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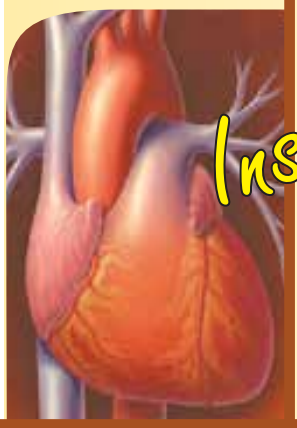

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2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults (JNC 8 Report)

Hypertension remains one of the most important preventable contributors to disease and death. Abundant evidence from randomized controlled trials (RCTs) has shown benefit of antihypertensive drug treatment in reducing important health outcomes in persons with hypertension.

The panel members appointed to the Eighth Joint National Committee (JNC 8) used rigorous evidence-based methods, developing Evidence Statements and recommendations for blood pressure (BP) treatment based on a systematic review of the literature to meet user needs, especially the needs of the primary care clinician. This report is an executive summary of the evidence and is designed to provide clear recommendations for all clinicians. Major differences from the previous JNC report are summarized in Table 1.

THE PROCESS

The panel members appointed to JNC 8 were selected from more than 400 nominees based on expertise in hypertension (n = 14), primary care (n = 6), including geriatrics (n = 2), cardiology (n = 2), nephrology (n = 3), nursing (n = 1), pharmacology (n = 2), clinical trials (n = 6), evidence-based medicine (n = 3), epidemiology (n = 1), informatics (n = 4), and the development and implementation of clinical guidelines in systems of care (n = 4).

THE EVIDENCE REVIEW

The evidence review focused on adults aged 18 years or older with hypertension and included studies with the following prespecified subgroups: diabetes, coronary artery disease, peripheral artery disease, heart failure, previous stroke, chronic kidney disease (CKD), proteinuria, older adults, men and women, racial and ethnic groups, and smokers. Studies with sample sizes smaller than 100 were excluded, as were studies with a follow-up period of less than 1 year, because small studies of brief duration are unlikely to yield enough health-related outcome information to permit interpretation of treatment effects. Studies were included in the evidence review only if they reported the effects of the studied interventions on any of these important health outcomes:

- Overall mortality, cardiovascular disease (CVD)–related mortality, CKD-related mortality
- Myocardial infarction, heart failure, hospitalization for heart failure, stroke
- Coronary revascularization (includes coronary artery bypass surgery, coronary angioplasty and coronary stent placement), other revascularization (includes carotid, renal, and lower extremity revascularization)
- End-stage renal disease (ESRD) (ie, kidney failure resulting in dialysis or transplantation), doubling of creatinine level, halving of glomerular filtration rate (GFR).

The panel limited its evidence review to RCTs because they are less subject to bias than other study designs and represent the gold standard for determining efficacy and effectiveness. Initial search dates for the literature review were January 1, 1966, through December 31, 2009. The search strategy and PRISMA diagram for each question is in the online Supplement. To ensure that no major relevant studies published after December 31, 2009, were excluded from consideration, 2 independent searches of PubMed and CINAHL between December 2009 and August 2013 were conducted with the same MeSH terms as the original search. Three panel members reviewed the results. The panel limited the inclusion criteria

of this second search to the following. (1) The study was a major study in hypertension (eg, ACCORD-BP, SPS3; however, SPS3 did not meet strict inclusion criteria because it included nonhypertensive participants. SPS3 would not have changed our conclusions/recommendations because the only significant finding supporting a lower goal for BP occurred in an infrequent secondary outcome). (2) The study had at least 2000 participants. (3) The study was multicentered. (4) The study met all the other inclusion/exclusion criteria. The relatively high threshold of 2000 participants was used because of the markedly lower event rates observed in recent RCTs such as ACCORD, suggesting that larger study populations are needed to obtain interpretable results. Additionally, all panel members were asked to identify newly published studies for consideration if they met the above criteria. No additional clinical trials met the previously described inclusion criteria. Studies selected were rated for quality using NHLBI's standardized quality rating tool and were only included if rated as good or fair.

