Module 5:

Management of Hypertension in Non-diabetes Patients with Chronic Kidney Disease

This program meets the accreditation criteria of The College of Family Physicians of Canada and has been accredited for up to 1.0 Mainpro-M1 credits.

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Hypertension CANADA

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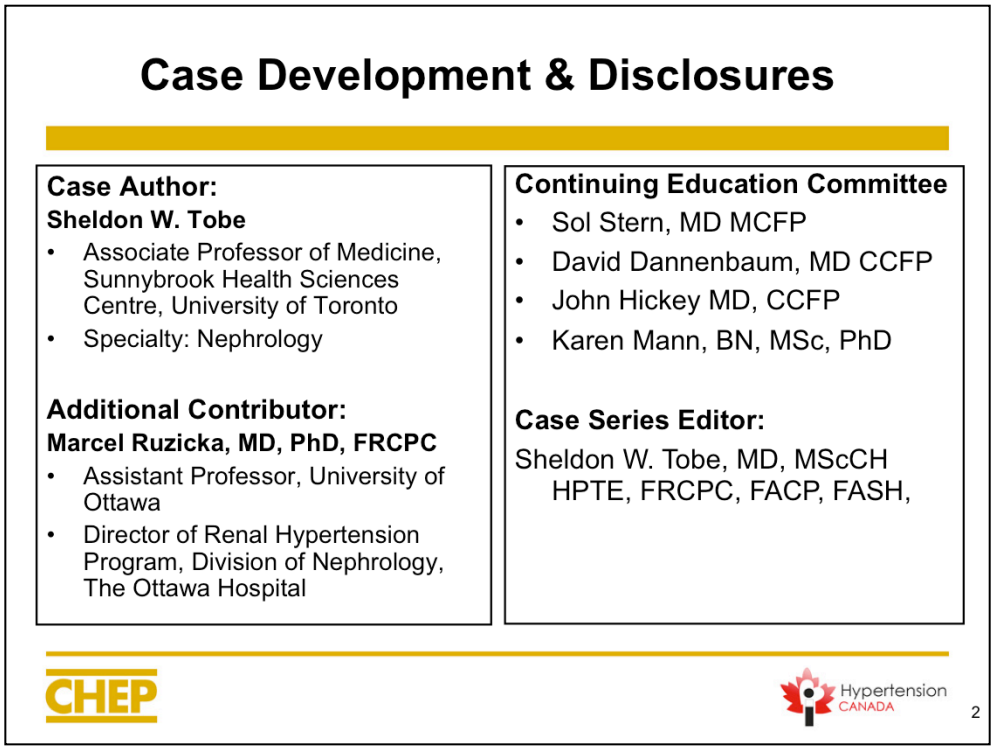
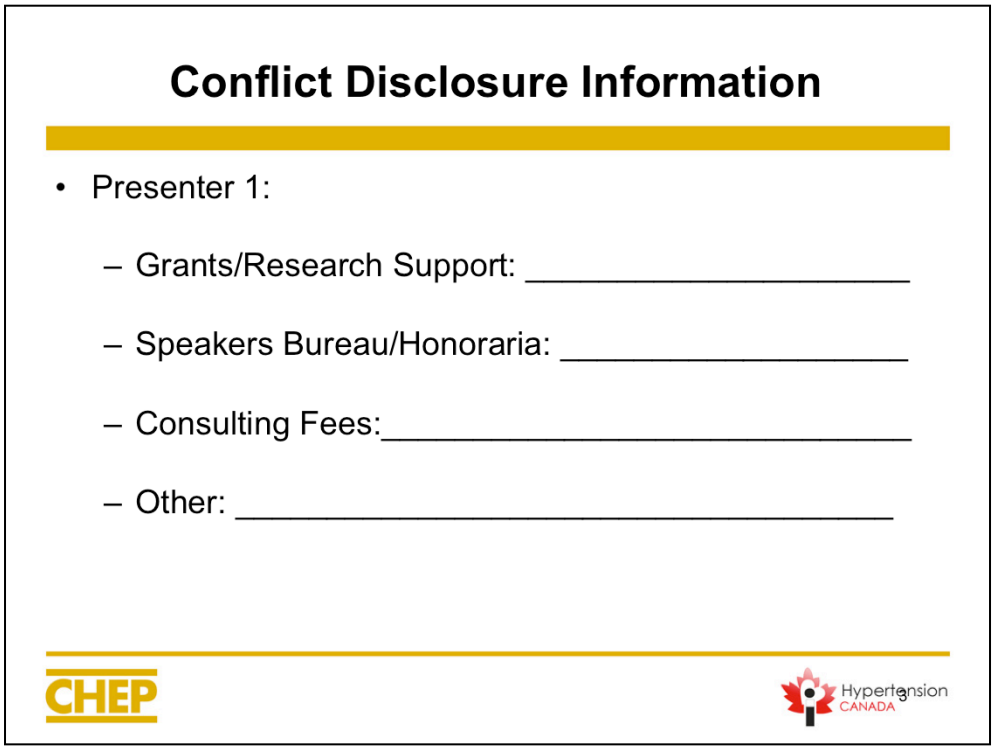


Instructions

Read out the case authors and their disclosure information.



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:

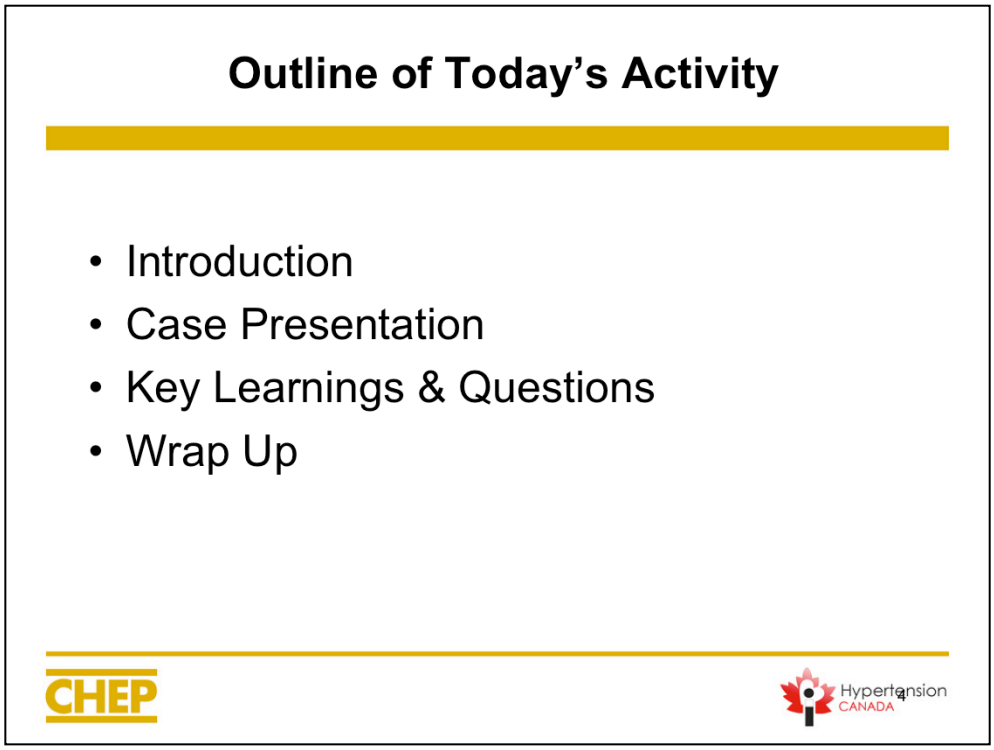
To ensure balance, independence, objectivity and scientific rigor, please disclose to program participants any real or apparent conflict(s) of interest that may have a direct bearing on the subject matter of this CME program. This pertains to relationships with pharmaceutical companies, biomedical device 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.



Instructions

Review the agenda for today's activity.

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

Module 5:

Management of Hypertension in Non-diabetes Patients with Chronic Kidney Disease

Gerald

An 78-year-old man with a 20 year history of hypertension is found to have a creatinine of 140 umol/L on his most recent blood tests

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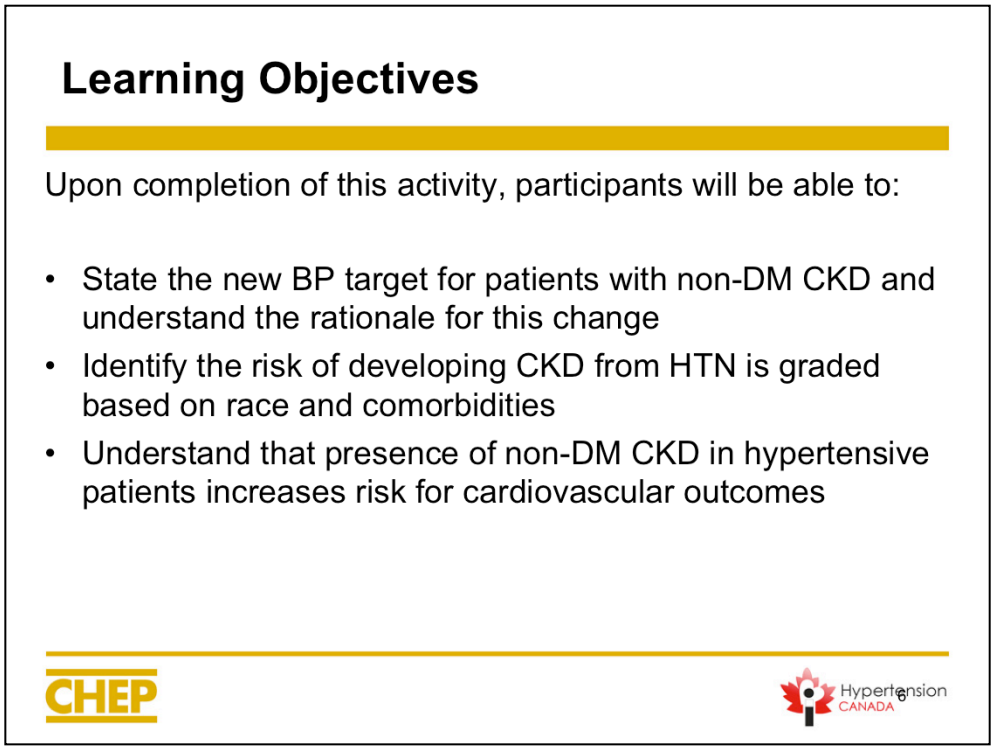
Instructions

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

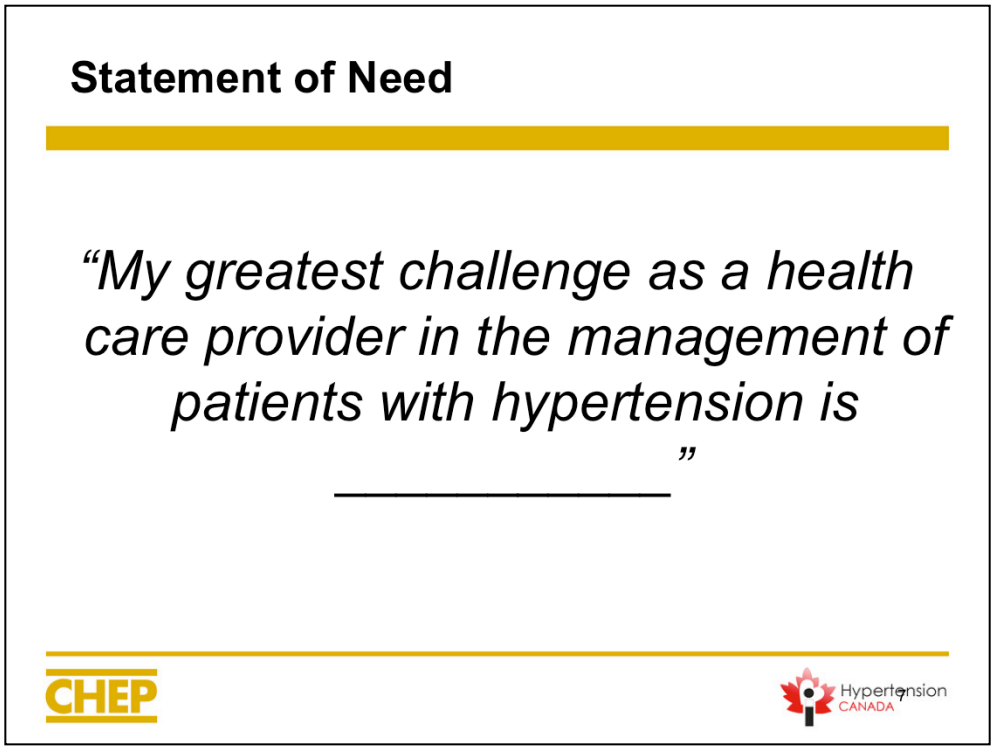
Notes

Hypertension is the second most common cause of chronic kidney disease and a major cause of renal deterioration in patients with diabetes or glomerulonephritis



