



HYPERTENSION: DIAGNOSIS AND MANAGEMENT

Sahil Bharat*, Rohit Kumar, Tanvay Jaithliya, Shubam Sehgal, Gulshan Singh and Atul Tiwari¹

*Faculty of Pharmaceutical Sciences, Mewar University, 312901, Chittorgarh, India.

¹Assistant Professor, Faculty of Pharmaceutical Sciences, Mewar University, Chittorgarh, 312901, India.

***Corresponding Author: Sahil Bharat**

Faculty of Pharmaceutical Sciences, Mewar University, 312901, Chittorgarh, India.

Article Received on 19/03/2018

Article Revised on 09/04/2018

Article Accepted on 30/04/2018

ABSTRACT

Systemic hypertension is a chief risk factor for cardiovascular disease and is present in 69% of patients with a first myocardial infarction, in 77% of patients with a first stroke, in 74% of patients with chronic heart failure, and in 60% of patients with peripheral arterial disease. Double-blind, randomized, placebo-controlled trials have found that antihypertensive drug therapy reduces cardiovascular events in patients aged younger than 80 years and in patients aged 80 years and older in the Hypertension in the Very Elderly Trial. Although the optimal blood pressure treatment goal has not been determined, existing epidemiologic and clinical trial data suggest that a reasonable therapeutic blood pressure goal should be <140/90 mm Hg in patients younger than 80 years and a systolic blood pressure of 140-145 mm Hg if tolerated in patients aged 80 years and older. Non-pharmacologic lifestyle measures should be reinvigorated both to prevent development of hypertension and as adjunctive therapy in patients with hypertension. Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, calcium channel blockers, and diuretics have all reduced cardiovascular events in randomized trials. The choice of specific drugs be contingent on efficacy, tolerability, presence of specific comorbidities, and cost.

KEYWORD: Systemic hypertension presence of specific comorbidities, and cost.

INTRODUCTION

Hypertension (HTN or HT), too known as high blood pressure (HBP), is a long-term medical condition in which the blood pressure in the arteries is persistently elevated.^[23] High blood pressure usually does not cause symptoms.^[1] Long-term high blood pressure, however, is a chief risk factor for coronary artery disease, stroke, heart failure, atrial fibrillation, peripheral vascular disease, vision loss, chronic kidney disease, and dementia.^{[15][16][17][24]} High blood pressure is classified as either primary (essential) high blood pressure or secondary high blood pressure.^[18] Nearly 90–95% of cases are primary, defined as high blood pressure due to nonspecific lifestyle and genetic factors.^{[18][19]} Lifestyle influences that increase the risk include excess salt in the diet, excess body weight, smoking, and alcohol abusive use.^{[1][18]} The remaining 5–10% of cases are categorized as secondary high blood pressure, defined as high blood pressure due to an identifiable cause, such as chronic kidney disease, narrowing of the kidney arteries, an endocrine disorder, or the use of birth control pills.^[18] Blood pressure is expressed by two measurements, the systolic and diastolic pressures, which are the maximum and minimum pressures, respectively.^[1] For most adults, normal blood pressure at rest is within the range of 100–130 millimetres mercury (mmHg) systolic and 60–80 mmHg diastolic.^{[20][25]} For most adults, high blood

pressure is existing if the resting blood pressure is persistently at or above 130/90 or 140/90 mmHg.^{[18][20]} Different numbers apply to children.^[26] Ambulatory blood pressure monitoring over a 24-hour period appears more accurate than office-based blood pressure measurement.^{[18][23]} Lifestyle changes and medications can lower blood pressure and decrease the risk of health complications.^[21] Lifestyle changes include weight loss, decreased salt intake, physical exercise, and a healthy diet.^[18] If lifestyle changes are not sufficient then blood pressure medications are used.^[21] Up to three medications can control blood pressure in 90% of people.^[18] The treatment of moderately high arterial blood pressure (defined as >160/100 mmHg) with medications is associated with an improved life expectancy.^[27] The effect of treatment of blood pressure between 130/80 mmHg and 160/100 mmHg is less clear, with some reviews finding benefit^{[20][28][30]} and others finding unclear benefit.^{[31][32][33]} High blood pressure affects between 16 and 37% of the population globally.^[18] In 2010 hypertension was believed to have been a factor in 18% of all deaths (9.4 million globally).^[22]

