



Module 4

Managing Patients with Hypertension and Diabetes

This program meets the accreditation criteria of The College of Family Physicians of Canada
and has been accredited for up to X Mainpro-M1 credits.

Canadian Hypertension Education Program



Notes

This program meets the accreditation criteria of The College of Family Physicians of Canada and has been accredited for up to 1.5 Mainpro-M1 credits

Case Development & Disclosures

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Instructions

Read out the case authors and their disclosure information.

Conflict Disclosure Information

- Presenter 1:

Grants/Research Support: _____

Speakers Bureau/Honoraria: _____

Consulting Fees: _____

Other: _____



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Instructions

Fill out prior to the meeting and disclose to the group any real or apparent conflict(s) of interest that may have a direct bearing on the subject matter of this CME program (based on the guidelines below).

Allow other participants to introduce themselves and give a brief outline of their practice and interests.

Guidelines for disclosure:

To ensure balance, independence, objectivity and scientific rigor, please disclose to program participants any real or apparent conflict(s) of interest that may have a direct bearing on the subject matter of this CME program. This pertains to relationships with pharmaceutical companies, biomedical device manufacturers, or other corporations whose products or services are related to the subject matter of this program. The intent of this disclosure is not to prevent a facilitator with a potential conflict of interest from making a presentation. It is merely intended that any potential conflict would be identified openly so that the participants may form their own judgments about the program with the full disclosure of the facts. It remains for the audience to determine whether the facilitator's outside interests may reflect a possible bias in either the exposition or the conclusions presented.

Example

Grants/research support: PharmaCorp ABC

Speakers bureau/honoraria: XYZ Biopharmaceuticals Ltd.

Consulting fees: MedX Group Inc.

Other: Employee of XXY Hospital Group

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.



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Instructions

Indicate to the group that this patient will be the focus of today's case discussion.

Notes

Hypertension, alone or in combination with coronary heart disease, precedes the development of heart failure in the majority of men and women.

Outline of Today's Activity

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



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Instructions

Review the agenda for today's activity.

For all slides, present the slide content and use the accompanying notes to describe them.

Statement of Need

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



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Instructions

Quickly go around the room and ask each participant to complete this statement. If there are members of the interprofessional team participating, tailor the statement accordingly.

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



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Instructions

Review the learning objectives for today's activity.

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



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Instructions

Review the learning objectives for today's activity.

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



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Instructions

Review the case study slide with the group.

Questions are integrated in the case presentation – when these appear on screen, allow the group to discuss their possible answers and the rationale behind them before moving on to review feedback from the case authors.

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



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Instructions

Review the case study slide with the group.

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



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Instructions

Review the case study slide with the group.

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



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Notes

Review the patient's past history.

Missing data are to be assumed NORMAL, to prevent prolonged discussions.

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



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Notes

Review the patient's family history.

Missing data are to be assumed NORMAL, to prevent prolonged discussions.

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



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Notes

These are the medications that the patient is taking at presentation.

They reflect an actual patient seen in clinic and are not intended to reflect current best practices.

Physical Examination

- Height: 160 cm
- Weight: 88 kg
- BMI: 33.7 kg/m²
- BP (left arm, seated):
 - 148/92 mmHg using an automated device
- Pulse: 56
- Funduscopy: 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



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Instructions

Based on the patient's history and examination, discuss possible next steps with the group.

Notes

The office automated device when used correctly, measures BP very accurately.

After the device is initiated, the healthcare provider leaves the room while it completes additional readings.

The initial reading is discarded and the subsequent readings are then averaged.

An office automated BP of 135/85 mmHg is equivalent to the daytime automated ambulatory BP of 135/85 mmHg or home BP monitoring.

The reading recorded in the office with the automated device of 148/92 mmHg can be considered a 'research quality' measurement.

Her murmurs have been noted before and are unchanged. It could suggest aortic sclerosis. These findings are all from the current visit.

Discussion Question 1

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



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Instructions

Discuss the question with the group.

Reminder: Allow the group to discuss their possible answers and the rationale behind them before moving on to review feedback from the case authors.

Discussion Question 1) This patient has hypertension and diabetes. What investigations are appropriate for this patient?

- a) What are the essential laboratory tests required in a patient with hypertension and diabetes?
- b) How frequently should you obtain these tests?



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Instructions

Discuss the question with the group.

Reminder: Allow the group to discuss their possible answers and the rationale behind them before moving on to review feedback from the case authors.

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



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Notes

Review the answer to the first question regarding essential laboratory investigations in patients with hypertension and diabetes.

Briefly discuss any rationale that participants may have for conducting other investigations not listed, or for not routinely conducting any of those listed.

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



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Notes

Review the answer to the next question regarding the timing of follow-up investigations in patients with hypertension and diabetes.

Briefly discuss any rationale that participants may have for answers different from those shown above.

Discussion Question 2

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



Instructions

Discuss the question with the group.

Reminder: Allow the group to discuss their possible answers and the rationale behind them before moving on to review feedback from the case authors.

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?

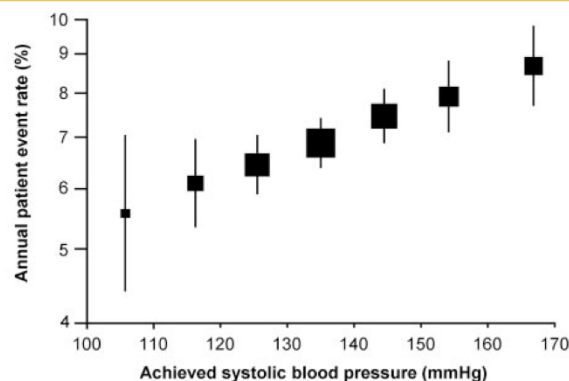


Instructions

Discuss the question with the group.

Reminder: Allow the group to discuss their possible answers and the rationale behind them before moving on to review feedback from the case authors.

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



De Galan BE cJASN 2009



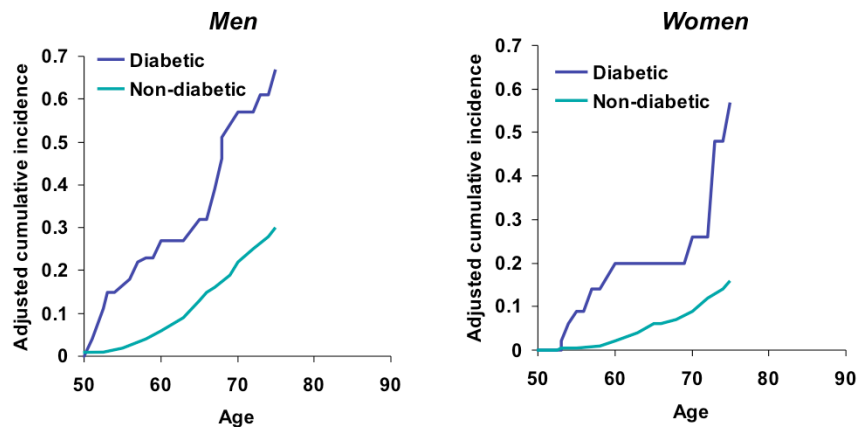
Key Points

- The Action in Diabetes and Vascular disease: preterAx and diamicroN-MR Controlled Evaluation (ADVANCE) study included patients with diabetes (n=11,140) randomized to either the combination of perindopril-indapamide or to placebo.
- The graph shows the relationship between renal event rate and systolic BP at follow-up. The rate of all renal events was significantly associated with achieved SBP levels ($p < 0.0001$ for trend). Patients who **achieved** the lowest SBP (median 106 mmHg) exhibited the lowest risk for renal events.

Reference

1. de Galan BE et al. Lowering blood pressure reduces renal events in type 2 diabetes. *J Am Soc Nephrol* 2009;2:883-92.

