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Background

Epidemiology
Cost Burden
High Blood Pressure Prevalence Adults ≥ 20 Years Stratified by Age/Sex

Dariush Mozaffarian et al. Circulation. 2015;131:e29-e322
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Age-Adjusted Trends for High Blood Pressure Prevalence Adults ≥ 20 years Stratified by Age/Race/Ethnicity/Sex

High Blood Pressure Stratified by Age
Awareness/Treatment/Control of Blood Pressure

Dariush Mozaffarian et al. Circulation. 2015;131:e29-e322
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Percentage Breakdown of Deaths Attributable to Cardiovascular Disease
United States 2011
Cardiovascular Disease (CVD) Deaths Versus Cancer Deaths by Age
United States 2011
Direct and Indirect Costs of Cardiovascular Disease (CVD) and Stroke (in billions of dollars)
United States 2011

- Heart disease: 215.6 billions of dollars
- Hypertension: 46.4 billions of dollars
- Stroke: 33.6 billions of dollars
- Other CVD: 24.6 billions of dollars
The 23 Leading Diagnoses for Direct Health Expenditures (in billions of dollars)
United States 2011

- Heart conditions: 116.3 billion dollars
- Cancer: 88.7 billion dollars
- Trauma-related disorders: 81.8 billion dollars
- Mental disorders: 77.6 billion dollars
- Osteoarthritis: 76.2 billion dollars
- COPD, asthma: 75.2 billion dollars
- Diabetes mellitus: 55.2 billion dollars
- Hypertension: 42.7 billion dollars
- Normal live births: 39.4 billion dollars
- Hyperlipidemia: 38.9 billion dollars
- Back problems: 38.1 billion dollars
- Systemic lupus and connective disorders: 36.2 billion dollars
- Kidney disease: 32.0 billion dollars
- Other central nervous system disorders: 28.6 billion dollars
- Infectious diseases: 26.9 billion dollars
- Residual codes: 24.2 billion dollars
- Skin disorders: 23.9 billion dollars
- Disorders of the upper GI: 23.7 billion dollars
- Gallbladder, pancreatic, and liver disease: 23.1 billion dollars
- Other circulatory conditions: 19.0 billion dollars
- Hereditary & other nervous system disorders: 16.9 billion dollars
- Other eye disorders: 17.7 billion dollars
- Stroke: 17.5 billion dollars
Projected Total Costs of Cardiovascular Disease (CVD), 2015 to 2030 (in billions of dollars)
United States 2012

Dariush Mozaffarian et al. Circulation. 2015;131:e29-e322
Copyright © American Heart Association, Inc. All rights reserved
Age-Specific Prevalence of Hypertension in US Adults
NHANES 1999-2004

NHANES Population by Age

Prevalence 1999-2004 (%)
Pathophysiology

Essential Hypertension
Secondary Hypertension
Causes of Hypertension

Secondary Hypertension
- Develops through the manifestation of other medical problems
- Occurs in about 5% of the population

Essential, Primary or Idiopathic Hypertension
- No definitive causes
- Multiple risk factors
- Present in 95% of the population

Hormones
- Renal problems
- Genetic
- Vascular problems
- Alcohol
- Stress
- Obesity
- Endocrine problems
- Over the counter Medications

http://papahealth.com
Schematic of the Pathophysiology of Hypertension
Conceptual Framework for Cardiovascular Adaptations to Arterial Stiffening that Occur with Aging

- Arterial stiffening
  - Arterial SBP and pulse pressure
  - Arterial DBP
  - CBF
  - Myocardial ischemia
  - LV wall thickness
  - LA size
  - Late LV filling
  - Preserved end-diastolic LV volume
- Pulse wave velocity
  - Earlier reflected pressure waves add to late systolic pressure; earlier reflected flow waves subtract from forward blood flow
- Aortic root size
  - Aortic wall thickness
- Aortic impedance and LV afterload (wall tension)
- Prolonged myocardial contraction
  - Early diastolic LV filling rate
- Partial normalization of LV wall tension
- Preserved end-systolic LV volume and EF