Detection

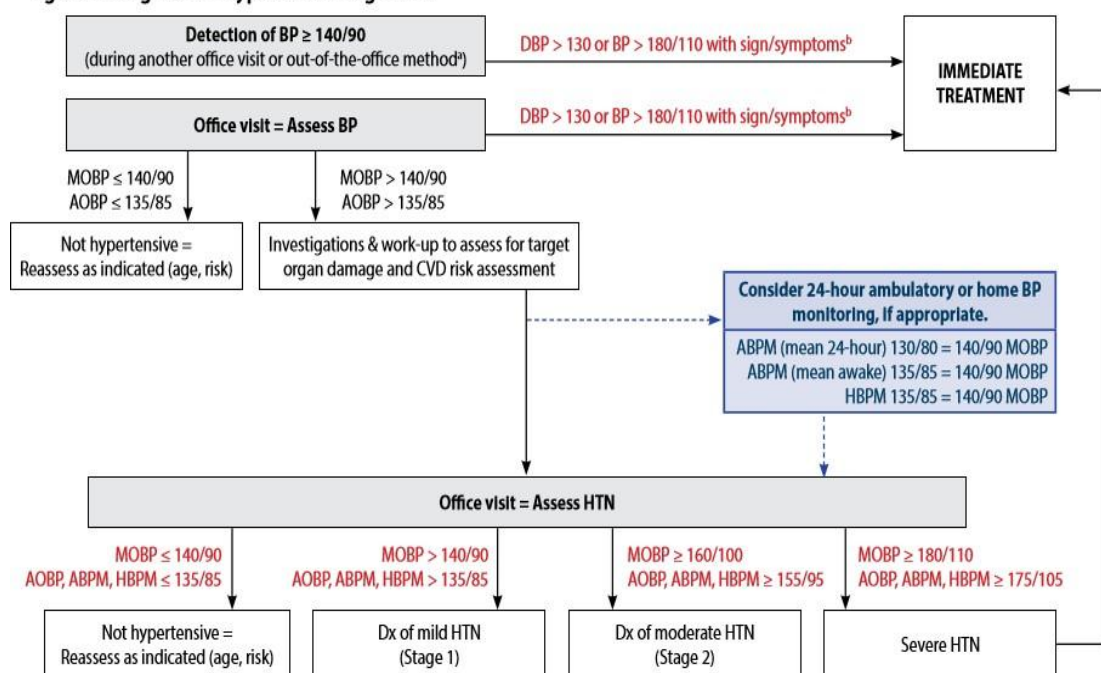
In patients aged ≥ 45 years, BP should be recorded at least once every 5 years. This recording should be the average of several measurements. Ensure standardized

technique (e.g., patient in a seated position, selecting the arm with the higher BP) and equipment are being used (refer to Appendix B: Recommended Methods and Techniques for Measuring Blood Pressure). When possible, use an automated office BP measuring electronic device, as an alternative to manual office BP technique.^[3] Using automated office BP reduces errors due to improper technique, avoiding an overestimation of BP values (white-coat HTN) or underestimation of BP values (masked HTN).

Diagnosis^[7,9]

Assessment of Elevated Blood Pressure If average BP is elevated again, proceed to investigations and work-up to assess target organ damage and cardiovascular disease (CVD) risk. Select which arm to use by measuring BP in both arms with the patient in a seated position. Measure BP three more times using the arm with the higher reading, then discard the 1st reading and average the latter two.

