

**“The Waitemata Renal Service,
has been, since its inception,
and always will be,
The finest renal service in New
Zealand”**

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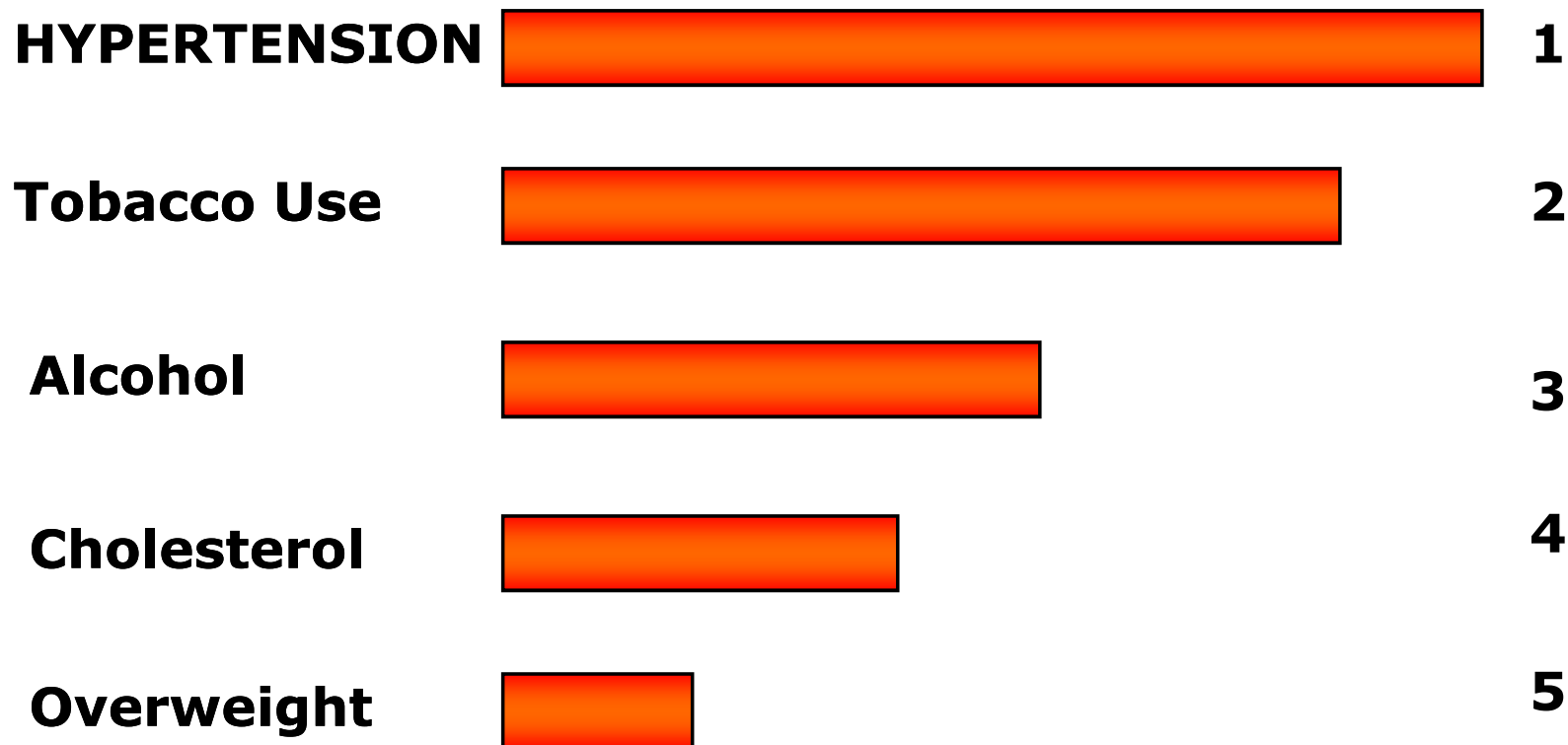
Hypertension: what to target?



