Blood Pressure

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February 2021

Virtual Preceptorship

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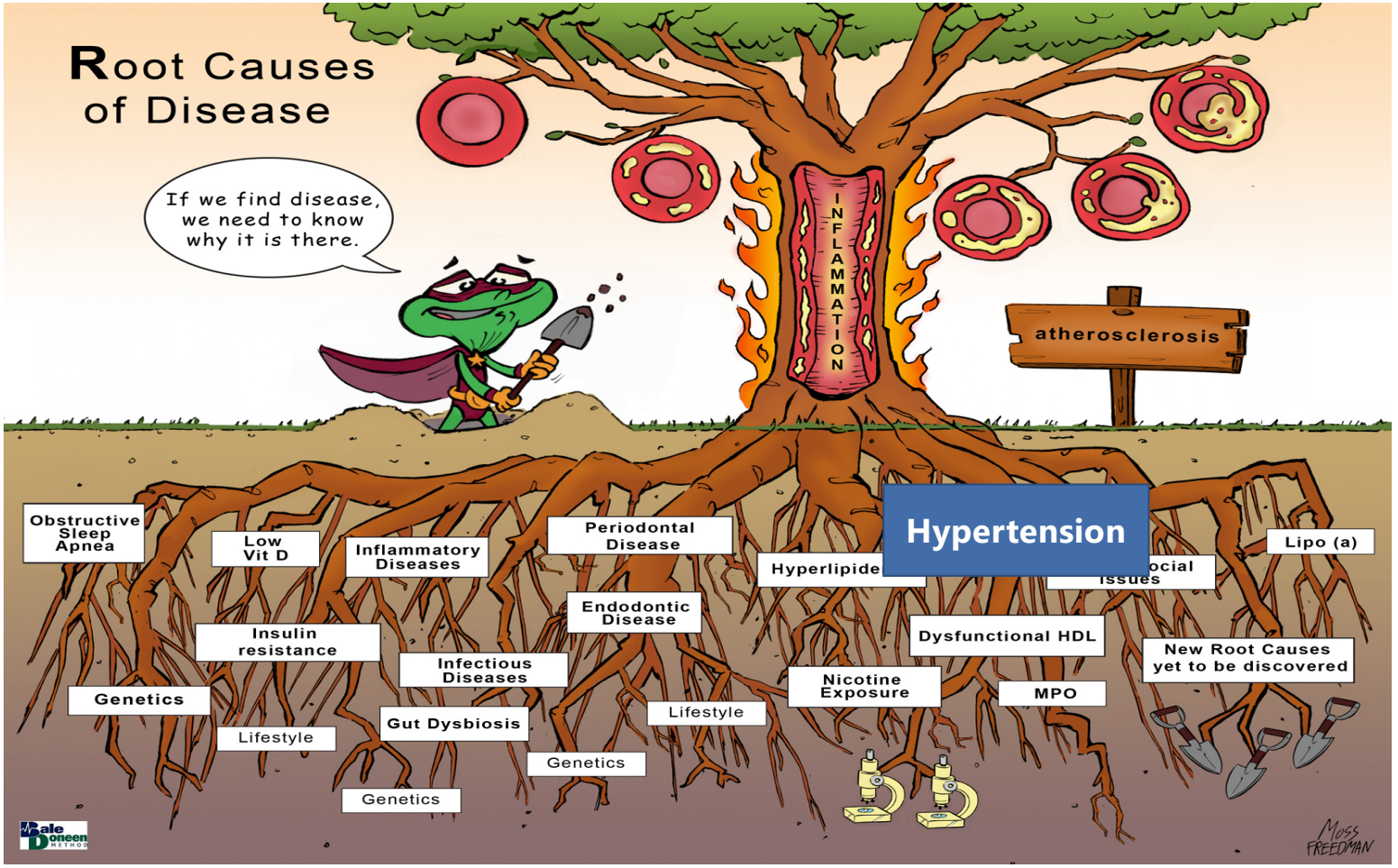

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Blood Pressure

Outline:

1. HTN and VSMC transformation
2. Incidence of hypertension
2. What is optimal
3. Establishment of new guideline
4. Microvascular disease and HTN
5. Hypertension in Adolescence
6. DBP in heart failure patients
7. When, why and how to measure
8. White coat HTN?

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Hypertension and Vascular Smooth Muscle Cell Transformation

Several mechanisms are responsible for the development of hypertension including excessive vasoconstriction and deficient vasodilatation.

<u>Contributes to the development and complications of HTN</u>:

The remodeling of large and small arteries

Renin-angiotensin system (RAS)

Angiotensin II (Ang II) is a potent vasoconstrictor

Li, F., Zhang, C., Lou, X., et al. (2019). Involvement of the MiR-181b-5p/HMGB1 pathway in Angiotensin II-induced phenotypic transformation of smooth muscle cells in hypertension. Aging and Disease (2019) April 2019;10(2);231-248.

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Hypertension and Vascular Smooth Muscle Cell Transformation

Vascular smooth muscle cells (VSMCs) are a dominant constituent of arteries and a critical determinant of vascular diseases.

VSMCs may undergo phenotype alternations between a differentiated phenotype (contractile phenotype) and a dedifferentiated phenotype (synthetic phenotype) in response to different stimuli.

Li, F., Zhang, C., Lou, X., et al. (2019). Involvement of the MiR-181b-5p/HMGB1 pathway in Angiotensin II-induced phenotypic transformation of smooth muscle cells in hypertension. Aging and Disease (2019) April 2019;10(2);231-248.

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Hypertension and Vascular Smooth Muscle Cell Transformation

VSMCs phenotypic transformation from contraction to synthesis is widely accepted as the pivotal process in vascular remodeling during hypertension.

The mechanisms responsible for VSMCs phenotypic transformation in hypertension are not fully understood.

Ang II has been shown to induce inflammatory reactions and Ang II-induced VSMCs phenotypic transformation contributes to the development of hypertension, suggesting a possible link between Ang II-induced VSMCs phenotypic transformation and inflammation.

Li, F., Zhang, C., Lou, X., et al. (2019). Involvement of the MiR-181b-5p/HMGB1 pathway in Angiotensin II-induced phenotypic transformation of smooth muscle cells in hypertension. Aging and Disease (2019) April 2019;10(2);231-248.

