visit. E
- All hypertensive patients with diabetes should monitor their blood pressure at home. A

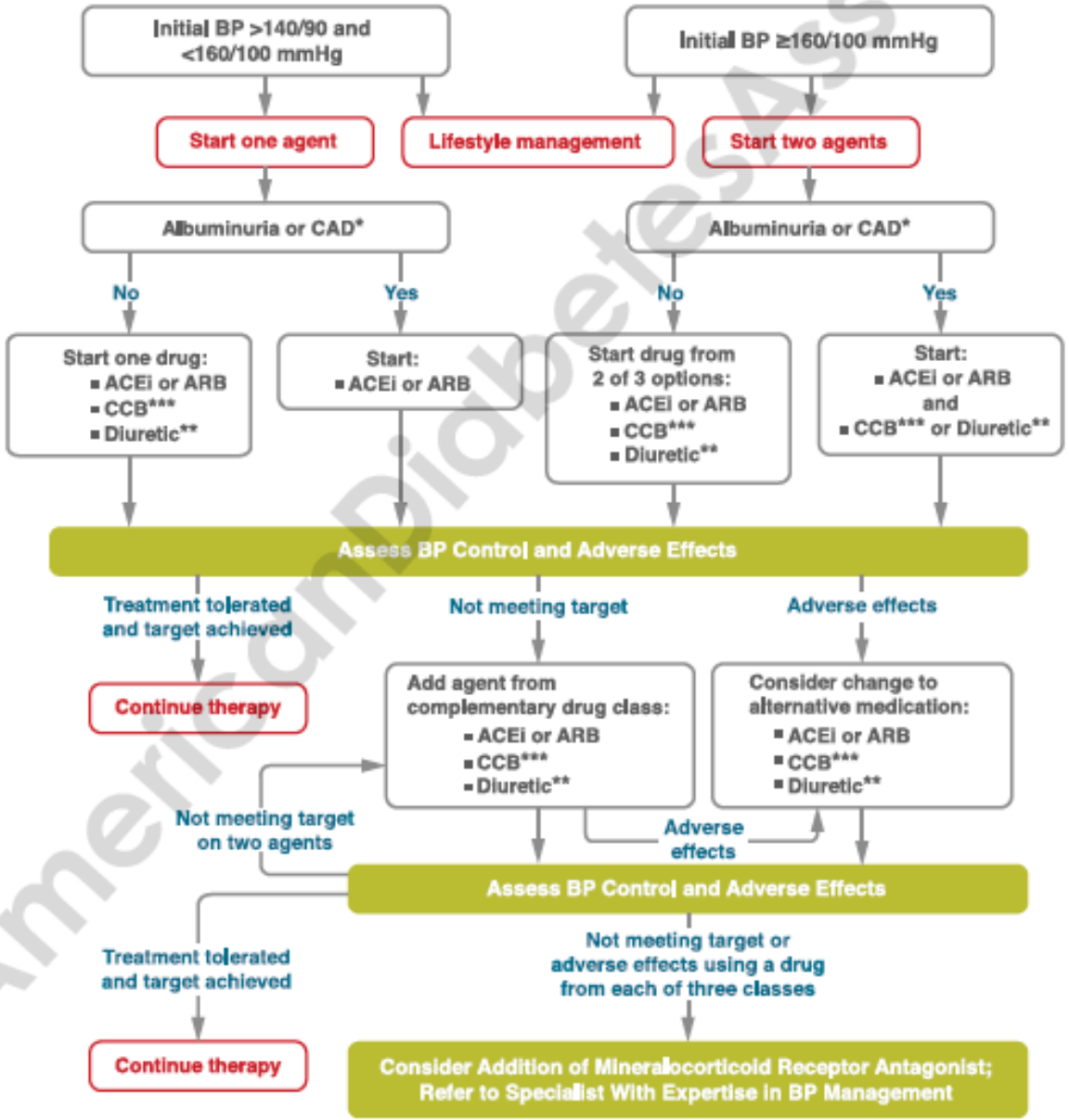
BP CONTROL

- Most patients with diabetes (cv risk< 15%) BP < 140 /90 mmHg
- For individuals with diabetes and hypertension at higher cv 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. B
- Pregnant patients with diabetes and preexisting hypertension BP≤ 110-135/ 85 mmHg

Blood pressure >120/80 mmHg

- 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

Recommendations for the Treatment of Confirmed Hypertension in People With Diabetes



BP

- Not a combination of ACE inhibitors and angiotensin receptor blockers

- ACEI + ARB

STATIN TREATMENT

Age (Years)		ASCVD or Target organ damage or ≥ 3 MRF Long duration ≥ 20 yrars	RF (+) or ≥ 10 DM	RF (-)
*Age 20–39	Dose of stain	High-intensity statin	Moderate intensity statin	No need for statin
	Goal	LDL<55	LDL<70	LDL<100
Age≥ 40- 75	Dose of statin	High-intensity statin	High-intensity(50-75 Years multiple RF) statin	Moderate intensity statin
	Goal	LDL<55	LDL<70	LDL<100

In adults with diabetes, it is reasonable to obtain a lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides) at the time of diagnosis at the initial medical evaluation, and at least every 5 years thereafter in patients under the age of 40 years. In younger patients with longer duration of disease (such as those with youth-onset type 1 diabetes), more frequent lipid profiles may be reasonable.

STATIN TREATMENT

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Statin therapy

- In adults with diabetes aged >75 years, it may be reasonable to initiate statin therapy after discussion of potential benefits and risks. C
- Statin therapy is contraindicated in pregnancy. B

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

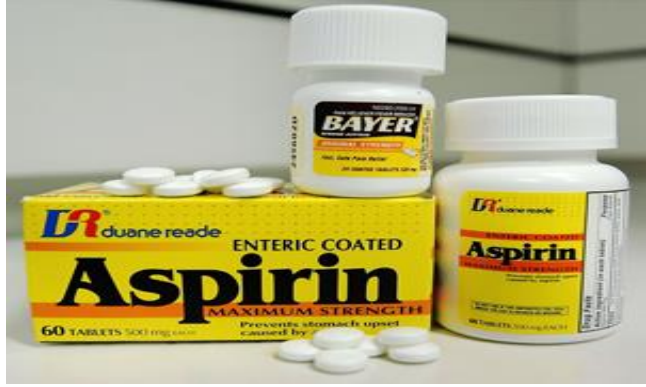
*Once-daily dosing. XL, extended release.

Ezetimibe or PCSK9 Inhibitor)

- If didnt recive to target LDL on maximally tolerated statin dose
- consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor).

- American Diabetes Association Standards of Medical Care in diabetes—2022

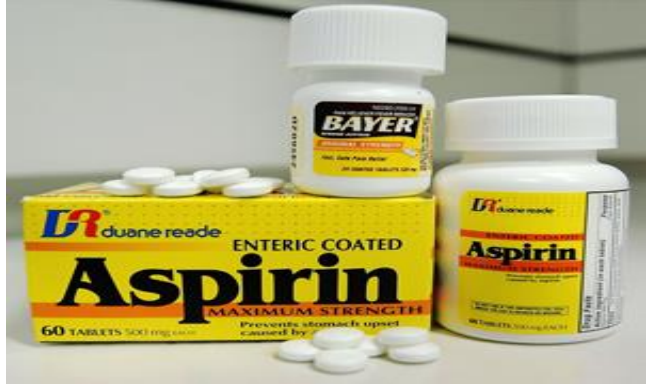
ANTIPLATELET AGENTS



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

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 bleeding. A

ANTIPLATELET AGENTS

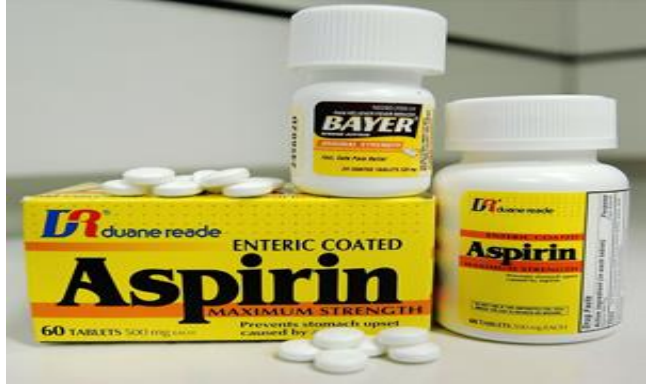


Consider aspirin therapy (75–162 mg/day) as **a primary prevention strategy** in those with type 2 diabetes who are at increased cardiovascular risk .

This includes most men or women with **diabetes aged >50 years who have at least one additional major risk factor** (family history of premature atherosclerotic cardiovascular disease, hypertension, smoking, dyslipidemia, or albuminuria) and are not at increased risk of bleeding.

Diabetes Care Volume 39, Supplement 1, January 2020

ANTIPLATELET AGENTS



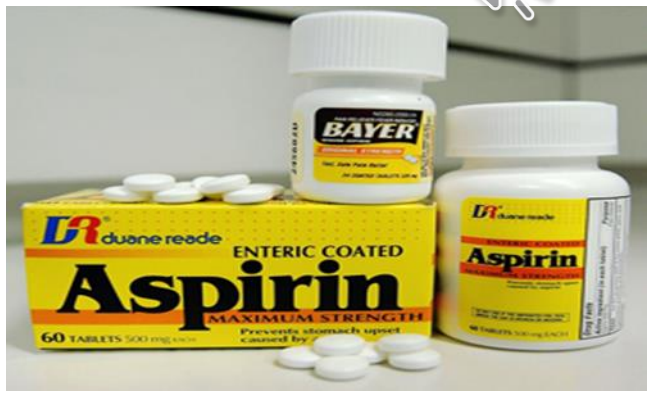
Aspirin **is not recommended** for those at low risk of ASCVD (such as men and women aged <50 years with diabetes with no other major ASCVD risk factors) as the low benefit is likely to be outweighed by the risks of bleeding.

Clinical judgment should be used for those at intermediate risk (younger patients with one or more risk factor)

Diabetes Care Volume 39, Supplement 1, January 2020

Over the age of 70 years

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



American Diabetes Association Standards of Medical Care in diabetes—2022

Conclusion

- Comprehensive Medical Evaluation
- Assessment of Comorbidities

References

- 1-Harrison's PRINCIPLES OF INTERNAL MEDICINE: 20TH EDITION
- 2-American Diabetes Association Standards of Medical Care in diabetes—2022
- 3-WILLIAMS textbook of ENDOCRINOLOGY 14 TH EDITION
- 4- UPTODATE 2022

Urinary albumin–to– creatinine ratio

- At least once a year, assess urinary albumin (e.g., spot urinary albumin–to– creatinine ratio) and estimated glomerular filtration rate in patients with type 1 diabetes with duration of > 5 years, in all patients with type 2 diabetes, and in all patients with comorbid hypertension.

Albuminuria

- Micro Albuminuria = spot urinary albumin-to-creatinine ratio
- >30–299 **mg/g**
- Or
- > 30–299 **µg/mg**
- Macro Albuminuria
- ≥ 300 mg/g
- Or
- ≥ 300 µg/mg creatinine

- خانم 60 ساله ای با دیابت تیپ 2 (از 7 سال پیش) با نتایج آزمایش آلبومین ادرار به شرح زیر مراجعه نموده است:

- **Urine Micro Albumin (Random) = 1.9 mg/dL**
- **Urine Creatinine (Random) = 380 mg/L**
- تفسیر شما از تست آلبومین اوری بیمار فوق چیست؟

Urine Micro Albumin (Random) = 1.9 mg/dL
Urine Creatinine (Random) = 380 mg/L

- **Urine Albumin(mg/L)/ Urine Creatinine(g/L)**
- **Urine Albumin(µg/L)/ Urine Creatinine(mg/L)**
- ابتدا برای بدست اوردن نسبت باید واحد حجم را یکسان کنید. مثلا واحد البومین را به لیتر تبدیل کنید، که میشود: 19 mg/L

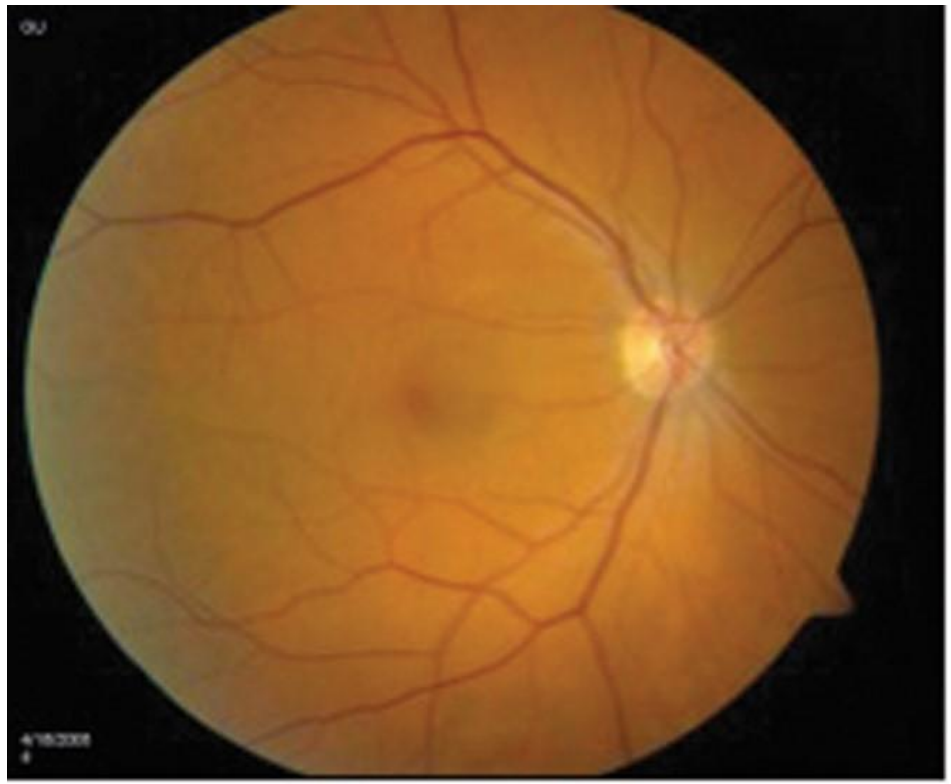
سپس واحد البومین را به میلیگرم و واحد کراتینین را به گرم تبدیل کنید که واحد کراتینین میشود: 0/38 g/L

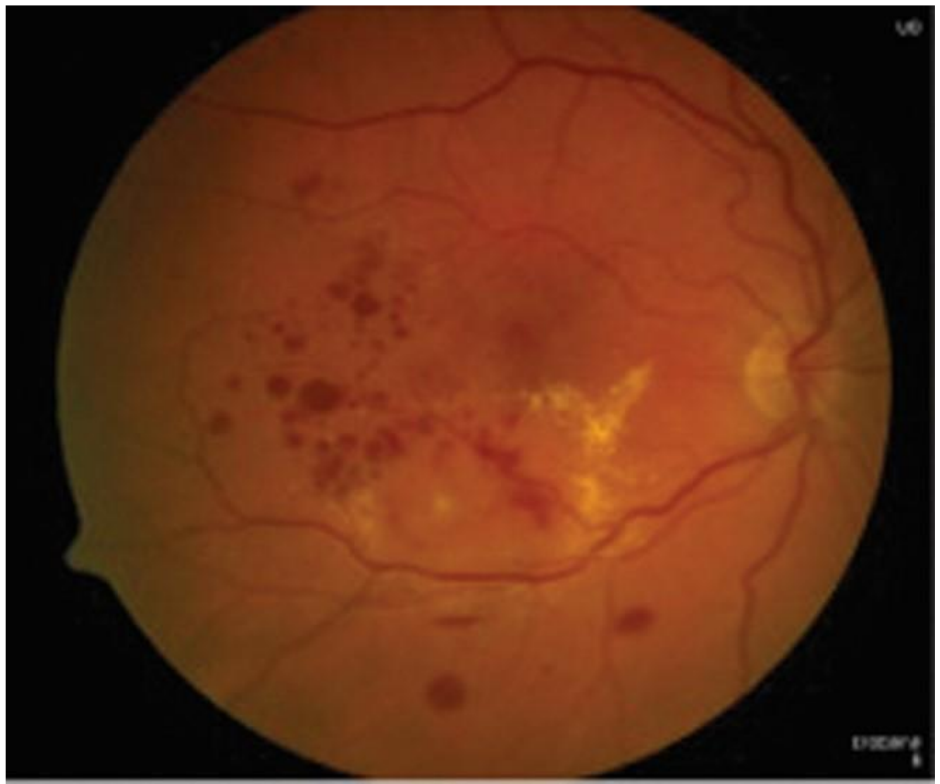
اینک نسبت را محاسبه کنید:

19 تقسیم بر 0/38 برابر 50 mg/g میزان میکرو البومین اوری بیمار محاسبه میشود.

