Module 4

Managing Patients with Hypertension and Diabetes

Case Development & Disclosures

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Conflict Disclosure Information

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  Other: _____

Module 4: Hypertension and Diabetes

Mrs. J.D.

A 58 year old patient who just moved to your city. She is on active treatment for her hypertension and her diabetes.

Outline of Today's Activity

- Introduction
- Case Presentation
- Key Learnings & Questions
- Wrap Up

Statement of Need

"My greatest challenge as a health care professional in the management of patients with hypertension is

"

_____

Learning Objectives

Upon completion of this activity, participants will be able to:

1. Plan the investigation of patients with hypertension and diabetes including evaluation for nephropathy
2. Assess the risk associated with diabetes in patients with hypertension including the impact of diabetic nephropathy
3. Demonstrate knowledge of the blood pressure target in hypertensives living with diabetes

Learning Objectives

4. Select treatment for patients with hypertension and diabetes with nephropathy
   - Contrast this with patients with hypertension and diabetes without nephropathy
   - Choose appropriate antihypertensive medications
   - Discuss the risks of dual RAAS blockade with ACEi or ARB

5. Identify patients with BP not at goal and plan their investigation and treatment

History of Present Illness

- Mrs. J.D. is a 58 year old patient who sees you because of her BP and diabetes
- She was told at age 45 years that her blood pressure was too high
- She had no symptoms except ankle edema which she noted in the evenings. She was given treatment with hydrochlorothiazide 12.5 mg daily
- She was followed intermittently for the next few years and was told that her BP was at the upper limit of normal and that her blood sugar was also borderline high

History of Present Illness

- At age 52 years, she was found to have BP over 155 mmHg and treatment with irbesartan 150 mg daily was added to her diuretic dose
- High blood glucose was found and metformin was started
- At age 55 years, her BP was still above 140/90 mmHg and atenolol 25 mg was added to her treatments

History of Present Illness

- At her initial visit to you, she complains of shortness of breath on climbing stairs and also that her ankles are swollen by the evening
- She has no chest pain. She does not sleep well and is tired during the day. She has nocturia 2 or 3 times and also frequent urination during the day
- She has pain in her knees and hips linked to her work in a supermarket where she must stand all day
- She has flushing episodes
- She is short of breath on mild exercise

Past History

- Married, lives with husband
- Works in a supermarket as a cashier for the last 15 years
- Does not smoke, drinks socially, sedentary, follows no diet but does not use the salt shaker
- No known allergies
- G2 P2 A0 (age 32 and 34 years)
- Cholecystectomy
- Menopause at age 52 years

Family History

- Father
  - Died at age 72 of MI and renal disease
- Mother
  - Alive and well at 84 years. She has been treated for hypertension for the last 25 years
- Brother
  - HTN, CAD, smoker
- Sister
  - Obesity, diabetes

Current Medications

- Hydrochlorothiazide 12.5 mg
- Ramipril 5 mg day
- Bisoprolol 5 mg day
- Metformin 500 mg BID
- ASA 81 mg day
- Lorazepam 1.0 mg HS
- Ibuprofen 1 to 3 tabs/day

Physical Examination

- Height: 160 cm
- Weight: 88 kg
- BMI: 33.7 kg/m^2
- BP (left arm, seated):
  - 148/92 mmHg using an automated device
- Pulse: 56
- Funduscopic: Gr I
- Neck-Thyroid palpable, no nodule
- Heart: Normal
- Lungs: Normal
- Abdomen: no murmurs
- Arteries: Normal
- Ankle edema: pitting ++
- Neuro: decreased vibration and monofilament in feet

Discussion Question 1

This patient has hypertension and diabetes. What investigations are appropriate for this patient?

Discussion Question1) This patient has hypertension and diabetes. What investigations are appropriate for this patient?

a) What are the essential laboratory test required in a patient with hypertension and diabetes?

b) How frequently should you obtain these tests?

a) Routine Laboratory Tests

Preliminary investigations of patients with hypertension and diabetes

1. Urinalysis
2. Blood chemistry (potassium, sodium and creatinine)
3. Fasting glucose
4. Fasting total cholesterol and high density lipoprotein cholesterol (HDL), low density lipoprotein cholesterol (LDL), triglycerides
5. Standard 12-leads ECG

- Currently there is insufficient evidence to recommend routine testing of microalbuminuria in people with hypertension who do not have diabetes

b) Frequency of Follow Up Investigations

- During the maintenance phase of hypertension management, tests (including electrolytes, creatinine, glucose, and fasting lipids) should be repeated with a frequency reflecting the clinical situation
- Diabetes develops in 1-3%/year of those with drug treated hypertension. The risk is higher in those treated with a diuretic or beta blocker, in the obese, sedentary, with higher fasting glucose and who have unhealthy eating patterns.
- Assess for diabetes more frequently in these patients

Discussion Question 2

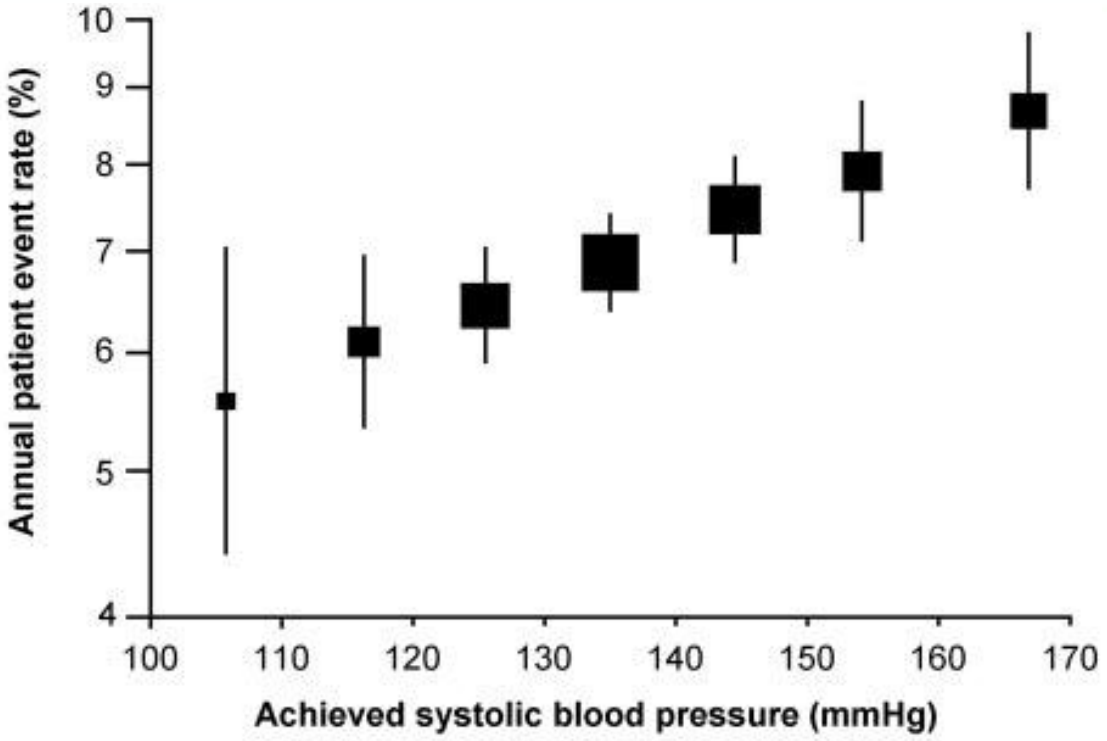
What is the impact of finding nephropathy in a patient with diabetes?

Discussion Question 2)
If you find nephropathy:

a) What is the impact of achieved BP on patient outcomes?
   - (the patient's BP is 148/92 mmHg using an automated device)

b) What is the impact for the patient?

Incidence of Renal Events by Achieved BP Levels in ADVANCE Study



Median systolic blood pressure (mmHg)	106	116	125	135	144	154	168
No. of person-years	1431	4266	8974	11983	9138	4942	3470

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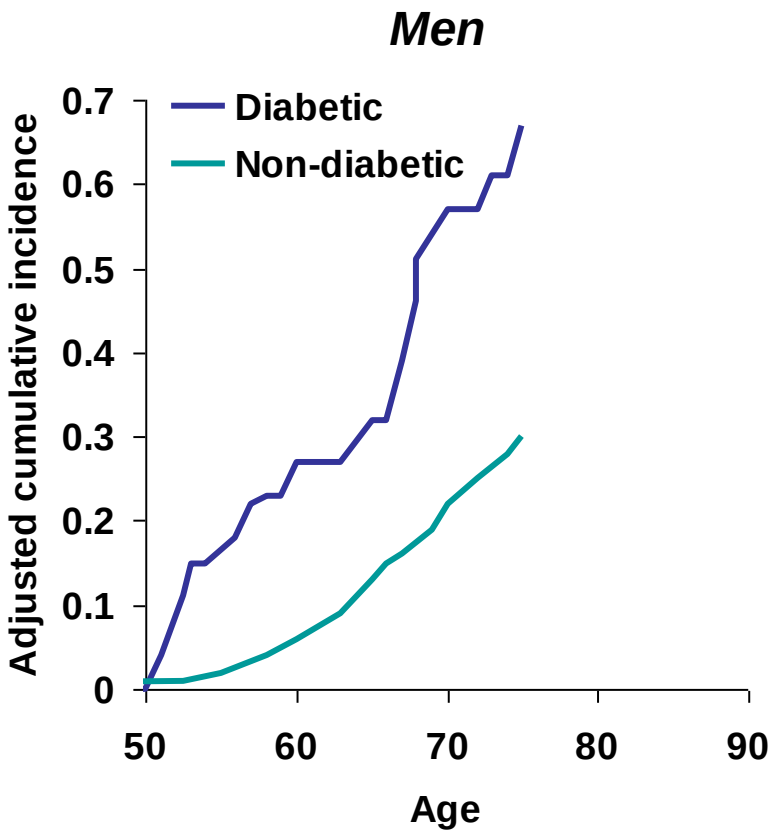
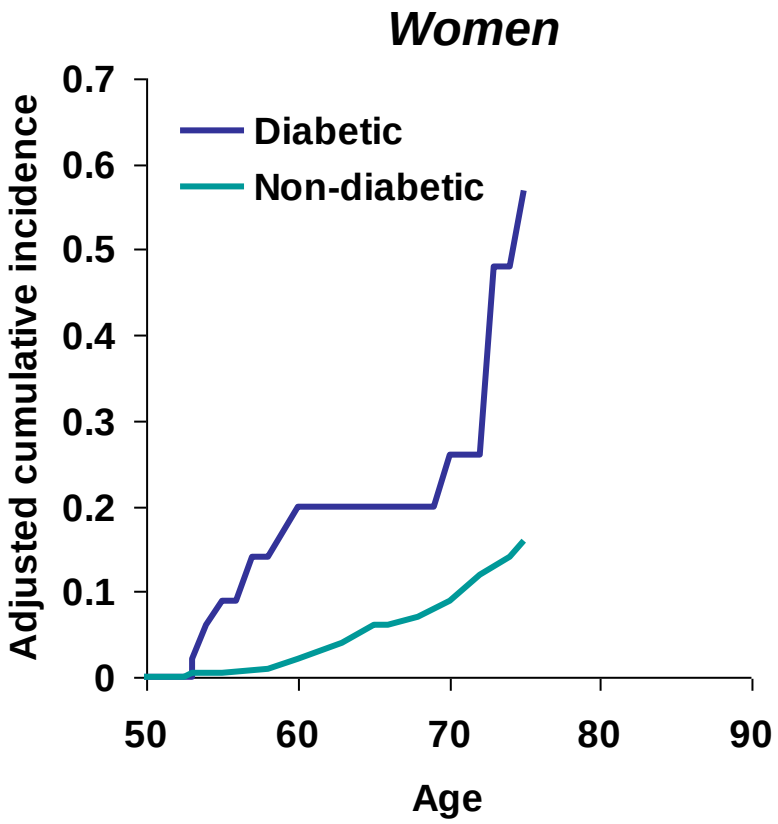
Hypertension CANADA