An external methodology team performed the literature review, summarized data from selected papers into evidence tables, and provided a summary of the evidence. From this evidence review, the panel crafted evidence statements and voted on agreement or disagreement with each statement. For approved evidence statements, the

Table 1. Comparison of Current Recommendations With JNC 7 Guidelines

Topic	JNC 7	2014 Hypertension Guideline
Methodology	Nonsystematic literature review by expert committee including a range of study designs Recommendations based on consensus.	Critical questions and review criteria defined by expert panel with input from methodology team. Initial systematic review by methodologists restricted to RCT evidence. Subsequent review of RCT evidence and recommendations by the panel according to a standardized protocol .
Definitions	Defined hypertension and prehypertension.	Definitions of hypertension and prehypertension not addressed, but thresholds for pharmacologic treatment were defined.
Treatment goals	Separate treatment goals defined for "uncomplicated" hypertension and for subsets with various comorbid conditions (diabetes and CKD).	Similar treatment goals defined for all hypertensive populations except when evidence review supports different goals for a particular subpopulation.
Lifestyle recommendations	Recommended lifestyle modifications based on literature review and expert opinion.	Lifestyle modifications recommended by endorsing the evidence based Recommendations of the Lifestyle Work Group.
Drug therapy	Recommended 5 classes to be considered as initial therapy but recommended thiazide-type diuretics as initial therapy for most patients without compelling indication for another class. Specified particular antihypertensive medication classes for patients with compelling indications, ie, diabetes, CKD, heart failure, myocardial infarction, stroke, and high CVD risk. Included a comprehensive table of oral antihypertensive drugs including names and usual dose ranges.	Recommended selection among 4 specific medication classes (ACEI or ARB, CCB or diuretics) and doses based on RCT evidence. Recommended specific medication classes based on evidence review for racial, CKD, and diabetic subgroups. Panel created a table of drugs and doses used in the outcome trials.
Scope of topics	Addressed multiple issues (blood pressure measurement methods, patient evaluation components, secondary hypertension, adherence to regimens, resistant hypertension, and hypertension in special populations) based on literature review and expert opinion.	Evidence review of RCTs addressed a limited number of questions, those judged by the panel to be of highest priority.
Review process prior to publication	Reviewed by the National High Blood Pressure Education Program Coordinating Committee, a coalition of 39 major professional, public, and voluntary organizations and 7 federal agencies.	Reviewed by experts including those affiliated with professional and public organizations and federal agencies; no official sponsorship by any organization should be inferred.

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; CKD, chronic kidney disease; CVD, cardiovascular disease; JNC, Joint National Committee; RCT, randomized controlled trial

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panel then voted on the quality of the evidence. Once all evidence statements for each critical question were identified, the panel reviewed the evidence statements to craft the clinical recommendations, voting on each recommendation and on the strength of the recommendation. For both evidence statements and recommendations, a record of the vote count (for, against, or recusal) was made without attribution. The panel attempted to achieve 100% consensus whenever possible, but a two-thirds majority was considered acceptable, with the exception of recommendations based on expert opinion, which required a 75% majority agreement to approve.

RESULTS (RECOMMENDATIONS)

Recommendation 1

In the general population aged ≥60 years, initiate pharmacologic treatment to lower blood pressure (BP) at systolic blood pressure (SBP) ≥150 mm Hg or diastolic blood pressure (DBP) ≥90 mm Hg and treat to a goal SBP <150 mm Hg and goal DBP <90 mm Hg. (Strong Recommendation – Grade A)

Corollary Recommendation

In the general population aged ≥60 years, if pharmacologic treatment for high BP results in lower achieved SBP (eg,

