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Hypertension Management at a Glance 1352Acknowledgments 1354References 1354To align with its mission to reduce the global burden of raised blood pressure (BP), the International Society of Hypertension (ISH) has developed worldwide practice guidelines for the management of hypertension in adults, aged 18 years and older.The ISH Guidelines Committee extracted evidence-based content presented in recently published extensively reviewed guidelines and tailored and standards of care in a practical format that is easy-to-use particularly in low, but also in high resource settings – by clinicians, but also nurses and community health workers, as appropriate. Although distinction between low and high resource settings often refers to high (HIC) and low- and middle-income countries (LMIC), it is well established that in HIC there are areas with low resource settings, and vice versa.Herein optimal care refers to evidence-based standard of care articulated in recent guidelines1,2 and summarized here, whereas standards recognize that standards would not always be possible. Hence essential standards refer to minimum standards of care. To allow specification of essential standards of care for low resource settings, the Committee was often confronted with the limitation or absence in clinical evidence, and thus applied expert opinion.In the Guidelines, differentiation between optimal and essential standards were not always possible, and were made in sections where it was most practical and sensible. The Guidelines Committee is also aware that some recommended essential standards may not be feasible in low resource settings, for example, out-of-office BP measurements, the requirement of multiple visits for the diagnosis of hypertension, or advising the use of single pill combination therapy. Although challenging to implement, these guidelines may aid in local initiatives to motivate policy changes and serve as an instrument to drive local improvements in standards of care. Every effort should be made to achieve essential standards of care to reduce hypertension-induced cardiovascular morbidity and mortality.MotivationRaised BP remains the leading cause of death globally, accounting for 10.4 million deaths per year.3 When reviewing global figures, an estimated 1.39 billion people had hypertension in 2010. 4 However, BP trends show a clear shift of the highest BPs from high-income to low-income regions,5 with an estimated 349 million with hypertension in HIC and 1.04 billion in LMICs.4The large disparities in the regional burden of hypertension are accompanied by low levels of awareness, treatment and control rates in LMIC, when compared to HIC. In response to poor global awareness for hypertension (estimated 67% in HIC and 38% in LMIC),4 the ISH launched a global campaign to increase awareness of raised BP, namely the May Measurement Month initiative.6,7Despite several initiatives, the prevalence of raised BP and adverse impact on cardiovascular morbidity and mortality are increasing globally, irrespective of income.4,5 It is therefore critical that population-based initiatives are applied to reduce the global burden of raised BP, such as salt-reduction activities and improving the availability of fresh fruit and vegetables. To improve the management of hypertension, the ISH has published in 2014 with the American Society of Hypertension, Clinical Practice Guidelines for the Management of Hypertension in the Community (See Section 11: Resources). Recently, we have observed a recent flurry of updated evidence-based guidelines arising mainly from high-income regions and countries, including the United States of America,2 Europe,1 United Kingdom,8 Canada9 and Japan.10 New developments include redefining hypertension,2 initiating treatment with a single pill combination therapy,1 advising wider out-of-office BP measurement,2,10 and lower BP targets.1,2,8,11,12Low- and middle-income regions often follow the release of guidelines from high-income regions closely, as their resources and health systems to develop and implement local guidelines remain challenging. In Africa only 25% of countries have hypertension guidelines13 and in many instances these guidelines are adopted from those of high-income regions. However, the adoption of guidelines from high-income regions are sometimes impractical as low resource settings are confronted with a substantial number of obstacles including severe lack of trained healthcare professionals, unreliable electricity in rural clinics, low access to basic office BP devices and limited ability to conduct basic recommended diagnostic procedures and poor access to affordable high-quality medications. In both low and high-income regions, the ambiguities of latest guidelines are often met with confusion among healthcare providers, anxiety among patients,14 and they resulted in a call for global harmonization.15 Guidelines from high-income regions may thus not fit global purpose.16Guideline Development ProcessThe 2020 ISH Global Hypertension Practice Guidelines were developed by the ISH Hypertension Guidelines