Diabetes and Lifetime CVD Risk





Lloyd Jones et al. *Circulation* 2006;113:791-8

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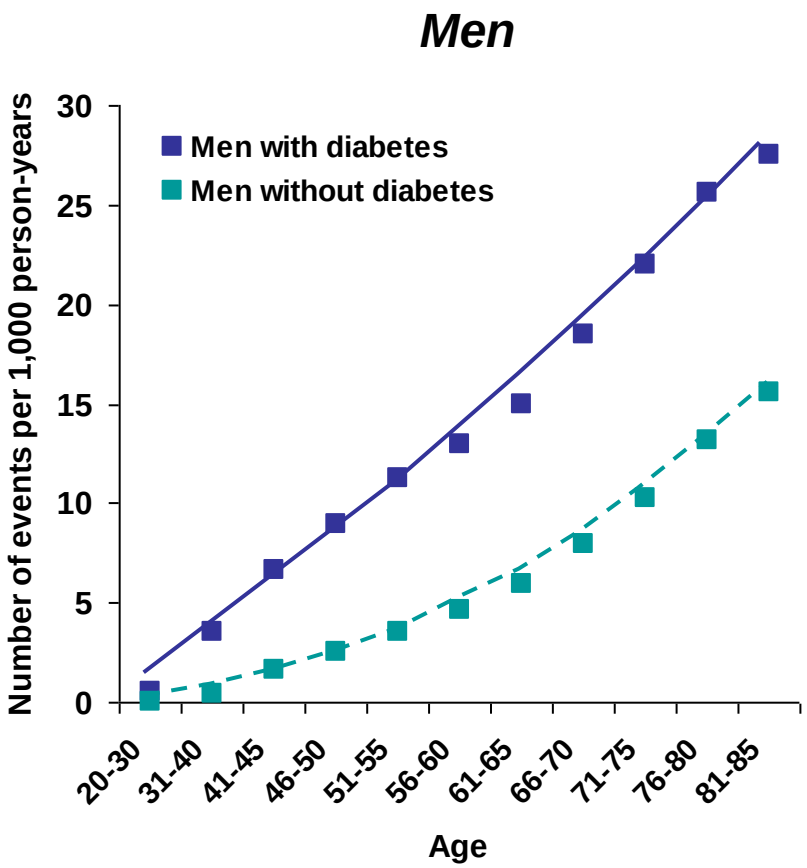
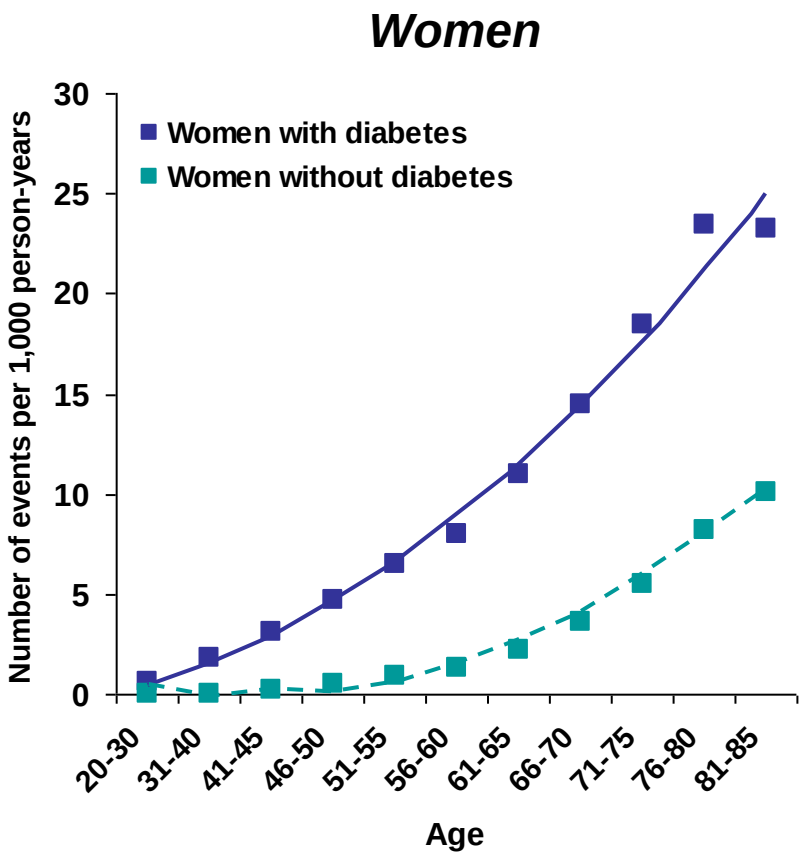
Hypertension CANADA

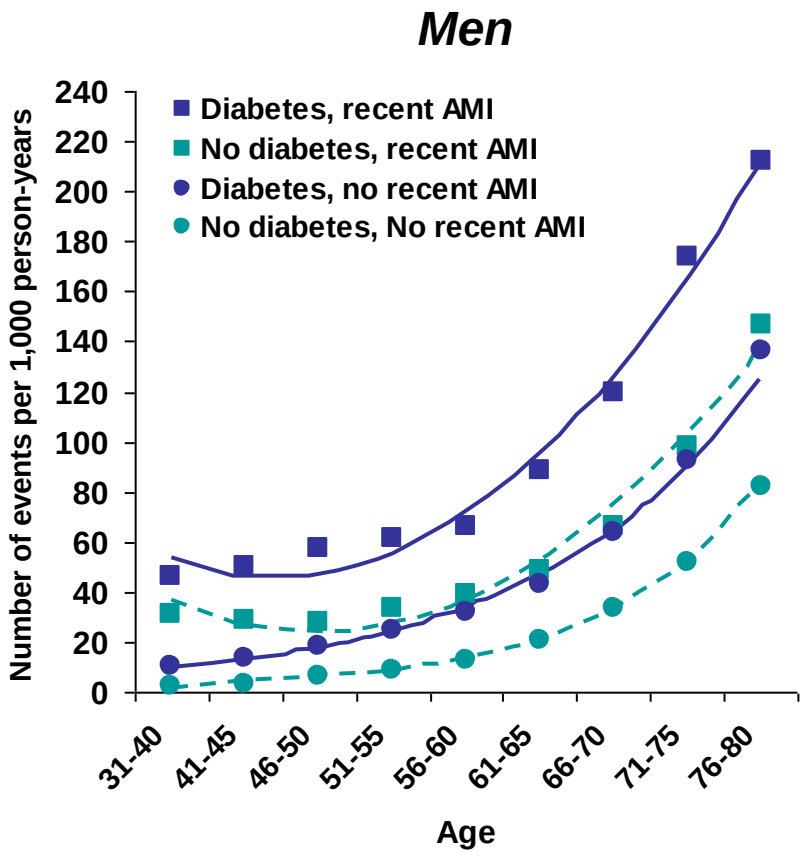
Relation Between Age and CVD in Patients with Diabetes Compared to Those Without

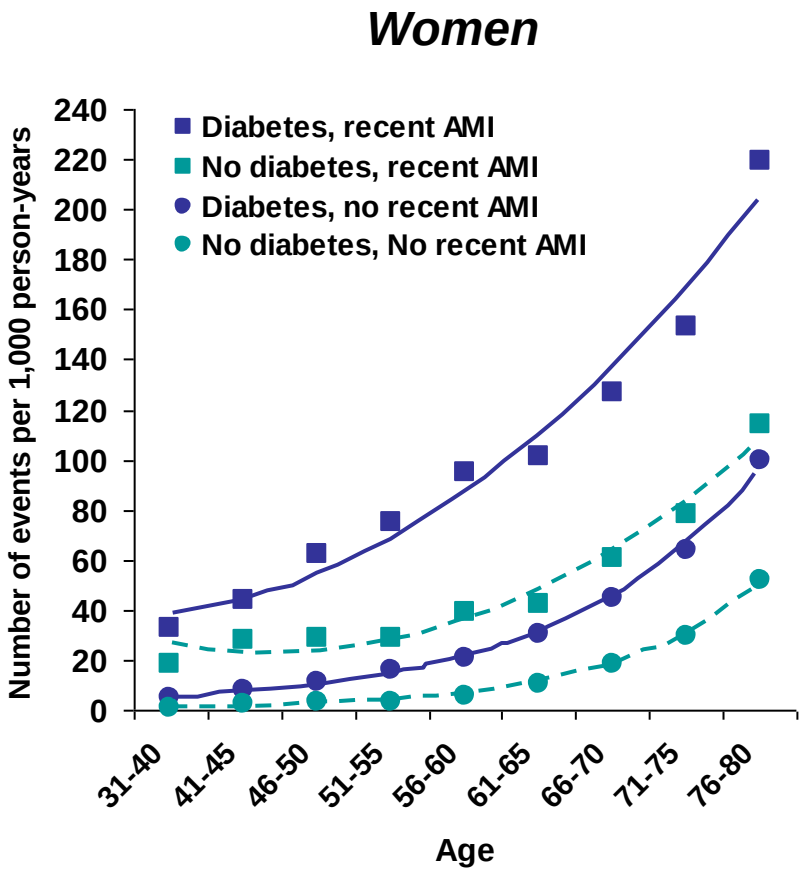




Booth et al. *Lancet* 2006;368:29-36

Relation Between Age and CVD in Patients with Diabetes Compared to Those Without ± Recent AMI





