

Hypertension and Hyperlipidemia Management for Patients with Diabetes

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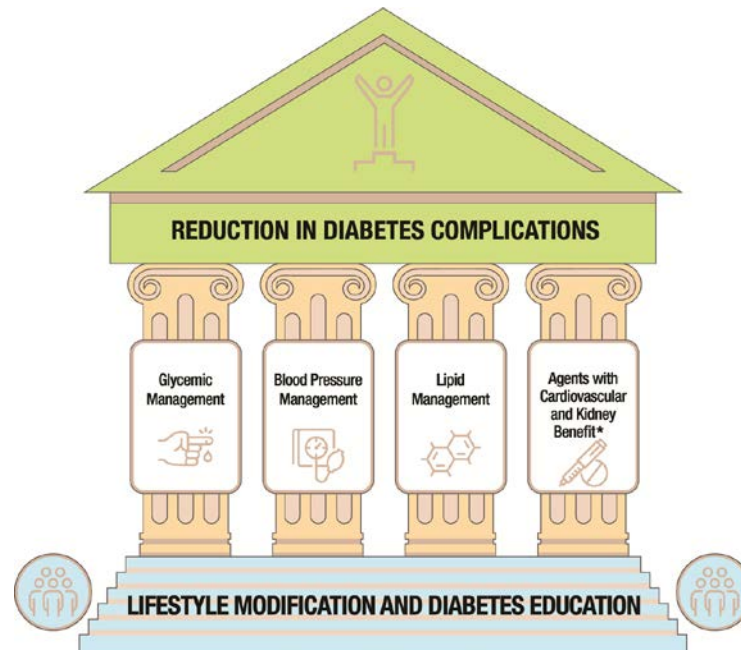


Figure Legend:

Multifactorial approach to reduction in risk of diabetes complications. *Risk reduction interventions to be applied as individually appropriate.



Hypertension

Atherosclerotic disease

- Coronary heart disease
- Cerebrovascular disease
- Peripheral arterial disease
- Leading cause of mortality and morbidity in individuals with diabetes
- Both HTN and Hyperlipidemia (HLD) are major risk factors for ASCVD
- Nearly 1 in 3 Americans have HTN and 2 of 3 people with diabetes have HTN²

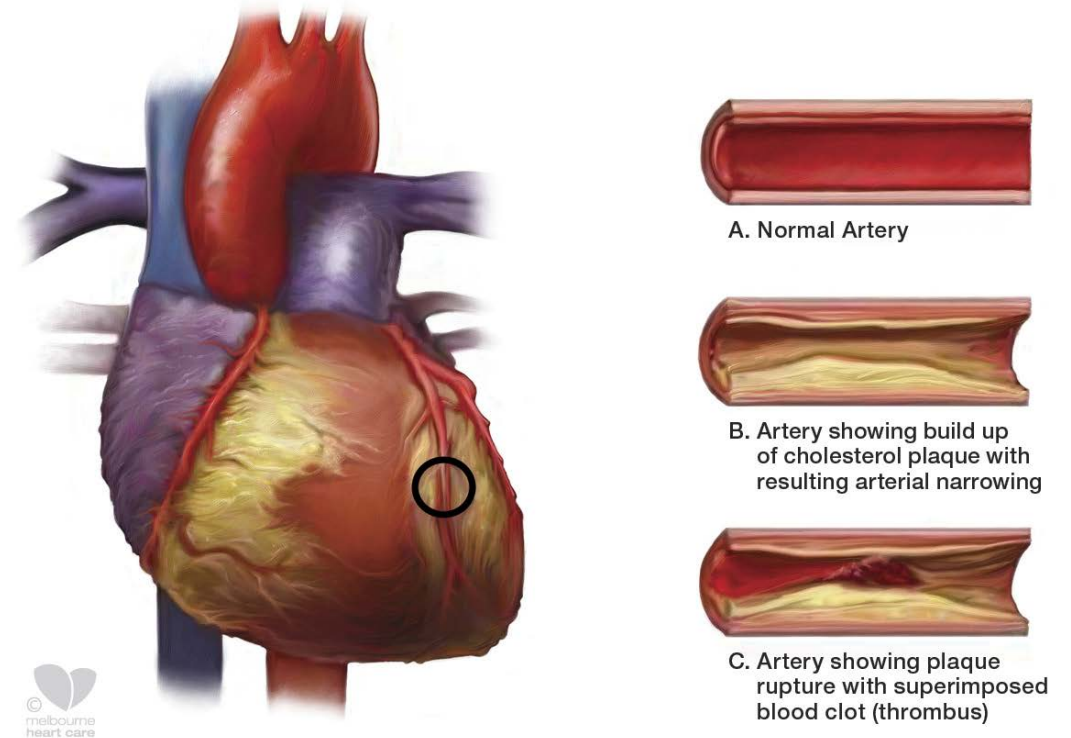


Figure 1: Atherosclerosis of arteries by Melbourne Heart Care, 2019;

