



# Hypertension management In type II diabetes

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# Cardiovascular Disease and Risk Management In DM



**Metabolic Disorders**:

Metabolic syndrom

Fatty Liver

\*Hyperlipidemia

**\*HTN** 

Overweight & Obesity

CVD
STROKE
STROKE
CANCER
CKD & ESRD
HEPATIC disorder
PAD





بيشترين							

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## **DM MANAGEMENT**:

**\*HIS** 

- **\* PE & FOOT EXAM**
- **\***REFFERALS
- **\***ASSESSMENT
- **<b>\***EVALUATION

## HIS:

- Age, DM onset
- **♦FH**
- **Common comorbid**:
- **CS & Alcohol**
- **\*PA** & Sleep
- Eating pattern & Weight history
- Social His & support
- \*Medication:
- Hypoglycemia +/-



### **General appearance**\*

Weight, WC, BMI **\*BP** : orthostatic +/-Hand: pulse , skin, nail **Pale** +/-\* Mouth Thyroid palpation Skin exam: acant nig, insulin injection Foot examination:

## **∻Lab**

- **\***Referrals
- **\***Assessment
- Goal setting
- Treatment plan

Selected standard laboratory tests for work-up of hypertensive patients

Hemoglobin and/or hematocrit

Fasting blood glucose and HbA1C

- Blood lipids: total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides
- Blood potassium and sodium
- Blood uric acid
- Blood creatinine (and/or cystatin C) for estimating GFR with eGFRa formulas
- Blood calcium

Urine analysis (first voided urine in the morning), multicomponent dipstick test in all patients, urinary albumin/creatinine ratio, microscopic examination in selected patients.

# **Referrals**:

- Annual dilated eye exam
- Family planning for women of reproductive age
- Registered dietitian for MNT
- Diabetes self-management education
- Dental examination
- Mental health professional, if needed

#### Table 4.2-Assessment and treatment plan\*

Assess risk of diabetes complications

- ASCVD and heart failure history
- ASCVD risk factors (see Table 10.2) and 10-year ASCVD risk assessment
- Staging of chronic kidney disease (see Table 11.1)
- Hypoglycemia risk (Table 4.3)

Goal setting

- Set A1C/blood glucose target
- If hypertension present, establish blood pressure target
- Diabetes self-management goals (e.g., monitoring frequency)

The rapeutic treatment plan

- Lifestyle management
- Pharmacologic therapy (glucose lowering)
- Pharmacologic therapy (cardiovascular disease risk factors and renal)
- 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 is an essential component of initial and all follow-up visits.



## Table 4.3-Assessment of hypoglycemia risk

Factors that increase risk of treatment-associated hypoglycemia

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

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#### **Comprehensive Medical Evaluation and Assessment of Comorbidities**:

#### **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
- Hypoglycemia risk
- Assessment for retinopathy
- Assessment for neuropathy

# The Risk Calculators:

#### **Comprehensive Medical Evaluation and Assessment of Comorbidities**:

#### 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)



For prevention and management of both ASCVD and heart failure, cardiovascular risk factors should be systematically assessed at least annually in all patients with diabetes.

#### Assessment:

CVD &HF risk:	1- http/tools.acc.org/ASCVD-Risk-Estimator- Plus				
	2- EF- LVH – Diastolic dysfunction				
CKD risk:	CKD-EPI Equations for GFR				
Hepatic Fibrosis:	FIB-4 calculator				
Hypoglycemic risk:	Table 4.3				
*Assessment for retinopathy:					
Assessment for neuro	opatny:				

**Therapeutic treatment plans:** 

Lifestyle management

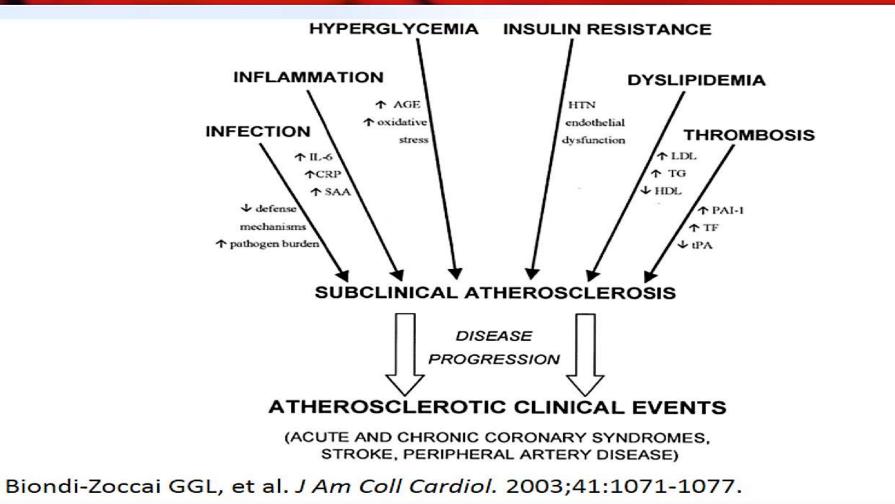
Pharmacologic therapy: glucose lowering

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)

