Hypertension Treatment in 2023

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Overview

- Prevalence
- NZ guidelines / international guidelines
- Pharmacotherapy
- Target BP for treatment
- Specific groups of patients
- Lifestyle changes
- Morning or evening dose?
- When to screen for secondary causes
- Case discussions

Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants

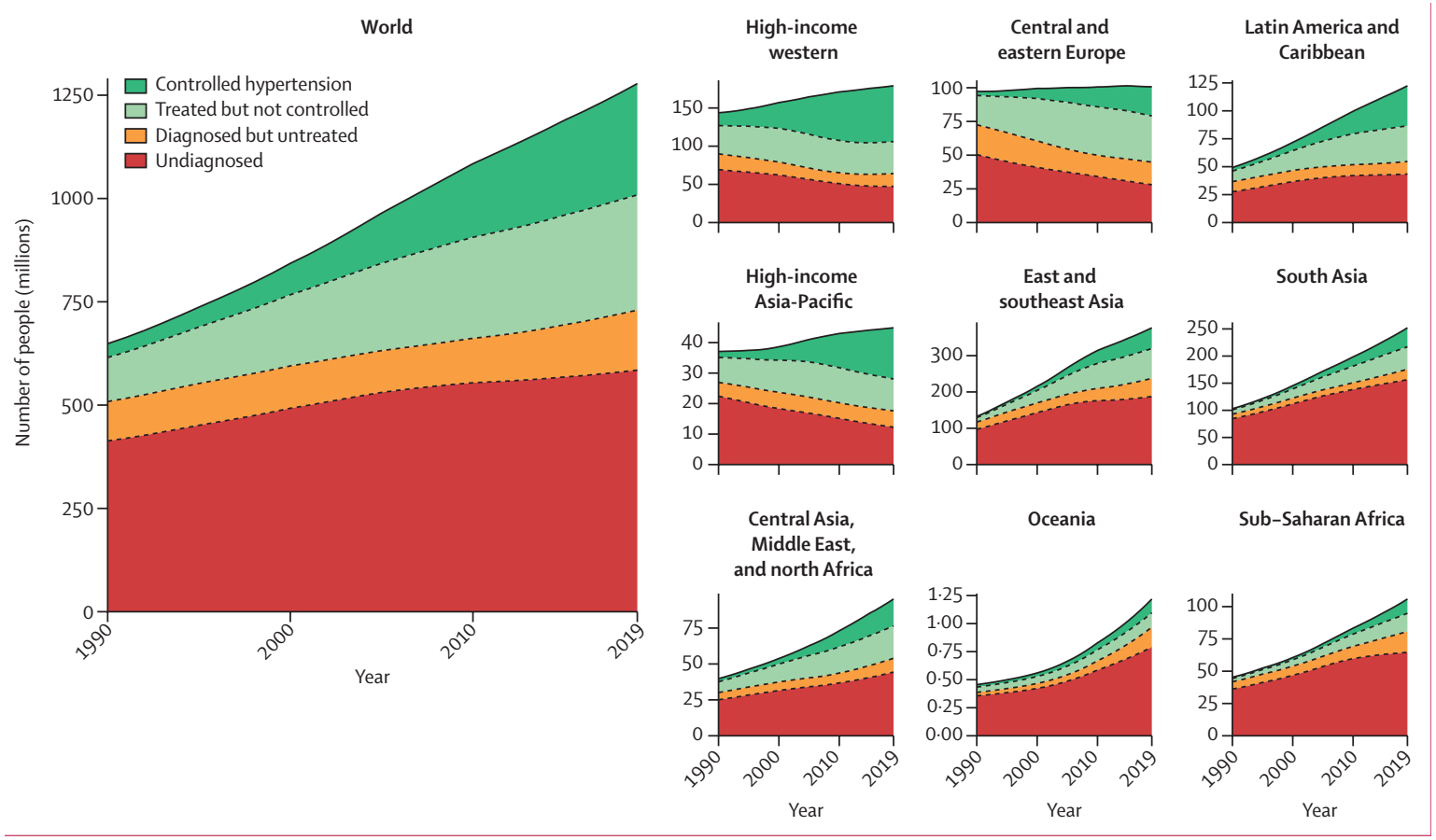
*NCD Risk Factor Collaboration (NCD-RisC)**

1.28 billion adults aged 30–79 years worldwide have hypertension, most (two-thirds) living in low- and middle-income countries

•46% of adults with hypertension are unaware that they have the condition.