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I'M KIND OF A BIG DEAL

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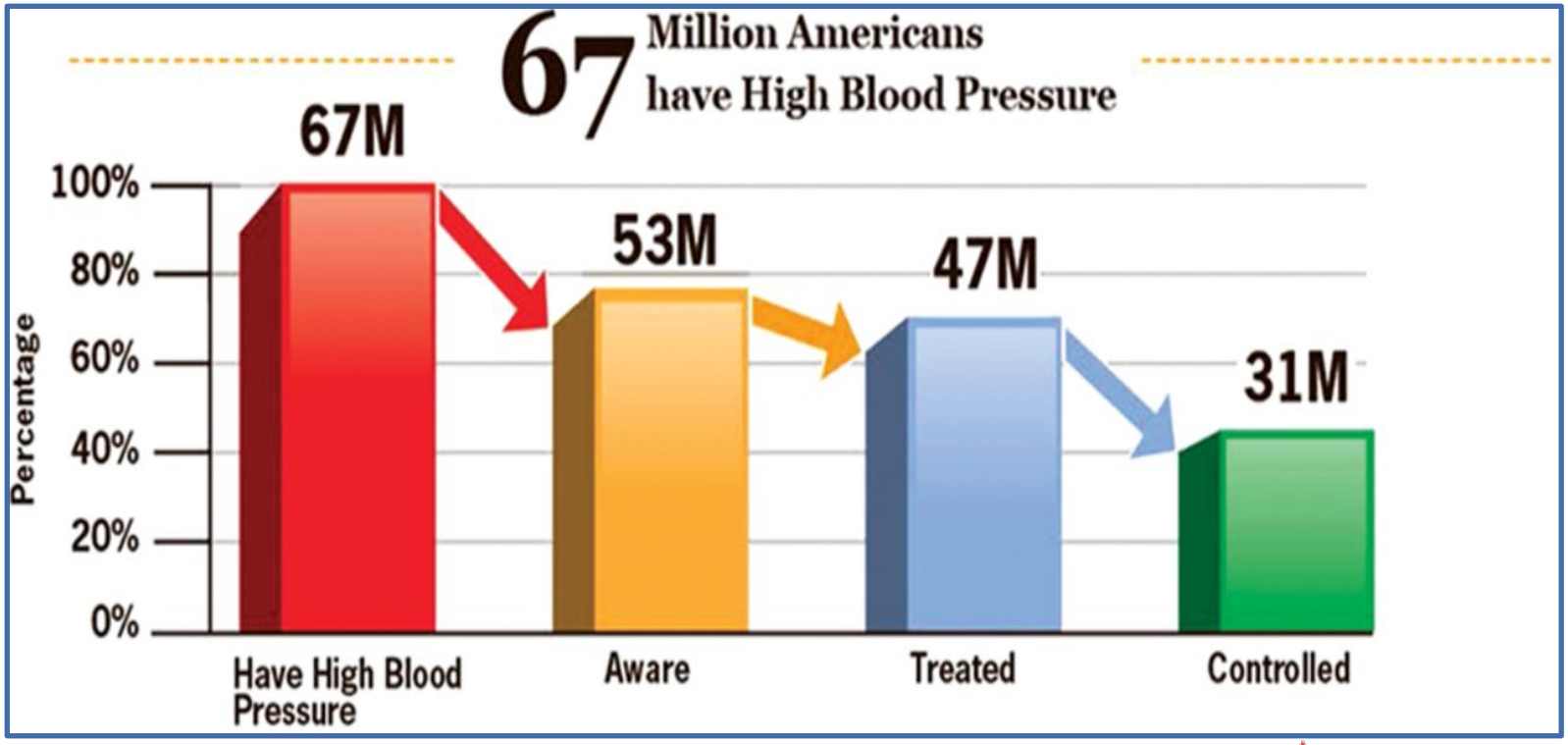
Nearly 1 in 3 Americans has hypertension, and nearly half of those people have out-of-control hypertension



Arnett D K Circulation 2013;127:2066-2070

American Heart Association
Learn and Live

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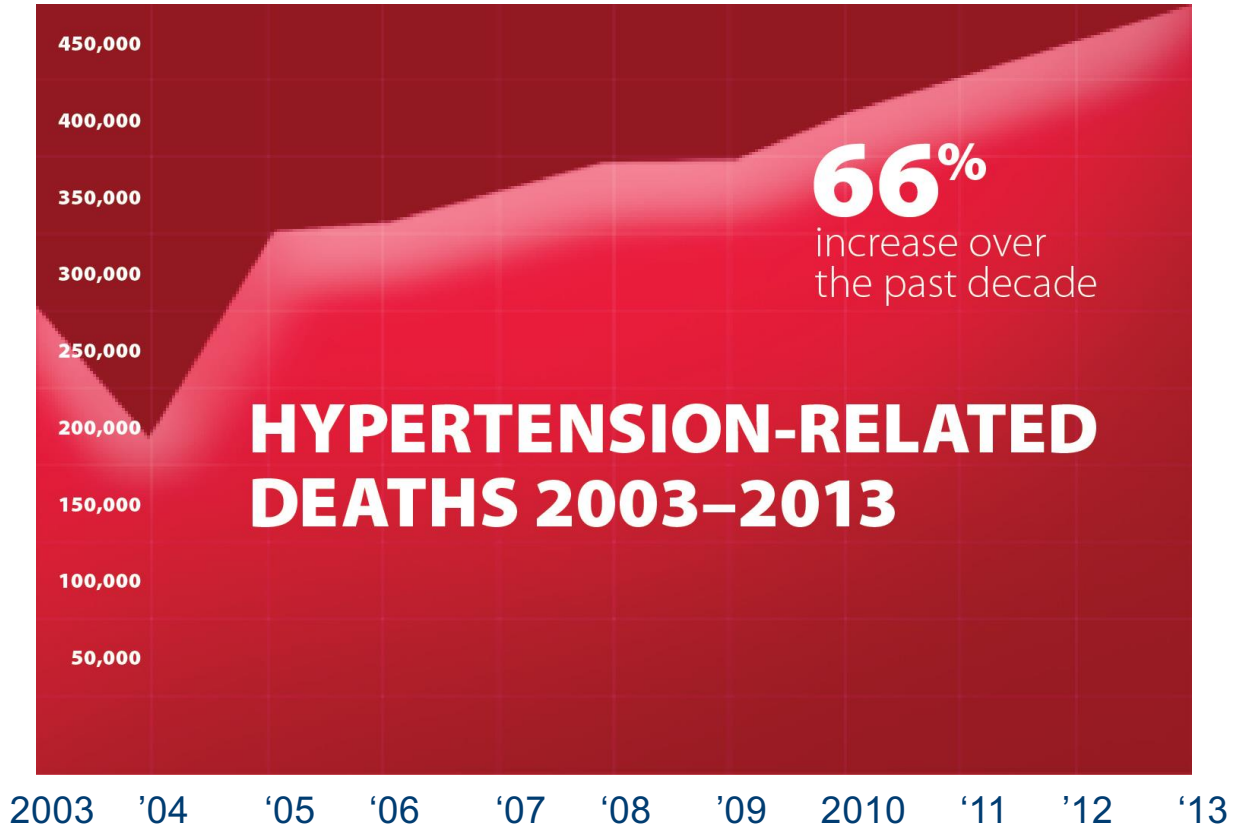
BP Related Deaths Skyrocketed



Kung HC, Xu JQ. (2015) Hypertension-related mortality in the United States, 2000–2013. NCHS data brief, no 193. Hyattsville, MD: National Center for Health Statistics.