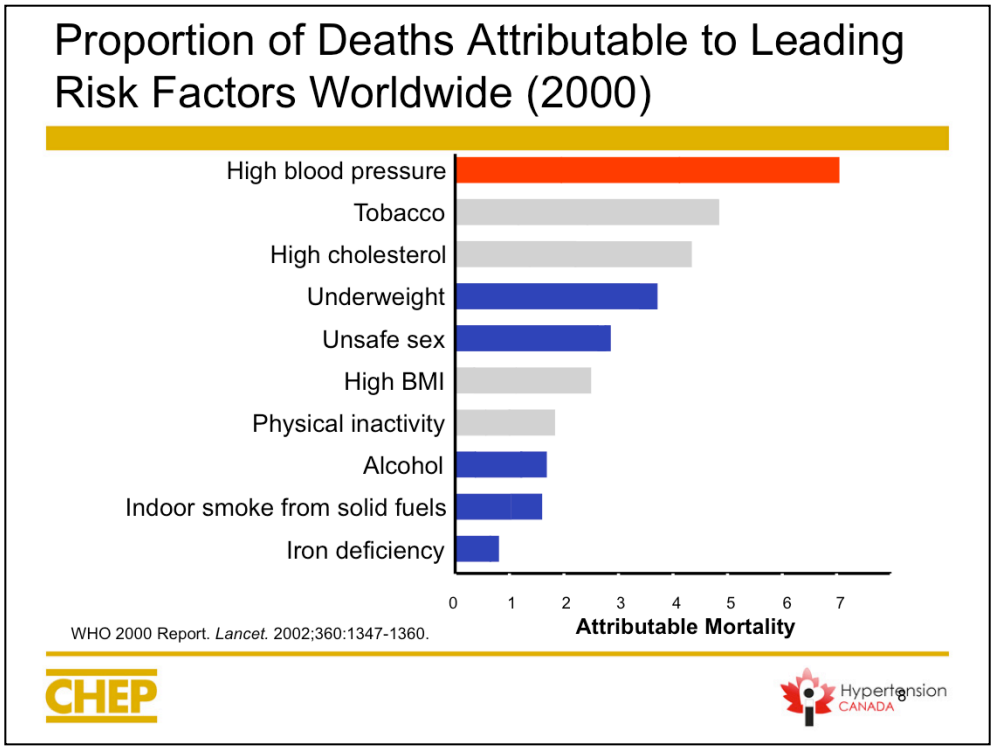
Instructions

Review the learning objectives for today's activity.



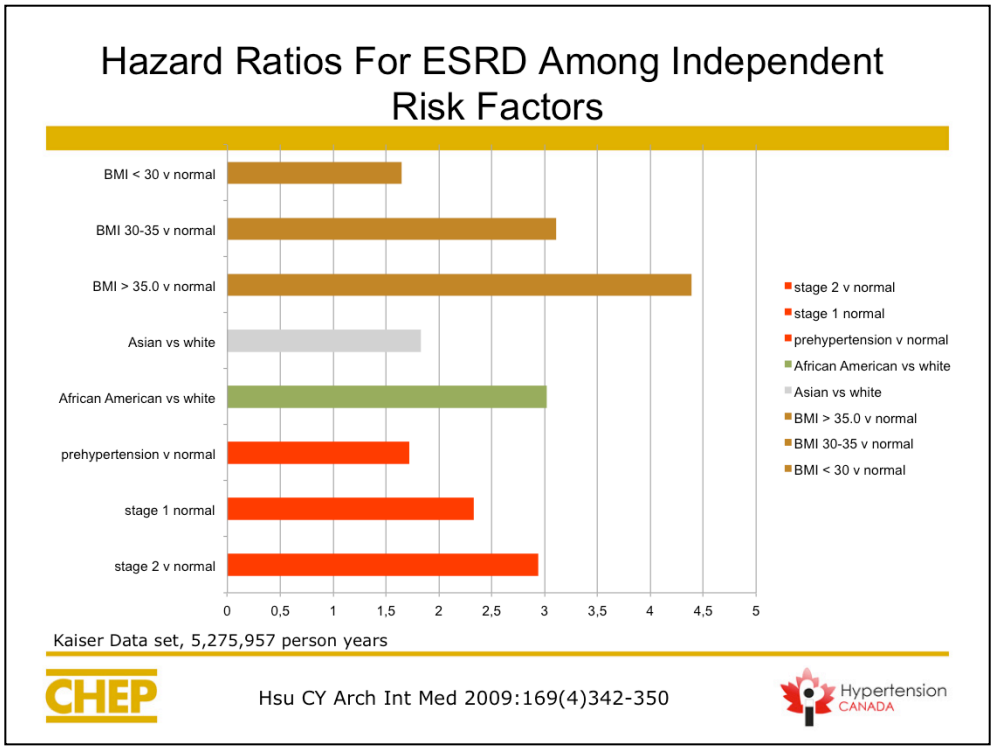
Instructions

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.



Notes

- Analysis conducted by the World Health Organization
- Estimate of the proportion of deaths in the world caused by major health risks
- Overall elevated blood pressure (systolic > 115 mmHg) is estimated to be the leading risk for death.
- Elevated blood pressure is a greater health risk in developed than under developed nations and in Europe than in North America



Notes:

Reference: Risk Factors for End-Stage Renal Disease 25-Year Follow-up

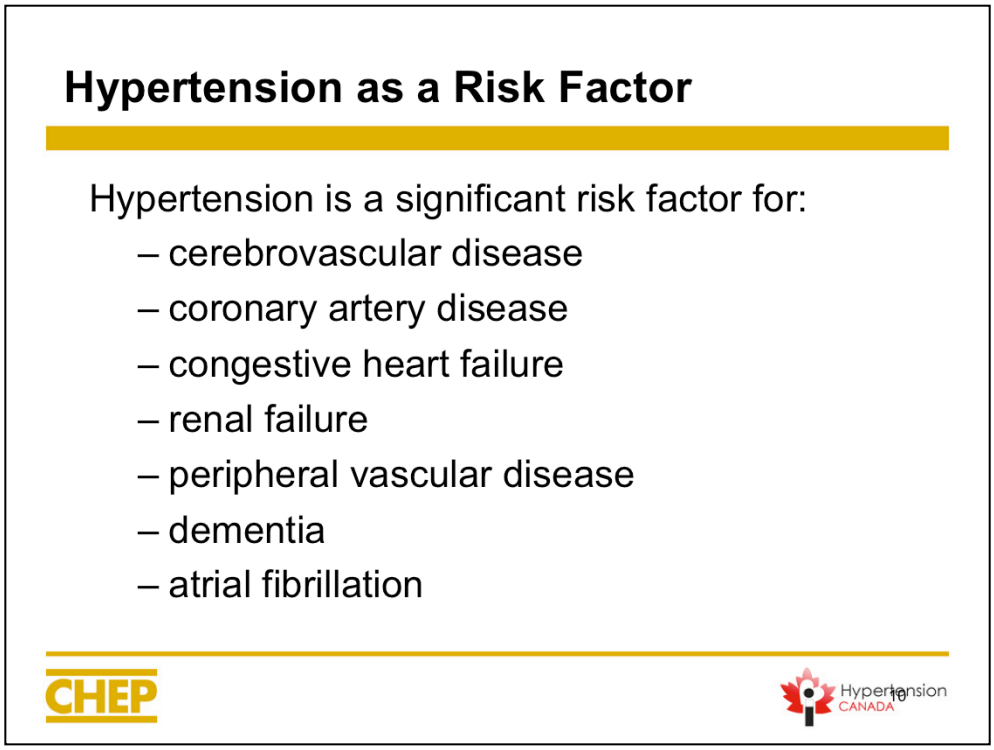
Chi-yuan Hsu, MD, MSc; Carlos Iribarren, MD, PhD; Charles E. McCulloch, PhD; Jeanne Darbinian, MPH; Alan S. Go, MD *Arch Intern Med*. 2009;169(4):342-350.

Background Few cohort studies have focused on risk factors for end-stage renal disease (ESRD). This investigation evaluated the prognostic value of several potential novel risk factors for ESRD after considering established risk factors.

Methods We studied 177 570 individuals from a large integrated health care delivery system in northern California who volunteered for health checkups between June 1, 1964, and August 31, 1973. Initiation of ESRD treatment was ascertained using US Renal Data System registry data through December 31, 2000.

Results A total of 842 cases of ESRD were observed during 5 275 957 person-years of follow-up. This comprehensive evaluation confirmed the importance of established risk factors, including the following: male sex, older age, proteinuria, diabetes mellitus, lower educational attainment, and African American race, as well as higher blood pressure, body mass index, and serum creatinine level. The 2 most potent risk factors were proteinuria and excess weight. For proteinuria, the adjusted hazard ratios (HRs) were 7.90 (95% confidence interval [CI], 5.35-11.67) for 3 to 4+ on urine dipstick, 3.59 (2.82-4.57) for 1 to 2+ on urine dipstick, and 2.37 (1.79-3.14) for trace vs negative on urine dipstick. For excess weight, the HRs were 4.39 (95% CI, 3.38-5.70) for class 2 to class 3 obesity, 3.11 (2.51-3.84) for class 1 obesity, and 1.65 (1.39-1.97) for overweight vs normal weight. Furthermore, several independent novel risk factors for ESRD were identified, including lower hemoglobin level (1.33 [1.08-1.63] for lowest vs highest quartile), higher serum uric acid level (2.14 [1.65-2.77] for highest vs lowest quartile), self-reported history of nocturia (1.36 [1.17-1.58]), and family history of kidney disease (HR, 1.40 [95% CI, 1.02-1.90]).

Conclusions We confirmed the importance of established ESRD risk factors in this large cohort with broad sex and racial/ethnic representation. Lower hemoglobin level, higher serum uric acid level, self-reported history of nocturia, and family history of kidney disease are independent risk factors for ESRD.