<https://www.melbourneheartcare.com.au/or-patients/conditions/atherosclerosis/>

Hypertension (HTN)

- Defined as a sustained blood pressure greater or equal to 140/90, must be confirmed with multiple readings and including measurements on separate days
- Major risk factor for both ASCVD (Atherosclerotic Cardiovascular Disease) and microvascular complications
- Several studies have indicated that antihypertensive therapy does reduce ASCVD events, heart failure and microvascular complications¹

Table 1: Blood Pressure Categories

- From American Heart Association: *Understanding blood pressure readings*. [www.heart.org](https://www.heart.org/en/health-topics/high-blood-pressure/understanding-blood-pressure-readings). (n.d.). <https://www.heart.org/en/health-topics/high-blood-pressure/understanding-blood-pressure-readings>.

Blood Pressure Categories



BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120-129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130-139	or	80-89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

©American Heart Association. 5/5/16 60 1/20

heart.org/bplevels

Blood Pressure Measurement

- Patients with blood pressure $\geq 180/110$ mmHg and CVD could be diagnosed with hypertension at a single visit.¹⁰

How to measure blood pressure

- Have patient avoid caffeine, exercise and smoking for at least 30 minutes before taking blood pressure⁵
- Ask them to empty their bladder
- Have your patient relax in a chair (feet on floor, back supported) for > 5 minutes. Don't take readings while your patient is sitting or lying on an exam table⁵
- No conversations or talking while measuring BP
- Arm should be bare when cuff is placed
- Use the correct cuff size, the bladder should go around 80% of the arm⁵
- Be sure the patient's arm is supported on a surface at the correct height (heart level)
- Wrist and finger monitors aren't recommended because they yield less accurate and reliable readings⁵
- Measure at the same time every day
- List of validated blood pressure monitors: <https://www.validatebp.org/>

Bladder Cuff Size

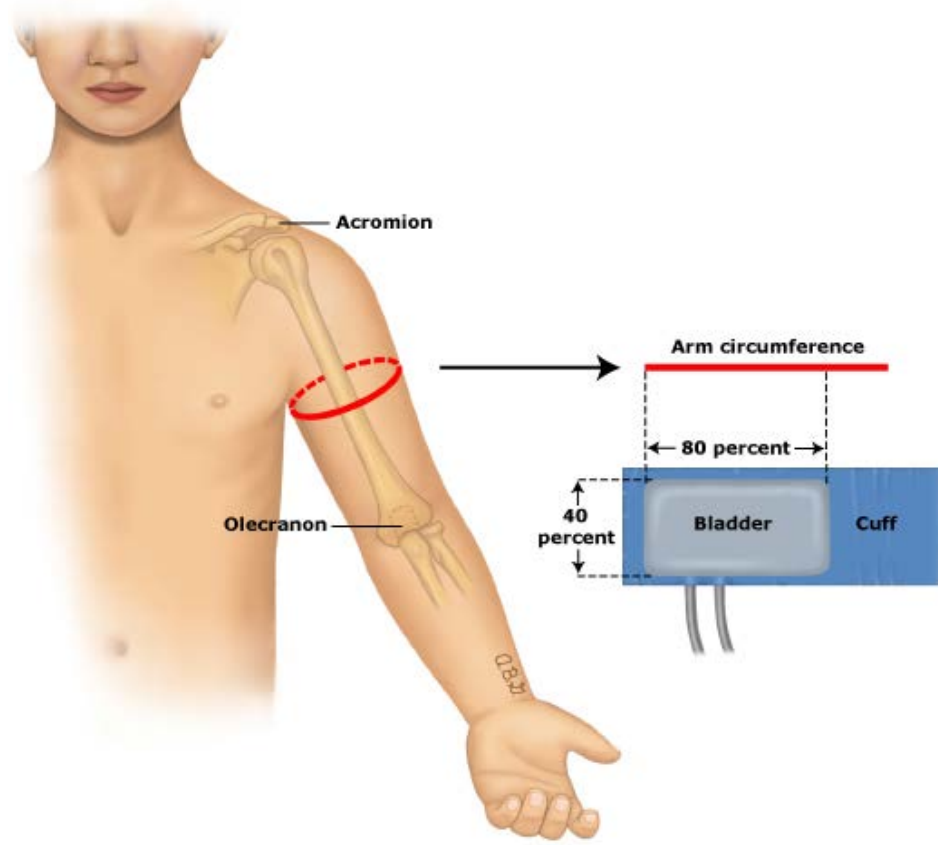


Figure 9:
<https://www.uptodate.com/contents/image?imageKey=PEDS%2F73414>



Figure 2: Infographic on how to get accurate BP reading from Target: BP, 2019; <https://targetbp.org/blood-pressure-improvement-program/control-bp/measure-accurately/>

