Hypertension Management Overview

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Hypertension
Prevalence and Burden

Hypertension remains the major preventable cause of cardiovascular disease and all-cause death globally

Recent 30 years

Number of people living with hypertension has doubled to

1.28 billion

2X

DALYs attributable to hypertension have increased by

40 %

19·2%

of all deaths

CVD: Cardiovascular disease, DALY: Disability-adjusted life years

Hypertension.2015;66:254-9, Lancet. 2020; 396: 1223–1249, Lancet. 2021;398:957-980

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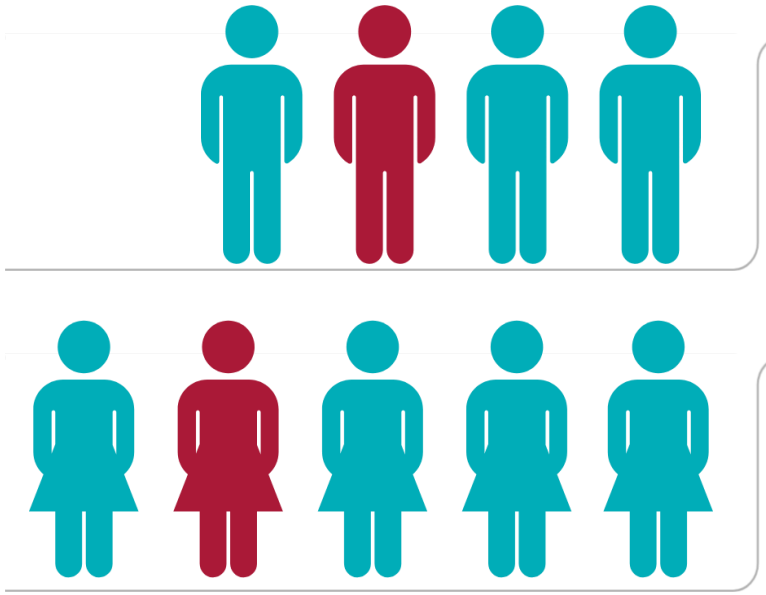
60%

Estimated number of adults with hypertension from 2000 to 2025.



1 in 4

men have hypertension

1 in 5

women have hypertension

World Health Organization

Eur Heart J. 2018;39:3021-3104, Circulation. 2021;143:991–1001

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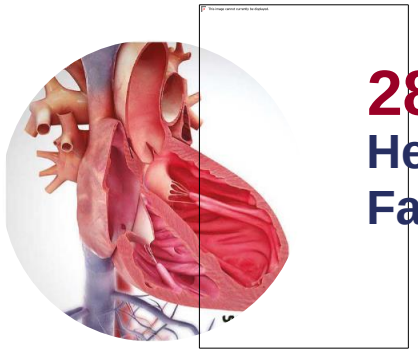
Blood pressure lowering significantly reduces cardiovascular event risk

Every **10 mmHg reduction** in systolic blood pressure can significantly reduce risk of:

17%
Coronary heart diseases

27%
Stroke



28%
Heart Failure

Hippokratia. 2007; 11: 114–119

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Hypertension
Classification and Definition

Blood pressure Classifications

Categories	Systolic blood pressure, mm Hg	And/or	Diastolic blood pressure, mm Hg
American College of Cardiology/American Heart Association			
Normal	<120	and	<80
Elevated	120–129	and	<80
Hypertension, stage 1	130–139	or	80–89
Hypertension, stage 2	≥140	or	≥90
European Society of Cardiology/European Society of Hypertension			
Optimal	<120	and	<80
Normal	120–129	and/or	80–84
High normal	130–139	and/or	85–89
Hypertension, grade 1	140–159	and/or	90–99
Hypertension, grade 2	160–179	and/or	100–109
Hypertension, grade 3	≥180	and/or	≥110
Isolated systolic hypertension	≥140	and	<90

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Circulation . 2022;146(11):868-877

Importance of Accurate Blood Pressure Measurement

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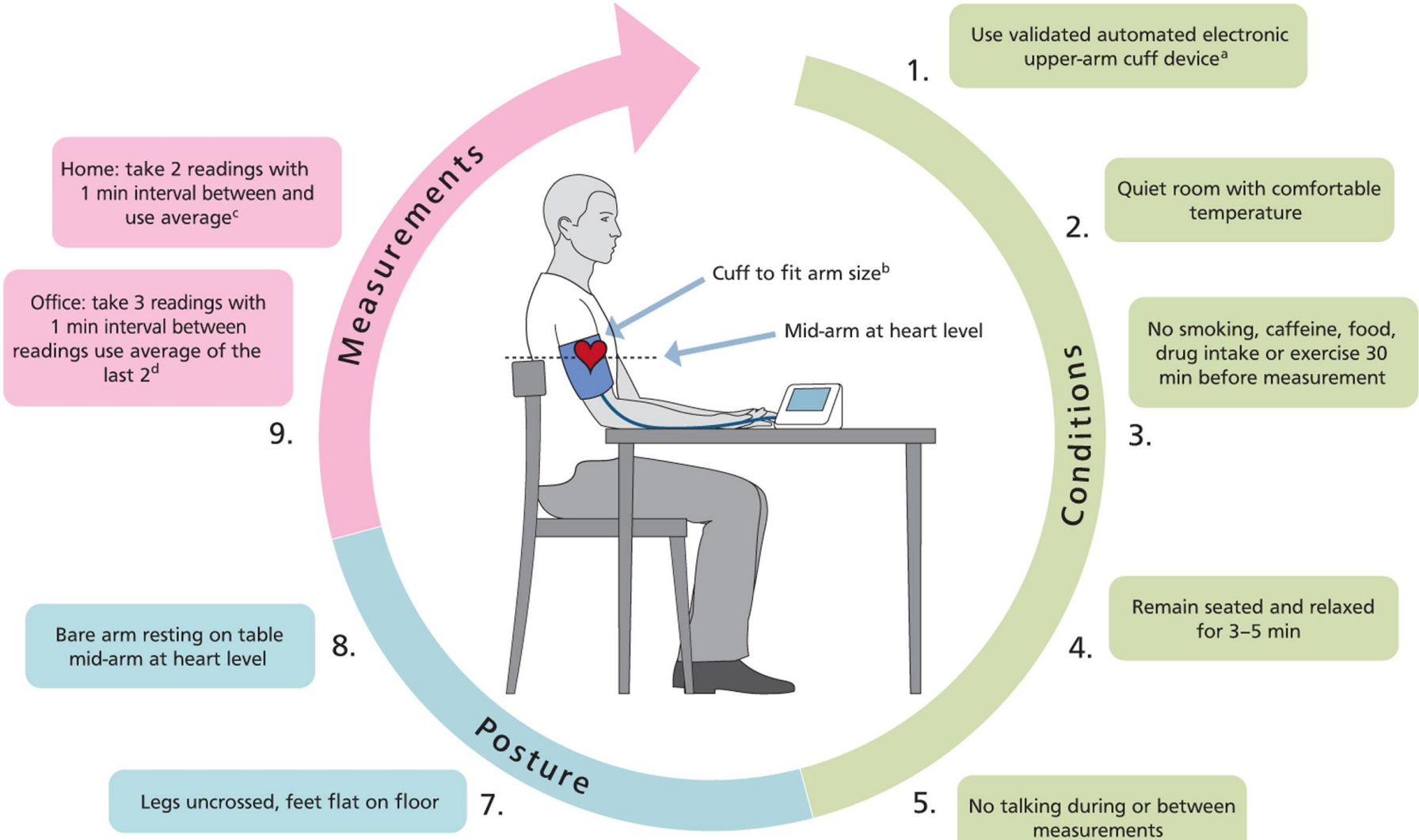
Recommendations for standard BP measurement in the office and at home



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Confirming the Diagnosis of Hypertension

Confirm Hypertension Diagnosis

- At least two to three visits (within 4 weeks) , unless the BP values recorded during the first visit are markedly elevated (grade 3 hypertension: ≥180/110 mmHg) or CV risk is high, including the presence of HMOD.

