

Are we understanding preHTN

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JNC 7 2003

BLOOD PRESSURE CLASSIFICATION	SBP MMHG	DBP MMHG
NORMAL	<120	and <80
PREHYPERTENSION	120–139	or 80–89
STAGE 1 HYPERTENSION	140–159	or 90–99
STAGE 2 HYPERTENSION	≥160	or ≥100

SBP, systolic blood pressure; DBP, diastolic blood pressure

- **JNC 7 (2003) created a new category designated as “pre-HTN” that recognizes the relationship between BP and the risk of CVD events and signaled the need for the increased education of healthcare professionals and the public in order to decrease BP levels and prevent the development of HTN.**
- **Although pre-HTN is a risk factor for CVD, pre-HTN is not a disease category in the JNC 7.**
- **The corresponding guideline (JNC 8) published in 2014 does not address pre-HTN.**

2017 Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure 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

Recent American guidelines used (elevated BP and stage 1 HTN) for the old category of pre-HTN

2018 ESC/ESH Guidelines for the management of arterial HTN

Category	Systolic (mmHg)		Diastolic (mmHg)
Optimal	<120	and	<80
Normal	120–129	and/or	80–84
High normal	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	160–179	and/or	100–109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension ^b	≥140	and	<90

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The recent European guidelines used the term (normal and high normal BP) for the old category of pre-HTN

**How should we (clinicians and healthcare providers)
consider pre-HTN in the strategy of management of HTN?**

Prevalence of Pre-HTN

- **The reported prevalence of pre-HTN varies from 15 to 59%, and the reported prevalence of HTN varies from 22 to 44%.**
- **Study populations in subjects with pre-HTN have shown a higher proportion of men and higher values of age, BMI, total cholesterol, triglyceride, LDL, and HbA1c, and lower HDL compared to subjects with optimal BP.**

Risk of New-Onset HTN

- **The 5-year rates of HTN onset are approx. 10, 30, and 50% for optimal, normal, and high normal BP, respectively.**
- **However, the rates of progression among different age groups is not constant.**
- **Framingham Heart Study showed that, among subjects aged 35–94 years, the odds ratios for developing HTN among the normal and high-normal BP participants compared with the optimum BP participants over a 4-year interval were higher in the participants aged 35–64 years (younger age).**
- **Many other studies showed that, the risk of developing HTN by BP category at baseline compared with optimal BP tends to be greater in younger subjects compared to older subjects.**

The Age-Related Difference in the Impact of Systolic Vs. Diastolic BP

- **A number of studies have examined whether systolic and/or diastolic BP is associated with the risk of new onset HTN or CVD in different age groups.**
- **The pressor mechanism differs at different ages.**
- **Younger patients' HTN is characterized by neuro-hormonal activation (SNS and the RAS system).**
- **Whereas age-related vascular change is the predominant leading cause of systolic HTN older patients.**

