Hypertension Canada's 2016 Canadian Hypertension Education Program guidelines for pharmacists: An update

Yazid N. Al Hamarneh, BSc(Pharm), PhD; Sherilyn K. D. Houle, BSP, PhD;
Raj Padwal, MD, MSc; Ross T. Tsuyuki, BSc(Pharm), PharmD, MSc, FCSHP, FACC

THE CANADIAN HYPERTENSION EDUCATION Program (CHEP) has been preparing and publishing guidelines for diagnosis and management of hypertension since 1999.¹ The 2016 guidelines,² released earlier this year, mark the 18th yearly production and update of evidence to date in the area of hypertension. Those guidelines, among other Hypertension Canada activities, can be considered as major contributors to the high levels of awareness and control of hypertension in Canada.^{3,4} Indeed, it has been reported that Canada has higher levels of awareness, treatment and control and lower prevalence of hypertension when compared with the United States and England.³

CHEP guidelines are synthesized and disseminated by a multidisciplinary expert committee. All committees to date have had physician, nurse and pharmacist representation, in addition to other disciplines. Indeed, based on the strong evidence of pharmacist-led interventions,⁵⁻¹¹ pharmacists' expanded role has been identified as a strategy to further enhance hypertension detection and management in Canada.

The *Canadian Pharmacists Journal* has published pharmacist-specific CHEP guidelines regularly, with the most recent full set of guidelines published in 2011¹² and regular updates since 2005.¹³⁻¹⁵ This article highlights the updates that have been introduced into the 2016 version, as well as what the authors think is still important from the previous versions. Readers who require the full CHEP guidelines are encouraged to refer

to the full guidelines in the *Canadian Journal of Cardiology*² or www.hypertension.ca or the previous pharmacist-specific publications.

What's new

Accurate measurement of blood pressure

Automated office blood pressure (AOBP) is the preferred method for measuring blood pressure in an office setting (Grade D). When using this method, an average blood pressure of $\geq 135/85$ mmHg is considered elevated (Grade D).² This recommendation builds on the one made in 2015 to support the use of automated electronic upper arm devices when measuring blood pressure.¹⁶

Using AOBP will eliminate patient-health care professional interaction during the blood pressure measurement, as it will be conducted via a fully automated device in a private area or a quiet room.² This approach prevents any conversation between patient and health care professional, minimizes the white coat influence, allows for more than one measurement and calculates the average of those measurements in one visit.² Such measurements were found to be consistent between visits¹⁷⁻¹⁹ and to closely resemble the average awake blood pressure measured using ambulatory blood pressure devices.^{17,20-26} Moreover, measurements made using AOBP do not seem to be affected by the location in which they were taken. Indeed, it has been reported that measurements taken at

a physician's office are similar to the ones taken in a pharmacy.²⁷ Similarly, comparable results were reported when AOBP was used in different settings such as an examination room, waiting room and ambulatory blood pressure monitoring unit.^{17,28-30} Padwal and colleagues compared serial blood pressure readings using an in-pharmacy automated blood pressure kiosk (PharmaSmart PS-2000) to daytime ambulatory blood pressure and AOBP measurements. The study authors reported that the serial kiosk results were similar to the AOBP readings when ambulatory blood pressure was used as the reference standard. This highlights the important role that well-validated kiosks can play in blood pressure assessment and management.³¹

Furthermore, it has been found that AOBP measurements can be helpful in forecasting end-organ damage.³²⁻³⁵ Indeed, it has been shown that the incidence of cardiovascular events can be predicted by uncontrolled AOBP measurements.³⁶ Myers and colleagues³⁶ reported that patients with untreated elevated blood pressure ($135 > \text{SBP} > 144 \text{ mmHg}$ or $80 > \text{DBP} > 89 \text{ mmHg}$) were at higher risk of having cardiovascular events when compared to those with lower blood pressure ($110 > \text{SBP} > 119 \text{ mmHg}$ or $60 > \text{DBP} > 69 \text{ mmHg}$). It is important to note that the study was conducted with seniors (≥ 65 years); as such, its generalizability might be limited. Yet it adds to the body of evidence for using AOBP as the preferred method of measuring blood pressure in the office setting.