•Approximately 1 in 5 adults (21%) with hypertension have it under control.

***Lancet* 2021; 398: 957–80**



Prevalence of hypertension and % of treated/untreated hypertension

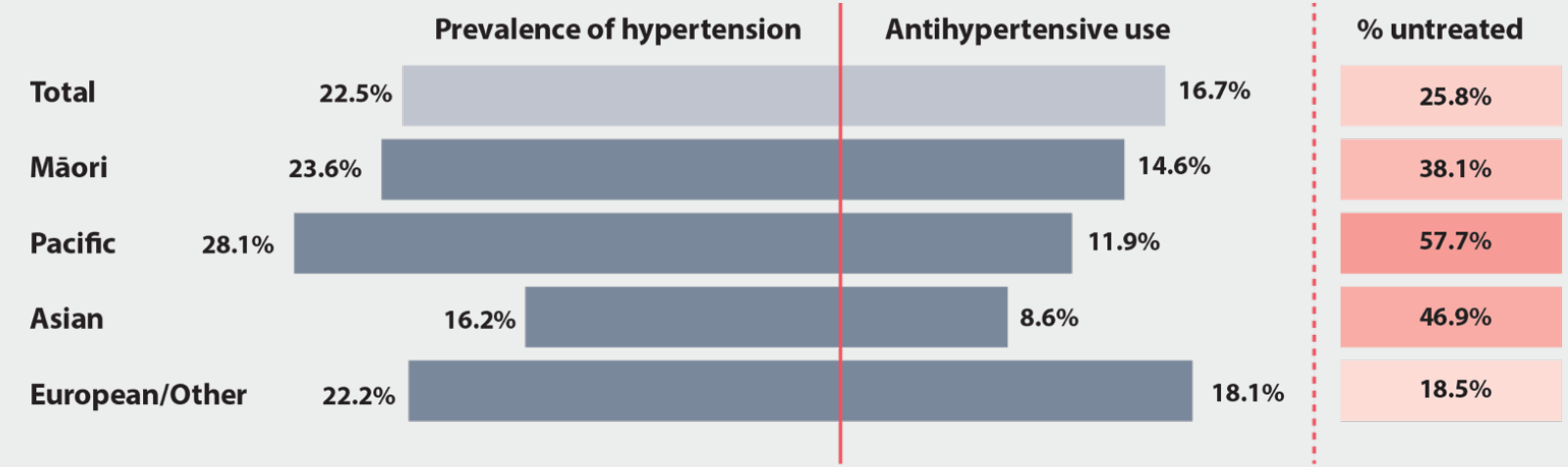


Figure 1. Prevalence of hypertension versus rates of antihypertensive use in New Zealand by ethnicity.[8] Data obtained from the 2020/21 Ministry of Health New Zealand Health Survey. The percentage of patients not taking an antihypertensive was calculated using the datasets for "Raised blood pressure (measured)" and "High blood pressure (medicated)".

Why is hypertension under-treated?