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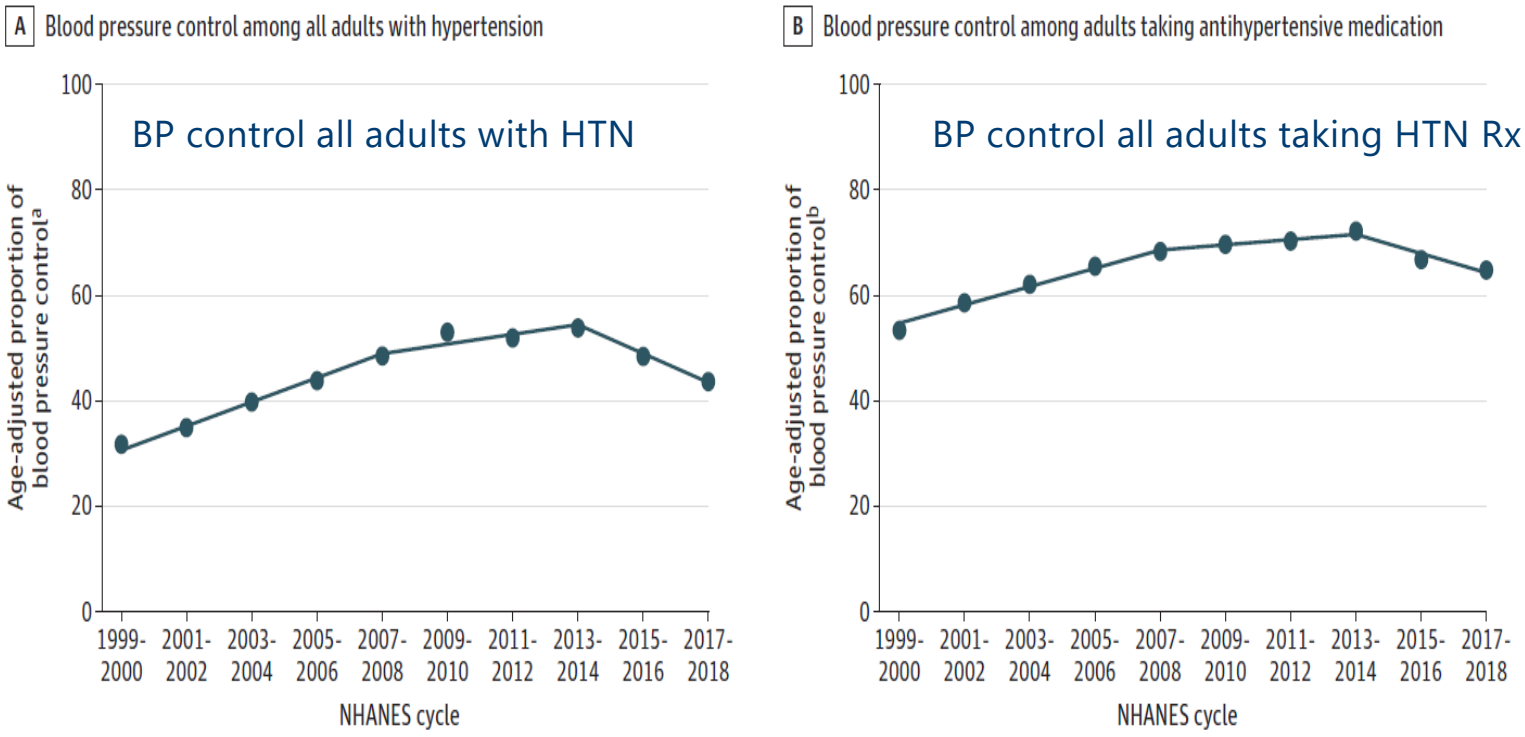
Good news! Really? Is it??

Figure. Age-Adjusted Estimated Proportion of Adults With Hypertension and Controlled Blood Pressure



Muntner, P., Hardy, Fine, L. et al. (Sept 2020). Trends in Blood Pressure Control Among US Adults With Hypertension, 1999-2000 to 2017-2018. JAMA Published online 9-2020

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Good news! Really? Is it??

National Health and Nutrition Examination Survey data, US adults, between 1999-2000 and 2017-2018 (10 cycles), including 18 262 US adults aged ≥18 years

The primary outcome of BP control was **<140/90 mmHg**

Is this good enough to protect our microvascular system?

Muntner, P., Hardy, Fine, L. et al. (Sept 2020). Trends in Blood Pressure Control Among US Adults With Hypertension, 1999-2000 to 2017-2018. JAMA Published online 9, 2020

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What about SBP ≥110mmHg?

SBP of ≥110mm Hg is associated with increased CVD and renal disease risk.

SBP elevation is causal of CAD, ischemic stroke and hemorrhagic stroke.

The burden of SBP of >110mmHg remains high despite the availability of preventive interventions which include low-cost, effective BP meds.

Forouzanfar, M. H., et. al. (2017). Global burden of hypertension and systolic blood pressure of at least 110 to 115 mm hg, 1990-2015. *JAMA, 317*(2), 165-182.

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What about SBP ≥110mmHg?

Data from 8.69 million people ≥25 yo. from 154 countries.

In last 25 yrs (‘90-’15) the rate of SBP ≥110 mm Hg has been increasing.

The estimated rate of annual deaths associated with SBP >110 mm Hg increased accordingly from 135.6 to 145.2 per 100 000 persons.

Forouzanfar, M. H., et. al. (2017). *JAMA, 317*(2), 165-182.

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What about SBP ≥110mmHg?

CAD and stroke accounted for majority of disease burden related to SBP of ≥110mm Hg.

Nearly 30% of this burden occurred in individuals with SBP between 115 &140 mm Hg.

Chronic kidney disease contributed to the burden almost as much as the CVD.

Forouzanfar, M. H., et. al. (2017). *JAMA, 317*(2), 165-182.

BaleDoneen METHOD®

What about SBP ≥110mmHg?

SBP of ≥110 mmHg remains one of the largest risks for decreased human health, greater than tobacco or high BMI.

Prevention and control of BP ≥ 110 mm Hg through a combination of behavioral, lifestyle, and drug treatment could mitigate this growing burden in healthcare!

Forouzanfar, M. H., et. al. (2017). *JAMA, 317*(2), 165-182.

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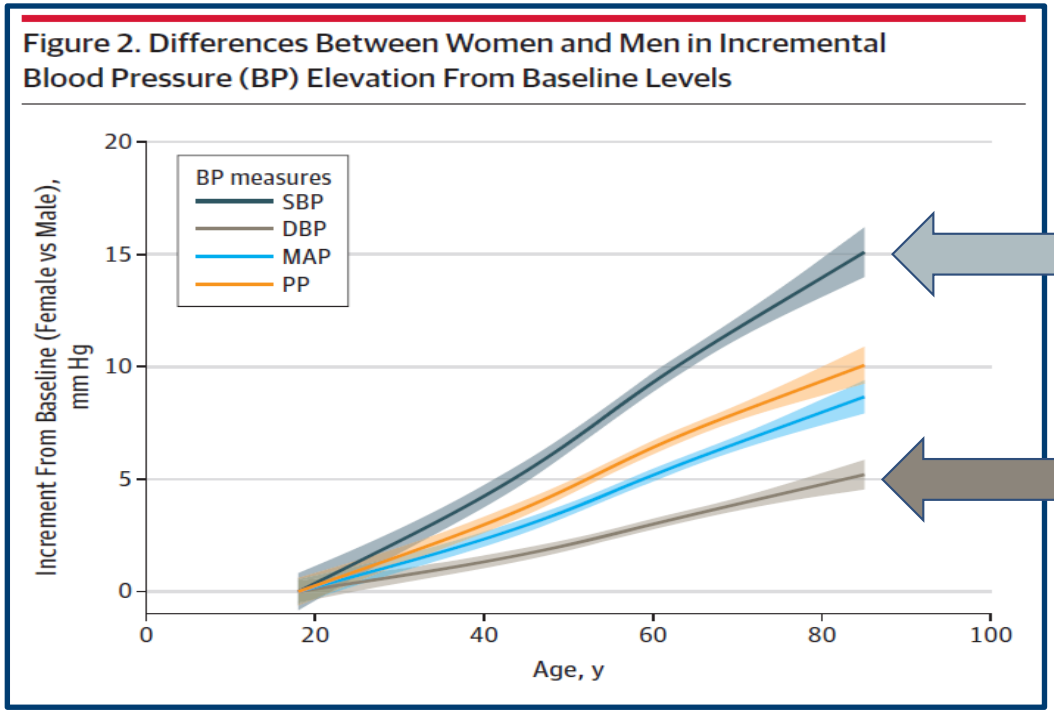
Blood Pressure elevation progresses more rapidly in women then in men



SBP – systolic BP

DBP – systolic BP

Hongwei, J., Kim, A., et al. (2020). Sex differences in blood pressure trajectories over the like course. JAMA Cardiology 2020;5(3):255-262

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What is optimal?