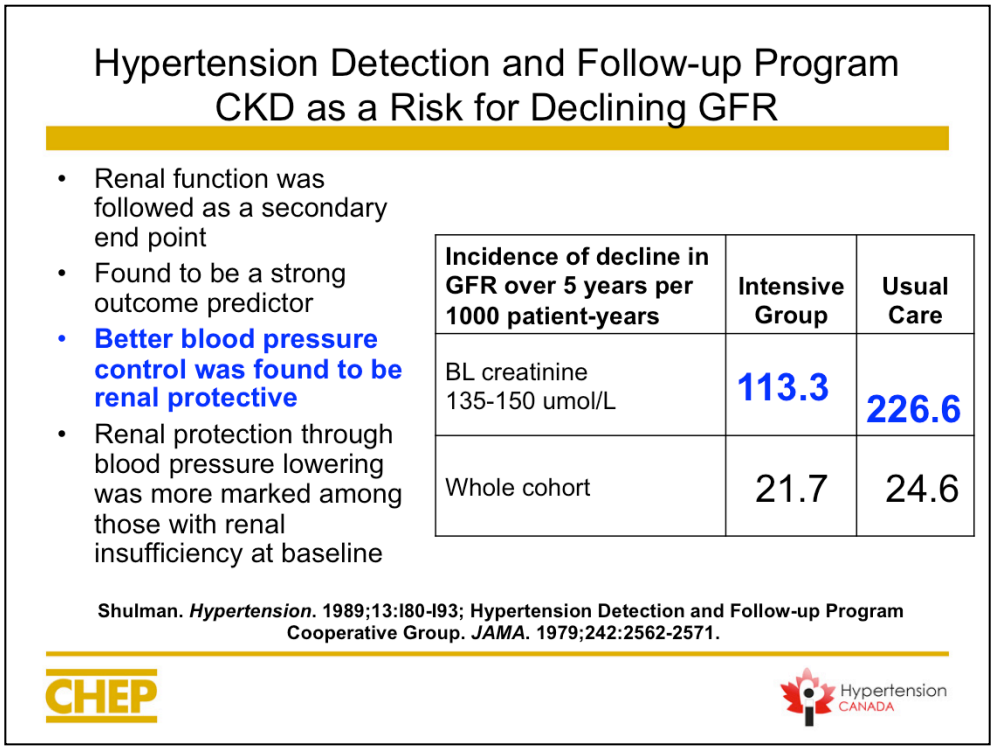
Notes

- Worldwide, attributable to high blood pressure:
  - 7.6 million premature deaths
  - 92 million disability-adjusted life years
  - 54% of stroke
  - 47% of coronary artery disease
- High blood pressure affects one in five Canadian adults and the majority of these will require pharmacological therapy to control their blood pressure.
- Hypertension is a major cause of heart failure. It is likely the most common cause of atrial fibrillation and atrial fibrillation may be the first presentation of an otherwise untreated hypertensive patient. Atrial fibrillation is of course a risk factor for stroke.

References

1.Joffres MR, Hamet P, Rabkin SW, Gelskey D, Hogan K, Fodor G. Prevalence, control and awareness of high blood pressure among Canadian adults. Canadian Heart Health Surveys Research Group. CMAJ 1992 Jun 1;146(11):1997-2005.

2.Khan N, Wardman D, Campbell N. Differences in need for antihypertensive drugs among those aware and unaware of their hypertensive status: a cross sectional survey. BMC Cardiovascular Disorders 2005;5(1):4.



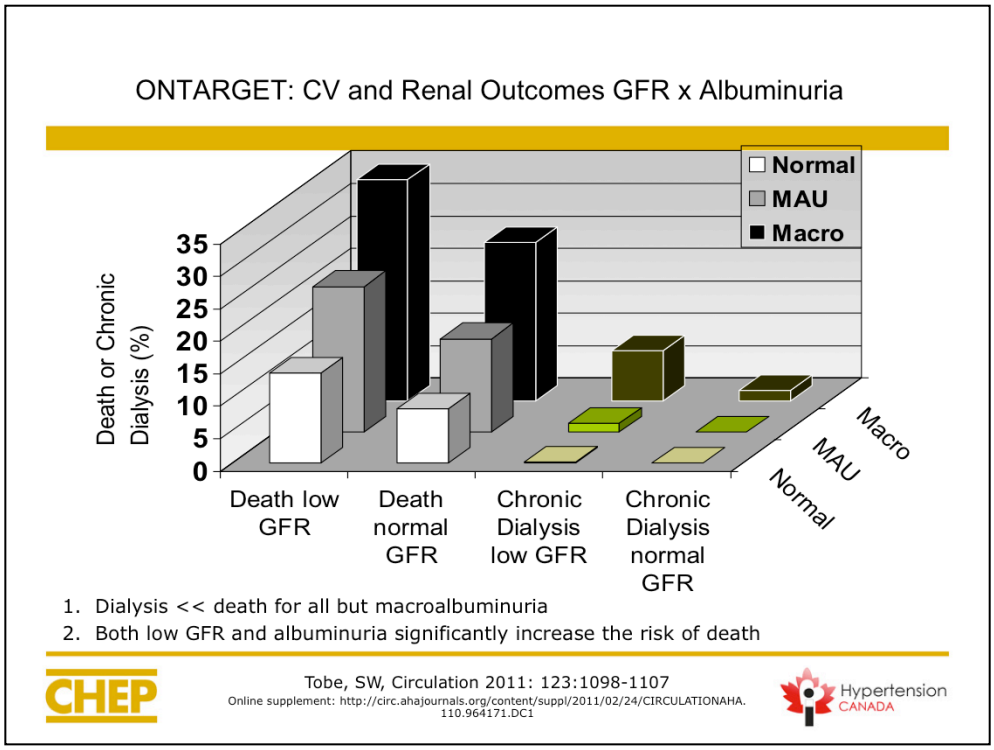
Notes:

•The Hypertension Detection and Follow-up Program followed 10,940 persons for 5 years in a community-based, randomized, controlled trial of treatment for hypertension. Importantly this study was done in the 1970's before ACEi's were available. Participants were randomized to one of two treatment groups, stepped care and referred care.

•The primary end point of the study was all-cause mortality, with morbid events involving the heart, brain, and kidney as secondary end points. Loss of renal function, ascertained by a change in serum creatinine, was among these secondary events. Baseline serum creatinine concentration had a significant prognostic value for 8-year mortality. For persons with a serum creatinine concentration greater than or equal to 1.7 mg/dl, 8-year mortality was more than three times that of all other participants.

•The overall estimated 5-year incidence of substantial decline in renal function was 21.7/1,000 in the stepped-care group and 24.6/1,000 in the referred-care group. Among persons with a baseline serum creatinine level between 1.5 and 1.7 mg/dl, the 5-year incidence of decline was 113.3/1,000 (stepped care) and 226.6/1,000 (referred care) (p less than 0.01).

This demonstrates: a) that people with elevated creatinine have a greatly



Notes:

•In the ONTARGET study, when the population was divided by GFR level (< 60 ml/min vs 60+) and urine albumin level (normal/Micro/MACRO) an interesting finding is seen.

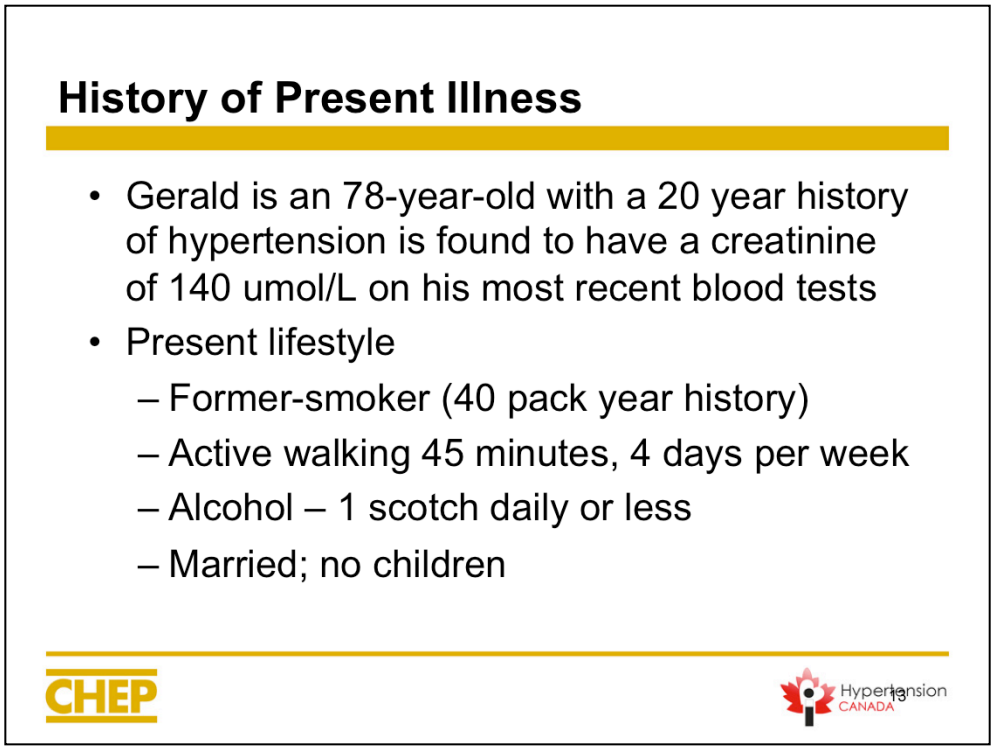
•Mortality rates are much higher than rates of progression to ESRD in patients with low GFR and normal albuminuria and even microalbuminuria.

•Only in patients with low GFR and macroalbuminuria does progression to ESRD approach 1/7th the risk of death.

•The conclusion from this slide is that for all patients with CKD, a focus on CV risk is paramount. Treating BP, using RAAS blockade, Diabetes management, lipid control, lifestyle changes all will benefit CV outcomes as well as being appropriate renal management. Focus on the heart and the kidneys will also be happy.

Background—In the Ongoing Telmisartan Alone and in Combination With Ramipril Global End Point Trial (ONTARGET),

Dual therapy did not reduce cardiovascular or renal outcomes compared with either angiotensin-converting enzyme inhibitors or angiotensin receptor blockers alone. Previous controlled trials with angiotensin-



Instructions

Review the case study slide with the group. Several 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

- He has been stable in your clinic for 10 years
  - Blood work over the last 10 years shows a slowly rising creatinine level

Date	May 2005	April 2006	May 2007	July 2008	May 2010	Aug 2011
Creatinine	95	102	98	96	112	140
eGFR*	62.5	58.2	60.5	61.8	53.0	42.4

*eGFR by Cockcroft and Gault (140-age)x Wt (kg)/Creat (umol/L) x 1.2 (for male)

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Cockcroft DW, Nephron 1976, 16(1) 31-41

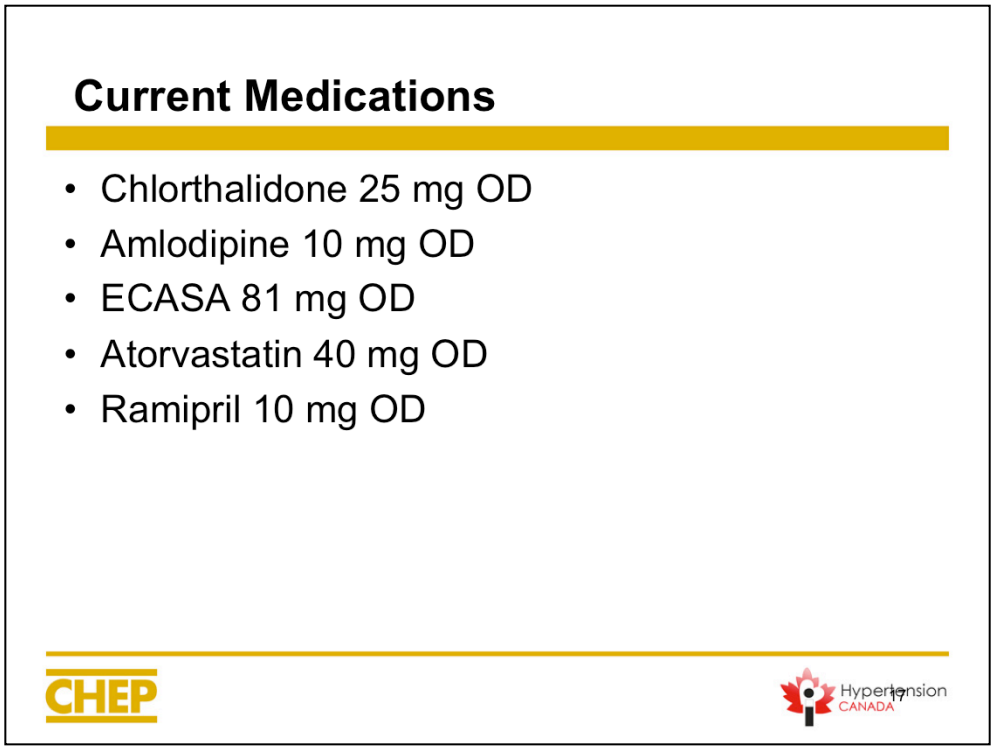
Hypertension CANADA

Past History

- Hypertension
  - diagnosed and treated for 20 years
- Stable coronary artery disease
  - coronary stent in 2004
- No history of peripheral vascular disease
- No history of diabetes