- Patient factors
  - Asymptomatic
  - In denial of the diagnosis (home BP recordings looked ‘OK’)
  - Not keen to start on a longterm medications, self belief of all medications are toxic and they will be “addicted” to the antihypertensive medications
  - Masked hypertension
  - Still trying lifestyle changes after years of noticing hypertension

- Factors facilitate initiating treatment
  - Experienced an adverse event
  - Family history of cardiovascular/cerebrovascular disease
  - Symptomatic severe hypertension

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When to initiate antihypertensive medicines

Patients with a blood pressure of ≥ 160/100 mmHg should be initiated on antihypertensive treatment immediately, in addition to lifestyle changes, regardless of their five-year CVD risk.[6]

For all other patients with a blood pressure persistently ≥ 130/80 mmHg, the 2018 Ministry of Health cardiovascular risk consensus statement recommends calculating their five-year CVD risk to guide antihypertensive medicine decisions. In patients with:[6]

- **Five-year CVD risk < 5%:** antihypertensive treatment is not recommended; proceed with lifestyle changes
- **Five-year CVD risk 5 – 15%:** consider antihypertensive treatment if blood pressure is ≥ 140/90 mmHg, in addition to lifestyle changes
- **Five-year CVD risk ≥ 15%:** antihypertensive treatment is recommended, in addition to lifestyle changes

For further information see: "Cardiovascular disease risk assessment and management for primary care" (available at: www.health.govt.nz/publication/cardiovascular-disease-risk-assessment-and-management-primary-care)

ESC 2018 guidelines

Category	Systolic (mm Hg)		Diastolic (mm Hg)
Normal BP	<130	and	<85
High-normal BP	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	≥160	and/or	≥100

ACC 2017 guidelines

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

Pharmacotherapy

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Class	Funded option as of Jan, 2023	Initial dose (may be lower in some patients)	Dose range
ACE inhibitors*	Enalapril	5 mg, once daily	Usual maintenance dose 20 mg, once daily; maximum 40 mg, once daily
	Lisinopril	10 mg, once daily	Usual maintenance dose 20 mg, once daily; maximum 80 mg, once daily
	Perindopril	4 mg, once daily in the morning	Maximum 8 mg, once daily
	Quinapril	10 mg, once daily	Usual maintenance dose 20 – 40 mg, daily in 1 – 2 divided doses; maximum 80 mg, daily
	Ramipril	2.5 mg, once daily	Maximum 10 mg, once daily
ARBs	Candesartan	8 mg, once daily	Usual maintenance dose 8 mg, once daily; maximum 32 mg, once daily
	Losartan	50 mg, once daily	Usual maintenance dose 50 mg, once daily; maximum 100 mg, once daily
Calcium channel blockers	Amlodipine	5 mg, once daily	Maximum 10 mg, once daily
	Diltiazem (modified release)	180 – 240 mg, once daily	Usual maintenance dose 240 – 360 mg, once daily
	Felodipine	5 mg, once daily in the morning	Usual maintenance dose 5 – 10 mg, once daily
	Verapamil (immediate release)	80 mg, two or three times daily	Maximum 160 mg, two or three times daily
	Verapamil (modified release)	120 – 240 mg, once daily	Maximum 240 mg, twice daily
Thiazide and thiazide-like diuretics	Bendroflumethiazide	2.5 mg, once daily in the morning	Maximum doses of 10 mg, daily have been used; however, doses higher than 2.5 mg daily, increase the risk of adverse effects and have a limited additional blood pressure lowering effect
	Chlortalidone	12.5 – 25 mg, once daily in the morning	
	Indapamide	2.5 mg, once daily in the morning	
Fixed-dose combination treatment†	Losartan + hydrochlorothiazide	1 tablet (50 mg losartan + 12.5 mg hydrochlorothiazide), once daily	Maximum 2 tablets, once daily

Pharmacotherapy – Blockers of renin-angiotensin system

ACE inhibitors and ARB

- ARBs are associated with lower treatment discontinuation rates for adverse events than all other classes of antihypertensive therapies
- ACEI and ARB should not be combined for treatment of hypertension as there is no added benefits and added renal adverse events
- Both ACEI and ARB
  - reduce albuminuria and are effective in delaying diabetic and non-diabetic CKDs.
  - appear to be effective in preventing or regressing hypertension mediated organ damage such as LVH and small artery remodelling