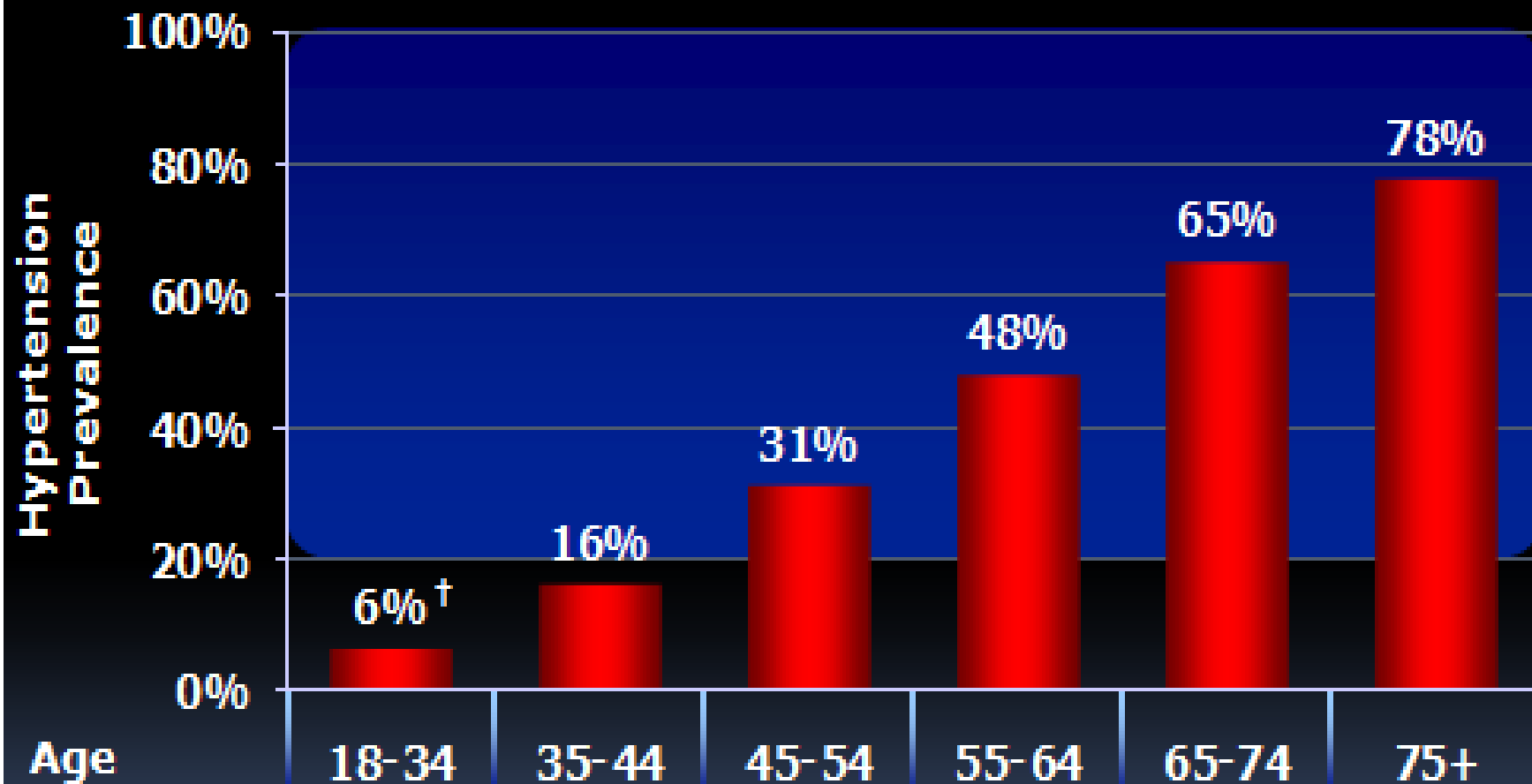


Inaugural meeting of the NZ Hypertension society (de Zoysa on right)

Leading remediable risks for premature death worldwide (WHO)



Prevalence of Hypertension in the United States by Age Group*



*Based on data from the 1999–2000 National Health and Nutrition Examination Survey. Hypertension is defined as blood pressure $\geq 140/90$ mm Hg or as receiving antihypertensive treatment.

[†]Low reliability due to large relative error.

Fields LE, et al. *Hypertension*. 2004;44:398-404.

Slide Source
Hypertension Online
www.hypertensiononline.org

BP targets

BP measurement

- Conventional office
- Office AOBP
- ABPM
- HBPM
- Central aortic pressure and augmentation index

Antihypertensive Drug Algorithms/ Titration

Drug class effects

Resistant hypertension

- pathophysiological targets

BP in CKD and renal transplant recipients

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BP targets

What have we learned in the last few years?

“Lower is not necessarily better and may sometimes be worse”

**< 130/80 target for diabetes and CKD
not strongly evidence-based**

Primary Cardiovascular Outcome

ACCORD

ONTARGET – post hoc analysis

INVEST – post hoc analysis

HOT

JATOS

Primary Renal Outcome (GFR)

AASK

MDRD

REIN-2

ABCD

Lewis

Strong evidence that targeting BP < 130/80 (rather than 140/90) benefits:

- cardiovascular outcomes in CKD X
- rate of progression of GFR loss in non-proteinuric CKD X

There is strong evidence, particularly in diabetics, that in CKD associated with >1g proteinuria, for the same achieved blood pressure, patients whose regimen includes a RAS-blocker have improved renal outcomes compared with patients whose regimen does not include a RAS-blocker

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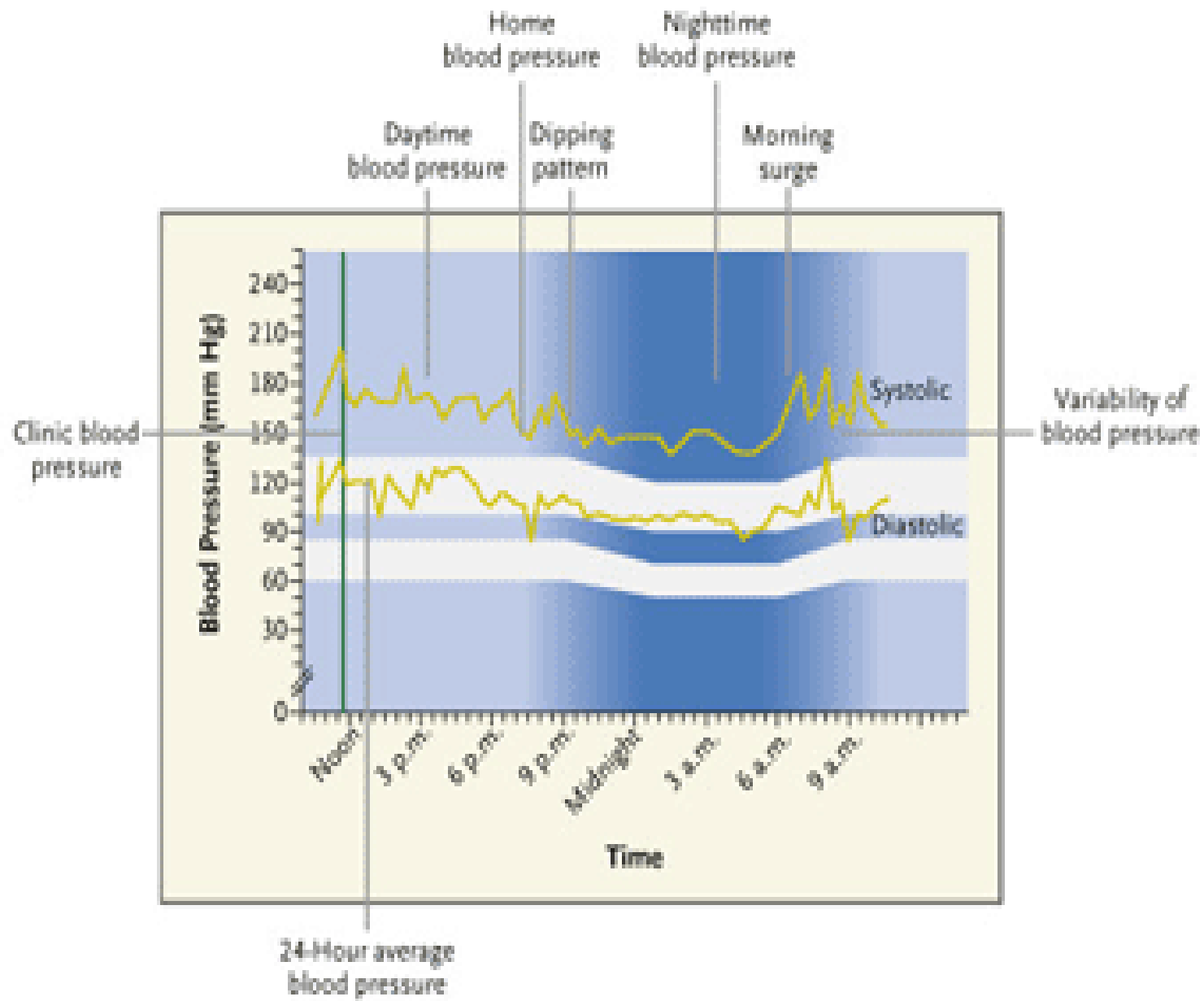