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Sprint Trial

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Blood Pressure Goal of < 120 mm Hg Reduces CV Risk in High Risk Adults

9,361 pts. ≥50 yo, syst BP ≥ 130 mm Hg; plus at least one additional risk factor- (known CVD; ≥ 75 yo; ≥ stage 3 CKD; FRS ≥15%).

Randomized to systolic goal of:

< 140 mm Hg vs < 120 mm Hg

Wright, J. T., et. al. (2015). A Randomized Trial of Intensive versus Standard Blood-Pressure Control. N Engl J Med, 373(22), 2103-2116.

BaleDoneen METHOD®

Blood Pressure Goal of < 120 mm Hg Reduces CV Risk in High-Risk Adults

Primary outcome: coronary artery event; stroke; CV death; HF

Secondary outcomes: dementia, CKD, all cause mortality

Intended to be a 5-year trial.

Wright, J. T., et. al. (2015). A Randomized Trial of Intensive versus Standard Blood-Pressure Control. N Engl J Med, 373(22), 2103-2116.

BaleDoneen METHOD®

Blood Pressure Goal of < 120 mm Hg Reduces CV Risk in High-Risk Adults

Achieved BP in < 140 mm Hg arm averaged ~ 134 mm Hg and took ~ 2 meds.

Achieved BP in < 120 mm Hg arm averaged ~ 119 mm Hg and took ~ 3 meds.

Wright, J. T., et. al. (2015). A Randomized Trial of Intensive versus Standard Blood-Pressure Control. N Engl J Med, 373(22), 2103-2116.

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Blood Pressure Goal of < 120 mm Hg Reduces CV Risk in High-Risk Adults

Trial stopped 6 months early due to a **significant 33% reduction in primary CV outcomes**

and a **significant 25% reduction in all-cause mortality** in the intensive treatment group.

Wright, J. T., et. al. (2015). A Randomized Trial of Intensive versus Standard Blood-Pressure Control. N Engl J Med, 373(22), 2103-2116.

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Treating Systolic BP (SBP) to <120 mm/Hg is Cost Effective: Background

Adults at high risk for CVD who have no hx of DM, HF or stroke have significant reduction in death & CV events when SBP is rx'ed <120.

These benefits must be weighed against the increased risk of serious adverse events (SAE) and higher implementation costs.

Bress, A. P., et. al. (2017). Cost-Effectiveness of Intensive versus Standard Blood-Pressure Control. *New England Journal of Medicine, 377*(8), 745-755.

BaleDoneen METHOD®

Treating BP to Systolic <120 mm/Hg is Cost Effective

~17 million U.S. adults meet SPRINT eligibility criteria and stand to benefit from SBP rx to < 120 mm/Hg.

Canada and Australia have already recognized this.

Bress, A. P., et. al. (2017). Cost-Effectiveness of Intensive versus Standard Blood-Pressure Control. *New England Journal of Medicine, 377*(8), 745-755.

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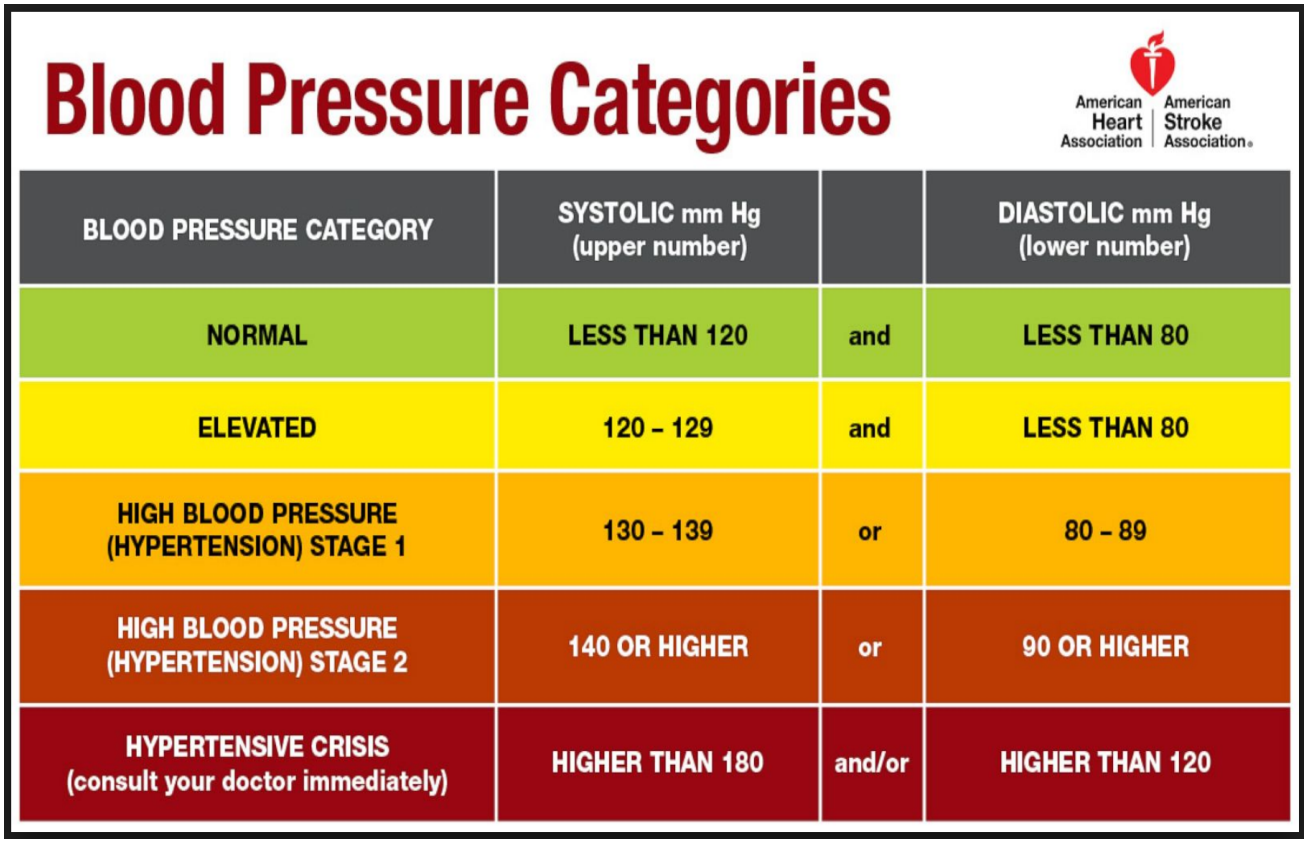
November 2017



Blood Pressure Categories

American Heart Association | American Stroke Association

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

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Microvascular Disease Health Consequences

MVD found in any vascular bed indicates a high probability of MVD in other organs perfused at a high rate of flow: the heart, the brain, the kidney, the retina and the lung.

The link appears multidirectional.

Hakim, A. M. (2019). "Small Vessel Disease."
Frontiers in Neurology **10**: 1020-1020.