Randomized control trials

- ACCORD- BP (Action to Control Cardiovascular Risk in Diabetes- Blood Pressure)¹
 - 4,733 participants with T2DM aged 40-79 years with prior evidence of CVD or multiple cardiovascular risk factors
 - Intensive BP (<120 mmHg) vs. Standard (130-140 mmHg)
 - No benefit in primary end point: composite of non fatal MI, non fatal stroke and CVD death
 - Stroke risk did reduce by 41% in intensive control but more adverse events were common in intensive group – particularly with electrolyte abnormalities and creatinine elevation
 - This trial largely drives ADA's recommendation of a higher blood pressure threshold for initiation of medications and target

Randomized control trials

- SPRINT (Systolic Blood Pressure Intervention Trial)¹
 - 9,361 participants without diabetes
 - Systolic blood pressure target <120 mmHg vs. Systolic blood pressure target: <140 mmHg
 - Intensive systolic blood pressure target lowered primary composite outcome 25% (MI, acute coronary syndrome, stroke, heart failure and death due to CVD)
 - Intensive target reduced risk of death 27%
 - Intensive therapy increased risk of electrolyte abnormalities and acute kidney injury
 - Even though SPRINT did exclude individuals with diabetes, a post hoc analysis was conducted and evaluated those with pre-DM (fasting glucose ≥ 100 mg/dL) compared to normoglycemia patients (fasting glucose <100 mg/dL)
 - Analysis suggest that the benefits of intensive blood pressure treatment are similar between both groups

Randomized control trials

- ADVANCE – BP (Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation – Blood Pressure)¹
 - 11,140 participants with T2DM aged 55 years and older with prior evidence of CVD or multiple cardiovascular risk factors
 - Placebo vs. Intervention (single pill, fixed dose combination of perindopril and indapamide)
 - Intervention reduced risk of primary composite and point of major macrovascular and microvascular events (9%), death from any cause (14%) and death from CVD (18%)
 - Reduction in death in interventional group attenuation was significant when observed over 6 year observational follow up

Randomized Control Trials

- HOT (Hypertension Optimal Treatment)¹
 - 18,790 participants including 1,501 with diabetes
 - Diastolic blood pressure target ≤ 80 vs. Diastolic blood pressure target ≤ 90 mmHg
 - An intensive diastolic target was associated with significantly reduced risk (51%) of CVD events

Table 2: Summary of Blood Pressure Goals and Initial Choice of Antihypertensive Agent for Patients With Diabetes Endorsed by Different Professional Societies or Expert Groups

Recommendation (Year)	Blood Pressure Goals (mmHg)	First-Line Pharmacological Treatment
American Diabetes Association (2018)	<140/90 (<130/80 ⁺)	ACEI/ARB [±] , thiazide-like diuretic, or dihydropyridine CCB
American College of Cardiology/American Heart Association (2017)	<130/80	No preference
Joint National Committee 8 (2014)	<140/90	Non-black: ACEI/ARB, thiazide-like diuretic, or CCB Black: thiazide-like diuretic or CCB
Veterans Affairs (VA) and Department of Defense (2014)	<150/85 (140/85 ⁺⁺)	Thiazide-like diuretic (chlorthalidone or indapamide)
Canadian Diabetes Association (2013)	<130/80	ACEI/ARB [±] , thiazide-like diuretic, or dihydropyridine CCB
European Society of Hypertension/European Society of Cardiology (2013)	<140/85	ACEI/ARB [±] , thiazide-like diuretic, or CCB

Adapted from : Passarella, P., Kiseleva, T. A., Valeeva, F. V., & Gosmanov, A. R. (2018). Hypertension management In diabetes: 2018 Update. *Diabetes Spectrum*, 31(3), 218–224. <https://doi.org/10.2337/ds17-0085>

Blood pressure goals

- The American Diabetes Association recommends treating to systolic and diastolic blood pressure of <140 mmHg and <90 mmHg respectively⁸
- Lower treatment targets (<130/80) may be appropriate for individuals at high risk of CVD without any undue treatment burden⁸
- American College of Cardiology/American Heart Association hypertension guidelines in 2017 recommend a goal blood pressure in patients with diabetes mellitus of <130/80 mmHg⁸

So what does this all mean?



Figure 3: Confusion
by Paul, A., 2013:
<https://www.kqed.org/mindshift/27166/why-confusion-can-be-a-good-thing>

Honestly, it depends on the patient

- Having an individual approach for patient's blood pressure goal is better than trying to fit a one size fits all model.
- The current blood pressure recommendations are based on studies with heterogeneous populations, different treatment goals and endpoints.
- Its still unclear if the ACC/AHA recommendations will lead to significant decrease in CVD events or increase in adverse events.⁷
- It's always best to review with your patients what fits best with their lifestyle, drug-drug interactions, potential adverse events and limiting pill burden as well as costs.