Pharmacotherapy- ACEI/ARB DO NOT cause lung cancer

Sipahi I, Debanne SM, Rowland DY, Simon DI, Fang JC, Angiotensin-receptor blockade and risk of cancer: meta-analysis of randomised controlled trials. Lancet Oncology 2010; 11:627–636

- The concern on possible link of lung cancer and renin angiotensin blockade originally came from the above meta-analysis by Sipahi et al. The paper mainly included an ARB, telmisartan (not an ACE inhibitor) and risk of lung cancer with a relatively short follow up period of 1.9 – 4.8 years.
- Only 9 out of 60 trials included in this paper had data on cancer incidence or cancer related deaths, as meeting the inclusion criteria of the meta-analysis.
- Further meta-analyses refuted the results by Sipahi et al.
- FDA and European Medicines Agency indicated no signal of harm associated with ARB or ACEi.

Journal of Cancer Research and Clinical Oncology (2021) 147:195–204

Pharmacotherapy- Calcium channel blockers

- Inhibit calcium influx into peripheral smooth muscle cells (peripheral vasodilator) and cardiac myocytes (negative inotropic effects) as well as sinoatrial and/ or AV nodal cells (bradycardia)
  - Dihydropyridine CCB (amlodipine, felodipine) - affects more peripheral vascular smooth muscle cells, therefore are primarily vasodilators and no clinical effect on cardiac contractility or conduction
    - Most randomized trials demonstrated benefits of CCBs on outcomes used dihydropyridines, especially amlodipine.
  - Non-dihydropyridine CCB - negative inotropic and chronotropic effect
    - Diltiazem (benzothiazepines) – equipotent in cardiac and vascular smooth muscle cells
    - Verapamil (phenylalkylamines) – More negative chronotropic effects than diltiazem
    - Avoid using in heart failure with reduced ejection fraction
    - Consider if rate control is required