Laboratory tests for the investigation of patients with hypertension

The 2016 guidelines² provide a revised recommendation when it comes to ordering a lipid panel. A lipid panel is still part of the recommended laboratory testing in patients with hypertension (Grade D)¹⁶; however, a nonfasting instead of a fasting lipid panel can now be considered adequate (Grade C).² Sidhu and Naugler³⁷ reported a minimal impact of the duration of fasting on total cholesterol, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol levels when they studied this impact among more than 200,000 individuals in Canada. However, they reported a larger difference when it came to triglyceride levels and duration of fasting.³⁷ Similar results have been reported by Doran and colleagues³⁸ and Langsted and colleagues.³⁹

Moreover, it has been reported that nonfasting lipid panels can be indicative of new cases of cardiovascular disease.³⁸⁻⁴³ Multiple studies, conducted in different settings, consistently reported that elevated nonfasting lipid panels were predictive of cardiovascular events, mortality and all-cause mortality.^{38,39,42}

Nonfasting lipid panel testing can also help alleviate the burden placed on laboratories with morning testing, reduce hypoglycemia in those with diabetes and improve patient adherence.⁴⁴⁻⁴⁶ It can thus provide a practical option for individuals with hypertension.

Health behaviour management

Increasing dietary potassium is now recommended in patients who are *not* at risk of hyperkalemia (Grade A). Patients can be at risk for hyperkalemia if they:

- Are receiving renin-angiotensin-aldosterone inhibitors
- Are receiving other drugs that can cause hyperkalemia (such as trimethoprim, sulfamethoxazole, amiloride, triamterene)
- Have chronic kidney disease (estimated glomerular filtration rate [eGFR] $< 60 \text{ mL/min/1.73 m}^2$)
- Have baseline serum potassium $> 4.5 \text{ mmol/L}$
- Have impaired urinary potassium excretion from renal failure

Aburto and colleagues⁴⁷ conducted a meta-analysis of 22 randomized controlled trials and 11 cohort studies and reported that increased potassium intake was associated with both systolic and diastolic blood pressure reduction (3.49 mmHg [95% confidence interval {CI} 1.82 to 5.15] and 1.96 mmHg [95% CI 0.86 to 3.06], respectively) only in individuals with hypertension. No significant adverse events were associated with this increased potassium intake.⁴⁷ As such, the 2016 guidelines recommend encouraging patients with hypertension to consume foods that are high in potassium (such as fresh fruits, vegetables and legumes) if they are not at risk for hyperkalemia.

New targets and thresholds for high-risk patients

Intensive systolic blood pressure management to target $\leq 120 \text{ mmHg}$ should be considered in high-risk patients who are ≥ 50 years old, have

blood pressure ≥ 130 mmHg and any of the following (Grade B):

- Clinical or subclinical cardiovascular disease
 - Previous myocardial infarction, percutaneous coronary intervention, coronary artery bypass grafting, carotid endarterectomy, carotid stenting
 - Acute coronary syndrome
 - Peripheral arterial disease with revascularization
 - Acute coronary syndrome
 - Ankle-brachial index ≤ 0.90 within the past 24 months
 - Left ventricular hypertrophy within the past 24 months
- Chronic kidney disease (nondiabetic nephropathy, proteinuria < 1 g/d, eGFR 20-59 mL/min/1.73 m²)
- Framingham risk score $\geq 15\%$
- Age ≥ 75 years

Patients should consent to receive such intensive treatment.

Intensive management should be avoided if the patient falls into any of the following categories (Grade B):

- Has heart failure (ejection fraction $< 35\%$) or recent myocardial infarction (within past 3 months)
- Indication for, but not currently receiving, a β -blocker
- Frail or institutionalized elderly individuals
- Has diabetes mellitus
- Had a previous stroke
- eGFR < 20 mL/min/1.73 m²
- Is unwilling or unable to adhere to multiple medications
- Has standing systolic blood pressure < 110 mmHg
- Unable to measure systolic blood pressure accurately
- Has known secondary cause(s) of hypertension