Diabetes and Lifetime CVD Risk



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

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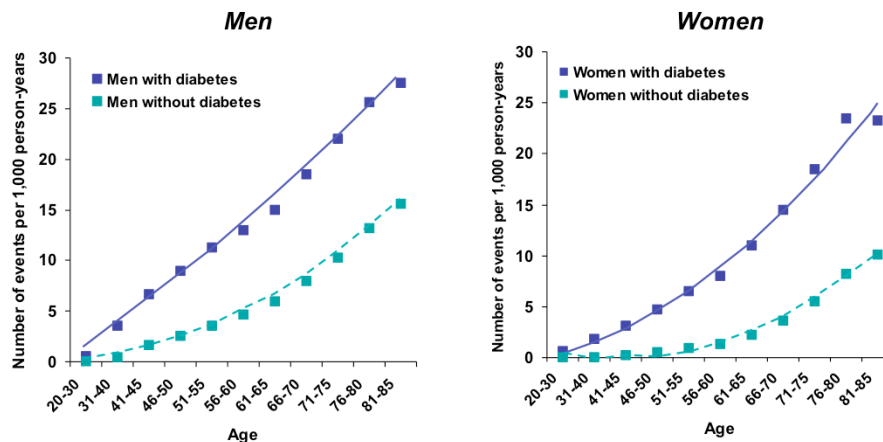
Key Points

- Diabetes has a substantial impact on lifetime CVD risk.
- The graphs show the lifetime CVD risk among patients in the Framingham cohort who had no cardiovascular disease (CVD) at age 50 (n=111,777 patient-years). Of individual risk factors present at age 50, diabetes conferred the highest lifetime CVD risk through age 75: 67.1% for men and 57.3% for women.

Reference

1. Lloyd-Jones DM, et al. Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age. *Circulation* 2006;113:791-8.

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



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



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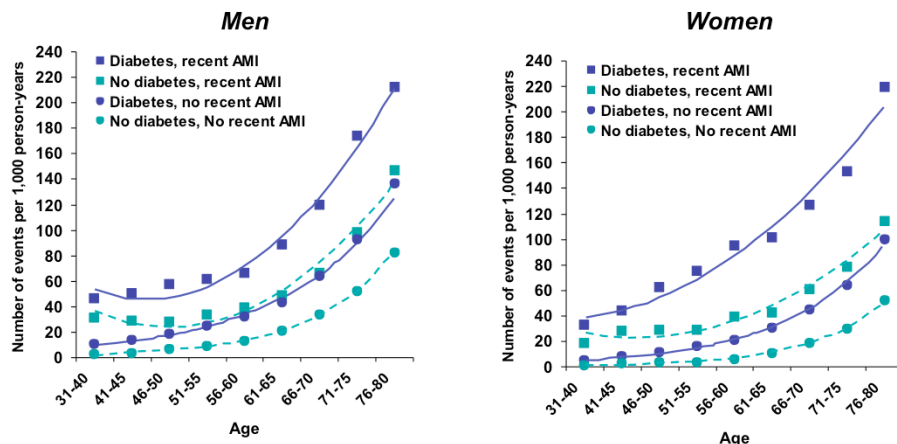
Key Points

- A retrospective analysis of an Ontario health claims database examined CVD events in patients with diabetes (n=379,003) as compared to the general population (n=9,018,082) over a 6 year period (1994-2000).
- The study found that patients with diabetes were more likely to experience a CVD event earlier than those without. Diabetes conferred an equivalent risk to aging 15 years.

Reference

1. Booth GL, et al. Relation between age and cardiovascular disease in men and women with diabetes compared with non-diabetic people: a population-based retrospective cohort study. *Lancet* 2006;368:29-36.

Relation Between Age and CVD in Patients with Diabetes Compared to Those Without $\pm$ Recent AMI



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



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Key Points

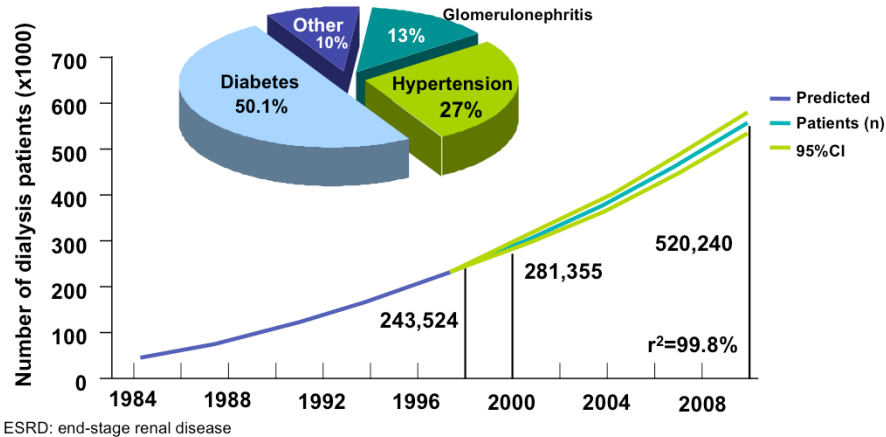
- These graphs show the impact on CVD events in men and women according to the presence of 3 risk factors: age, diabetes and previous myocardial infarction.
- For example, in men the highest risk was among those with diabetes and recent MI, while the lowest risk was among those with neither. The risk was almost equivalent among men without diabetes who had a recent AMI vs. men with diabetes who had not had a recent AMI, particularly among men ages 50-65 years.
- However, in men and women of all ages, those with diabetes had consistently higher CVD-event rates than those without diabetes.

Reference

1. Booth GL, et al. Relation between age and cardiovascular disease in men and women with diabetes compared with non-diabetic people: a population-based retrospective cohort study. *Lancet* 2006;368:29-36.

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



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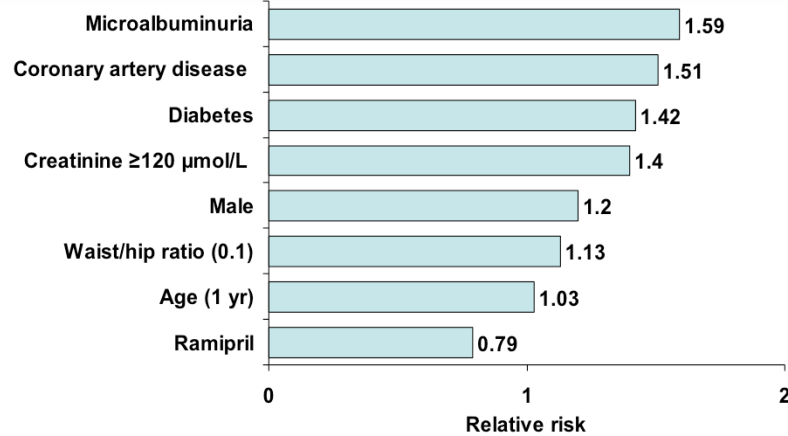
Key Points

- Diabetes is a common cause of end stage renal disease (ESRD). The number of people on dialysis increases by about 10% per year, and the main cause of this exponential increase is chronic diabetic nephropathy.
- It is important to note that both of the major causes of ESRD (diabetes and hypertension) are associated with increased CV risk.

Reference

1. United States Renal Data System. Annual data report. 2000. Available at: <http://www.usrds.org/adr.htm>. Accessed April 25, 2001.

Multivariate Relative Risks for Primary Outcomes in the HOPE Study



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



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Key Points

- The Heart Outcomes and Prevention Evaluation (HOPE) study, in 9287 patients, included 980 patients with mild renal insufficiency and 8,307 without. Patients received ramipril, vitamin E, or placebo and were followed-up for a median of 4.5 years.
- The graph shows the results of a multivariate analysis of risk factors for the primary outcome measure (incidence of CV death, MI, or stroke). Microalbuminuria, prior CAD, and diabetes were key factors associated with increased incidence, while ramipril was associated with a decrease.

Reference

1. Mann, JFE et al. Renal insufficiency as a predictor of cardiovascular outcomes and the impact of ramipril: the HOPE randomized trial. *Ann Intern Med* 2001;134:629-36.