بیمار میکروآلبومین اوری دارد.

- A 32-year-old woman in her second trimester of pregnancy presents to the ophthalmologist for a dilated eye examination. She has no known history of diabetic ophthalmopathy or any other diabetes-associated complications. The left image shows a picture of her dilated fundus from an examination several years ago, and the right image shows a picture from her current examination.





The images shown depict which of the following:

Answer	Left Image	Right Image
A.	Normal retina	Microaneurysms
B.	Normal retina	Severe nonproliferative diabetic retinopathy with retinal hemorrhages and hard exudates
C.	Nonproliferative diabetic retinopathy	Proliferative diabetic retinopathy
D.	Nonproliferative diabetic retinopathy	Proliferative retinopathy with laser scars
E.	Soft exudates	Hard exudates

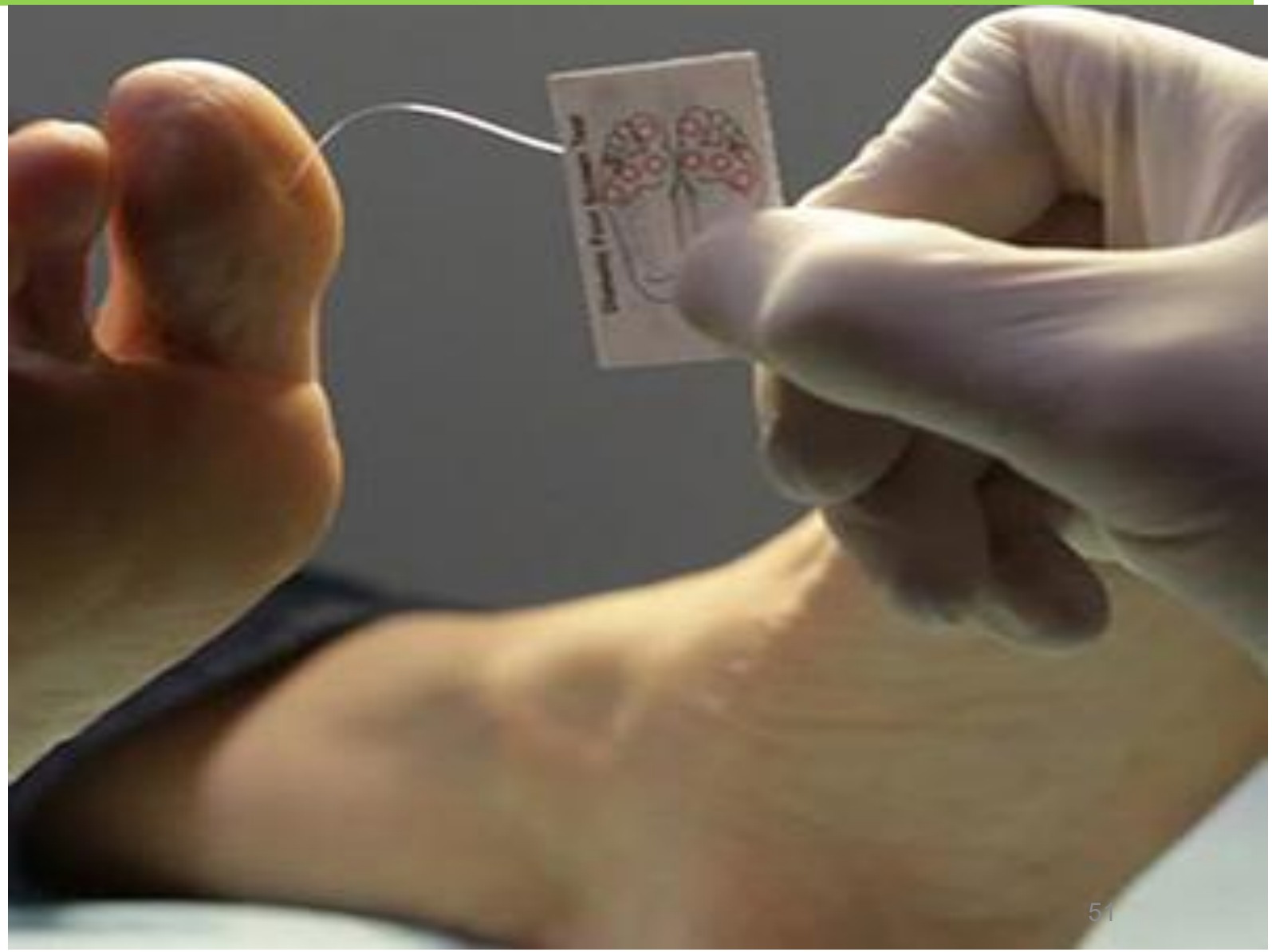
Correct Answer: B. B

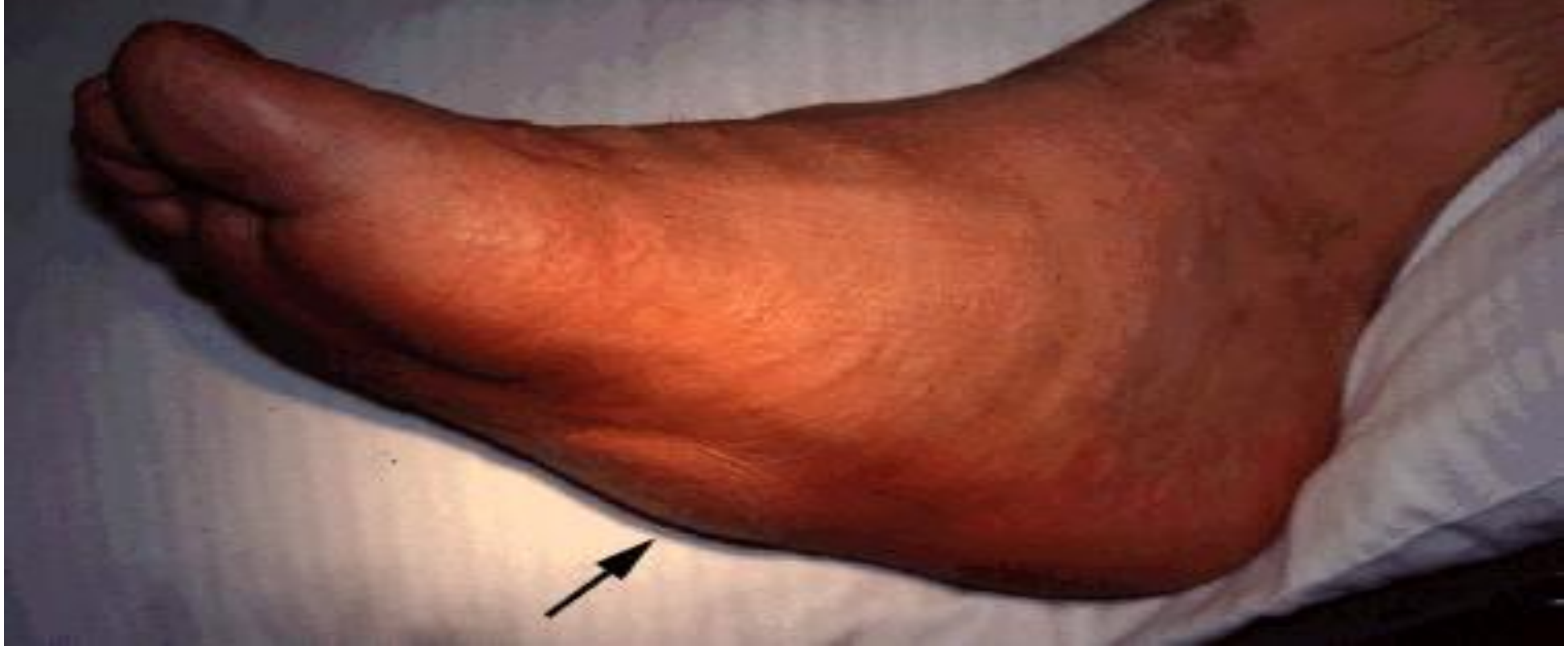
Foot examination

- An annual foot examination should:
- 1- Assess blood flow (pedal pulses)
- 2-Assessment of small nerve fiber function by testing thermal or pin prick sensation.
- Assessment of large nerve fiber function by testing:
  - **vibration** sensation with a 128 Hz tuning fork at the base of the great toe
  - proprioception (joint **position** sensation)
  - light touch perception with a 10 g **monofilament** on the dorsal aspect of the distal great toe
  - deep **tendon reflexes** at the ankle as compared with more proximal locations
- **nail**

Vibratory Sensation

monofilament





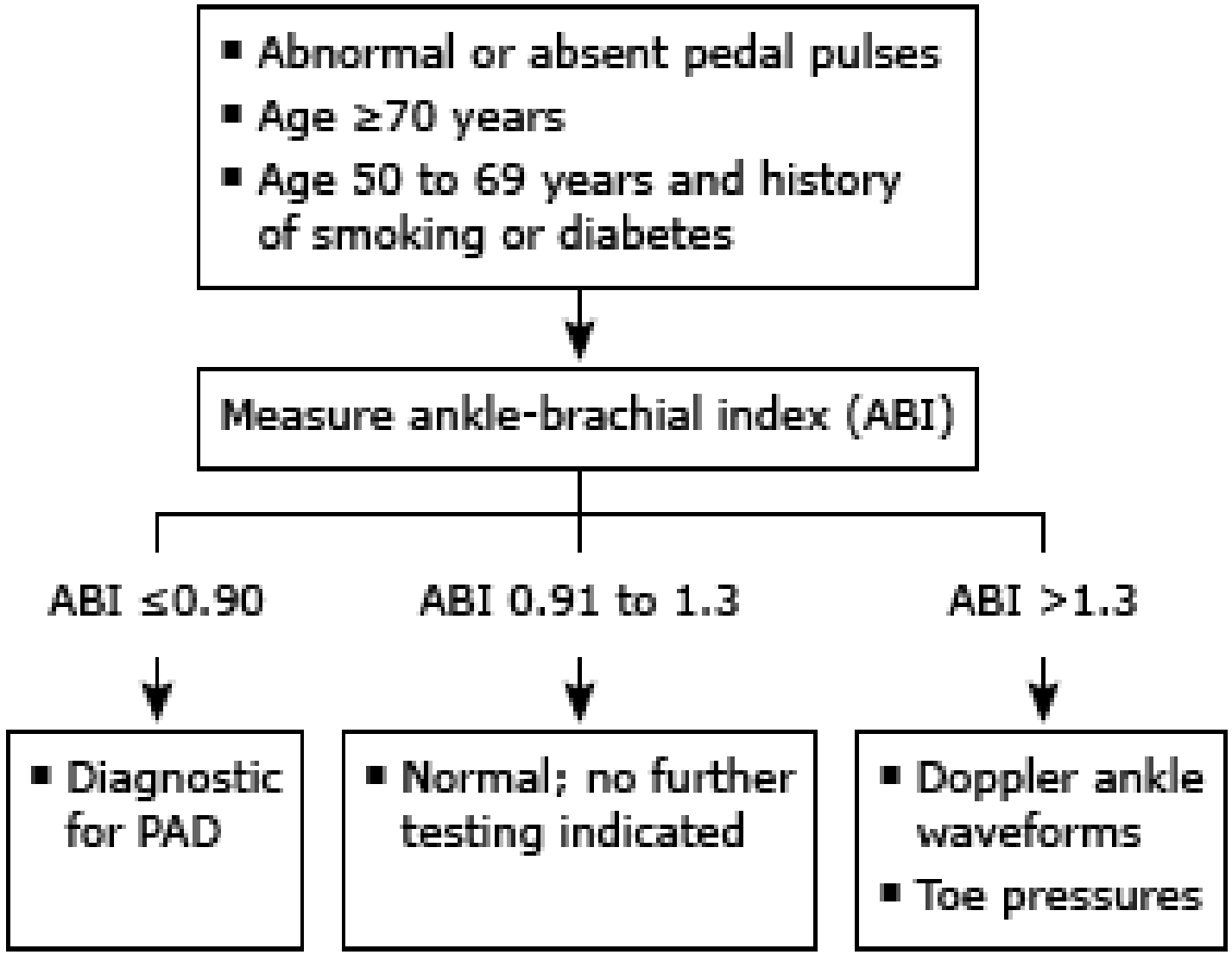
Diabetic patient with Charcot arthropathy characterized by collapse of the arch of the midfoot, which is replaced by a bony prominence (arrow). Several factors contribute to this painless condition, including small muscle wasting, decreased sensation, and maldistribution of weight bearing.

Ankle-brachial index

- simple and inexpensive
- arterial occlusive disease
- predictive of coronary heart disease and cerebrovascular disease

Algorithm for vascular testing in asymptomatic PAD

Patients with **diabetes** or **end-stage kidney disease** may have falsely elevated ABIs as a result of arterial calcification. The toe-brachial index may be more accurate.



STATIN TREATMENT

Age (Years)		ASCVD or Target organ damage or ≥ 3 MRF Long duration ≥ 20 yrars	RF (+) or ≥ 10 DM	RF (-)
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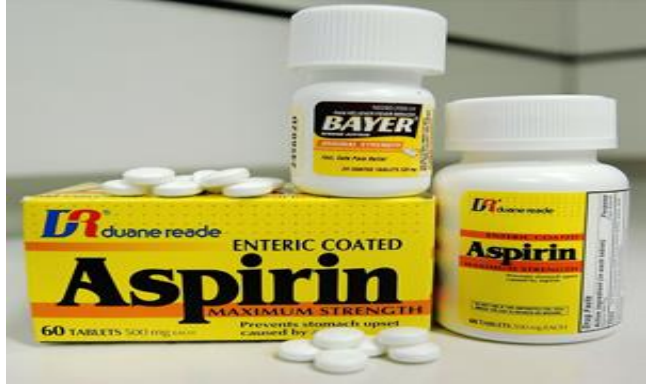
- American Diabetes Association Standards of Medical Care in diabetes—2022

ANTIPLATELET AGENTS



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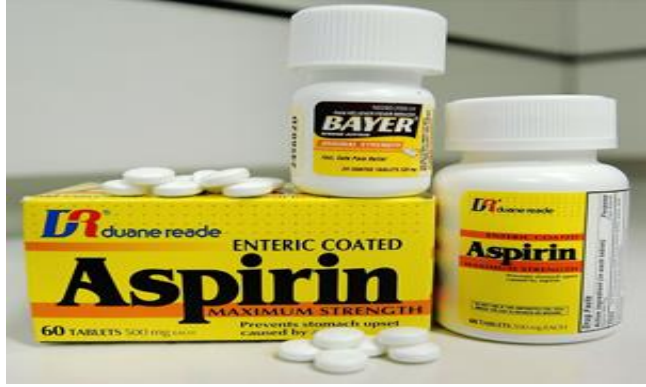
Aspirin therapy (75–162 mg/day) may be considered as a primary prevention strategy in those with diabetes who are at increased cardiovascular risk, after a comprehensive discussion with the patient on the benefits versus the comparable increased risk of bleeding. A

ANTIPLATELET AGENTS

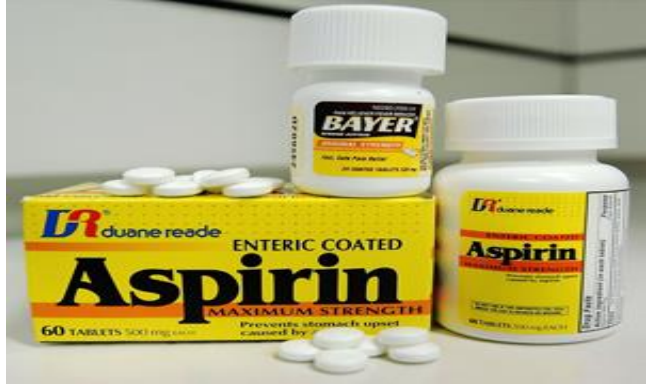


Consider aspirin therapy (75–162 mg/day) as **a primary prevention strategy** in those with type 2 diabetes who are at increased cardiovascular risk .

This includes most men or women with **diabetes aged >50 years who have at least one additional major risk factor** (family history of premature atherosclerotic cardiovascular disease, hypertension, smoking, dyslipidemia, or albuminuria) and are not at increased risk of bleeding.