Lifestyle Modifications

- ALWAYS A PART OF MANAGEMENT
- Reducing salt intake to less than 1.5 grams per day
- Increasing consumption of fruits and vegetables (8-10 servings per day)
- Increasing consumption of low fat dairy products (2-3 servings/day)
- Losing weight (loss of 1 kg of body weight has been associated with a decrease of BP of ~1 mmHg)⁴
- Avoiding alcohol consumption – less than 2 drinks/day for men and 1 drink/day for women⁴
- Increase exercise (at least 30-45 minutes a day)
- Always remember to ask about sleep! Treatment of obstructive sleep apnea has shown to reduce BP in patients with diabetes⁴

Initiating blood pressure medications

BP ^b Category	Pressure Ranges	Recommendations
Normal BP	<120/<80 mmHg	Promote healthy lifestyle; reassess BP annually.
Elevated BP	120-129/<80 mmHg	Start with nonpharmacologic therapy, reassess BP in 3-6 months.
Stage1 Hypertension	130-139/80-89 mmHg	ASCVD^c or 10-year CVD^d risk $\geq 10\%$: Start with both nonpharmacologic and pharmacologic therapy. Reassess BP in 1 month. If at goal, reassess every 3-6 months. If not at goal, assess for adherence and consider intensification of therapy.
		No ASCVD and 10-year CVD risk <10%: Start with nonpharmacologic therapy, reassess BP in 3-6 months. If not at goal, consider initiation of pharmacologic therapy.
Stage 2 Hypertension	$\geq 140/\geq 90$ mmHg	Start with both nonpharmacologic and pharmacologic therapy. Reassess BP in 1 month. If at goal, reassess every 3-6 months. If not at goal, assess for adherence and consider intensification of ther

Table 3: AHA/ACC Guideline Recommendations by Blood Pressure Category.

Adapted from American Heart Association:
New guidance on blood pressure management in low-risk adults with stage 1 hypertension. American College of Cardiology. (n.d.).
<https://www.acc.org/Latest-in-Cardiology/Articles/2021/06/21/13/05/New-Guidance-on-BP-Management-in-Low-Risk-Adults-with-Stage-1-HTN>.

How to calculate risk

- ASCVD Risk Estimator Risk
- <https://tools.acc.org/ascvd-risk-estimator-plus/#!/calculate/estimate/>

Atherosclerotic Cardiovascular Disease (ASCVD) Prevention Tool

Enter Patient Data Shared Decision

Intended for use in people at risk for ASCVD and the LDL cholesterol is >190mg/dL.

Age (years)	65
African American	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Gender	<input checked="" type="checkbox"/> Male <input type="checkbox"/> Female
Current	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
On BP Medication	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Smoker	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Total Cholesterol	200 mg/dL
HDL Cholesterol	50 mg/dL
Systolic Blood Pressure	100 mmHg
LDL Cholesterol	150 mg/dL

Estimated Risk

41.9% Your Estimated 10-Year ASCVD Risk

KP Guideline Recommendations

Start High-Intensity Statin
Start atorvastatin 40 mg.

Consider Aspirin at 81 mg
Consider initiating aspirin in adults aged 50-69 years with a ≥10% 10-year ASCVD risk.

Smoking Cessation
Smoking Cessation should be encouraged to reduce the risk of ASCVD.

Recalculate Risk

Figure 4: Example of ASCVD Risk Calculated Score. Kaiser Permanente, 2020; <https://wa.kaiserpermanente.org/static/pdf/public/guidelines/ascvd-primary.pdf>

Recommendations for the Treatment of Confirmed Hypertension in People With Diabetes