Abnormal Urinary Albumin Levels

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

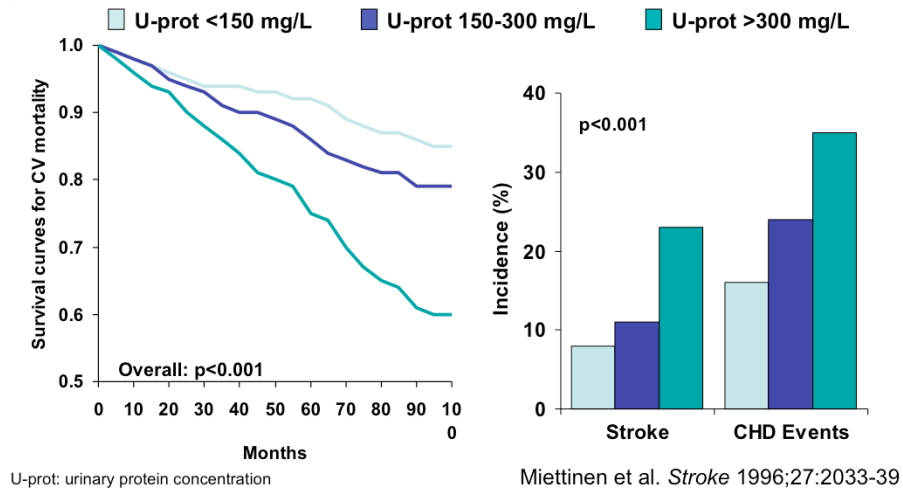


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Key Points

- The table shows abnormal urinary albumin/creatinine ratios for men and women.
- In diabetes, the presence of microalbuminuria and hypertension is known to confer increased renal and cardiovascular risk. Renal risk can be reduced by blocking the renin-angiotensin-aldosterone system (RAAS) in addition to controlling blood pressure.
- In chronic kidney disease, there is evidence of additional renal benefit of blockade of the RAAS system beyond that provided for BP control alone, in patients with urine protein levels >500 mg/day. This level is equivalent to a urine albumin:creatinine ratio of ~30.

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



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Key Points

- This study was a 7-year follow-up of cohorts of nondiabetic ($n=1375$) and diabetic ($n=1056$) subjects in Finland. The urinary protein concentration at baseline was stratified into three categories: no proteinuria (<150 mg/L), borderline (150 to 300 mg/L), and clinical proteinuria (>300 mg/L).
- The graph on the left shows the survival curves for CVD mortality in patients with diabetes according urinary protein concentration. CVD mortality was significantly higher in those with clinical proteinuria than in patients with borderline proteinuria or without proteinuria.
- The graph on the right shows that the incidence of stroke and CHD events (CHD death or nonfatal MI) demonstrated a similar pattern to mortality, being highest in those with clinical proteinuria.

Reference

1. Miettinen H, et al. Proteinuria predicts stroke and other atherosclerotic vascular disease events in nondiabetic and non-insulin-dependent diabetic subjects. *Stroke* 1996;27:2033-39.

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



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Instructions

Review the results of lab tests that were performed prior to the next office visit.

Discuss any implications of these findings.

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



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Instructions

Review the results of lab tests that were performed prior to the next office visit.

Discuss any implications of these findings.

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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Instructions

Review the results of lab tests that were performed prior to the next office visit.

Discuss any implications of these findings.

Discussion Question 3

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



Instructions

Discuss the question with the group.

Reminder: Allow the group to discuss their possible answers and the rationale behind them before moving on to review feedback from the case authors.

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?



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Instructions

Discuss the question with the group.

Reminder: Allow the group to discuss their possible answers and the rationale behind them before moving on to review feedback from the case authors.

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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Instructions

Discuss how you would classify this patient.

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 🇨🇦



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Instructions

Discuss when you would initiate pharmacotherapy in patients with diabetes and hypertension.

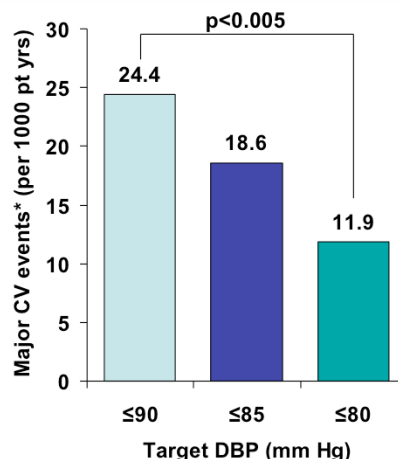
Notes

The BP levels for treatment initiation are the same as the BP target levels.

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



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

Hypertension
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Key Points

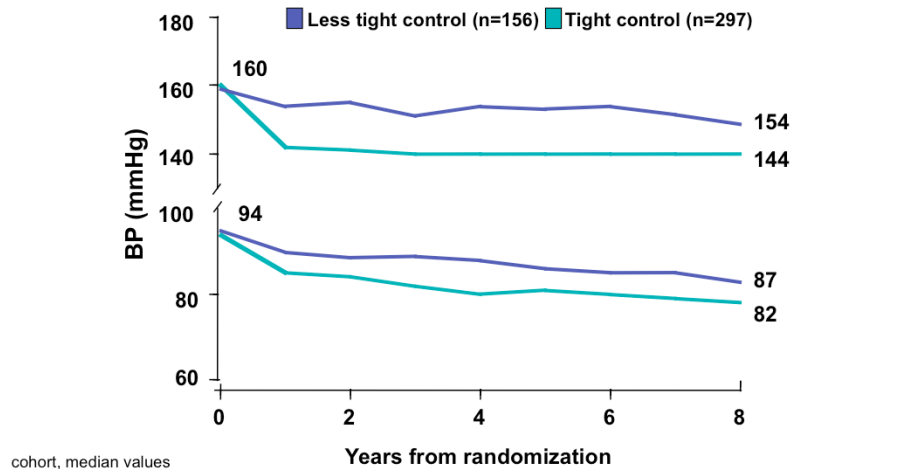
- The Hypertension Optimal Treatment (HOT) trial showed a reduction in cardiovascular events with tighter control of diastolic blood pressure in patients with diabetes. HOT included 18,790 patients, with hypertension and diastolic blood pressure (DBP) between 100-115 mm Hg who were randomly assigned a target DBP ≤90, ≤85, or ≤80 mm Hg.
- The table on the left shows the target values of BP and DBP levels achieved.
- The graph on the right shows major CV events according to target DBP group.
- In the subgroup of patients with diabetes, major cardiovascular events were reduced by about 51% in the <80 mm Hg target group compared with the <90 mm Hg group (p=0.005).

•

Reference

1. Hansson L, et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. *Lancet* 1998;351:1755-62.

Blood Pressure: Tight vs. Less Tight Control



CHEP

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



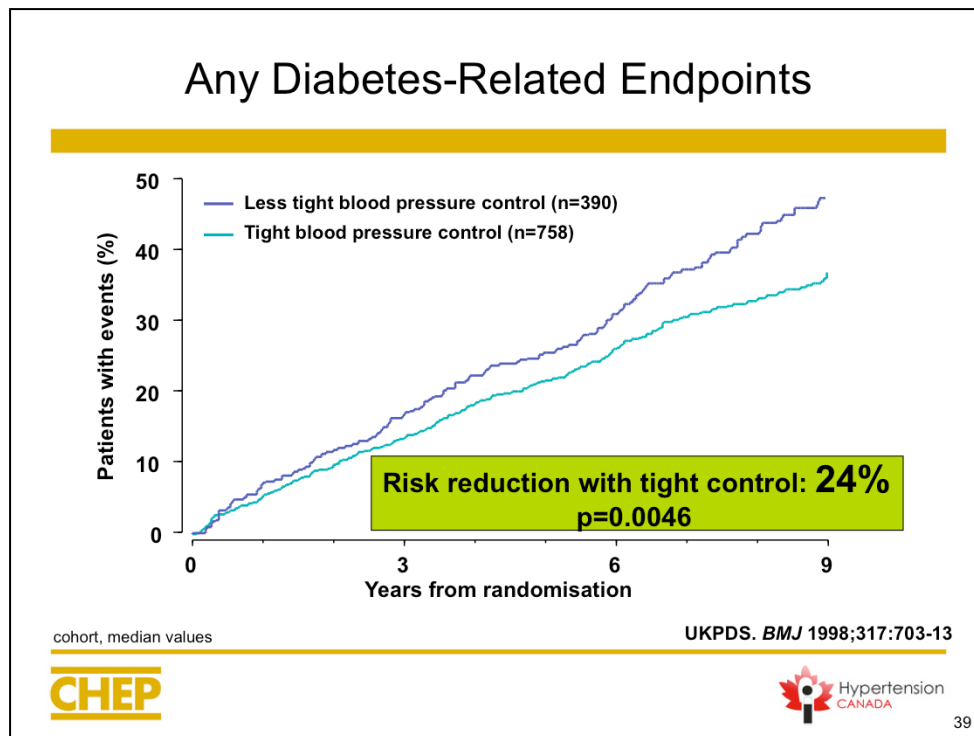
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Key Points