Diabetes Care Volume 39, Supplement 1, January 2020

ANTIPLATELET AGENTS



Aspirin **is not recommended** for those at low risk of ASCVD (such as men and women aged <50 years with diabetes with no other major ASCVD risk factors) as the low benefit is likely to be outweighed by the risks of bleeding.

Clinical judgment should be used for those at intermediate risk (younger patients with one or more risk factor)

Diabetes Care Volume 39, Supplement 1, January 2020

Over the age of 70 years

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

American Diabetes Association Standards of Medical Care in diabetes—2022

Conclusion

- Comprehensive Medical Evaluation
- Assessment of Comorbidities

References

- 1-Harrison's PRINCIPLES OF INTERNAL MEDICINE: 20TH EDITION
- 2-American Diabetes Association Standards of Medical Care in diabetes—2022
- 3-WILLIAMS textbook of ENDOCRINOLOGY 14 TH EDITION
- 4- UPTODATE 2022


Thanks for your attention

IN THE NAME OF GOD

Approaches to CVD Treatment

By: Dr Mozhgan Karimifar

Assistant Prof. of Endocrinology

Isfahan University Of Medical Sciences

16 Farvardin 1397

CASE

مرد ۶۰ ساله ای با DM و HTN در معاینه : قد= ۱۷۰ سانتی متر وزن=۹۵ کیلوگرم و **فشارخون = ۱۵۰/۹۵** mmHg دارد. BMI=32.87 بروی عروق کاروتید و شکم بروئی ندارد. ادم روی تیبیا ندارد. سایر معاینات نرمال است. چه داروئی برای فشارخون ؟

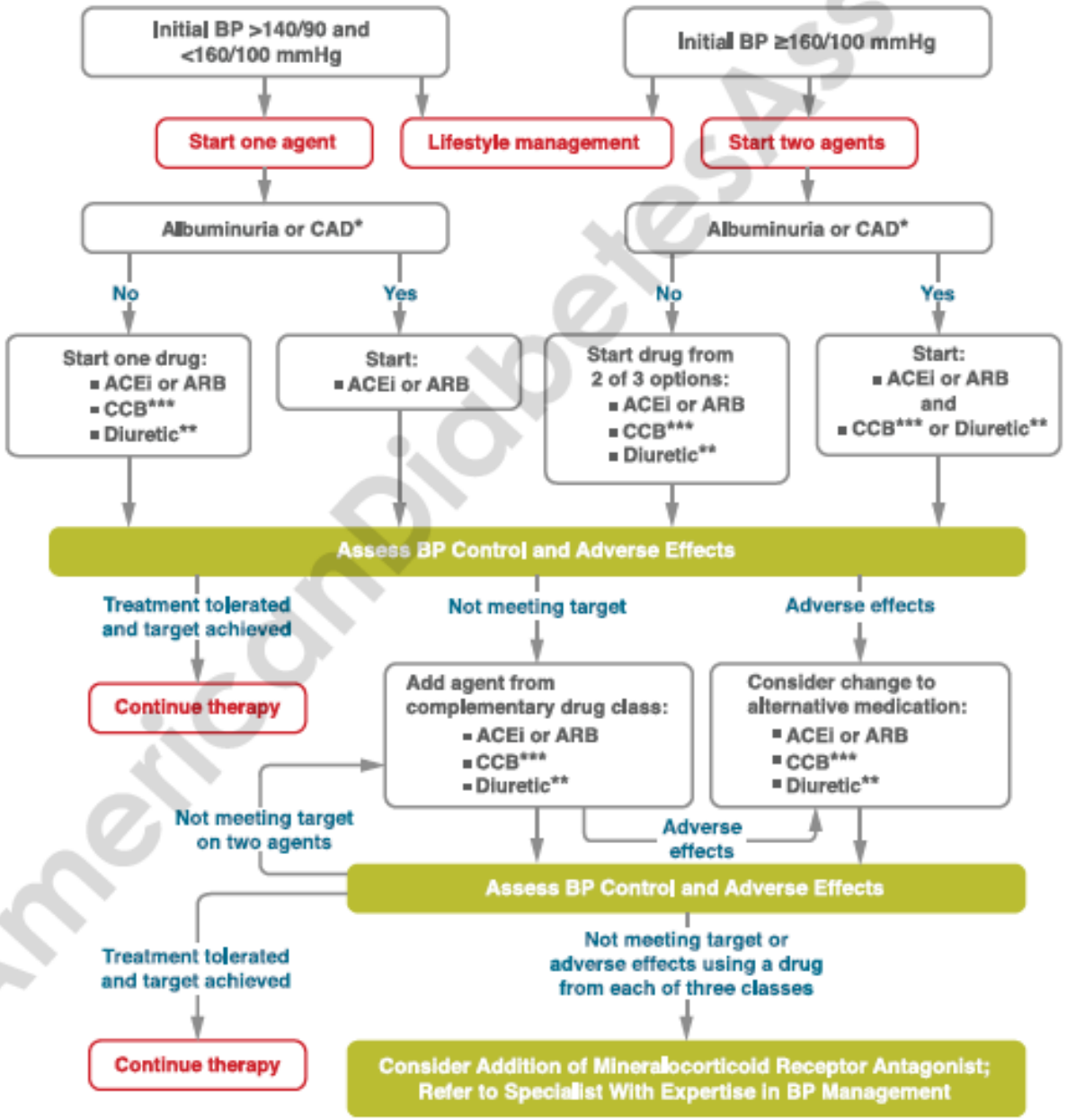
Hb= 15.9 g/dl	**Cr= 1.2**
TG=300 mg/dl	HbA1c= 8.2 %
Cholesterol=225 mg/dl	UA
HDL= 35 mg/dl	Glu=+
LDL= 130 mg/dl	Prot=neg
urine albumin= 4 mg/dl	urine creatinine= 600 mg/L

ACR= 40 /0.6= 66.6 mg/g

ACR= Micro Albumin/ Urine Creatinine
ACR= mg/g or micg/mg

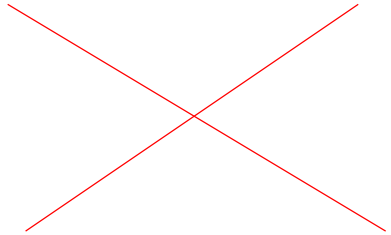
- Micro Albumin (Random) = 4 mg/dl
- Urine Creatinine (Random) = 600 mg/L
- ACR=?
- 40 /0.6= 66.6 mg/g

Recommendations for the Treatment of Confirmed Hypertension in People With Diabetes



BP

- Not a combination of ACE inhibitors and angiotensin receptor blockers



- ACEI + ARB

مرد ۶۰ ساله ای با DM و HTN در معاینه : قد= ۱۷۰ سانتی متر وزن=۹۵ کیلوگرم و **فشارخون = ۱۵۰/۹۵** mmHg دارد. BMI=32.87 بروی عروق کاروتید و شکم بروئی ندارد. ادم روی تیبیا ندارد. سایر معاینات نرمال است. چه داروئی برای فشارخون ؟

Hb= 15.9 g/dl	**Cr= 1.2**
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urine albumin= 4 mg/dl urine creatinine= 600 mg/L	

ACR= 40 /0.6= 66.6 mg/g

چه داروئی برای کنترل چربی خون ؟

آترووواستاتین (moderate-intensity statin یا high-intensity) یا

رزواستاتین

هدف؟

Hb= 15.9 g/dl	**Cr= 1.2**
TG=300 mg/dl	HbA1c= 8.2 %
Cholesterol=225 mg/dl	UA
HDL= 35 mg/dl	Glu=+
LDL= 130 mg/dl	Prot=neg
urine albumin= 4 mg/dl	urine creatinine= 600 mg/L

ACR= 40 /0.6= 66.6 mg/g

STATIN TREATMENT

Age (Years)		ASCVD or Target organ damage or ≥ 3 MRF Long duration ≥ 20 yrars	RF (+) or ≥ 10 DM	RF (-)
*Age 20–39	Dose of stain	High-intensity statin	Moderate intensity statin	No need for statin
	Goal	LDL<55	LDL<70	LDL<100
Age≥ 40- 75	Dose of statin	High-intensity statin	High-intensity(50-75 Years multiple RF) statin	Moderate intensity statin
	Goal	LDL<55	LDL<70	LDL<100

In adults with diabetes, it is reasonable to obtain a lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides) at the time of diagnosis at the initial medical evaluation, and at least every 5 years thereafter in patients under the age of 40 years. In younger patients with longer duration of disease (such as those with youth-onset type 1 diabetes), more frequent lipid profiles may be reasonable.

STATIN TREATMENT

Age (Years)	Dose of stain	ASCVD or Target organ damage or ≥ 3 MRF Long duration ≥ 20 yrars	RF (+) or ≥ 10 DM	RF (-)
*Age 20–39	Dose of stain	High-intensity statin	Moderate intensity statin	No need for statin
	Goal	LDL<55	LDL<70	LDL<100
Age≥ 40-75	Dose of statin	High-intensity statin	High-intensity(50-75 Years multiple RF) statin	Moderate intensity statin
	Goal	LDL<55	LDL<70	LDL<100

Statin

- Atorvastatin and rosuvastatin are generally well tolerated if started at **lower doses** and titrated up to meet lipid goals.
- Atorvastatin is the statin of choice in patients with renal disease. If statin intolerant or the LDL cholesterol goal is not met, consider the addition of *ezetimibe* or a *PCSK9 inhibitor*.

Statin therapy

- In adults with diabetes aged >75 years, it may be reasonable to initiate statin therapy after discussion of potential benefits and risks. C
- Statin therapy is contraindicated in pregnancy. B

مرد ۶۰ ساله ای با DM و HTN در معاینه : قد= ۱۷۰ سانتی متر وزن=۹۵ کیلوگرم و **فشارخون** = **۱۵۰/۹۵** mmHg دارد. BMI=32.87 بروی عروق کاروتید و شکم بروئی ندارد. ادم روی تیبیا ندارد. سایر معاینات نرمال است. چه داروئی برای کنترل لیپید؟

Hb= 15.9 g/dl	**Cr= 1.2**
TG=**650** mg/dl	HbA1c= 8.2 %
Cholesterol=225 mg/dl	FBS= 250
HDL= 35 mg/dl	Urine Glu=+++
LDL= 130 mg/dl	Urine Prot=neg
urine albumin= 4 mg/dl urine creatinine= 600 mg/L	
ACR= 40 /0.6= 66.6 mg/g	

Icosapent

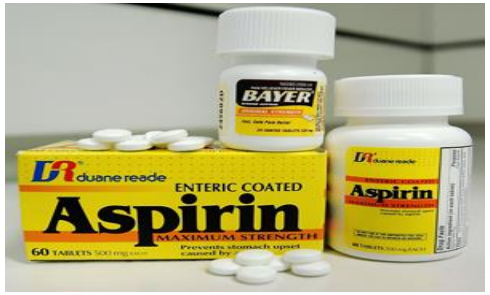
- **Icosapent** results in cardiovascular risk reduction on top of statin treatment and may have a larger benefit in diabetic individuals.
- 2 g twice daily with meals
- **Niacin** use is associated with an even greater increased risk for type 2 DM or worsening glycemic control and is not recommended because of a lack of improvement in cardiovascular outcomes.

مرد ۶۰ ساله ای با DM و HTN در معاینه : قد= ۱۷۰ سانتی متر وزن=۹۵ کیلوگرم و **فشارخون** = **۱۵۰/۹۵** mmHg دارد. BMI=32.87 بروی عروق کاروتید و شکم بروئی ندارد. ادم روی تیبیا ندارد. سایر معاینات نرمال است. آیا **آسپرین** تجویز می کنید؟

Hb= 15.9 g/dl	**Cr= 1.2**
TG=300 mg/dl	HbA1c= 8.2 %
Cholesterol=225 mg/dl	UA
HDL= 35 mg/dl	Glu=+
LDL= 130 mg/dl	Prot=neg
urine albumin= 4 mg/dl	urine creatinine= 600 mg/L

ACR= 40 /0.6= 66.6 mg/g

ANTIPLATELET AGENTS



Consider aspirin therapy (75–162 mg/day) as **a primary prevention strategy** in those with type 2 diabetes who are at increased cardiovascular risk .

This includes most men or women with **diabetes aged >50 years who have at least one additional major risk factor** (family history of premature atherosclerotic cardiovascular disease, hypertension, smoking, dyslipidemia, or albuminuria) and are not at increased risk of bleeding.

مرد ۴۲ ساله ای با DM و HTN در معاینه : قد= ۱۷۰ سانتی متر وزن=۸۵ کیلوگرم و **فشارخون** = **۱۹۰/۱۲۰** mmHg دارد. بروی عروق کاروتید و شکم بروئی ندارد. ادم روی تیبیا ندارد. سایر معاینات نرمال است. تحت درمان با والزارتان و آملودیپین و هیدروکلرتیازیداست.از ۱۲ سال قبل DMوHTN دارد و از ۶ سال قلب فشارخون و DMکنترل نبوده تشخیص چیست؟

چه اقداماتی برای کنترل فشارخون انجام می دهید؟

۱- فشارخون مقاوم به درمان

۲- آیا دارو می خورد؟

۳- بررسی علل ثانویه فشارخون

۴- سونو کلیه و سونوداپلر شریان رنال

۵- آزمایشات مربوطه و ECG

Renovascular disease
Primary kidney disease
Drug-induced hypertension: Oral contraceptives Anabolic steroids NSAIDs Chemotherapeutic agents (eg, tyrosine kinase inhibitors/VEGF blockade) Stimulants (eg, cocaine, methylphenidate) Calcineurin inhibitors (eg, cyclosporine) Antidepressants (eg, venlafaxine)
Pheochromocytoma
Primary aldosteronism
Cushing's syndrome
Sleep apnea syndrome
Coarctation of the aorta
Hypothyroidism
Primary hyperparathyroidism

مرد ۴۲ ساله ای با DM و HTN در معاینه : قد= ۱۷۰ سانتی متر وزن=۸۵ کیلوگرم و **فشارخون** = **۱۹۰/۱۲۰** mmHg دارد. بروی عروق کاروتید و شکم بروئی ندارد. ادم روی تیبیا ندارد. سایر معاینات نرمال است. تحت درمان با والزارتان و آملودیپین و هیدروکلرتیازیداست.از ۱۲ سال قبل HTNوDM دارد و از ۶ سال قلب فشارخون و DMکنترل نبوده چه داروئی برای فشارخون ؟

Hb= 15.9 g/dl	**Cr= 1.2**
K= 3.2 mEq/L	HbA1c= 10 %
Na= 139 mEq/L	UA
Aldosterone= 79 ng/dl (1.2-35)	Glu=+
Renin= 0.05 µiu/ml (5.3-99.1)	Prot=neg
FBS= 300 ACR= 80 mg/g	

- Serum potassium and renal function should be monitored.
- Because of the high prevalence of atherosclerotic disease in individuals with type 2 DM, the possibility of renovascular hypertension should be considered when the blood pressure is not readily controlled.

PHYSICAL ACTIVITY

- Most adults with with type 1 C and type 2 B diabetes should engage in *150 min* or more of moderate-to vigorous intensity physical activity per week, spread over at least 3 days/week, with no more than 2 consecutive days without activity. *Shorter durations* (minimum 75 min/week) of *vigorous-intensity* or interval training may be sufficient for younger and more physically fit individuals.

PHYSICAL ACTIVITY

- All adults, and particularly those with type 2 diabetes, should decrease the amount of time spent in daily sedentary behavior. B Prolonged sitting should be interrupted every 30 min for blood glucose benefits, particularly in adults with type 2 diabetes. C

PHYSICAL ACTIVITY

- *Children and adolescents* with type 1 or type 2 diabetes or prediabetes should engage in 60 min/day or more of moderate- or vigorous intensity aerobic activity, with vigorous muscle-strengthening and bone-strengthening activities at least 3 days/week. C

HYPERTENSION/BLOOD PRESSURE CONTROL

- Screening and Diagnosis
- Blood pressure should be measured *at every routine visit*.
- Patients found to have elevated blood pressure should have blood pressure confirmed on a *separate day*. B

BP

- چه داروئی پیشنهاد می کنید؟
- الف)ACEI
- ب)ARB
- ج)CCB
- د)Diuretic
- ه) Mineralocorticoid RA

BP CONTROL(Systolic Targets)

•Goals

- Most patients with diabetes and hypertension should be treated to a systolic blood pressure goal of < 140 mmHg and a diastolic blood pressure goal of < 90 mmHg. A
- Patients with *blood pressure ≥180/110 mmHg* and cardiovascular disease could be diagnosed with hypertension at a single visit. E
- All hypertensive patients with diabetes should monitor their blood pressure at home.