Figure 1. Diagnosis of hypertension algorithm



Abbreviations: AOBP = automatic office blood pressure; ABPM = ambulatory blood pressure monitoring; BP = blood pressure; CVD = cardiovascular disease; DBP = diastolic blood pressure; Dx = diagnosis; HBPM = home blood pressure monitoring; HTN = hypertension; MOBP = manual office blood pressure. Footnote: a Out-of-office method may include automated BP machines at pharmacies or grocery stores. b Sign/symptoms may include papilledema and retinal haemorrhage.


Investigations and work-up includes

- Medical history - ask about risk factors and rule out any exogenous factors Risk Factors o Modifiable: smoking; physical activity levels/sedentary lifestyle; poor diet; body composition (e.g., body weight, body mass index, waist circumference); poor sleep; psychological factors (e.g., stress levels). o Non-modifiable: age; family history; ethnicity (e.g., African, Caribbean, South Asian (East Indian, Pakistani, Bangladeshi, Sri Lankan) origin). Exogenous Factors o White-coat HTN (~20% of patients with high manual office BP readings); prescription drugs (e.g., nonsteroidal anti-inflammatory drugs (NSAIDs), steroids, oral contraceptives, decongestants); and others (e.g., alcohol, stimulants, sodium).
- Physical examination - fundoscopy, central and peripheral cardiovascular examination, and abdominal examination

- Urinalysis - albumin to creatinine ratio (ACR), haematuria.
- Test for blood chemistry - potassium, sodium, creatinine/estimated glomerular filtration rate (eGFR)
- Test for type 2 diabetes - fasting blood glucose OR haemoglobin A1c level
- Test for lipids - full lipid profile
- Electrocardiogram (ECG) standard 12-lead
- CVD risk assessment - Framingham Risk Score or www.bestsciencemedicine.com/chd/calc2.html.

Consider 24-hour ambulatory or home BP monitoring for appropriate patients (e.g., suspected white-coat HTN, unusual fluctuating office-based BP readings).^[4]

Table 1. Ranking of preferred methods for measuring blood pressure by accuracy and accessibility^{3,7,10,11}

1. Automated Office BP (e.g., BpTRU)	
135/85 (automated office BP) = 135/85 (ambulatory BP monitoring: mean awake)	
Advantages	1) Measurements are comparable to ambulatory BP monitoring (the gold standard); 2) readings are consistent from visit-to-visit; 3) reduces white-coat and masked HTN; and 4) correlates well with CV outcomes (e.g., acute MI and cerebrovascular events).
2. Ambulatory BP Monitoring	
130/80 (ambulatory BP monitoring: mean 24-hour) = 135/85 (ambulatory BP monitoring: mean awake) = 140/90 (manual office BP)	
Advantages	Ambulatory BP monitoring is considered the gold standard for accurate BP measurements.
Limitations	1) May cost (patient-pay ~ \$50); 2) accessibility issues (both in actual devices and trained professionals to interpret results); and 3) patient may not be able to tolerate ambulatory BP monitoring.
Technical Notes	Offer ambulatory BP monitoring to patients with elevated BP and who can tolerate keeping the cuff position correctly and dry for 24 hours.
3. Home BP Monitoring	
135/85 (home BP monitoring) = 135/85 (ambulatory BP monitoring: mean awake) = 140/90 (manual office BP)	
Advantages	1) Measurements are comparable to ambulatory BP monitoring (the gold standard); 2) correlates well with target organ damage and CV mortality.
Technical Notes	Offer home BP monitoring if ambulatory BP monitoring is not tolerated. Ensure device is appropriate (e.g., cuff size) and validated (i.e., includes the endorsement logo and/or listed on www.hypertension.ca)
	
4. Manual Office BP	
Advantages	1) Considered a more accurate reading for patients with arrhythmias; and 2) no accessibility issues.
Limitations	1) Known issues with the accuracy of manual office BP (e.g., white-coat effect, improper technique) that may result in approximately 10/5 mm Hg higher readings; and 2) relatively poor predictor of CV risk related to BP status.

Abbreviations: BP = blood pressure; CV = cardiovascular; HTN = hypertension; mm Hg = millimetre of mercury; MI = myocardial infarction.