- In the UK Prospective Diabetes Study (UKPDS), patients with diabetes and hypertension were randomized to tight or less tight BP control, and followed up for 8 years.
- The average BP was 144/82 mmHg in the tight BP control group, and 154/87 mmHg in the less tight control group.

Reference

1. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *BMJ* 1998;317:703-13.



Key Points

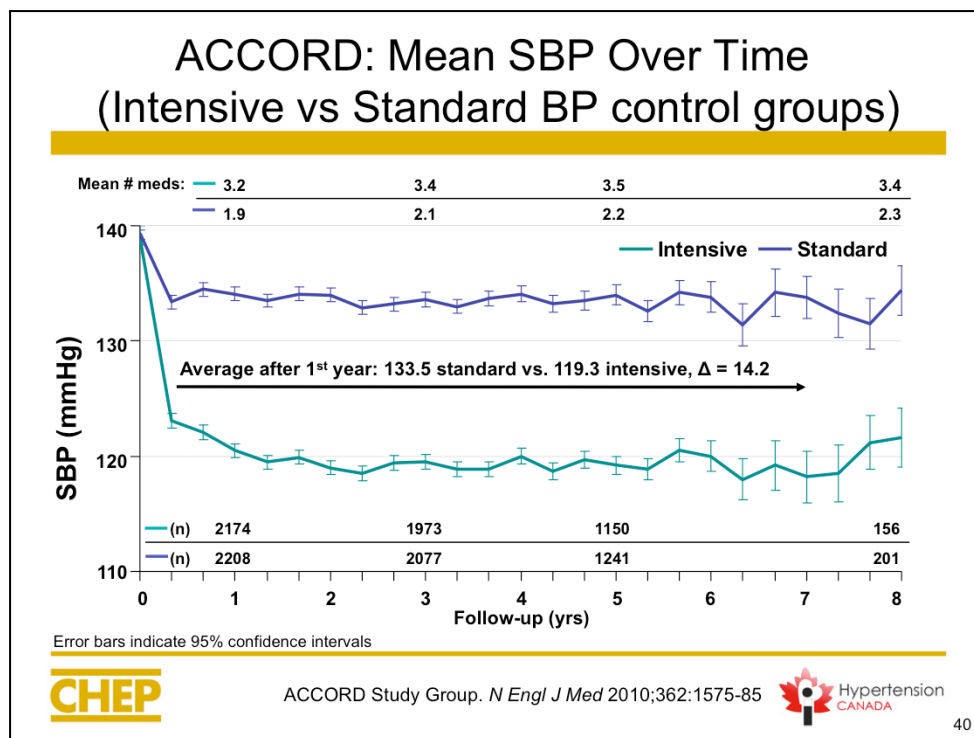
- In the UK Prospective Diabetes Study (UKPDS), patients with diabetes and hypertension were randomized to tight or less tight BP control, and followed up for 8 years.
- Patients in the tight BP control group, achieved a 24% greater reduction in risk of any diabetes related endpoint compared to those in the less tight BP control group (95% CI 8-38; $p=0.0046$).

Notes

- Clinical end points related to diabetes (non-fatal): Myocardial infarction, angina, heart failure, stroke, renal failure, amputation (of at least one digit), vitreous hemorrhage, retinal photocoagulation, blindness in one eye, or cataract extraction
- Mortality endpoints related to diabetes: Death due to myocardial infarction, sudden death, stroke, peripheral vascular disease, renal disease, hyperglycemia, or hypoglycemia

Reference

1. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *BMJ*



Key Points

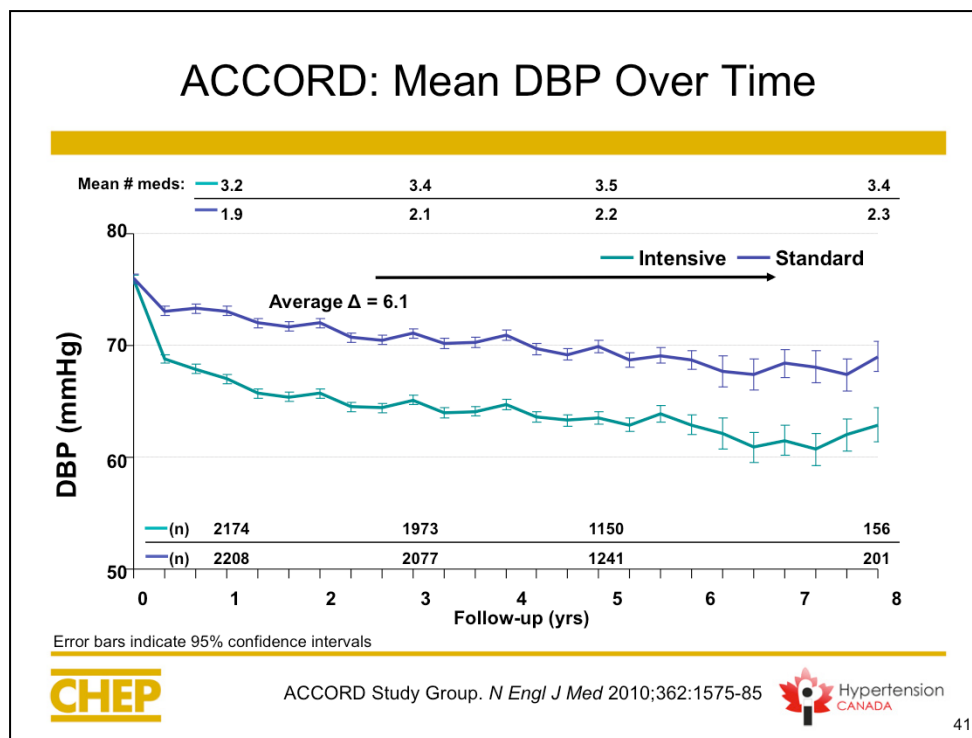
- These data are from the Action to Control Cardiovascular Risk in Diabetes (ACCORD) BP sub-study in 4733 randomized to intensive therapy (target SBP <120 mm Hg) or standard therapy (target SBP <140 mm Hg).
- The graph shows the mean achieved SBP over the 8-year follow-up. After the first year, the average SBP was 133.5 mm Hg in patients receiving standard therapy compared to 119.3 mm Hg in those receiving intensive therapy – a difference of 14.2 mm Hg.

Notes

- The Action to Control Cardiovascular Risk in Diabetes (ACCORD) study was a randomized, double-blind trial conducted across Canada and the US. The BP sub-study was conducted in a subgroup of patients (n=4733) who were randomized to either intensive therapy (target SBP <120 mm Hg) or standard therapy (target SBP <140 mm Hg). The primary endpoint was a composite of nonfatal MI, nonfatal stroke, or CV-related death. Mean BP at baseline was 139.2/70.6 mm Hg.
- Patients in the intensive therapy arm were given a greater mean number of medications than those in the standard therapy group over the course of the trial.