BP

- Optimize blood pressure control (<140/90 mmHg) to reduce the risk or slow the progression of diabetic kidney disease. A

Treatment for hypertension should include drug classes

- ACE inhibitors,
- angiotensin receptor blockers
- thiazide- like diuretics
- or dihydropyridine calcium channel blockers
  - nifedipine, isradipine, felodipine, nicardipine, nisoldipine, lacidipine, and amlodipine
- Multiple drug therapy is generally required to achieve blood pressure targets (but not a combination of ACE inhibitors and angiotensin receptor blockers). A

BP in older adults (>65)

- In older adults, pharmacological therapy to achieve treatment goals of < 130/70 mmHg is *not recommended;* treating to systolic blood pressure <130 mmHg has not been shown to improve cardiovascular outcomes and
- treating to diastolic blood pressure < 70 mmHg has been associated with higher mortality. C

LIPID MANAGEMENT

Cardiovascular risk factors

- Dyslipidemia
- Hypertension
- Smoking
- Family history of premature coronary disease
- Albuminuria.

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Table 9.2—Recommendations for statin and combination treatment in adults with diabetes

Age	ASCVD	Recommended statin intensity^ and combination treatment*
<40 years	No	None†
	Yes	High • If LDL cholesterol ≥70 mg/dL despite maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor)#
≥40 years	No	Moderate‡
	Yes	High • If LDL cholesterol ≥70 mg/dL despite maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor)

*In addition to lifestyle therapy. ^For patients who do not tolerate the intended intensity of statin, the maximally tolerated statin dose should be used. †Moderate-intensity statin may be considered based on risk-benefit profile and presence of ASCVD risk factors. ASCVD risk factors include LDL cholesterol ≥100 mg/dL (2.6 mmol/L), high blood pressure, smoking, chronic kidney disease, albuminuria, and family history of premature ASCVD. ‡High-intensity statin may be considered based on risk-benefit profile and presence of ASCVD risk factors. #Adults aged <40 years with prevalent ASCVD were not well represented in clinical trials of non-statin–based LDL reduction. Before initiating combination lipid-lowering therapy, consider the potential for further ASCVD risk reduction, drug-specific adverse effects, and patient preferences.

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Table 9.3—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% to 50%)
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 2–4 mg

*Once-daily dosing. XL, extended release.

ANTIPLATELET AGENTS

- Consider aspirin therapy (75–162 mg/day) as a primary prevention strategy in those with type 1 or type 2 diabeteswho are at increased cardiovascular risk (10-year risk >10%). This includes most men or women with diabetes aged ≥ 50 years who have at least one additional major risk factor:
- FH of premature atherosclerotic cardiovascular disease
- Hypertension
- Smoking
- Dyslipidemia
- Albuminuria
- and are not at increased risk of bleeding. C

ANTIPLATELET AGENTS

- For patients with atherosclerotic cardiovascular disease and documented aspirin allergy, *clopidogrel* (75 mg/day) should be used. B
- Dual antiplatelet therapy is reasonable for up to a year after an acute coronary syndrome. B

CORONARY HEART DISEASE

- Screening
- 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

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

urinary albumin–to– creatinine ratio

- At least once a year, assess urinary albumin (e.g., spot urinary albumin–to– creatinine ratio) and estimated glomerular filtration rate in patients with type 1 diabetes with duration of > 5 years, in all patients with type 2 diabetes, and in all patients with comorbid hypertension. B

DIABETIC RETINOPATHY

- Screening
- Adults with type 1 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist within 5 years after the onset of diabetes. B

- Patients with type 2 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist at the time of the diabetes diagnosis. B

NEUROPATHY

- Screening
- All patients should be assessed for diabetic peripheral neuropathy starting at diagnosis of type 2 diabetes and 5 years after the diagnosis of type 1 diabetes and at least annually thereafter. B

FOOT CARE

- Perform a comprehensive foot evaluation each year to identify risk factors for ulcers and amputations. B

between groups. The
ease rate was lower
oup over follow-up.
ollow-up of the VADT
a reduction in the risk
events (52.7 [control
ntervention group]
erson-years) with no
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s in ACCORD (42) and
of VADT (50) suggest
sks of intensive glyce-
tweigh its benefits in
In all three trials, se-
was significantly more
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Table 5.2—Summary of glycemic recommendations for 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. 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.
†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.

of <7% (53 mmol/mol). The issue of preprandial versus postprandial SMBG targets is complex (54). Elevated postchallenge (2-h oral glucose tolerance test) glucose values have been associated with increased cardiovascular risk independent of fasting plasma glucose in some epidemiological studies. In subjects with diabetes, surrogate measures

and landmark glycemic control trials such as the DCCT and UKPDS relied overwhelmingly on preprandial SMBG. Additionally, a randomized controlled trial in patients with known CVD found no CVD benefit of insulin regimens targeting postprandial glucose compared with those targeting preprandial glucose

CASE 1

مرد ۶۰ ساله ای با شکایت خشکی دهان که از چند ماه قبل شروع شده است به شما مراجعه میکند. داروئی مصرف نمیکند. کاهش وزن و تغبیر روش زندگی نداشته است. سابقه فامیلی دیابت را در دو خواهر و برادر کوچکتر از خودش میدهد. سابقه بیماری خاصی را نمی دهد، فقط متذکر است که دو ماه پیش نیز فشارخون وی ۱۵ بوده است در آزمایش دو ماه پیش که همراه ایشان است، نیز قند خون ۱۶۰ داشته است. در معاینه :

قد= ۱۷۰ سانتی متر وزن=۹۵ کیلوگرم و فشارخون = ۱۵۰/۹۵ میلیمتر جیوه دارد.

BMI=32.87

بروی عروق کاروتید و شکم بروئی ندارد. ادم روی تیبیا ندارد.

سایر معاینات نرمال است.

CASE 1

- ازمایشات وی به شرح زیر است:

Hb= 15.9 g/dl	TG=300 mg/dl	HDL= 35 mg/dl
FBS= 190 mg/dl	Cholesterol=225 mg/dl	LDL= 125 mg/dl
Cr= 1.2	HbA1c= 8.2 %	
UA	Glu=+	Pro=neg

Pharmacologic Approaches to Glycemic Treatment

- چه داروی کاهنده قند خون را پیشنهاد میکنید؟

A1C GOALS

- A reasonable A1C goal for many nonpregnant adults is ,< 7% (53 mmol/mol). A

A1C goals < 6.5%

- short duration of diabetes:

- type 2 diabetes treated with lifestyle or metformin only
- long life expectancy
- no significant cardiovascular disease. C

CASE 1

- با 2000 میلیگرم مت فورمین قند خون بیمار مدت 15 ماه کنترل بود ولی در آزمایشات جدید:

- FBS=180
- BS 2hPP= 240
- HbA1c= 9%

- دارد چه داروئی راپیشنهاد میکنید؟

- Mean glucose levels for specified A1C levels = (Patient HbA1c – 2) * 30
- (9 – 2) * 30 =210mg/dl

Start with Monotherapy unless:

A1C is greater than or equal to 9%, **consider Dual Therapy.**

A1C is greater than or equal to 10%, blood glucose is greater than or equal to 300 mg/dL, or patient is markedly symptomatic, **consider Combination Injectable Therapy** (See Figure 8.2).

Monotherapy — Metformin — Lifestyle Management

EFFICACY*	high
HYPO RISK	low risk
WEIGHT	neutral/loss
SIDE EFFECTS	GI/lactic acidosis
COSTS*	low

If A1C target not achieved after approximately 3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

Dual Therapy — Metformin + — Lifestyle Management

	Sulfonylurea	Thiazolidinedione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist	Insulin (basal)
EFFICACY*	high	high	intermediate	intermediate	high	highest
HYPO RISK	moderate risk	low risk	low risk	low risk	low risk	high risk
WEIGHT	gain	gain	neutral	loss	loss	gain
SIDE EFFECTS	hypoglycemia	edema, HF, fxs	rare	GU, dehydration, fxs	GI	hypoglycemia
COSTS*	low	low	high	high	high	high

If A1C target not achieved after approximately 3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

Triple Therapy — Metformin + — Lifestyle Management

Sulfonylurea +	Thiazolidinedione +	DPP-4 inhibitor +	SGLT2 inhibitor +	GLP-1 receptor agonist +	Insulin (basal) +
TZD	SU	SU	SU	SU	TZD
or DPP-4-i	or DPP-4-i	or TZD	or TZD	or TZD	or DPP-4-i
or SGLT2-i	or SGLT2-i	or SGLT2-i	or DPP-4-i	or SGLT2-i	or SGLT2-i

Dual Therapy Metformin + Lifestyle Management

	Sulfonylurea	Thiazolidinedione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist	Insulin (basal)
EFFICACY*	high	high	intermediate	intermediate	high	highest
HYPO RISK	moderate risk	low risk	low risk	low risk	low risk	high risk
WEIGHT	gain	gain	neutral	loss	loss	gain
SIDE EFFECTS	hypoglycemia	edema, HF, fxs	rare	GU, dehydration, fxs	GI	hypoglycemia
COSTS*	low	low	high	high	high	high

If A1C target not achieved after approximately 3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

Triple Therapy Metformin + **Lifestyle Management**

Sulfonylurea +	Thiazolidinedione +	DPP-4 inhibitor +	SGLT2 inhibitor +	GLP-1 receptor agonist +	Insulin (basal) +
TZD	SU	SU	SU	SU	TZD
or DPP-4-i	or DPP-4-i	or TZD	or TZD	or TZD	or DPP-4-i
or SGLT2-i	or SGLT2-i	or SGLT2-i	or DPP-4-i	or SGLT2-i	or SGLT2-i
or GLP-1-RA	or GLP-1-RA	or Insulin§	or GLP-1-RA	or Insulin§	or GLP-1-RA
or Insulin§	or Insulin§		or Insulin§		

If A1C target not achieved after approximately 3 months of triple therapy and patient (1) on oral combination, move to basal insulin or GLP-1 RA, (2) on GLP-1 RA, add basal insulin, or (3) on optimally titrated basal insulin, add GLP-1 RA or mealtime insulin. Metformin therapy should be maintained, while other oral agents may be discontinued on an individual basis to avoid unnecessarily complex or costly regimens (i.e., adding a fourth antihyperglycemic agent).

Combination Injectable Therapy (See Figure 8.2)

Figure 8.1—Antihyperglycemic therapy in type 2 diabetes: general recommendations. The order in the chart was determined by historical availability and the route of administration, with injectables to the right; it is not meant to denote any specific preference. Potential sequences of antihyperglycemic therapy for patients with type 2 diabetes are displayed, with the usual transition moving vertically from top to bottom (although horizontal movement within therapy stages is also possible, depending on the circumstances). DPP-4-i, DPP-4 inhibitor; fxs, fractures; GI, gastrointestinal; GLP-1 RA, GLP-1 receptor agonist; GU, genitourinary; HF, heart failure; Hypo, hypoglycemia; SGLT2-i, SGLT2 inhibitor; SU, sulfonylurea; TZD, thiazolidinedione. *See ref. 21 for description of efficacy and cost categorization. §Usually a basal insulin (NPH, glargine, detemir, degludec). Adapted with permission from Inzucchi et al. (21).

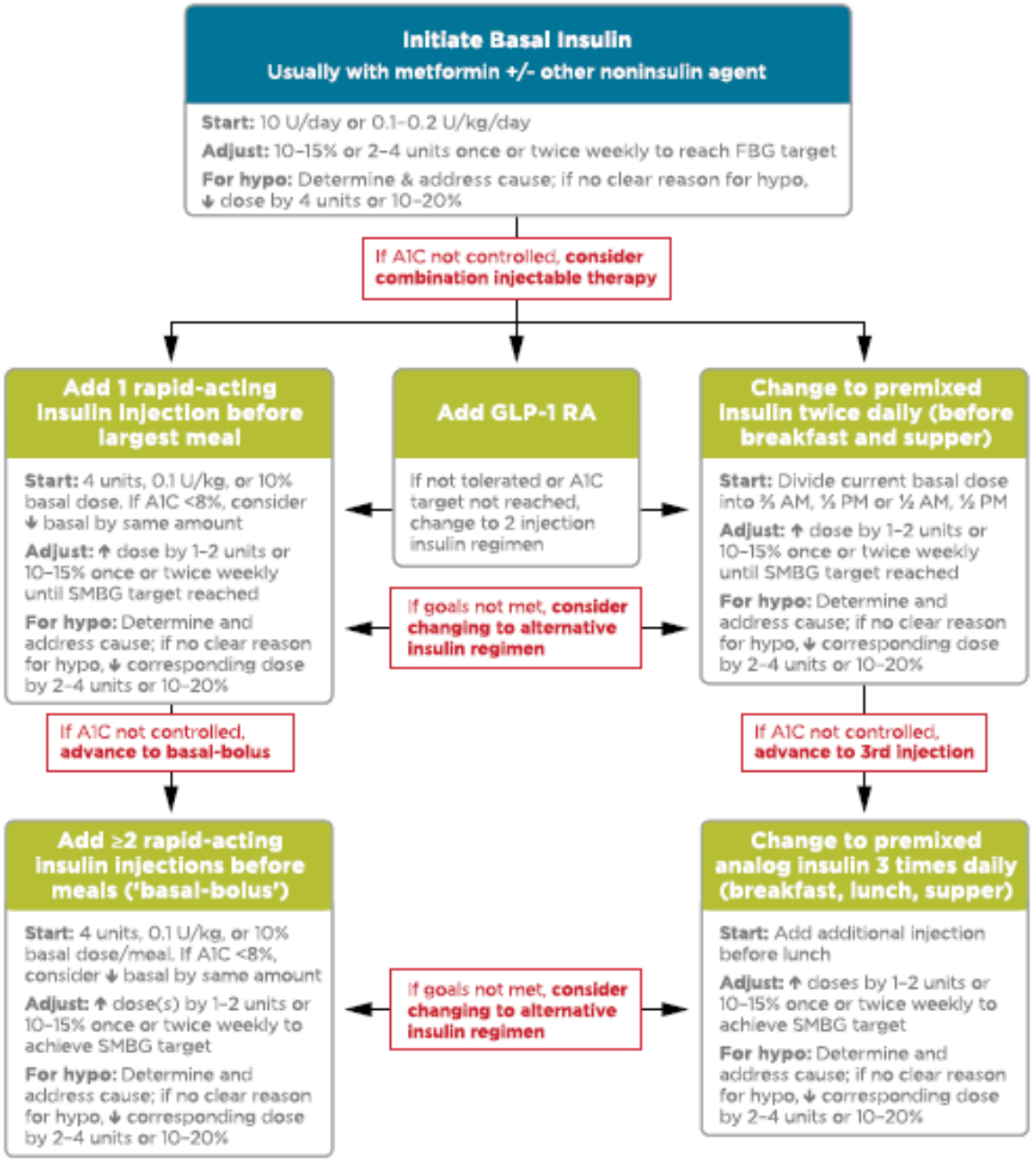


Figure 8.2—Combination injectable therapy for type 2 diabetes. FBG, fasting blood glucose; hypo, hypoglycemia. Adapted with permission from Inzucchi et al. (31).