- Assessment of of Hypertension If ambulatory or home BP monitoring was not conducted, measure office BP again. A HTN diagnosis may be confirmed at this visit. If a HTN diagnosis cannot be confirmed or ruled out, consider ambulatory or home BP monitoring. Further office visits may be required.
- Indications for Consultation with a Specialist Indications for consultation with a specialist include:
 - Hypertensive emergency – DBP > 130 or BP > 180/110 with signs/symptoms;
 - Sudden onset in the elderly;
 - Abnormal nocturnal BP differences¹² – an extreme nocturnal BP dip (>20%), non/small nocturnal BP dip (<10%), or an increase in nocturnal BP are at risk for CVD;
 - Signs or symptoms suggesting of secondary causes of the HTN; and
 - Resistant HTN – BP still difficult to control after treating with 3 antihypertensive medications.

Management

Once a diagnosis has been confirmed, conduct a patient-specific discussion to decide upon desirable BP readings and an individualized treatment plan. This discussion

should consider any benefits and potential harms.

Desirable Blood Pressure Readings

140/90 or lower is the desirable blood pressure reading for an adult with no-comorbid conditions, diabetes, chronic kidney disease or other target organ damage.^[2] However, an individual patient's desirable BP is influenced by their age, presence of target organ damage, CVD risk level and/or the presence of other CVD risk factors.

This guideline uses the term 'desirable BP' instead of 'targets' to encourage clinical judgement when dealing with an individual patient. The suggested desirable BP readings of 140/90 is provided as guidance only, since recommending a uniform threshold for all patients or even patient groups is not optimal. Also, the term 'targets' is not used because the treat-to-target approach is not recommended.

Controversies in Care: Blood Pressure Readings in the Diabetes Population

This guideline recommends a desirable BP reading of 140/90 for the diabetes population. There is an

acknowledgement that this does not align with the Canadian Hypertension Education Program's^[7] or the Canadian Diabetes Association's^[12] recommendation of a 130/80 target; but it does align with the Eighth Joint National Committee's^[9] and National Institute for Health and Care Excellence's^[8] guidance. The target of 130/80 is not supported by any randomized controlled trials, and therefore is mostly consensus based. However, there is no evidence to completely discard the 130/80 either. A desirable BP of 140/90 is based on a recent large clinical trial^[2] that found no significant difference between a target of 140/90 versus 120/80, thus a 130/80 would unlikely be beneficial versus 140/90. Future trials are needed to bring clarity to this issue.

Lifestyle Management

Recommend lifestyle management for patients with mild HTN (average BP = 140 – 159/90 – 99), low-risk for

CVD and no co-morbidities (refer to Table 3 for list of co-morbidities).^[6]

The benefits of pharmacologic treatment in the mild HTN group is unknown, and may not outweigh the potential harms (e.g., increased risk of falls).^[14] In a recent systematic review, pharmaceutical treatment within this patient group did not reduce total mortality, total CV events, coronary heart disease or stroke, when compared to a placebo treatment.^[14] Whereas, the benefits of lifestyle management (e.g., smoking cessation, increasing physical activity, obtaining or maintaining a healthy body composition, eating a well-balanced diet, and monitoring salt intake) with this patient group has been documented (refer to Table 3).

Table 2. Impact of health behaviours on blood pressure^{7,8}

Intervention	SBP (mm Hg)	DBP (mm Hg)	Goal
Diet and weight control	-6.0	-4.8	• BMI < 25 kg/m ² ; WC ≤ 102/88 cm (Caucasian men/women), ≤ 90/80 cm (Asian men/women)
Reduced salt/sodium intake	-5.4	-2.8	• < 2000 mg of sodium ^a
Reduced alcohol intake (heavy drinkers)	-3.4	-3.4	• ≤ 2 drinks/day
DASH diet ^b	-11.4	-5.5	-
Physical activity	-3.1	-1.8	• 30-40 minutes 4-7 days/week
Smoking cessation	unknown	unknown	• Smoke free environment
Relaxation therapies	-3.7	-3.5	-
Multiple interventions	-5.5	-4.5	-

Abbreviations: BMI = body mass index; DASH = dietary approaches to stop hypertension; DBP = diastolic blood pressure; kg/m² = kilogram per square metre; mm Hg = millimetre of mercury; SBP = systolic blood pressure; WC = waist circumference.