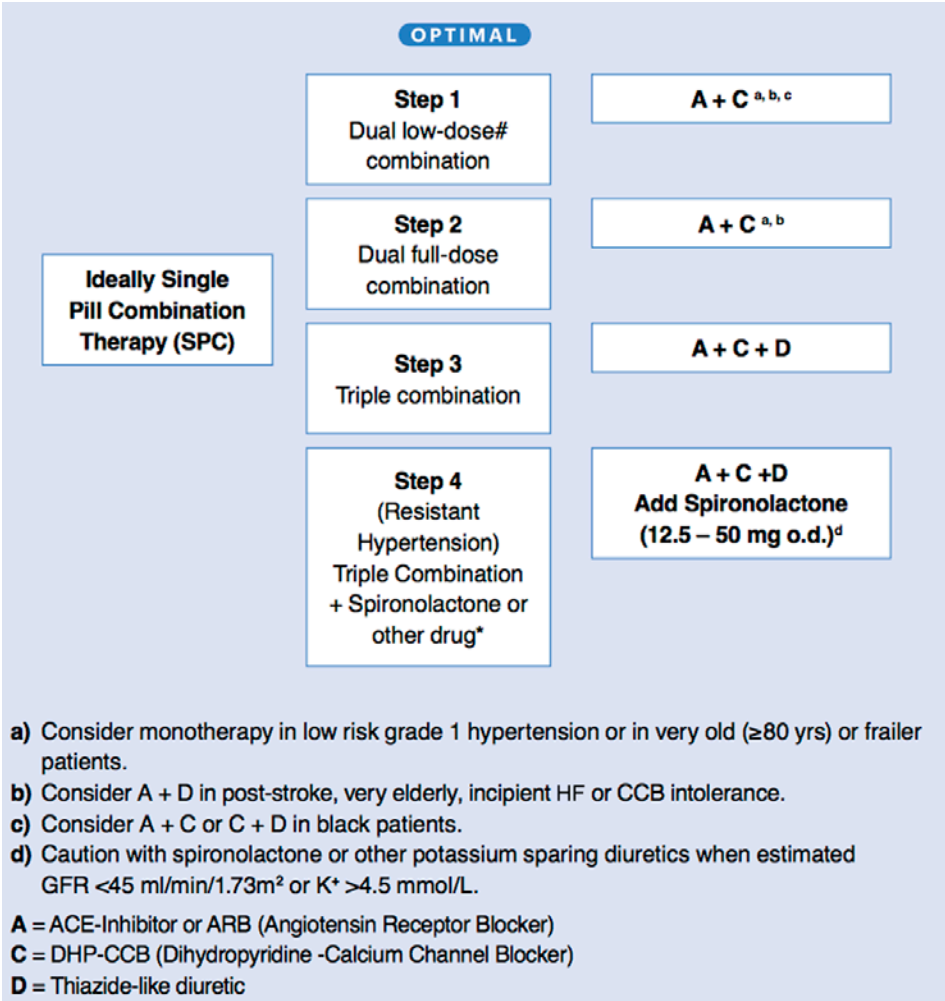
Pharmacotherapy – Beta-blockers

- Beta blocker should be considered at any step if there is symptomatic angina, post MI, heart failure with reduced ejection fraction, or atrial fibrillation requires rate control
- Should be considered as an alternative to ACEI/ARB in young women with hypertension planning pregnancy
- When compared with other antihypertensive agents, BBs are equivalent in lowering cardiovascular events, but less effective in preventing stroke

Pharmacotherapy – Other antihypertensive agents

- Alpha-1 blockers
  - indicated as a third line agent if there is concurrent benign prostatic hypertrophy
  - it is more effective than placebo, but less effective than spironolactone at lowering BP in resistant hypertension (PATHWAY-2 study)
- Centrally active drugs are less frequently used now, mainly due to poorer tolerability

Pharmacotherapy , when to introduce a second antihypertensive agent



ESC guidelines on hypertension treatment 2017

Specific groups

- Hypertension with IHD, ACEI/ARB or BB
- Hypertension with HF, ACEI/ARB, BB, mineralocorticoid receptor antagonist; diuretics for symptomatic improvement; CCB only if poor BP control
- Thoracic aortic aneurysm, BB/ARB

Target BP of treatment

- < 130/80 to prevent major adverse events / target organ damage

Thoracic aortic disease

- Evidence supports aggressive BP lowering to reduce vascular-related adverse events and all-cause mortality in patients with thoracic aortic disease. SPRINT (Systolic Blood Pressure Intervention Trial) showed that intensive BP control to a SBP <120 mm Hg, if tolerated, reduced cardiovascular events by 25% and all-cause mortality rate by 27% in patients without diabetes over a median of 3.3 years, compared with a control with a SBP target of <140 mm Hg.

  Group et al. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015;373:2103-2116

- BB + ARB better than BB alone to slow the growth of thoracic aortic aneurysm.

Lifestyle changes

- Salt reduction
- Healthy diet
- Reduction in alcohol consumption
- Weight reduction
- Smoking cessation
- Regular aerobic exercise (at least 30 min moderate intensity, ≥ 5 times weekly)