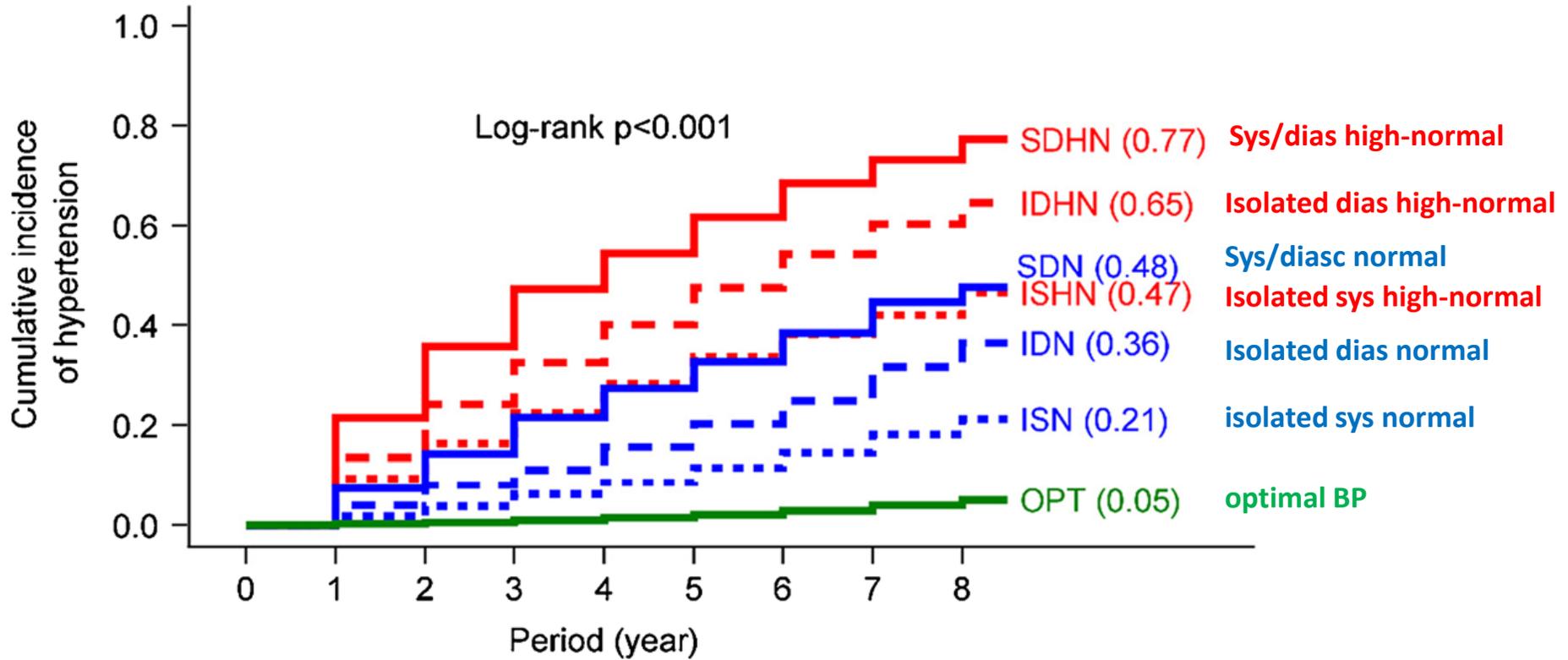
The Age-Related Difference in the Impact of Systolic Vs. Diastolic BP

- **The effect of DBP is greater than that of SBP on the risk of developing HTN and CVD in younger adults. The elevation of DBP is closely related to increased vascular resistance caused by SNS activation and/or RAS activation.**
- **Conversely, mainly increased vascular stiffness contributes to elevated SBP in elderly individuals.**
- **Moreover, it was shown that increased SBP variability (which is more closely associated with vascular stiffness) was related to age, whereas DBP variability showed no relation to age .**