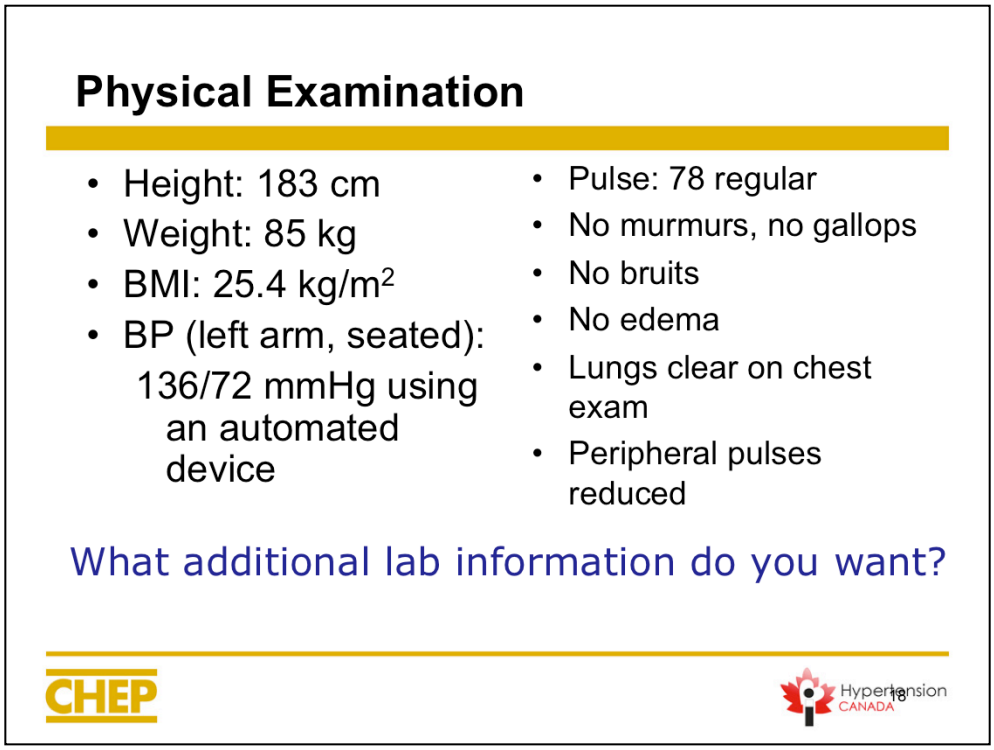
Family History

- Mother
  - history of hypertension
- Father
  - history of hypertension
- Sister
  - 1 sister has hypertension
- Brothers
  - 2 younger brothers also hypertensive



Notes

These are the meds that the patient is taking on presentation. They reflect an actual patient seen in clinic and are not intended to reflect current best practices.



Instructions

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

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 automate device of 136/72 mmHg can be considered a 'research quality' measurement

Lab Tests

- Electrocardiogram (ECG)
- Fasting glucose and lipids
- Electrolytes, urea, and creatinine
- Complete blood count (CBC)
- Calcium, Phosphate, Parathyroid Hormone Test (PTH)
- Urinalysis and urine, albumin/creatinine ratio (ACR)
- Abdominal ultra-sound

Laboratory Investigations

Test	Results	Normal Values
Glucose	5.5 mmol/L	4.0-8.0 mmol/L
Urea	7.8 mmol/L	3.0-7.0 mmol/L
Creatinine	144 µmol/L eGFR 41 ml/min	44-106 umol/L
K	4.4 mmol/L	3.5-5.0 mmol/L
Hb	114 g/L	115-165 g/L
ACR	19 mg/mmol	< 2.8 mg/mmol

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Hypertension CANADA

Instructions

Review the labs that were performed prior to the next office visit.

Discuss any implications of these findings. The CBC has a normochromic, normocytic pattern.

Last colonoscopy one year ago for routine screening and was normal. Hb noted to be low but retics were also a little low consistent with stage 3 chronic kidney disease at that time.

Laboratory Investigations

Test	Results	Normal Values
LDL	2.2 mmol/L	<2.50 mmol/L
Total Chol	3.8 mmol/L	<5.20 mmol/L
TG	2.2 mmol/L	<1.70 mmol/L
HDL	1.1 mmol/L	>0.99 mmol/L
TC:HDL	3.75	High risk target: <4.0 Mod risk target: <5.0 Low risk target: <6.0

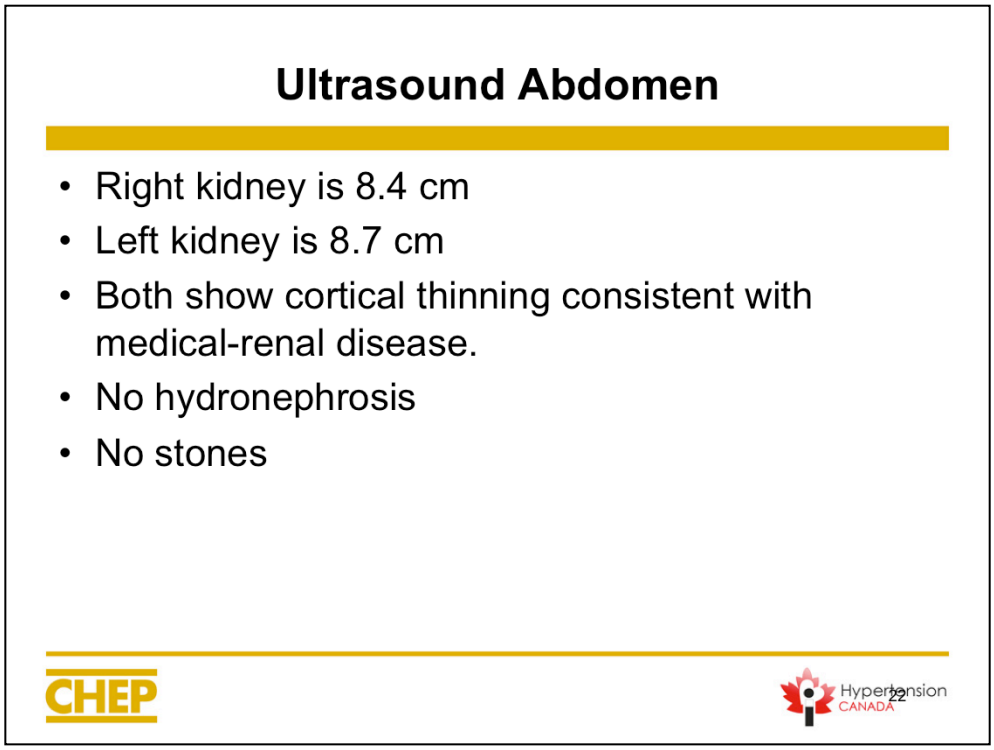
CHEP

Hypertension CANADA

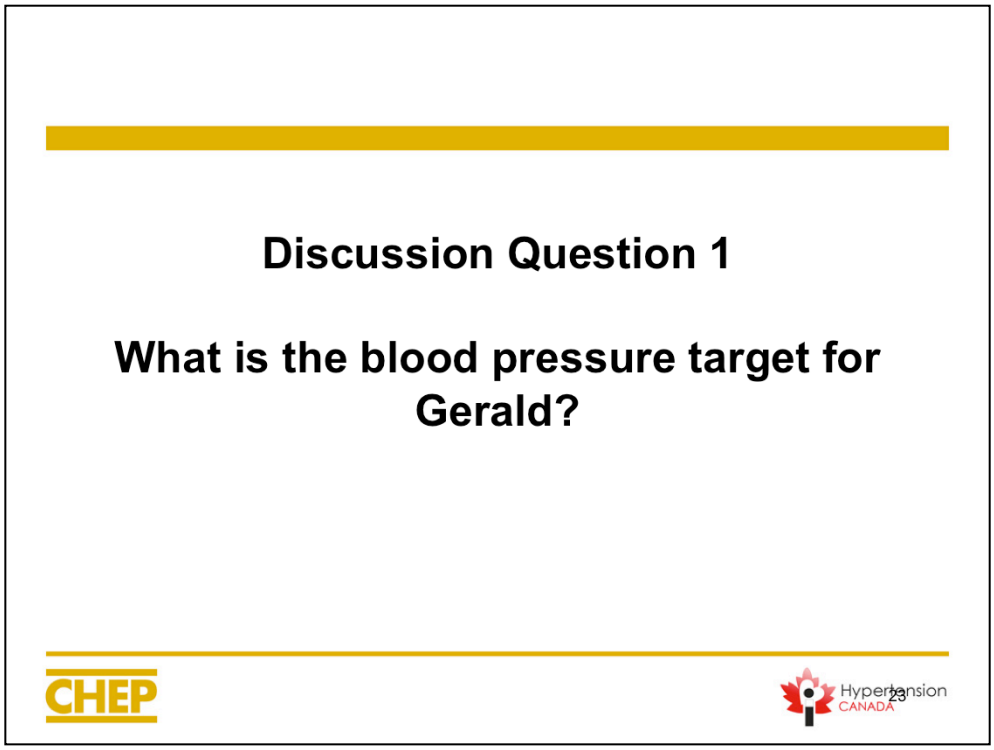
Instructions

Review the labs that were performed prior to the next office visit.

Discuss any implications of these findings. The CBC has a normochromic, normocytic pattern.

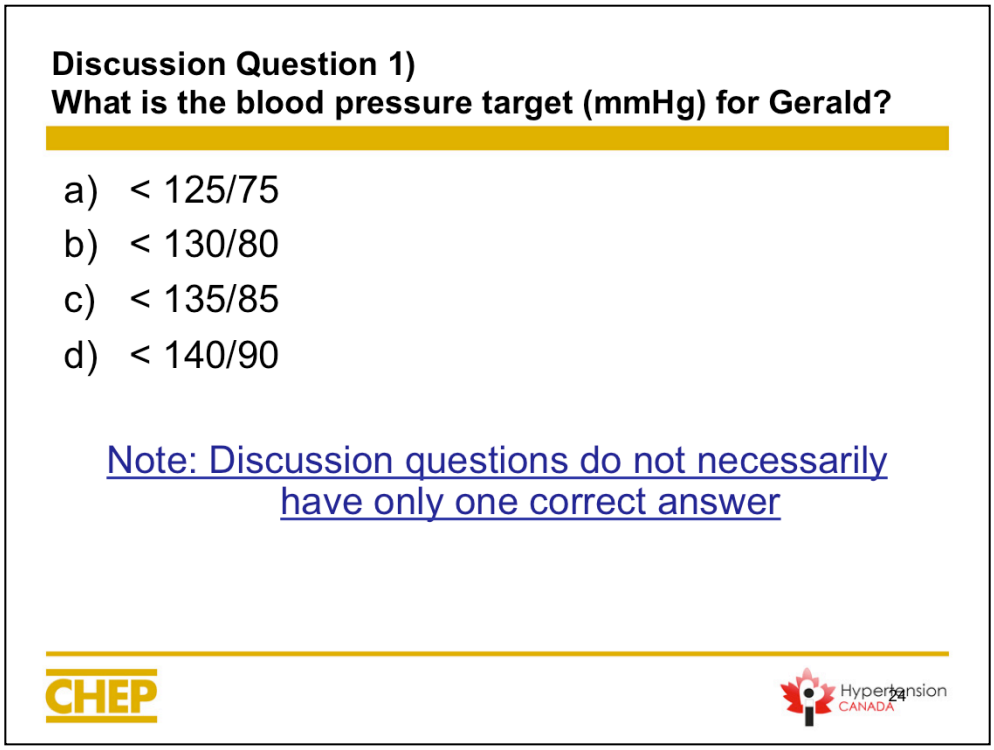


The u/s shows bilaterally small kidneys typical of microvascular disease from long standing hypertension plus or minus renovascular disease.