Table 2. Evidence-Based Dosing for Antihypertensive Drugs

Antihypertensive Medication	Initial Daily Dose, mg	Target Dose in RCTs Reviewed, mg	No. of Doses per Day
ACE inhibitors			
Captopril	50	150-200	2
Enalapril	5	20	1-2
Lisinopril	10	40	1
Angiotensin receptor blockers			
Eprosartan	400	600-800	1-2
Candesartan	4	12-32	1
Losartan	50	100	1-2
Valsartan	40-80	160-320	1
Irbesartan	75	300	1
β-Blockers			
Atenolol	25-50	100	1
Metoprolol	50	100-200	1-2
Calcium channel blockers			
Amlodipine	2.5	10	1
Diltiazem extended release	120-180	360	1
Nitrendipine	10	20	1-2
Thiazide-type diuretics			
Bendroflumethiazide	5	10	1
Chlorthalidone	12.5	12.5-25	1
Hydrochlorothiazide	12.5-25	25-100[a]	1-2
Indapamide	1.25	1.25-2.5	1

Abbreviations: ACE, angiotensin-converting enzyme; RCT, randomized controlled trial.
[a]Current recommended evidence-based dose that balances efficacy and safety is 25-50 mg daily.

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<140 mm Hg) and treatment is well tolerated and without adverse effects on health or quality of life, treatment does not need to be adjusted. (Expert Opinion – Grade E)

Recommendation 2

In the general population ≤60 years, initiate pharmacologic treatment to lower BP at DBP >90 mm Hg and treat to a goal DBP <90 mm Hg. (For ages 30-59 years, Strong Recommendation – Grade A; For ages 18-29 years, Expert Opinion – Grade E)

Recommendation 3

In the general population <60 years, initiate pharmacologic treatment to lower BP at SBP ≥140 mm Hg and treat to a goal SBP <140 mm Hg. (Expert Opinion – Grade E)

Recommendation 4

In the population aged ≥18 years with chronic kidney disease (CKD), initiate pharmacologic treatment to lower BP at SBP ≥140 mm Hg or DBP ≥90 mm Hg and treat to goal SBP <140 mm Hg and goal DBP <90 mm Hg. (Expert Opinion – Grade E)

Recommendation 5

In the population aged ≥18 years with diabetes, initiate pharmacologic treatment to lower BP at SBP ≥140 mm Hg or DBP ≥90 mm Hg and treat to a goal SBP <140 mm Hg and goal DBP <90 mm Hg. (Expert Opinion – Grade E)

Recommendation 6

In the general nonblack population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic, calcium channel blocker (CCB), angiotensin-converting enzyme inhibitor (ACEI), or angiotensin receptor blocker (ARB). (Moderate Recommendation – Grade B)

Recommendation 7

In the general black population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic or CCB. (For general black population: Moderate Recommendation – Grade B; for black patients with diabetes: Weak Recommendation – Grade C)

Recommendation 8

In the population aged ≥18 years with CKD, initial (or add-on) antihypertensive treatment should include an ACEI or ARB to improve kidney outcomes. This applies to all CKD patients with hypertension regardless of race or diabetes status. (Moderate Recommendation – Grade B)

Recommendation 9

The main objective of hypertension treatment is to attain and maintain goal BP. If goal BP is not reached within a month of treatment, increase the dose of the initial drug or add a second drug from one of the classes in recommendation 6 (thiazide-type diuretic, CCB, ACEI, or ARB). The clinician should continue to assess BP and adjust the treatment regimen until goal BP is reached. If goal BP cannot be reached with 2 drugs, add and titrate a third drug from the list provided. Do not use an ACEI and an ARB together in the same patient. If goal BP cannot be reached using only the drugs in recommendation 6 because of a contraindication or the need to use more than 3 drugs to reach goal BP, antihypertensive drugs from other classes can be used. Referral to a hypertension specialist may be indicated for patients in whom goal BP cannot be attained using the above strategy or for the management of complicated patients for whom additional clinical consultation is needed. (Expert Opinion – Grade E)

LIMITATIONS

This evidence-based guideline for the management of high BP in adults is not a comprehensive guideline and is limited in scope because of the focused evidence review to address the 3 specific questions (Table 1). Clinicians often provide care for patients with numerous comorbidities or other important issues related to hypertension, but the decision was made to focus on 3 questions considered to be relevant to most physicians and patients.