The SPRINT study randomized 9361 individuals at high risk for cardiovascular events (without diabetes or prior stroke) to receive either standard (targeting systolic blood pressure < 140 mmHg) or intensive (targeting systolic blood

pressure < 120 mmHg) treatment to assess the impact of lower systolic blood pressure on clinical events.²⁰ While the study was designed to follow the patients for 5 years, it was stopped early (after a median of 3.26 years) because of the significant difference in the primary composite outcome (myocardial infarction, other acute coronary syndromes, stroke, heart failure or death from cardiovascular causes) in the intensive treatment group compared with the standard treatment group (1.65%/year vs 2.19%/year; hazard ratio 0.75; 95% CI, 0.64 to 0.89; $p < 0.001$).²⁰ The findings of the SPRINT study were supported by 2 more recent systematic reviews and meta-analyses, which also demonstrated a strong relationship between lower blood pressure and the reduction in cardiovascular events.^{48,49}

Caution should be practised when choosing intensive treatment because:

- The evidence comes from a highly selected population including those with:
 - Clinical or subclinical cardiovascular disease
 - Chronic kidney disease (nondiabetic nephropathy, proteinuria < 1 g/d, eGFR 20-59 mL/min/1.73 m²)
 - Framingham risk score $\geq 15\%$
 - Age ≥ 75 years
- It is not suitable for everyone, as intensive treatment involves putting patients at higher risk for adverse events such as hypotension.
- Patients should consent to treatment to these lower targets, as it involves intensifying the treatment regimen and increasing the frequency of the follow-up visits.

Treatment for hypertension in association with ischemic heart disease

β -blocker or calcium channel blocker can be used as first-line therapy in patients with stable angina and without prior heart failure, myocardial infarction or coronary artery bypass surgery (Grade B).

Pepine and colleagues⁵⁰ randomized 22,576 patients with hypertension and coronary artery disease to receive either verapamil or atenolol with a target blood pressure of $< 140/90$ mmHg (or $< 130/85$ if the patient had diabetes or chronic kidney disease) to compare mortality and morbidity between those 2 groups. Patients who did

FIGURE 1 Hypertension diagnostic algorithm

not achieve the blood pressure target on monotherapy were further treated with hydrochlorothiazide and/or trandolapril. Similar blood pressure reduction was achieved (−18.7/−10 mmHg for the verapamil group and −19/−10.2 mmHg for the atenolol group), and no statistical difference in all-cause mortality, nonfatal myocardial infarction or nonfatal stroke was noted between the 2 groups (relative risk 0.98, 95% CI 0.9 to 1.06).⁵⁰ Those findings are in line with what has been reported by Dargie and colleagues⁵¹ and Rehnqvist and colleagues.⁵² Those 3 trials support the use of β -blocker or calcium channel blocker to prevent major cardiovascular events in patients with stable coronary artery disease.

What's still important

Diagnosis

Figure 1 illustrates the recommended steps for diagnosing hypertension. Out-of-office measurement is the preferred method for diagnosing hypertension as it has better predictive ability for cardiovascular outcomes when compared with office blood pressure measurements. It also has

the ability to identify white coat hypertension.¹⁶ The recommended out-of-office measurement method is ambulatory blood pressure monitoring (Grade D). Patients can be diagnosed with hypertension if the mean 24-hour ambulatory blood pressure is $\geq 130/80$ mmHg or the mean awake ambulatory blood pressure is $\geq 135/85$ mmHg (Grade C).

Home blood pressure monitoring can be used as an alternative if ambulatory blood pressure monitoring is not available, cannot be tolerated or due to patient preference (Grade D). A patient can be diagnosed with hypertension if his or her mean home blood pressure is $\geq 135/85$ (Grade C).

If the patient's blood pressure is elevated in the office (AOBP $\geq 135/85$) but the mean awake ambulatory blood pressure is $< 135/85$ or the mean 24-hour blood pressure is $< 130/80$ or the mean of a series of home blood pressure measurements is $< 135/85$, then white coat hypertension can be diagnosed. If white coat hypertension diagnosis is confirmed, pharmacologic treatment should not be initiated (Grade C).

Masked hypertension occurs when blood pressure is controlled in the office but elevated when out-of-office measurements are conducted

FIGURE 2 Types of hypertension based on manual office and ambulatory blood pressure measurements

(Grade C). The prevalence of such a phenomenon can reach 10% in the general population, 20% in patients with hypertension (controlled and uncontrolled) and more than 30% in patients with controlled hypertension.⁵³ Patients may be at high risk for masked hypertension if they have diabetes, are obese older men with borderline systolic office blood pressure, have central obesity or have a family history of elevated blood pressure.^{53,54} As such, it is recommended to conduct out-of-office measurements in individuals with such risk factors, even if their office blood pressure was at target.^{53,54}

It has also been reported that individuals with masked hypertension are at higher risk of cardiovascular events compared to individuals with white coat hypertension and those with normal blood pressure.⁵⁵ Figure 2 provides a breakdown of the different types of hypertension based on manual office and ambulatory blood pressure measurements.