Reference

1. ACCORD Study Group. Effects of intensive blood-pressure control in type 2 diabetes mellitus. *N Engl J Med* 2010;362:1575-85.



Key Points

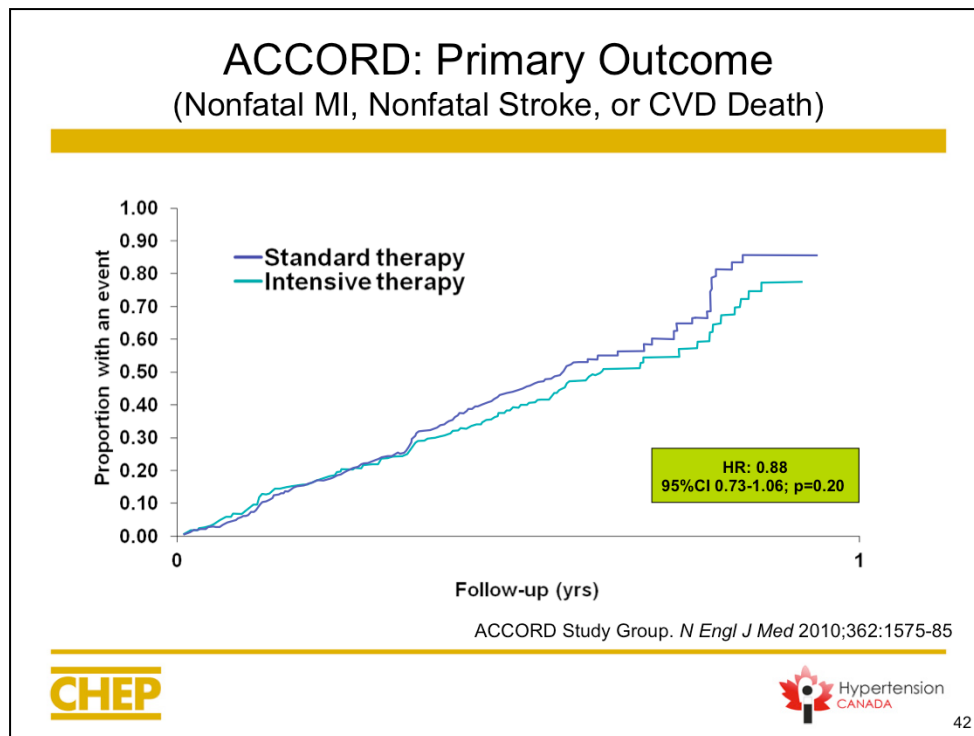
- These data are from the ACCORD BP sub-study in 4733 randomized to intensive therapy (target SBP <120 mm Hg) or standard therapy (target SBP <140 mm Hg).
- The graph shows the mean achieved DBP over the 8-year follow-up. After the first year, the average DBP was 70.5 mm Hg in patients receiving standard therapy and 64.4 mm Hg in those receiving intensive therapy – a difference of 6.1 mm Hg.

Notes

- The Action to Control Cardiovascular Risk in Diabetes (ACCORD) study was a randomized, double-blind trial conducted across Canada and the US. The BP sub-study was conducted in a subgroup of patients (n=4733) who were randomized to either intensive therapy (target SBP <120 mm Hg) or standard therapy (target SBP <140 mm Hg). The primary endpoint was a composite of nonfatal MI, nonfatal stroke, or CV-related death. Mean BP at baseline was 139.2/70.6 mm Hg.
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1. ACCORD Study Group. Effects of intensive blood-pressure control in type 2 diabetes mellitus. *N Engl J Med* 2010;362:1575-85.



Key Points

- These data are from the ACCORD BP sub-study in 4733 randomized to intensive therapy (target SBP <120 mm Hg) or standard therapy (target SBP <140 mm Hg).
- There was no significant reduction in the rate of the primary composite outcome: 1.87% per year in the intensive therapy group vs. 2.09% per year in the standard therapy group (hazard ratio: 0.88, 95% CI 0.73-1.06; p=0.20). However the rate of stroke was significantly reduced (data not shown).

Notes

- The Action to Control Cardiovascular Risk in Diabetes (ACCORD) study was a randomized, double-blind trial conducted across Canada and the US. The BP sub-study was conducted in a subgroup of patients (n=4733) who were randomized to either intensive therapy (target SBP <120 mm Hg) or standard therapy (target SBP <140 mm Hg). The primary endpoint was a composite of nonfatal MI, nonfatal stroke, or CV-related death. Mean BP at baseline was 139.2/70.6 mm Hg.
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Reference

1. ACCORD Study Group. Effects of intensive blood-pressure control in type 2 diabetes mellitus. *N Engl J Med* 2010;362:1575-85.

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



ACCORD study NEJM 2010



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Key Points

- The ACCORD BP sub-study did not find a significant reduction in CV events in patients with type 2 diabetes and high risk of CV events with a target SBP <120 mm Hg vs. <140 mm Hg.
- Reasons for the lack of superiority of tighter BP control are discussed in the slide.

Notes

- The Action to Control Cardiovascular Risk in Diabetes (ACCORD) study was a randomized, double-blind trial conducted across Canada and the US. The BP sub-study was conducted in a subgroup of patients (n=4733) who were randomized to either intensive therapy (target SBP <120 mm Hg) or standard therapy (target SBP <140 mm Hg). The primary endpoint was a composite of nonfatal MI, nonfatal stroke, or CV-related death. Mean BP at baseline was 139.2/70.6 mm Hg.
- Patients in the intensive therapy arm were given a greater mean number of medications than those in the standard therapy group over the course of the trial.

Reference

1. ACCORD Study Group. Effects of intensive blood-pressure control in type 2 diabetes mellitus. *N Engl J Med* 2010;362:1575-85.

Discussion Question 4

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



Instructions

Discuss the question with the group.

Reminder: Allow the group to discuss their possible answers and the rationale behind them before moving on to review feedback from the case authors.

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



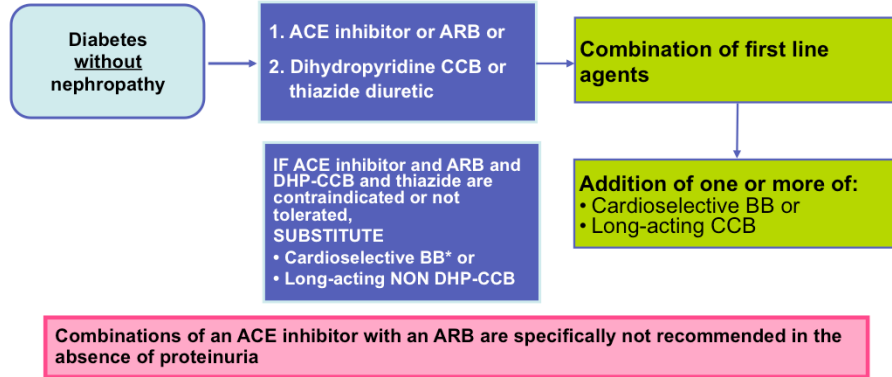
Instructions

Discuss the question with the group.

Reminder: Allow the group to discuss their possible answers and the rationale behind them before moving on to review feedback from the case authors.

Treatment of Systolic-Diastolic Hypertension without Diabetic Nephropathy

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



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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Key Points

- The algorithm shows the CHEP treatment recommendations for patients with hypertension and diabetes without nephropathy.
- The recommended target is <130/80 mm Hg.
- For patients with cardiovascular or kidney disease, including microalbuminuria or with cardiovascular risk factors in addition to diabetes and hypertension, an ACE inhibitor or an ARB is recommended as initial therapy (Grade A).
- For patients with diabetes and hypertension not included in the above recommendation, appropriate choices include (in alphabetical order): ACE inhibitors (Grade A), angiotensin receptor blockers (Grade B), dihydropyridine CCBs (Grade A) and thiazide/thiazide-like diuretics (Grade A).
- Combination therapy using 2 first-line agents may also be considered as initial treatment (Grade B) if the SBP is 20 mm Hg above the target or if DBP is 10 mm Hg above the target.
- If target BP is not achieved with standard-dose monotherapy, additional antihypertensive therapy should be used. For patients in whom combination therapy with an ACE inhibitor is being considered, a dihydropyridine CCB is preferable to hydrochlorothiazide (Grade A).