Footnotes: ^a Canadian Hypertension Education Program now recommends a sodium intake threshold 2000 mg (5 g of salt) per day. The previous threshold was ≤ 1500 mg (3.75 g of salt) and was changed based on clinical trial evidence from two systematic reviews published in 2013. The aim is to identify salt sensitive patients. ^b There are no mortality outcome studies of the DASH diet.

Pharmacologic Management^[7]

Instigate pharmacologic management in context of the patient's overall CVD risk (e.g., not solely based on a patient's BP) and in conjunction with lifestyle management.^[5] Pharmacologic management may be considered if:

- 1) Average BP is > 140/90 and with target organ damage or CVD risk >20%;
- 2) Average BP is > 140/90 with 1+ co-morbidities (refer to Table 3 for co-morbidities list);
- 3) Average BP is ≥ 160/100
- 4) Desirable BP is not reached with lifestyle management.

Table 3. Pharmacologic treatment recommendations of hypertension complicated by co-morbidity⁷

Co-morbidity	Pharmacologic Treatment Recommendations	Notes	
Cardiovascular Disease			
Coronary heart disease	First-line	ACE-I or ARB or Beta-blockers (for patients with stable angina)	1) Do not use short-acting nifedipine; 2) Do not use ACE-I + ARB if no systolic HF; 3) Caution when lowering SBP to a goal, if DBP is \leq 60 mm Hg.
	Second-line	Long-acting CCB or DHP-CCB (for high-risk patients and in combination with a first-line ACE-I)	
Myocardial infarction (recent)	First-line	Beta-blockers + ACE-I/ARB (if ACE-I intolerant)	1) Do not use non-DHP-CCB (diltiazem, verapamil) if heart failure is present. 2) Caution when lowering SBP to a goal, if DBP is \leq 60 mm Hg.
	Second-line	Long-acting CCB (if beta-blockers contraindicated or ineffective)	
Left ventricular hypertrophy	First-line	ACE-I/ARB (if ACE-I intolerant) or Thiazide/Thiazide-like diuretic or Long-acting CCB	Do not use direct arterial vasodilators such as hydralazine and minoxidil.
	Second-line	Combination of first-line drugs.	
Heart failure	First-line	Beta-blockers + ACE-I/ARB (if ACE-I intolerant) • Aldosterone antagonist may be added in patients with recent CV hospitalization, acute MI, elevated BNP or NT-proBNP level, or NYHA Class II to IV symptoms.	1) If combining aldosterone antagonist to ACE-I/ARB, monitor for hyperkalemia. 2) If combining ACE-I + ARB, monitor for potential adverse events including hypotension, hyperkalemia and worsening of renal function. 3) If bradycardia is also present, avoid use of beta-blockers.
	Second-line	ACE-I + ARB or Hydralazine + Isosorbide dinitrate (if ACE-I + ARB intolerant or contraindicated) • Thiazide/thiazide-like for BP control or loop diuretics for volume control as additive therapy. DHP-CCB may also be used.	
Cerebrovascular disease After acute stroke	First-line	ACE-I + Thiazide/Thiazide-like diuretic	1) During acute stroke and not eligible for thrombolytic therapy do not treat HTN unless extreme BP increase. 2) Combination of ACE-I + ARB is not recommended.
	Second-line	Long-acting DHP-CCB or combination of additional drugs	
Diabetes			
Diabetes with microalbuminuria ^a , CKD, CVD or CVD risk factors	First-line	ACE-I/ARB (if ACE-I intolerant)	Loop diuretic could be considered in hypertensive CKD patients with extracellular fluid volume overload.
	Second-line	DHP-CCB	
Diabetes	First-line	ACE-I or ARB or Thiazide/Thiazide-like diuretic or DHP-CCB	
	Second-line	Combination of first-line drugs • In combination with ACE-I or ARB, a DHP-CCB is preferable to a thiazide/thiazide-like diuretic.	
Chronic Kidney Disease			
Chronic kidney disease without diabetes	First-line	ACE-I/ARB (if ACE-I intolerant) • Thiazide/thiazide-like diuretic as additive therapy. Loop diuretics for those with volume overload.	1) If using ACE-I or ARB, monitor renal function and potassium. 2) Combination of ACE-I + ARB is not recommended for patients without proteinuria ^a .
	Second-line	Combination of additional drugs	
Renovascular disease	First-line	Thiazide diuretic or ACE-I or ARB (if ACE-I intolerant) or Long-acting CCB	Avoid ACE-I or ARB if bilateral renal artery stenosis or unilateral disease with solitary kidney.
	Second-line	Combination of first-line drugs	