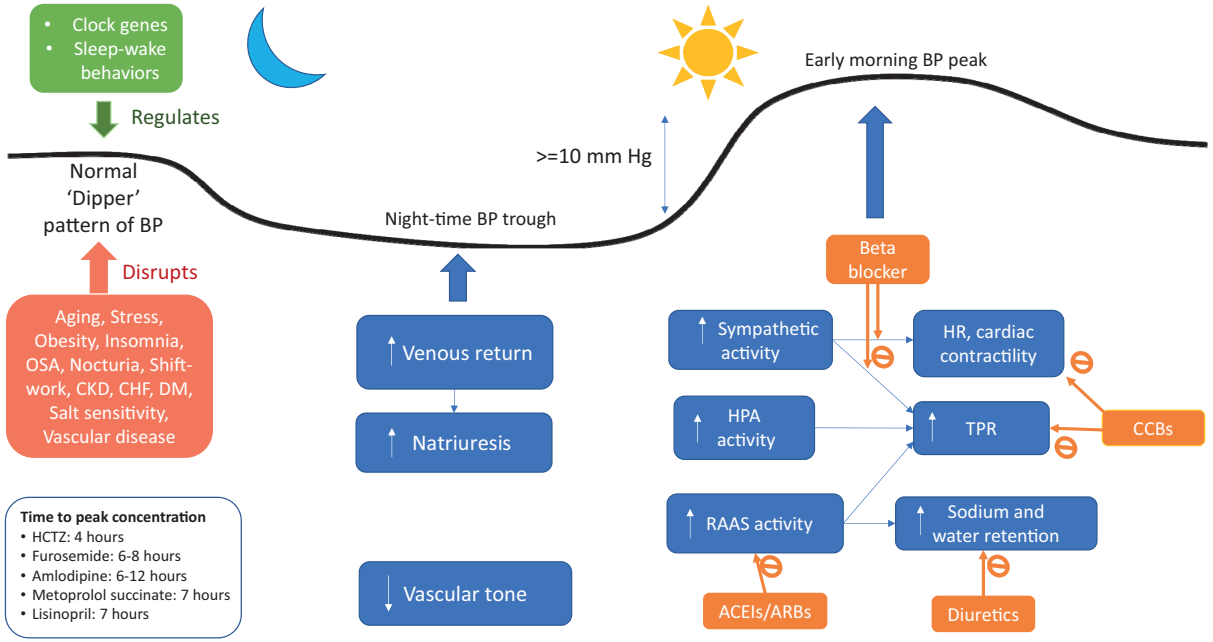
Lifestyle changes

Table 15. Best Proven Nonpharmacological Interventions for Prevention and Treatment of Hypertension*

	Nonpharmacological Intervention	Dose	Approximate Impact on SBP		
			Hypertension	Normotension	Reference
Weight loss	Weight/body fat	Best goal is ideal body weight, but aim for at least a 1-kg reduction in body weight for most adults who are overweight. Expect about 1 mm Hg for every 1-kg reduction in body weight.	–5 mm Hg	–2/3 mm Hg	S6.2-1
Healthy diet	DASH dietary pattern	Consume a diet rich in fruits, vegetables, whole grains, and low-fat dairy products, with reduced content of saturated and total fat.	–11 mm Hg	–3 mm Hg	S6.2-6,S6.2-7
Reduced intake of dietary sodium	Dietary sodium	Optimal goal is <1500 mg/d, but aim for at least a 1000-mg/d reduction in most adults.	–5/6 mm Hg	–2/3 mm Hg	S6.2-9,S6.2-10
Enhanced intake of dietary potassium	Dietary potassium	Aim for 3500–5000 mg/d, preferably by consumption of a diet rich in potassium.	–4/5 mm Hg	–2 mm Hg	S6.2-13
Physical activity	Aerobic	90–150 min/wk 65%–75% heart rate reserve	–5/8 mm Hg	–2/4 mm Hg	S6.2-18,S6.2-22
	Dynamic resistance	90–150 min/wk 50%–80% 1 rep maximum 6 exercises, 3 sets/exercise, 10 repetitions/set	–4 mm Hg	–2 mm Hg	S6.2-18
	Isometric resistance	4 × 2 min (hand grip), 1 min rest between exercises, 30%–40% maximum voluntary contraction, 3 sessions/wk 8–10 wk	–5 mm Hg	–4 mm Hg	S6.2-19,S6.2-31
Moderation in alcohol intake	Alcohol consumption	In individuals who drink alcohol, reduce alcohol† to: Men: ≤2 drinks daily Women: ≤1 drink daily	–4 mm Hg	–3 mm Hg	S6.2-22—S6.2-24

ACC 2017 guidelines

Best time for administration of antihypertensive medications: Morning or evening?