Assessing cardiovascular risk in patients with hypertension

Cardiovascular risk engines can be used to predict the patient's overall risk of having a cardiovascular event more accurately (Grade A) and to use the blood pressure reduction lowering medications more efficiently (Grade D). To improve the effectiveness of risk factor modification and management, it is recommended to communicate the patients' overall cardiovascular risk to them (Grade B).

Tsuyuki and colleagues¹¹ used individualized cardiovascular risk assessment and education as the base of the intervention when they evaluated the effect of a community pharmacy-based case finding and intervention on cardiovascular

risk factors. They reported a greater reduction in blood pressure ($-9.37/-2.92$ mm Hg, $p < 0.001$) and other cardiovascular risk factors in the intervention group when compared with the control group.¹¹ Those findings are in line with those reported by Grover and colleagues.⁵⁶ Such findings, combined with the fact that 80% of patients with hypertension have at least 1 extra cardiovascular risk factor,⁵⁷ should emphasize the importance of calculating the overall cardiovascular risk in this population.

Statin therapy is recommended in patients with hypertension who have ≥ 3 of the following risk factors:

- Male sex
- Age ≥ 55 years
- Left ventricular hypertrophy
- Electrocardiogram abnormalities
- Peripheral arterial disease
- Previous stroke or transient ischemic attack
- Albuminuria or chronic kidney disease
- Diabetes
- Tobacco use
- Family history of premature cardiovascular disease
- Total cholesterol to high-density lipoprotein ratio ≥ 6

Low-dose aspirin can be considered in patients with hypertension if they are 50 years or older (Grade B). Extra caution should be paid if the patient's blood pressure is uncontrolled (Grade C).

In patients with hypertension, tobacco use status should be assessed regularly (Grade C). Tobacco users with hypertension should receive advice in combination with pharmacotherapy (e.g., nicotine replacement therapy, varenicline, bupropion) with the goal of quitting (Grade C).

These recommendations were based on the findings of Stead and colleagues⁵⁸ and Cahill and Lancaster.⁵⁹ Higher quit rates and sustained cessation were reported in those who received clinician advice when compared with usual care.⁵⁸ Combining advice with pharmacotherapy was associated with even higher quit rates when compared to advice combined with placebo.

Adherence

Drugs don't work in patients who don't take them.

—C. Everett Koop

The most important step in hypertension treatment is to get the patient to take the medications regularly as prescribed.

Adherence to hypertension medications can be improved by the following steps:

- Educating patient, family members and caregivers about the condition and the prescribed treatment
- Using a multidisciplinary team approach
 - Involving other health care professionals and work-site health care providers when possible
- Encouraging the patient to become more involved and monitor his or her blood pressure at home regularly
- Assessing adherence to therapy at each encounter with the patient
- Working with the patient to associate taking medications with daily habits
- When possible, using unit-of-dose packing and single-pill combinations and simplifying treatment regimens

Conclusion

The 2016 CHEP guidelines present 4 changes relevant to pharmacists:

1. AOBP is the recommended method for measuring blood pressure in an office setting.

2. Increasing dietary potassium is recommended in patients who are not at risk of hyperkalemia.
3. Intensive blood management to target systolic blood pressure ≤ 120 mmHg should be considered in high-risk patients who are ≥ 50 years old, have systolic blood pressure ≥ 130 mmHg and have any of the following:
 - Clinical or subclinical cardiovascular disease
 - Chronic kidney disease (nondiabetic nephropathy, proteinuria < 1 g/d, eGFR $20\text{--}59$ mL/min/ 1.73 m²)
 - Framingham risk score $\geq 15\%$
 - Age ≥ 75 years
4. β -blocker or calcium channel blocker can be used as first-line therapy in patients with stable angina and without prior heart failure, myocardial infarction or coronary artery bypass surgery.