# Mechanisms by Which Diabetes Leads to CHD



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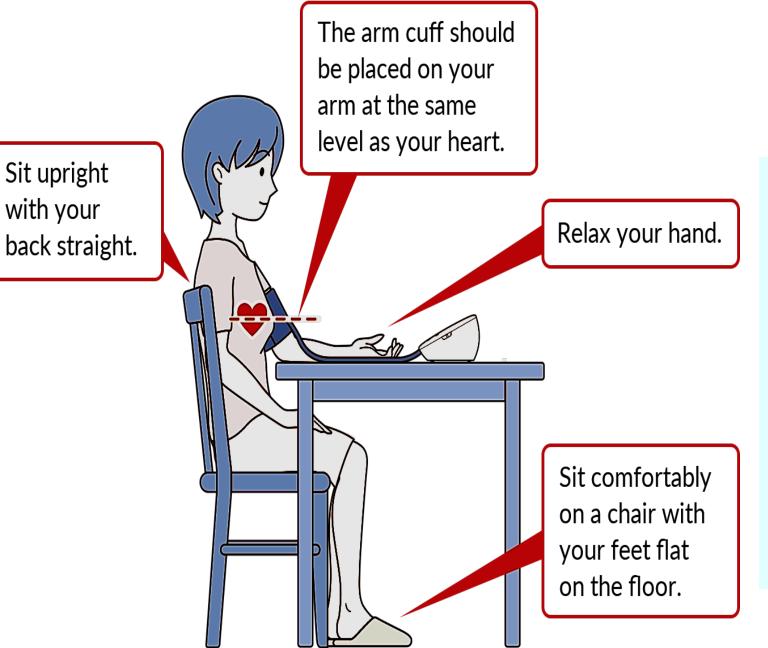




Major risk factor for ASCVD & microvascular complications:

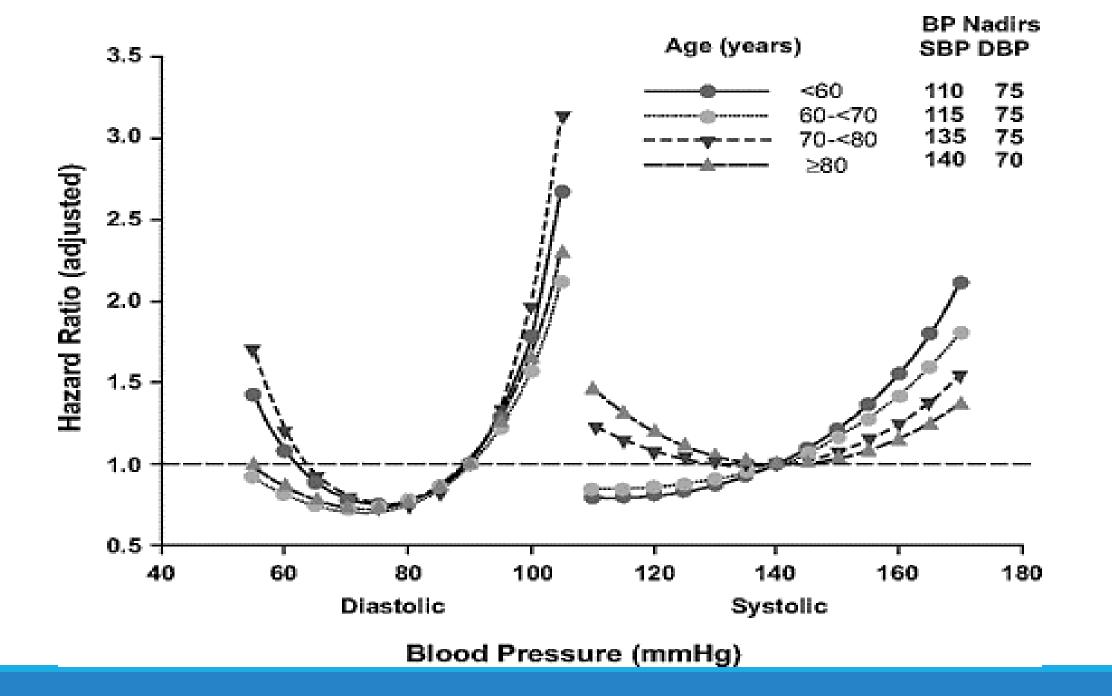
In T<sub>1</sub>DM, HTN often results from underlying kidney disease.

In T<sub>2</sub>DM, HTN coexists with other cardiometabolic risk factors.