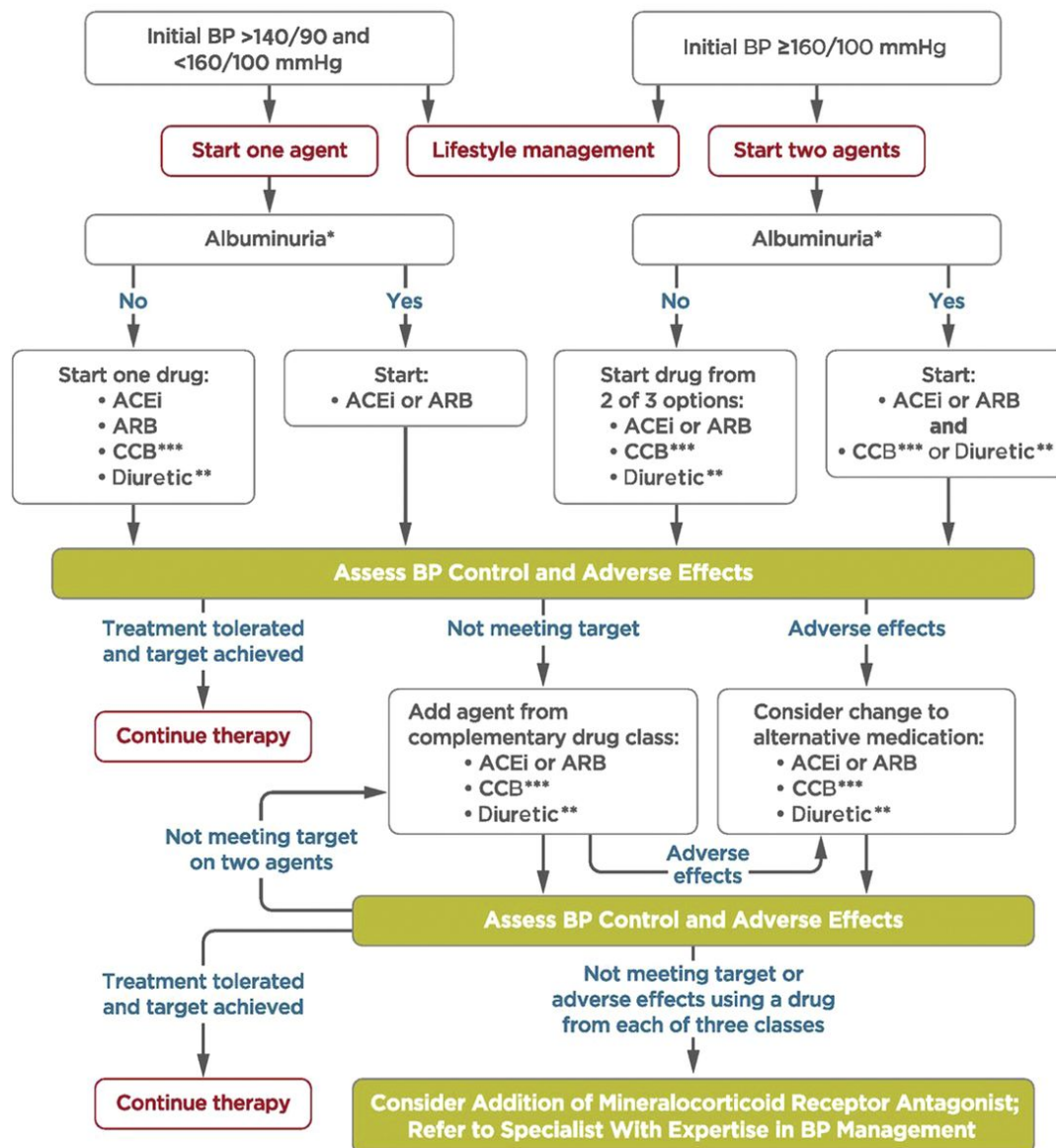


Figure 5: Recommendations for Treatment of Confirmed HTN in People with Diabetes.

Adapted from de Boer IH, Bangalore S, Benetos A, et al. Diabetes Care 2017;40:1273–1284.

American Diabetes Association Dia Care 2020;43:S111-S134

Table 4 Classes of Anti-hypertensive Medications.

Adapted from American Heart Association: *Types of blood pressure medications*.
[www.heart.org](https://www.heart.org/en/health-topics/high-blood-pressure/changes-you-can-make-to-manage-high-blood-pressure/types-of-blood-pressure-medications#ARB). (n.d.).
<https://www.heart.org/en/health-topics/high-blood-pressure/changes-you-can-make-to-manage-high-blood-pressure/types-of-blood-pressure-medications#ARB>.

Classes of Antihypertensive Medications	
Mechanism of Action	Examples
Angiotensin Renin Inhibitors (ACE-I)	Lisinopril Enalapril Captopril
Angiotensin Receptor Blockers (ARB)	Losartan Potassium Valsartan Irbesartan
Dihydropyridine Calcium Channel Blockers (DHP CCB)	Amlodipine Felodipine Nifedipine Nicardipine
Thiazide Diuretics	Chlorthalidone* Indapamide* Hydrochlorothiazide
Beta Blockers	Metoprolol Tartrate/Succinate Atenolol Labetalol
Potassium-Sparing Diuretics	Amiloride hydrochloride Spironolactone Triamterene
Blood Pressure Vasodilators	Hydralazine Hydrochloride Minoxidil
Non Dihydropyridine Calcium Channel Blockers (Non-DHP CCB)*	Diltiazem Verapamil
Alpha Blockers	Doxazosin Terazosin
Loop Diuretic	Furosemide Bumetanide
Central Agonists	Clonidine Hydrochloride Alpha Methyl dopa