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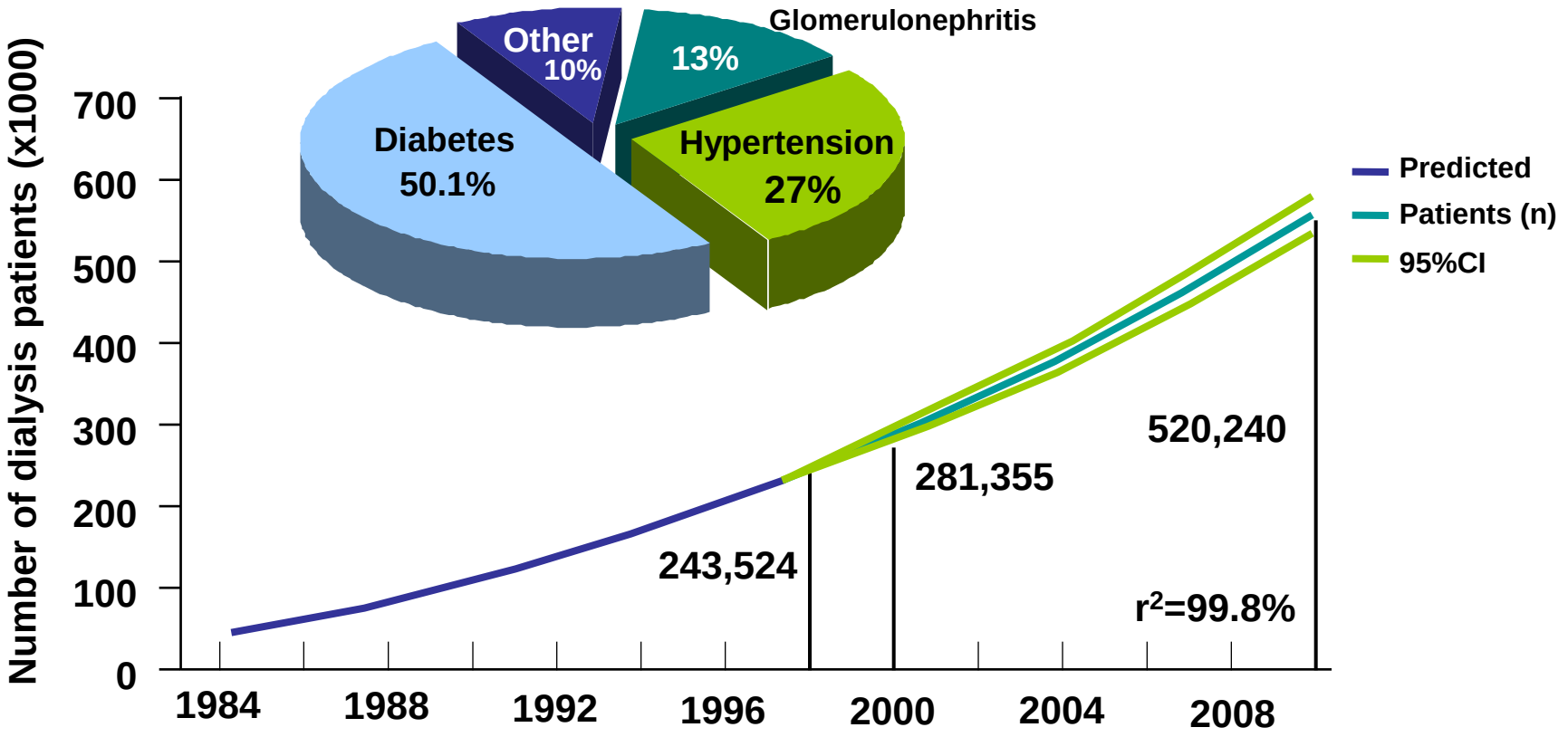
Booth et al. *Lancet* 2006;368:29-36

Hypertension CANADA

Major Causes of ESRD

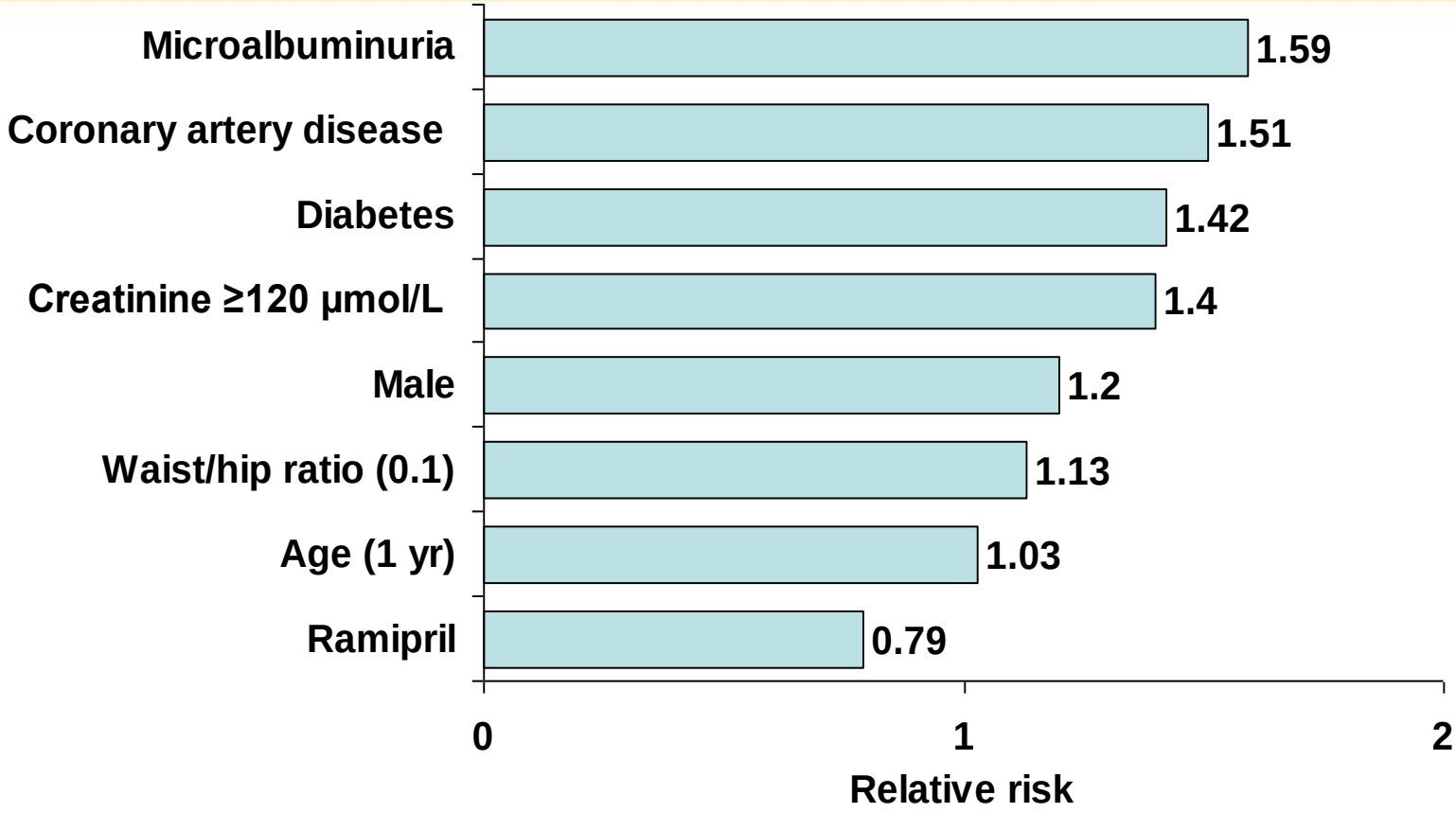
Primary diagnosis in patients who start dialysis



ESRD: end-stage renal disease

United States Renal Data System. Annual data report. 2000

Multivariate Relative Risks for Primary Outcomes in the HOPE Study



Mann et al. *Ann Intern Med* 2001;134:629-36

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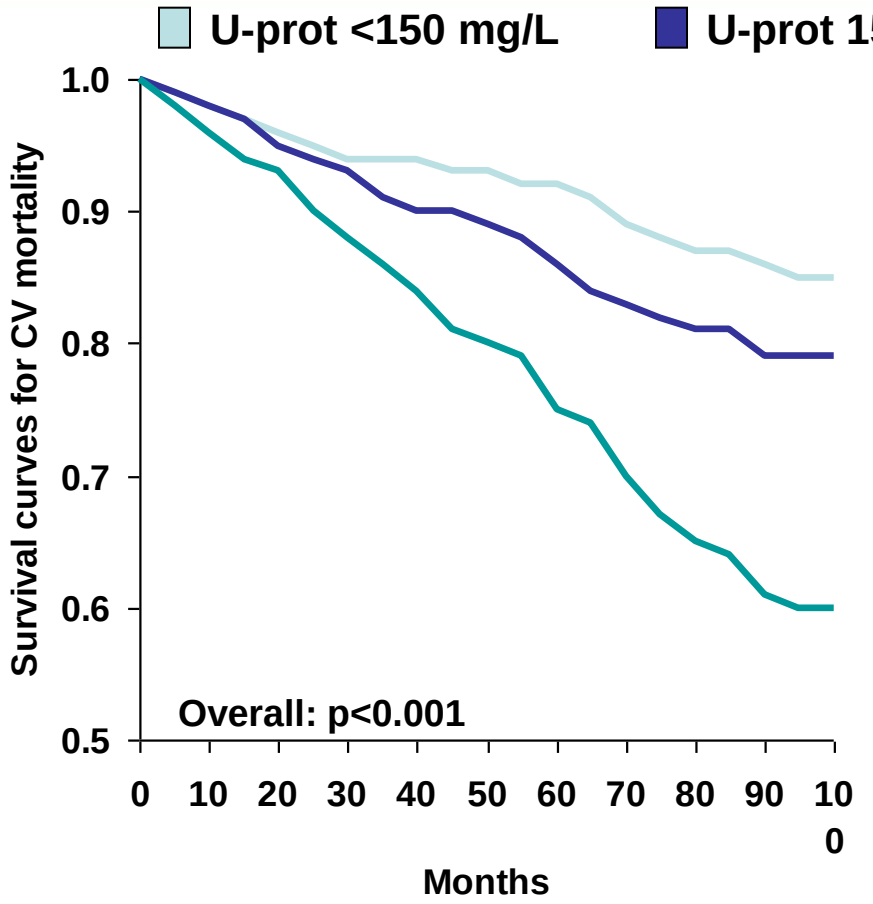
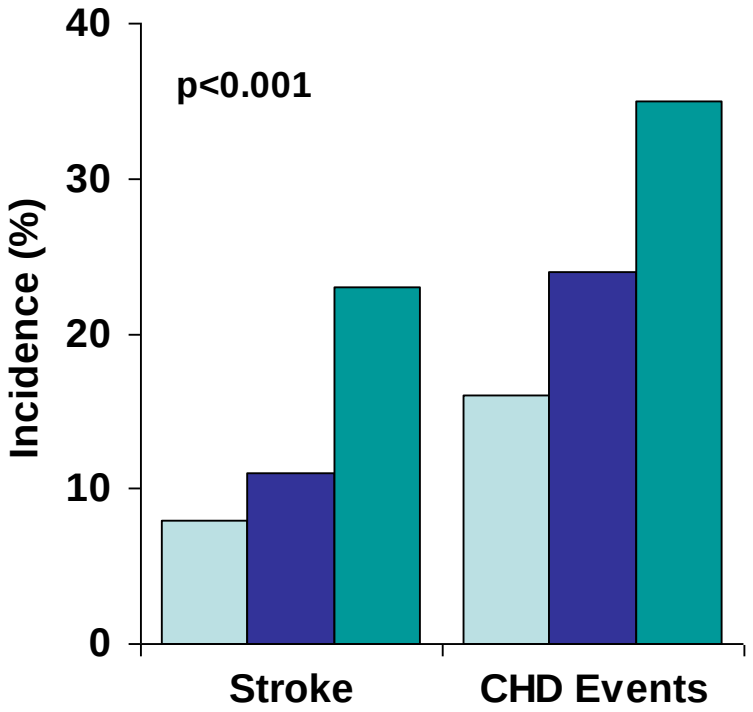
Abnormal Urinary Albumin Levels

Setting	Urinary albumin/creatinine level (mg/mmol)	
	Men	Women
Chronic kidney disease	>30	
Diabetes	>2	>2.8

Proteinuria Levels a Predictor of Stroke and Cardiovascular Events in Type 2 Diabetes





U-prot: urinary protein concentration

Miettinen et al. *Stroke* 1996;27:2033-39

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Laboratory Investigations

Test	Results	Normal values
Glucose	8.6 mmol/L	4.0-8.0 mmol/L
Uric acid	475 mmol/L	mmol/L
Creatinine	90 µmol/L eGFR 80 ml/min	44-106 µmol/L
K	3.8 mmol/L	3.5-5.0 mmol/L
Na	136 mmol	135-145 mmol/l

• Note that labs are done prior to the next visit

Laboratory Investigations

Test	Results	Normal values
HbA1c	0.074	0.045 - 0.057 mmol/L
Urinalysis	Negative for proteinuria	Neg
Alb/creat	1.0 mg/mmol	0.0 - 2.8 mg/mmol
CK	125	30-213 u/l
TSH	4.2	0.35-5.50 mUI/l

- Note that labs are done prior to the next visit

Laboratory Investigations

Test	Results	Normal values
LDL	4.2 mmol/L	<2.0 mmol/L
Total chol	6.8 mmol/L	<5.20 mmol/L
TG	3.6 mmol/L	<1.70 mmol/L
HDL	0.8 mmol/L	>0.99 mmol/L
TC:HDL	8.5	High risk target: <4.0 Mod risk target: <5.0 Low risk target: <6.0

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Hypertension CANADA

Discussion Question 3

What is the blood pressure target in people with diabetes and hypertension?