- At the first office visit, BP should be measured in both arms. A consistent between-arm SBP difference >15-20 mmHg suggests atheromatous disease and is associated with increased CV risk. All subsequent measurements should be made on the arm with the highest BP readings.

- ABPM, HBPM or data should be collected whenever feasible when office BP is elevated, to confirm the diagnosis of hypertension.

Home BP measurement

تاریخ	صبح (قبل داروها)		شب (قبل شام)	
	بار اول	بار دوم	بار اول	بار دوم

لطفا نکات زیر را رعایت‌فرمایید:

- همیشه فشار خون دستی را که فشارش بالاتر است، ثبت‌کنید.
- سی دقیقه قبل از اندازه‌گیری، سیگار نکشیده و چای و قهوه نیز میل‌نکنید.
- پنج دقیقه قبل از اندازه‌گیری، در حالت استراحت باشید.
- برای اندازه‌گیری فشار خون، روی صندلی نشسته، پاهایتان باید به زمین رسیده باشد.
- هنگام اندازه‌گیری، پاها را روی هم نیندازید.
- دستتان باید در حالت راحت روی دسته ای باشد که در سطح قلب قرار گیرد.
- در هر نوبت، دو بار فشار خونتان را به‌فاصله یک دقیقه اندازه‌بگیرید.
- زمان اندازه‌گیری فشار خون، صبح قبل از مصرف داروی فشار خون و شب قبل شام باشد.
- در صورت نیاز به دستشویی، حتما قبل از اندازه‌گیری فشار خون به دستشویی بروید.
- در هر نوبت ویزیت، دستگاه خود را جهت بررسی از نظر درستی، به کلینیک بیاورید.

- HBPM is recommended to identify white-coat hypertension or masked hypertension.

- HBPM is recommended for long-term follow-up of treated hypertension because it improves BP control, especially when combined with education and counselling.

- Home BP should be monitored for 7 (not fewer than 3) days with duplicate morning (with 1 minute between them) and evening measurements before office visits. Average home BP should be calculated after discarding readings of the first day.

Using automated electronic devices select cuff size according to the device's instructions. At the initial visit, measure BP in both arms.

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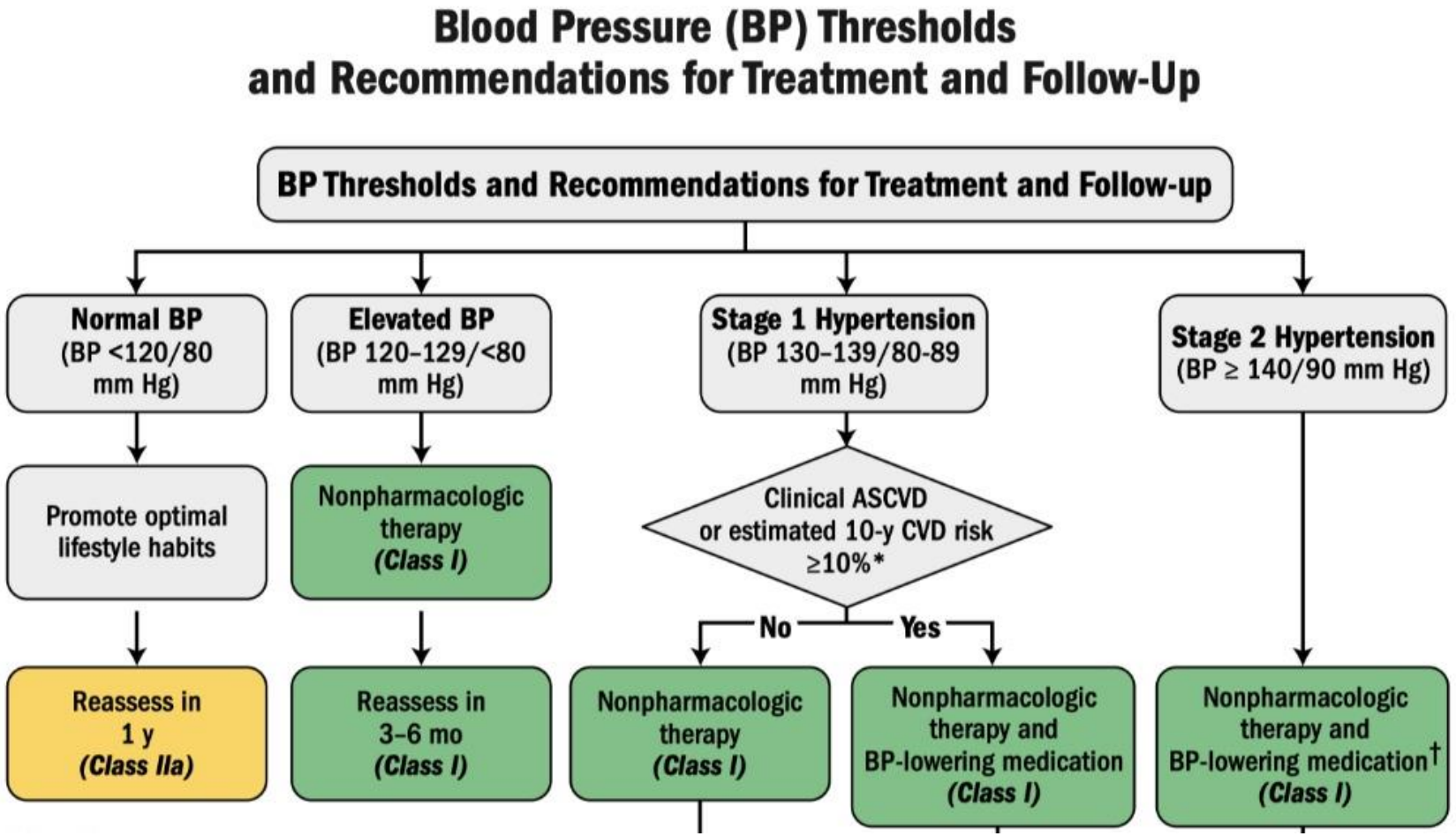
Determining the BP stage based on corresponding office BP numbers

TABLE 11 Corresponding Values of SBP/DBP for Clinic, HBPM, Daytime, Nighttime, and 24-Hour 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