Committee based on evidence criteria, (1) to be used globally; (2) to be fit for application in low and high resource settings by advising on essential and optimal standards; and (3) to be concise, simplified, and easy to use. They were critically reviewed and evaluated by numerous external hypertension experts from HIC and LMIC with expertize in the optimal management of hypertension and management in resource-constraint settings. These Guidelines were developed without any support from industry or other sources.Composition of the ISH Hypertension Guidelines Committee and Selection of External ReviewersThe ISH Hypertension Guidelines Committee was composed of members of the ISH Council; they were included on the basis of (1) specific expertize in different areas of hypertension; (2) previous experience with the generation of hypertension guidelines, as well as (3) representation of different regions of the world. A similar strategy was followed concerning the selection of external reviewers with particular consideration of representatives from LMICs.Section 2: Definition of HypertensionIn accordance with most major guidelines it is recommended that hypertension be diagnosed when a person's systolic blood pressure (SBP) in the office or clinic is ≥140 mm Hg and/or their diastolic blood pressure (DBP) is ≥90 mm Hg following repeated examination (see below, Section 3). Table 1 provides a classification of BP based on office BP measurement, Table 2 provides ambulatory and home BP values used to define hypertension; these definitions apply to all adults (>18 year old). These BP categories are designed to align therapeutic approaches with BP levels.High-normal BP is intended to identify individuals who could benefit from lifestyle interventions and who would receive pharmacological treatment if compelling indications are present (see Section 9).Isolated systolic hypertension defined as elevated SBP (≥140 mm Hg) and low DBP (10 mm Hg in repeated measurements, use the arm with the higher BP. If the difference is >20 mm Hg consider further investigation.Standing blood pressure: Measure in treated hypertensives after 1 min and again after 3 min when there are symptoms suggesting postural hypotension and at the first visit in the elderly and people with diabetes.Unattended office blood pressure: Multiple automated BP measurements taken while the patient remains alone in the office provide a more standardized evaluation but also lower BP levels than usual office measurements with uncertain threshold for hypertension diagnosis.17,18,23,24 Confirmation with out-of-office BP is again needed for most treatment decisions.Out-of-office BP measurements (by patients at home or with 24-hour ambulatory blood pressure monitoring [ABPM]) are more reproducible than office measurements, more closely associated with hypertension-induced organ damage and the risk of cardiovascular events and identify the white coat and masked hypertension phenomena (see below).Out-of-office BP measurement is often necessary for the accurate diagnosis of hypertension and for treatment decisions. In untreated or treated subjects with office BP classified as high-normal BP or grade 1 hypertension (systolic 130–159 mm Hg and/or diastolic 85–99 mm Hg), the BP level needs to be confirmed using home or ambulatory BP monitoring (Table 5).1,2,17,21Recommendations for performing home and ambulatory BP measurement are presented in Table 5.White Coat and Masked HypertensionThe use of office and out-of-office (home or ambulatory) BP measurements identifies individuals with white coat hypertension, who have elevated BP only in the office (nonelevated ambulatory or home BP), and those with masked hypertension, who have nonelevated BP in the office but elevated BP out of the office (ambulatory or home).1,2,17–21,25–27 These conditions are common among both untreated subjects and those treated for hypertension. About 10%–30% of subjects attending clinics due to high BP have white coat hypertension and 10%–15% have masked hypertension.White coat hypertension: These subjects are at intermediate cardiovascular risk between normotensives and sustained hypertensives. The diagnosis needs confirmation with repeated office and out-of-office BP measurements. If their total cardiovascular risk is low and there is no hypertension-mediated organ damage (HMOD), drug treatment may not be prescribed. However, they should be followed with lifestyle modification, as they may develop sustained hypertension requiring drug treatment.1,2,17–21,25–27Masked hypertension: These patients are at similar risk of cardiovascular events as sustained hypertensives. The diagnosis needs confirmation with repeated office and out-of-office measurements. Masked hypertension may require drug treatment aiming to normalize out-of-office BP.1,2,17–21,25–27Section 4: Diagnostic / Clinical TestsPatients with hypertension are often asymptomatic, however specific symptoms can suggest secondary hypertension or hypertensive complications that require further investigation. A complete medical and family history is recommended and should include1:Blood pressure: New onset hypertension, duration, previous BP levels, current and previous antihypertensive medication, other medications/over-the counter medicines that can influence BP, history of intolerance (side-effects) of antihypertensive medications, adherence to antihypertensive treatment, previous hypertension with oral contraceptives or pregnancy.Risk factors: Personal history of CVD (myocardial infarction, heart failure [HF], stroke, transient ischemic attacks [TIA], diabetes, dyslipidemia, chronic kidney disease [CKD], smoking status, diet, alcohol intake, physical activity, psychosocial aspects, history of depression). Family history of hypertension, premature CVD, (familial) hypercholesterolemia, diabetes.Assessment of overall cardiovascular risk: In line with local guidelines/recommendations (see risk scores in Section 11 at the end of the document).Symptoms/signs of hypertension/coexistent illnesses: Chest pain, shortness of breath, palpitations, claudication, peripheral edema, headaches, blurred vision, nocturia, hematuria, dizziness.Symptoms suggestive of secondary hypertension: Muscle weakness/tetany, cramps, arrhythmias (hypokalemia/primary aldosteronism), flash pulmonary edema (renal artery stenosis), sweating, palpitations, frequent headaches (pheochromocytoma), snoring, daytime sleepiness (obstructive sleep apnea), symptoms suggestive of thyroid disease (see Section 10 for full list of symptoms).A thorough physical examination can assist with confirming the diagnosis of hypertension and the identification of HMOD and/or secondary hypertension and should include:Circulation and heart: Pulse rate/rhythm/character, jugular venous pulse/pressure, apex beat, extra heart sounds, basal crackles, peripheral edema, bruits (carotid, abdominal, femoral), radio-femoral delay.Other organs/systems: Enlarged kidneys, neck circumference >40 cm (obstructive sleep apnea), enlarged thyroid, increased body mass index (BMI)/waist circumference, fatty deposits and coloured striae (Cushing disease/syndrome).Blood tests: Sodium, potassium, serum creatinine and estimated glomerular filtration rate (eGFR). If available, lipid profile and fasting glucose.Urine test: Dipstick urine test.12-lead ECG: Detection of atrial fibrillation, left ventricular hypertrophy (LVH), ischemic heart disease.Additional investigations when indicated can be undertaken to assess and confirm suspicion of HMOD, coexistent diseases or/and secondary hypertension.Imaging TechniquesEchocardiography: LVH, systolic/diastolic dysfunction, atrial dilation, aortic coarctation.Carotid ultrasound: Plaques (atherosclerosis), stenosis.Kidneys/renal artery and adrenal imaging: Ultrasound/renal artery Duplex; CT-/MR-angiography: renal parenchymal disease, renal artery stenosis, adrenal lesions, other abdominal pathology.Fundoscopy: Retinal changes, hemorrhages, papilledema, tortuosity, nipping.Brain CT/MRI: Ischemic or hemorrhagic brain injury due to hypertension.Functional Tests and Additional Laboratory InvestigationsAnkle-brachial index: Peripheral (lower extremity) artery disease.Further testing for secondary hypertension if suspected: Aldosterone-renin ratio, plasma free metanephrines, late-night salivary cortisol or other screening tests for cortisol excess.Urinary albumin/creatinine ratioSerum uric acid (s-UA) levelsLiver function testsSection 5: Cardiovascular Risk FactorsDiagnostic ApproachMore than 50% of hypertensive patients have additional cardiovascular risk factors.28,29The most common additional risk factors are diabetes (15%–20%), lipid disorders (elevated low-density lipoprotein-cholesterol [LDL-C] and triglycerides [30%]), overweight-obesity (40%), hyperuricemia (25%) and metabolic syndrome (40%), as well as unhealthy lifestyle habits (eg, smoking, high alcohol intake, sedentary lifestyle).28–30The presence of one or more additional cardiovascular risk factors proportionally increases the risk of coronary, cerebrovascular, and renal diseases in hypertensive patients.1An evaluation of additional risk factors should be part of the diagnostic workup in hypertensive patients particularly in the presence of a family history of CVD.Cardiovascular risk should be assessed in all hypertensive patients by easy-to-use scores based on BP levels and additional risk factors according to a simplified version of the approach proposed by ESC-ESH Guidelines (Table 6).1A reliable estimate of cardiovascular risk can be obtained in daily practice by including:Other Risk Factors: Age (>65 years), sex (male>female), heart rate (>80 beats/min), increased body weight, diabetes, high LDL-C/triglyceride, family history of CVD, family history of hypertension, early-onset menopause, smoking habits, psychosocial or socioeconomic factors. HMOD: LVH (LVH with ECG), moderate-severe CKD (CKD; eGFR 6 mg/dl [0.357 mmol/L]).An increase in cardiovascular risk must be considered in patients with hypertension and chronic inflammatory diseases, chronic obstructive pulmonary disease (COPD), psychiatric disorders, psychosocial stressors where an effective BP control is warranted.1Section 6: Hypertension-Mediated Organ Damage (HMOD)Definition