“Conventional office BP measurement can no longer be regarded as the standard of care and has been replaced by automated office BP measurement (AOBPM)”

Up to date review of AOBPM literature

“The great myth of office BP
measurement”

*Myers MG. J Hypertens 2012 Aug 4 (E pub
ahead of print)*



Diagnosis (1)

If clinic blood pressure is 140/90 or higher, offer ambulatory blood pressure monitoring (ABPM) to confirm the diagnosis of hypertension

August 2011

NICE clinical guideline 127

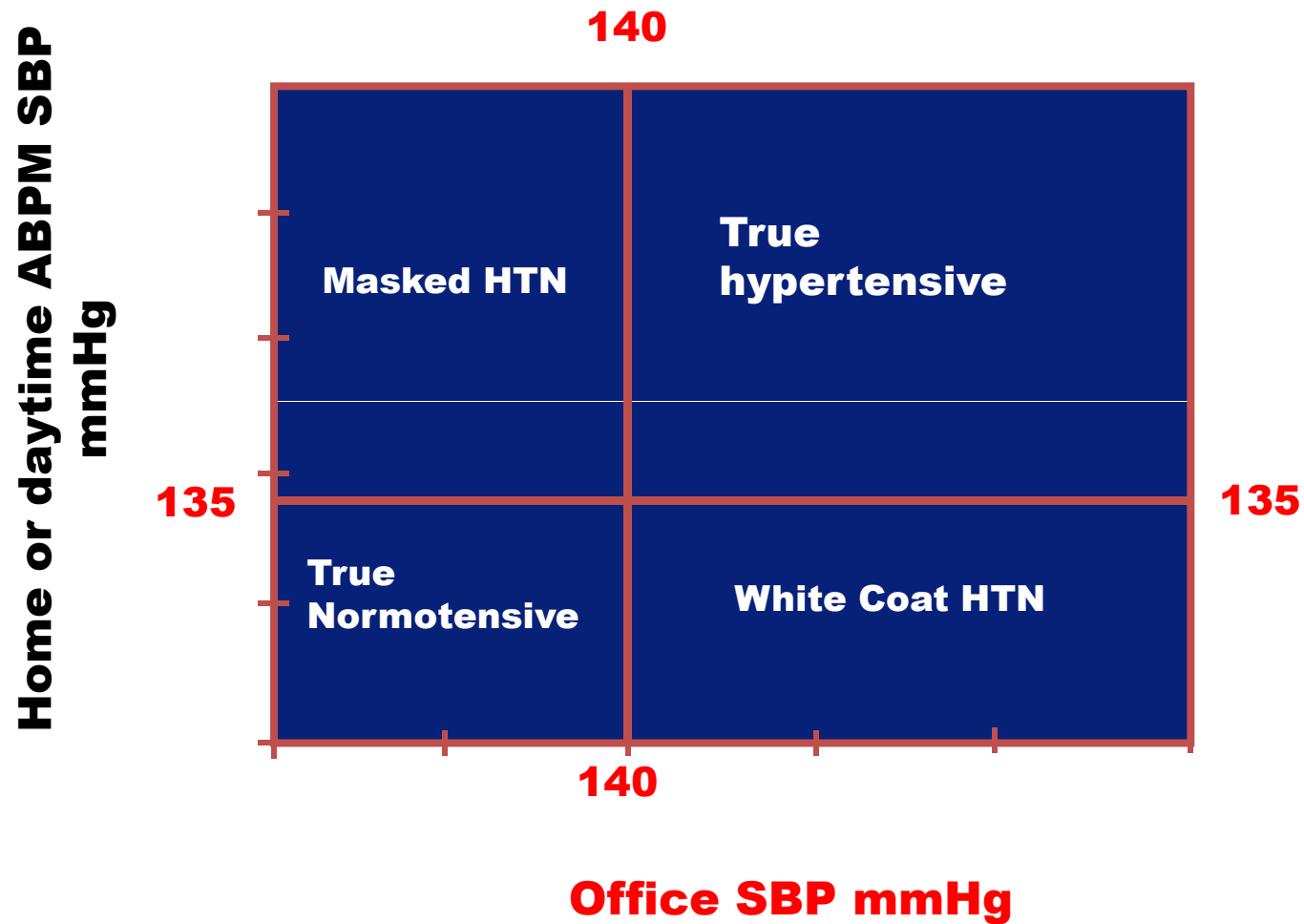


In the general hypertensive population

20-25% of patients with elevated office BP
have a normal ABPM profile

10-15% of patients with normal office BP
have abnormal ABPM profile

The concept of masked hypertension



From Pickering, Hypertension 1992

Home BP monitoring

- Accuracy and prognostic value – intermediate between office BPM and ABPM
- Useful tool as an aid to compliance
- Useful tool in monitoring patients with White Coat Hypertension and assessing response to therapy in patients with established hypertension
- Gives no information about overnight (asleep) blood pressure