CASE 2

CASE 2

- -خانم 60 ساله ای جهت بهبود کنترل قند خون به درمانگاه مراجعه کرده است. سابقه 8 ساله ابتلاء به دیابت تیپ 2 دارد. سابقه هیپرتانسیون، استئوپروز ، ناراحتی گوارشی، نفخ شکم، تری گلیسرید بالا، و جدیدا سابقه کاهش خفیف عملکرد کلیه را میدهد. تحت درمان با لوزارتان، فنوفیبرات و دوز کامل گلی بن کلامید و متفورمین میباشد. در معاینه بجز افزایش وزن خفیف و ادم 2 مثبت اندامها ، مشکل دیگری ندارد. آزمایشات وی به شرح زیر است:

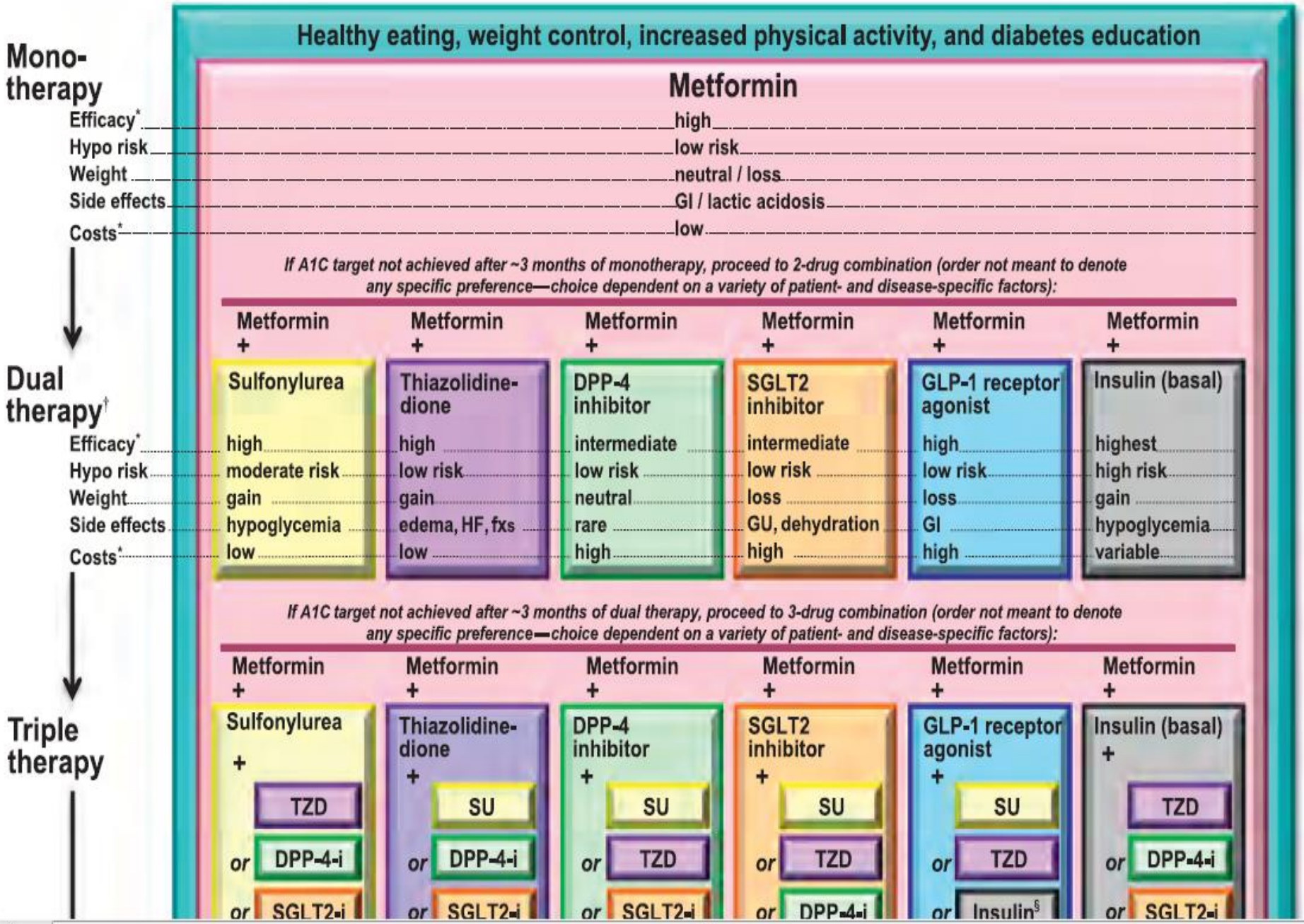
- FBS=145 mg/dl TG=450 mg/dl
- BS 2hPP=200 mg/dl
- Cholesterol=220 mg/dl HbA1C=8%

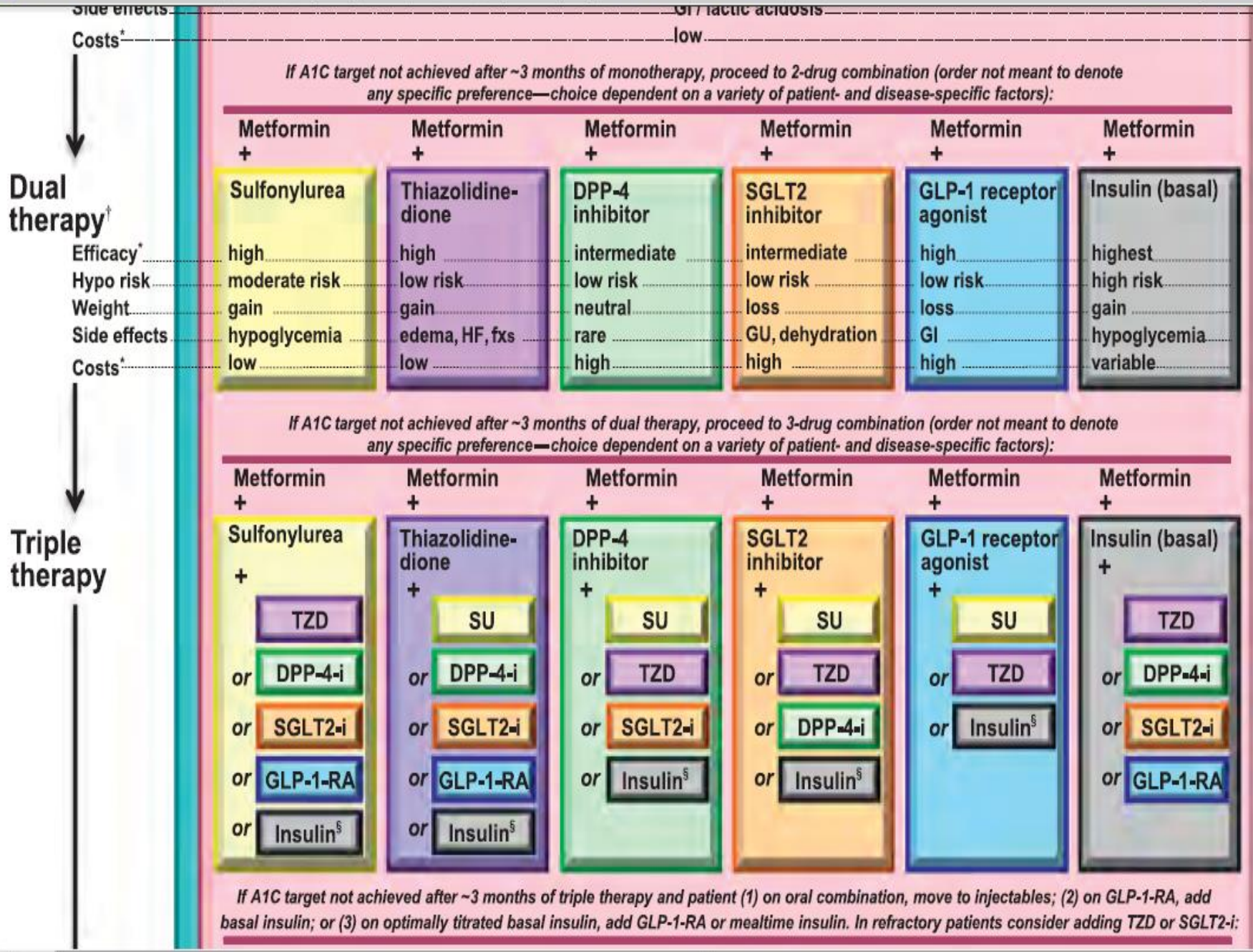
- به شدت از قبول داروهای تزریقی امتناع میورزد. کدام داروی خوراکی را جهت بهبود کنترل قند خون مناسبتر میدانید؟
- 1-آکربوز
- 2-پیوگلیتازون
- 3-کلوزوالوم
- 4-سیتاگلیپتین

CASE 3

CASE 3

- 10-خانم 65 ساله با سابقه 10 ساله دیابت نوع 2 بدلیل بروز حملات هیپوگلیسمی شبانه و قبل از ناهار به شما مراجعه میکند. از چند ماه قبل درمان وی به انسولین NPH و رگولار قبل از صبحانه و شام تغییر یافته است. ولیکن همچنان HbA1C 9% دارد.
- کدام گزینه زیر بهترین راه حل مشکل زیر است؟
- 1-تزریق انسولین NPH شبانه را به قبل از خواب منتقل میکنید.
- 2-قطع تزریق انسولین رگولار و انتقال زمان تزریق انسولین NPH به هنگام خواب.
- 3-جایگزین کردن انسولین NPH با گلارژین و ادامه انسولین رگولار.
- 4-تزریق انسولین NPH شبانه به قبل از خواب و به جای انسولین رگولار از نوع سریع الاثر استفاده میکنید.





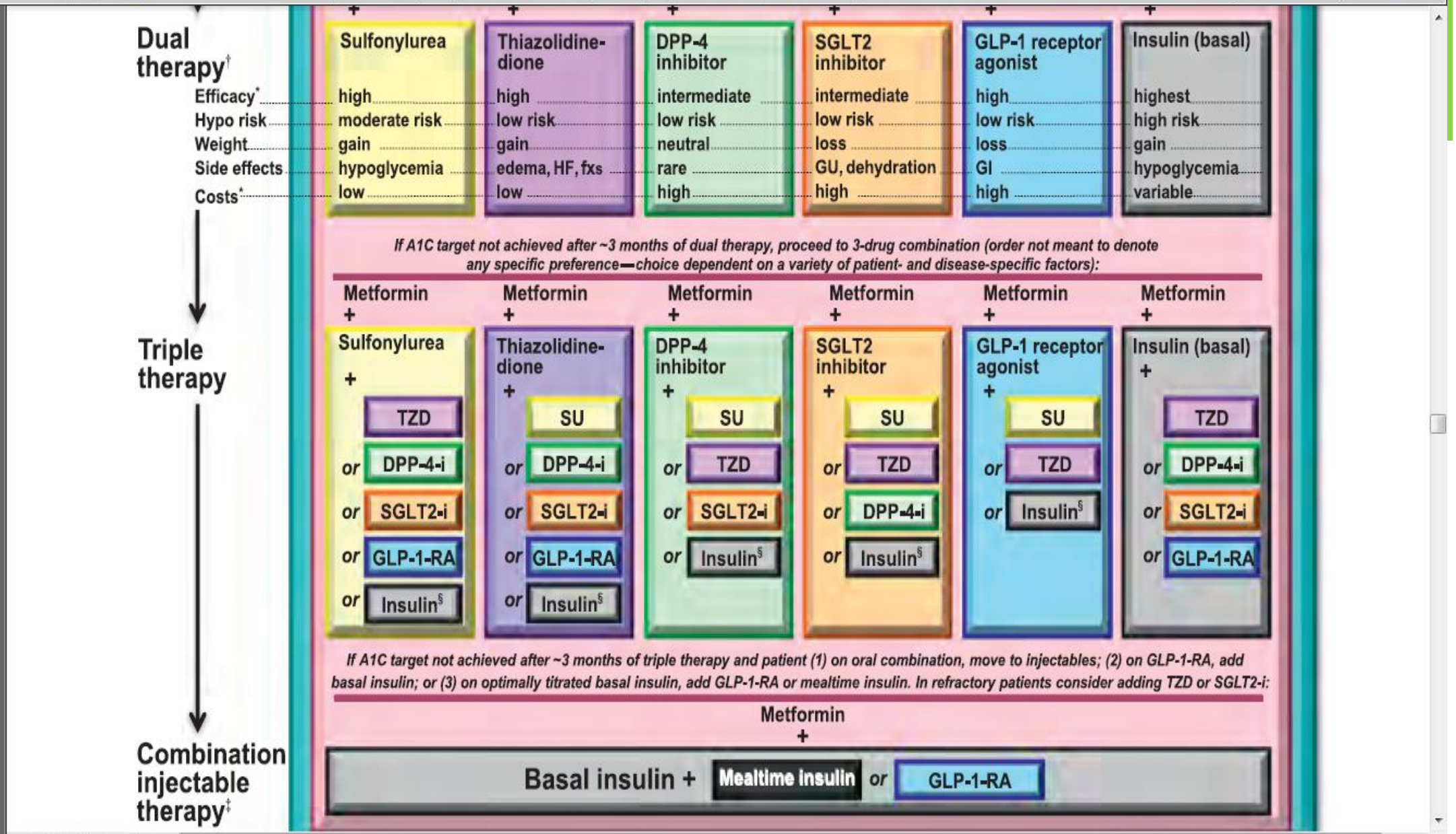


Table 7.1—Properties of available glucose-lowering agents in the U.S. and Europe that may guide individualized treatment choices in patients with type 2 diabetes (17)

Class	Compound(s)	Cellular mechanism(s)	Primary physiological action(s)	Advantages	Disadvantages	Cost*
Biguanides	• Metformin	Activates AMP-kinase (? other)	• ↓ Hepatic glucose production	• Extensive experience • No hypoglycemia • ↓ CVD events (UKPDS)	• Gastrointestinal side effects (diarrhea, abdominal cramping) • Vitamin B_{12} deficiency • Contraindications: CKD, acidosis, hypoxia, dehydration, etc. • Lactic acidosis risk (rare)	Low
Sulfonylureas	2nd Generation • Glyburide/ glibenclamide • Glipizide • Gliclazide† • Glimepiride	Closes K_{ATP} channels on β-cell plasma membranes	• ↑ Insulin secretion	• Extensive experience • ↓ Microvascular risk (UKPDS)	• Hypoglycemia • ↑ Weight	Low
Meglitinides (glinides)	• Repaglinide • Nateglinide	Closes K_{ATP} channels on β-cell plasma membranes	• ↑ Insulin secretion	• ↓ Postprandial glucose excursions • Dosing flexibility	• Hypoglycemia • ↑ Weight • Frequent dosing schedule	Moderate
TZDs	• Pioglitazone‡ • Rosiglitazone§	Activates the nuclear transcription factor PPAR-γ	• ↑ Insulin sensitivity	• No hypoglycemia • Durability • ↑ HDL-C • ↓ Triglycerides (pioglitazone) • ? ↓ CVD events (PROactive, pioglitazone)	• ↑ Weight • Edema/heart failure • Bone fractures • ↑ LDL-C (rosiglitazone) • ? ↑ MI (meta-analyses, rosiglitazone)	Low
α-Glucosidase inhibitors	• Acarbose • Miglitol	Inhibits intestinal α-glucosidase	• Slows intestinal carbohydrate digestion/absorption	• No hypoglycemia • ↓ Postprandial glucose excursions • ? ↓ CVD events (STOP-NIDDM) • Nonsystemic	• Generally modest A1C efficacy • Gastrointestinal side effects (flatulence, diarrhea) • Frequent dosing schedule	Low to moderate
DPP-4 inhibitors	• Sitaglintin	Inhibits DPP-4 activity, increasing	• ↑ Insulin secretion (glucose	• No hypoglycemia	• Angioedema/urticaria and other	High

				pioglitazone)		
α-Glucosidase inhibitors	• Acarbose • Miglitol	Inhibits intestinal α-glucosidase	• Slows intestinal carbohydrate digestion/absorption	• No hypoglycemia • ↓ Postprandial glucose excursions • ? ↓ CVD events (STOP-NIDDM) • Nonsystemic	• Generally modest A1C efficacy • Gastrointestinal side effects (flatulence, diarrhea) • Frequent dosing schedule	Low to moderate
DPP-4 inhibitors	• Sitagliptin • Vildagliptin† • Saxagliptin • Linagliptin • Alogliptin	Inhibits DPP-4 activity, increasing postprandial active incretin (GLP-1, GIP) concentrations	• ↑ Insulin secretion (glucose dependent) • ↓ Glucagon secretion (glucose dependent)	• No hypoglycemia • Well tolerated	• Angioedema/urticaria and other immune-mediated dermatological effects • ? Acute pancreatitis • ? ↑ Heart failure hospitalizations	High
Bile acid sequestrants	• Colesevelam	Binds bile acids in intestinal tract, increasing hepatic bile acid production	• ? ↓ Hepatic glucose production • ? ↑ Incretin levels	• No hypoglycemia • ↓ LDL-C	• Generally modest A1C efficacy • Constipation • ↑ Triglycerides • May ↓ absorption of other medications	High
Dopamine-2 agonists	• Bromocriptine (quick release)§	Activates dopaminergic receptors	• Modulates hypothalamic regulation of metabolism • ↑ Insulin sensitivity	• No hypoglycemia • ? ↓ CVD events (Cycloset Safety Trial)	• Generally modest A1C efficacy • Dizziness/syncope • Nausea • Fatigue • Rhinitis	High