The evidence review did not include observational studies, systematic reviews, or meta-analyses, and the panel did not conduct its own meta-analysis based on prespecified inclusion criteria. Thus, information from these types of studies was not incorporated into the evidence statements or recommendations. Although this may be considered a limitation, the panel decided to focus only on RCTs because they represent the best scientific evidence and because there were a substantial number of studies that included large numbers of patients and met our inclusion criteria. Randomized controlled trials that included participants with normal BP were excluded from our formal analysis. In cases in which high-quality evidence was not available or the evidence was weak or absent, the panel relied on fair-quality evidence, panel members' knowledge of the published literature beyond the RCTs reviewed, and personal experience to make recommendations. The duration of the guideline development process following completion of the systematic search may have caused the panel to miss studies published after our literature review. However, a bridge search was performed through August 2013, and the panel found no additional studies that would have changed the recommendations.

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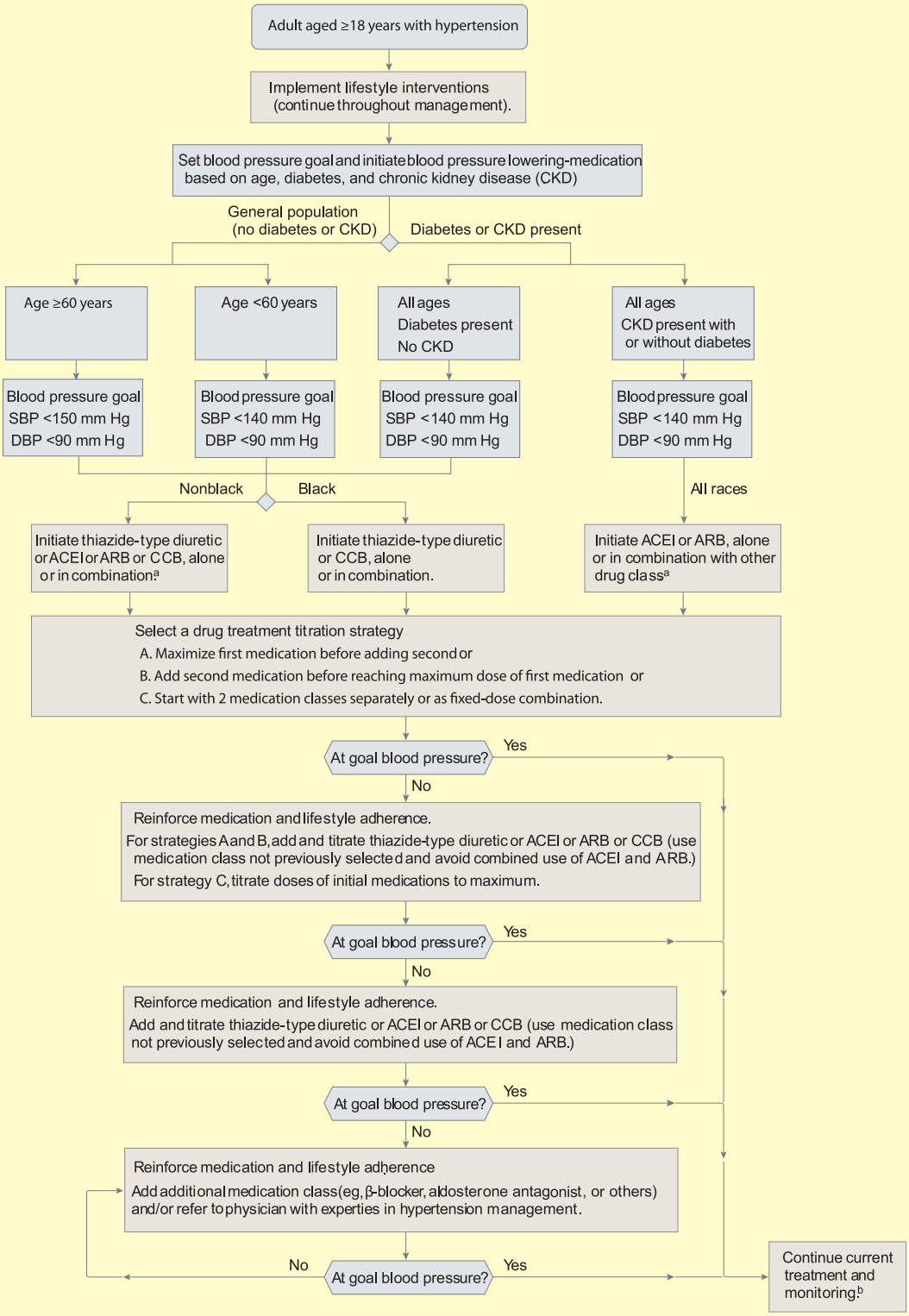
Figure 2014 Hypertension Guideline Management Algorithm