Circulation

American Heart
Association®

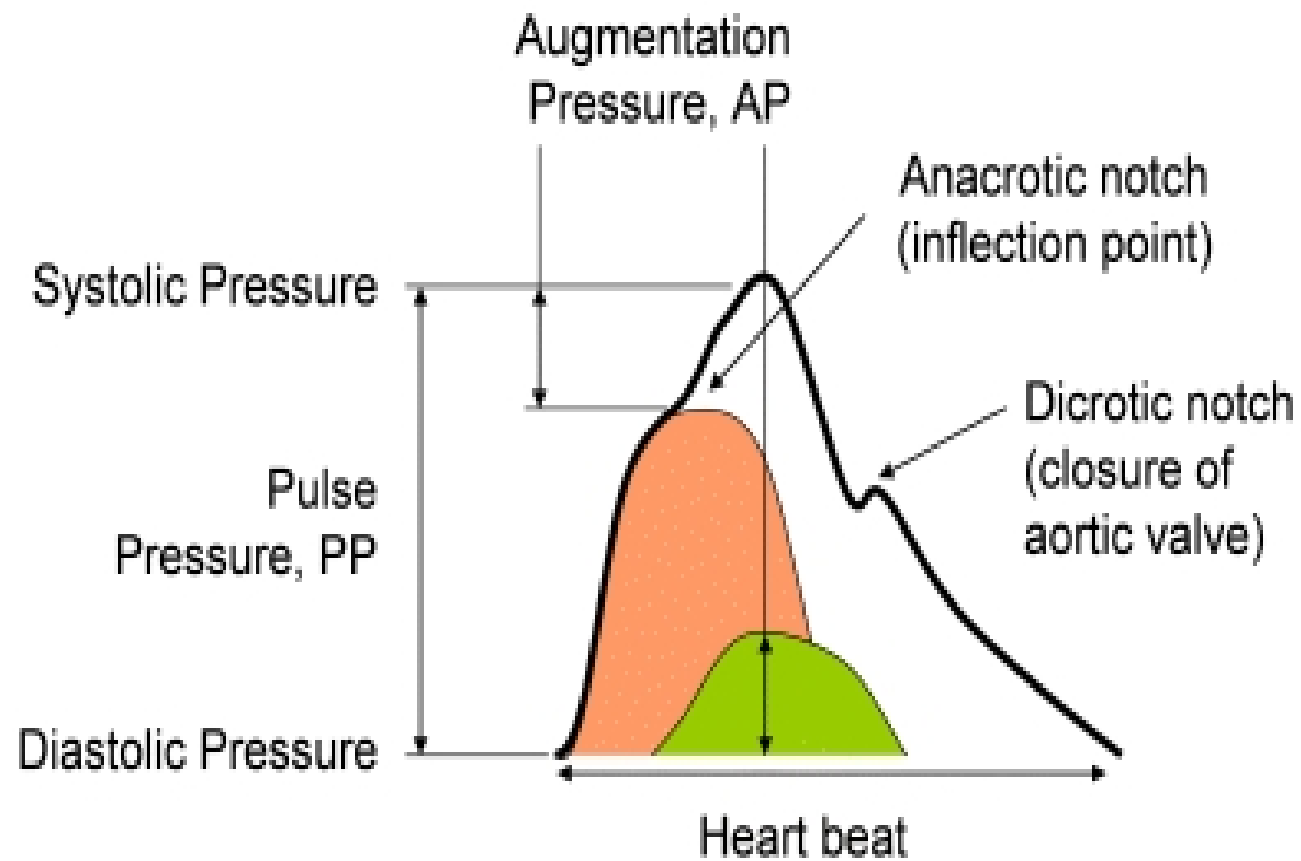


2006; 113: 1213-1225

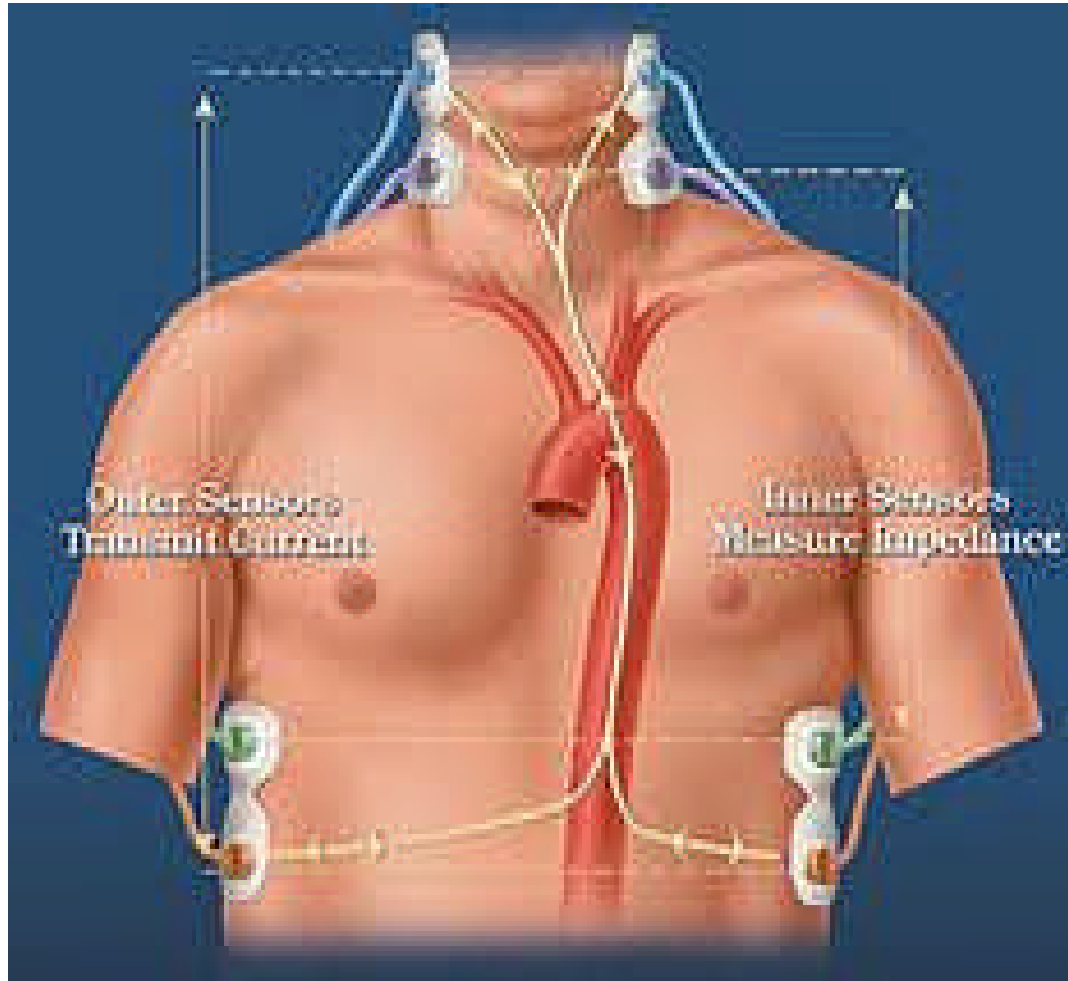
**Differential Impact of Blood Pressure–
Lowering Drugs on Central Aortic Pressure
and Clinical Outcomes
Principal Results of the Conduit Artery
Function Evaluation (CAFE) Study**

Central aortic blood pressure and augmentation index





Thoracic Bioimpedance



“Not ready for prime time but may be useful in post-transplant hypertension”
S Taler. Mayo

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Stage 2 hypertension under 75 years

Lisinopril 10mg mane (Candesartan 8mg if ACE-inhibitor intolerant) +
amlodipine 5mg mane or diltiazem CD 120mg mane
(start with candesartan 8mg if ACE-inhibitor intolerant)

Increase lisinopril 20 mg OR candesartan 16mg daily

Increase Lisinopril to 40mg OR Candesartan to 32mg daily

Increase amlodipine to 10mg OR diltiazem CD to 240-360mg

Add chlorthalidone 12.5mg daily, titrating to 25mg daily

Add spironolactone 12.5mg daily, titrating to 25mg daily

Add atenolol 25mg BD and doxazosin 1mg nocte, titrating to
atenolol 50mg BD and doxazosin 2mg nocte

Central sympatholytic (clonidine, methyldopa, moxonidine)

Direct vasodilator (hydralazine, minoxidil)

Thiazide intolerance – consider loop diuretic
Spironolactone intolerance – consider eplerenone or amiloride
Beta blocker intolerance - consider adding diltiazem to amlodipine
ARB intolerance – consider aliskerin

ALLOW 2 WEEKS
Between each
dose adjustment

CHECK
urea creatinine
and electrolytes
two weeks after