Blood pressure thresholds and treatment recommendations



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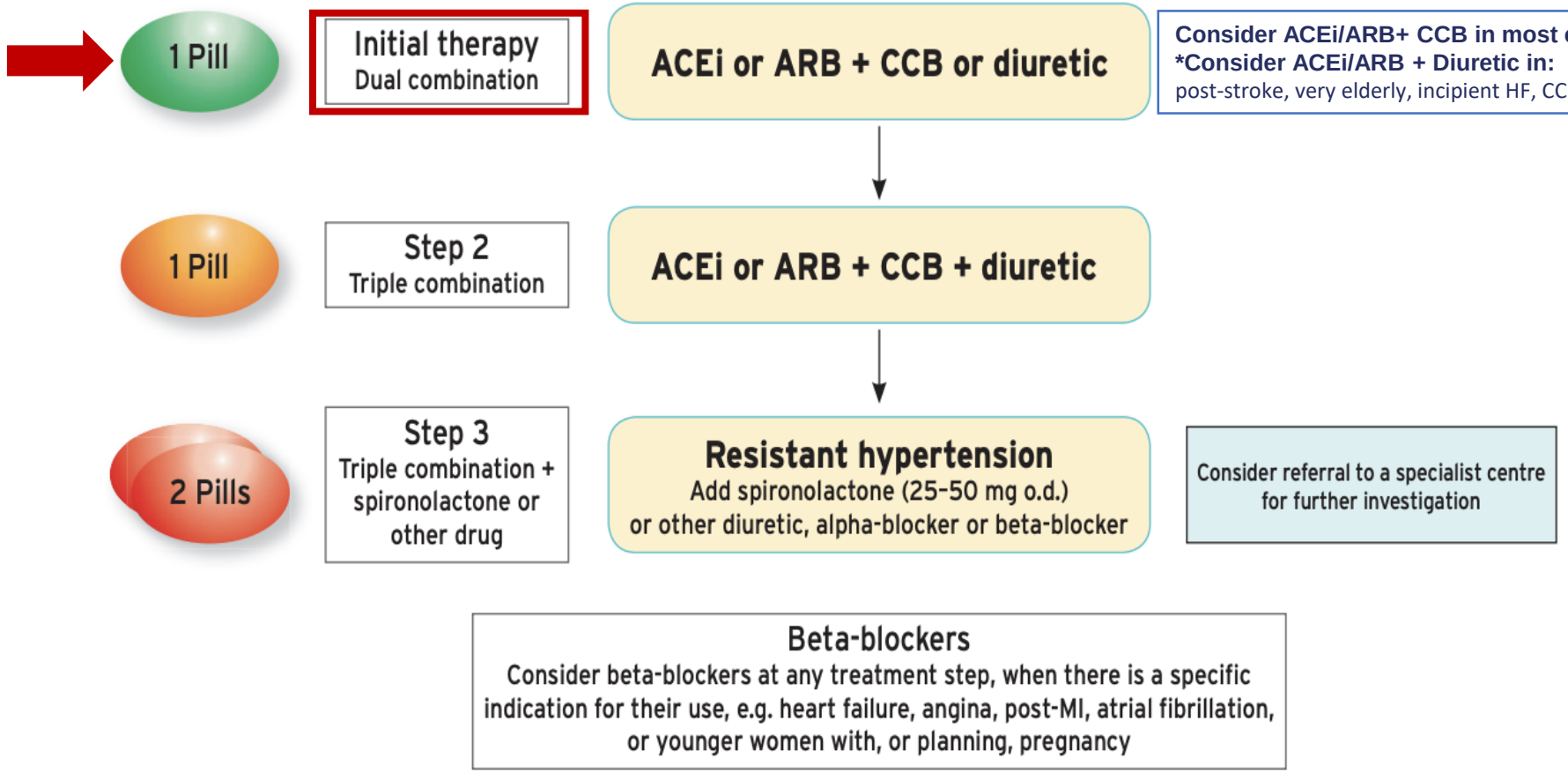
Single pill combination is the latest recommended strategy for hypertension initial therapy



J Clin Hypertens. 2018;20:902–907.

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Why Single Pill Combination instead of Free Combination?

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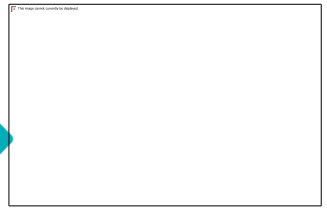
Suboptimal control of blood pressure is associated with higher risk of cardio-vascular events

Poor patient adherence to treatment

- Multiple medications
- Medications with multiple daily doses

Rate of adherence to treatment: Less than half of the patients with hypertension

50%



Cardiovascular risk

Eur Heart J. 2018 ;39:3021-3104, Hypertension. 2006;47:345-351, Vasc Health Risk Manag. 2010;6:321-325.

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Single Pill Combination: One Pill, Once Daily

Situation: Nonadherence in patients with hypertension

Solution: **Single pill combination**

One pill per day vs. polypharmacy by single pill combinations

AND

Once daily over multiple times per day by single pill combinations

Better compliance to antihypertensive medications

Cardiovascular risk reduction

Vasc Health Risk Manag. 2010 ;6:321-325, J Hypertens. 2011;29:610-618, BMJ Open. 2019 ;9:e023995.

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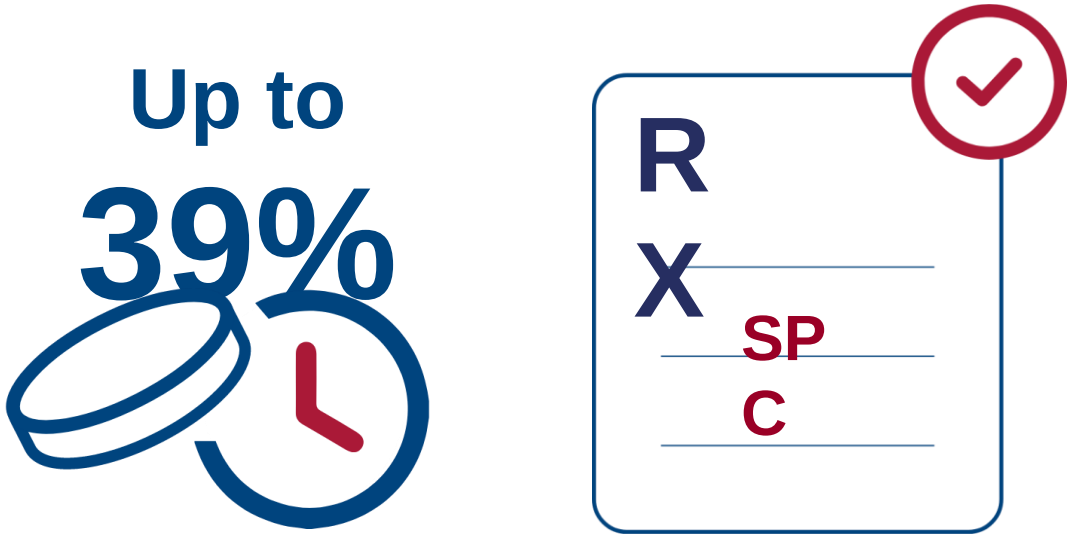
Up to 39% medication adherence with single pill combination versus free combination of antihypertensive medication

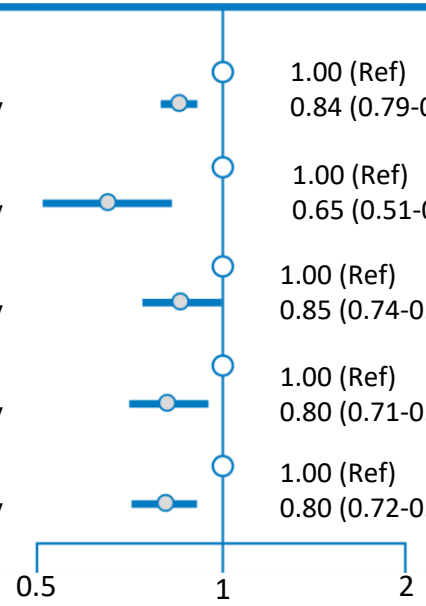


Meta- analysis of 62, 481 patients with hypertension, with 30, 103 patients taking single pill combinations and 32, 378 patients taking free-equivalent combinations.

J Clin Hypertens. 2018;20:902–907.