	1st Blood Pressure	1 <sup>st</sup> Pulse	2 <sup>nd</sup> Blood Pressure	2 <sup>nd</sup> Pulse	
	(mmHg)	(beats/minute)	(mmHg)	(beats/minute)	Comments
Day 1 AM	1		1		
РМ	1		1		
Day 2 AM	1		1		
PM	1		1		
Day 3 AM	1		1		
РМ	1		1		
Day 4 AM	1		1		
PM	1		1		
Day 5 AM	1		1		
PM	1		1		
Day6 AM	1		1		
PM	1		1		
Day 7 AM	1		1		
PM	1		1		





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Therefore, it maybe reasonable to target blood pressure,
<130/80mmHg among patients with diabetes and either clinically diagnosed cardiovascular disease (particularly stroke, which was significantly reduced in ACCORDBP) or 10-year ASCVDrisk>15%, if it can be attained safely.

#### Hypertension, defined as a sustained blood pressure >130/80 mmHg, is common among patients with either type 1 or type 2 diabetes.

All hypertensive patients with diabetes should monitor their blood pressure at home.

Home blood pressure self-monitoring and 24-h ambulatory blood pressure monitoring may provide evidence of white coat hypertension, masked hypertension, or other discrepancies between office and "true" blood pressure.

# **Categories of BP in Adults\***

BP Category	SBP		DBP			
Normal	<120 mm Hg	and	<80 mm Hg			
Elevated	120-129 mm Hg	and	<80 mm Hg			
Hypertension						
Stage 1	130-139 mm Hg	or	80-89 mm Hg			
Stage 2 ≥140 mm Hg		or	≥90 mm Hg			

\*Individuals with SBP and DBP in 2 categories should be designated to the higher BP category.

# Corresponding Values of Systolic BP/Diastolic BP for Clinic, Home (HBPM), Daytime, Nighttime, and 24-Hour Ambulatory (ABPM) Measurements.

Clinic	HBPM	Daytime ABPM	Nighttime ABPM	24-Hour ABPM
120/80	120/80	120/80	100/65	115/75
130/80	130/80	130/80	110/65	125/75
140/90	135/85	135/85	120/70	130/80
160/100	145/90	145/90	140/85	145/90

# **Outpatient Management:**

Lifestyle modification

- Lipid management
- Bp control
- Cigar discontinuous
- Glycemic control

# Management:

## **New onset DM:** Lipid, Bp, Glucose control

## Advance DM : Lipid ,BP ,but less glucose control

## Older age DM : Bp, lipid ,but less glucose control

Clinical trial	Population	rials of intensive versus stan Intensive	Standard	Outcomes
ACCORD BP (28)	aged 40-79 years with	Systolic blood pressure target: <120 mmHg Achieved (mean) systolic/ diastolic: 119.3/64.4 mmHg	Systolic blood pressure target: 130–140 mmHg Achieved (mean) systolic/ diastolic: 133.5/70.5 mmHg	<ul> <li>No benefit in primary end point: composite of nonfatal MI, nonfatal stroke, and CVD death</li> <li>Stroke risk reduced 41% with intensive control, not sustained through follow-up beyond the period of active treatment</li> <li>Adverse events more common in intensive group, particularly elevated serum creatinine and electrolyte abnormalities</li> </ul>
A DVANCE BP (29)	aged 55 years and older with prior evidence of CVD	Intervention: a single-pill, fixed- dose combination of perindopril and indapamide Achieved (mean) systolic/ diastolic: 136/73 mmHg	Control: placebo Achieved (mean) systolic/ diastolic: 141.6/75.2 mmHg	<ul> <li>Intervention reduced risk of primary composite end point of major macrovascular and microvascular events (9%), death from any cause (14%), and death from CVD (18%)</li> <li>6-year observational follow-up found reduction in risk of death in intervention group attenuated but still significant (174)</li> </ul>
HOT (173)	18,790 participants, including 1,501 with diabetes	Diastolic blood pressure target: :≤80 mmHg	Diastolic blood pressure target: ⊴90 mmHg	<ul> <li>In the overall trial, there was no cardiovascular benefit with more intensive targets</li> <li>In the subpopulation with diabetes, an intensive diastolic target was associated with a significantly reduced risk (51%) of C/D events</li> </ul>
SPRINT (39)	9,361 participants without diabetes	Systolic blood pressure target: <120 mmHg Achieved (mean): 121.4 mmHg	Systolic blood pressure target: <140 mmHg Achieved (mean): 136.2 mmHg	<ul> <li>Intensive systolic blood pressure target lowered risk of the primary composite outcome 25% (MI, ACS, stroke, HF, and death due to CVD)</li> <li>Intensive target reduced risk of death 27%</li> <li>Intensive therapy increased risks of electrolyte abnormalities and AKI</li> </ul>

Intensive systolic blood pressure lowered risk of the primary

composite outcome 25% (MI, ACS, stroke, HF, and death due to CVD)

Intensive target reduced risk of death 27%

Intensive therapy increased risks of electrolyte abnormalities and

AKI

### Stroke risk reduced 41% with intensive control, not sustained

through follow-up beyond the period of active treatment

**Adverse events more common in intensive group, particularly** 

elevated serum creatinine and electrolyte abnormalities.

In the overall trial, there was no cardiovascular benefit with more intensive targets.