SBP indicates systolic blood pressure; DBP, diastolic blood pressure; ACEI, angiotensin-converting enzyme inhibitor; ARB , angiotensin receptor blocker; and CCB, calcium channel blocker.

[a] ACEIs and ARBs should not be used in combination.

[b] If blood pressure fails to be maintained at goal, reenter the algorithm where appropriate based on the current individual therapeutic plan.

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Many of the reviewed studies were conducted when the overall risk of cardiovascular morbidity and mortality was substantially higher than it is today; therefore, effect sizes may have been overestimated. In many studies focused on DBP, participants also had elevated SBP so it was not possible to determine whether the benefit observed in those trials arose from lowering DBP, SBP, or both. In addition, the ability to compare studies from different time periods was limited by differences in clinical trial design and analytic techniques.

While physicians use cost, adherence, and often observational data to make treatment decisions, medical interventions should whenever possible be based first and foremost on good science demonstrating benefits to patients. Randomized controlled trials are the gold standard for this assessment and thus were the basis for providing the evidence for our clinical recommendations. Although adverse effects and harms of antihypertensive treatment documented in the RCTs were considered when the panel made its decisions, the review was not designed to determine whether therapy-associated adverse effects and harms resulted in significant changes in important health outcomes. In addition, this guideline was not endorsed by any federal agency or professional society prior to publication and thus is a departure from previous JNC reports.

DISCUSSION

The recommendations based on RCT evidence in this guideline differ from recommendations in other currently used guidelines supported by expert consensus (Table 4). For example, JNC 7 and other guidelines recommended treatment to lower BP goals in patients with diabetes and CKD based on observational studies. Recently, several guideline documents such as those from the American Diabetes Association have raised the systolic BP goals to values that are similar to those recommended in this evidence-based guideline. Other guidelines such as those of the European Society of Hypertension/European Society of Cardiology also recommend a systolic BP goal of lower than 150 mm Hg, but it is not clear at what age cutoff in the general population this goal specifically applies. This changing landscape is understandable given the lack of clear RCT evidence in many clinical situations.

CONCLUSIONS

It is important to note that this evidence-based guideline has not redefined high BP, and the panel believes that the 140/90 mm Hg definition from JNC 7 remains reasonable. The relationship between naturally occurring BP and risk is linear down to very low BP, but the benefit of treating to

Table 3. Strategies to Dose Antihypertensive Drugs[a]