Hospitalization risk for cardiovascular events was lower with initial 2-drug single pill combination versus monotherapy

Outcome	Treatment strategy	HR (95% CI)	p
Any CV events	Monotherapy	1.00 (Ref)	<0.001
	Combination therapy	0.84 (0.79-0.90)	
Heart failure	Monotherapy	1.00 (Ref)	<0.001
	Combination therapy	0.65 (0.51-0.82)	
Cerebrovascular disease	Monotherapy	1.00 (Ref)	0.027
	Combination therapy	0.85 (0.74-0.98)	
Ischemic heart disease	Monotherapy	1.00 (Ref)	<0.001
	Combination therapy	0.80 (0.71-0.91)	
Death	Monotherapy	1.00 (Ref)	<0.001
	Combination therapy	0.80 (0.72-0.89)	



Hazard ratios (HR) and 95% CI estimating the risk of cardiovascular (CV) outcomes and death between patients with initial antihypertensive monotherapy and initial 2-drug single pill combination therapy.

During 3-year follow-up of 19627 patients, significant reduction in the risk of hospitalization for all considered outcomes displayed in patients prescribed an initial single pill 2-drug combination vs. patients with initial monotherapy and remaining on monotherapy. The risk reduction was largest for heart failure.

Circ Res. 2019;124:1113–1123, Hypertension. 2018;72:846-853

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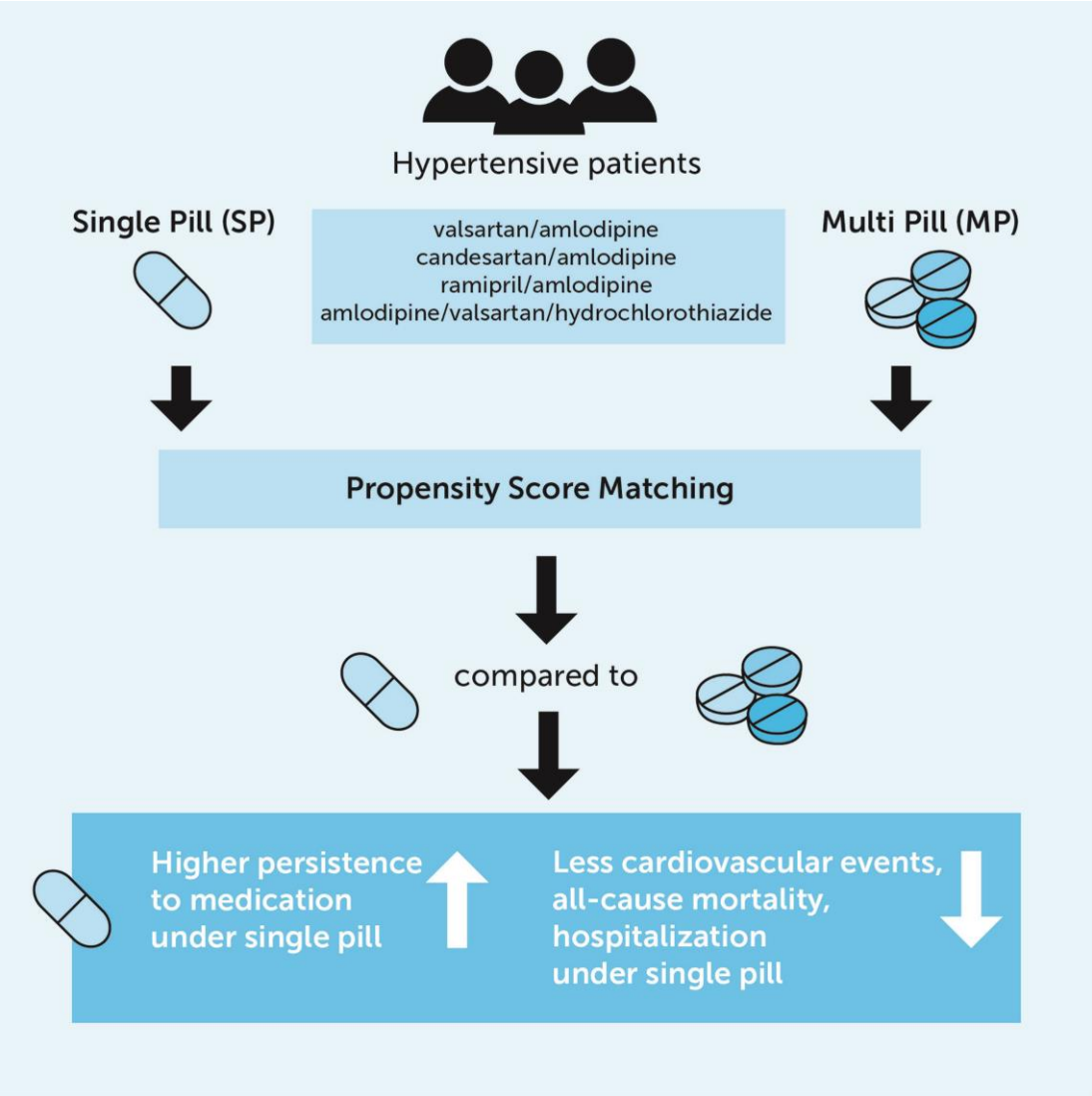
Improved Persistence with Single Pill Combinations



Antihypertensive combination therapy reduces all-cause mortality and cardiovascular events when provided as single pill compared to identical drugs as multipills.

HypertensionVolume 80, Issue 5, May 2023; Pages 1127-1135

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Simplicity, better compliance and tolerability all together with single pill combination versus free combination

	Free combination therapy	Single-pill combination therapy
Efficacy	++	++
Time to reach BP target	++	++
BP variability	+	+
Simplicity	-	+
Compliance	-	+
Tolerability	+	++

Comparison between different HTN management strategies

Adapted from Integr Blood Press Control. 2013; 6:69-78, Hypertension. 2021;77:692–705

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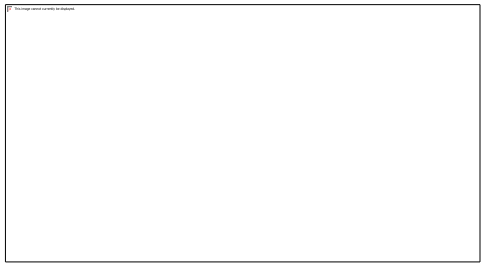
Dual and Triple Single Pill Combinations

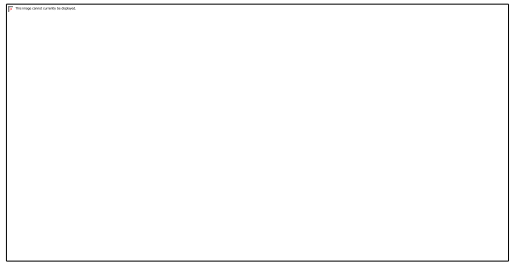
Amlodipine/Valsartan combination has significant cardiovascular benefits over other combinations



Cardiovascular mortality

Nonfatal cerebral vascular disease

Nonfatal myocardial infarction



Mortality of hypertensive patients with type 2 diabetes mellitus

Drugs in Context 2018; 7: 212531.