Abbreviations: ACE-I = angiotensin-converting enzyme inhibitors; ACR = albumin to creatinine ratio; ARB = angiotensin II receptor blocker; BP = blood pressure; BNP = brain natriuretic peptide; CCB = calcium channel blocker; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; DBP = diastolic blood pressure; DHP = dihydropyridine; HF = heart failure; HTN = hypertension; MI = myocardial infarction; mm Hg = millimeter of mercury; NYHA = New York Heart Association functional classification system; NT-proBNP = N-terminal prohormone of brain natriuretic peptide; SBP = systolic blood pressure.
Footnotes: ^a Proteinuria is defined as urinary protein > 500 mg/24hr or ACR > 30 mg/mmol in 2 of 3 specimens. ^b The term microalbuminuria is being phased out, which is now referred to as moderately increased albuminuria and as defined as ACR = 3 mg/mmol - 30 mg/mmol.

CONCLUSION

Adolescents with significant hypertension or obesity or those who are not successful in lowering their blood pressure may require intensive counseling from a registered dietitian or nutritionist. Referral to a public health nurse and/or coordination with the school nurse for on-going monitoring may also be useful. Smokers may benefit from an age-appropriate smoking cessation program.

Those who abuse alcohol or other drugs may need referral to a chemical dependency counselor for in-depth evaluation and treatment. The hypertensive adolescent needs the positive support and role modeling of all family members. Their commitment to also make necessary lifestyle changes, including increased physical activity, smoking cessation, reduction in dietary sodium, and adopting the DASH eating plan will make it possible for the adolescent to be successful in managing hypertension.

REFERENCES

1. "High Blood Pressure Fact Sheet". CDC. 19 February 2015. Archived from the original on 6 March 2016. Retrieved 6 March 2016.
2. Cushman WC, Evans GW, Byington RP, et al. ACCORD Study Group. Effects of intensive blood-pressure control in type 2 diabetes mellitus. *N Engl J Med.*, 2010; 362(17): 507-515.
3. Myers MG, Kaczorowski J, Dawes M, et al. Automated office blood pressure measurement in primary care. *Can Fam Physician*, 2014; 60: 127-32.
4. Hodgkinson J, Mant J, Martin U, et al. Relative effectiveness of clinic and home blood pressure monitoring compared with ambulatory blood pressure monitoring in diagnosis of hypertension: Systematic review. *BMJ (Clinical Research Ed.)*, 2011; 342: d3621.
5. The Blood Pressure Lowering Treatment Trialists' Collaboration. Blood pressure-lowering treatment based on cardiovascular risk: A meta-analysis of individual patient data. *Lancet*, 2014; 384: 591-98.
6. Dickinson HO, Mason JM, Nicolson DJ, et al. Lifestyle interventions to reduce raised blood