Continued on p. S56

Table 7.1—Continued

Class	Compound(s)	Cellular mechanism(s)	Primary physiological action(s)	Advantages	Disadvantages	Cost*
SGLT2 inhibitors	• Canagliflozin • Dapagliflozin‡ • Empagliflozin	Inhibits SGLT2 in the proximal nephron	• Blocks glucose reabsorption by the kidney, increasing glucosuria	• No hypoglycemia • ↓ Weight • ↓ Blood pressure • Effective at all stages of type 2 diabetes • Associated with lower CVD event rate and mortality in patients with CVD (EMPA-REG OUTCOME)	• Genitourinary infections • Polyuria • Volume depletion/hypotension/ dizziness • ↑ LDL-C • ↑ Creatinine (transient) • DKA, urinary tract infections leading to urosepsis, pyelonephritis	High
GLP-1 receptor agonists	• Exenatide • Exenatide extended release • Liraglutide • Albiglutide • Lixisenatide† • Dulaglutide	Activates GLP-1 receptors	• ↑ Insulin secretion (glucose dependent) • ↓ Glucagon secretion (glucose dependent) • Slows gastric emptying • ↑ Satiety	• No hypoglycemia • ↓ Weight • ↓ Postprandial glucose excursions • ↓ Some cardiovascular risk factors	• Gastrointestinal side effects (nausea/vomiting/diarrhea) • ↑ Heart rate • ? Acute pancreatitis • C-cell hyperplasia/medullary thyroid tumors in animals • Injectable • Training requirements	High
Amylin mimetics	• Pramlintide§	Activates amylin receptors	• ↓ Glucagon secretion • Slows gastric emptying • ↑ Satiety	• ↓ Postprandial glucose excursions • ↓ Weight	• Generally modest A1C efficacy • Gastrointestinal side effects (nausea/vomiting) • Hypoglycemia unless insulin dose is simultaneously reduced • Injectable • Frequent dosing schedule • Training requirements	High
Insulins	• Rapid-acting analogs - Lispro - Aspart - Glulisine - Inhaled insulin • Short-acting - Human Regular • Intermediate-acting - Human NPH • Basal insulin analogs	Activates insulin receptors	• ↑ Glucose disposal • ↓ Hepatic glucose production • Suppresses ketogenesis	• Nearly universal response • Theoretically unlimited efficacy • ↓ Microvascular risk (UKPDS)	• Hypoglycemia • Weight gain • ? Mitogenic effects • Training requirements • Patient reluctance • Injectable (except inhaled insulin) • Pulmonary toxicity (inhaled insulin)	Moderate to high#

	• Albiglutide • Lixisenatide† • Dulaglutide		• Slows gastric emptying • ↑ Satiety	• ↓ Some cardiovascular risk factors	• C-cell hyperplasia/medullary thyroid tumors in animals • Injectable • Training requirements	
Amylin mimetics	• Pramlintide§	Activates amylin receptors	• ↓ Glucagon secretion • Slows gastric emptying • ↑ Satiety	• ↓ Postprandial glucose excursions • ↓ Weight	• Generally modest A1C efficacy • Gastrointestinal side effects (nausea/vomiting) • Hypoglycemia unless insulin dose is simultaneously reduced • Injectable • Frequent dosing schedule • Training requirements	High
Insulins	• Rapid-acting analogs - Lispro - Aspart - Glulisine - Inhaled insulin • Short-acting - Human Regular • Intermediate-acting - Human NPH • Basal insulin analogs - Glargine - Detemir - Degludec† • Premixed (several types)	Activates insulin receptors	• ↑ Glucose disposal • ↓ Hepatic glucose production • Suppresses ketogenesis	• Nearly universal response • Theoretically unlimited efficacy • ↓ Microvascular risk (UKPDS)	• Hypoglycemia • Weight gain • ? Mitogenic effects • Training requirements • Patient reluctance • Injectable (except inhaled insulin) • Pulmonary toxicity (inhaled insulin)	Moderate to high#

CKD, chronic kidney disease; CVD, cardiovascular disease; DKA, diabetic ketoacidosis; EMPA-REG OUTCOME, BI 10773 (Empagliflozin) Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients (31); GIP, glucose-dependent insulinotropic peptide; HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; MI, myocardial infarction; PPAR-γ, peroxisome proliferator–activated receptor γ; PROactive, Prospective Pioglitazone Clinical Trial in Macrovascular Events (32); STOP-NIDDM, Study to Prevent Non-Insulin-Dependent Diabetes Mellitus (33); TZD, thiazolidinedione; UKPDS, UK Prospective Diabetes Study (34,35). Cycloset trial of quick-release bromocriptine (36). *Cost is based on lowest-priced member of the class (see ref. 17). †Not licensed in the U.S. ‡Initial concerns regarding bladder cancer risk are decreasing after subsequent study. §Not licensed in Europe for type 2 diabetes. #Cost is highly dependent on type/brand (analogs > human insulins) and dosage. Adapted with permission from Inzucchi et al. (17).

CASE 4

CASE 4

- خانم ۷۰ ساله ای با سابقه ابتلاء به دیابت از ۵ سال پیش جهت کنترل قند خون مراجعه کرده است. از خشکی دهان و تکرر ادرار شبانه شاکی است. بجز شکستگی دوبل ساعد بدنبال زمین خوردن روی قالی، سابقه بیماری دیگری ندارد. رتینوپاتی و نوروپاتی ندارد. داروهای مصرفی شامل آتورواستاتین ۲۰ میلیگرم، اسپیرین ۸۰، مت فورمین ۱۵۰۰ میلیگرم میباشد.در معاینه

- BMI=24 Kg/ m^2 BP=120/80 mm/Hg
- سایر معاینات نرمال است.
- آزمایشات وی به شرح زیر است:

- FBS=150 mg/dl BS 2hPP=200 mg/dl
- HbA1c=8.3% Cr=0.8 mg/dl

CASE 4

- جهت بهبود کنترل قند کدام دارو را توصیه میکنید؟
- 1-گلی بن کلامید 1 عدد هرصبح
- 2-پیوگلیتازون 15 میلیگرم روزانه
- 3-سیتاگلیپنین 100 میلیگرم روزانه
- 4-لیراگلوتاید 1/2 میلیگرم زیرجلدی روزانه

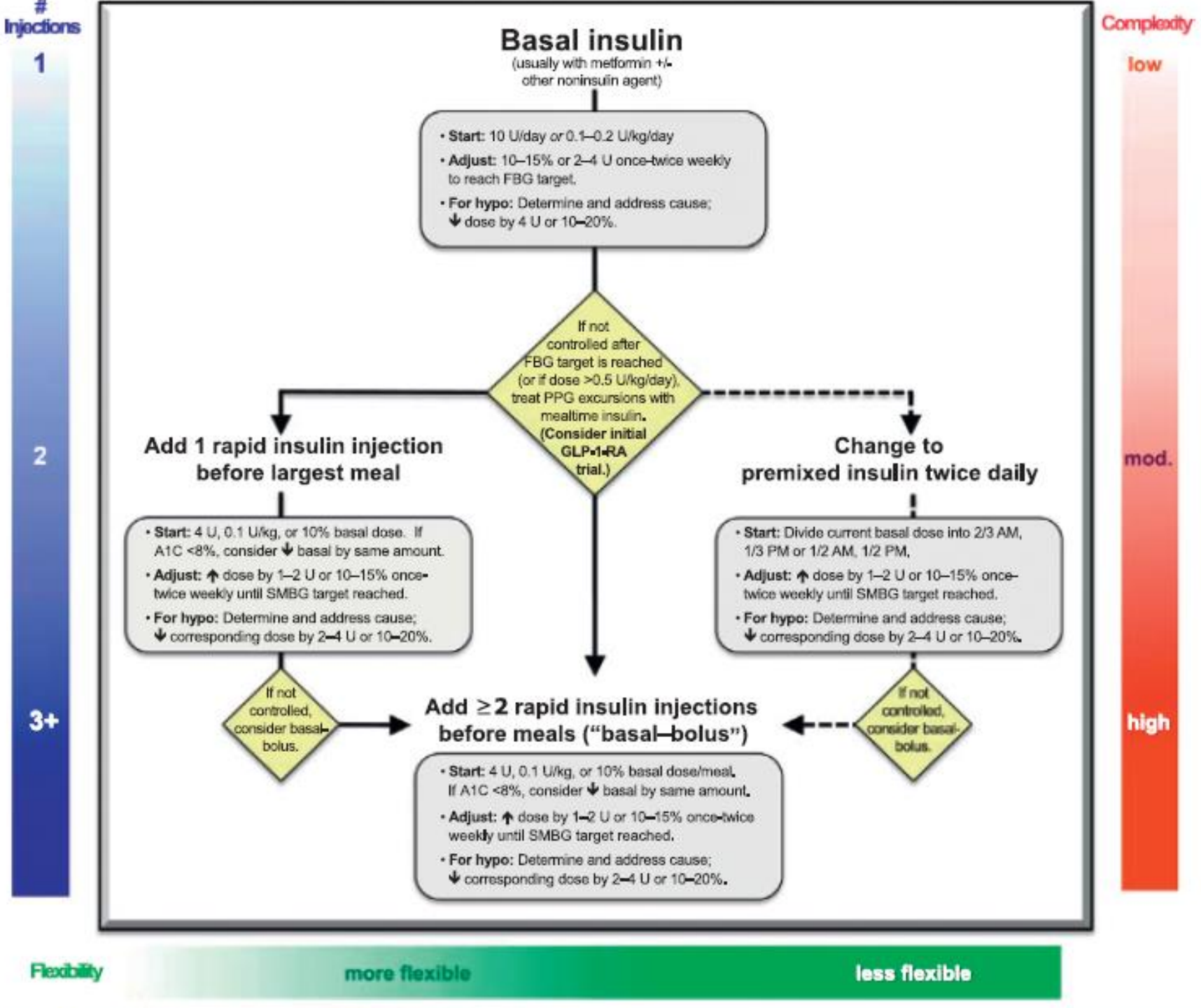
CASE 5

CASE 5

- اقای 62 ساله ای با سابقه دیابت از 9 سال قبل مراجعه کرده است. وی از کاهش وزن 7 کیلوگرمی طی 6 ماه گذشته شاکی است. سابقه فشارخون و کم کاری تیروئید را میدهد. داروی مصرفی وی شامل مت فورمین 1500 میلیگرم روزانه، گلی بن کلامید 3 عدد روزانه، اسپرین 80، آتورواستاتین 40، لوزارتان 100، لوستاتین 1/. میلیگرم روزانه میباشد.در معاینه:
- BW=70 Kg Height=180 cm BP=130/80 mmhg
- در معاینه تیروئید نکته مثبتی ندارد.سایر معاینات نرمال است. روی کاروتید بروئی ندارد.آزمایشات وی به شرح زیر است:
- FBS=250 mg/dl BS2hPP=280 mg/dl
- HbA1C=11% Cr=1.1 mg/dl TSH=6 m IU/L

CASE 5

- جهت بهبود کنترل قند خون چه داروئی را پیشنهاد میکنید؟
- 1-سیتاگلیپتین 100 میلیگرم روزانه
- 2-افزایش دوز گلی بن کلامید به 4عدد روزانه
- 3-قطع گلی بن کلامید و شروع گلیکلازید ام ار 60 دو بار در روز
- 4- اضافه کردن انسولین لنتوس 10 واحد روزانه زیر جلدی
- 5-اضافه کردن دوز لوتیروکسین


Injections
1
2
3+
Complexity
low
mod.
high
Basal insulin
(usually with metformin +/- other noninsulin agent)
• Start: 10 U/day or 0.1–0.2 U/kg/day
• Adjust: 10–15% or 2–4 U once-twice weekly to reach FBG target.
• For hypo: Determine and address cause; ↓ dose by 4 U or 10–20%.
If not controlled after FBG target is reached (or if dose >0.5 U/kg/day), treat PPG excursions with mealtime insulin. (Consider initial GLP-1-RA trial.)
Add 1 rapid insulin injection before largest meal
• Start: 4 U, 0.1 U/kg, or 10% basal dose. If A1C <8%, consider ↓ basal by same amount.
• Adjust: ↑ dose by 1–2 U or 10–15% once-twice weekly until SMBG target reached.
• For hypo: Determine and address cause; ↓ corresponding dose by 2–4 U or 10–20%.
If not controlled, consider basal-bolus.
Change to premixed insulin twice daily
• Start: Divide current basal dose into 2/3 AM, 1/3 PM or 1/2 AM, 1/2 PM.
• Adjust: ↑ dose by 1–2 U or 10–15% once-twice weekly until SMBG target reached.
• For hypo: Determine and address cause; ↓ corresponding dose by 2–4 U or 10–20%.
If not controlled, consider basal-bolus.
Add ≥2 rapid insulin injections before meals ("basal–bolus")
• Start: 4 U, 0.1 U/kg, or 10% basal dose/meal. If A1C <8%, consider ↓ basal by same amount.
• Adjust: ↑ dose by 1–2 U or 10–15% once-twice weekly until SMBG target reached.
• For hypo: Determine and address cause; ↓ corresponding dose by 2–4 U or 10–20%.
Flexibility
more flexible
less flexible

طریقه تبدیل انسولین نومیکس 30 و انسولین NPH به انسولین لنتوس

- اگر انسولین ان پی اچ یکبار در روز تزریق میشده است معادل همان میزان لنتوس تجویز شود.
- اگر انسولین ان پی اچ دو بار در روز تزریق می شده است معادل 80% انسولینNPH = میزان لنتوس
- اگر انسولین نومیکس 30 یکبار در روز تزریق میشده است معادل همان میزان انسولین متوسط الاثر = انسولین لنتوس
- اگر انسولین نومیکس 30 دو بار در روز تزریق میشده است:
- معادل 80% میزان انسولین متوسط الاثر = انسولین لنتوس

طریقه تبدیل انسولین به انسولین لنتوس نومیکس نومیکس 30 و

CASE 6

CASE 6

- خانم 59 ساله ای با سابقه دیابت از 9 سال قبل مراجعه کرده است. وی از افزایش وزن 7 کیلوگرمی طی چند سال گذشته شاکی است. سابقه فشارخون و کم کاری تیروئید را میدهد. داروی مصرفی وی شامل مت فورمین 1500 میلیگرم روزانه، گلی بن کلامید 3 عدد روزانه، اسپرین 80، آتورواستاتین 40، لوزارتان 100، لوستاتین 1/. میلیگرم روزانه میباشد.در معاینه:

- BW=70 Kg Height=180 cm BP=130/80 mmhg

- در معاینه تیروئید نکته مثبتی ندارد.سایر معاینات نرمال است. روی کاروتید بروئی ندارد.آزمایشات وی به شرح زیر است:

- FBS=250 mg/dl BS2hPP=280 mg/dl
- HbA1C=11% Cr=1.1 mg/dl TSH=2.4

CASE 6

- جهت بهبود کنترل قند خون چه داروئی را پیشنهاد میکنید؟
- 1-سیتاگلیپتین 100 میلیگرم روزانه
- 2-افزایش دوز گلی بن کلامید به 4عدد روزانه
- 3-قطع گلی بن کلامید و شروع گلیکلازید ام ار 60 دو بار در روز
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- 5- اضافه کردن لیراگلوتاید