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 / 



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Instructions

Discuss BP targets for patients with diabetes and hypertension.

Notes

Target blood pressure is <140/90 in patients with systolic or diastolic hypertension, and lower (<130/80) in patients with comorbid diabetes.

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



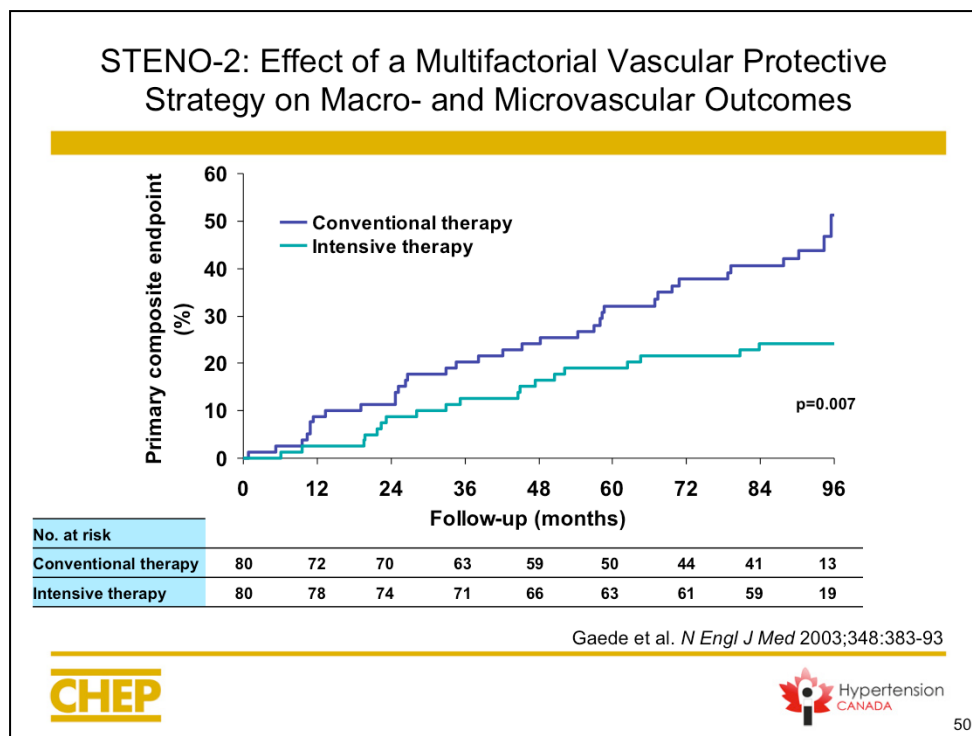
49

Key Points

- The STENO-2 study compared the effects of a multifactorial more intensive therapy vs. conventional treatment on reductions in the rate of all-cause mortality and CV-related mortality in patients with diabetes and persistent microalbuminuria (n=160).
- Defined targets included: glycated hemoglobin <6.5%, fasting serum total cholesterol <4.5 mmol/L, fasting serum triglycerides <1.7 mmol/L, SBP <130 mm Hg, and DBP <80mm Hg.

Reference

1. Gaede, P et al. Effect of a multifactorial intervention on mortality in type 2 diabetes. *N Engl J Med* 2008;358:580-91.



Key Points

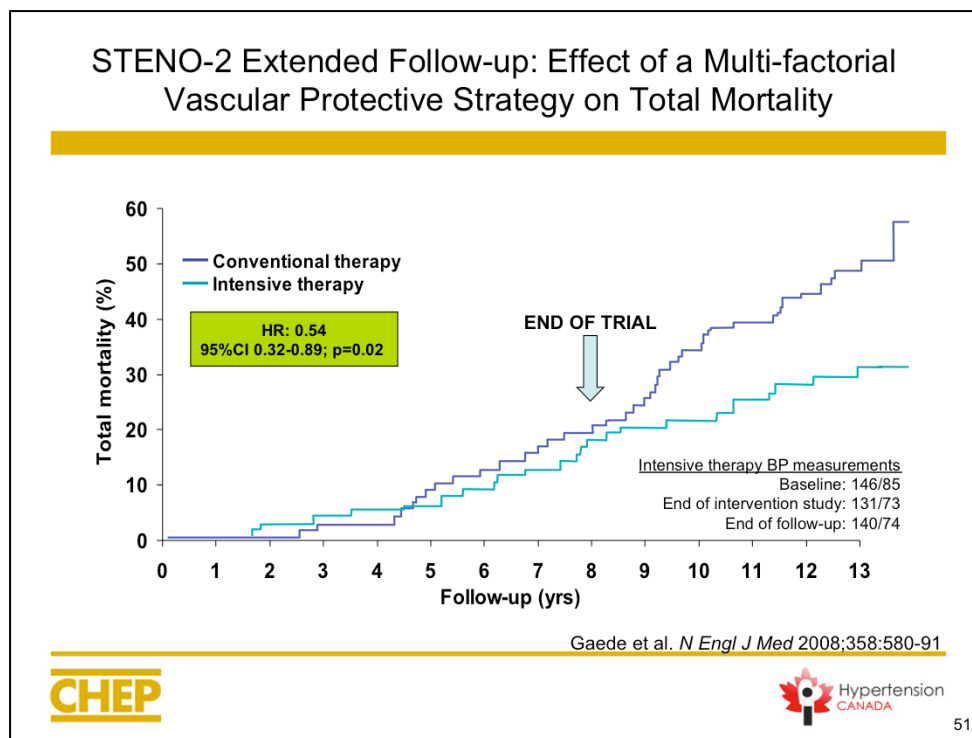
- The STENO-2 study found that significant reductions in event rates with more intense therapy vs. conventional treatment
- The graph shows the time to first event curves for the primary composite endpoint. Throughout follow-up, the curves continued to separate, with intensive therapy resulting in a risk reduction of approximately 50% over standard therapy. This suggests that more aggressive management of patients with diabetes and elevated BP will likely reduce the risk of both micro- and macrovascular complications.

Notes

The STENO-2 study compared the effects of a multifactorial more intensive therapy vs. conventional treatment on reductions in the rate of all-cause mortality and CV-related mortality in patients with diabetes and persistent microalbuminuria (n=160).

Reference

1. Gaede P, et al. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med* 2003;348:383-93.



Key Points

- The STENO-2 study also showed a significant reduction in mortality with more intense therapy vs. conventional treatment.
- The hazard ratio for mortality was 0.54 (95% CI 0.32-0.89; p=0.02) with intensive therapy vs. standard therapy. Over the mean 13.3 year follow-up period, the absolute risk reduction for all-cause mortality was 20% with intensive vs. standard therapy.