Instructions

Read the question to the group. A selection of multiple choice answers will follow on the next slide.



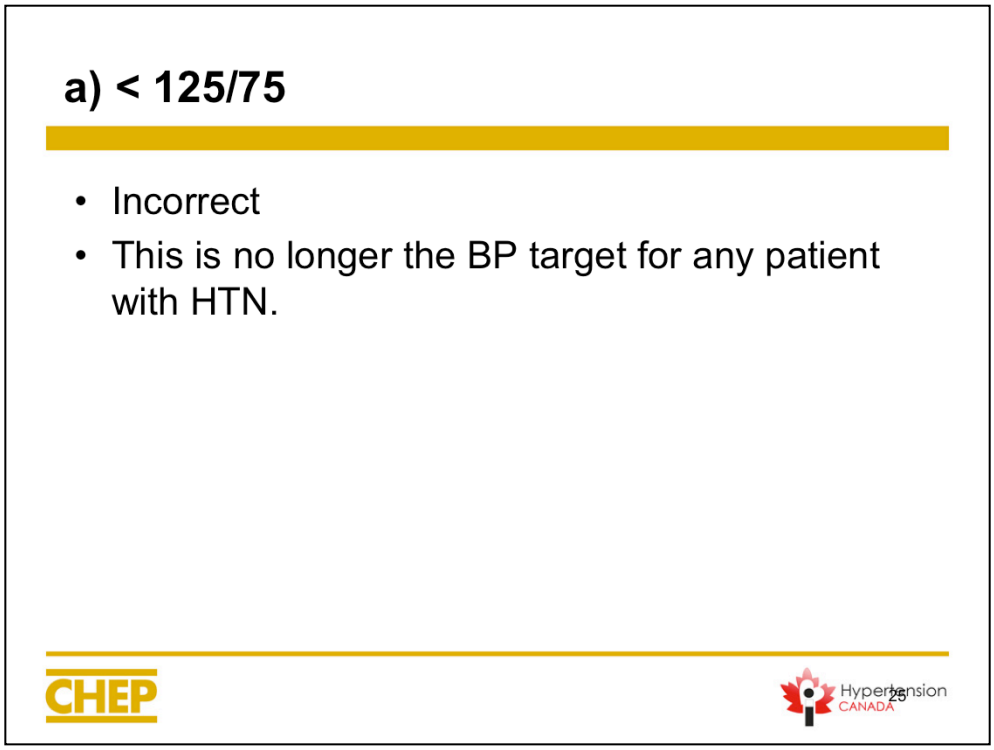
Instructions

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

Discuss the potential merits of each answer.

There is not necessarily one right answer; the goal of the exercise is to have an open discussion.

When you have discussed each possible answer, proceed to see the feedback provided by the case authors.



Notes:
Based on the MDRD study by Peterson, Ann Intern Med 1995 123:754-762 – BP control, proteinuria, and progression of renal disease – MDRD a re-analysis of MDRD study showing benefit of treating to 125/75 if more than 3g/d of proteinuria and to less than 130/80 (MAP 98) if less than 3g per day. Thus 125/75 became the target for patients with 3 g/day or more of protein in the urine in the past.

However the following are important points to consider about this data:

•Subgroup analysis

•Not pre-specified and randomization not stratified by level of proteinuria

•Proteinuria categories not pre-specified

•No a priori power calculations done for subgroups

•Level of statistical significance not adjusted for multiple testing

•Baseline characteristics were not presented according to subgroup

•The use of ACE-inhibitors was significantly higher in the group that was assigned to the low BP target

Also, the REIN study Ruggenenti P et al. Lancet 2005

b) < 130/80

- Incorrect in this case
- < 130/80 mmHg is the BP target for people with diabetes with or without CKD

C) < 135/85

- Incorrect
- This is the correct answer if you use home BP readings or an automated device in your office, such as BpTRU

d) < 140/90

- Correct
- This is the new BP target for people with chronic kidney disease and no diabetes

In 2012, CHEP revisited the CKD BP targets following publication of significant new data

CHEP 2011	CHEP 2012
For patients with nondiabetic chronic kidney disease, target BP is <130/80 mm Hg (Grade C).	**For patients with nondiabetic chronic kidney disease, target blood pressure is <140/90 mm Hg (Grade B).**

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Hypertension CANADA

Notes:

BP target in Chronic Kidney Disease (CKD) without Diabetes is now < 140/90 mmHg

The target BP for CKD without diabetes has been <130/80 mmHg [1-3]. In recent years there has been a retrenchment from this lower target. In 2008, the NICE chronic kidney disease guidelines maintained the target of <130/80 mmHg but only when the urine protein was 1g/day or greater, otherwise targeting < 140/90 mmHg [4]. This recommendation was based on a meta-analysis showing a relative risk of 4.5 for doubling of serum creatinine or end stage renal disease (ESRD) in individuals with > 1 g/day proteinuria who achieved a systolic BP of 110-119 vs. 130-139 mmHg [5] and a sub-analysis of the Modification of Diet in Renal Disease (MDRD) study showing a greater decline in GFR in patients with over 3g/day of proteinuria [6]. It was on the strength of the MDRD study that BP targets for non-diabetic chronic kidney disease with proteinuria were set at < 120/75 mmHg in 1999 [4-7]. In 2006 however, the African American Study of Kidney Disease (AASK) and the Blood Pressure Control for Renoprotection in Patients with Chronic Renal Disease (REIN-2) studies [8] showed no renal benefit for the lower BP target of < 120/75 mmHg. Blood pressure targets for all patients with chronic kidney disease were kept at < 130/80 mmHg, largely on the strength of the MDRD[9].

A new AASK trial analysis including an additional cohort phase, found that patients with proteinuria (but not those without) benefited from the lower targeted BP, supporting the NICE guidelines approach of a differential blood pressure target of < 130/80 mmHg for proteinuria (> 1 gm/day) and < 140/90 mmHg for those with less proteinuria [10]. The AASK trial included 1094 African American individuals with hypertensive CKD and assessed the effect on GFR of reducing BP to a usual BP goal (achieved BP 141/85 mmHg) or a low BP goal (achieved BP 128/78mmHg). In the cohort phase, the blood pressure target was < 130/80 mmHg and follow-up ranged from 8.8 to 12.2 years. On critical appraisal of this study it was noted that a secondary outcome from the original study was used as the primary outcome (change in creatinine) and no benefit was found for the primary outcome of the original study, the change of GFR over time, even in participants with proteinuria [11]. This post-hoc subgroup analysis of a secondary endpoint would therefore be considered only as hypothesis generating. A critical appraisal of the MDRD study for patients with proteinuria, noted that the finding of slower loss of GFR in patients with proteinuria ≥3 grams/day was a post-hoc subgroup analysis in only 32 patients[6]. The lack of strong evidence for a benefit of more intensive blood pressure lowering for patients with non-diabetic chronic kidney disease with or without proteinuria, led to the change of blood pressure target to < 140/90 mmHg. An intensive review of the blood pressure target in patients with hypertension and diabetes including those with chronic kidney disease confirmed the blood pressure target of < 130/80 mmHg (see Rabi D, CMAJ in Press).

Another AASK sub-study shed interesting light on the impact of adherence to recommended therapy. While no differences were found in GFR outcomes between randomly assigned BP goals, there was a substantial slowing of loss of GFR for patients observed to achieve lower BPs within each group [12]. Further, patients in the low BP group who failed to achieve target-BP had significantly worse outcomes than those in the usual-BP group with the same blood pressure, suggesting that a confounding of comorbidities may have been involved[12].

In summary, randomized controlled trials do not provide sufficient evidence to recommend a lower BP target in individuals with non-diabetic chronic kidney disease, even with proteinuria.

Reference List

(1) Rabi DM, Daskalopoulou SS, Padwal RS, Khan NA, Grover SA, Hackam DG et al. The 2011 canadian hypertension education program recommendations for the management of hypertension: blood pressure measurement, diagnosis, assessment of risk, and therapy. *Can J Cardiol* 2011; 27(4):415-433.

(2) Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G et al. 2007 Guidelines for the Management of Arterial Hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens* 2007; 25(6):1105-1187.

(3) NKF-K/DOQI Clinical Practice Guidelines. Chronic Kidney Disease. *American Journal of Kidney Diseases* 2002;39(2 Suppl 1):S170-S212.

(4) National Collaborating Centre for Chronic Conditions. *Chronic kidney disease: national clinical guideline for early identification and management in adults in primary and secondary care*. Royal College of Physicians, editor. 2011. London, Royal College of Physicians. NICE clinical practice guidelines.
Ref Type: Online Source

(5) Jafar TH, Stark PC, Schmid CH, Landa M, Maschio G, De Jong PE et al. Progression of chronic kidney disease: the role of blood pressure control, proteinuria, and angiotensin-converting enzyme inhibition: a patient-level meta-analysis. *Ann Intern Med* 2003; 139(4):244-252.

(6) Klahr S, Levey AS, Beck GJ, Caggiula AW, Hunsicker L, Kusek JW et al. The effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. Modification of Diet in Renal Disease Study Group [see comments]. *New England Journal of Medicine* 1994; 330(13):877-884.

(7) Klahr S. Primary and secondary results of the modification of diet in renal diseases study. *Mineral & Electrolyte Metabolism* 1996;22(1-3):138-142.

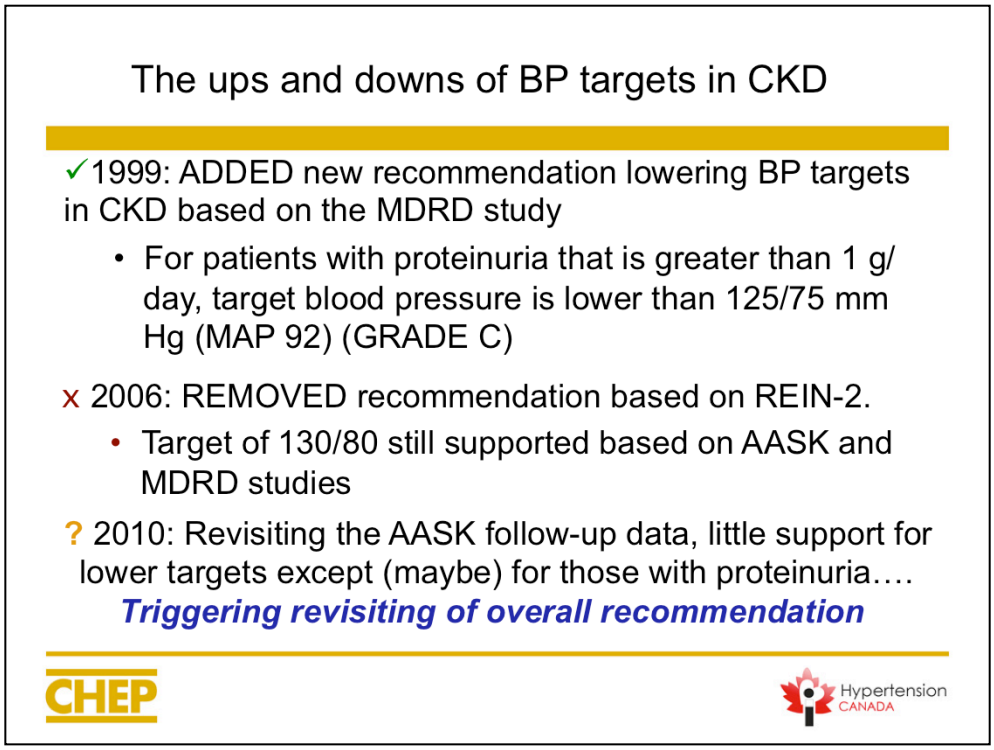
(8) Ruggenenti P, Perna A, Loriga G, Ganeva M, Ene-Iordache B, Turturro M et al. Blood-pressure control for renoprotection in patients with non-diabetic chronic renal disease (REIN-2): multicentre, randomised controlled trial. *Lancet* 2005; 365(9463):939-946.