- pressure: A systematic review of randomized controlled trials. *J Hypertens*, 2006; 24(2): 215–233.
7. Dasgupta K, Quinn RR, Zarnke KB, et al. The 2014 Canadian Hypertension Education Program recommendations for blood pressure measurement, diagnosis, assessment of risk, prevention and treatment of hypertension. *Can J Cardiol*, 2014; 30: 485-501.
 8. National Institute for Health and Care Excellence. Hypertension: The clinical management of primary hypertension in adults (Clinical Guidance 127). 2011. London: National Institute for Health and Care Excellence.
 9. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: Report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA*. doi:10.1001/jama.2013.284427.
 10. 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.
 11. Kaczorowski J, Dawes M, Gelfer M. Measurement of blood pressure: New developments and challenges. *BCMJ*, 2012; 54(8): 399-403.
 12. Fagard RH. Dipping pattern of nocturnal blood pressure in patients with hypertension. *Expert Rev Cardiovasc Ther.*, 2009; 7(6): 599-605.
 13. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee, Gilbert R, Rabi D, LaRochelle P, et al. Treatment of hypertension. *Can J Diabetes*, 2013; 37(1): S117-8.
 14. Diao D, Wright JM, Cundiff DK, et al. Pharmacotherapy for mild hypertension. *Cochrane Database Syst Rev.*, 2012; 8: CD006742.
 15. Lackland, DT; Weber, MA. "Global burden of cardiovascular disease and stroke: hypertension at the core". *The Canadian journal of cardiology*, May 2015; 31(5): 569–71. doi:10.1016/j.cjca.2015.01.009. PMID 25795106.
 16. Mendis, Shanthi; Puska, Pekka; Norrving, Bo. Global atlas on cardiovascular disease prevention and control (PDF) (1st ed.). Geneva: World Health Organization in collaboration with the World Heart Federation and the World Stroke Organization, 2011; 38. ISBN 9789241564373. Archived (PDF) from the original on 17 August 2014.
 17. Hernandorena, I; Duron, E; Vidal, JS; Hanon, O. "Treatment options and considerations for hypertensive patients to prevent dementia". *Expert Opinion on Pharmacotherapy (Review)*, July 2017; 18(10): 989–1000. doi:10.1080/14656566.2017.1333599. PMID 28532183.
 18. Poulter, NR; Prabhakaran, D; Caulfield, M. "Hypertension". *Lancet*, 22 August 2015; 386(9995): 801–12. doi:10.1016/s0140-6736(14)61468-9. PMID 25832858.
 19. Carretero OA, Oparil S; Oparil. "Essential hypertension. Part I: definition and etiology". *Circulation*, January 2000; 101(3): 329–35. doi:10.1161/01.CIR.101.3.329. PMID 10645931. Archived from the original on 12 February 2012.
 20. Whelton, Paul K.; Carey, Robert M.; Aronow, Wilbert S.; Casey, Donald E.; Collins, Karen J.; Dennison Himmelfarb, Cheryl; DePalma, Sondra M.; Gidding, Samuel; Jamerson, Kenneth A.; Jones, Daniel W.; MacLaughlin, Eric J.; Muntner, Paul; Ovbiagele, Bruce; Smith, Sidney C.; Spencer, Crystal C.; Stafford, Randall S.; Taler, Sandra J.; Thomas, Randal J.; Williams, Kim A.; Williamson, Jeff D.; Wright, Jackson T. (13 November 2017). "2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults". *Hypertension: HYP*.0000000000000065. doi:10.1161/HYP.0000000000000065.
 21. "How Is High Blood Pressure Treated?". National Heart, Lung, and Blood Institute. 10 September 2015. Archived from the original on 6 April 2016. Retrieved 6 March 2016.
 22. Campbell, NR; Lackland, DT; Lisheng, L; Niebylski, ML; Nilsson, PM; Zhang, XH. "Using the Global Burden of Disease study to assist development of nation-specific fact sheets to promote prevention and control of hypertension and reduction in dietary salt: a resource from the World Hypertension League". *Journal of clinical hypertension (Greenwich, Conn.)*, March 2015; 17(3): 165–67. doi:10.1111/jch.12479. PMID 25644474.
 23. Naish, Jeannette; Court, Denise Syndercombe. *Medical sciences*, 2014; (2 ed.): 562. ISBN 9780702052491. Archived from the original on 26 December 2016.
 24. Lau, DH; Nattel, S; Kalman, JM; Sanders, P. "Modifiable Risk Factors and Atrial Fibrillation". *Circulation (Review)*, August 2017; 136(6): 583–96. doi:10.1161/CIRCULATIONAHA.116.023163. PMID 28784826.
 25. Giuseppe, Mancia; Fagard, R; Narkiewicz, K; Redon, J; Zanchetti, A; Bohm, M; Christiaens, T; Cifkova, R; De Backer, G; Dominiczak, A; Galderisi, M; Grobbee, DE; Jaarsma, T; Kirchhof, P; Kjeldsen, SE; Laurent, S; Manolis, AJ; Nilsson, PM; Ruilope, LM; Schmieder, RE; Sirnes, PA; Sleight, P; Viigimaa, M; Waeber, B; Zannad, F; Redon, J; Dominiczak, A; Narkiewicz, K; Nilsson, PM; et al. "2013 ESH/ESC 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)". *European Heart Journal*, July 2013; 34(28): 2159–219. doi:10.1093/eurheartj/eh151. PMID 23771844.
 26. James, PA.; Oparil, S.; Carter, BL.; Cushman, WC.; Dennison-Himmelfarb, C.; Handler, J.; Lackland, DT.; Lefevre, ML.; et al. "2014 Evidence-Based