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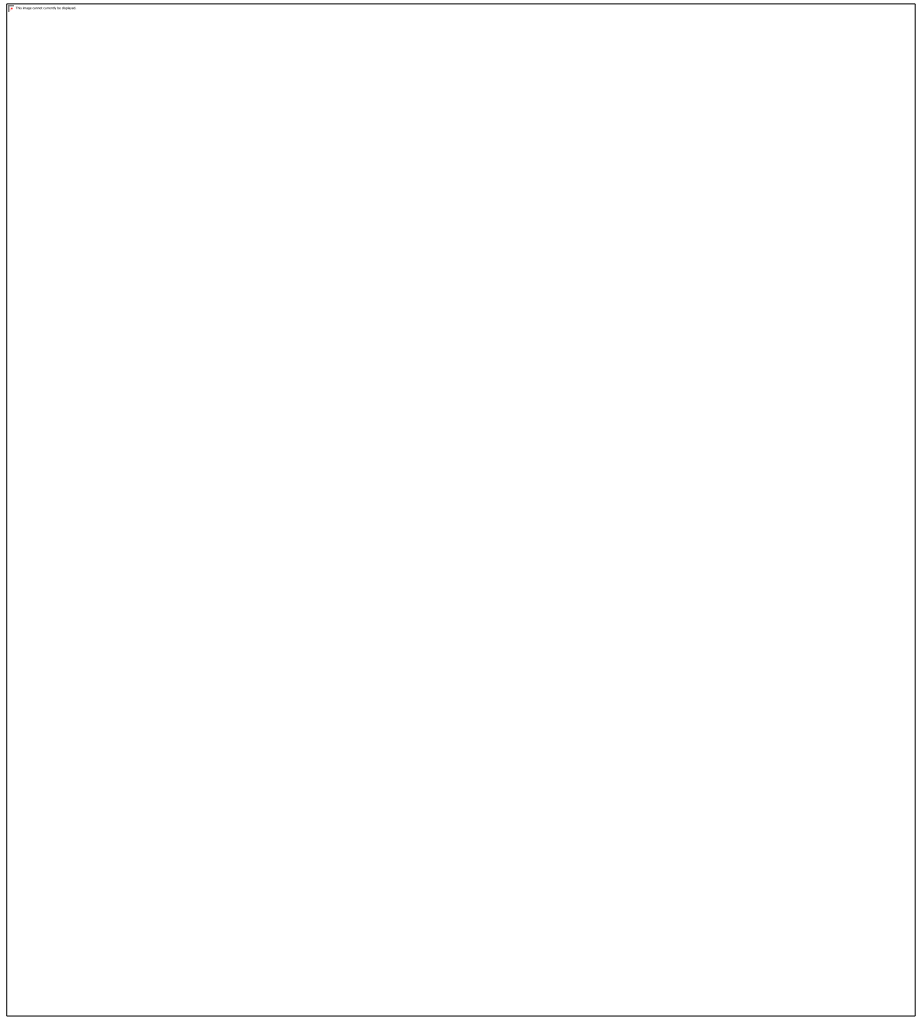
Amlodipine + Valsartan = Valzomix®

Around 90% individual response to Amlodipine/ Valsartan across different hypertension severities

EXCITE study:



A prospective, multinational, non-interventional real-world study of SPC therapies in 9,794 adult patients with hypertension from middle east and Asia observed for 26±8 weeks. Effectiveness outcome measure was change from baseline. SPC administered as single therapy or as add-on therapy to diuretics, Beta-blockers, CCBs, ACEIs or ARBs, as part of clinical practice. Decreases in msSBP and msDBP were greater in patients with more severe systolic hypertension at baseline. Reductions of 53.6/ 21.7 mmHg in SBP≥ 180 mmHg at baseline.

blood pressure response defined as SBP <140 mmHg (<130 mmHg in patients with diabetes) or a reduction of ≥20 mmHg, and DBP <90 mmHg (<80 mmHg in patients with diabetes) or a reduction of ≥10 mmHg.
BL: baseline, EXCITE: Clinical EXperienCe of amlodipine and valsarTan in hypErtension
Curr Med Res Opin 2014; 30: 1937-1945

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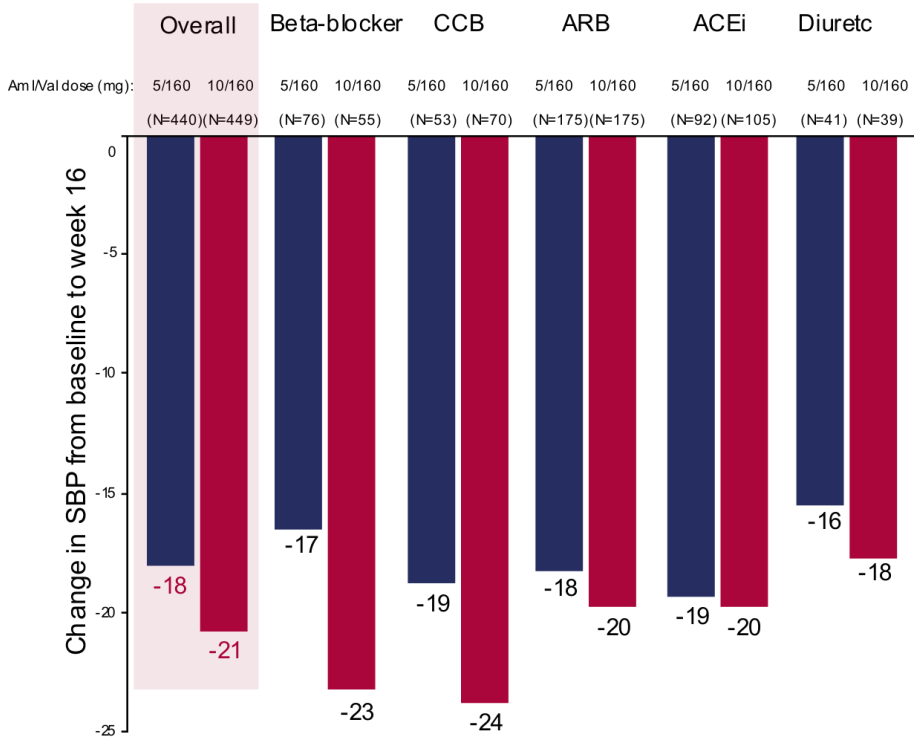
Nonresponders to monotherapy with any class of antihypertensive medications benefit from additional blood pressure lowering of Amlodipin/ Valsartan

EX-FAST study:



A randomized, double-blind, multinational, parallel-group study conducted at 132 centers in 8 countries. BP control rates in the individual treatment groups did not differ over time by previous antihypertensive monotherapies. the proportion of patients in whom BP control was achieved at the study end point (week 16). After 16 weeks, BP control (levels <140/90 mm Hg or <130/80 mm Hg for diabetics) was achieved in 72.7% of patients receiving amlodipine/valsartan 5/160 mg and in 74.8% receiving amlodipine/valsartan 10/160 mg.

ACEi: Angiotensin converting enzyme inhibitors, Aml/Val: Amlodipine/Valsartan, ARB: Angiotensin Receptor Blockers, BP: Blood pressure, EXFAST: EXFORGE in Failure After Single Therapy.
J Clin Hypertens. 2008; 10: 185-194. Presented in 2007 ASH.