Discussion Question 3) What is the blood pressure target in people with diabetes and hypertension?

1. What is the classification of hypertension and what are the BP threshold and target values for a patient with hypertension and diabetes?

2. How does recent evidence support these recommendations?

European Society of Hypertension Classification of Blood Pressure

Category	Systolic		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	<90

The category pertains to the highest risk blood pressure

*ISH: isolated systolic hypertension

***J Hypertension* 2007;25:1105-87**

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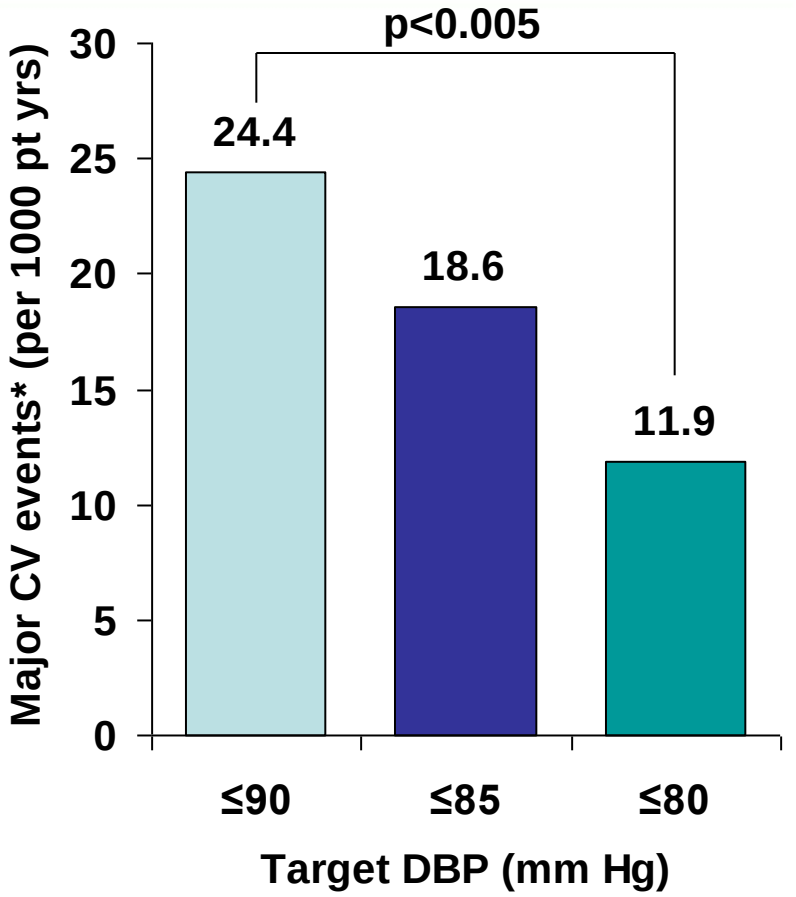
II. Indications for Pharmacotherapy

Usual blood pressure threshold values for initiation of pharmacological treatment of hypertension

Condition	Initiation
	SBP or DBP mmHg
• Systolic or diastolic hypertension	≥140/90
• Diabetes	≥130/80
• Chronic kidney disease	≥140/90

Strict BP Control Reduces Cardiovascular Events in Patients with Diabetes: HOT Trial

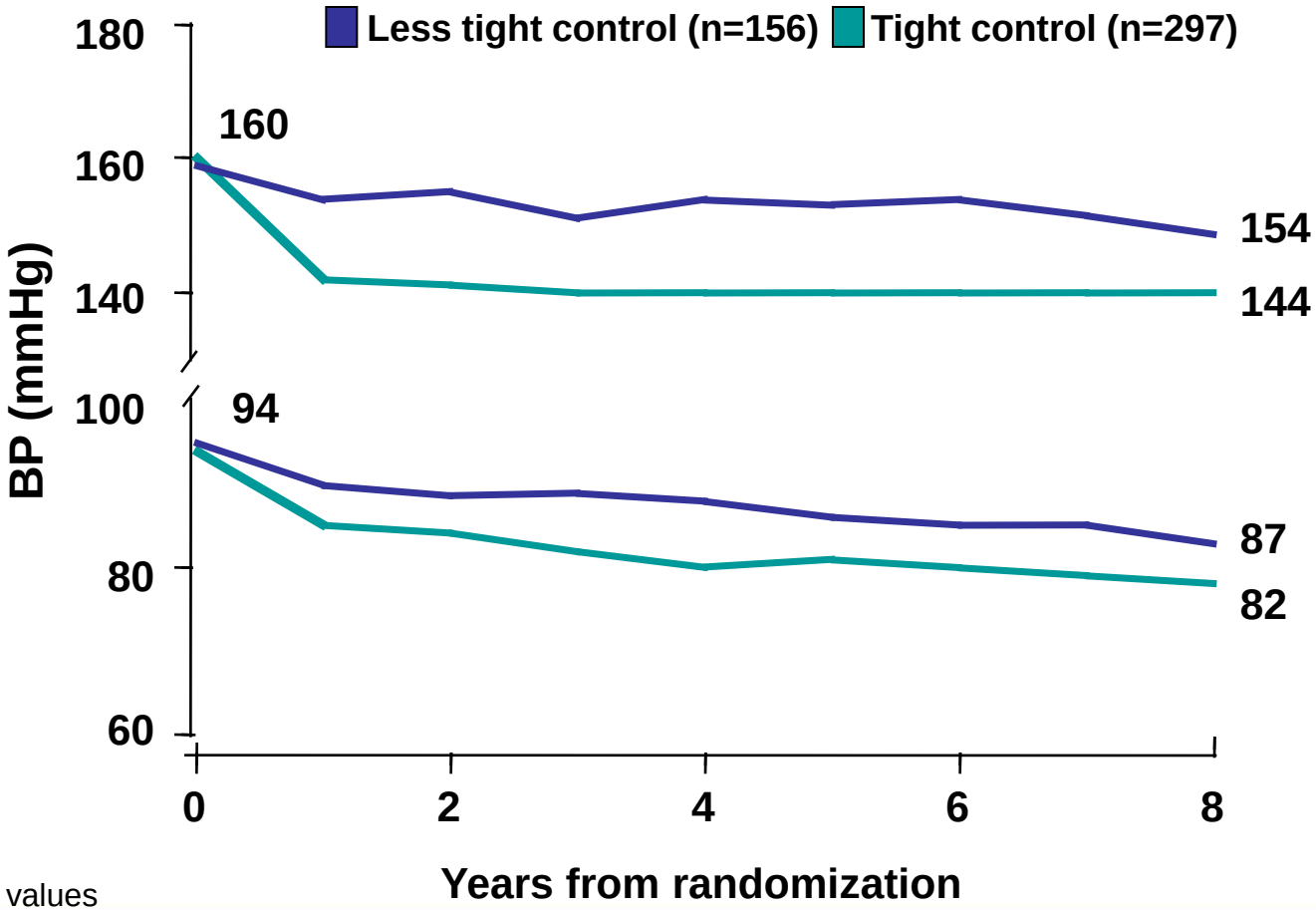
Target DBP (mmHg)	Patients (n)	Achieved SBP** (mmHg)	Achieved DBP** (mmHg)
≤90	501	143.7	85.2
≤85	501	141.4	83.2
≤80	499	139.7	81.1



*includes myocardial infarction,
stroke and all other causes of death from CV;
**mean of all BPs from 6 months of follow-up to end of study

Hansson et al. *Lancet* 1998;351:1755-62

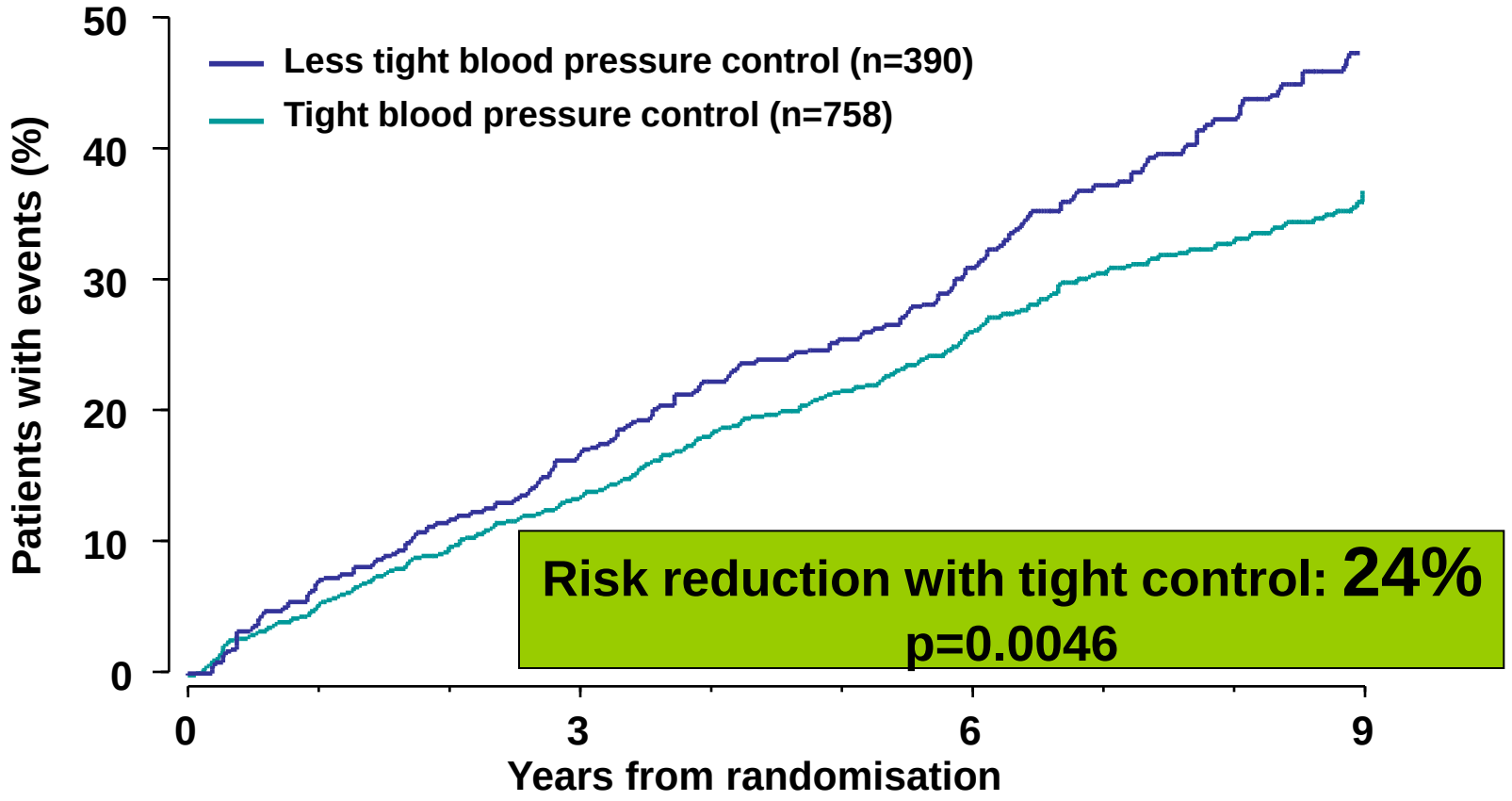
Blood Pressure: Tight vs. Less Tight Control