(9) Khan NA, McAlister FA, Rabkin SW, Padwal R, Feldman RD, Campbell NR et al. The 2006 Canadian Hypertension Education Program recommendations for the management of hypertension: Part II - Therapy. *Can J Cardiol* 2006; 22(7):583-593.

(10) Appel LJ, Wright JT, Jr., Greene T, Agodoa LY, Astor BC, Bakris GL et al. Intensive blood-pressure control in hypertensive chronic kidney disease. *N Engl J Med* 2010; 363(10):918-929.

(11) Wright JT, Jr., Bakris G, Greene T, Agodoa LY, Appel LJ, Charleston J et al. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial.[comment]. *JAMA* 2002; 288(19):2421-2431.

(12) Davis EM, Appel LJ, Wang X, Greene T, Astor BC, Rahman M et al. Limitations of analyses based on achieved blood pressure: lessons from the African American study of kidney disease and hypertension trial. *Hypertension* 2011; 57(6):1061-1068.



Notes:
1999 added new recommendation based on findings from MDRD suggesting that patients with proteinuria that is greater than 1 g/day, target blood pressure is lower than 125/75 mm Hg (MAP 92).
CHEP panel concluded that the AASK followup data was methodologically suspect based on their switch of primary outcomes from that used in the original study.

Studies of BP targets in CKD patients

Upadhyay , Ann Intern Med. 2011;154:541-548

	MDRD	AASK	REIN-2
n	840	1094	334
Target BP	~125/75 vs.~140/90	~125/75 vs.~140/90	130/80 vs. x/90
1° outcome	change in GFR	composite	ESRD
Mortality	ND	ND	ND
CVD events	ND	ND	x
GFR decline	ND	ND	ND
ESRD	ND	ND	ND

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Notes:

BP target in Chronic Kidney Disease (CKD) without Diabetes is now <140/90 mmHg

The target BP for CKD without diabetes has been <130/80 mmHg [1-3]. In recent years there has been a retrenchment from this lower target. In 2008, the NICE chronic kidney disease guidelines maintained the target of <130/80 mmHg but only when the urine protein was 1g/day or greater, otherwise targeting < 140/90 mmHg [4]. This recommendation was based on a meta-analysis showing a relative risk of 4.5 for doubling of serum creatinine or end stage renal disease (ESRD) in individuals with > 1 g/day proteinuria who achieved a systolic BP of 110-119 vs. 130-139 mmHg [5] and a sub-analysis of the Modification of Diet in Renal Disease (MDRD) study showing a greater decline in GFR in patients with over 3g/day of proteinuria [6]. It was on the strength of the MDRD study that BP targets for non-diabetic chronic kidney disease with proteinuria were set at < 120/75 mmHg in 1999 [4,7]. In 2006 however, the African American Study of Kidney Disease (AASK) and the Blood Pressure Control for Renoprotection in Patients with Chronic Renal Disease (REIN-2) studies [8] showed no renal benefit for the lower BP target of < 120/75 mmHg. Blood pressure targets for all patients with chronic kidney disease were kept at < 130/80 mmHg, largely on the strength of the MDRD[9].

A new AASK trial analysis including an additional cohort phase, found that patients with proteinuria (but not those without) benefited from the lower targeted BP, supporting the NICE guidelines approach of a differential blood pressure target of < 130/80 mmHg for proteinuria (> 1 gm/day) and < 140/90 mmHg for those with less proteinuria [10]. The AASK trial included 1094 African American individuals with hypertensive CKD and assessed the effect on GFR of reducing BP to a usual BP goal (achieved BP 141/85 mmHg) or a low BP goal (achieved BP 128/78mmHg). In the cohort phase, the blood pressure target was < 130/80 mmHg and follow-up ranged from 8.8 to 12.2 years. On critical appraisal of this study it was noted that a secondary outcome from the original study was used as the primary outcome (change in creatinine) and no benefit was found for the primary outcome of the original study, the change of GFR over time, even in participants with proteinuria [11]. This post-hoc subgroup analysis of a secondary endpoint would therefore be considered only as hypothesis generating. A critical appraisal of the MDRD study for patients with proteinuria, noted that the finding of slower loss of GFR in patients with proteinuria ≥3 grams/day was a post-hoc subgroup analysis in only 32 patients[6]. The lack of strong evidence for a benefit of more intensive blood pressure lowering for patients with non-diabetic chronic kidney disease with or without proteinuria, led to the change of blood pressure target to < 140/90 mmHg. An intensive review of the blood pressure target in patients with hypertension and diabetes including those with chronic kidney disease confirmed the blood pressure target of < 130/80 mmHg (see Rabi D, CMAJ in Press). Another AASK sub-study shed interesting light on the impact of adherence to recommended therapy. While no differences were found in GFR outcomes between randomly assigned BP goals, there was a substantial slowing of loss of GFR for patients observed to achieve lower BPs within each group [12]. Further, patients in the low BP group who failed to achieve target-BP had significantly worse outcomes than those in the usual-BP group with the same blood pressure, suggesting that a confounding of comorbidities may have been involved[12].

Summary: randomized controlled trials do not provide sufficient evidence to recommend a lower BP target in individuals with non-diabetic chronic kidney disease, even with proteinuria.

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(2) Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G et al. 2007 Guidelines for the Management of Arterial Hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens* 2007; 25(6):1105-1187.

(3) NKF-K/DOQI Clinical Practice Guidelines; Chronic Kidney Disease. *American Journal of Kidney Diseases* 2002; 39(2 Suppl 1):S170-S212.

(4) National Collaborating Centre for Chronic Conditions. *Chronic kidney disease: national clinical guideline for early identification and management in adults in primary and secondary care*. Royal College of Physicians, editor. 2011. London, Royal College of Physicians. NICE clinical practice guidelines. Ref Type: Online Source

(5) Jafar TH, Stark PC, Schmid CH, Landa M, Maschio G, De Jong PE et al. Progression of chronic kidney disease: the role of blood pressure control, proteinuria, and angiotensin-converting enzyme inhibition: a patient-level meta-analysis. *Ann Intern Med* 2003; 139(4):244-252.

(6) Klahr S, Levey AS, Beck GJ, Caggiula AW, Hunsicker L, Kusek JW et al. The effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. Modification of Diet in Renal Disease Study Group [see comments]. *New England Journal of Medicine* 1994; 330(13):877-884.

(7) Klahr S. Primary and secondary results of the modification of diet in renal disease study. *Mineral & Electrolyte Metabolism* 1996; 22(1-3):138-142.

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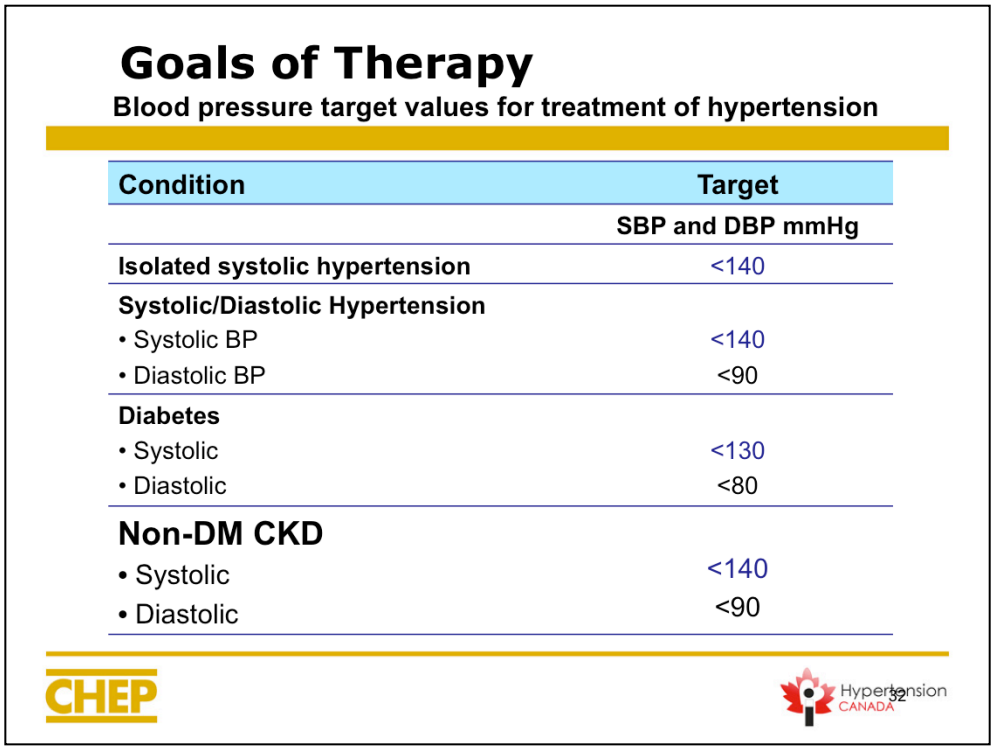
(9) Khan NA, McAlister FA, Rabkin SW, Padwal R, Feldman RD, Campbell NR et al. The 2006 Canadian Hypertension Education Program recommendations for the management of hypertension: Part II - Therapy. *Can J Cardiol* 2006; 22(7):583-593.

(10) Appel LJ, Wright JT, Jr., Greene T, Agodoa LY, Astor BC, Bakris GL et al. Intensive blood-pressure control in hypertensive chronic kidney disease. *N Engl J Med* 2010; 363(10):918-929.

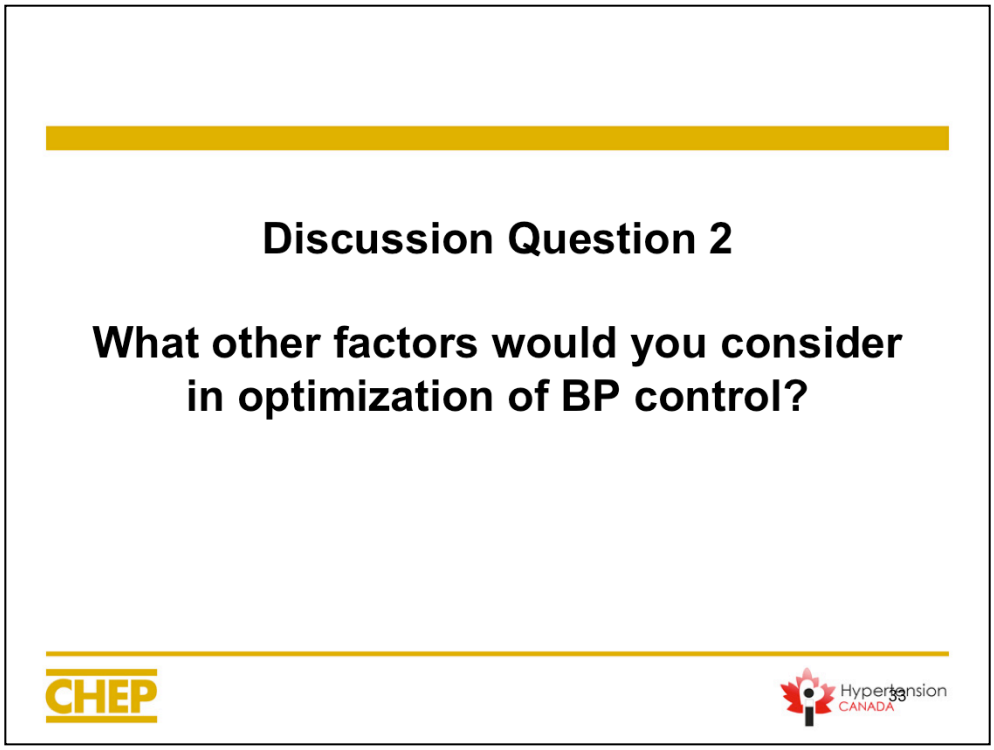
(11) Wright JT, Jr., Bakris G, Greene T, Agodoa LY, Appel LJ, Charleston J et al. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial.[comment]. *JAMA* 2002; 288(19):2421-2431.

