



Better Blood Pressure Control: the earlier the better

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Conflict of Interest Declaration: Tobe

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Major Shareholder	N/A
Other Financial/Material Support	N/A

Objectives

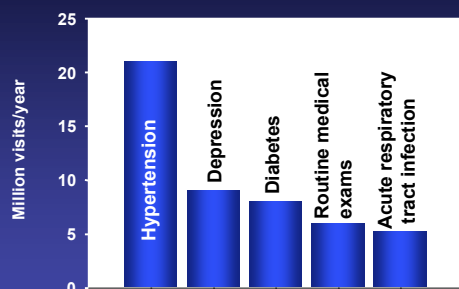
- To discuss new data regarding high normal BP and new recommendations for these patients
- To review the role of screening for urine albumin in hypertensives without and with diabetes

Hypertension as a Risk Factor

Hypertension is a significant risk factor for:

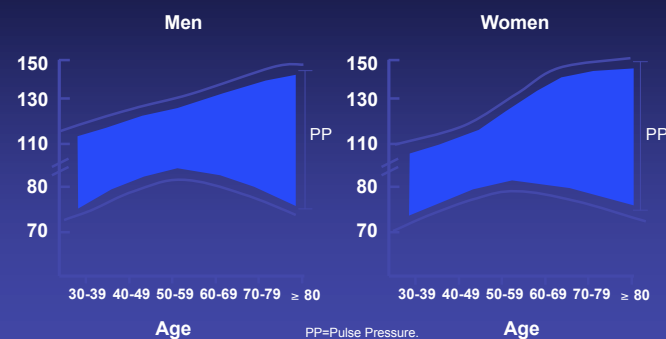
- cerebrovascular disease
- coronary artery disease
- congestive heart failure
- renal failure
- peripheral vascular disease
- dementia
- atrial fibrillation

Leading diagnoses resulting in visits to physician offices in Canada



Source: IMS HEALTH Canada 2002. <http://www.imshealthcanada.com/>

Blood Pressure Distribution in the Population According to Age



Adapted from : Third National Health and Nutrition Examination Survey. *Hypertension* 1995;25:305-13

Classification of Hypertension

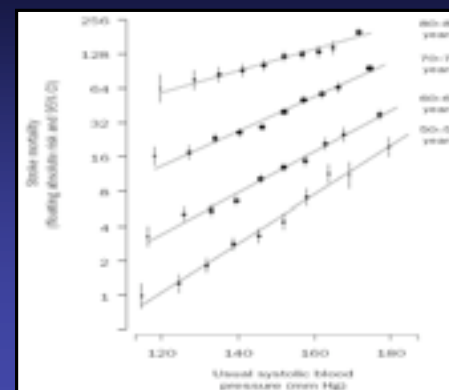
(Pre Hypertension) 120-139 / 80-89

Category	Systolic	and / or	Diastolic
Optimal	<120	and / or	<80
Normal	<130	and / or	<85
High-Normal	130-139	and / or	85-89
Grade 1 (mild hypertension)	140-159	and / or	90-99
Grade 2 (moderate hypertension)	160-179	and / or	100-109
Grade 3 (severe hypertension)	≥ 180	and / or	≥ 110
Isolated Systolic Hypertension (ISH)	≥140	and / or	<90

The category pertains to the highest risk blood pressure

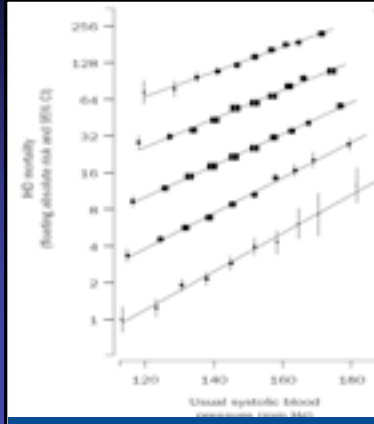
*ISH=International Society of Hypertension. Chalmers J et al. *J Hypertens* 1999;17:151-85.