Strategy	Description	Details
A	Start one drug, titrate to maximum dose, and then add a second drug.	If goal BP is not achieved with the initial drug, titrate the dose of the initial drug up to the maximum recommended dose to achieve goal BP. If goal BP is not achieved with the use of one drug despite titration to the maximum recommended dose, add a second drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB) and titrate up to the maximum recommended dose of the second drug to achieve goal BP. If goal BP is not achieved with 2 drugs, select a third drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB), avoiding the combined use of ACEI and ARB. Titrate the third drug up to the maximum recommended dose to achieve goal BP.
B	Start one drug and then add a second drug before achieving maximum dose of the initial drug.	Start with one drug then add a second drug before achieving the maximum recommended dose of the initial drug, then titrate both drugs up to the maximum recommended doses of both to achieve goal BP If goal BP is not achieved with 2 drugs, select a third drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB), avoiding the combined use of ACEI and ARB. Titrate the third drug up to the maximum recommended dose to achieve goal BP.
C	Begin with 2 drugs at the same time, either as 2 separate pills or as a single pill combination.	Initiate therapy with 2 drugs simultaneously, either as 2 separate drugs or as a single pill combination. Some committee members recommend starting therapy with ≥2 drugs when SBP is >160 mm Hg and/or DBP is >100 mm Hg, or if SBP is >20 mm Hg above goal and/or DBP is >10 mm Hg above goal. If goal BP is not achieved with 2 drugs, select a third drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB), avoiding the combined use of ACEI and ARB. Titrate the third drug up to the maximum recommended dose.

Abbreviations: ACEI, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; CCB, calcium channel blocker; DBP, diastolic blood pressure; SBP, systolic blood pressure.

[a]This table is not meant to exclude other agentswithin the classes of antihypertensive medications that have been recommended but reflects those agents and dosing used in randomized controlled trials that demonstrated improved outcomes.

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these lower levels with antihypertensive drugs is not established. For all persons with hypertension, the potential benefits of a healthy diet, weight control, and regular exercise cannot be overemphasized. These lifestyle treatments have the potential to improve BP control and even reduce medication needs.

The recommendations from this evidence-based guideline from panel members appointed to the Eighth Joint National Committee (JNC 8) offer clinicians an analysis of what is known and not known about BP treatment thresholds, goals, and drug treatment strategies to achieve those goals based on evidence from RCTs. However, these recommendations are not a substitute for clinical judgment, and decisions about care must carefully consider and incorporate the clinical characteristics and circumstances of each individual patient. We hope that the algorithm will facilitate implementation and be useful to busy clinicians. The strong evidence base of this report should inform quality measures for the treatment of patients with hypertension.

Extracted from 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 Published online December 18, 2013.

Table 4. Guideline Comparisons of Goal BP and Initial Drug Therapy for Adults With Hypertension

Guideline	Population	Goal BP, mm Hg	Initial Drug Treatment Options
2014 Hypertension guideline	General ≥60 y	<150/90	Nonblack: thiazide-type diuretic, ACEI, ARB, or CCB; black: thiazide-type <140/90 diuretic or CCB
	General <60 y	<140/90	
	Diabetes	<140/90	Thiazide-type diuretic, ACEI, ARB, or CCB
	CKD	<140/90	ACEI or ARB
ESH/ESC 2013	General nonelderly	<140/90	Diuretic, β-blocker, CCB, ACEI, or ARB
	General elderly <80 y	<150/90	
	General ≥80 y	<150/90	
	Diabetes	<140/90	ACEI or ARB
	CKD no proteinuria	<140/90	ACEI or ARB
	CKD + proteinuria	<130/90	
ESH/ESC 2013	General <80 y	<140/90	Thiazide, â-blocker (age <60y), ACEI (nonblack), or ARB
	General ≥80 y	<150/90	
	Diabetes	<130/80	ACEI or ARB with additional CVD risk ACEI, ARB, thiazide, or DHPCCB without additional CVD risk
	CKD	<140/90	ACEI or ARB
ADA 2013	Diabetes	<140/80	ACEI or ARB
KDIGO 2012	CKD no proteinuria	≤140/90	ACEI or ARB
	CKD + proteinuria	≤130/80	
NICE 2011	General <80 y	<140/90	<55 y: ACEI or ARB
	General ≥80 y	<150/90	≥55 y or black: CCB
ISHIB 2010	Black, lower risk	<135/85	Diuretic or CCB
	Target organ damage or CVD risk	<130/80	