Readers are encouraged to refer to the full guidelines in the *Canadian Journal of Cardiology*² or at www.hypertension.com, where additional professional and patient resources can be found. Pharmacists can find educational materials on hypertension assessment and management on the Hypertension Canada website in different forms such as documents, presentations and videos. ■

From the EPICORE Centre/COMPRIS (Al Hamarneh, Tsuyuki) and the Department of Medicine (Al Hamarneh, Tsuyuki), University of Alberta, Edmonton, Alberta; and the University of Waterloo School of Pharmacy (Houle), Kitchener, Ontario. Contact yazid.alhamarneh@ualberta.ca.

Author Contributions: Y. Al Hamarneh drafted the manuscript, based closely on the 2016 CHEP guidelines. All authors reviewed, edited and approved the final version of the manuscript.

Declaration of Conflicting Interests: The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Funding: The authors received no financial support for the research, authorship and/or publication of this article.

References

1. Campbell NR, Burgess E, Choi BCK, et al. Methods and overview of the Canadian recommendations. *CMAJ* 1999;160(9 suppl):S1-S6.
2. Leung AA, Nerenberg K, Daskalopoulou SS, et al. Hypertension Canada's 2016 Canadian Hypertension Education Program guidelines for blood pressure measurement, diagnosis, assessment of risk, prevention, and treatment of hypertension. *Can J Cardiol* 2016;32:569-88.
3. Joffers M, Falaschetti E, Gillespie C, et al. Hypertension prevalence, awareness, treatment and control in national surveys from England, the USA and Canada, and correlation with stroke and ischaemic heart disease mortality: a cross-sectional study. *BMJ Open* 2013;3(8):e003423.
4. Padwal RS, Bienek A, McAlister FA, Campbell NR. Epidemiology of hypertension in Canada: an update. *Can J Cardiol* 2016;32:687-94.