introduction or
increase of ACE
inhibitor or ARB
or diuretic

THE NEW ZEALAND MEDICAL JOURNAL

New Zealand Medical Association 25 May 2012 Vol 125
No.1355: 31-40

Nurse titration clinics to achieve rapid control of blood pressure

Dominic Taylor, Veronica van der Merwe,
Walter van der Merwe

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Three mechanisms known to contribute to blood pressure elevation in essential hypertension

- renin angiotensin system
- volume
- sympathetic nervous system

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Aldosterone

- Effects not limited to regulation of sodium and potassium handling in distal nephron
- In all animal models studies aldosterone causes vascular inflammation and myocardial injury and proteinuria independent of blood pressure
- Non-adrenal sites of aldosterone production not regulated by systemic RAAS (**fat cells** and cardiac, vascular)
- Mineralocorticoid receptors in heart and blood vessels

Spironolactone

- Most effective add-on 4th drug in resistant hypertension
- Efficacy not limited to patients with high aldosterone levels
- Beneficial effects on glucose and lipid metabolism
- Antiproteinuric effects
- Particularly effective in hypertension assoc with metabolic syndrome
- Improved outcomes in heart failure
- Counteracts thiazide-induced K⁺ and Mg⁺⁺ wasting

In essence in a patient with RH and normal renal function you can't be sure they have hidden Na⁺/volume until

they are on

chlorthalidone 25mg daily (or equivalent)

+

spironolactone 25mg daily (or equivalent)