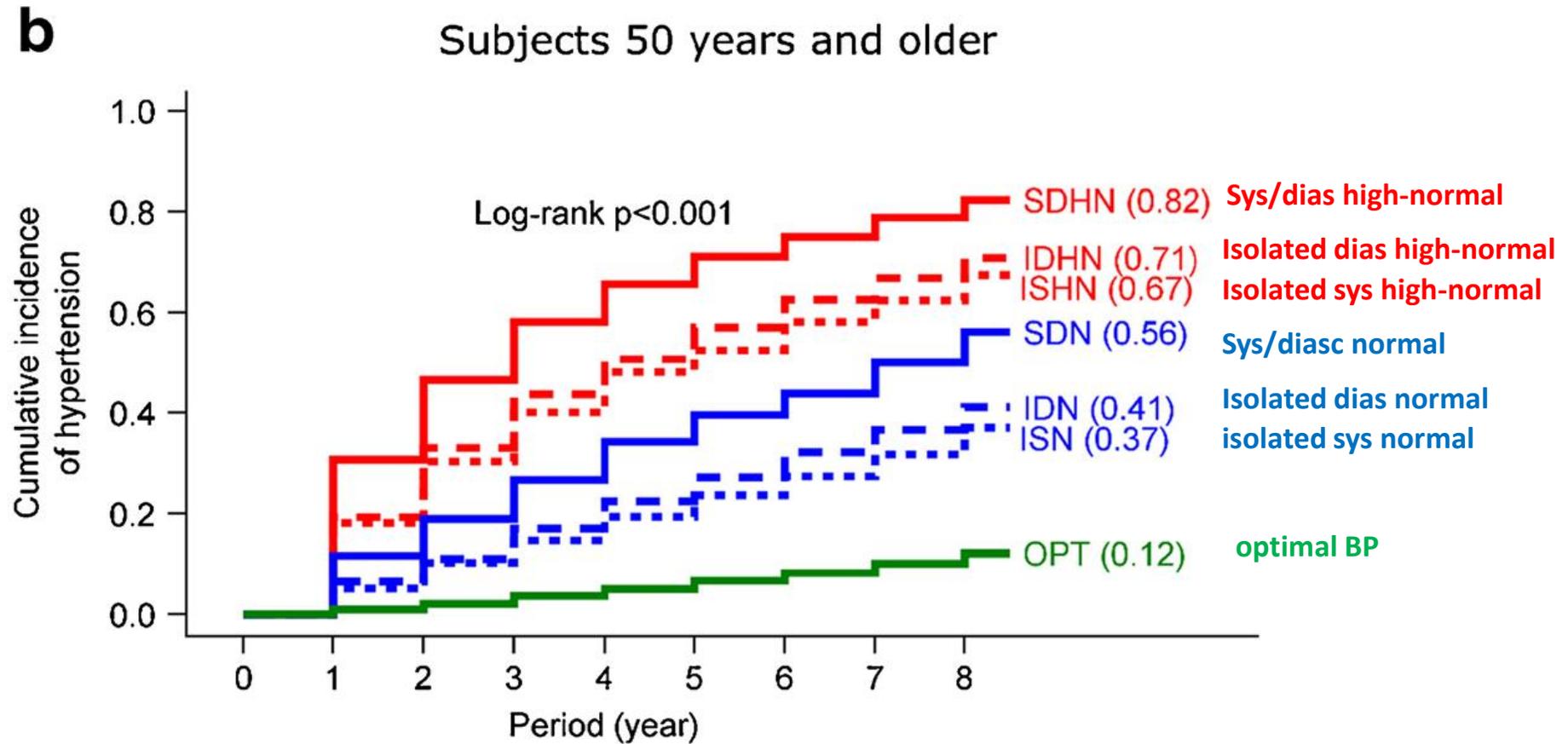
Cumulative incidence of HTN among normotensive subjects

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Subjects younger than 50 years