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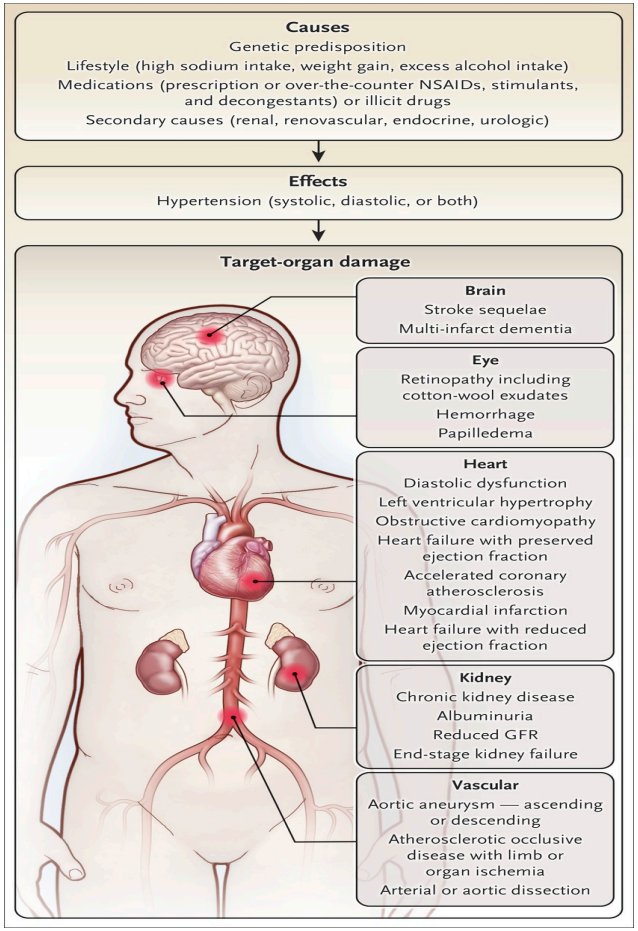
Initial Treatment of Hypertension



<u>Why identify and treat hypertension early?</u>

Stroke
Dementia
Retinopathy
Retinal hemorrhage
Papilledema
Diastolic dysfunction
Left ventricular hypertrophy
Obstructive cardiomyopathy
Heart Failure with preserved EF
Accelerated coronary atherosclerosis
Heart Failure with reduced EF
Chronic Kidney Disease
Albuminuria
Reduced GFR
End-stage Kidney Disease
Aortic aneurysm – ascending or descending
Limb or organ ischemia
Arterial or aortic dissection

Taler SJ. N Engl J Med 2018;378:636-644

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Midlife Hypertension and cognitive impairment later in life

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Midlife hypertension confers increased risk for cognitive impairment in late life

Midlife HTN is associated with late-life dementia risk and with risk of clinically diagnosed Alzheimer's disease.

Extensive published literature describes the positive association between HTN and cerebral small vessel disease.

HTN has also been associated with smaller brain volumes, with more consistent associations seen with midlife, rather than late life.

Lane, C., Barnes, J., Nicholas, J. et al. 2019. Associations between blood pressure across adulthood and late-life brain structure and pathology in the neuroscience substudy of the 1946 British birth cohort: an epidemiological study. Lancet neuro. August 20, 2019(19)30228-5

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Midlife hypertension confers increased risk for cognitive impairment in late life

Researchers investigated associations between BP and BP changes at different ages: 36, 43, 53, 60–64, and 69 years

Examining white matter changes, amyloid-β status using logistic regression, whole-brain volume and hippocampal volumes using linear regression, with adjustment for potential confounders.

Lane, C., Barnes, J., Nicholas, J. et al. 2019. Associations between blood pressure across adulthood and late-life brain structure and pathology in the neuroscience substudy of the 1946 British birth cohort: an epidemiological study. Lancet neuro. August 20, 2019(19)30228-5

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Midlife hypertension confers increased risk for cognitive impairment in late life

Higher BP in midlife is associated with greater cerebral small vessel disease burden and smaller whole-brain and hippocampal volumes at age 70.

Both SBP and DBP at 53 years of age were associated with late-life cerebral small vessel disease

Lane, C., Barnes, J., Nicholas, J. et al. 2019. Associations between blood pressure across adulthood and late-life brain structure and pathology in the neuroscience substudy of the 1946 British birth cohort: an epidemiological study. Lancet neuro. August 20, 2019(19)30228-5

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BP >120/80mmHg risk in young adults

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BP of ≥120/80 mm/Hg in Young Adults is Associated with Higher CV Event Risk:

Data from the Coronary Artery Risk Development in Young Adults (CARDIA) Study will be analyzed to determine if elevated BP or hypertension in adults <40yo is associated with higher CV event risk later in life compared to normal BP.

The study will also exam whether any association differs by race and sex.

Yano, Y., et al. (2018). *JAMA, 320*(17), 1774-1782.

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BP of ≥120/80 mm/Hg in Young Adults is Associated with Higher CV Event Risk

After adjustment for: age when follow-up started, race, sex, educational level, study site, BMI, smoking, physical activity, TC, HDL, FBG, the HRs for CVD events were significantly higher in all groups compared to normal BP:

Elevated BP- HR-1.67 (95% CI, 1.01-2.77)

Stage 1 BP- HR-1.75 (95% CI, 1.22-2.53)

Stage 2 BP- HR-3.49 (95% CI, 2.42-5.05)

Yano, Y., et al. (2018). *JAMA, 320*(17), 1774-1782.

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Abnormal BP in Young Korean Adults is Associated with Premature CV Event Risk:

Awareness and management of hypertension in young adults is < 20%.

The potential association of the current definition of BP with CV risk in young adults needs clarification.

Son, J., Choi, S., Kim, K., & et al. (2018). *JAMA, 320*(17), 1783-1792.

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Abnormal BP in Young Korean Adults is Associated with Premature CV Event Risk

BP defined by recent guidelines.

40% - normal BP

10.5% - elevated BP

38% - stage 1 BP

11.5% - stage 2 BP

44,813 premature CVD events occurred.

Son, J., Choi, S., Kim, K., & et al. (2018). Association of blood pressure classification in korean young adults according to the 2017 american college of cardiology/american heart association guidelines with subsequent cardiovascular disease events. *JAMA, 320*(17), 1783-1792.

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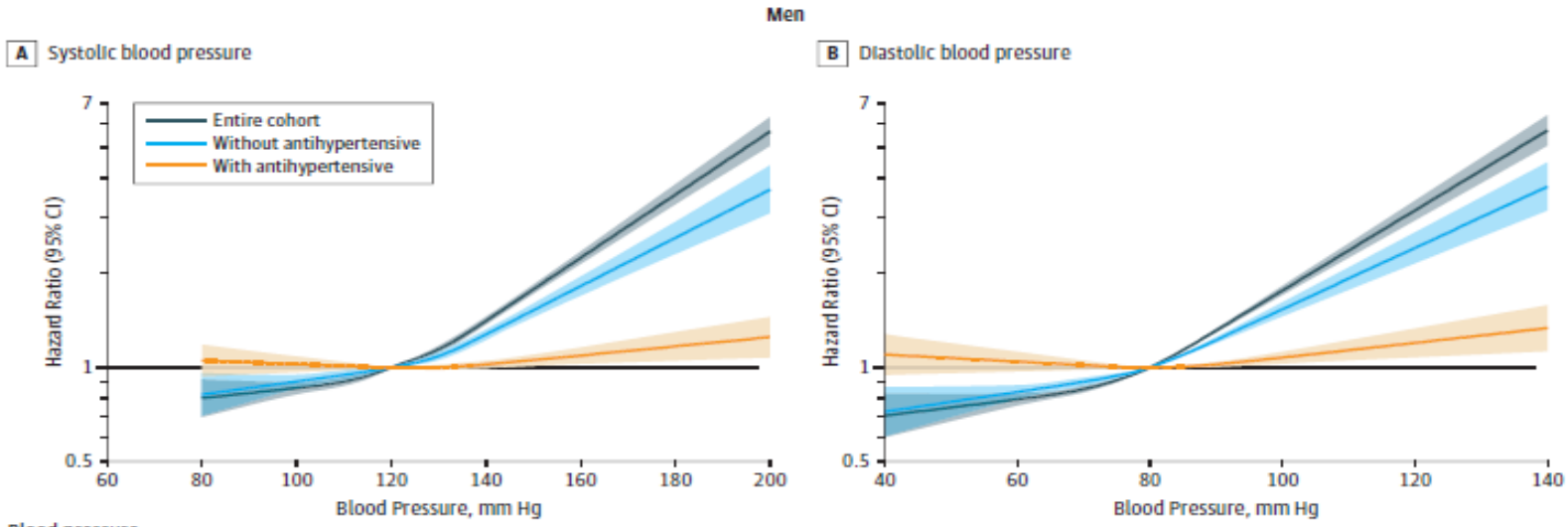
Abnormal BP in Young Korean Adults is Associated with Premature CV Event Risk