CASE 7

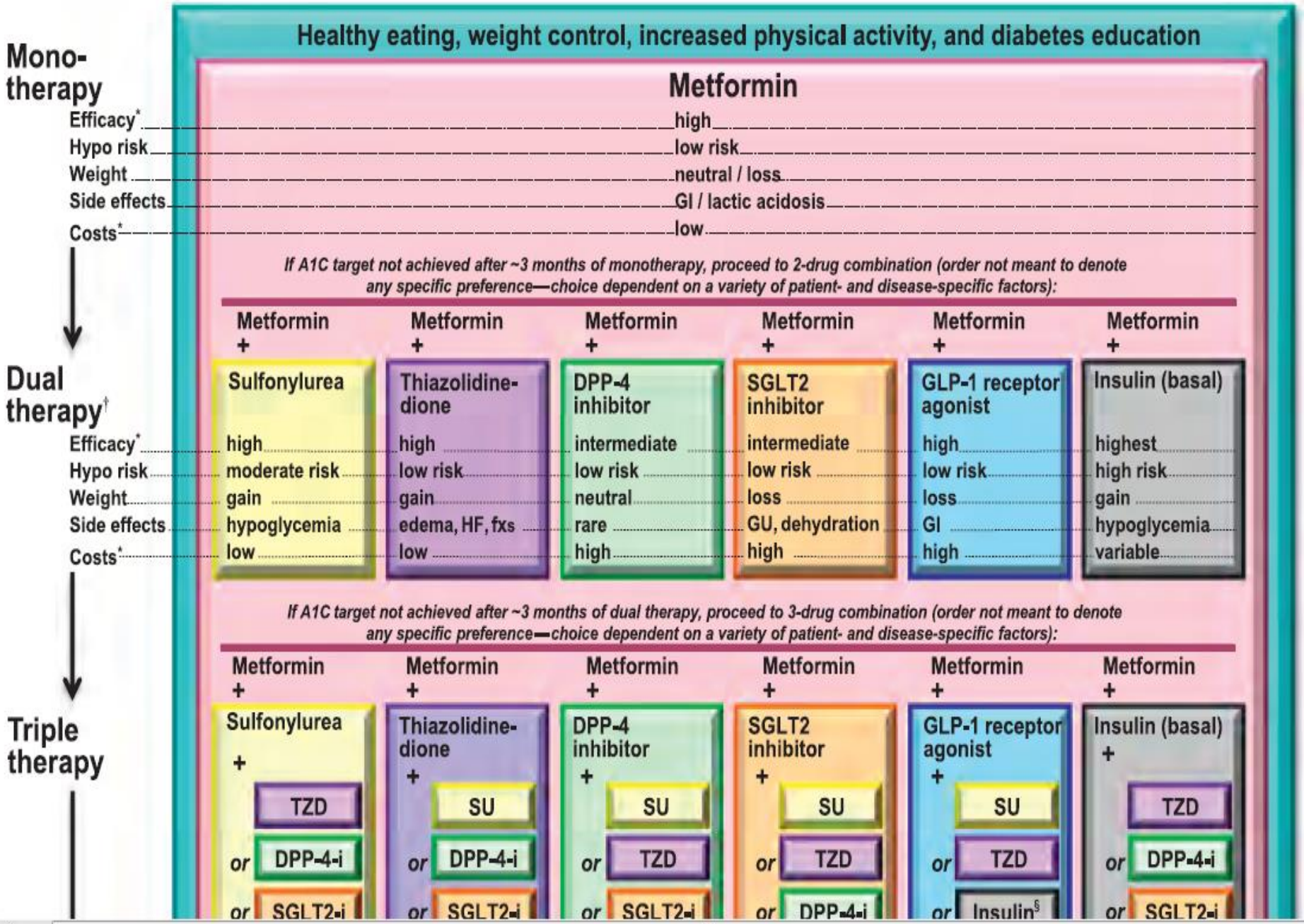
CASE 7

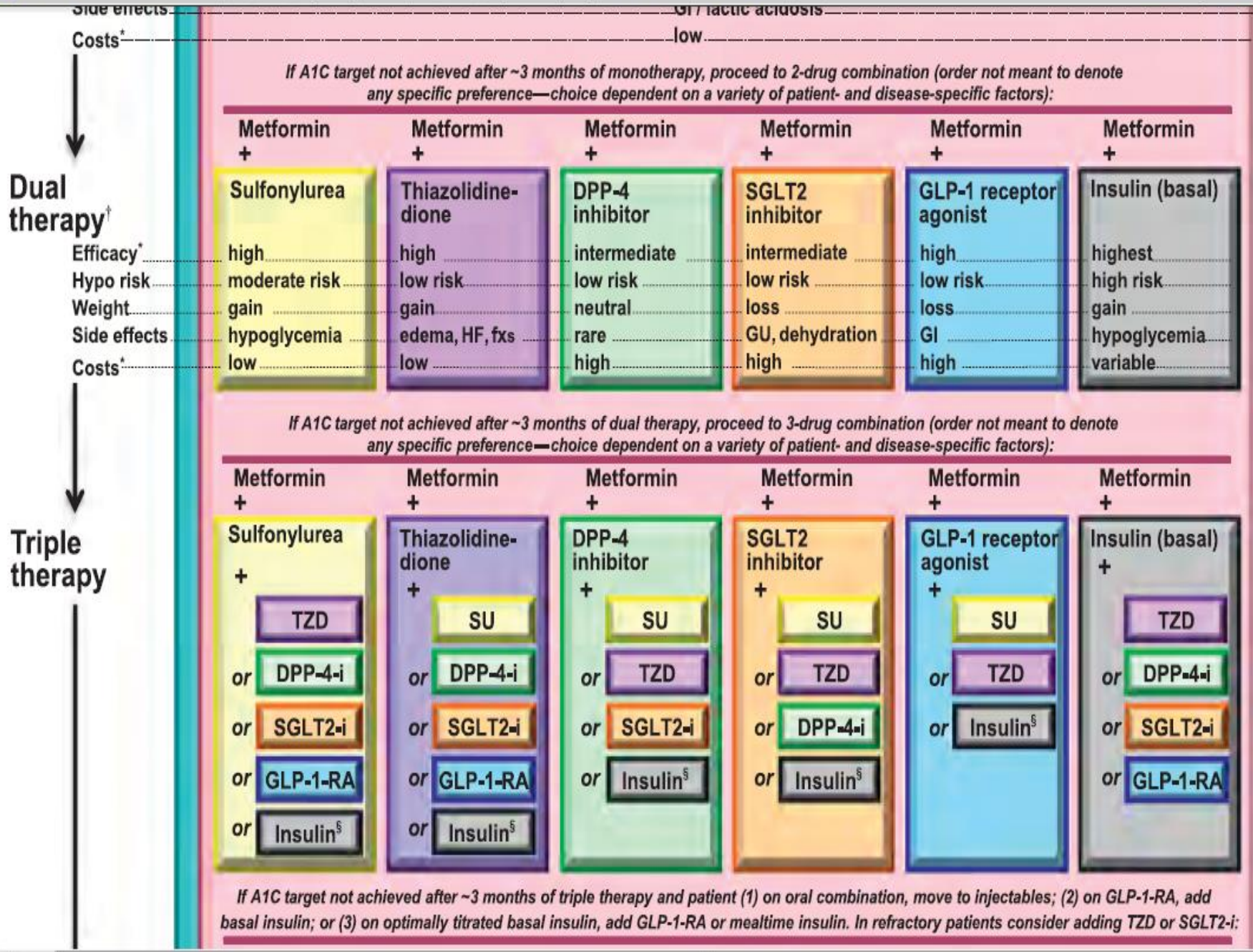
- خاتم 57 ساله ای با پرنوشی و پر ادراری به درمانگاه مراجعه کرده است.از سوزش کف پا شاکی است.سابقه بیماری خاصی نمیدهد.شرح حال کاهش وزن و مصرف داروی خاصی رانمی دهد.در معاینه:
- BW=63 Kg Height =165 cm BP=120/80 mmHg
- آزماییشات وی به شرح زیر است:
- FBS=250 mg/dl Bs 2hPP=280 mg/dl HbA1C=9.5% Cr=0.7 mg/dl
- جهت کتترل قند خون وی کدام دارو را پیشنهاد میکنید؟

CASE 7

- 1-مت فورمین 2500 میلیگرم
- 2-گلی بن کلامید یک عدد هر 12 ساعت
- 3-مت فورمین 1000 میلیگرم و گلی کلازید 40 میلیگرم
- 4-متفورمین 1500 میلیگرم و آکربوز 100 میلیگرم

IN THE NAME OF GOD





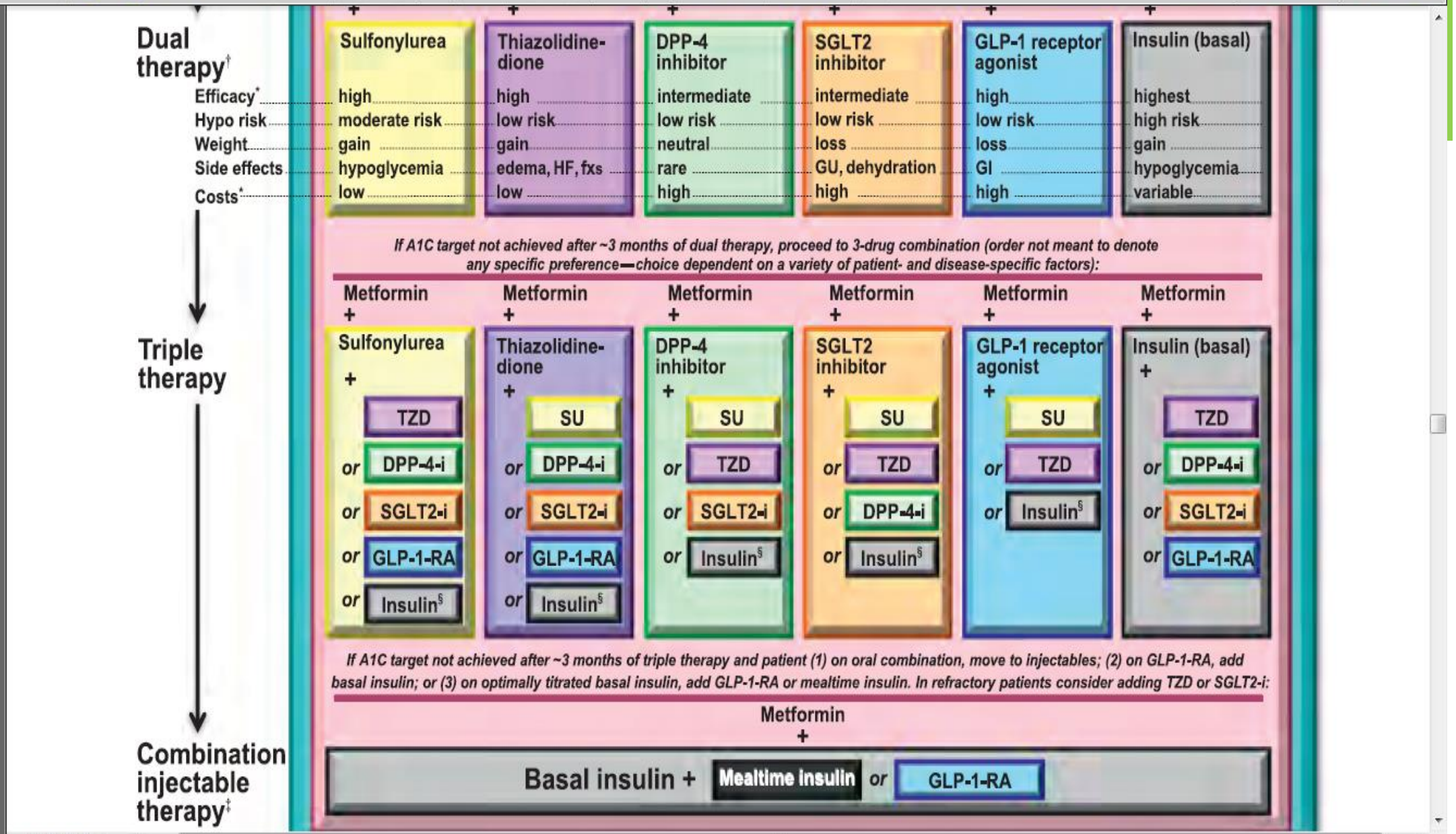


Table 7.1—Properties of available glucose-lowering agents in the U.S. and Europe that may guide individualized treatment choices in patients with type 2 diabetes (17)

Class	Compound(s)	Cellular mechanism(s)	Primary physiological action(s)	Advantages	Disadvantages	Cost*
Biguanides	• Metformin	Activates AMP-kinase (? other)	• ↓ Hepatic glucose production	• Extensive experience • No hypoglycemia • ↓ CVD events (UKPDS)	• Gastrointestinal side effects (diarrhea, abdominal cramping) • Vitamin B_{12} deficiency • Contraindications: CKD, acidosis, hypoxia, dehydration, etc. • Lactic acidosis risk (rare)	Low
Sulfonylureas	2nd Generation • Glyburide/ glibenclamide • Glipizide • Gliclazide† • Glimepiride	Closes K_{ATP} channels on β-cell plasma membranes	• ↑ Insulin secretion	• Extensive experience • ↓ Microvascular risk (UKPDS)	• Hypoglycemia • ↑ Weight	Low
Meglitinides (glinides)	• Repaglinide • Nateglinide	Closes K_{ATP} channels on β-cell plasma membranes	• ↑ Insulin secretion	• ↓ Postprandial glucose excursions • Dosing flexibility	• Hypoglycemia • ↑ Weight • Frequent dosing schedule	Moderate
TZDs	• Pioglitazone‡ • Rosiglitazone§	Activates the nuclear transcription factor PPAR-γ	• ↑ Insulin sensitivity	• No hypoglycemia • Durability • ↑ HDL-C • ↓ Triglycerides (pioglitazone) • ? ↓ CVD events (PROactive, pioglitazone)	• ↑ Weight • Edema/heart failure • Bone fractures • ↑ LDL-C (rosiglitazone) • ? ↑ MI (meta-analyses, rosiglitazone)	Low
α-Glucosidase inhibitors	• Acarbose • Miglitol	Inhibits intestinal α-glucosidase	• Slows intestinal carbohydrate digestion/absorption	• No hypoglycemia • ↓ Postprandial glucose excursions • ? ↓ CVD events (STOP-NIDDM) • Nonsystemic	• Generally modest A1C efficacy • Gastrointestinal side effects (flatulence, diarrhea) • Frequent dosing schedule	Low to moderate
DPP-4 inhibitors	• Sitaglintin	Inhibits DPP-4 activity, increasing	• ↑ Insulin secretion (glucose	• No hypoglycemia	• Angioedema/urticaria and other	High

				pioglitazone)		
α-Glucosidase inhibitors	• Acarbose • Miglitol	Inhibits intestinal α-glucosidase	• Slows intestinal carbohydrate digestion/absorption	• No hypoglycemia • ↓ Postprandial glucose excursions • ? ↓ CVD events (STOP-NIDDM) • Nonsystemic	• Generally modest A1C efficacy • Gastrointestinal side effects (flatulence, diarrhea) • Frequent dosing schedule	Low to moderate
DPP-4 inhibitors	• Sitagliptin • Vildagliptin† • Saxagliptin • Linagliptin • Alogliptin	Inhibits DPP-4 activity, increasing postprandial active incretin (GLP-1, GIP) concentrations	• ↑ Insulin secretion (glucose dependent) • ↓ Glucagon secretion (glucose dependent)	• No hypoglycemia • Well tolerated	• Angioedema/urticaria and other immune-mediated dermatological effects • ? Acute pancreatitis • ? ↑ Heart failure hospitalizations	High
Bile acid sequestrants	• Colesevelam	Binds bile acids in intestinal tract, increasing hepatic bile acid production	• ? ↓ Hepatic glucose production • ? ↑ Incretin levels	• No hypoglycemia • ↓ LDL-C	• Generally modest A1C efficacy • Constipation • ↑ Triglycerides • May ↓ absorption of other medications	High
Dopamine-2 agonists	• Bromocriptine (quick release)§	Activates dopaminergic receptors	• Modulates hypothalamic regulation of metabolism • ↑ Insulin sensitivity	• No hypoglycemia • ? ↓ CVD events (Cycloset Safety Trial)	• Generally modest A1C efficacy • Dizziness/syncope • Nausea • Fatigue • Rhinitis	High

Continued on p. S56

Table 7.1—Continued

Class	Compound(s)	Cellular mechanism(s)	Primary physiological action(s)	Advantages	Disadvantages	Cost*
SGLT2 inhibitors	• Canagliflozin • Dapagliflozin‡ • Empagliflozin	Inhibits SGLT2 in the proximal nephron	• Blocks glucose reabsorption by the kidney, increasing glucosuria	• No hypoglycemia • ↓ Weight • ↓ Blood pressure • Effective at all stages of type 2 diabetes • Associated with lower CVD event rate and mortality in patients with CVD (EMPA-REG OUTCOME)	• Genitourinary infections • Polyuria • Volume depletion/hypotension/ dizziness • ↑ LDL-C • ↑ Creatinine (transient) • DKA, urinary tract infections leading to urosepsis, pyelonephritis	High
GLP-1 receptor agonists	• Exenatide • Exenatide extended release • Liraglutide • Albiglutide • Lixisenatide† • Dulaglutide	Activates GLP-1 receptors	• ↑ Insulin secretion (glucose dependent) • ↓ Glucagon secretion (glucose dependent) • Slows gastric emptying • ↑ Satiety	• No hypoglycemia • ↓ Weight • ↓ Postprandial glucose excursions • ↓ Some cardiovascular risk factors	• Gastrointestinal side effects (nausea/vomiting/diarrhea) • ↑ Heart rate • ? Acute pancreatitis • C-cell hyperplasia/medullary thyroid tumors in animals • Injectable • Training requirements	High
Amylin mimetics	• Pramlintide§	Activates amylin receptors	• ↓ Glucagon secretion • Slows gastric emptying • ↑ Satiety	• ↓ Postprandial glucose excursions • ↓ Weight	• Generally modest A1C efficacy • Gastrointestinal side effects (nausea/vomiting) • Hypoglycemia unless insulin dose is simultaneously reduced • Injectable • Frequent dosing schedule • Training requirements	High
Insulins	• Rapid-acting analogs - Lispro - Aspart - Glulisine - Inhaled insulin • Short-acting - Human Regular • Intermediate-acting - Human NPH • Basal insulin analogs	Activates insulin receptors	• ↑ Glucose disposal • ↓ Hepatic glucose production • Suppresses ketogenesis	• Nearly universal response • Theoretically unlimited efficacy • ↓ Microvascular risk (UKPDS)	• Hypoglycemia • Weight gain • ? Mitogenic effects • Training requirements • Patient reluctance • Injectable (except inhaled insulin) • Pulmonary toxicity (inhaled insulin)	Moderate to high#