Blood Pressure and Risk of Stroke Mortality



Lancet 2002;360: 1903-13

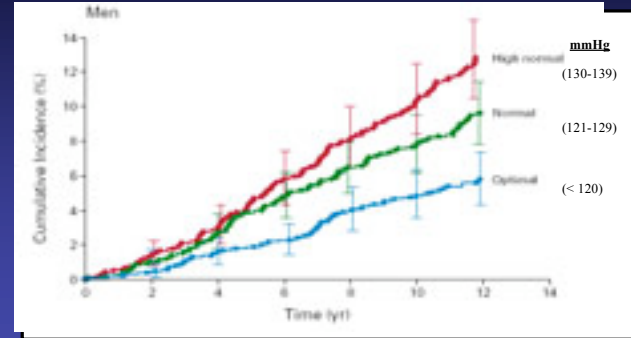
Blood Pressure and Risk of IHD Mortality



Lancet 2002;360: 1903-13

Impact of High-Normal Blood Pressure on the Risk of Cardiovascular Disease

CUMULATIVE INCIDENCE OF CV EVENTS IN MEN WITHOUT HYPERTENSION ACCORDING TO BASELINE BLOOD PRESSURE



N Engl J Med 2001;345:1291-7

2007 Canadian Recommendations for the Management of Hypertension

A slide kit for medical education can be downloaded from:

<http://www.hypertension.ca>

Incidence rates of hypertension at 1, 2 and 3 yrs

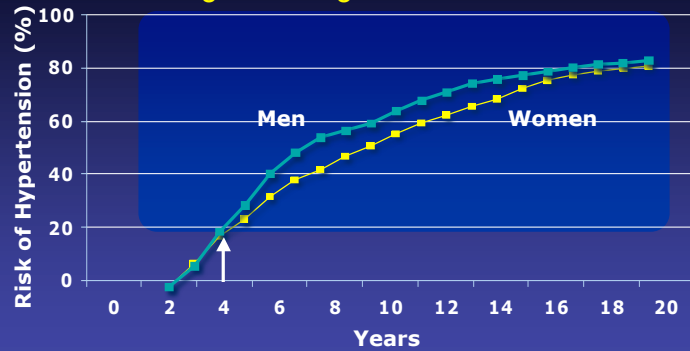
Baseline BP category	Age 35-64 years	Age 65-94 years
% hypertension at 1 year (95% CI)*		
Optimum BP	1.3 (1.1-1.6)	4.3 (3.1-5.7)
Normal BP	4.7 (4.0-5.5)	7.1 (5.5-9.0)
High normal BP	11.0 (9.6-12.6)	15.7 (13.0-18.8)
% hypertension at 2 years (95% CI)*		
Optimum BP	2.7 (2.2-3.2)	8.3 (6.2-11.1)
Normal BP	9.2 (7.9-10.7)	13.7 (10.8-17.2)
High normal BP	20.8 (18.3-23.5)	28.9 (24.2-34.0)
% hypertension at 3 years (95% CI)*		
Optimum BP	4.0 (3.3-4.8)	12.2 (9.2-16.1)
Normal BP	13.5 (11.6-15.7)	19.8 (15.7-24.6)
High normal BP	29.6 (26.2-33.1)	40.1 (34.0-46.4)

*Rates are per 100, and are adjusted for sex, age, body-mass index, baseline examinations, and baseline systolic and diastolic BP.

Optimum < 120/80
Normal 120-129/80-84
High normal 130-139/85-89

Vasan. Lancet 2001

Lifetime Risk of Developing Hypertension Among Adults Aged 55 to 65 Years*



*Residual lifetime risk of developing hypertension among adults aged 55 to 65 years with a blood pressure <140/90 mmHg.

Vasan RS, et al. *JAMA*. 2002; 287:1003-1010. Copyright 2002, American Medical Association.