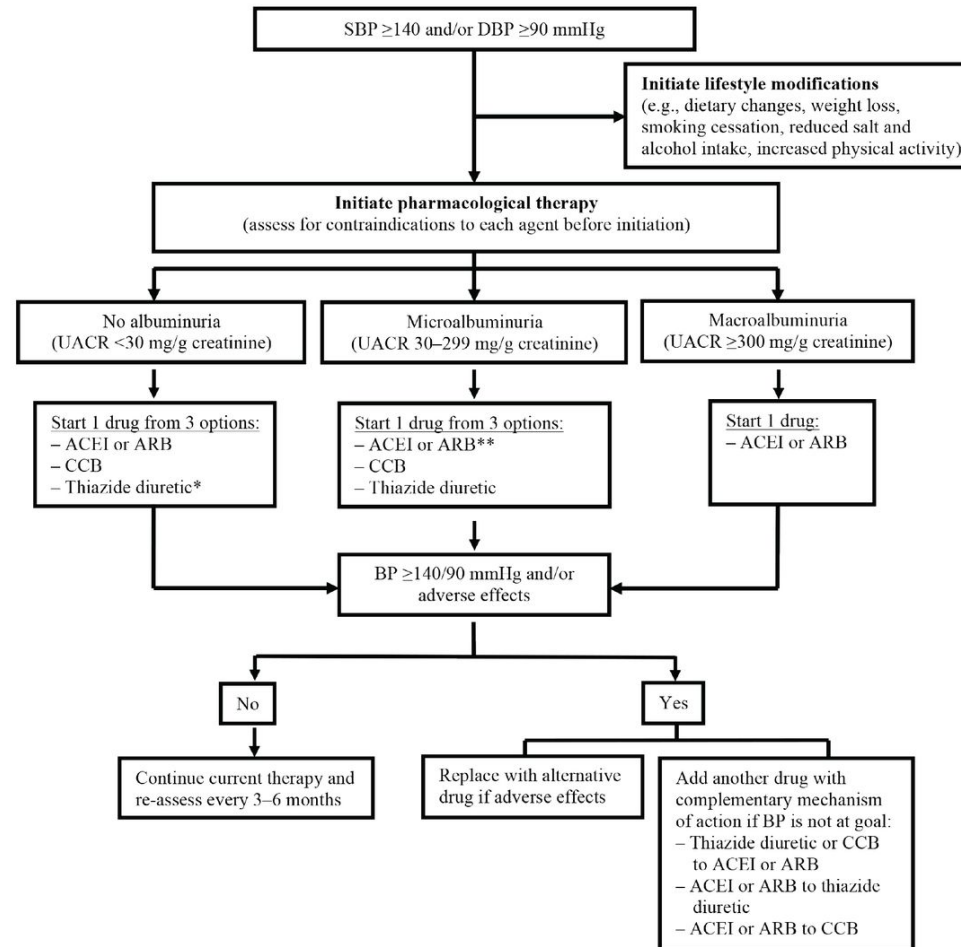
Angiotensin Renin Inhibitors and Angiotensin Receptor Blockers

- Tends to be first line for patients with diabetes
- An ACE inhibitor (ACE- I) or Angiotensin Receptor Blocker (ARB) is suggested to treat hypertension for patients with urine albumin-to-creatinine ratio 30–299 mg/g creatinine and strongly recommended for patients with urine albumin-to-creatinine ratio ≥ 300 mg/g creatinine⁴
- Don't combine the two! Has higher risk of renal side effects.
- ARB has lower side effect profile⁴
- In general, use one or the other depending on patient's tolerance to medication

Pathway to initial antihypertensive therapy in patients with diabetes. *Use of chlorthalidone or indapamide is preferred. **Can be suggested as first-line therapy in patients with microalbuminuria.

Figure 6: Anti-HTN algorithm for patients with microalbuminuria.

Adapted from: Passarella, P., Kiseleva, T. A., Valeeva, F. V., & Gosmanov, A. R. (2018, August 1). *Hypertension management In diabetes: 2018 Update*. Diabetes Spectrum. <https://spectrum.diabetesjournals.org/content/31/3/218>.



Pasquale Passarella et al. Diabetes Spectr 2018;31:218-224

Thiazide diuretics

- ****Thiazide-like diuretic; long-acting agents shown to reduce cardiovascular events, such as chlorthalidone and indapamide, are preferred¹**

Calcium Channel Blockers (CCB)

- *****Dihydropyridine calcium channel blocker (CCB) are preferred¹**
 - More potent vasodilators
 - Longer lasting
 - Has higher effects on systemic vascular resistance



Hyperlipidemia

Lipid disorders

- Most common pattern of dyslipidemia is elevated triglycerides and decreased high density lipoprotein (HDL) levels³
- Dyslipidemia is extremely common in T2DM affecting around 72-85% of patients³
- LDL-cholesterol has been the primary predictor of CVD

When to screen and monitor

- Obtain a lipid profile at the time of diagnosis or initial medical evaluation
- You can screen every 5 years if under the age of 40 or more frequently if indicated (generally 1-2 years if abnormal)³
- Obtain a lipid profile about 4-12 weeks after you initiate a statin to see if there is a change to see if dose needs to be titrated³

Hyperlipidemia Recommendations

- For patients with diabetes aged 40-75 years without ASCVD, use moderate-intensive statin therapy in addition to lifestyle therapy
- For patients of all ages with diabetes AND ASCVD, high intensity statin therapy should be initiated with lifestyle therapy¹
- In patients with diabetes at higher risk especially those with multiple ASCVD risk factors or aged 50-70 years, it is reasonable to use high intensity statin therapy¹
- Statins not recommended in pregnancy*¹

Other considerations

- Can consider moderate intensity statin for the following¹
 - Patients younger than 40 years of age
 - Type 1 Diabetes with other ASCVD risk factors
 - Patients with diabetes who are 75 years or older

When to go beyond statins?