and Role of HMOD in Hypertension ManagementHypertension-mediated organ damage (HMOD) is defined as the structural or functional alteration of the arterial vasculature and/or the organs it supplies that is caused by elevated BP. End organs include the brain, the heart, the kidneys, central and peripheral arteries, and the eyes.Figure 1. How to measure blood pressure.While assessment of overall cardiovascular risk is important for the management of hypertension, additional detection of HMOD is unlikely to change the management of those patients already identified as high risk (ie, those with established CVD, stroke, diabetes, CKD, or familial hypercholesterolemia). However, it can provide important therapeutic guidance on (1) management for hypertensive patients with low or moderate overall risk through reclassification due to presence of HMOD, and (2) preferential selection of drug treatment based on the specific impact on HMOD.1Specific Aspects of HMOD and AssessmentBrain: TIA or strokes are common manifestations of elevated BP. Early subclinical changes can be detected most sensitively by magnetic resonance imaging (MRI) and include white matter lesions, silent microinfarcts, microbleeds, and brain atrophy. Due to costs and limited availability brain MRI is not recommended for routine practice but should be considered in patients with neurologic disturbances, cognitive decline and memory loss.Heart: A 12-lead ECG is recommended for routine workup of patients with hypertension and simple criteria (Sokolow-Lyon index: SV1+RV5 ≥35 mm, Cornell index: SV3+RaVL >28 mm for men or >20 mm for women and Cornell voltage duration product: >2440 mm•ms) are available to detect presence of LVH. Sensitivity of ECG-LVH is very limited and a two-dimensional transthoracic echocardiogram (TTE) is the method of choice to accurately assess LVH (left ventricular mass index [LVMI]: men >115 g/m2; women >95 g/m2) and relevant parameters including LV geometry, left atrial volume, LV systolic and diastolic function and others.Kidneys: Kidney damage can be a cause and consequence of hypertension and is best assessed routinely by simple renal function parameters (serum creatinine and eGFR) together with investigation for albuminuria (dipstick or urinary albumin creatinine ratio [UACR]) in early morning spot urine).Arteries: Three vascular beds are commonly assessed to detect arterial HMOD: (1) the carotid arteries through carotid ultrasound to detect atherosclerotic plaque burden/stenosis and intima media thickness (IMT); (2) the aorta by carotid-femoral pulse wave velocity (PWV) assessment to detect large artery stiffening; and (3) the lower extremity arteries by assessment of the ankle-brachial index (ABI). Although there is evidence to indicate that all three provide added value beyond traditional risk factors, their routine use is currently not recommended unless clinically indicated, that is, in patients with neurologic symptoms, isolated systolic hypertension, or suspected peripheral artery disease, respectively.Eyes: Fundoscopy is a simple clinical bedside test to screen for hypertensive retinopathy although interobserver and intraobserver reproducibility is limited. Fundoscopy is particularly important in hypertensive urgencies and emergencies to detect retinal hemorrhage, microaneurysms, and papilledema in patients with accelerated or malignant hypertension. Fundoscopy should be performed in patients with grade 2 hypertension, ideally by experienced examiners or alternative techniques to visualize the fundus (digital fundus cameras) where available.The following assessments to detect HMOD should be performed routinely in all patients with hypertension:Serum creatinine and eGFRDipstick urine test12-lead ECGAll other techniques mentioned above can add value to optimize management of hypertension in affected individuals and should be considered where clinically indicated and available. Serial assessment of HMOD (LVH and albuminuria) to monitor regression with antihypertensive treatment may be helpful to determine the efficacy of treatment in individual patients but this has not been sufficiently validated for most measures of HMOD.Section 7: Exacerbators and Inducers of HypertensionBackgroundSeveral medications and substances may increase BP or antagonize the BP-lowering effects of antihypertensive therapy in individuals (Table 7). It is important to note that the individual effect of these substances on BP can be highly variable with greater increases noted in the elderly, those with higher baseline BP, using antihypertensive therapy or with kidney disease.Screen all patients (with hypertension and those at risk for hypertension) for substances that may increase BP or interfere with the BP-lowering effect of antihypertensive medications.Where appropriate, consider reducing or eliminating substances that raise BP. If these substances are required or preferred, then treat BP to target regardless. (See resource31 on possible antihypertensive therapies that target mechanisms underlying the raised BP induced by these substances).Section 8: Treatment of Hypertension8.1 Lifestyle