Impact of high-normal BP on risk of cardiovascular disease.

- Framingham cohort (n=6859)
- High normal BP at baseline
- 10-year cumulative incidence of CVD (CV death, MI, stroke, CHF)

	35-64 years	65-90 years
Men	8% (6% - 10%)	25% (17% - 34%)
Women	4% (2% - 5%)	18% (12% - 23%)

NEJM 2001;345:1291-7

TROPHY Study

- 4-year, multicenter, RCT
- Does candesartan reduce progression to hypertension from prehypertension, compared with placebo
- Treatment-naïve, mean BP \leq 139/85-89 mmHg or 130-139/<89 mmHg

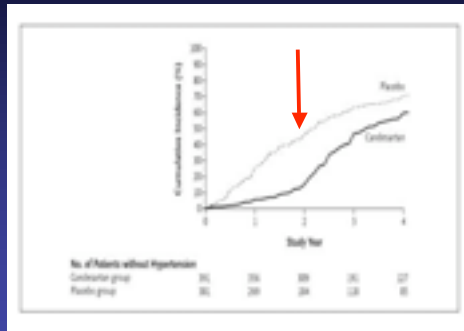
Julius et al. *N Engl J Med* 2006

Incidence of hypertension in those identified with borderline hypertension

- 772 subjects, mean age 48.5
- Not receiving tx for HTN
- Avg of 3 BPs at baseline:
SBP 130-139 and DBP < 89 OR
SBP < 139 and DBP 85-89
- Primary endpoint – new onset HTN
- Note that mean BMI was 30!

NEJM 2006;354:1685-97

Kaplan-Meier Plot of New Onset HTN in an RCT



Baseline BP 130-139 / 85-89 mmHg

Julius et al. *NEJM* 2006;354:1685-97

High risk of developing hypertension in those with high normal blood pressure

- 40% of patients with systolic 130-139 or diastolic 85-89 mmHg developed hypertension in 2 years and 63% in 4 years *NEJM* 2006;354:1685-97
- Annual follow-up of patients with high normal blood pressure is recommended.



NEJM 2006;354:1685-97

Impact of Lifestyle Therapies on Blood Pressure in Hypertensive Adults

Intervention	Amount	SBP/DBP
Reduce foods with added sodium	1.8g or 78 mmol/d	-5.1 / -2.7
Weight loss	per kg lost	-1.1 / -0.9
Alcohol intake	- 3.6 drinks/day	-3.9 / -2.4
Aerobic exercise	120-150 min/week	-4.9 / -3.7
Dietary patterns	DASH diet	-11.4 / -5.5
	Hypertensive Normotensive	-3.6 / -1.8

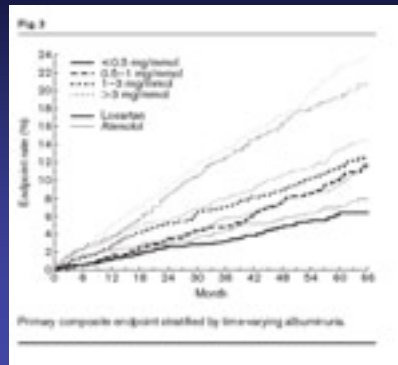
Applying the 2005 Canadian Hypertension Education Program recommendations: 3. Lifestyle modifications to prevent and treat hypertension Padwal R. et al. *CMAJ* · SEPT. 27, 2005; 173 (7): 749-751

Lifestyle Modification can reduce and prevent hypertension – if advice is followed correctly



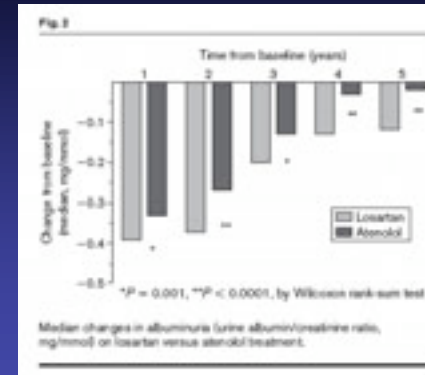
“My Doc told me to walk my dog regularly”