(12) Davis EM, Appel LJ, Wang X, Greene T, Astor BC, Rahman M et al. Limitations of analyses based on achieved blood pressure: lessons from the African American study of kidney disease and hypertension trial. *Hypertension* 2011; 57(6):1061-1068.



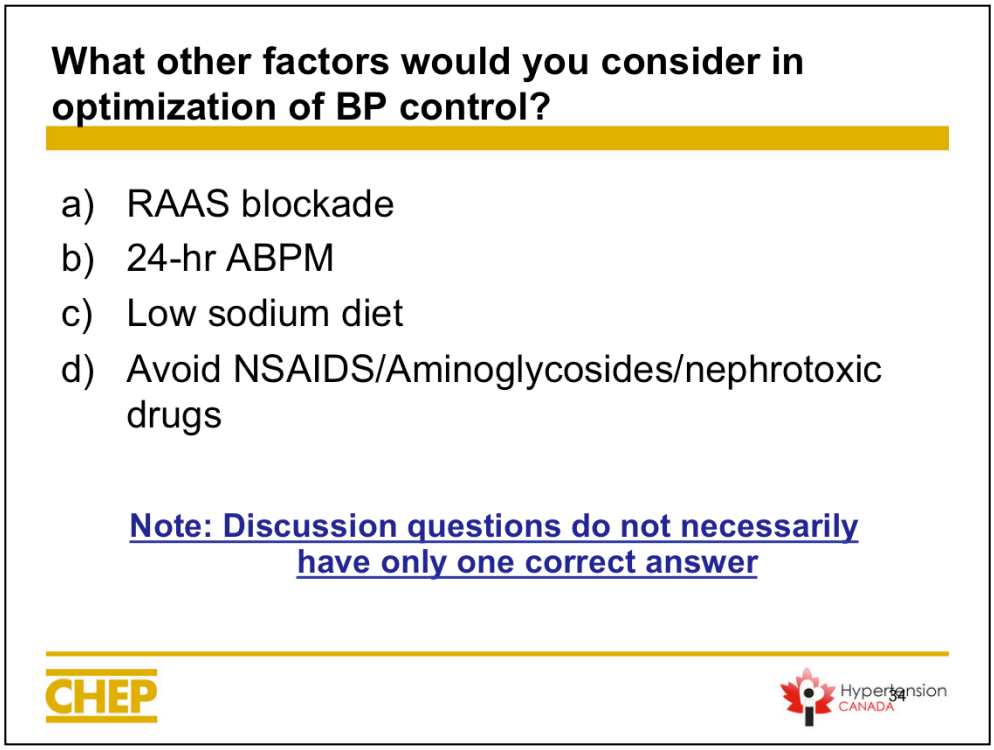
Notes:

The new change in BP target for patients with CKD without diabetes. If someone has CKD and diabetes, then their BP target would be < 130/80 mmHg.



Instructions

Read the question to the group. A selection of multiple choice answers will follow on the next slide.



Instructions

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

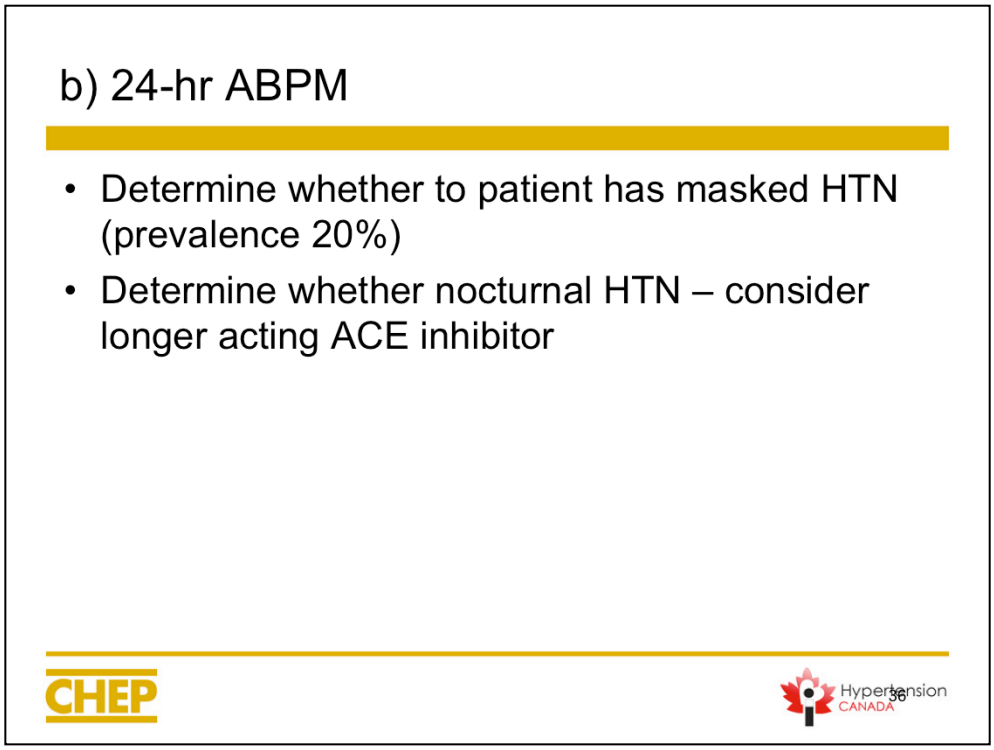
Discuss the potential merits of each answer.

There is not necessarily one right answer; the goal of the exercise is to have an open discussion.

When you have discussed each possible answer, proceed to see the feedback provided by the case authors.

a) RAAS blockade

- The patient is taking ramipril 10 mg/day



Review Jafar Meta-analysis

c) Low sodium diet

- High dietary sodium is an key contributor to high blood pressure.
- To decrease blood pressure, consider reducing sodium intake towards 2,000 mg (5g of salt or 87mmol of sodium) per day.

d) Avoid NSAIDS/Aminoglycosides/nephrotoxic drugs

- Nephrotoxic drugs can cause hemodynamic compromise of kidney in patients with CKD
- Examples of nephrotoxic drugs
  - Aminoglycosides
  - Nonsteroidal anti-inflammatory drugs (NSAIDs)
  - Acyclovir
  - Amphotericin B
  - Lithium
  - Phenytoin
  - Sulfonamides
  - Vancomycin
  - Zoledronic acid

Baumgarten, Gehr. *Am Fam Physician* 2011;84:1138-48

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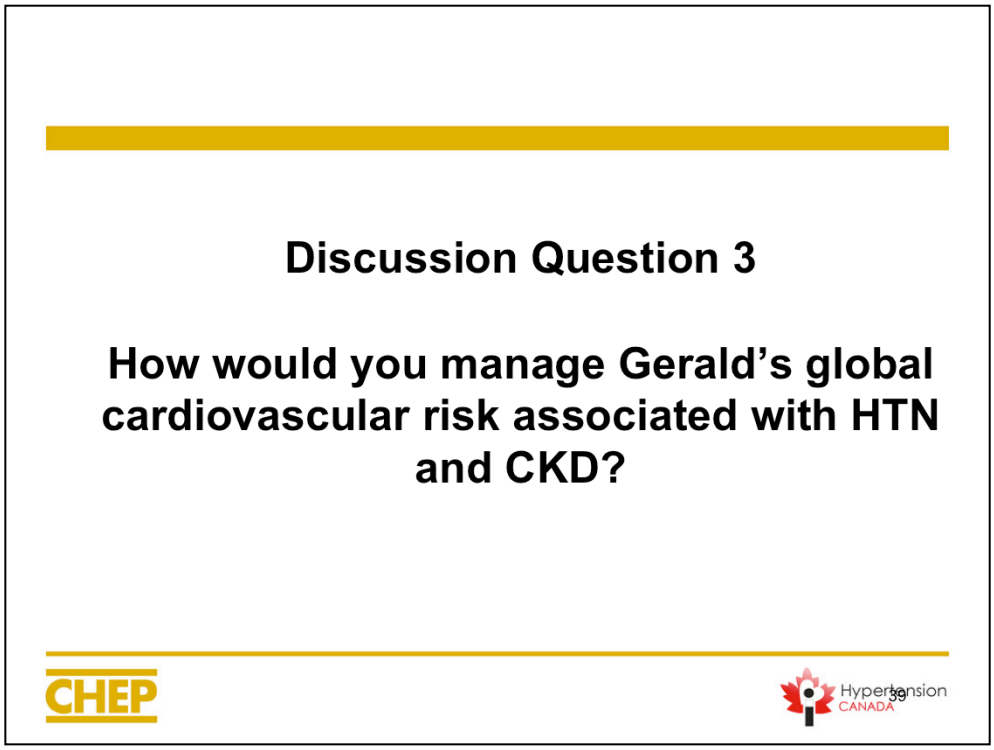
Notes:

•SAIDS such as ibuprofen, advil, motrin, and the prescription NSAIDS such as voltaren and coxib such as cellebrex all reduce protective renal prostaglandins setting up the kidney to be injured in the setting of a volume depletion event. Further they can sometime cause interstitial nephritis.

•Aminoglycosides such gentamycin and tobramycin can cause nephrotoxicity with long term use.

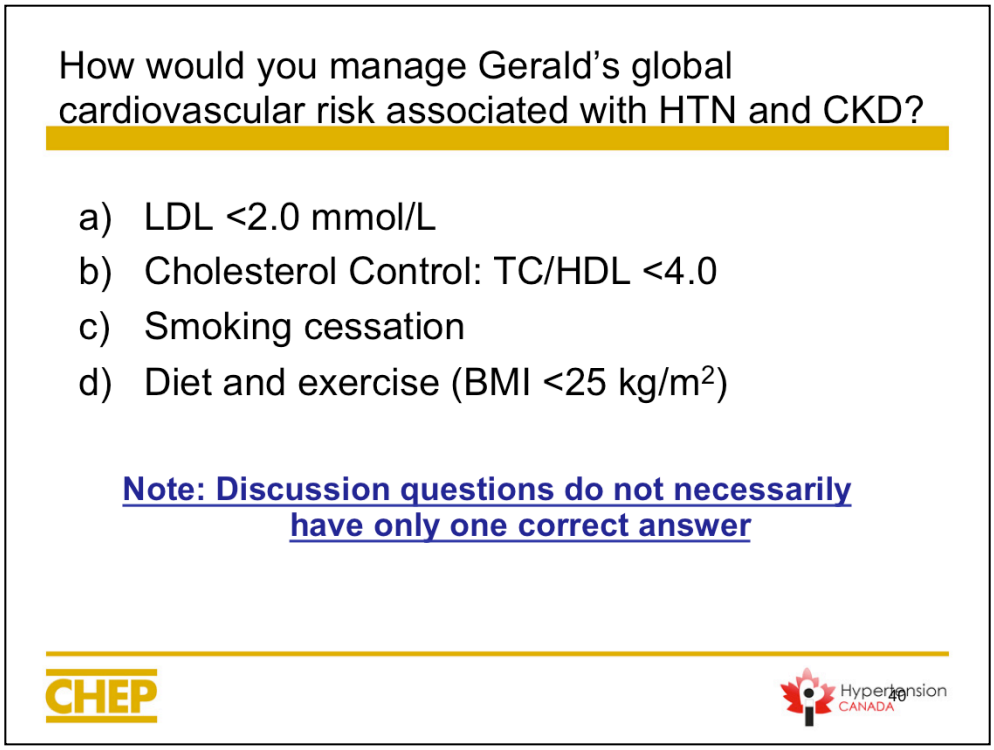
•Other nephrotoxics include contrast dye in patients with diabetes, myeloma or CKD. Also cisplatinin and amphotericin B are nephrotoxins.