Figure 2. Hazard Ratios for Cardiovascular Disease According to Index Blood Pressure Among Young Adults With and Without Stratification According to Antihypertensive Medication Prescription Within the First 5 Years of Follow-up



Blood pressure, mm Hg	<100	100-119	120-139	140-159	160-179	≥180
No. of participants	20582	550451	962634	148099	155572	1493
No. of events	338	9272	20579	5070	856	145

	<60	60-79	80-99	100-119	≥120
No. of participants	17782	764727	869474	45035	1813
No. of events	277	13047	20674	2073	189

Son, J., Choi, S., Kim, K., & et al. (2018). *JAMA, 320*(17), 1783-1792.

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Abnormal BP in Young Korean Adults is Associated with Premature CV Event Risk

Conclusion:

Young adults with abnormal BP have higher risk for premature CV events.

Son, J., Choi, S., Kim, K., & et al. (2018). *JAMA, 320*(17), 1783-1792.

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As exciting as it is to lower blood pressure to these levels –

Be aware that not everyone can handle low pressures

SBP <120 mm/Hg in patients with HF with preserved EF (HFpEF) shows poorer outcomes

Discharge SBP levels less than 120mmHg. 30-day, 1-year, and overall all-cause mortality and heart failure readmission through December 31, 2008.

SBP <120mmHg was also associated with

Higher risk of **mortality** at

1 year (HR, 1.36; *P* < .001)

6 years (HR, 1.17; *P* = .005)

Higher risk of **heart failure readmission** at 30 days:

(HR, 1.47; *P* = .02) but not at 1 or 6 yrs

Tsimploulis, A., Lam, P, Arundel, C. et al. Systolic BP and outcomes in patients with HFpEF. JAMA Cardiology. Published Feb 14, 2018 online. Doi 10.001

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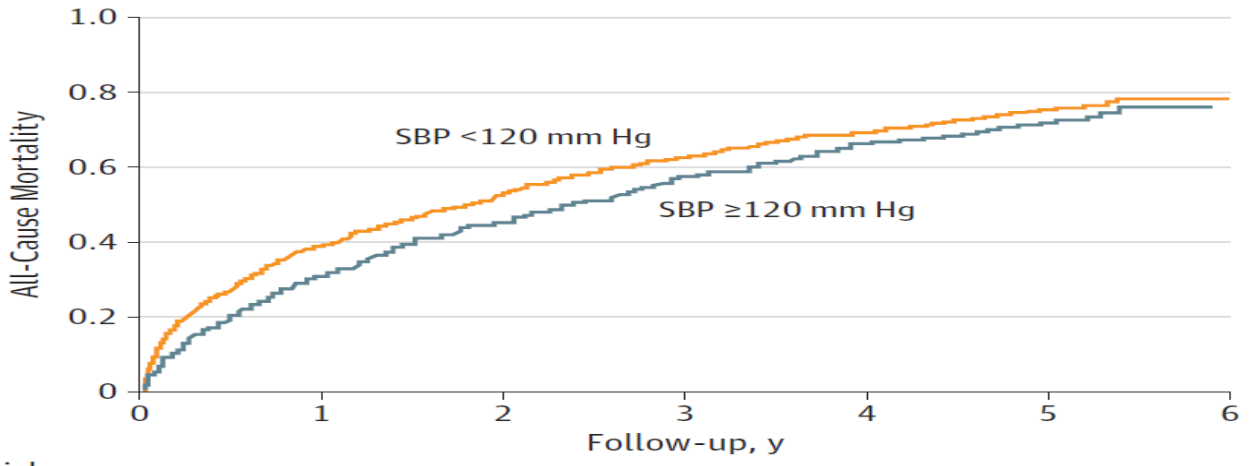
SBP <120 mm/Hg in patients with HF with preserved EF (HFpEF) shows poorer outcomes

Figure 1. Kaplan-Meier Plots for All-Cause Mortality by Systolic Blood Pressure (SBP) Level



No. at risk						
SBP <120 mm Hg	901	552	425	338	278	93
SBP ≥120 mm Hg	901	623	496	385	306	86

Tsimploulis, A., Lam, P, Arundel, C. et al. Systolic BP and outcomes in patients with HFpEF. JAMA Cardiology. Published Feb 14, 2018 online. Doi 10.001

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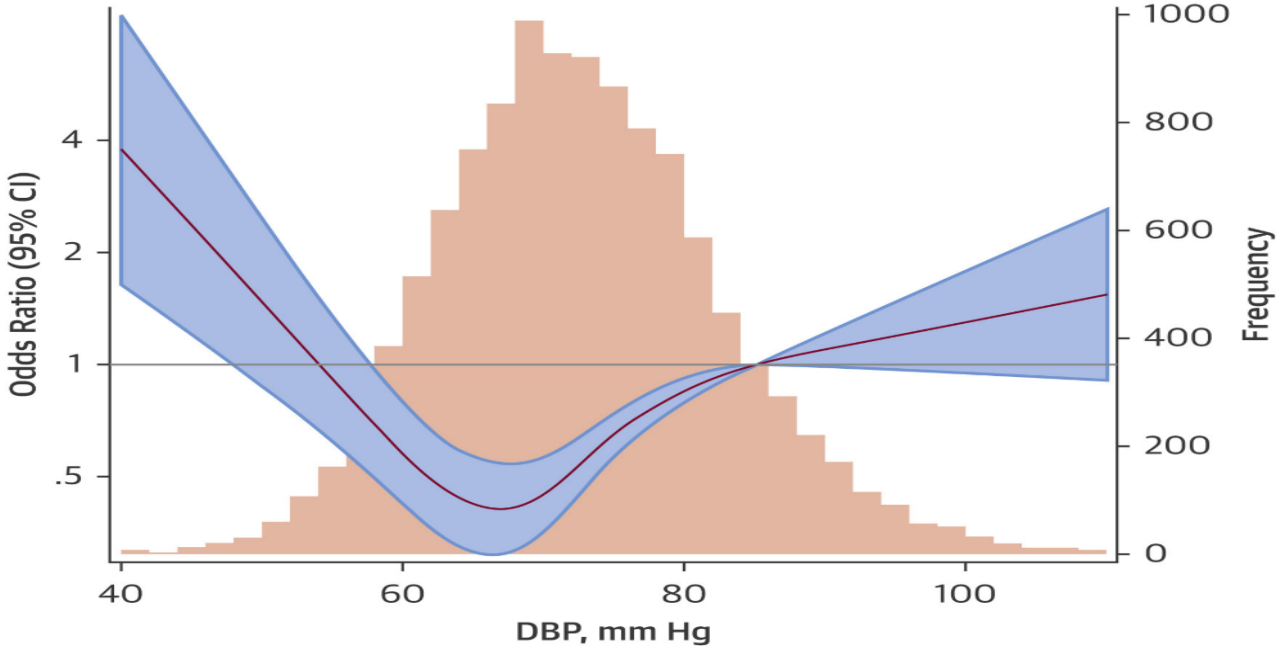
Relationship Between DBP and Elevated hs-cTnT



When DBP <65 mm Hg, a linear inverse relationship between DBP and hs-cTnT

McEvoy, J., Chen, Y., Rawlings, A., et al. Diastolic blood pressure, subclinical myocardial damage, and cardiac events. J Am Coll Cardiol 2016.