LIFE MAU Substudy Risk of primary composite endpoint related to the in-treatment level of albuminuria



Ibsen H. *J Hypertension* 2004

Albuminuria Level Fell During LIFE Study in Both Atenolol and Losartan Groups



Ibsen H. *Hypertension* 2004

End Points in LIFE study in those with a fall in ACR from Baseline to 1 Year from above the median to below the median compared to those remaining above the median:

BL	1 Year	Composite n (%)	CV mortality n (%)	Stroke n (%)	MI N (%)
Above Median	Below Median	92/978 (9.4%)	34/995 (3.4%)	44/984 (4.5%)	37/990 (3.7%)
Above Median	Above Median	351/2601 (13.5%)	161/2643 (6.1%)	169/2616 (6.5%)	123/2628 (3.4%)

Ibsen H. *Hypertension* 2005;45, 198

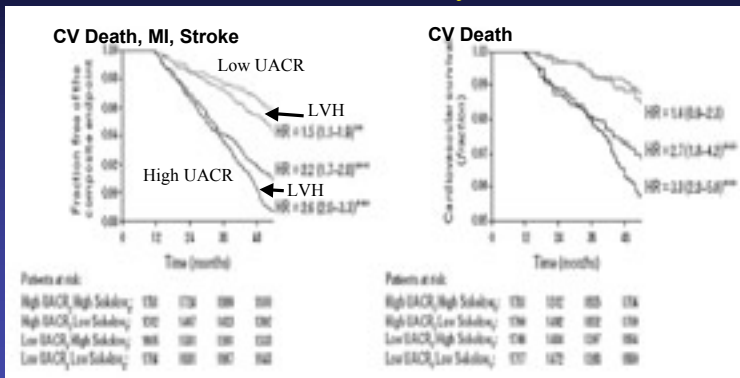
Baseline EKG-LVH and MAU as independent predictors in LIFE

- 6679 hypertensive patients from the LIFE study
- Question was whether LVH and MAU were independent predictors of CVD mortality/ MI/CVA
- 3-4 year follow-up. Excluded patients with events in the first year.

Olsen MH. *J Hypertension* 2006;24:775

Olsen et al. *J Hypertens* 2006;24:775

Baseline EKG-LVH and abnormal Urine Albumin Levels are independent predictors in LIFE sub-Study

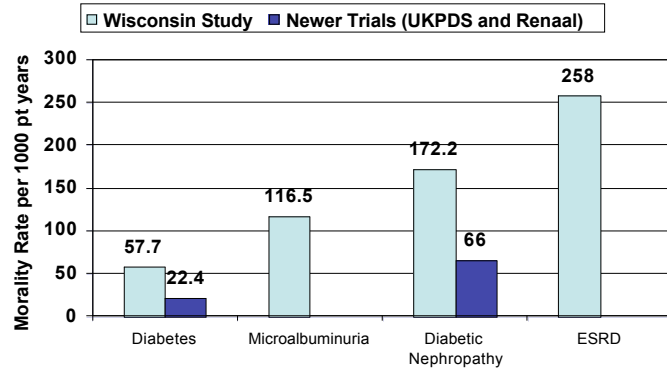


Olsen MH, J Hypertension 2006;24:775
 Olsen et al. J Hypertens 2006;24:775

Measuring Urine Albumin in Hypertensives at High Risk

- A greater fall in urine albumin with treatment was associated with better outcome, but:
 - A significant fraction had diabetes
 - Targeting lower urine albumin levels was not the intervention
 - Most of the patients had urine albumin within the normal range
 - Most of the albumin lowering effect was due to reduction of BP
- Therefore this is not sufficient evidence to recommend urine albumin screening in non-diabetic hypertensives