cohort, median values

UKPDS. *BMJ* 1998;317:703-13

Any Diabetes-Related Endpoints



cohort, median values

UKPDS. *BMJ* 1998;317:703-13

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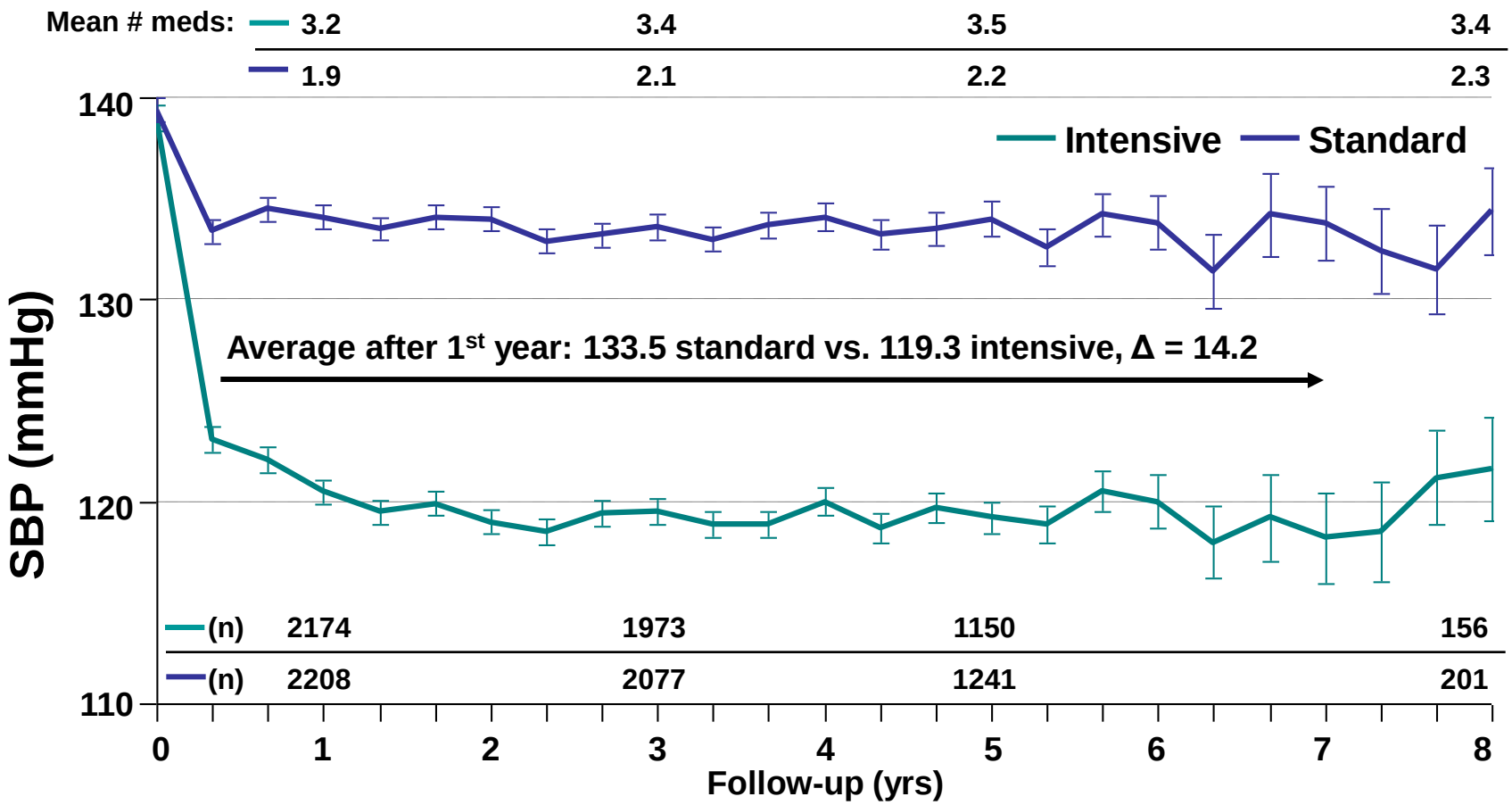
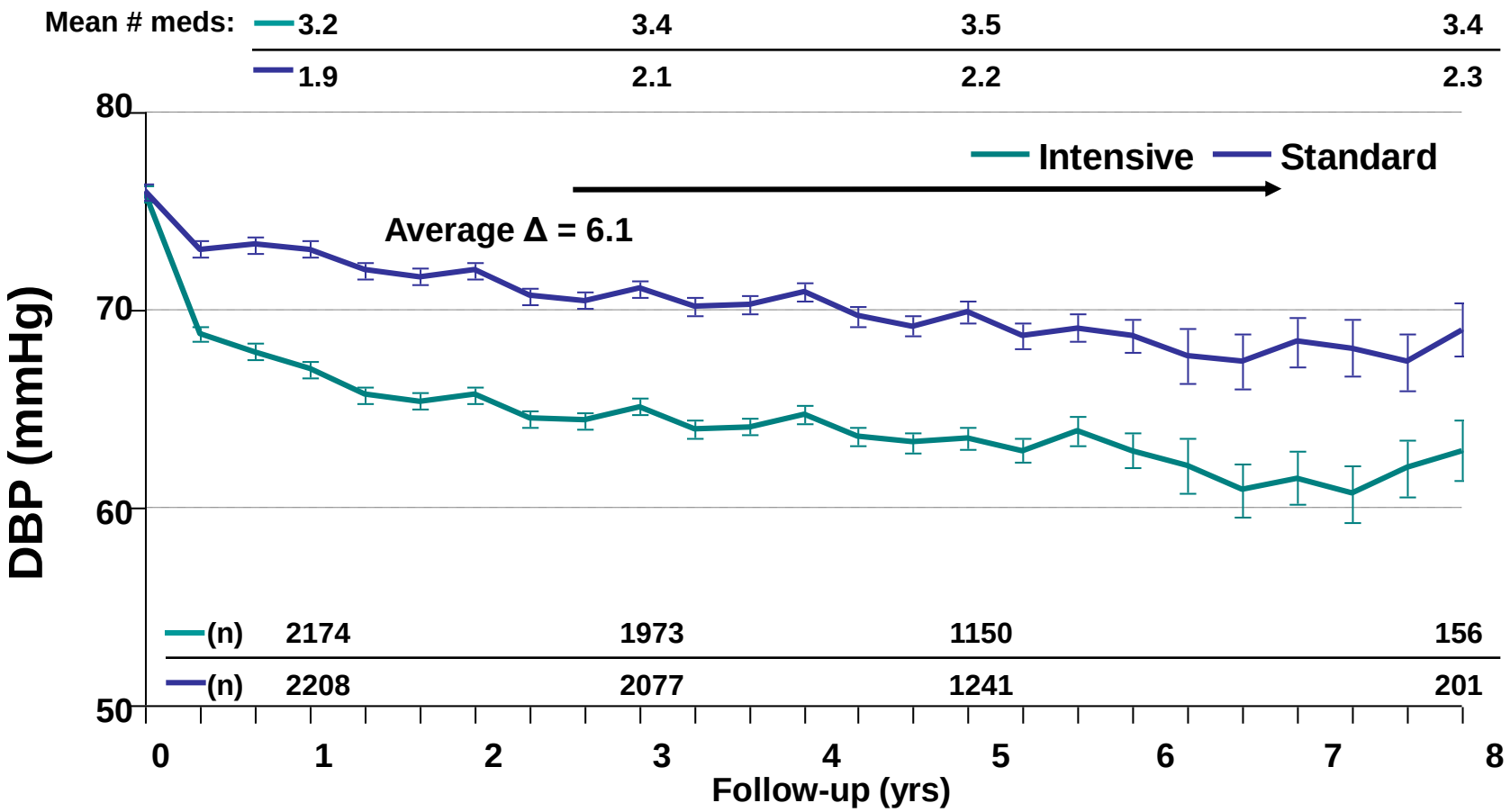
ACCORD: Mean SBP Over Time (Intensive vs Standard BP control groups)