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Diastolic Blood Pressure Subclinical myocardial damage and CV events

Compared baseline DBP between 80 to 89 mmHg, the adjusted OR of having hs-cTnT >14 ng/l at baseline was:

2.2 (95% CI:1.2-4.1) in those with DBP <60 mmHg

1.5 (95% CI: 1.0-2.3) in those with DBP 60 to 69 mm Hg.

McEvoy, J., Chen, Y., Rawlings, A., et al. Diastolic blood pressure, subclinical myocardial damage, and cardiac events. J Am Coll Cardiol 2016.

BaleDoneen METHOD®

Diastolic Blood Pressure Subclinical myocardial damage and CV events

BaleDoneen Take-Away:

1. Remember – Optimal = Individualized
2. Always use the data to shape decision process but remember we are treating the n of 1 = the unique patient.
3. SPRINT data is powerful! Going from 140 to 120 SBP reduced events by 33% and reduced all-cause mortality by 25%
4. DBP reduction must be balanced with SBP optimization.
5. Utilize hs-cTn to determine safety of DBP regulation.

McEvoy, J., Chen, Y., Rawlings, A., et al. Diastolic blood pressure, subclinical myocardial damage, and cardiac events. J Am Coll Cardiol 2016.

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When, why and how to measure BP

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Morning Home BP Predicts Stroke and Heart Attack Risk

Morning BP is generally the highest and most CV events occur in the morning.

Ambulatory systolic BP (SBP) taken upon awakening is the strongest predictor of strokes, but it is not definite for heart attacks.

Kario, K., et. al. (2016). Morning Home Blood Pressure Is a Strong Predictor of Coronary Artery DiseaseThe HONEST Study. *J Am Coll Cardiol, 67*(13), 1519-1527.

BaleDoneen METHOD®

Morning Home BP Predicts Stroke and Heart Attack Risk

21,591 essential hypertensive pts; versed in taking HBP; pts rx'ed with olmesartan plus any combo of BP med; management and goals of BP at providers discretion.

Pts followed mean of 2 yrs.

127 strokes & 121 heart attacks occurred.

Kario, K., et. al. (2016). Morning Home Blood Pressure Is a Strong Predictor of Coronary Artery DiseaseThe HONEST Study. *J Am Coll Cardiol, 67*(13), 1519-1527.

BaleDoneen METHOD®

Morning Home BP Predicts Stroke and Heart Attack Risk

Results demonstrate that morning high blood pressure is a strong predictor of future heart attacks and strokes.

The data indicate morning home blood pressure may be superior to clinic blood pressure.

Kario, K., et. al. (2016). Morning Home Blood Pressure Is a Strong Predictor of Coronary Artery DiseaseThe HONEST Study. *J Am Coll Cardiol, 67*(13), 1519-1527.

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“My blood pressure is only high when I come in here because I get nervous coming to the dentist.”

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White Coat HTN, Ambulatory & Home Blood Pressure readings and CV mortality.

The prognostic value of white coat hypertension (WCH) is still debated.

N=2051 representative of the general population – measured office, ambulatory, and home blood pressure.

The risk of cardiovascular and all-cause mortality was assessed over 16 years in normotensive, sustained hypertensive, and WCH subjects.

Mancia, G., et al. Hypertension May 28, 2013 published online.

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White Coat HTN, Ambulatory & Home Blood Pressure readings and CV mortality.

White Coat Hypertension (WCH):
An office BP elevation and ambulatory (24 hours) or home BP normality.

Sustained Hypertension (HT):
Elevation of all 3 BPs respectfully (office, home, amb).

Normal Tension (NT):
Defined by normality

Average follow-up was 16 years.

Mancia, G., et al. Hypertension May 28, 2013 published online.

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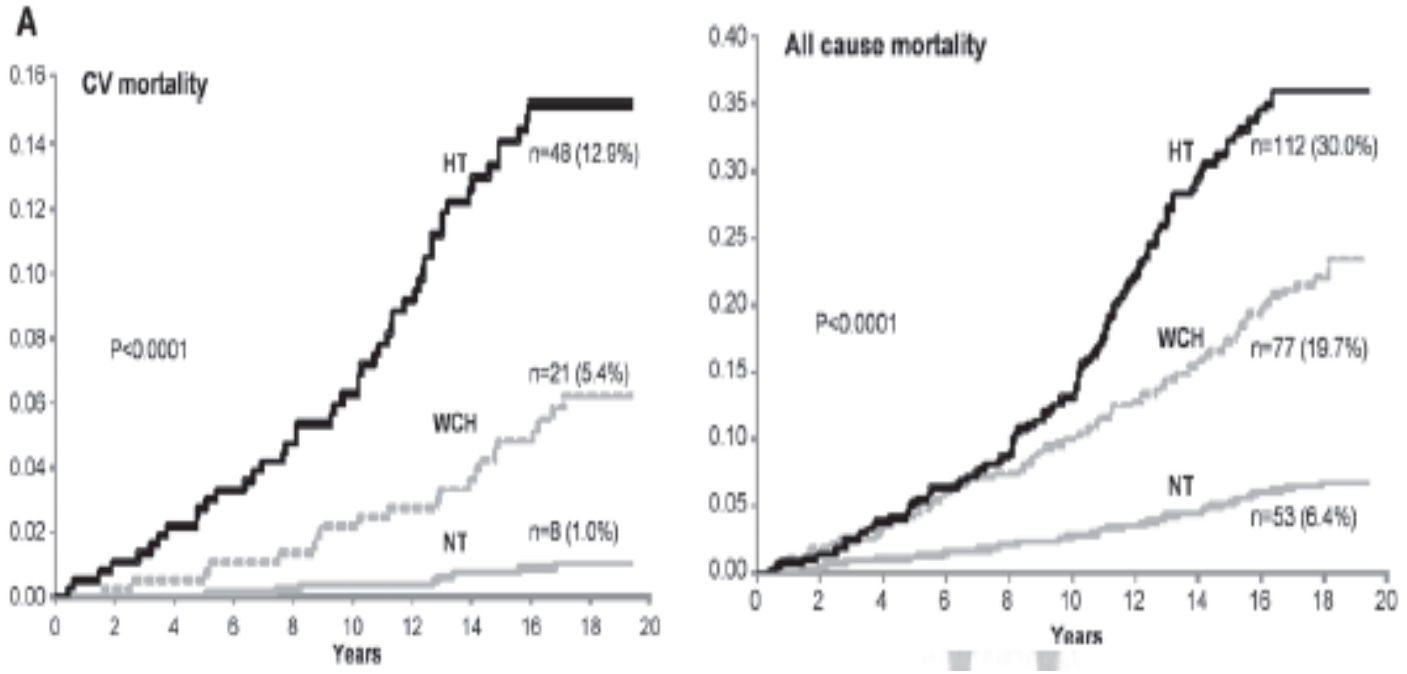
White Coat HTN, Ambulatory & Home Blood Pressure readings and CV mortality.



Kaplan-Meier curves for CV and all-cause mortality in NT, WCH, and HT

Mancia, G., et al. Hypertension May 28, 2013 published online.