### This approach is consistent with guidelines from the American

**College of Cardiology/American Heart Association, which advocate** 

a blood pressure target <130/80 mmHg for all patients, with or

without diabetes.

## **Medical Therapy in HTN**:



## **\***ACE inhibitors

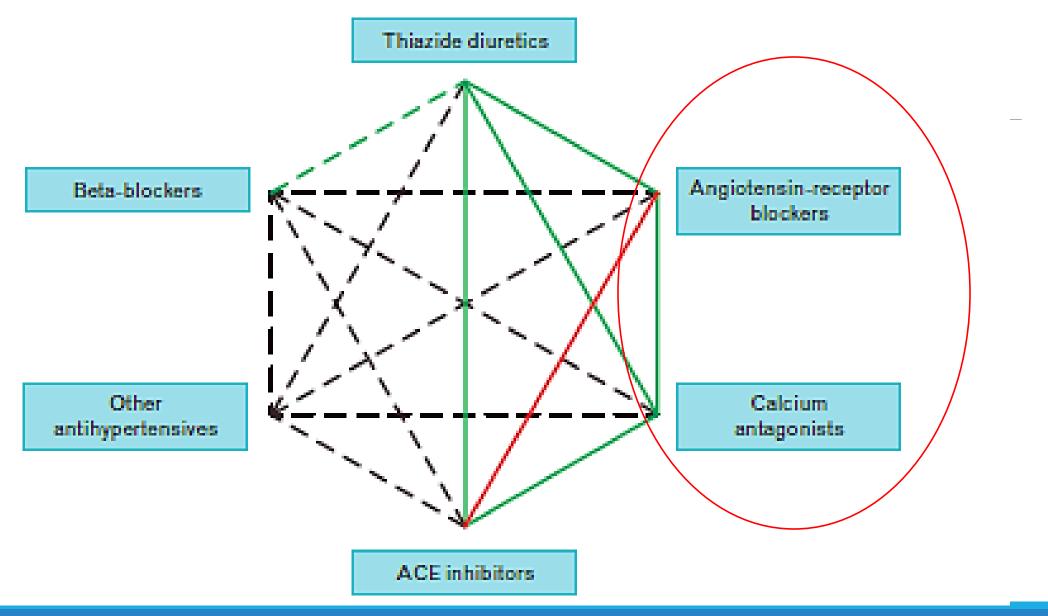
## Ca blockers (Dihydropyridine)

Thiazid like

### B-Blockers may be used for the treatment of prior MI, active angina,

or heart failure.

But have not been shown to reduce mortality as blood pressure lowering agents in the absence of these conditions.



2013 ESH/ESC Guidelines for the management of arterial hypertension

## **Treatment Strategies:**

✤ ACE inh and ARB in combination is not recommended given the lack of added ASCVD benefit and increased rate of adverse events –

namely hyperkalemia ,syncope ,and acute kidney injury.

In the absence of albuminuria, risk of progressive kidney disease

is low, and ACE inhibitors and ARBs have not been found to afford superior cardio protection when compared with thiazide-like diuretics or dihydropyridine calcium channel blockers. An ACE inhibitor or angiotensin receptor blocker, at the maximum tolerated dose indicated for blood pressure treatment, is the recommended first-line treatment for hypertension in patients with diabetes and urinary albumin-to- creatinine ratio  $\geq$ 300 mg/g creatinine (A) Or 30-299 mg/g creatinine (B)

If one class is not tolerated, the other should be substituted.(B)

American Diabetes Association Standards of Medical Care in Diabetes. Cardiovascular disease and risk management. Diabetes Care 2017; 40 (Suppl. 1): S75-S87

# **Treatment:**

An ACE inhibitor or angiotensin receptor blocker, at the maximum tolerated dose indicated for blood pressure treatment, is the recommended first-line treatment for hypertension in patients with diabetes and urinary albumin–to–creatinine ratio ≥300 mg/g creatinine (A) or 30–299 mg/g creatinine (B).

For patients with blood pressure >120/80 mmHg, lifestyle intervention consists of weight loss if overweight or obese; a Dietary Approaches to Stop Hypertension-style dietary pattern including reducing sodium and increasing potassium intake; moderation of alcohol intake; and increased physical activity.(B)