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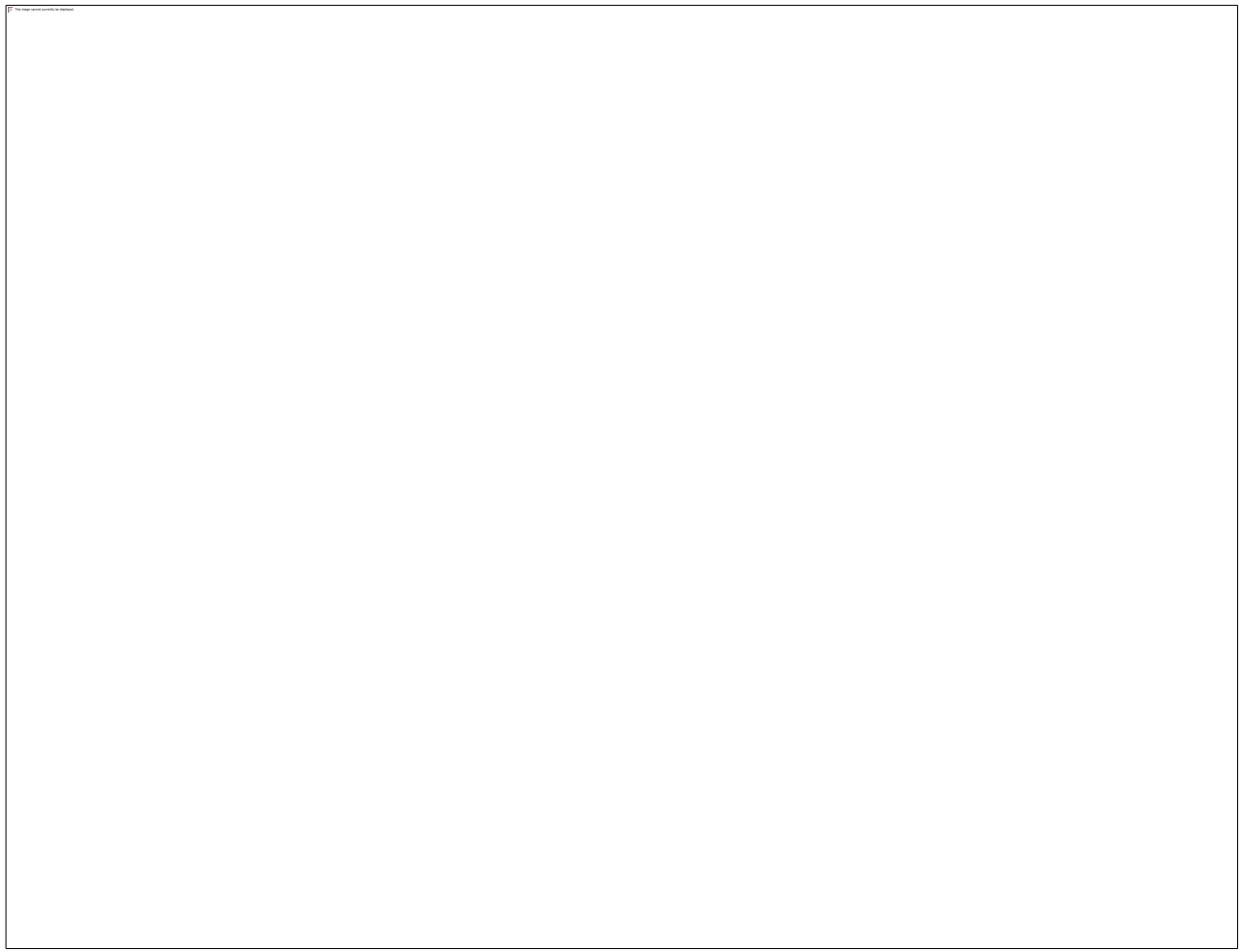
Amlodipine/ Valsartan combination has favorable safety profile



4-week placebo period, 80 grade 1–2 hypertensive patients, SBP>140mmHg and DBP>90mmHg and <110 were randomized to Amlodipine 10mg or Valsartan 160mg or Amlodipine 10mg plus Valsartan 160mg for 6 weeks.

AFV: ankle foot volume
J Hum Hypertens 2007;21:220– 224

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Valsartan + HTC

Valzodec-HCT®
Valsartan / Hydrochlorothiazide

- **Newly diagnosed hypertension patients with SBP≥140 mmHg or DBP≥90 mmHg* benefit more from Val/HCT SPC:**

Post stroke (Secondary prevention of stroke)

Incipient heart failure (primary prevention of heart failure)

Very elderly

CCBs intolerance

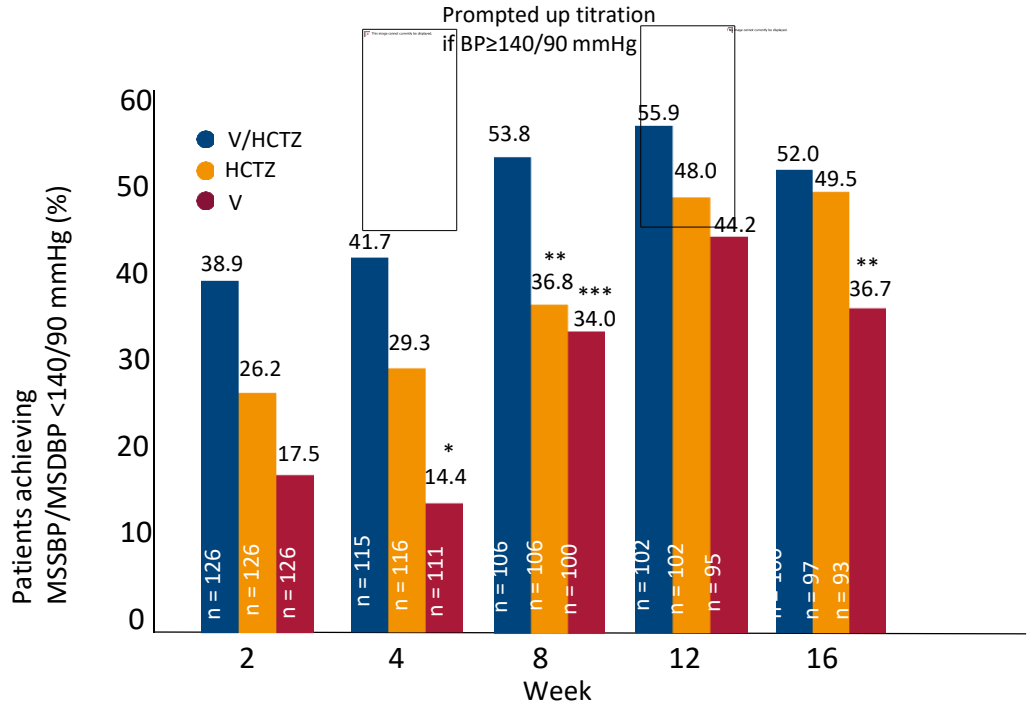
- **Uncontrolled Hypertension with Valsartan or Hydrochlorothiazide monotherapy†.**

*Exceptions: Frail older, low risk grade 1 (140-159/90-99 mmHg, esp. <150 mmHg), †Not adequately controlled: above 130/80 mmHg (in ≥ 65yrs. Above 139 mmHg).

Hypertension. 2020;75:1334-1357, Hypertension. 2018;71:e13-e115, FDA label Valsartan/ Hydrochlorothiazide. Reference ID: 4659158.

ValVET Trial

In elderly with systolic hypertension, initial low-dose combination therapy with Valsartan/HCT was more effective than either component monotherapy



Proportion of achieving mean sitting systolic blood pressure mean sitting diastolic blood pressure <140/90 mmHg
*p<0.0001 **p<0.05 ***p=0.0044

A 16-week trial in 384 randomized patients ≥70 years old with systolic hypertension(n=128 in each of the 3 treatment groups: V/HCT 160/12.5 mg, HCT 12.5 mg, or V 160 mg). Greater mean in msSBP from baseline with single pill V/HCT vs V and HCT, 17.3 mmHg vs 8.6 mmHg and 13.6 mmHg, respectively. Reductions of BP reduction in the V/HCT group generally persisted. Goal attainment rates were greater with V/HCT than HCT treatment and Valsartan treatment at weeks 8 and 16 (P<.05).