Cumulative incidence of HTN among normotensive subjects



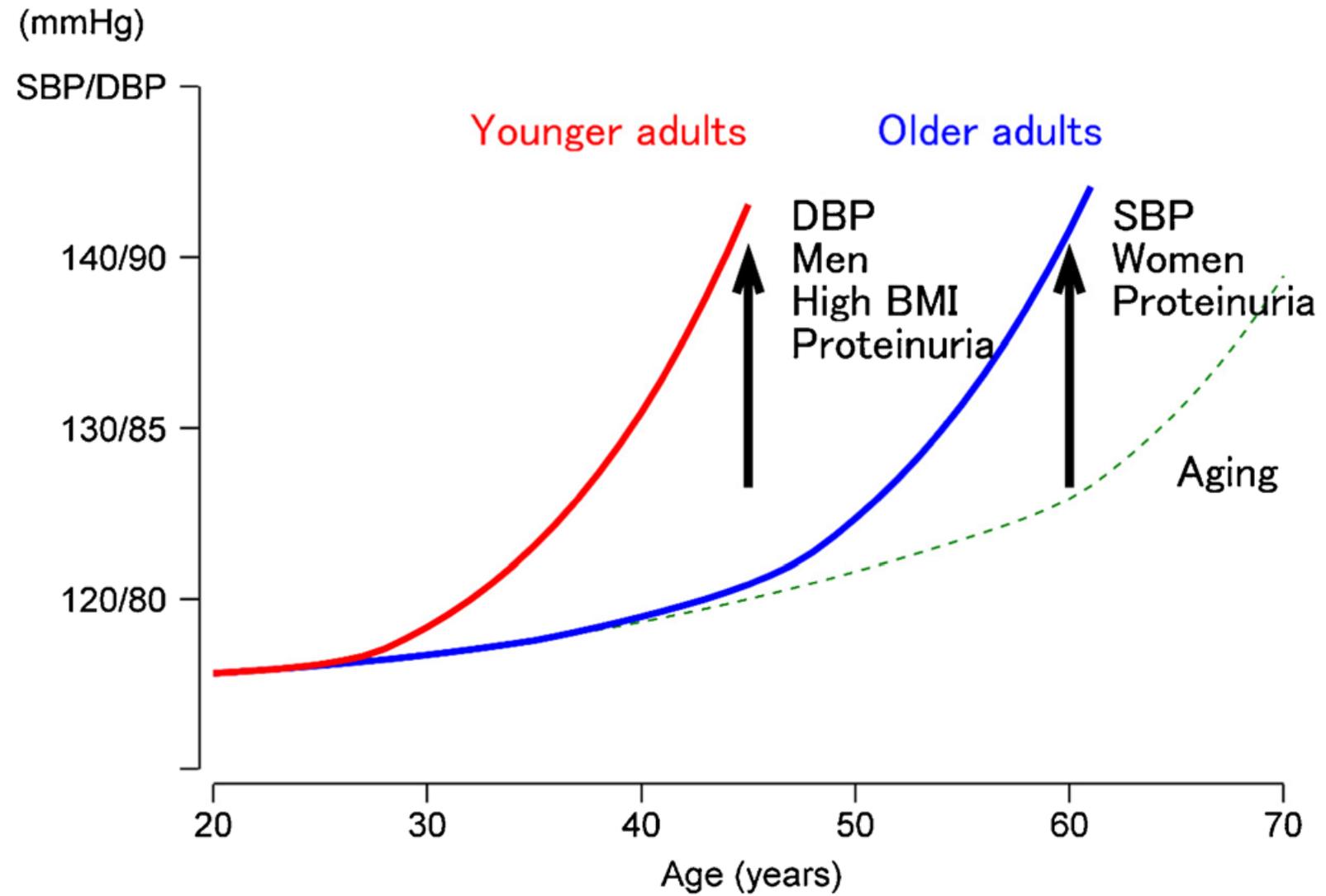
Obesity and Sex

- **The impact of obesity and sex on the new onset of HTN was greater in the younger adults compared to the older adults.**
- **Framingham Heart Study, showed that the OR for developing HTN for a 2-kg/m² increase in BMI over 4-year interval was higher in subjects aged 35–64 years compared to those aged 65–94 years, but sex was not an important risk of HTN.**
- **Other studies showed that BMI at baseline was a consistent predictor of risk of HTN, irrespective of age.**
- **females have a greater risk of HTN in the younger (<50 years), but not older subjects (HR = 0.74 for males, HR = 1.0 for females).**

Proteinuria

- **It was observed that proteinuria presented a risk of HTN in both younger and older adults.**
- **In one study to evaluate the association between proteinuria and the development of HTN in normotensive subjects (19–89 years old) showed that, proteinuria increased the risk of HTN by twofold.**
- **The early detection of proteinuria would be useful for the identification of individuals at high risk of developing HTN and for the individuals' motivation to modify their lifestyle.**