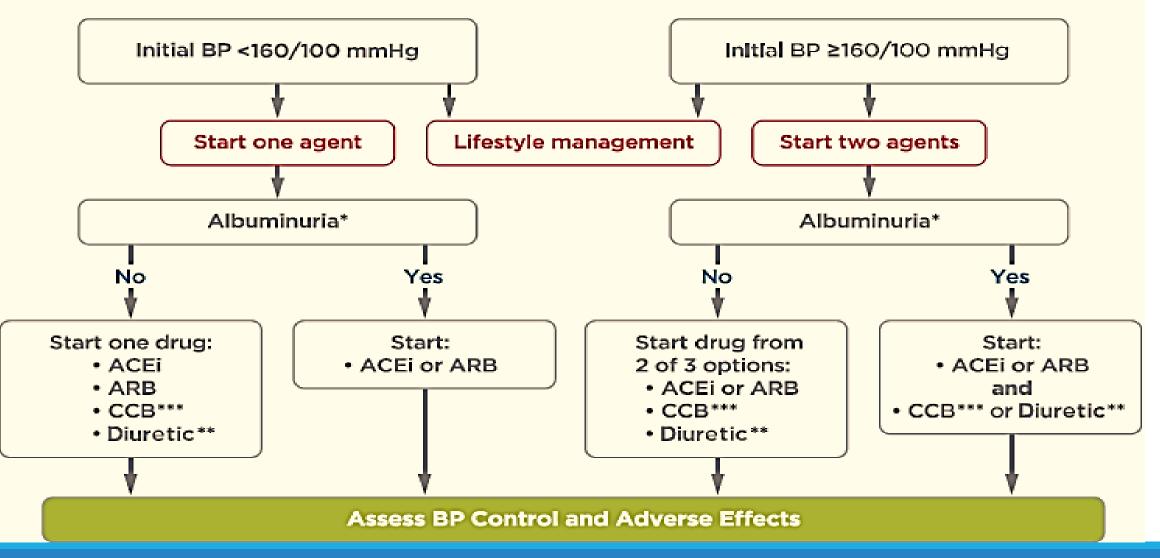
## **Treatment:**

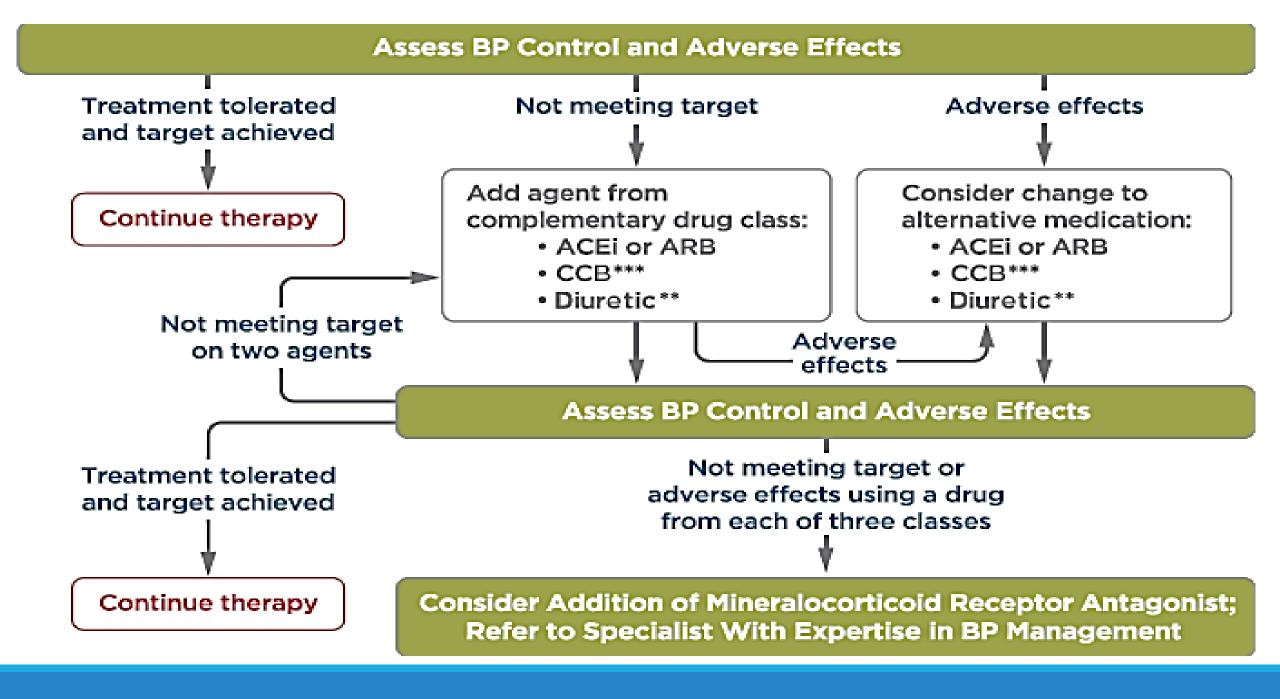
An important caveat is that most patients with diabetes and hypertension require multiple-drug therapy to reach blood pressure treatment goals.

Identifying and addressing barriers to medication adherence (such as cost and side effects) should routinely be done. If blood pressure remains uncontrolled despite confirmed adherence to optimal doses of at least three antihypertensive agents of different classes, one of which should be a diuretic, clinicians should consider an evaluation for secondary causes of hypertension.