ModificationsHealthy lifestyle choices can prevent or delay the onset of high BP and can reduce cardiovascular risk.46 Lifestyle modification is also the first line of antihypertensive treatment. Modifications in lifestyle can also enhance the effects of antihypertensive treatment. Lifestyle modifications should include the following (Table 8).47–64Seasonal BP Variation65BP exhibits seasonal variation with lower levels at higher temperatures and higher at lower temperatures. Similar changes occur in people traveling from places with cold to hot temperature, or the reverse. A meta-analysis showed average BP decline in summer of 5/3 mm Hg (systolic/diastolic). BP changes are larger in treated hypertensives and should be considered when symptoms suggesting over-treatment appear with temperature rise, or BP is increased during cold weather. BP below the recommended goal should be considered for possible downtitration, particularly if there are symptoms suggesting overtreatment.8.2 Pharmacological TreatmentContemporary data from over 100 countries66,67 suggest that on average, less than 50% of adults with hypertension receive BP-lowering medication, with few countries performing better than this and many worse. This is despite the fact that a difference in BP of 20/10 mm Hg is associated with a 50% difference in cardiovascular risk.68The pharmacological treatment strategies recommended here (Figures 2–4) are largely compatible with those made in the most recent US2 and European guidelines.1,8Figure 2. Pharmacological treatment of hypertension: general scheme. See Table 2 (Section 2) for equivalent BP levels based on ambulatory or home BP recordings.Figure 3. Office blood pressure targets for treated hypertension.Figure 4. ISH core drug-treatment strategy. Data from references 69–73. Ideal characteristics of drug treatment (see Table 9).Figure 5. ISH 2020 recommendations (minimum standards of care).Figure 6. ISH 2020 recommendations (evidence-based standards of care).8.3 Adherence to Antihypertensive TreatmentBackgroundAdherence is defined as to the extent to which a person's behaviors such as taking a medication, following a diet or executing lifestyle changes corresponds with agreed recommendations from a healthcare provider.74 Nonadherence to antihypertensive treatment affects 10%–80% of hypertensive patients and is one of the key drivers of suboptimal BP control.75–77 Poor adherence to antihypertensive treatment correlates with the magnitude of BP elevation and is an indicator of poor prognosis in hypertensive patients.78–81 The etiology of nonadherence to antihypertensive treatment is multifactorial and includes causes associated with the healthcare system, pharmacological therapy, the disease, patients and their socioeconomic status.74Recommendations: Adherence to Antihypertensive TherapyEvaluate adherence to antihypertensive treatment as appropriate at each visit and prior to escalation of antihypertensive treatment.Consider the following strategies to improve medication adherence82-87a. reducing polypharmacy – use of single pill combinationsb. once-daily dosing over multiple times per day dosingc. linking adherence behavior with daily habitsd. providing adherence feedback to patientse. home BP monitoringf. reminder packaging of medicationsg. empowerment-based counseling for self-managementh. electronic adherence aids such as mobile phones or short messages servicesi. multidisciplinary healthcare team approach (ie, pharmacists) to improve monitoring for adherenceObjective indirect (ie, review of pharmacy records, pill counting, electronic monitoring devices) and direct (ie, witnessed intake of medications, biochemical detection of medications in urine or blood) are generally preferred over subjective methods to diagnose nonadherence to antihypertensive treatment.80,85The most effective methods for management of nonadherence require complex interventions that combine counseling, self-monitoring, reinforcements and supervision.Section 9: Common and Other Comorbidities and Complications of HypertensionBackgroundHypertensive patients have several common and other comorbidities that can affect cardiovascular risk and treatment strategies.The number of comorbidities increases with age, with the prevalence of hypertension and other diseases.Common comorbidities include coronary artery disease (CAD), stroke, CKD, HF, and COPD.Uncommon comorbidities include rheumatic diseases and psychiatric diseases.Uncommon comorbidities are largely underestimated by guidelines and frequently treated with drugs often self-prescribed and possibly interfering with BP control.Common and uncommon comorbidities should be identified and managed according to available evidence.Common Comorbidities and ComplicationsHypertension and Coronary Artery Disease (CAD)A strong epidemiological interaction exists between CAD and hypertension that accounts for 25%–30% of acute myocardial infarctions.88Lifestyle changes are recommended (smoking cessation, diet and exercise).BP should be lowered if ≥140/90 mm Hg and treated to a target 180 mm HgImmediate, 130

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