Age-related risk factors for new-onset HTN



Non-pharmacologic Approaches to Pre-HTN

- **The approach to the primary prevention of HTN is a combination of lifestyle changes: weight loss in overweight persons; increased physical activity; moderation of alcohol intake; and consumption of a diet that is higher in fruits, vegetables, and low-fat dairy products and lower in sodium content.**
- **The HTN Prevention Trial (subjects aged 25– 49 years, DBP 78–89 mmHg) was conducted to assess the effect of dietary changes on BP for 3 years. All four dietary-counseling treatment groups (reduced calories, reduced sodium, reduced sodium and calories, or reduced sodium and increased potassium) showed lower mean BPs than the control group and experienced fewer hypertensive events.**

Non-pharmacologic Approaches to Pre-HTN

- **In the Trial of HTN Prevention (THOP- 1 and THOP-2), weight reduction and sodium reduction were the effective short-term strategies for reducing BP in normotensives.**
- **Although the effects on average BP declined over time, reductions in the HTN incidence were achieved.**
- **In these studies, people with pre-HTN assigned to a sodium reduction intervention experienced a 25–30% lower risk of CV outcomes for 10 to 15 years after the trial.**

Pharmacologic Approaches to Pre-HTN

- **The early treatment of BP may reduce the incidence of HTN and the long-term consequences of HTN.**
- **The TRial Of Preventing HTN (TROPHY) study conducted to investigate pharmacologic interventions in patients with pre-HTN. The TROPHY results confirmed that treatment with an ARB can prevent or postpone the development of HTN, demonstrating a 66.3% reduction in HTN incidence relative to placebo at 2 years, and a 15.6% reduction in HTN incidence relative to placebo at 4 years.**
- **The pharmacologic treatment of pre-HTN thus appears to be feasible.**

Pharmacologic Approaches to Pre-HTN

- **The Danish HTN Prevention Project investigated whether early treatment with an ARB in young normotensive offspring of hypertensive parents persistently lowered BP after treatment withdrawal.**
- **The temporary treatment of subjects at high familial risk of future HTN with an ARB is feasible, but the treatment had no persistent effect on BP when treatment was withdrawn.**
- **In the Prevention of HTN with the ACE-I Ramipril in patients with high-normal BP (PHARAO) study, ramipril was more effective in reducing the incidence of HTN at 3 years follow-up (34.4% relative risk reduction).**

Pharmacologic Approaches to Pre-HTN

- **The Prevention of HTN in Patients with Pre-HTN (PREVER-Prevention) trial aimed to evaluate the efficacy and safety of a low-dose diuretic for the prevention of HTN and end-organ damage.**
- **The incidence of HTN at 18-month follow-up was significantly lower in the diuretics group compared to the placebo group (HR 0.56), resulting in a cumulative incidence of 11.7% in the diuretic arm versus 19.5% in the placebo arm (p = 0.004).**
- **In addition, the LV mass decreased to a greater extent in the participants allocated to diuretic therapy compared to placebo (p = 0.02).**

Pharmacologic Approaches to Pre-HTN

- **The clinical trials showed that, early pharmacologic treatment of BP is feasible and reduces the incidence of HTN and the end-organ damage, at least during the on-medication period.**
- **The persistent effects of the withdrawal of the medication may postpone the development of HTN for a while.**
- **We should consider the cost and the benefits of pharmacologic intervention in regard to the prevention of HTN and subsequent CV risks.**

Conclusions

- **Lifestyle modifications including weight loss, increased physical activity, and dietary changes have been shown to reduce the incidence of HTN and should be recommended for all persons and especially those with pre-HTN.**
- **Careful observation is recommended for younger adults with pre-HTN who have risk factors such as high DBP, male sex, high BMI, or proteinuria, and the appropriate timing of pharmacologic treatment should not be missed.**