Error bars indicate 95% confidence intervals

ACCORD Study Group. *N Engl J Med* 2010;362:1575-85

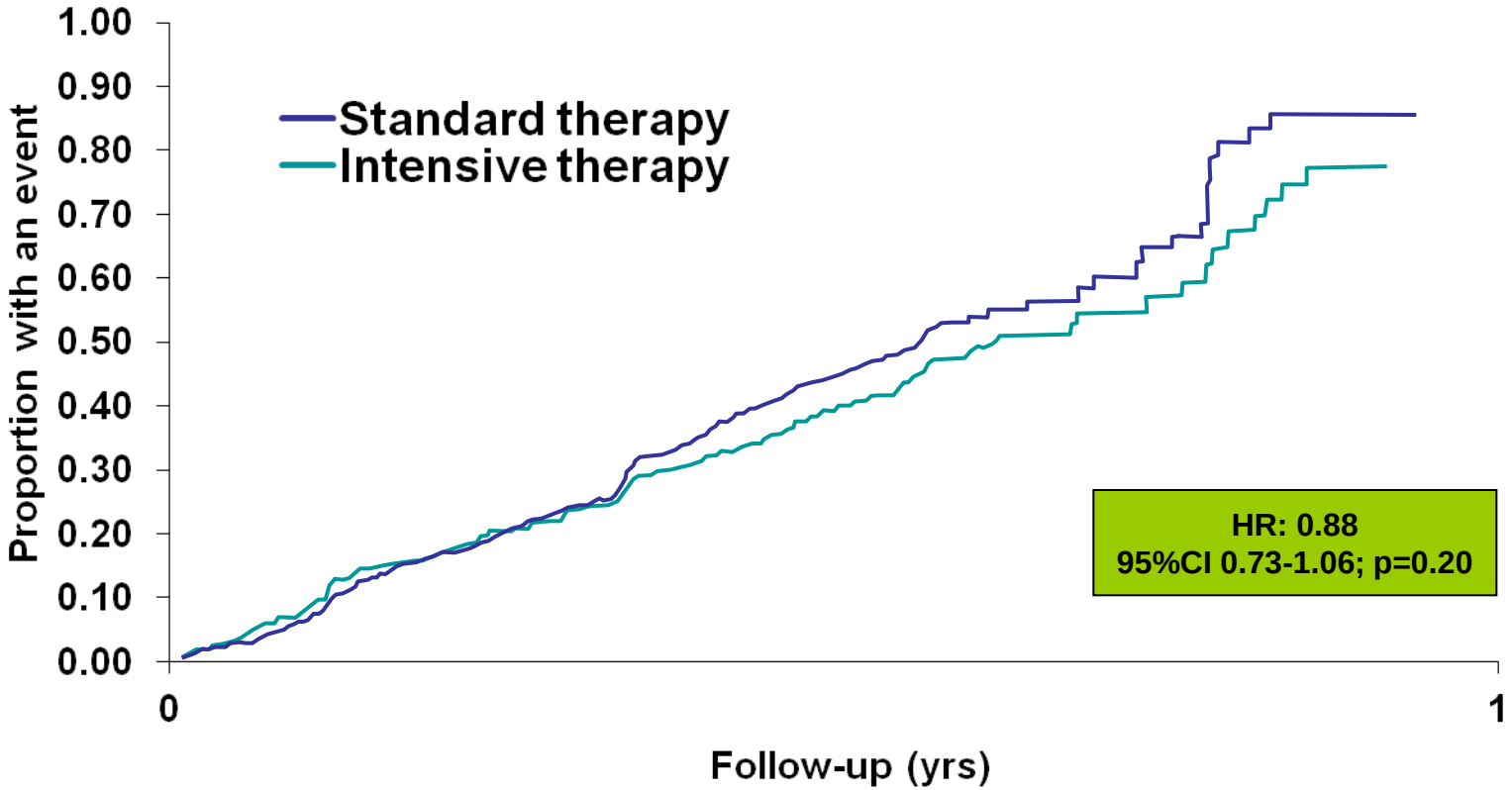
ACCORD: Mean DBP Over Time



Error bars indicate 95% confidence intervals

ACCORD Study Group. *N Engl J Med* 2010;362:1575-85

ACCORD: Primary Outcome
(Nonfatal MI, Nonfatal Stroke, or CVD Death)



ACCORD Study Group. *N Engl J Med* 2010;362:1575-85

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ACCORD: Results and Rationale for Lack of Impact on BP Recommendations

- Overall BP study was neutral with no benefit of systolic target <120 mmHg vs. <140 mmHg for primary outcome, yet:
- Power issue: annual rate of primary outcome 1.87% in the intensive arm versus 2.09% in the standard arm vs 4%/year event rate projected during sample size calculations
- Significant interaction between BP and glycaemia control studies such that those in usual care glycaemia group (A1c 7%+) had a significant improvement in primary outcome with lower BP target
- Secondary outcome for stroke reduction showed a benefit for lower BP target (41% RRR)

Therefore no clear evidence supporting a change in BP targets for people with diabetes at this point

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ACCORD study NEJM 2010

Hypertension CANADA

Discussion Question 4

What is the management of a patient with diabetes and above target blood pressure without nephropathy?

Discussion Question 4) What is the management of a patient with diabetes and BP above target?

1. Treatment of hypertension in diabetes without nephropathy
2. Treatment targets
3. Multi-risk factor intervention

Treatment of Systolic-Diastolic Hypertension without Diabetic Nephropathy

Threshold equal or over 130/80 mmHg and TARGET below 130/80 mmHg

Diabetes without nephropathy

→ **1. ACE inhibitor or ARB or**
2. Dihydropyridine CCB or thiazide diuretic

→ **Combination of first line agents**

→ **Addition of one or more of:**
- Cardioselective BB or
- Long-acting CCB

IF ACE inhibitor and ARB and DHP-CCB and thiazide are contraindicated or not tolerated,
SUBSTITUTE
- **Cardioselective BB* or**
- **Long-acting NON DHP-CCB**

Combinations of an ACE inhibitor with an ARB are specifically not recommended in the absence of proteinuria

More than 3 drugs may be needed to reach target values for diabetic patients

DHP: dihydropyridine

*cardioselective BB: acebutolol, atenolol, bisoprolol, metoprolol

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Treatment Targets

Usual blood pressure targets

Condition	Initiation
	SBP or DBP mmHg
• Systolic or diastolic hypertension	<140/90
• Diabetes	<130/80
• Chronic kidney disease	<140/90

Multi-risk factor intervention

- Target A1c of 7.0%
- Target LDL < 2.0
- Smoking cessation if appropriate
- Diet
- Exercise
- BP control and use of RAAS blockers

STENO-2 Study (Type 2 DM)

- 160 patients randomly assigned to intensified intervention with achievement of blood pressure targets, tight glucose regulation, use of the RAAS blockers, aspirin, lipid lowering agents and focused behaviour modifications
- Treatment to target in STENO-2
  - HbA1c less than 6.5%
  - Cholesterol less than 4.5 mmol
  - Triglycerides less than 1.7 mmol
  - BP less than 130/80 mmHg
  - Use of RAAS blockade

Gaede et al. *N Engl J Med* 2008;358:580-91

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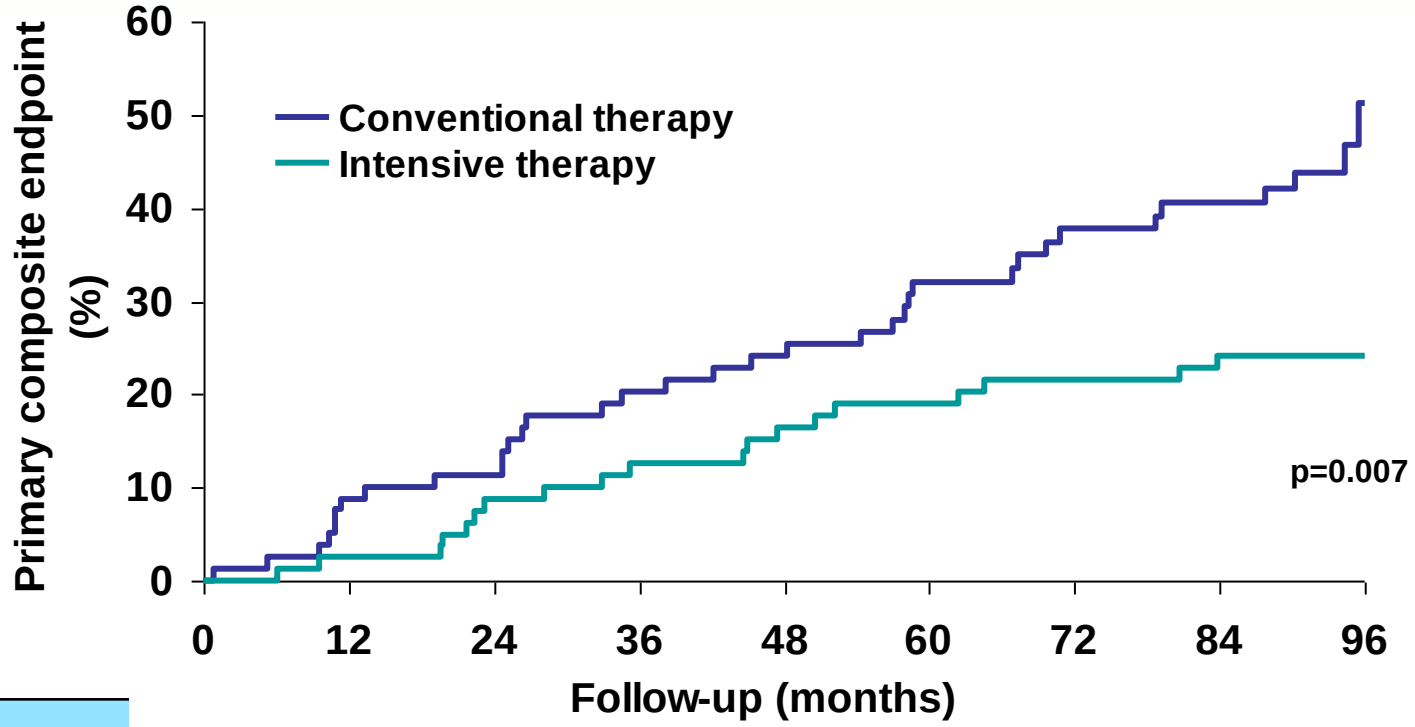
STENO-2: Effect of a Multifactorial Vascular Protective Strategy on Macro- and Microvascular Outcomes



No. at risk									
Conventional therapy	80	72	70	63	59	50	44	41	13
Intensive therapy	80	78	74	71	66	63	61	59	19

Gaede et al. *N Engl J Med* 2003;348:383-93

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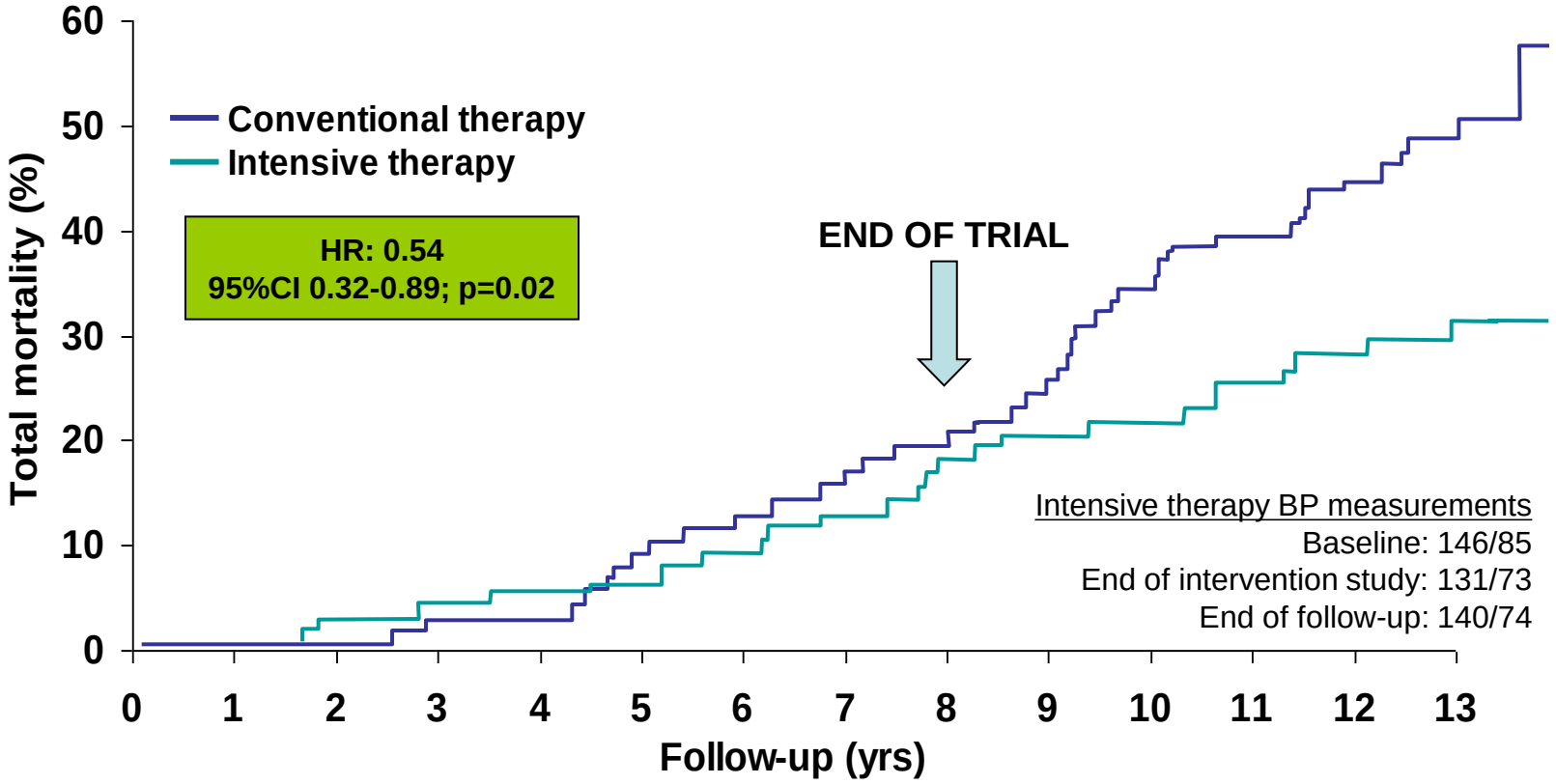
STENO-2 Extended Follow-up: Effect of a Multi-factorial Vascular Protective Strategy on Total Mortality