5. Chisholm-Burns MA, Kim Lee J, Spivey CA, et al. US pharmacists' effect as a team member on patient care: systematic review and meta-analyses. *Med Care* 2010;48:923-33.
6. Santschi V, Chiolerio A, Burnand A, et al. Impact of pharmacist care in the management of cardiovascular disease risk factors: a systematic review and meta-analysis of randomized trials. *Arch Intern Med* 2011;171:1441-53.
7. Santschi V, Chiolerio A, Paradis G, et al. Pharmacist interventions to improve cardiovascular disease risk factors in diabetes: a systematic review and meta analysis of randomized controlled trials. *Diabetes Care* 2012;35:2706-17.
8. Santschi V, Chiolerio A, Colosimo AL, et al. Improving blood pressure control through pharmacist interventions: a meta-analysis of randomized controlled trials. *J Am Heart Assoc* 2014;3:e000718.
9. Tsuyuki R, Houle S, Charrois T, et al. A randomized trial of the effect of pharmacist prescribing on improving blood pressure in the community: the Alberta clinical trial in optimizing hypertension (RxACTION). *Circulation* 2015;132:93-100.
10. Pojskic N, Jackson M, Malek A, Cimino S. Impact of community pharmacist interventions in hypertension management on patient outcomes: a randomized controlled trial. *Can Pharm J (Ott)* 2014;147:S17.
11. Tsuyuki RT, Al Hamarneh YN, Jones CA, Hemmelgarn BR. Effectiveness of community pharmacist prescribing and care on cardiovascular risk reduction: randomized controlled Rx EACH trial. *J Am Coll Cardiol* 2016;67(24):2846-54. doi:10.1016/j.jacc.2016.03.528
12. Houle SKD, Tsuyuki RT, Campbell NRC. The Canadian Hypertension Education Program (CHEP) 2011 guidelines for pharmacists. *Can Pharm J (Ott)* 2011;144:295-304.
13. Houle SKD, Padwal R, Tsuyuki RT. The 2012-2013 Canadian Hypertension Education Program (CHEP) guidelines for pharmacists: an update. *Can Pharm J (Ott)* 2013;146:146-50.
14. Houle SKD, Padwal R, Poirier L, Tsuyuki RT. The 2014 Canadian Hypertension Education Program (CHEP) guidelines for pharmacists: an update. *Can Pharm J (Ott)* 2014;147:203-8.
15. Houle SKD, Padwal R, Poirier L, Tsuyuki RT. The 2015 Canadian Hypertension Education Program (CHEP) guidelines for pharmacists: an update. *Can Pharm J (Ott)* 2015;148:180-6.
16. Daskalopoulou SS, Rabi DM, Zarnke KB, et al. The 2015 Canadian Hypertension Education Program recommendations for blood pressure measurement, diagnosis, assessment of risk, prevention, and treatment of hypertension. *Can J Cardiol* 2015;31:549-68.
17. Myers MG, Godwin M, Dawes M, et al. Conventional versus automated measurement of blood pressure in primary care patients with systolic hypertension: randomised parallel design controlled trial. *BMJ* 2011;342:d286.
18. Myers MG, Valdivieso M, Kiss A. Consistent relationship between automated office blood pressure recorded in different settings. *Blood Press Monit* 2009;14:108-11.
19. Myers MG, Valdivieso M, Kiss A. Use of automated office blood pressure measurement to reduce the white coat response. *J Hypertens* 2009;27:280-6.
20. Wright JT Jr, Williamson JD, Whelton PK, et al. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med* 2015;373:2103-16.
21. Brouwers MC, Kho ME, Browman GP, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. *CMAJ* 2010;182:E839-42.
22. Myers MG. A proposed algorithm for diagnosing hypertension using automated office blood pressure measurement. *J Hypertens* 2010;28:703-8.
23. Myers MG. The great myth of office blood pressure measurement. *J Hypertens* 2012;30:1894-8.
24. Myers MG. Eliminating the human factor in office blood pressure measurement. *J Clin Hypertens (Greenwich)* 2014;16:541-2.
25. Myers MG, Godwin M. Automated measurement of blood pressure in routine clinical practice. *J Clin Hypertens (Greenwich)* 2007;9:267-70.
26. Myers MG, Godwin M, Dawes M, et al. Conventional versus automated measurement of blood pressure in the office (CAMBO) trial. *Fam Pract* 2012;29:376-82.
27. Greiver M, White D, Kaplan DM, et al. Where should automated blood pressure measurements be taken? Pilot RCT of BpTRU measurements taken in private or nonprivate areas of a primary care office. *Blood Press Monit* 2012;17:137-8.
28. Myers MG, Godwin M, Dawes M, et al. Measurement of blood pressure in the office: recognizing the problem and proposing the solution. *Hypertension* 2010;55:195-200.
29. Myers MG, Oh PI, Reeves RA, Joyner CD. Prevalence of white coat effect in treated hypertensive patients in the community. *Am J Hypertens* 1995;8:591-7.
30. Armstrong D, Matangi M, Brouillard D, Myers MG. Automated office blood pressure—being alone and not location is what matters most. *Blood Press Monit* 2015;20:204-8.
31. Padwal RS, Townsend RR, Trudeau L, et al. Comparison of an in-pharmacy automated blood pressure kiosk to day-time ambulatory blood pressure in hypertensive subjects. *J Am Soc Hypertens* 2015;9:123-9.
32. Chambers LW, Kaczorowski J, O'Rielly S, et al. Comparison of blood pressure measurements using an automated blood pressure device in community pharmacies and family physicians' offices: a randomized controlled trial. *CMAJ Open* 2013;1:E37-42.
33. Andreadis EA, Agaliotis GD, Angelopoulos ET, et al. Automated office blood pressure and 24-h ambulatory measurements are equally associated with left ventricular mass index. *Am J Hypertens* 2011;24:661-6.
34. Andreadis EA, Agaliotis GD, Angelopoulos ET, et al. Automated office blood pressure is associated with urine albumin excretion in hypertensive subjects. *Am J Hypertens* 2012;25:969-73.
35. Campbell NR, McKay DW, Conradson H, et al. Automated oscillometric blood pressure versus auscultatory