- TIME randomised trial in more than 21,000 patients with high blood pressure followed for over five years has concluded that protection against heart attack, stroke and vascular death is not affected by whether antihypertensive medications are taken in the morning or evening.
- Average age 65 years with 5.2 years of median follow up

HM Salah et al. The Lancet Oct 2022 Vol 400, 10361, P1383

When to screen for secondary causes

Table 27 **Incidence and typical causes of secondary hypertension according to age**

Age group	Per cent with underlying cause	Typical causes
Young children (<12 years)	70 - 85	• Renal parenchymal disease • Coarctation of the aorta • Monogenic disorders
Adolescents (12–18 years)	10–15	• Renal parenchymal disease • Coarctation of the aorta • Monogenic disorders
Young adults (19–40 years)	5–10	• Renal parenchymal disease • Fibromuscular dysplasia (especially in women) • Undiagnosed monogenic disorders
Middle-aged adults (41–65 years)	5–15	• Primary aldosteronism • Obstructive sleep apnoea • Cushing's syndrome • Phaeochromocytoma • Renal parenchymal disease • Atherosclerotic renovascular disease
Older adults (>65 years)	5–10	• Atherosclerotic renovascular disease • Renal parenchymal disease • Thyroid disease

Resistant hypertension

- Don't forget prescribed and re-creational drugs could also cause hypertention

Table 24 **Resistant hypertension characteristics, secondary causes, and contributing factors (adapted from reference[385])**

Characteristics of patients with resistant hypertension	Causes of secondary resistant hypertension	Drugs and substances that may cause raised BP
Demographics ● Older age (especially >75 years) ● Obesity ● More common in black people ● Excess dietary sodium intake ● High baseline BP and chronicity of uncontrolled hypertension	**More common causes** ● Primary hyperaldosteronism ● Atherosclerotic renovascular disease ● Sleep apnoea ● CKD	**Prescribed drugs** ● Oral contraceptives ● Sympathomimetic agents (e.g. decongestants in proprietary cold remedies) ● Non-steroidal anti-inflammatory drugs ● Cyclosporin ● Erythropoietin ● Steroids (e.g. prednisolone and hydrocortisone) ● Some cancer therapies
Concomitant disease ● HMOD: LVH and/or CKD ● Diabetes ● Atherosclerotic vascular disease ● Aortic stiffening and isolated systolic hypertension	**Uncommon causes** ● Phaeochromocytoma ● Fibromuscular dysplasia ● Aortic coarctation ● Cushing's disease ● Hyperparathyroidism	**Non-prescription drugs** ● Recreational drugs (e.g. cocaine, amphetamines, and anabolic steroids) ● Excessive liquorice ingestion ● Herbal remedies (e.g. ephedra and ma huang)

When to screen for secondary causes

- ≤ 40 years without other risk factors for hypertension e.g. metabolic syndrome, obesity
- Resistant hypertension (BP ≥ 140/90 when on 3 or more antihypertensive agents)
- Sudden change in BP control/ hypertensive crisis (>200/120)

Possible secondary causes:

1. Renal parenchymal disease
2. Primary aldosteronism
3. Renal artery stenosis
4. Phaeochromocytoma
5. Cushings syndrome
6. Coarctation of aorta
7. OSA
8. Thyroid disease

Cases for discussion

- 65-year-old Indian woman referred for exertional shortness of breath and rest onset chest pain. Normal ETT at 6 min 30 sec. Baseline BP 145/90, Peak BP 226/100. On Losartan 25mg daily.
- 60-year-old European man with BMI of 32kg/m2, asymptomatic perioperative AF while having elective prostate biopsy. Baseline BP 148/92 while on sotalol.
- 82-year-old frail European woman on three antihypetensive medications with resistant hypertension,165/90 in clinic room. What needs to be done next?
- 38-year-old Samoan man with multiple BP readings more than 160/100 at GPs. Not keen to take any meds. DNAed all the Cardiology appointments.

Thank you