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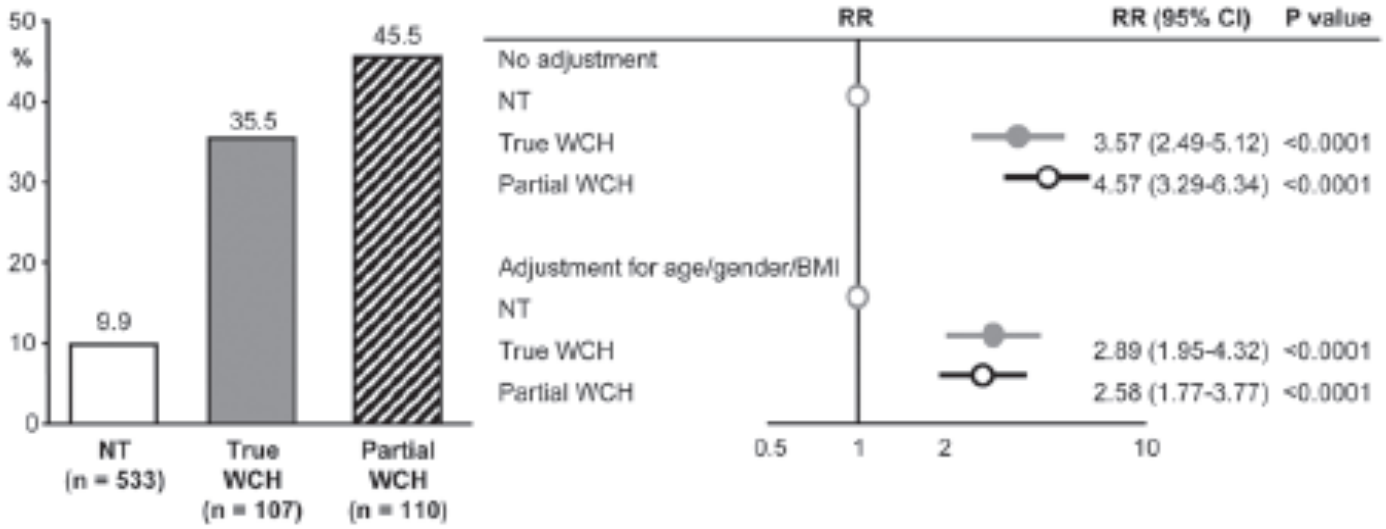
10 yr incidence & RR of developing sustained HTN

Over the 10 years, the percentage of subjects who developed sustained HT was progressively greater from NT to true and partial WCH.

Compared with NT, the risk of new-onset HTN was also sign greater in the 2 WCH groups when data were adjusted for age, sex and BMI.



Mancia, G., et al. Hypertension May 28, 2013 published online.

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How to take Blood Pressure correctly when using a wrist cuff (dental and home)

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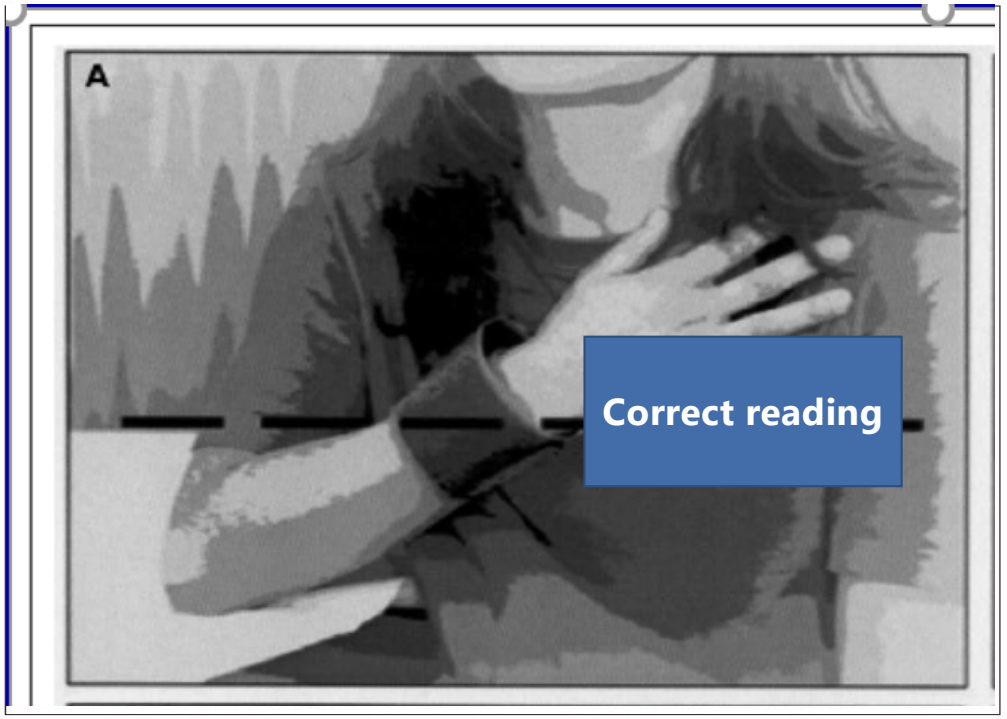
BP Taken By Wrist is Inaccurate Unless the Device is Positioned at Heart Level

correct reading

falsely high



falsely low

falsely high

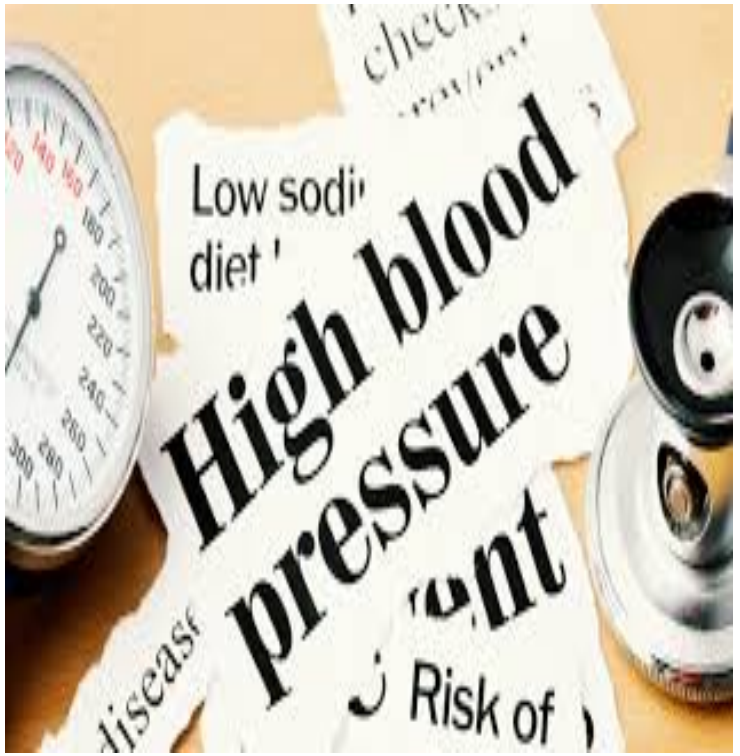
Figure 1. Correct (**A**) and incorrect (**B**–**D**) forearm positions in wrist blood pressure measurement. Dashed line indicates heart level. Position **B** (wrist higher than heart level) leads to falsely lower values. Positions **C** and **D** (forearm in horizontal position or vertical close to the body) lead to falsely higher values.

Casiglia, E., et. al. (2016). Poor Reliability of Wrist Blood Pressure Self-Measurement at Home: A Population-Based Study. *Hypertension, 68*(4), 896-903.

BaleDoneen METHOD®

Blood Pressure

1. Incidence of hypertension is high
2. What is optimal - SBP<120
3. Establishment of new guideline
4. Microvascular disease and HTN
5. Hypertension in Adolescence
6. DBP a concern in heart failure
7. White coat HTN does exist
8. When, why and how to measure



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