- blood pressure as a predictor of carotid intima-medial thickness in male firefighters. *J Hum Hypertens* 2007;21:588-90.
36. Myers MG, Kaczorowski J, Paterson JM, et al. Thresholds for diagnosing hypertension based on automated office blood pressure measurements and cardiovascular risk. *Hypertension* 2015;66:489-95.
 37. Sidhu D, Naugler C. Fasting time and lipid levels in a community-based population: a cross-sectional study. *Arch Intern Med*. 2012;172:1707-10.
 38. Doran B, Guo Y, Xu J, et al. Prognostic value of fasting versus nonfasting low-density lipoprotein cholesterol levels on long-term mortality: insight from the National Health and Nutrition Examination Survey III (NHANES-III). *Circulation* 2014;130:546-53.
 39. Langsted A, Freiberg JJ, Nordestgaard BG. Fasting and nonfasting lipid levels: influence of normal food intake on lipids, lipoproteins, apolipoproteins, and cardiovascular risk prediction. *Circulation* 2008;118: 2047-56.
 40. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group [erratum in *Lancet* 1999;354:602]. *Lancet* 1998;352:837-53.
 41. Bansal S, Buring JE, Rifai N, et al. Fasting compared with nonfasting triglycerides and risk of cardiovascular events in women. *JAMA* 2007;298:309-16.
 42. Emerging Risk Factors Collaboration, Di Angelantonio E, Sarwar N, et al. Major lipids, apolipoproteins, and risk of vascular disease. *JAMA* 2009;302:1993-2000.
 43. Nordestgaard BG, Varbo A. Triglycerides and cardiovascular disease. *Lancet* 2014;384:626-35.
 44. Aldasouqi S, Sheikh A, Klosterman P, et al. Hypoglycemia in patients with diabetes on antidiabetic medications who fast for laboratory tests. *Diabetes Care* 2011;34:e52.
 45. de Vries M, Klop B, Castro Cabezas M. The use of the non-fasting lipid profile for lipid-lowering therapy in clinical practice—point of view. *Atherosclerosis* 2014;234:473-5.
 46. Khera AV, Mora S. Fasting for lipid testing: is it worth the trouble? *Arch Intern Med* 2012;172:1710-2.
 47. Aburto NJ, Hanson S, Gutierrez H, et al. Effect of increased potassium intake on cardiovascular risk factors and disease: systematic review and meta-analyses. *BMJ* 2013; 346:f1378.
 48. Ettehad D, Emdin CA, Kiran J, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta analysis. *Lancet* 2016;387:957-67.
 49. Xie X, Atkins E, Lv J, et al. Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: updated systematic review and meta-analysis. *Lancet* 2016;387:435-43.
 50. Pepine CJ, Handberg EM, Cooper-DeHoff RM, et al. A calcium antagonist vs a non-calcium antagonist hypertension treatment strategy for patients with coronary artery disease. The International Verapamil/Trandolapril Study (INVEST): a randomized controlled trial. *JAMA* 2003;290:2805-16.
 51. Dargie HJ, Ford I, Fox KM. Total Ischaemic Burden European Trial (TIBET). Effects of ischaemia and treatment with atenolol, nifedipine SR and their combination on outcome in patients with chronic stable angina. The TIBET Study Group. *Eur Heart J* 1996;17:104-12.
 52. Rehnqvist N, Hjemdahl P, Billing E, et al. Effects of metoprolol vs verapamil in patients with stable angina pectoris. The Angina Prognosis Study in Stockholm (APSIS). *Eur Heart J* 1996;17:76-81.
 53. Andalib A, Akhtari S, Rigal R, et al. Determinants of masked hypertension in hypertensive patients treated in a primary care setting. *Intern Med J* 2012;42:260-6.
 54. Pickering TG, Davidson K, Gerin W, Schwartz JE. Masked hypertension. *Hypertension* 2002;40:795-796.
 55. Ohkubo T, Kikuya M, Metoki H, et al. Prognosis of “masked” hypertension and “white-coat” hypertension detected by 24-h ambulatory blood pressure monitoring 10-year follow-up from the Ohasama study. *J Am Coll Cardiol* 2005;46:508-15.
 56. Grover SA, Lowensteyn I, Joseph L, et al. Discussing coronary risk with patients to improve blood pressure treatment: secondary results from the CHECK-UP study. *J Gen Intern Med* 2009;24:33-9.
 57. Gee ME, Bienek A, McAlister FA, et al. Factors associated with lack of awareness and uncontrolled high blood pressure among Canadian adults with hypertension. *Can J Cardiol* 2012;28:375-82.
 58. Stead LF, Hartmann-Boyce J, Perera R, Lancaster T. Telephone counselling for smoking cessation. *Cochrane Database Syst Rev* 2013;CD002850.
 59. Cahill K, Lancaster T. Workplace interventions for smoking cessation. *Cochrane Database Syst Rev* 2014;CD003440.