	• Albiglutide • Lixisenatide† • Dulaglutide		• Slows gastric emptying • ↑ Satiety	• ↓ Some cardiovascular risk factors	• C-cell hyperplasia/medullary thyroid tumors in animals • Injectable • Training requirements	
Amylin mimetics	• Pramlintide§	Activates amylin receptors	• ↓ Glucagon secretion • Slows gastric emptying • ↑ Satiety	• ↓ Postprandial glucose excursions • ↓ Weight	• Generally modest A1C efficacy • Gastrointestinal side effects (nausea/vomiting) • Hypoglycemia unless insulin dose is simultaneously reduced • Injectable • Frequent dosing schedule • Training requirements	High
Insulins	• Rapid-acting analogs - Lispro - Aspart - Glulisine - Inhaled insulin • Short-acting - Human Regular • Intermediate-acting - Human NPH • Basal insulin analogs - Glargine - Detemir - Degludec† • Premixed (several types)	Activates insulin receptors	• ↑ Glucose disposal • ↓ Hepatic glucose production • Suppresses ketogenesis	• Nearly universal response • Theoretically unlimited efficacy • ↓ Microvascular risk (UKPDS)	• Hypoglycemia • Weight gain • ? Mitogenic effects • Training requirements • Patient reluctance • Injectable (except inhaled insulin) • Pulmonary toxicity (inhaled insulin)	Moderate to high#

CKD, chronic kidney disease; CVD, cardiovascular disease; DKA, diabetic ketoacidosis; EMPA-REG OUTCOME, BI 10773 (Empagliflozin) Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients (31); GIP, glucose-dependent insulinotropic peptide; HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; MI, myocardial infarction; PPAR-γ, peroxisome proliferator–activated receptor γ; PROactive, Prospective Pioglitazone Clinical Trial in Macrovascular Events (32); STOP-NIDDM, Study to Prevent Non-Insulin-Dependent Diabetes Mellitus (33); TZD, thiazolidinedione; UKPDS, UK Prospective Diabetes Study (34,35). Cycloset trial of quick-release bromocriptine (36). *Cost is based on lowest-priced member of the class (see ref. 17). †Not licensed in the U.S. ‡Initial concerns regarding bladder cancer risk are decreasing after subsequent study. §Not licensed in Europe for type 2 diabetes. #Cost is highly dependent on type/brand (analogs > human insulins) and dosage. Adapted with permission from Inzucchi et al. (17).

Table 8.1—Properties of available glucose-lowering agents in the U.S. that may guide individualized treatment choices in patients with type 2 diabetes (21)

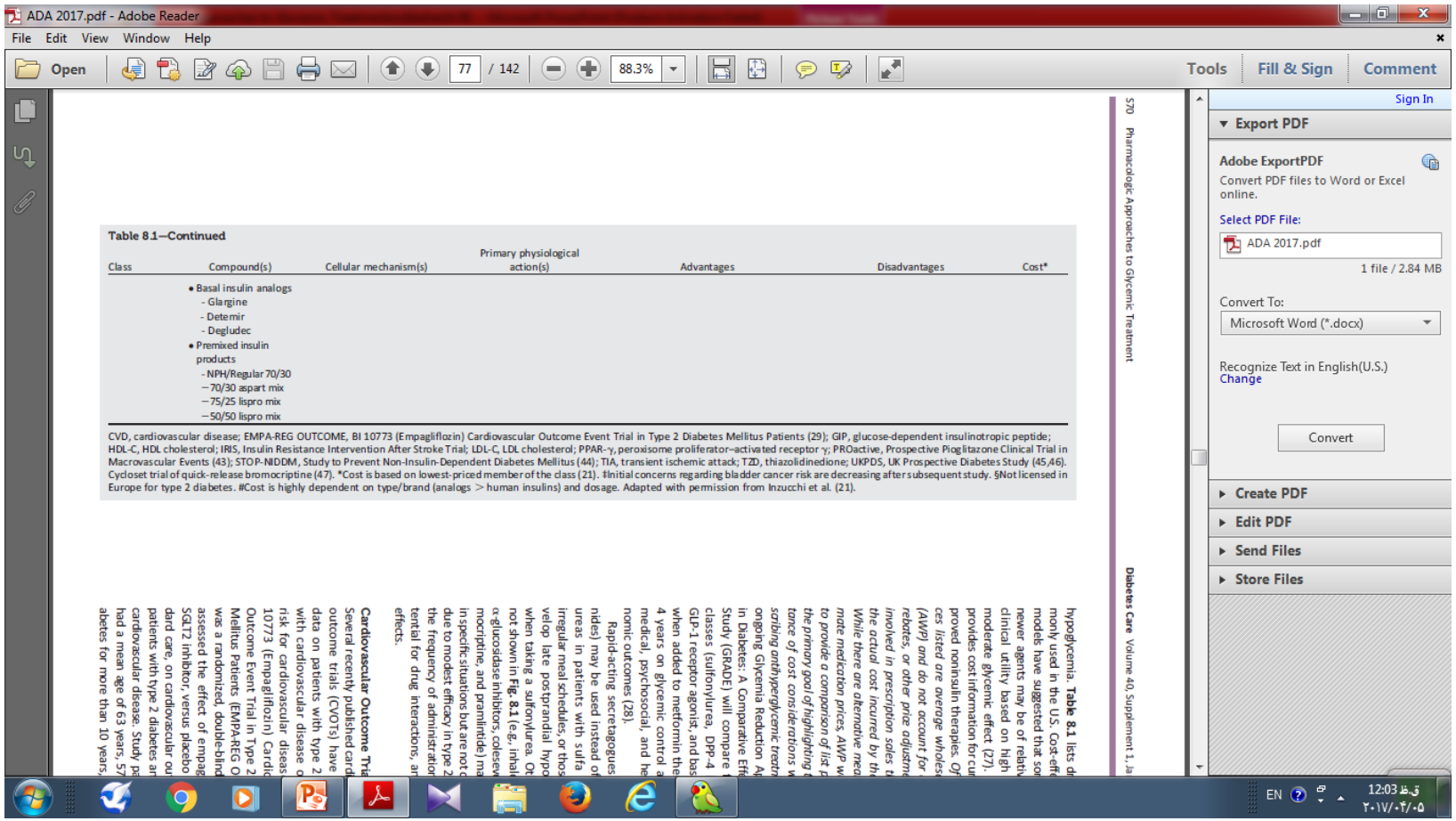
Class	Compound(s)	Cellular mechanism(s)	Primary physiological action(s)	Advantages	Disadvantages	Cost*
Biguanides	• Metformin	Activates AMP-kinase (? other)	• ↓ Hepatic glucose production	• Extensive experience • Rare hypoglycemia • ↓ CVD events (UKPDS) • Relatively higher A1C efficacy	• Gastrointestinal side effects (diarrhea, abdominal cramping, nausea) • Vitamin B12 deficiency • Contraindications: eGFR <30 mL/min/1.73 m^2, acidosis, hypoxia, dehydration, etc. • Lactic acidosis risk (rare)	Low
Sulfonylureas	2nd generation • Glyburide • Glipizide • Glimepiride	Closes K_{ATP} channels on β-cell plasma membranes	• ↑ Insulin secretion	• Extensive experience • ↓ Microvascular risk (UKPDS) • Relatively higher A1C efficacy	• Hypoglycemia • ↑ Weight	Low
Meglitinides (glinides)	• Repaglinide • Nateglinide	Closes K_{ATP} channels on β-cell plasma membranes	• ↑ Insulin secretion	• ↓ Postprandial glucose excursions • Dosing flexibility	• Hypoglycemia • ↑ Weight • Frequent dosing schedule	Moderate
TZDs	• Pioglitazone‡ • Rosiglitazone§	Activates the nuclear transcription factor PPAR-γ	• ↑ Insulin sensitivity	• Rare hypoglycemia • Relatively higher A1C efficacy • Durability • ↓ Triglycerides (pioglitazone) • ? ↓ CVD events (PROactive, pioglitazone) • ↓ Risk of stroke and MI in patients without diabetes and with *insulin resistance* and history of recent stroke or TIA (IRIS study [42], pioglitazone)	• ↑ Weight • Edema/heart failure • Bone fractures • ↑ LDL-C (rosiglitazone)	Low
α-Glucosidase inhibitors	• Acarbose • Miglitol	Inhibits intestinal α-glucosidase	• Slows intestinal carbohydrate digestion/absorption	• Rare hypoglycemia • ↓ Postprandial glucose excursions • ? ↓ CVD events in prediabetes (STOP-NIDDM) • Nonsystemic	• Generally modest A1C efficacy • Gastrointestinal side effects (flatulence, diarrhea) • Frequent dosing schedule	Low to moderate
DPP-4 inhibitors	• Sitagliptin • Saxagliptin • Linagliptin • Alogliptin	Inhibits DPP-4 activity, increasing postprandial incretin (GLP-1, GIP) concentrations	• ↑ Insulin secretion (glucose dependent) • ↓ Glucagon secretion (glucose dependent)	• Rare hypoglycemia • Well tolerated	• Angioedema/urticaria and other immune-mediated dermatological effects • ? Acute pancreatitis • ↑ Heart failure hospitalizations (saxagliptin; ? alogliptin)	High
Bile acid sequestrants	• Colesevelam	Binds bile acids in intestinal tract, increasing hepatic bile acid production	• ? ↓ Hepatic glucose production • ? ↑ Incretin levels	• Rare hypoglycemia • ↓ LDL-C	• Modest A1C efficacy • Constipation • ↑ Triglycerides • May ↓ absorption of other medications	High

Continued on p. S69

Table 8.1—Continued

Class	Compound(s)	Cellular mechanism(s)	Primary physiological action(s)	Advantages	Disadvantages	Cost*
Dopamine-2 agonists	• Bromocriptine (quick release)§	Activates dopaminergic receptors	• Modulates hypothalamic regulation of metabolism • ↑ Insulin sensitivity	• Rare hypoglycemia • ? ↓ CVD events (Cycloset Safety Trial)	• Modest A1C efficacy • Dizziness/syncope • Nausea • Fatigue • Rhinitis	High
SGLT2 inhibitors	• Canagliflozin • Dapagliflozin‡ • Empagliflozin	Inhibits SGLT2 in the proximal nephron	• Blocks glucose reabsorption by the kidney, increasing glucosuria	• Rare hypoglycemia • ↓ Weight • ↓ Blood pressure • Associated with lower CVD event rate and mortality in patients with CVD (empagliflozin EMPA-REG OUTCOME)	• Genitourinary infections • Polyuria • Volume depletion/hypotension/dizziness • ↑ LDL-C • ↑ Creatinine (transient) • DKA, urinary tract infections leading to urosepsis, pyelonephritis	High
GLP-1 receptor agonists	• Exenatide • Exenatide extended release • Liraglutide • Albiglutide • Lixisenatide • Dulaglutide	Activates GLP-1 receptors	• ↑ Insulin secretion (glucose dependent) • ↓ Glucagon secretion (glucose dependent) • Slows gastric emptying • ↑ Satiety	• Rare hypoglycemia • ↓ Weight • ↓ Postprandial glucose excursions • ↓ Some cardiovascular risk factors • Associated with lower CVD event rate and mortality in patients with CVD (liraglutide LEADER) (30)	• Gastrointestinal side effects (nausea/vomiting/diarrhea) • ↑ Heart rate • ? Acute pancreatitis • C-cell hyperplasia/medullary thyroid tumors in animals • Injectable • Training requirements	High
Amylin mimetics	• Pramlintide§	Activates amylin receptors	• ↓ Glucagon secretion • Slows gastric emptying • ↑ Satiety	• ↓ Postprandial glucose excursions • ↓ Weight	• Modest A1C efficacy • Gastrointestinal side effects (nausea/vomiting) • Hypoglycemia unless insulin dose is simultaneously reduced • Injectable • Frequent dosing schedule • Training requirements	High
Insulins	• Rapid-acting analogs - Lispro - Aspart - Glulisine - Inhaled insulin • Short-acting - Human Regular • Intermediate-acting - Human NPH	Activates insulin receptors	• ↑ Glucose disposal • ↓ Hepatic glucose production • Suppresses ketogenesis	• Nearly universal response • Theoretically unlimited efficacy • ↓ Microvascular risk (UKPDS)	• Hypoglycemia • Weight gain • Training requirements • Patient and provider reluctance • Injectable (except inhaled insulin) • Pulmonary toxicity (inhaled insulin)	High#

Continued on p. S70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Recognize Text in English(U.S.)
Change
Convert
Create PDF
Edit PDF
Send Files
Store Files
S70 Pharmacologic Approaches to Glycemic Treatment
Diabetes Care Volume 40, Supplement 1, Ja
Table 8.1—Continued
Class
Compound(s)
Cellular mechanism(s)
Primary physiological action(s)
Advantages
Disadvantages
Cost*
• Basal insulin analogs
- Glargine
- Determir
- Degludec
• Premixed insulin products
- NPH/Regular 70/30
—70/30 aspart mix
—75/25 lispro mix
—50/50 lispro mix
CVD, cardiovascular disease; EMPA-REG OUTCOME, BI 10773 (Empagliflozin) Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients (29); GIP, glucose-dependent insulinotropic peptide; HDL-C, HDL cholesterol; IRIS, Insulin Resistance Intervention After Stroke Trial; LDL-C, LDL cholesterol; PPAR-γ, peroxisome proliferator–activated receptor γ; PROactive, Prospective Pioglitazone Clinical Trial in Macrovascular Events (43); STOP-NIDDM, Study to Prevent Non-Insulin-Dependent Diabetes Mellitus (44); TIA, transient ischemic attack; TZD, thiazolidinedione; UKPDS, UK Prospective Diabetes Study (45,46). Cycloset trial of quick-release bromocriptine (47). *Cost is based on lowest-priced member of the class (21). ‡Initial concerns regarding bladder cancer risk are decreasing after subsequent study. §Not licensed in Europe for type 2 diabetes. #Cost is highly dependent on type/brand (analogs > human insulins) and dosage. Adapted with permission from Inzucchi et al. (21).
hypoglycemia. Table 8.1 lists d
monly used in the U.S. Cost-eff
models have suggested that so
newer agents may be of relativ
clinical utility based on high
moderate glycemic effect (27),
provides cost information for cu
proved noninsulin therapies. Of
ces listed are average wholes
(AWP) and do not account for
rebates, or other price adjustm
involved in prescription sales t
the actual cost incurred by th
While there are alternative mec
mate medication prices, AWP w
to provide a comparison of list p
the primary goal of highlighting
tance of cost considerations w
scribing antihyperglycemic treatm
ongoing Glycemia Reduction A
in Diabetes: A Comparative Eff
Study (GRADE) will compare
classes (sulfonylurea, DPP-4
GLP-1 receptor agonist, and bas
when added to metformin the
4 years on glycemic control a
medical, psychosocial, and he
nomic outcomes (28).
Rapid-acting secretagogues
nides) may be used instead of
ureas in patients with sulfa
irregular meal schedules, or thos
velop late postprandial hypo
when taking a sulfonylurea. Ot
not shown in Fig. 8.1 (e.g., inhal
α-glucosidase inhibitors, colesev
mocriptine, and pramlintide) ma
in specific situations but are not c
due to modest efficacy in type 2
the frequency of administration
tential for drug interactions, ar
effects.
Cardiovascular Outcome Tri
Several recently published card
outcome trials (CVOTs) have
data on patients with type 2
with cardiovascular disease o
risk for cardiovascular diseas
10773 (Empagliflozin) Cardio
Outcome Event Trial in Type 2
Mellitus Patients (EMPA-REG O
was a randomized, double-blind
assessed the effect of empag
SGLT2 inhibitor, versus placebo
dard care, on cardiovascular ou
patients with type 2 diabetes ar
cardiovascular disease. Study pa
had a mean age of 63 years, 57
abetes for more than 10 years,
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