or

renal function goes off

Hypertension

JOURNAL OF THE AMERICAN HEART ASSOCIATION



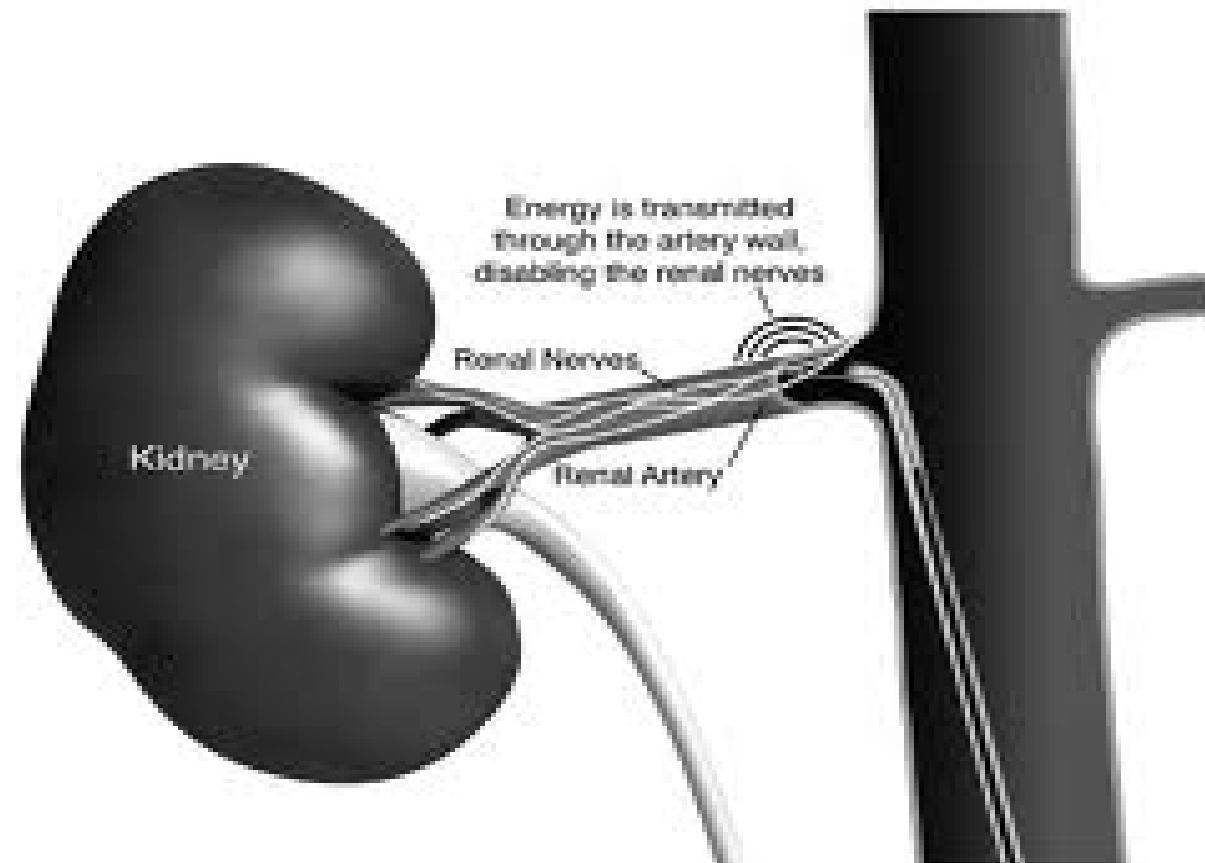
2007;49:839-845

Effect of Spironolactone on Blood Pressure in Subjects With Resistant Hypertension

Neil Chapman, Joanna Dobson, Sarah Wilson, Björn Dahlöf, Peter S. Sever, Hans Wedel and Neil R Poullter

Three mechanisms known to contribute to blood pressure elevation in essential hypertension

- renin angiotensin system
- volume
- **sympathetic nervous system**





"I suppose it is tempting, if the only tool you have is a hammer, to treat everything as if it were a nail."

Abraham Maslow 1908-1970

Catheter-based renal sympathetic nerve ablation
procedure

*irreversible, expensive, painful, risks of contrast and
aortic catheterisation*

“Clinic-based reversible sympathetic receptor
blockade”

reversible, cheap, safe, effective

Sympathetically mediated blood pressure reactivity is associated with increased catecholamine stimulation of beta receptors (increase in cardiac output and heart rate) and alpha receptors (increase peripheral resistance) often with one or other effect predominating



Monotherapy with either alpha or beta blockers for hypertension is often disappointing



Beta blockers ↓ HR and cardiac output, but unopposed alpha activity increases peripheral vasoconstriction and mutes BP-lowering effect



Alpha blockers ↑ peripheral vasodilation, but
unopposed beta activity increases cardiac output
and heart rate and mutes BP-lowering effect



Combining alpha and beta blockers may have a
disproportionately beneficial BP-lowering effect



Really???



So why hasn't it hit the prime time?



We ain't doing it right

Bioavailability

- bioavailability extremely variable and often low due to cytochrome P450–mediated first-pass hepatic metabolism