- “For patients with diabetes and ASCVD considered high risk if LDL cholesterol is ≥ 70 mg/dL on maximally tolerated statin dose, consider adding additional LDL lowering therapy such as ezetimibe or PCSK9 inhibitor” (Jialal 2019)
 - Ezetimibe is often cheaper in cost
- In adults with diabetes and 10 year ASCVD risk of 20% or higher, it may be reasonable to add ezetimibe to maximally tolerated statin therapy to reduce LDL cholesterol levels by 50% or more¹
- “If patients with ASCVD or other CV 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 CVD risk.” (Jialal 2019)
- Statin + Fibrate combination generally not recommended, hasn’t been shown to improve ASCVD outcomes¹
- Statin + Niacin combination therapy hasn’t been shown to prove additional CV benefit above statins only and may increase the risk of stroke¹

Table 5: Summary of low-density lipoprotein-cholesterol lowering medications

Drug class	Mechanism of action	Clinical efficacy	Adverse reactions
Statins	Inhibition of HMG coenzyme A Reductase	Highly effective	Myalgia, myositis, rhabdomyolysis, elevation in liver enzymes, new onset diabetes
Ezetimibe	Decrease intestinal cholesterol absorption by binding to Niemann-Pick C1-like 1 protein	Moderately effective; Safe addition to statin therapy	Worsening of liver function, myopathy or rhabdomyolysis if added to statins; Nasopharyngitis, diarrhea, upper respiratory tract infection
PCSK9 inhibitors	Inhibition of Proprotein Convertase Subtilisin/Kexin Type 9	Very highly effective in combination with statin therapy	Injection site reaction including itching, swelling, erythema and pain
Bile acid sequestrants	Bind bile acids in the small intestine and prevent reabsorption	Moderately effective, safe addition to statin therapy, not desirable if triglycerides are > 300 mg/dL	Constipation, abdominal pain, bloating, drug malabsorption

HMG: Hydroxymethylglutaryl; PCSK9: Proprotein convertase subtilisin/kexin type 9.