#### Recommendations for the Treatment of Confirmed Hypertension in People With Diabetes









# **Albuminuria in DM1**



## **Renal assessment**:



## **Approach:**

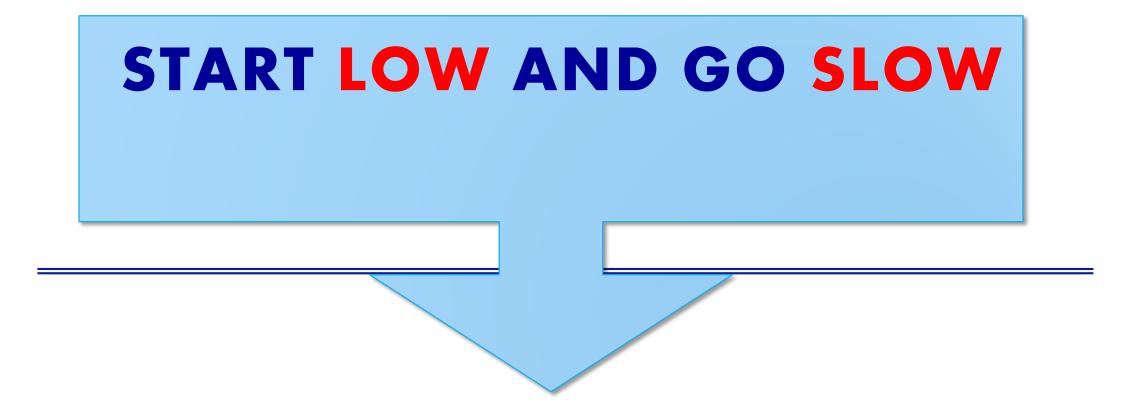
Look to UA:

## **Measurement** of **ACR** or **Proteinuria**

**MicroAlbuminuria** 

MacroAlbuminuria

Proteinuria



# 20/10 rule



# When BP is greater than 20/10mmHg above the goal

## therapy should be initiated with two drugs rather

than one.

Potential adverse effects of antihypertensive therapy (e.g., hypotension, syncope, falls, acute kidney injury, and electrolyte abnormalities) should also be taken into account. Patients with older age, chronic kidney disease, and frailty have been shown to be at higher risk of adverse effects of intensive blood pressure control.

- In addition, patients with orthostatic hypotension, substantial
  - comorbidity, functional limitations, or polypharmacy may be at high risk of adverse effects, and some patients may prefer higher
  - blood pressure targets to enhance quality of life.

# **Treatment Strategies:**

◆ACE inhibitor and ARB in combination is not recommended given the lack of added ASCVD benefit and increased rate of adverse events – namely hyperkalemia ,syncope ,and acute kidney injury. Table 10.1-Framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes

Patient characteristics/ health status	Rationale	Reasonable A1C goal‡	Fasting or preprandial glucose	Bedtime glucose	Blood pressure	Lipids
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.5% (58 mmol/mol)	90–130 mg/dL (5.0–7.2 mmol/L)	90–150 mg/dL (5.0–8.3 mmol/L)	<140/90 mmHg	Statin unless contraindicated or not tolerated
Complex/intermediate (multiple coexisting chronic illnesses* or 2+ instrumental ADL impairments or mild-to- moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	<8.0% (64 mmol/mol)	90–150 mg/dL (5.0–8.3 mmol/L)	100–180 mg/dL (5.6–10.0 mmol/L)	<140/90 mmHg	Statin unless contraindicated or not tolerated
Very complex/poor health (LTC or end-stage chronic illnesses** or moderate- to-severe cognitive impairment or 2 + ADL dependencies)	Limited remaining life expectancy makes benefit uncertain	<8.5%† (69 mmol/mol)	100-180 mg/dL (5.6-10.0 mmol/L)	110–200 mg/dL (6.1–11.1 mmol/L)	<150/90 mmHg	Consider likelihood of benefit with statin (secondary prevention more so than primary)



## **Treatment Strategies**:

SBP < 130 ;overall

SBP < 120 ;no Cv outcome in older people (age >65 years),

**DBP** < 80 ;**overall** 

DBP < 80 ; appropriate for: CKD, ACR+ CVD, additional riskfactors..

DBP < 70 ; avoided in older adult with greater risk of mortality

**IN DM1**: **HTN** +, **Alb**+ : **ACE inh** 

## IN DM<sub>2</sub>: HTN + ,Alb+ : ACE inh ,ARB

### **IN DM** without Alb : ACE inh , ARB , Thiazid , CCB

**Bedtime Dosing**, growing evidence suggests that there is an association between the absence of nocturnal blood pressure dipping and the incidence of ASCVD.

moving at least one antihypertensive medication to bedtime significantly reduced cardiovascular events ?

# In patient visit:

**BP** measurement

**Orthostatic symptom** 

**Albuminuria** +/-

**Bedtime dosing** 

FU; cr , K

If using ACE inhibitors, ARBs, or diuretics, monitor serum creatinine / eGFR & potassium levels.