Propranolol, metoprolol, labetalol and carvedilol

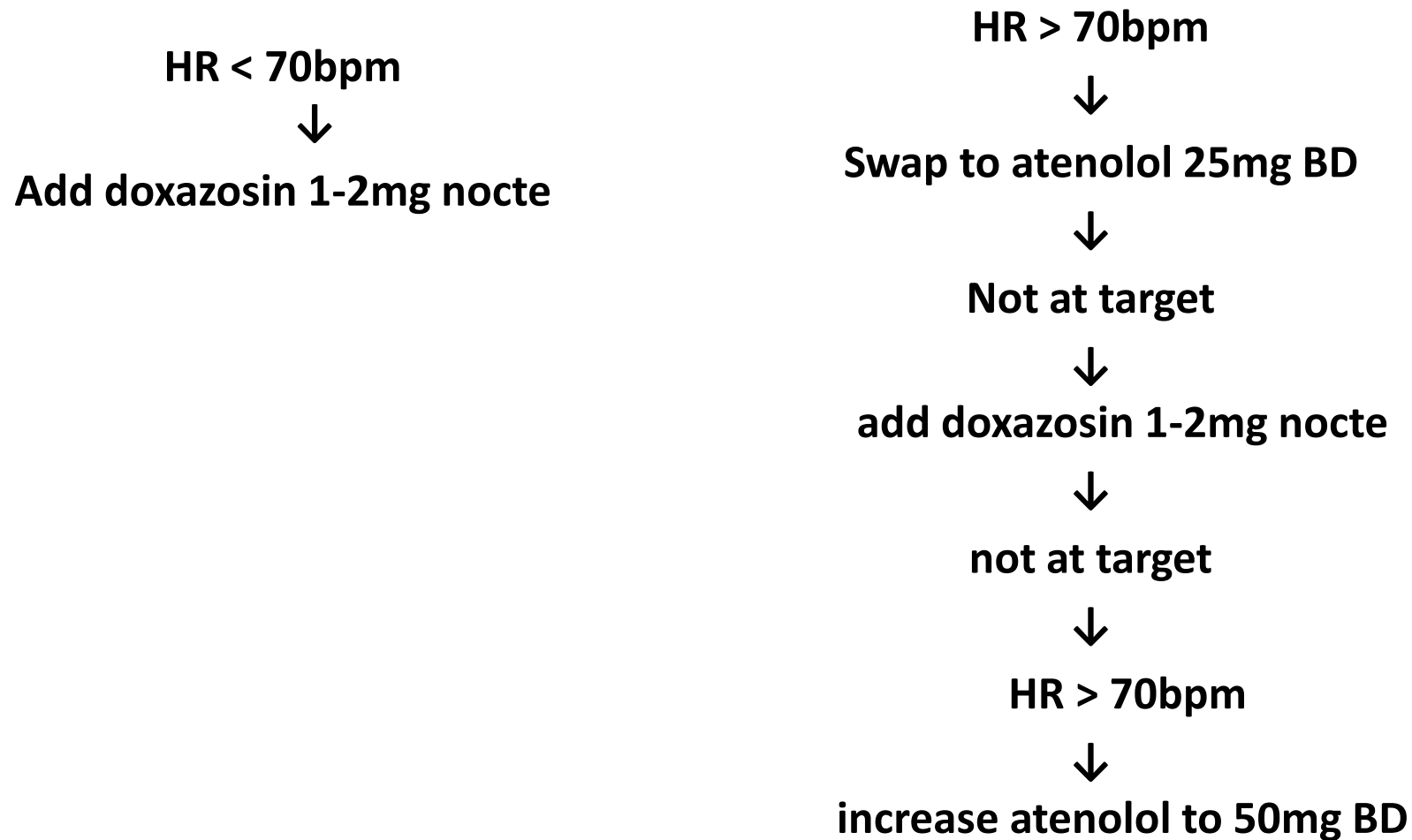
- not subject to this metabolic process

Atenolol, pindolol

Most reliable way of achieving effective combined alpha and beta blockade is to combine atenolol and doxazosin

BP not at target on optimal doses of 4 drugs?

Already on metoprolol or carvedilol?



BP not at target on optimal doses of 4 drugs?

Not yet on a beta blocker?



HR > 70bpm



add doxazosin 1-2mg nocte and atenolol 25mg BD



not at target



HR > 70bpm



increase atenolol to 50mg BD

***The Journal of Clinical
Hypertension***

***Volume 14, Issue 4, pages 191–
197, April 2012***

***Article available free on-line via
JCH website***

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Drug class effects

- Inter-individual blood pressure variability
- Worse outcomes in thiazide arm of ACCOMPLISH trial

THE LANCET

2010;375:895-905

Prognostic significance of visit-to-visit variability,
maximum systolic blood pressure, and episodic
hypertension

Rothwell P et al

Drug class effects

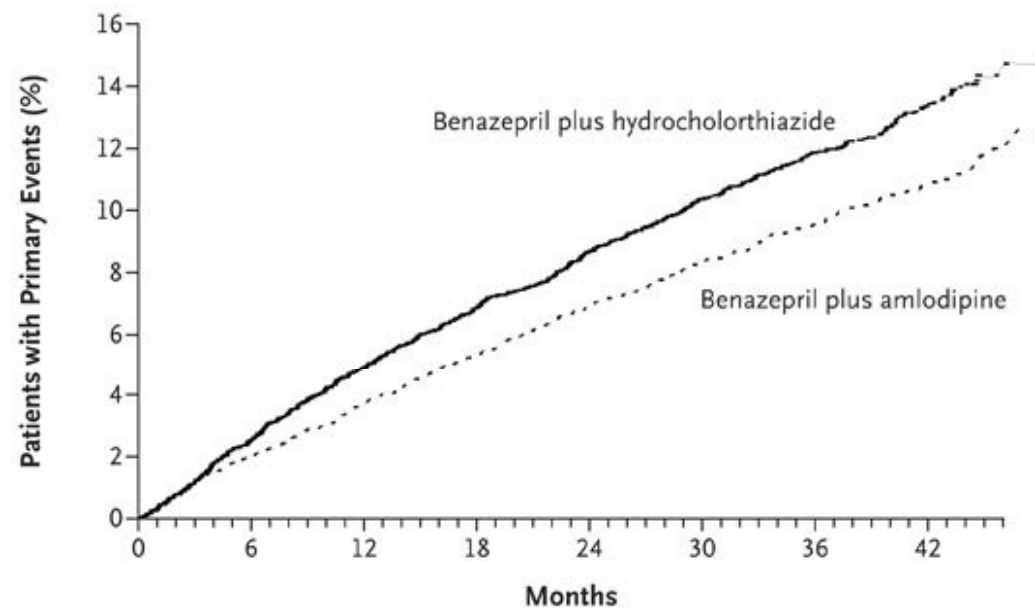
- Inter-individual blood pressure variability
- Worse outcomes in thiazide arm of ACCOMPLISH trial

Original Article

Benazepril plus Amlodipine or Hydrochlorothiazide for Hypertension in High-Risk

**Jamerson, M.D., Michael A. Weber, M.D., George L. Bakris, M.D., Björn
Dahlöf, M.D., Bertram Pitt, M.D., Victor Shi, M.D., Allen Hester, Ph.D., Jitendra
Gupte, M.S., Marjorie Gatlin, M.D., Eric J. Velazquez, M.D., for the ACCOMPLISH
Trial Investigators**

N Engl J Med
Volume 359(23):2417-2428
December 4, 2008



No. at Risk

Benazepril plus amlodipine	5512	5317	5141	4959	4739	2826	1447
Benazepril plus hydrochlorothiazide	5483	5274	5082	4892	4655	2749	1390



All excess risk in thiazide arm
in non-obese individuals

(Obesity paradox in
hypertension)