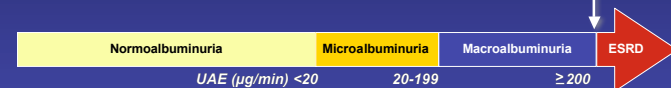
Ibsen H, Hypertension 2005;45, 198
 Olsen MH, J Hypertension 2006;24:775



UKPDS 33. Lancet 1998;352:837-53.
 Valmadrid CT. The Wisconsin Study: Risk of CV mortality with microalbuminuria and gross proteinuria in Type 2 DM *Archives of Int Medicine* 2000;160:1093-100.
 Brenner BM. The RENAAL study. Type 2 diabetes and nephropathy. *NEJM* 2001;345:861-9.

Lewis 1, RENAAL and IDNT have shown prevention of progression to ESRD for ACE and ARB

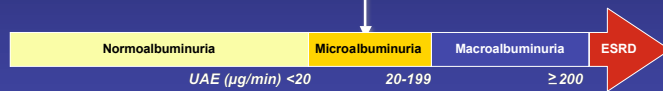
Lewis 1 T1DM
 RENAAL T2DM
 IDNT T2DM



Brenner BM, et al. *N Engl J Med* 2001; 345: 861-9.
 Lewis EJ, et al. *N Engl J Med* 2001; 345: 851-60.
 Lewis EJ, et al. *N Engl J Med* 1993;329:1456-1462.

Ahmad, Ravid and IRMA 2 showed we can Prevent Progression from MAU to Overt Nephropathy

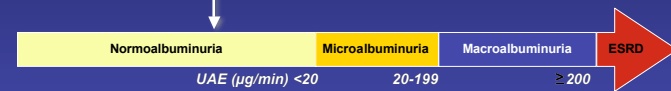
Ahmad T2DM
Ravid T2DM
IRMA 2 T2DM



Ahmad J, et al. *Diabetes Care* Oct. 1997;20(10):1576-81.
Ravid M, et al. *Arch Intern Med* 1996;156:286-9
Parving H-H, et al. *N Engl J Med* 2001; 345: 870-8.

Good Blood Sugar and BP Control Prevent Progression to MAU

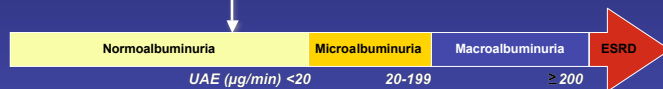
DCCT T1DM
UKPDS T2DM



Brenner BM, et al. *N Engl J Med* 2001; 345: 861-9.
Lewis EJ, et al. *N Engl J Med* 2001; 345: 851-60.
ADA. *Diabetes Care* 2004; 27(Suppl. 1): S79-S83.

ACE to Prevent Progression from DM to Microvascular Disease

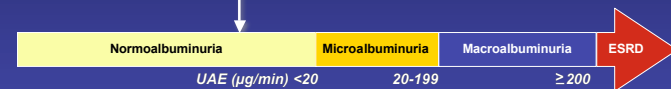
Micro HOPE
BENEDICT
EUCLID



Euclid *Lancet* 358, 28-3, 1998
Ruggenenti P, et al. *N Engl J Med* 2004; 351: 1941-51.

Can an ARB Prevent Microvascular Complications in T1 and T2 DM?

DIRECT
Study



Euclid *Lancet* 358, 28-3, 1998
Ruggenenti P, et al. *N Engl J Med* 2004; 351: 1941-51.

Conclusion 1:

Follow-up for patients with high normal blood pressure (130-139 / 85-89)

If BP is high-normal (SBP 130-139 mm Hg and/or DBP 85-89 mm Hg) patients should be followed annually

Conclusion 2: Urine Albumin Levels

- In non-diabetic hypertensives:
 - Signifies CV risk
 - No indication for screening
- In People with Diabetes
 - Signifies Renal and CV risk
 - Treat all risk factors aggressively and include an ACEi or ARB