ValVET: Valsartan Very Elderly Trial
J Clin Hypertens. 2011; 13:722-730

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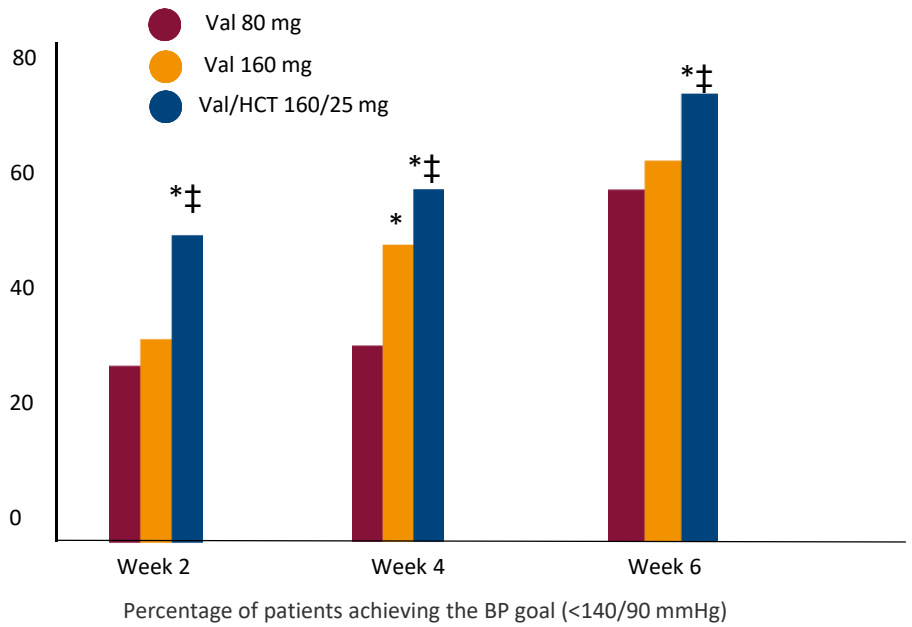
Less titration steps required with Valsartan/HCT initiation compared to Valsartan monotherapy to achieve blood pressure goal



Percentage of patients achieving the BP goal (<140/90 mmHg)

A prospective, 6-week, multicenter, double-blind study examined the benefits of initiating treatment with combination valsartan/ Hydrochlorothiazide compared with initial valsartan monotherapy in 648 patients with stage-1 or stage-2 hypertension. The BP goal of 140/90mmHg achieved in a shorter period of time (2.8 weeks) ($P<0.0001$). *$p<0.001$ vs V-low;‡ $p<0.05$ vs. V-high

V-high, valsartan 160 mg; V-low, valsartan 80 mg.
J Hum Hypertens. 2010;24:483–491

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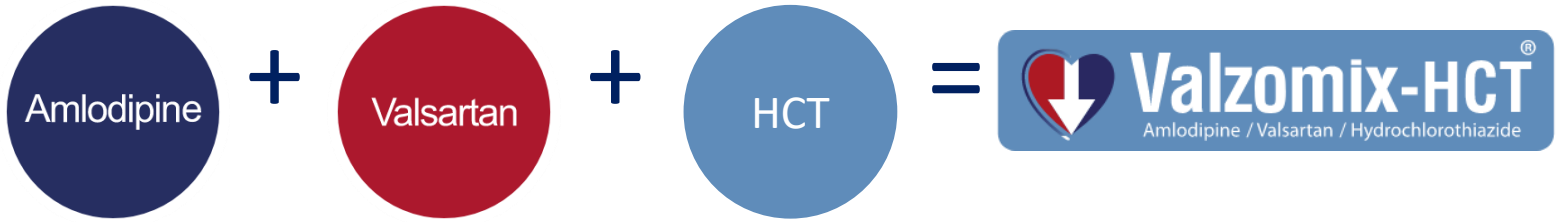

* Adequately controlledin ≥ 65yrs. SBP 130-139/80 mmHg.
FDA label Amlodipine and Valsartan and Hydrochlorothiazide. 2019 Revision

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Valzomix-HCT®
Amlodipine / Valsartan / Hydrochlorothiazide

1/3 of Hypertensive patients

Need 3 or more Antihypertensive agents

To Achieve Blood Pressure Control

Vasc Health Risk Manag 2010; 6: 321–325

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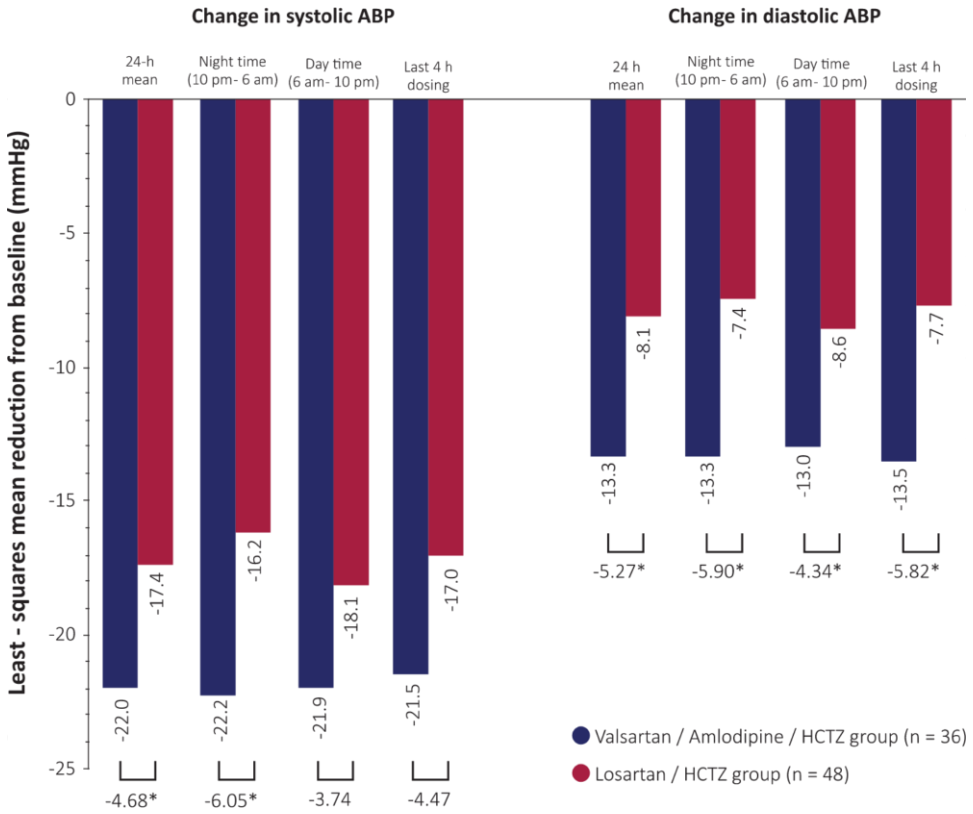
Moderate doses of ARB/CCB/ diuretic is more effective in lowering nighttime and daytime ABP than a maximal dose of an ARB with a diuretic



A randomized, double-blind, parallel-group study of patients with Stage 2 hypertension. The efficacy variables of this ABPM substudy were change from baseline in MSSBP and MSDBP at week 6.

Mean reduction in mean ABP at week 6 were significantly greater in the Valsartan/Amlodipine/HCT group than in the Losartan/ HCT group (-22.0 ±1.7/-13±1.0 versus -17.4±1.5/ -8.1±0.8 mmHg, P = 0.043/P < 0.001, respectively).