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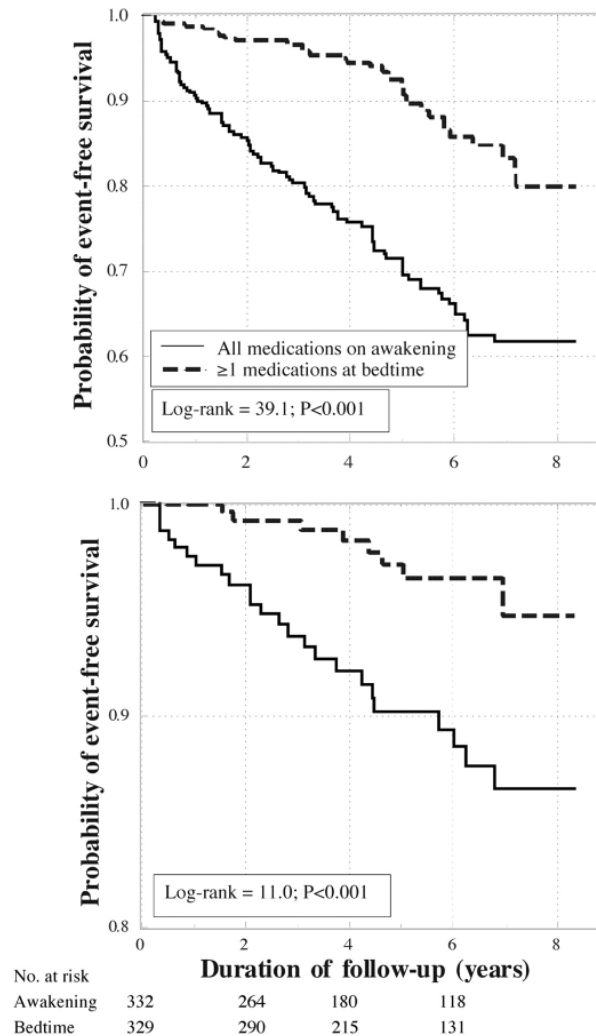
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Kaplan-Meier survival curves as a function of time-of-day of hypertension treatment, i.e., for patients with CKD ingesting either all their BP-lowering medications upon awakening or ≥ 1 medication at bedtime, for total CVD events (top) and major CVD events (...)



Hermida R C et al. JASN

©2011 by American Society of Nephrology

2011;22:2313-2321



Transplant hypertension

Office blood pressure

Target < 130/80

ABPM

Target 24h <125/75

Target awake average < 130/80

Target asleep average < 120/70

Concordant normotension

Office BP < 130/80 and all ABPM parameters at target

Concordant hypertension

Office BP \geq 130/80 with any ABPM parameter above target

White Coat Hypertension

Office BP \geq 130/80 with all ABPM parameters at target

Masked Hypertension

Office BP < 130/80 with any ABPM parameter above target

Results

Concordant normotension **34%**

Office BP < 130/80 and all ABPM parameters at target

Concordant hypertension **14%**

Office BP \geq 130/80 with any ABPM parameter above target

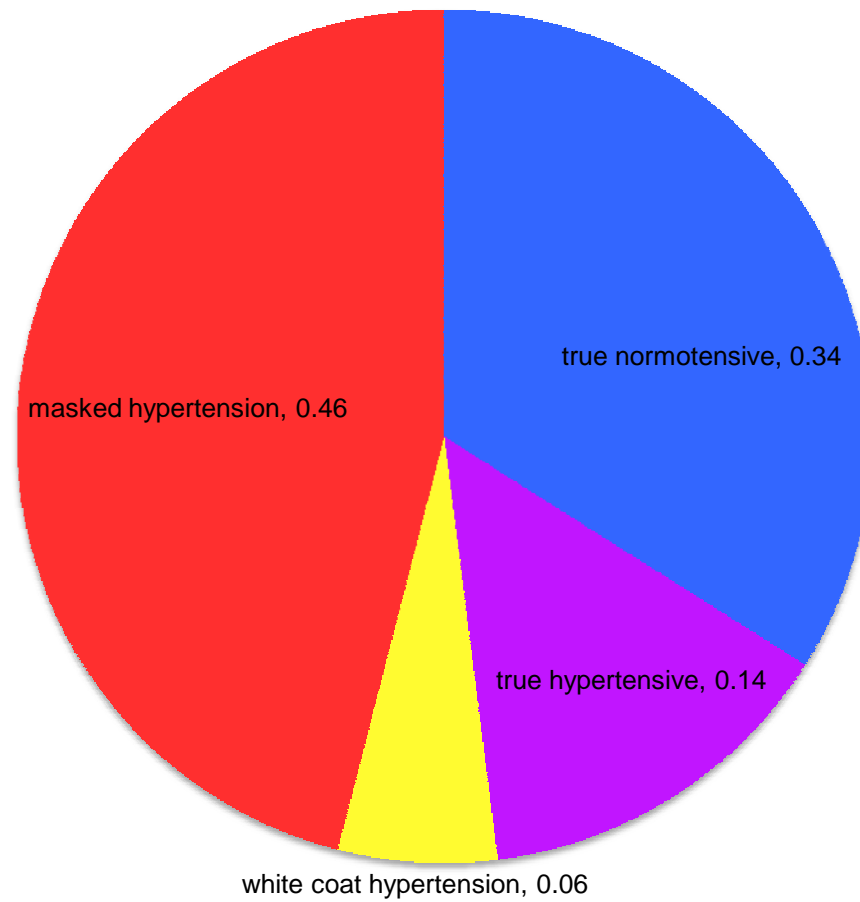
White Coat Hypertension **6%**

Office BP \geq 130/80 with all ABPM parameters at target

Masked Hypertension **46%**

Office BP < 130/80 with any ABPM parameter above target

Office BP and ABPM concordance



2020 New Zealand Hypertension Society Meeting