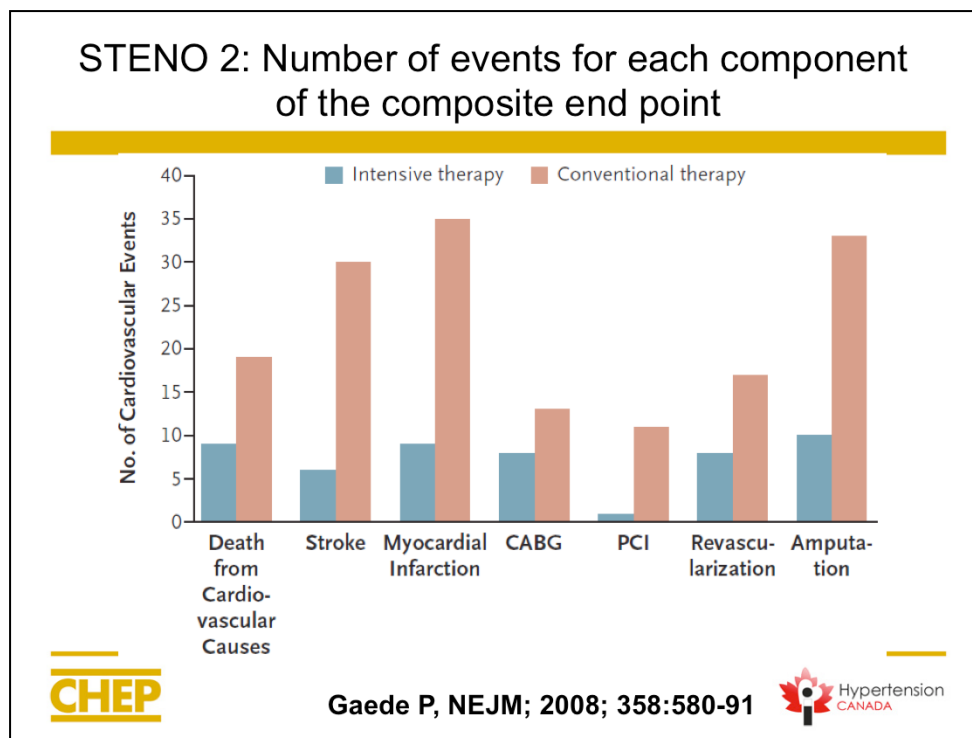
Notes

The STENO-2 study compared the effects of a multifactorial more intensive therapy vs. conventional treatment on reductions in the rate of all-cause mortality and CV-related mortality in patients with diabetes and persistent microalbuminuria (n=160).

The rate of death in the conventional treatment group was 50% over the entire follow-up period high-lighting the poor prognosis for patients with type 2 diabetes and microalbuminuria in the absence of intensive treatment.

Reference

1. Gaede, P et al. Effect of a multifactorial intervention on mortality in type 2 diabetes. *N Engl J Med* 2008;358:580-91.



Notes

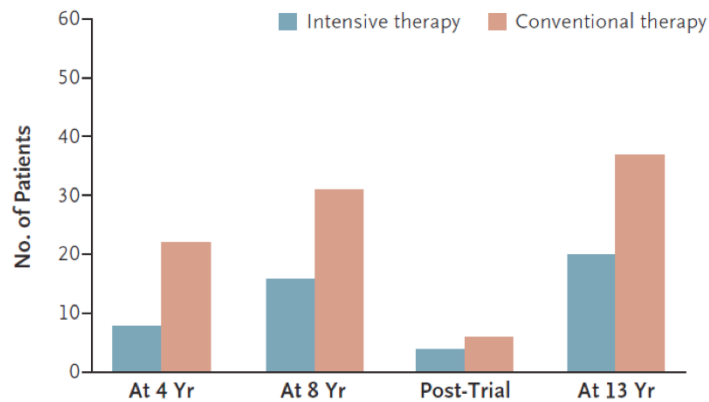
The STENO-2 At 13 years there was an absolute risk reduction for death from any cause of 20% for patients with type 2 diabetes and microalbuminuria who received intensive therapy, compared to those in the usual care group. This leads to a number needed to treat NNT of only 5 over 13 years for all cause mortality.

Reference

1. Gaede, P et al. Effect of a multifactorial intervention on mortality in type 2 diabetes. *N Engl J Med* 2008;358:580-91.

STENO-2: Progression to Macroalbuminuria

A Nephropathy



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



Notes

- The STENO-2 At 13 years there was an absolute risk reduction for death from any cause of 20% for patients with type 2 diabetes and microalbuminuria who received intensive therapy, compared to those in the usual care group. This leads to a number needed to treat NNT of only 5 over 13 years for all cause mortality.
- The reduction of progression of nephropathy was associated with a significant absolute reduction of 6.3% in the need for dialysis. This yields a number needed to treat (NNT) of 16 over the 13 years to prevent one dialysis.

Reference

1. Gaede, P et al. Effect of a multifactorial intervention on mortality in type 2 diabetes. *N Engl J Med* 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



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Instructions

Review the case progress slide with the group.

Reminder: Questions are integrated in the case presentation. Allow the group to discuss their possible answers and the rationale behind them before moving on to review feedback from the case authors.

Discussion Question 5

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



Instructions

Discuss the question with the group.

Reminder: Allow the group to discuss their possible answers and the rationale behind them before moving on to review feedback from the case authors.

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



Notes

These are the medications that the patient is currently taking.

They reflect an actual patient seen in clinic and are not intended to reflect current best practices.

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)



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Instructions

Briefly discuss possible changes to her current medications.

Notes

These were the meds that the patient was currently taking. They reflect an actual patient seen in clinic and are not intended to reflect current best practices.

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



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Instructions

Briefly discuss possible changes to her current medications.

Notes

These were the meds that the patient was currently taking. They reflect an actual patient seen in clinic and are not intended to reflect current best practices.

Key Points:

- a. Replacing Ibuprofen by other analgesics: by blocking prostaglandin production through blockade of the COX-2 enzyme. NSAIDs block the vasodilating and natriuretic effects of prostaglandins. They also blunt the antihypertensive effect of some medications mainly ACEI. NSAID may also diminish the cardioprotective effect of aspirin
- b. Options of replacing the beta blocker with a DHP-CCB (amlodipine-nifedipine-felodipine) is a more effective combination
- c. Adding a DHP-CCB to the actual medication: Following the results of the ACCOMPLISH trial, CHEP has recommended that ACEI+DHP-CCB combination be preferred combination for hypertensive –diabetics at risk of CV complications. The BB+ACEI combination has also not been proven to have additive effect

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.



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Instructions

Briefly discuss possible changes to her current medications.

Key Points

- d. Increasing the doses of the diuretic and the ACEI. Most common errors in resistant hypertension: inadequate doses of medications and more specifically the diuretic or lack of diuretic
- e. Replacing the hydrochlorothiazide with other diuretics which could be more effective at similar doses such as chlorthalidone. The use of spironolactone, a mineralocorticoid receptor antagonist is also an option but there is risk of hyperkalemia in the presence of an ACEI (ramipril) already prescribed. There are no guidelines for the monitoring of potassium but sampling at one week and 3 weeks would be reasonable and then regular follow up such as every 3 months or less if the patient is stable.

Notes

These were the meds that the patient was currently taking. They reflect an actual patient seen in clinic and are not intended to reflect current best practices.

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.



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Instructions

Briefly discuss possible changes to her current medications.

Key Points

- e. Addition of a mineralocorticoid receptor antagonist (spironolactone) while monitoring for hyperkalemia since patient already a potassium retaining agent: ARB or ACEI
- f. Another option would be the addition of an alpha blocker such as doxazosin while monitoring for hypotension

Notes

These were the meds that the patient was currently taking. They reflect an actual patient seen in clinic and are not intended to reflect current best practices.

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



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Instructions

Review the case progress slide with the group.

Reminder: Questions are integrated in the case presentation. Allow the group to discuss their possible answers and the rationale behind them before moving on to review feedback from the case authors.

Note: The proteinuria is despite a full dose of a RAAS blocker.

Discussion Question 6

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



Instructions

Discuss the question with the group.

Reminder: Allow the group to discuss their possible answers and the rationale behind them before moving on to review feedback from the case authors.

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



Instructions

Discuss the question with the group.

Reminder: Allow the group to discuss their possible answers and the rationale behind them before moving on to review feedback from the case authors.