# Free combination & Single-Pill combination

## FDA-Approved Combination Products to Treat Hypertension

Amlodipine-Based Combinations*		HCTZ-Based Combination	Other Combinations*	
Aliskiren: am lodipine	Aliskiren:HCTZ	Fosinopril:HCTZ	Olmesartan:HCTZ	Aliskiren:valsartan
Benazepril:amlodipine	Amiloride:HCTZ	Irbesartan:HCTZ	Propranolol:HCTZ	Atenolol:chlorthalidone
Olmesartan: am lodipine	Benazepril:HCTZ	Lisinopril:HCTZ	Quinapril:HCTZ	Azilsartan: chlorthalidone
Telmisartan: am lodipine	Bisoprolol:HCTZ	Losartan:HCTZ	Spironolactone:HCTZ	Bendroflumethiazide:nadolol
Valsartan: amlodipine	Candesartan:HCTZ	Methyldopa:HCTZ	Telmisartan:HCTZ	Chlorthalidone:clonidine
Aliskiren:amlodipine:HCTZ†	Captopril:HCTZ	Metoprolol:HCTZ		
(extended release)	Triamterene:HCTZ	Trandolapril:verapamil		
Amlodipine:HCTZ:olmesartan†	Enalapril:HCTZ	Metoprolol:HCTZ	Valsartan:HCTZ	
Amlodipine:HCTZ:valsartan†	Eprosartan:HCTZ	Moexipril:HCTZ		

## A promising choice in hypertension treatment: Fixed-dose combinations

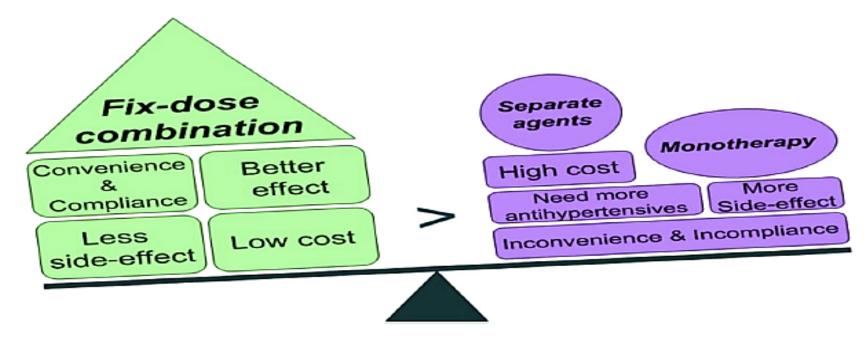


Fig. 1 – Advantages of fixed-dose combinations versus monotherapy and separate agents.

asian journal of pharmaceuticalsciences 9; (2014), 1-7

# **Resistant hypertension**:

♦ Resistant hypertension is defined as blood pressure >130/80 mmHg despite a therapeutic strategy that includes appropriate lifestyle management plus a diuretic and two other antihypertensive drugs belonging to different classes at adequate doses. Prior to diagnosing resistant hypertension, a number of other conditions should be excluded, including:

Medication nonadherence

White coat hypertension

Secondary hypertension

Mineralocorticoid receptor antagonists also reduce albuminuria an have additional cardiovascular benefits.

✤ For patients treated with an ACE inhibitor, angiotensin receptor blocker, or diuretic, serum creatinine/estimated glomerular filtration rate and serum potassium levels should be monitored at least annually. (B)

#### **Antidiabetic Drugs as Antihypertensives:**

SGLT2i: Are novel antidiabetic drugs with antihypertensive properties. Canagliflozin, dapagliflozin, and empagliflozin all have BP-reducing properties. They reduce SBP/ DBP by 3–5/2–3 mmHg, respectively.

The mechanisms are diuresis, nephron remodeling, reduced arterial stiffness, and weight loss.

Reducing the doses of diuretics or other antihypertensive drugs is essential.

This class of drugs is effective in patients with high glucose, BP, and weight.

## **Antidiabetic Drugs as Antihypertensives:**

◆GLP1-RA : Exenatide and liraglutide significantly reduced SBP and DBP by 1– 5 mmHg in a meta-analysis of 16 RCTs compared with antidiabetic drugs including insulin, glimepiride, and placebo for patients with T2DM. Liraglutide reduces SBP by nearly 1.5 mmHg, while the 1-mg dose of semaglutide reduces it by 2.6 mmHg (p\0.01).

Both drugs reduce glucose and weight in diabetes patients. They have a mild reduction effect on BP, are cardioprotective, but should not be used as an alternative to antihypertensive drugs.

#### **Antidiabetic Drugs as Antihypertensives:**

DPP4i : Sitagliptin has shown SBP reduction of 1–3 mmHg while in other studies it reduced BP significantly (p\0.01) without reducing body mass index and also reduced office as well as home BP (p\0.01), thus confirming pleotropic effects of this class.

Vildagliptin also was shown to lower central BP, which is a glucose-independent beneficial effect of gliptins.