Abbreviations: ADA, American Diabetes Association; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; CHEP, Canadian Hypertension Education Program; CKD, chronic kidney disease; CVD, cardiovascular disease; DHPCCB, dihydropyridine calcium channel blocker; ESC, European Society of Cardiology; ESH, European Society of Hypertension; ISHIB, International Society for Hypertension in Blacks; JNC, Joint National Committee; KDIGO, Kidney Disease: Improving Global Outcome; NICE, National Institute for Health and Clinical Excellence.

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Cardiology News

Long-term Air Pollution Ups Risk of CVD: European Study

A large meta-analysis of 11 cohorts in five European countries suggests that long-term exposure to air pollution is a cardiovascular risk factor. According to the recent report on the Global Burden of Disease, particulate air pollution is estimated to cause 3.1 million deaths each year worldwide, but the effect of air pollution on the incidence of acute MI and unstable angina was unclear. ESCAPE included 100 166 participants who were enrolled in cohorts in Finland, Sweden, Denmark, Germany, and Italy from 1997 to 2007 and had no previous coronary events at baseline. During a mean follow-up of 11.5 years, 5157 participants had an incident of acute coronary event. In statistical models that adjusted for age, sex, year of enrollment, smoking, and socioeconomic factors, the researchers found that a 5-μg/m^3 increase in annual exposure to fine ($PM_{2.5}$) particulate matter was associated with a 13% increased risk of coronary events, and a 10-μg/m^3 increase in annual exposure to coarse (PM_{10}) particulate matter was associated with a 12% increased risk of coronary events.

Medscape. Jan 27, 2014.

Multistage CVD Screening Could Eliminate LDL Lab Tests

A screening approach that selectively uses laboratory-based cholesterol testing to assess cardiovascular risk is able to identify patients at risk for cardiovascular disease to a similar extent as a widely used risk model. The multistage primary cardiovascular disease screening approach, in which only patients first identified as at intermediate risk of cardiovascular events are sent to the laboratory to measure cholesterol levels, performed as well as the Framingham Risk Score (FRS), which utilizes laboratory testing in all patients to assess cholesterol levels, in terms of discriminating risk of cardiovascular disease. The researchers used a multistage screening strategy that calculated an individual's risk of fatal or nonfatal cardiovascular outcomes using multiple non-laboratory-based risk markers. These included age, sex, smoking status, history of diabetes, blood-pressure treatment, systolic blood pressure, and body-mass index (BMI). From here, patients were classified as high, intermediate, or low risk for cardiovascular disease. In this multistage-screening approach, those at the polar ends of the risk spectrum would require no further testing and would be assigned treatment with statins (high-risk patients) or monitored without treatment (low-risk patients). Only individuals in the intermediate-risk category would be sent for laboratory tests to assess cholesterol levels.

January 14, 2014 in Circulation: Cardiovascular Quality and Outcomes

Anatomy Bests Ischemia for Risk Prediction: COURAGE

Coronary anatomy, and not ischemic disease burden, significantly predicts the risk of death, MI, and non-ST-elevation acute coronary syndrome (NSTE-ACS) in patients with stable ischemic heart disease. Despite being a better predictor of clinical outcomes, the anatomic burden of coronary artery disease assessed by angiography did not identify patients who would benefit from an invasive revascularization strategy over optimal medical therapy. These are the findings from a new post hoc analysis of the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial. The only predictors of clinical events were left ventricular ejection fraction (LVEF) and anatomic burden of disease.

January , 2014 the Journal of the American College of Cardiology

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Editorial Note

Dear Doctor,

We are happy to present the 32nd issue of "Insight Heart" is a small endeavor to provide you compiled & updat information on cardiovascular diseases and management. This issue is focused on " ***The JNC report on hypertension***". We will appreciate yo thoughtful comments.

Thanks and regards.

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