- Guideline for the Management of High Blood Pressure in Adults: Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)". *JAMA*, Dec 2013; 311(5): 507–20. doi:10.1001/jama.2013.284427. PMID 24352797.
27. Musini, VM; Tejani, AM; Bassett, K; Wright, JM. "Pharmacotherapy for hypertension in the elderly". *The Cochrane Database of Systematic Reviews*, 7 October 2009; 4: CD000028. doi:10.1002/14651858.CD000028.pub2. PMID 19821263.
 28. Sundström, Johan; Arima, Hisatomi; Jackson, Rod; Turnbull, Fiona; Rahimi, Kazem; Chalmers, John; Woodward, Mark; Neal, Bruce. "Effects of Blood Pressure Reduction in Mild Hypertension". *Annals of Internal Medicine*, February 2015; 162: 184–91. doi:10.7326/M14-0773. PMID 25531552.
 29. Xie, X; Atkins, E; Lv, J; Bennett, A; Neal, B; Ninomiya, T; Woodward, M; MacMahon, S; Turnbull, F; Hillis, GS; Chalmers, J; Mant, J; Salam, A; Rahimi, K; Perkovic, V; Rodgers, A. "Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: updated systematic review and meta-analysis". *Lancet*, 30 January 2016; 387(10017): 435–43. doi:10.1016/S0140-6736(15)00805-3. PMID 26559744.
 30. Diao, D; Wright, JM; Cundiff, DK; Gueyffier, F (Aug 15, 2012). "Pharmacotherapy for mild hypertension". *The Cochrane Database of Systematic Reviews*. 8: CD006742. doi:10.1002/14651858.CD006742.pub2. PMID 22895954.
 31. Garrison, SR; Kolber, MR; Korownyk, CS; McCracken, RK; Heran, BS; Allan, GM (8 August 2017). "Blood pressure targets for hypertension in older adults". *The Cochrane Database of Systematic Reviews*. 8: CD011575. doi:10.1002/14651858.CD011575.pub2. PMID 28787537.
 32. Musini, VM; Gueyffier, F; Puil, L; Salzwedel, DM; Wright, JM (16 August 2017). "Pharmacotherapy for hypertension in adults aged 18 to 59 years". *The Cochrane Database of Systematic Reviews*. 8: CD008276. doi:10.1002/14651858.CD008276.pub2. PMID 28813123