Gaede et al. *N Engl J Med* 2008;358:580-91

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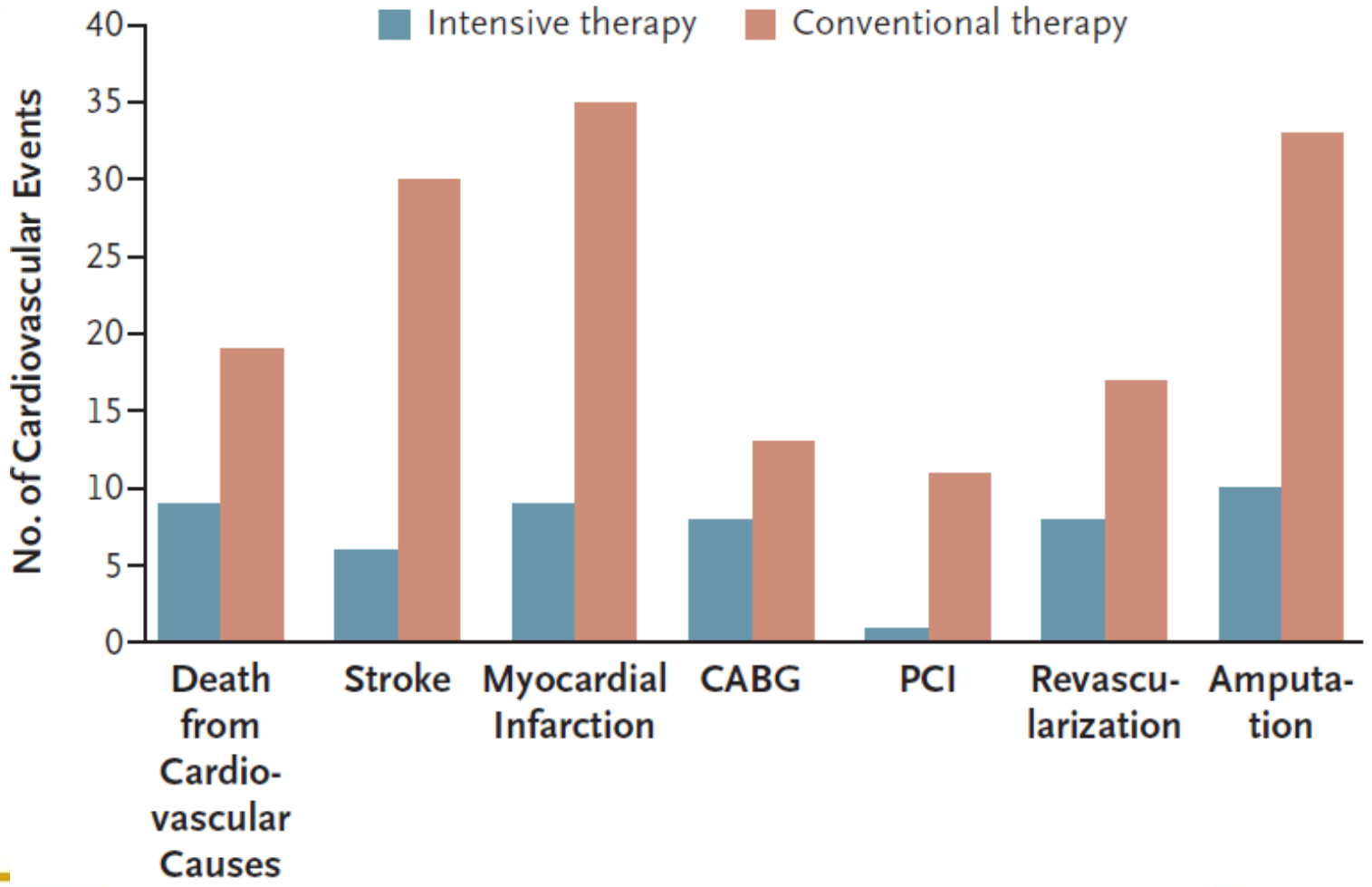
STENO 2: Number of events for each component of the composite end point



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Gaede P, NEJM; 2008; 358:580-91

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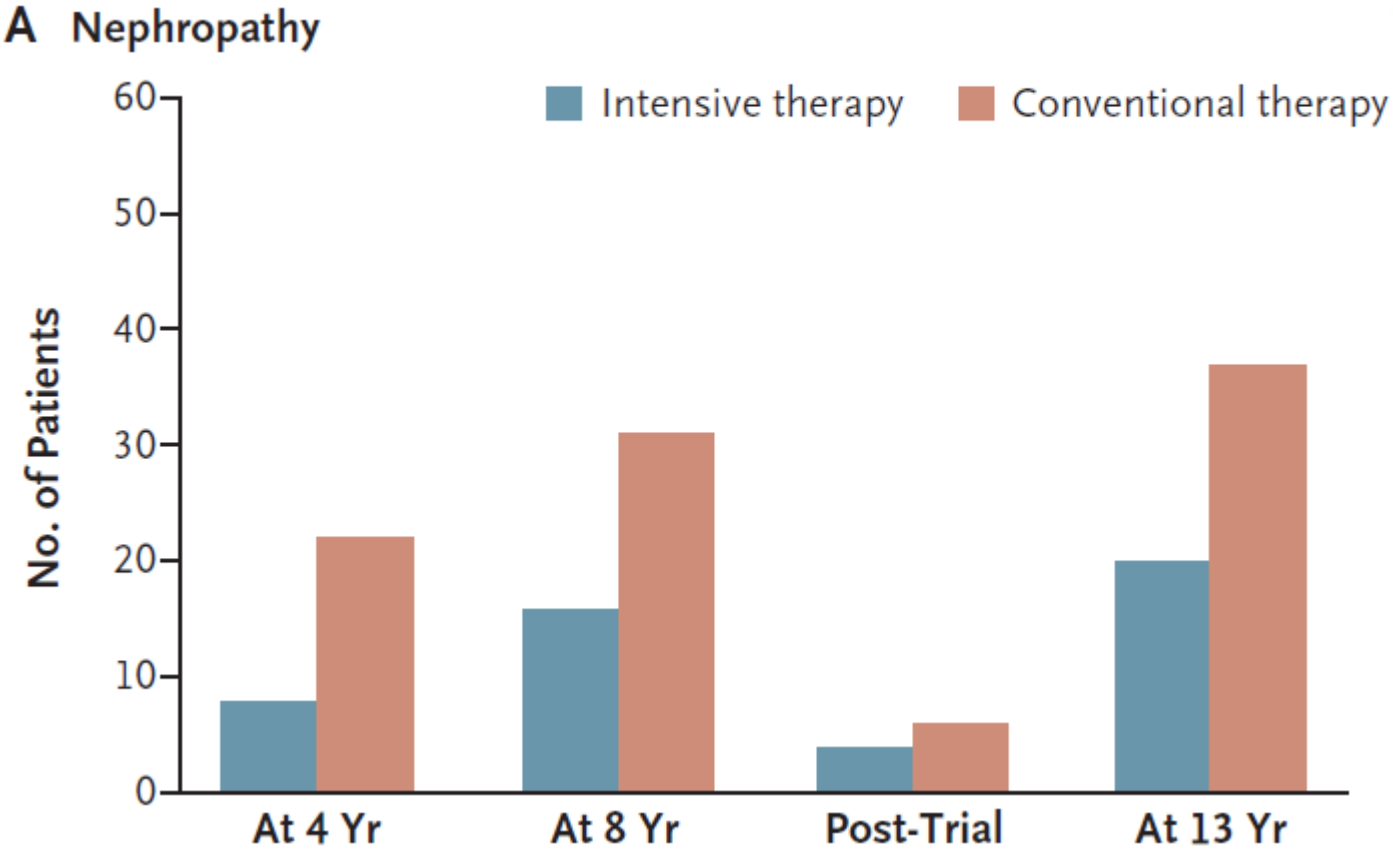
STENO-2: Progression to Macroalbuminuria



Gaede P, NEJM; 2008; 358:580-91

Case Progression

Mrs. J.D. returns to your office. What is your treatment plan?

- Height: 160 cm; weight: 92 kg; BMI: 35.3
- BP: 152/90 mmHg, by BpTru
- SOB: ankle edema
- Creatinine: 90mmol/l
- K: 4.0 mmol
- Na: 136 mmol
- Alb/creat: 26.2 mg/mmol

Discussion Question 5

Mrs. J.D. returns to your office. What is your treatment plan for her BP?

Case Progression

Current medications of Mrs J.D. are listed below. What changes would you propose?

- Hydrochlorothiazide 12.5 mg
- Ramipril 5 mg day
- Bisoprolol 5 mg day
- Metformin 500 mg BID
- ASA 81 mg day
- Lorazepam 1.0 mg HS
- Ibuprofen 1 to three tabs day

What changes would you propose the current medications? What are the benefits and risks?

a) Stopping Ibuprofen
b) Replacing bisoprolol with a DHP-CCB (amlodipine-nifedipine-felodipine)
c) Adding a DHP-CCB to the actual combination as a fourth medication
d) Increasing the dose of the diuretic and the ACE-I
e) Replacing hydrochlorothiazide with other diuretics (chlorthalidone or spironolactone)
f) Adding a peripheral alpha blocker(doxazosin)
g) Adding an alpha 2 agonist (clonidine)

Current Medications of Mrs. J.D. What Changes Could You Propose?

a) The use of ibuprofen (NSAID) is associated with an increase of BP

b) Replacing bisoprolol with a DHP-CCB.
   - An ACEI+DHP-CCB combination can be preferred combination for hypertensive –diabetics at risk of CV complications.

c) Adding a DHP-CCB to the combination is an option of four medications, if bisoprolol is maintained

Current Medications of Mrs. J.D. What Changes Could You Propose?

d) Increasing the dose of the diuretic HCTZ and ACEI.