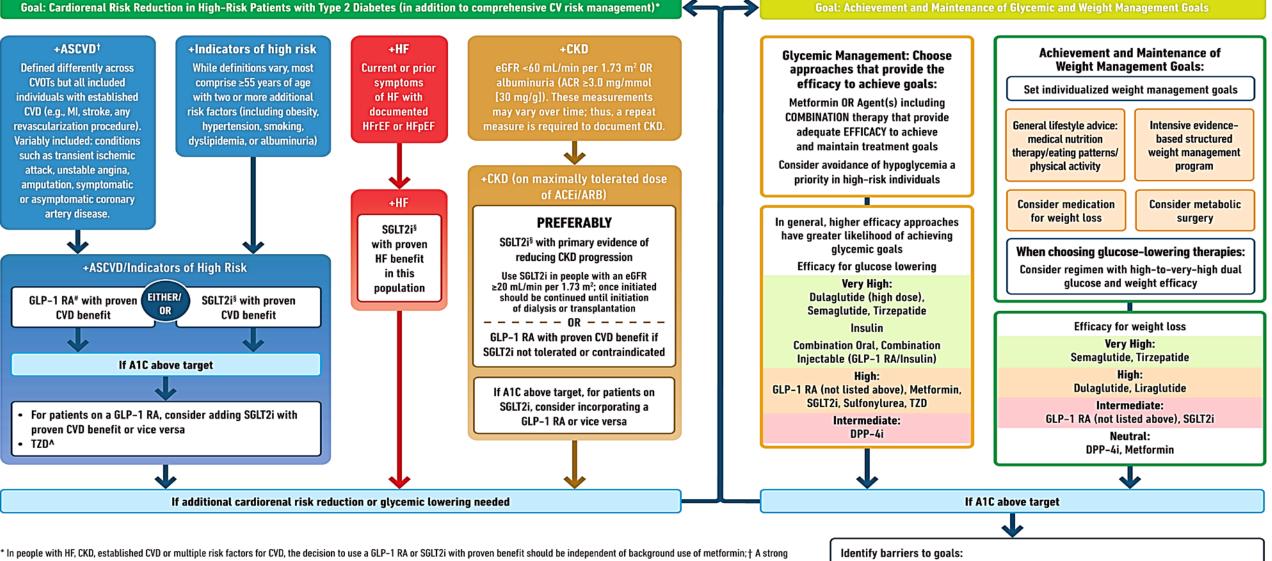
DPP4i have been shown to have various effects on BP, and their overall effect may be considered as neutral.

Though they have pressure-reducing effects, they should not be used as an alternative to antihypertensive drugs, at present.

#### **USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES**

HEALTHY LIFESTYLE BEHAVIORS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)





\* In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin; † A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details; ^ Low-dose TZD may be better tolerated and similarly effective; § For SGLT2i, CV/ renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF, and renal outcomes in individuals with T2D with established/high risk of CVD; # For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and renal endpoints in individuals with T2D with established/high risk of CVD.

· Consider DSMES referral to support self-efficacy in achievement of goals

Consider technology (e.g., diagnostic CGM) to identify therapeutic gaps and tailor therapy

Identify and address SDOH that impact achievement of goals

Secondary HTN Secondard HTN Although in more than 90% of patients with high blood pressure no underlying causes could be identified, up to 10% of hypertensives have a secondary hypertension.

This emphasizes the role of screening in order to rule out underlying causes of hypertension or so-called secondary hypertension. The most common cause for secondary hypertension is:

Chronic renal disease Renovascular hypertension Primary aldosteronism Pheochromocytoma.

Followings are some steps to follow when investigating the secondary causes of hypertension.



**Two arm measurement/ orthostatic change** 

**Auscultation : Carotid / Renal arteries** 

**Lower limb BP** 

End organ damage

## **Pheochromocytoma:**

Pheochromocytoma should be suspected in those who have one or more of the following conditions:

- A family history of pheochromocytoma.
- Incidentaloma of adrenal.
- Presser response during anesthesia, surgery or
  - angiography (hypotension or hypertension with or
  - without cardiac arrhythmia).
- Onset of hypertension at a young age (< 20 years).</p>
- Idiopathic dilated cardiomyopathy.
- **A** history of gastric stromal tumor or pulmonary chondromas (carney triad).
- Hypertension and diabetes.

Pheochromocytoma:

24 h urine for: volume

Cr

**Metanephrines** 

Normetanephrines

# **HTN+ Hypokalemia**

## spontaneous or diuretic induced

## HTN+ Hypokalemia:

1-secondary Hyperaldosteronism: RVH

2- Min Excess: CAH, DOC, Liddle syn

**3-** Primary Aldosteronism (PA)

#### Box 2

### Conditions that make the search for PA mandatory in a hypertensive patient

- Unexplained hypokalemia (spontaneous or diuretic-induced)
- Resistant hypertension and Grade 2 or 3 hypertension
- Early onset (juvenile) hypertension and/or stroke (<50 years)
- Incidentally discovered apparently nonfunctioning adrenal mass ("incidentaloma")
- Evidence of organ damage (left ventricular hypertrophy, diastolic dysfunction, atrioventricular block, carotid atherosclerosis, microalbuminuria, endothelial dysfunction), particularly if disproportionate for the severity of hypertension
- Overweight/obesity
- Obstructive sleep apnea syndrome