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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Key Points

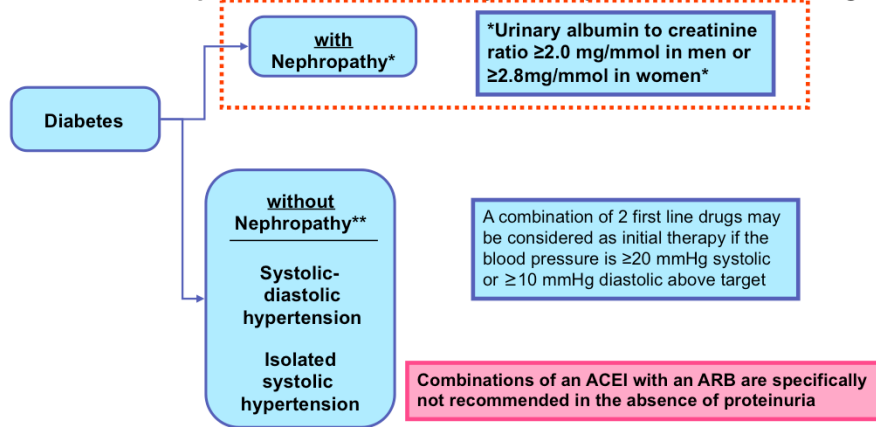
- Guidelines recommend considering lifestyle interventions as part of an overall strategy to reduce BP in patients above target. These may include: achieving and maintaining a healthier weight, limiting the intake of sodium and alcohol, increased physical activity, and smoking cessation.
- Discuss the role of sodium reduction, reducing intake of foods with added sodium.

Note

The extent of blood pressure change from each intervention should not be compared because the participants, the type and duration of intervention, and the basic design of the trials differed substantially.

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

CHEP

Hypertension CANADA

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Key Points

- The algorithm shows the CHEP treatment recommendations for patients with hypertension with or without diabetic nephropathy.
- The recommended target is $<130/80$ mm Hg.
- Nephropathy is defined as a UAC ratio ≥ 2.8 mg/mmol in women, or ≥ 2.0 mg/mmol in men, in a minimum of 2 out of 3 measurements.
- For patients with cardiovascular or kidney disease, including microalbuminuria or with cardiovascular risk factors in addition to diabetes and hypertension, an ACE inhibitor or an ARB is recommended as initial therapy (Grade A).
- For patients with diabetes and hypertension not included in the above recommendation, appropriate choices include (in alphabetical order): ACE inhibitors (Grade A), angiotensin receptor blockers (Grade B), dihydropyridine CCBs (Grade A) and thiazide/thiazide-like diuretics (Grade A).
- Combination therapy using 2 first-line agents may also be considered as initial treatment (Grade B) if the SBP is 20 mm Hg above the target or if DBP is 10 mm Hg above the target.
- If target BP is not achieved with standard-dose monotherapy, additional antihypertensive therapy should be used. For patients in whom combination therapy with an ACE inhibitor is being considered, a dihydropyridine CCB is preferable to hydrochlorothiazide (Grade A).
- When proteinuria is not present, use of an ACE-I + ARB combination is not recommended.

Definitions of Microalbuminuria and Macroalbuminuria

Care	Normal	Microalbuminuria	Macroalbuminuria
Urinary excretion of albumin ($\mu\text{g}/\text{min}$)	<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



Instructions

Discuss how you would classify this patient.

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?



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Instructions

Discuss the questions with the group.

Reminder: Allow the group to discuss their possible answers and the rationale behind them before moving on to review feedback from the case authors.

Notes:

1. Adding an ACEi to an ARB results in an improvement of albuminuria (Kunz R, Friedrich C, Wolbers M, Mann JF: Meta-analysis: effect of monotherapy and combination therapy with inhibitors of the renin angiotensin system on proteinuria in renal disease. Ann Intern Med 2008, 148:30–48.)
2. However, the data is still lacking to demonstrate that this leads to an improvement of renal and cardiovascular outcomes. There is also a significant risk of hyperkalemia with dual therapy (5% risk of $K > 5.5$ mmol/L) and acute renal failure (approximately 0.3%) compared to monotherapy with an ACEi or ARB alone.

References:

- Tobe SW, Clase CM, Gao P, McQueen M, Grosshennig A, Wang X et al. Cardiovascular and Renal Outcomes With Telmisartan, Ramipril, or Both in People at High Renal Risk: Results From the ONTARGET and

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.



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Instructions

Review the answers and pause here to discuss with the group.

Briefly discuss any rationale that participants may have for answers different from those shown above.

Notes:

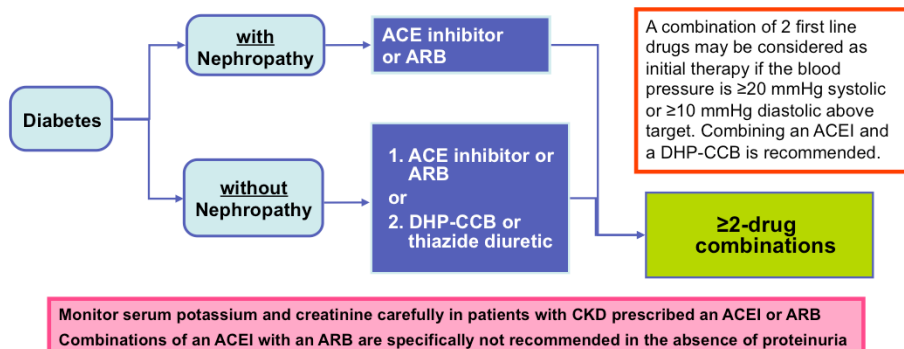
1. Adding an ACEi to an ARB results in an improvement of albuminuria (Kunz R, Friedrich C, Wolbers M, Mann JF: Meta-analysis: effect of monotherapy and combination therapy with inhibitors of the renin angiotensin system on proteinuria in renal disease. Ann Intern Med 2008, 148:30–48.)
2. However, the data is still lacking to demonstrate that this leads to an improvement of renal and cardiovascular outcomes. There is also a significant risk of hyperkalemia with dual therapy (5% risk of K > 5.5 mmol/L) and acute renal failure (approximately 0.3%) compared to monotherapy with an ACEi or ARB alone.
3. For monitoring of patients on dual therapy, suggest working with the patient's nephrologist or specialist and monitoring renal function and electrolytes every three months.

References:

- Tobe SW, Clase CM, Gao P, McQueen M, Grosshennig A, Wang X et al. Cardiovascular and Renal Outcomes With Telmisartan, Ramipril, or Both in People at High Renal Risk: Results From the ONTARGET and TRANSCEND Studies. Circulation 2011;CIRCULATION.
- Tobe SW, Dai MO. Outcomes of antiproteinuric RAAS blockade: high-dose compared with dual therapy. Curr Hypertens Rep 2009; 11(5):345-353

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

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



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

If creatinine over 150 $\mu\text{mol/L}$ 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

CHEP

Hypertension
CANADA

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Key Points

- The algorithm shows the CHEP treatment recommendations for patients with hypertension and diabetes without nephropathy.
- The recommended target is $<130/80$ mm Hg.
- For patients with cardiovascular or kidney disease, including microalbuminuria or with cardiovascular risk factors in addition to diabetes and hypertension, an ACE inhibitor or an ARB is recommended as initial therapy (Grade A).
- For patients with diabetes and hypertension not included in the above recommendation, appropriate choices include (in alphabetical order): ACE inhibitors (Grade A), angiotensin receptor blockers (Grade B), dihydropyridine CCBs (Grade A) and thiazide/thiazide-like diuretics (Grade A).
- Combination therapy using 2 first-line agents may also be considered as initial treatment (Grade B) if the SBP is 20 mm Hg above the target or if DBP is 10 mm Hg above the target.
- If target BP is not achieved with standard-dose monotherapy, additional antihypertensive therapy should be used. For patients in whom combination therapy with an ACE inhibitor is being considered, a dihydropyridine CCB is preferable to hydrochlorothiazide (Grade A).
- When proteinuria is not present, use of an ACE-I + ARB combination is not recommended.
- In patients with CKD receiving an ACE-I or ARB, clinicians are reminded to carefully monitor serum potassium and creatinine levels.

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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Instructions

Review key points from the Canadian Hypertension Education Program with the group.

The full slide set of the
2015 CHEP Recommendations
is available at
www.hypertension.ca