•Examples of nephrotoxic drugs are listed in the slide. Reference: Baumgarten M, Gehr T. Chronic kidney disease: detection and evaluation. *Am Fam Physician* 2011;84:1138-48.



Instructions

Read the question to the group. A selection of multiple choice answers will follow on the next slide.



Instructions

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

Discuss the potential merits of each answer.

There is not necessarily one right answer; the goal of the exercise is to have an open discussion.

When you have discussed each possible answer, proceed to see the feedback provided by the case authors.

a) LDL <2.0

- Primary lipid targets for adults with diabetes at high risk for CVD <2.0 mmol/L
- Achievable with statin monotherapy

b) Cholesterol Control

- High risk for CVD, secondary target TC/HDL of <4.0

c) Smoking cessation

- Maintain present lifestyle of non-smoking (former smoker with 40 pack year history)

d) Diet and exercise (BMI <25 kg/m^2)

- Lifestyle changes are a critical component of hypertension management and prevention

- An accumulation of 30-60 minutes of dynamic exercise of moderate intensity four to seven days per week in addition to the routine activities of daily living.

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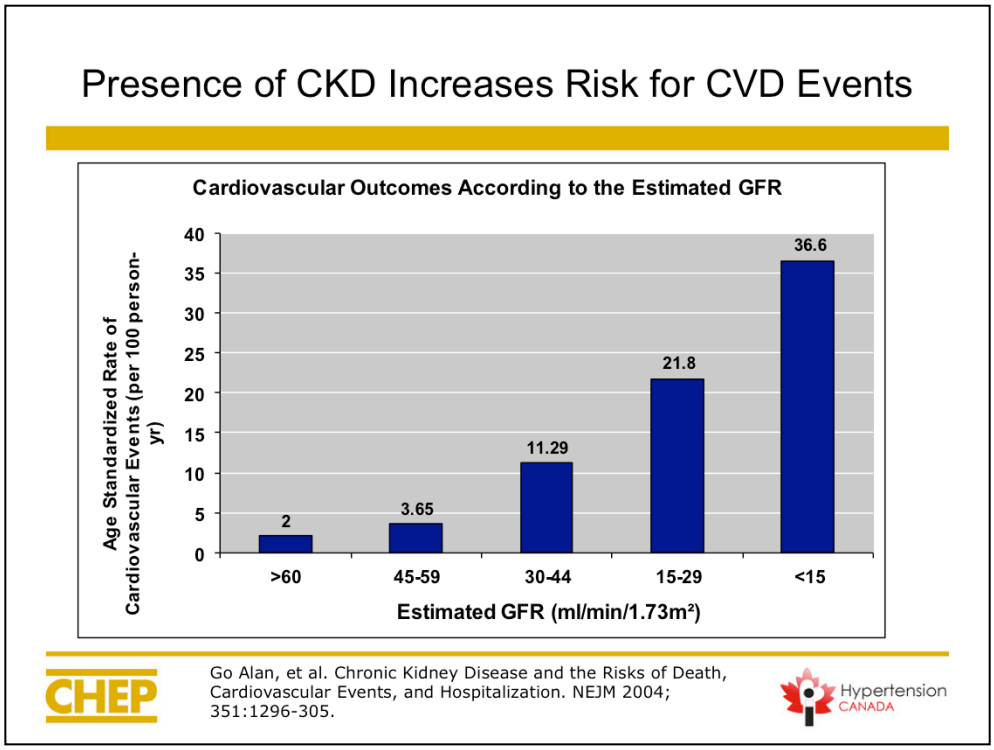

Notes:

Age-Standardized Rates of Cardiovascular Events According to the Estimated GFR among 1,120,295 Ambulatory Adults.

A cardiovascular event was defined as hospitalization for coronary heart disease, heart failure, ischemic stroke, and peripheral arterial disease. Error bars represent 95 percent confidence intervals. The rate of events is listed

above each bar.

Reference:

Go Alan, et al. Chronic Kidney Disease and the Risks of Death, Cardiovascular Events, and Hospitalization. NEJM 2004; 351:1296-305.

Adverse Outcomes Related to eGFR

Adjusted Hazard Ratio According to the Estimated GFR			
Estimated GFR	**Death from Any Cause**	**Any Cardiovascular Event**	**Any Hospitalization**
≥60 ml/min/1.73 m²†	1.0	1.0	1.0
45–59 ml/min/1.73 m²	1.2 (1.1–1.2)	1.4 (1.4–1.5)	1.1 (1.1–1.1)
30–44 ml/min/1.73 m²	1.8 (1.7–1.9)	2.0 (1.9–2.1)	1.5 (1.5–1.5)
15–29 ml/min/1.73 m²	3.2 (3.1–3.4)	2.8 (2.6–2.9)	2.1 (2.0–2.2)
<15 ml/min/1.73 m²	5.9 (5.4–6.5)	3.4 (3.1–3.8)	3.1 (3.0–3.3)

*Adjusted hazard ratio (95 percent confidence interval)

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Go Alan, et al. Chronic Kidney Disease and the Risks of Death, Cardiovascular Events, and Hospitalization. NEJM 2004; 351:1296-305.

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Notes:

•The analyses were adjusted for age, sex, income, education, use or nonuse of dialysis, and the presence or absence of prior coronary heart disease, prior chronic heart failure, prior ischemic stroke or transient ischemic attack, prior peripheral arterial disease, diabetes mellitus, hypertension, dyslipidemia, cancer, a serum albumin level of 3.5 g per deciliter or less, dementia, cirrhosis or chronic liver disease, chronic lung disease, documented proteinuria, and prior hospitalizations.
† This group served as the reference group.

Reference:

Go Alan, et al. Chronic Kidney Disease and the Risks of Death, Cardiovascular Events, and Hospitalization. NEJM 2004; 351:1296-305.

Large-Scale Statin Studies in CKD

	ALERT[1]	4D[2]	AURORA[3]	SHARP*
Primary Endpoint	Cardiac death, nonfatal MI or coronary intervention procedure	Death from cardiac causes, nonfatal MI, and stroke	Death from cardiovascular causes, nonfatal MI, or nonfatal stroke.	First major athero event (non-fatal MI or coronary death, non haemorrhagic stroke, or any arterial revascularisation procedure
Results	RR 0.83 P=0.139	RR 0.92 P=0.37	HR 0.96 P=0.59	RR 0.83 CI 0.74-0.94 P=0.0021

[1]Holdass et al. Lancet 2003; 361:2024-31
[2]Wanner et al. NEJM 2005; 353(3):238-248
[3]Fellstrom et al. NEJM 2009; 360(14):1395-1407
*Baigent et al. Lancet 2011; 377(11):2181-92

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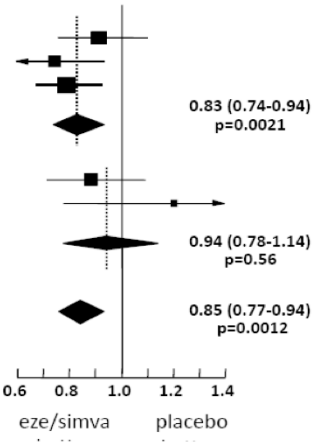
Notes:

The result of ALERT and 4D are broadly consistent with results from lipid-lowering trials in the general population. However, neither study was conclusive. There is therefore a need for more randomized evidence so that the size of any treatment effect can be assessed reliably across the spectrum of CKD (from stage 3 CKD through to patients on renal replacement therapy).

Major Atherosclerotic Coronary Events and Major Vascular Events

Event	eze/simva (n=4650)		placebo (n=4620)		Risk ratio & 95% CI
Major coronary event	213	(4.6%)	230	(5.0%)	
Non-hemorrhagic stroke	131	(2.8%)	174	(3.8%)	
Any revascularization procedure	284	(6.1%)	352	(7.6%)	
Major Atherosclerotic Event	**526**	**(11.3%)**	**619**	**(13.4%)**	**0.83 (0.74-0.94) p=0.0021**
Other cardiac death	162	(3.5%)	182	(3.9%)	
Hemorrhagic stroke	45	(1.0%)	37	(0.8%)	
Other Major Vascular Events	**207**	**(4.5%)**	**218**	**(4.7%)**	**0.94 (0.78-1.14) p=0.56**
Major Vascular Event	**701**	**(15.1%)**	**814**	**(17.6%)**	**0.85 (0.77-0.94) p=0.0012**



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Baigent C et al *Lancet* 2011; 377: 2181–92

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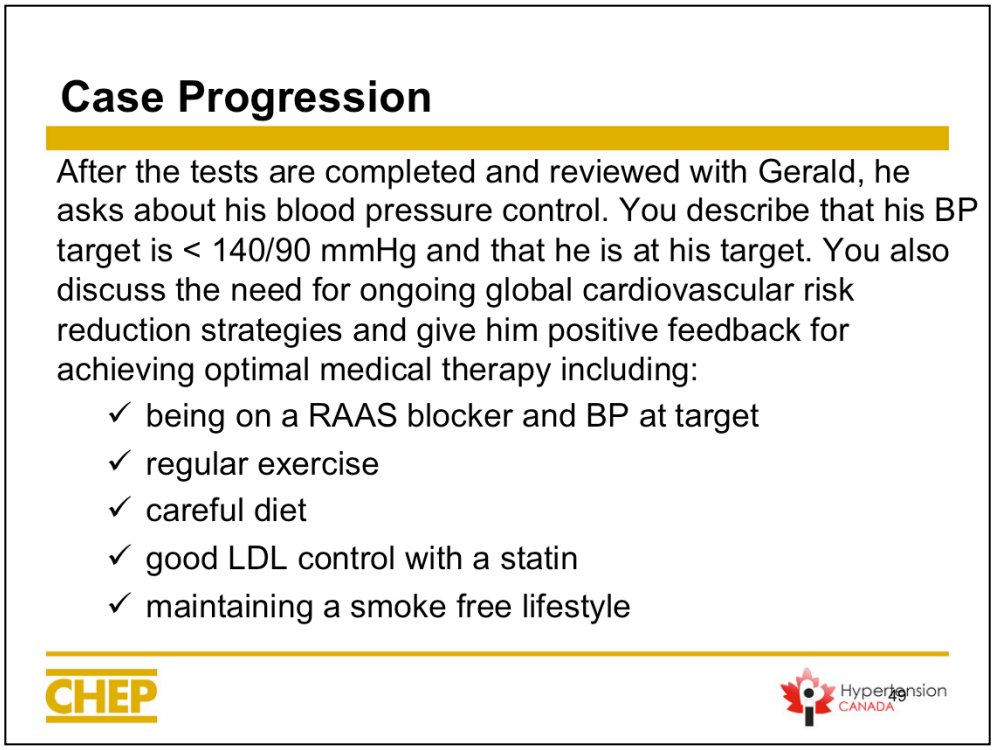

Instructions

Review the progress of the patient case and his current values and then proceed to the next slide.

Key Learnings

- ✓ For patients with nondiabetic chronic kidney disease, target blood pressure should be **<140/90 mmHg**
- ✓ Maintaining a healthy lifestyle and weight lowers blood pressure and prevents hypertension
- ✓ Promote: reducing dietary sodium and increased physical activity

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2015 CHEP Recommendations
is available at
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