Vasc Health Risk Manag. 2011; 7: 701–708

Three blood pressure lowering drugs in low dose combination would reduce stroke by 60% and heart disease by 50%

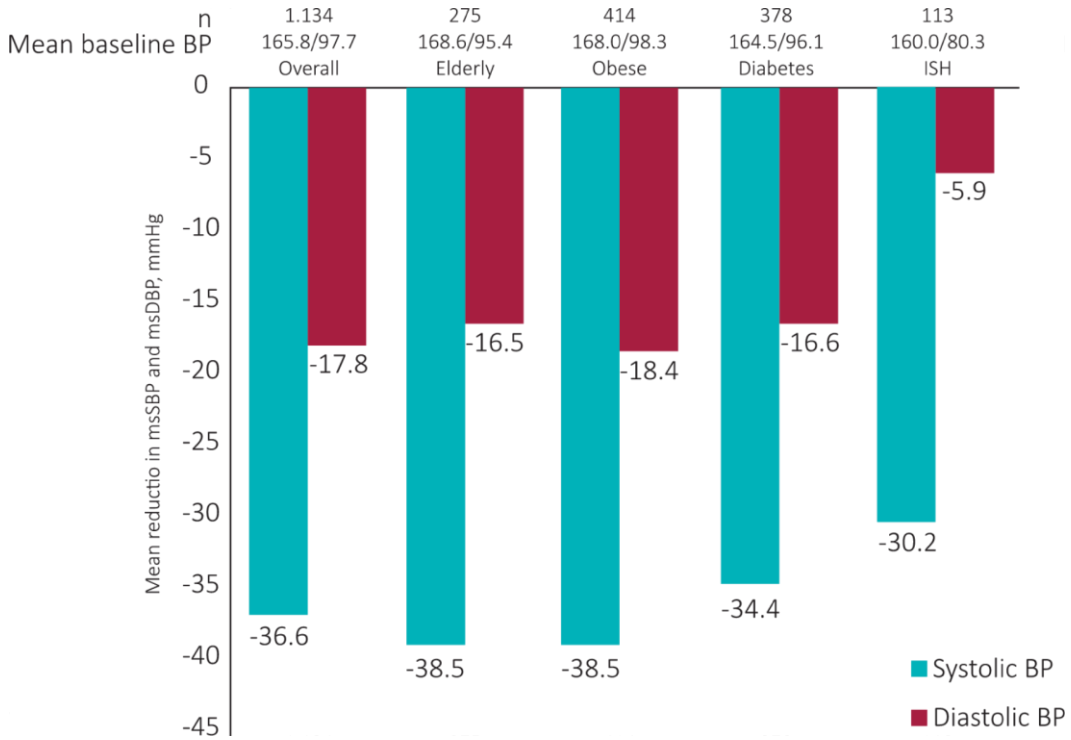
Percentage (95% CI) reduction in incidence

Disease	One drug	Two drugs	Three drugs
Stroke	29 (26 to 31)	49 (42 to 55)	63 (55 to 70)
Ischaemic heart disease events	19 (17 to 21)	34 (29 to 40)	46 (39 to 53)

Effects of blood pressure lowering drugs on reducing the incidence of stroke and ischemic heart disease events when used separately and in combination at half standard dose*

*Calculated from reductions in blood pressure in table 4 and estimates of association between blood pressure and disease events at age 60-69 years from the Prospective Studies Collaboration.
BMJ. 2003 ;326:1427

Triple combination therapy reduces blood pressure significantly in diverse hypertension subgroups



Mean reductions in msSBP and msDBP at 26±8 weeks in subgroups treated with Aml/Val/HCT

9,794 patients analyzed, 8,603 and 1,191 patients were prescribed Aml/Val and Aml/Val/HCT, respectively.

Vasc Health Risk Manag. 2015;11: 71–78

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Follow up
&
Targets of Hypertension Management

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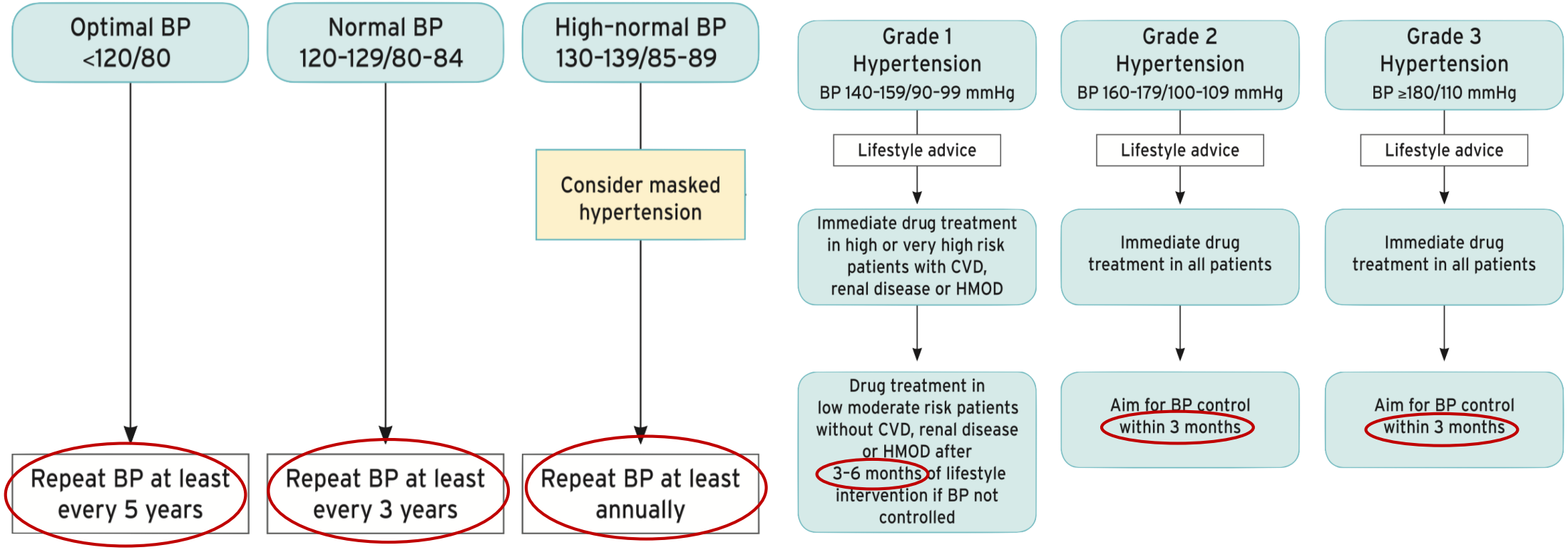
Follow-up in Hypertension



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Recommended Office Blood Pressure Target Ranges

Age group	Office SBP treatment target ranges (mmHg)				
	Hypertension	+ DM	+ CKD	+ CAD	+ Stroke/TIA
18 – 69 years	120–130	120–130	<140–130	120–130	120–130
	Lower SBP acceptable if tolerated				
≥70 years	**<140 mmHg, down to 130 mmHg if tolerated**				
	Lower SBP acceptable if tolerated				
DBP treatment target (mmHg)	<80 for all treated patients				

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Take Home Messages

- Most patients with **blood pressure ≥ 140/90 mmHg** need combination therapy for blood pressure control.
- Guidelines recommend **initiation** of hypertension treatment with **dual SPC**.
- In case of nonachievement to BP goal within 3 months with maximum tolerated dosage of dual SPC, uptitartion to **triple SPC,** is recommended.
- **Single pill combination benefits**:

✓ More efficacy

✓ Less adverse effect

✓ More adherence

✓ Less titration steps

✓ Better clinical outcome

- **Follow-up** the patient with hypertension, not only until goal achievement, but also for life long, to keep it controlled, and preventing HMOD and cardiovascular events.

THANK YOU FOR YOUR ATTENTION

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