When to initiate hyperlipidemia/dyslipidemia medications

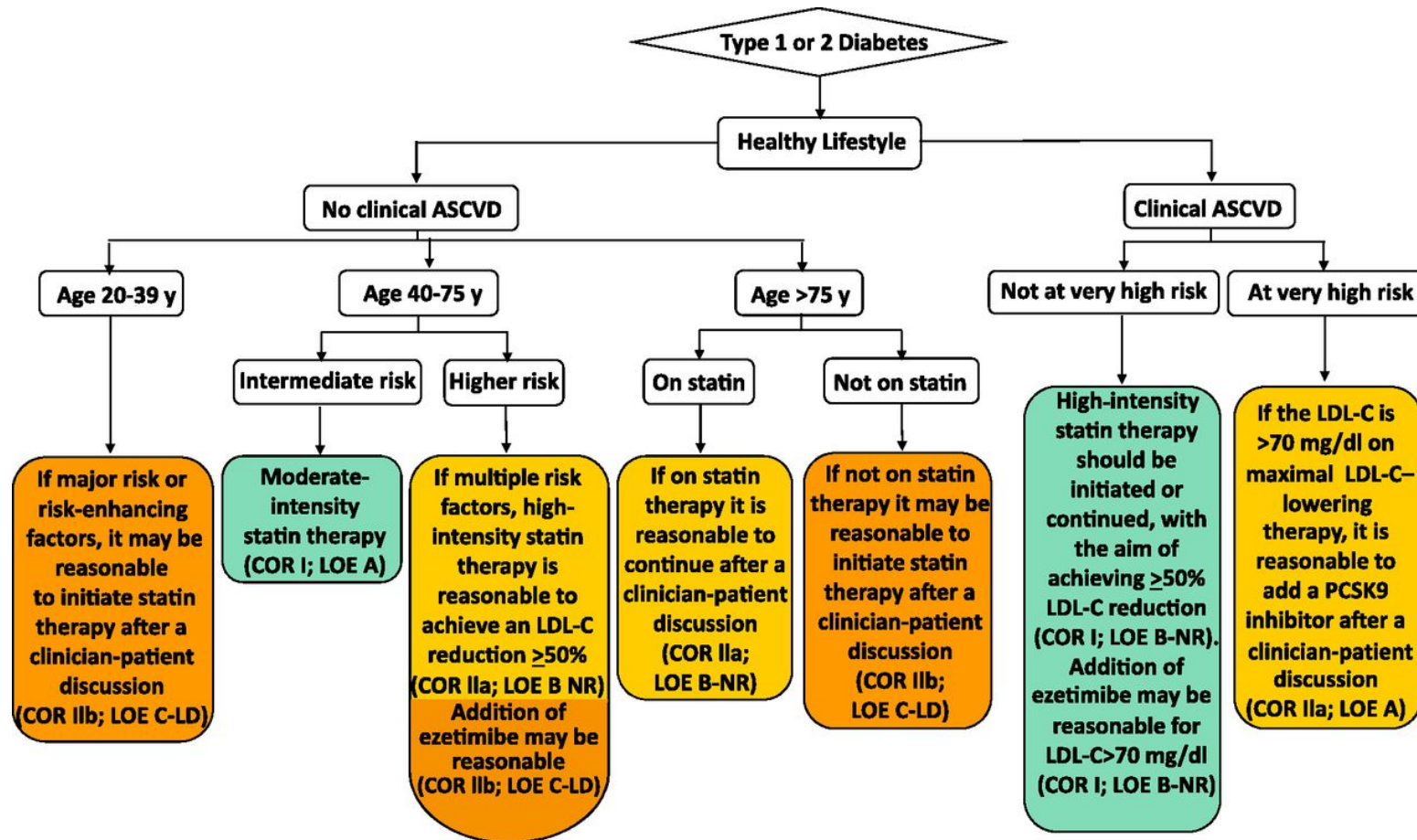


Figure 7: Statin Algorithm. Goldberg, 2018.

Adapted from Goldberg, R. B., Stone, N. J., & Grundy, S. M. (2020). The 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APHA/ASPC/NLA/PCNA guidelines on the management of blood cholesterol in diabetes. *Diabetes Care*, 43(8), 1673–1678.

<https://doi.org/10.2337/dci19-0036>

Moderate to High dose Statins

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

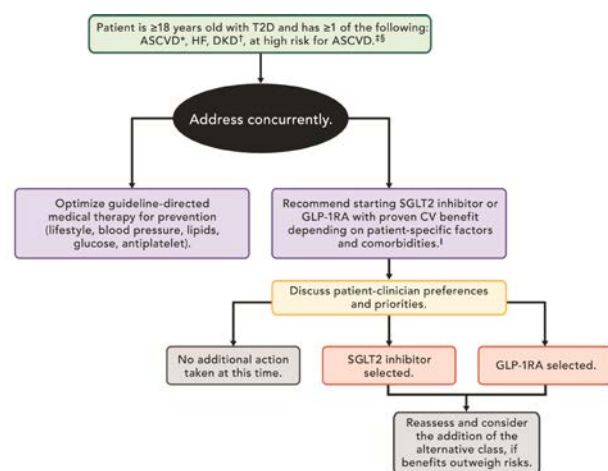
Table 6: Statin Potency Chart:
Diabetes Care, 2020.

Adapted from: Cardiovascular
disease and risk Management:
Standards of medical care In
Diabetes—2021. (2020). *Diabetes
Care*, 44(Supplement 1).
<https://doi.org/10.2337/dc21-s010>

What is the goal?

- Lowering of LDL by 50% or more if your ASCVD risk is 20% or higher³
 - Can add second agent if needing to reduce LDL cholesterol levels by 50% or more
- No specified LDL goals but do provide some general guidelines for secondary prevention in those who have CVD
- For those who are 20-39, it's reasonable to start moderate dose statin³
- Diabetes is considered a high risk condition for ASCVD

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*ASCVD is defined as a history of an acute coronary syndrome or MI, stable or unstable angina, coronary heart disease with or without revascularization, other arterial revascularization, stroke, or peripheral artery disease assumed to be atherosclerotic in origin.

†DKD is a clinical diagnosis marked by reduced eGFR, the presence of albuminuria, or both.

‡Consider an SGLT2 inhibitor when your patient has established ASCVD, HF, DKD or is at high risk for ASCVD. Consider a GLP-1RA when your patient has established ASCVD or is at high risk for ASCVD.

§Patients at high risk for ASCVD include those with end organ damage such as left ventricular hypertrophy or retinopathy or with multiple CV risk factors (e.g., age, hypertension, smoking, dyslipidemia, obesity).

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

ASCVD = atherosclerotic cardiovascular disease; CV = cardiovascular; DKD = diabetic kidney disease; eGFR = estimated glomerular filtration rate; GLP-1RA = glucagon-like peptide-1 receptor agonist; HF = heart failure; MI = myocardial infarction; SGLT2 = sodium-glucose cotransporter-2; T2D = type 2 diabetes

Figure Legend:

Approach to risk reduction with SGLT2 inhibitor or GLP-1 receptor agonist therapy in conjunction with other traditional, guideline-based preventive medical therapies for blood pressure, lipids, and glycemia and antiplatelet therapy. Reprinted with permission from Das et al. (220).



Questions?

Works Cited and Footnotes

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- Figure 9: <https://www.uptodate.com/contents/image?imageKey=PEDS%2F73414>

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Thank you!
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