– Ramipril and HCTZ are both prescribed at low doses for this patient. Ramipril is also a short acting ACEI which could be replaced by a longer acting RAAS blocker or the dose of ramipril be doubled or given BID

e) Replacing the HCTZ with chlorthalidone (long acting more potent diuretic.)

–Blood glucose, potassium and uric acid would have to be monitored.

Current Medications of Mrs. J.D. What Changes Could You Propose?

f) Adding a peripheral alpha2 receptor blocker (Doxazosin, terazosin or prazosin) an option

–Adverse effect is mainly orthostatic hypotension.

g) Adding an alpha2 agonist (clonidine) also an option in non responsive patients

–Adverse effects are mainly dry mouth, bradycardia mainly in combination with a beta-blocker and withdrawal hypertension if medication is suddenly stopped.

Case Progression: How would you manage Mrs. JD if she presented with ankle edema, shortness of breath and the following lab reports?

- Ankle edema, shortness of breath
- Creatinine: 102 mmol/l
- Sodium: 135 mmol/l
- Uric acid: 550µmol/l
- Potassium: 3.5 mmol/l
- 24 h urinary proteins 550 mg/L

Discussion Question 6

What is the management of a patient with diabetes and above target blood pressure in the setting of nephropathy?

Discussion Question 6) What is the management of a patient with diabetes and above target blood pressure in the setting of nephropathy?

1. Treatment of hypertension in diabetes with nephropathy
   - Role of blockade of the RAAS system
   - For severe nephropathy, role and risks of dual blockade of the RAAS system

Lifestyle Therapies in Adults with Hypertension: Summary

Intervention	Target
Reduce foods with added sodium	<2300 mg /day
Weight loss	BMI <25 kg/m^2
Alcohol restriction	≤2 drinks/day
Physical activity	30-60 minutes 4-7 days/week
Dietary patterns	DASH diet
Smoking cessation	Smoke free environment
Waist circumference	Men <102 cm Women <88 cm

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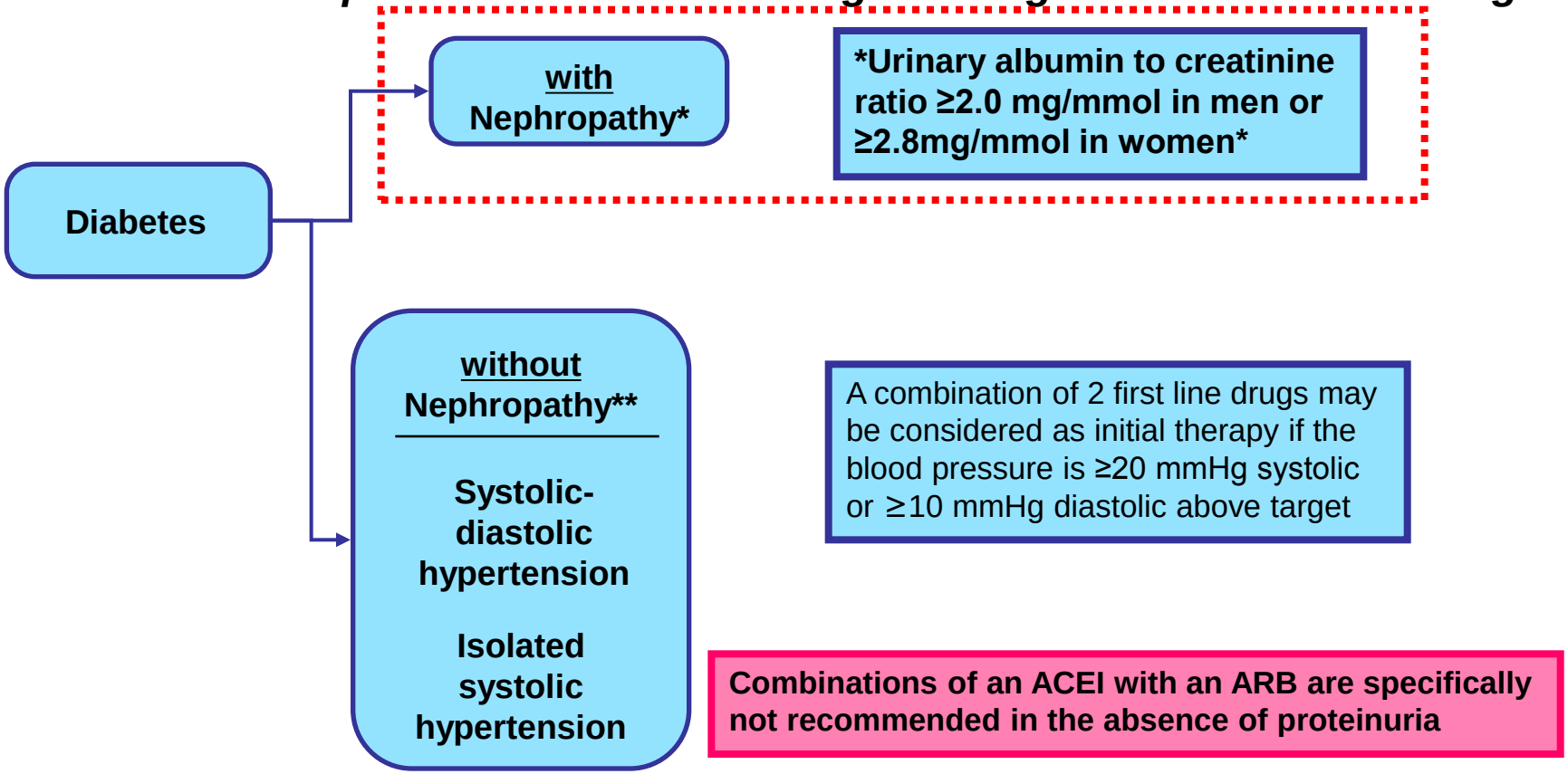
Hypertension CANADA

Treatment of Hypertension in Association with Diabetes Mellitus

Threshold equal or over 130/80 mmHg and target below 130/80 mmHg



*based on at least 2 of 3 measurements

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Hypertension CANADA

Definitions of Microalbuminuria and Macroalbuminuria

Care	Normal	Microalbuminuria	Macroalbuminuria
Urinary excretion of albumin (μg/min)	<20	20–200	>200
Urinary excretion of albumin (mg/24h)	<30	30–300	>300
Urine albumin to creatinine ratio (mg/gm)	<30	30–300	>300
Urine albumin to creatinine ratio (mg/mmol)	<2.0	2.0–20.0	>20.0

Expert Committee on Clinical Practice Guidelines of the Canadian Diabetes Association. Clinical practice guidelines of the 2008 Canadian Diabetes Association for the Prevention and Management of Diabetes in Canada. *Can J Diabetes* 2008

How would you manage Mrs. JD if she presented with ankle edema and shortness of breath?

1. Is an ACEI-ARB combination an acceptable treatment option for patients with hypertension, diabetes and proteinuria?
2. What risks have been associated with this combination?
3. How would you monitor this patient?

How would you manage Mrs. JD if she presented with ankle edema, shortness of breath?

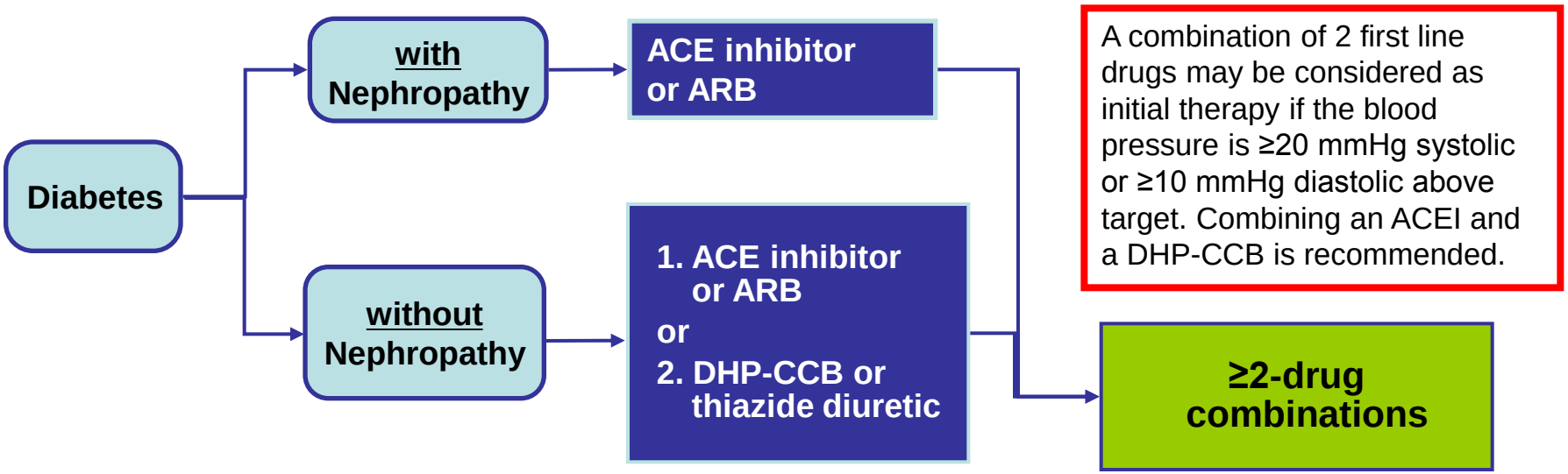
1. The combination of ACEI-ARB is acceptable in patients who have hypertension, diabetes and macroalbuminuria despite treatment with an ACEi or ARB

2. Risks associated with this combination include: increased risk of renal dysfunction, progression to dialysis, hypotension and hyperkalemia

3. Monitor Mrs. J.D.’s BP, renal function and potassium.

XII. Treatment of Hypertension in Association with Diabetes Mellitus: Summary

Threshold equal or over 130/80 mmHg and TARGET below 130/80 mmHg



Monitor serum potassium and creatinine carefully in patients with CKD prescribed an ACEI or ARB

Combinations of an ACEI with an ARB are specifically not recommended in the absence of proteinuria

More than 3 drugs may be needed to reach target values for diabetic patients

If creatinine over 150 µmol/L or creatinine clearance below 30 ml/min (0.5 ml/sec), a loop diuretic should be substituted for a thiazide diuretic if control of volume is desired

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IV. Optional Laboratory Tests

Investigation in specific patient subgroups

- For those with diabetes or chronic kidney disease: assess urinary albumin excretion, since therapeutic recommendations differ if proteinuria is present.
- For those suspected of having an endocrine cause for the high blood pressure, or renovascular hypertension, see following slides.
- Other secondary forms of hypertension require specific testing.

2015 Canadian Hypertension Education Program

- ✓ Patients with diabetes are at high cardiovascular risk
- ✓ Most patients with diabetes have hypertension
- ✓ Treatment of hypertension in patients with diabetes reduces total mortality, myocardial infarction, stroke, retinopathy and progressive renal failure rates
- ✓ Treating hypertension in patients with diabetes reduces death and disability and reduces health care system costs
- ✓ In diabetes, TARGET <130 systolic and <80 mmHg diastolic
- ✓ If a patient has both diabetes and CKD, TARGET <130 systolic and <80 mmHg diastolic
- ✓ The use of the combination of ACE inhibitor with an ARB should only be considered in selected and closely monitored people with advanced heart failure or proteinuric nephropathy

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The full slide set of the

2015 CHEP Recommendations

is available at

www.hypertension.ca