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Pathophysiology of hypertension

INAPPROPRIATELY HIGH SYMPATHETIC OUTFLOW

Increased large arterial stiffness

Abnormal venoconstriction and high venous return

Inappropriately high cardiac output

INAPPROPRIATELY HIGH RENIN RELEASE

Increased systemic resistance

ABNORMAL RENAL SALT/WATER HANDLING

Courtesy of JL Izzo Jr, MD.
CV and renal continuum: RAAS as a mediator of pathophysiology

Adapted from Dzau V et al. Circulation. 2006;114:2850-70.

RAAS

Risk factors

Early tissue dysfunction

Oxidative & mechanical stress inflammation

Vasoconstriction/Na/H₂O retention (High BP)

Atherothrombosis & progressive CVD

Tissue injury (MI, stroke, renal insufficiency, PAD)

Pathological remodeling

Target organ damage

End-organ failure (CHF, ESRD)

Death

ESRD = end-stage renal disease

Adapted from Dzau V et al. Circulation. 2006;114:2850-70.
RAAS overview: Key targets

Adapted from Staessen JA et al. Lancet. 2006;368:1449-56.
Treatment
Lifestyle Modification
Blood Pressure >140/90 in Adults Aged >18 years
(For age >80 years, pressure >150/90 or >140/90 if high risk [diabetes, kidney disease])

Start Lifestyle Changes
(Lose weight, reduce dietary salt and alcohol, stop smoking)

Drug Therapy
(Consider a delay in uncomplicated Stage 1 patients)*

Stage 1
140-159/90-99

Black Patients
- CCB or Thiazide
  - If Needed, Add ...
ACE-i or ARB
OR combine CCB+Thiazide
  - If Needed ...

ACE-i or ARB
  - If Needed ...

non-Black Patients
- Age <60 Years
  - CCB or Thiazide
  - If Needed ...
  - ACE-i or ARB

Age ≥60 Years
- CCB or Thiazide
  - If Needed ...
  - ACE-i or ARB

Stage 2
>160/100

All Patients
- Start with 2 Drugs
  - CCB or Thiazide
  - ACE-i or ARB

Special Cases
- Kidney disease
- Diabetes
- Coronary disease
- Stroke history
- Heart failure
  [see table of recommended drugs for these conditions]

Special Cases

* In stage 1 patients without other cardiovascular risk factors or abnormal findings, some months of regularly monitored lifestyle management without drugs can be considered.
Exercise and maintenance of a healthy weight

Lifestyle changes and/or medication may reduce high blood pressure to healthy levels:

Medications such as diuretics, beta-blockers, potassium replacements, calcium channel blockers and ACE inhibitors

A healthy, low sodium (salt) diet rich in natural sources of potassium, calcium, and fiber
RAAS Blockade With ARBs Can Be Considered a Foundation of Antihypertensive Therapy

<table>
<thead>
<tr>
<th>CCB</th>
<th>Alpha Blockers</th>
<th>Beta Blockers</th>
<th>Diuretics</th>
<th>Other</th>
</tr>
</thead>
</table>

ARB Foundation

ARB=angiotensin receptor blocker; BP=blood pressure; CCB=calcium channel blocker; RAAS=renin-angiotensin-aldosterone system.

BP Control Usually Requires Combination Therapy

Most patients require ≥2 antihypertensives to reach BP goal

Trial/SBP Achieved

- AASK (128 mmHg)
- MDRD (132 mmHg)
- ABCD (132 mmHg)
- INVEST (133 mmHg)
- ASCOT (138 mmHg)
- HOT (138 mmHg)
- IDNT (138 mmHg)
- ALLHAT (138 mmHg)
- RENAAL (141 mmHg)
- UKPDS (144 mmHg)

BP=blood pressure; SBP=systolic blood pressure.

Special Populations

Treatment of Hypertension in Patients With Coronary Artery Disease
# Summary of BP Goals

<table>
<thead>
<tr>
<th>BP Goal, mm Hg</th>
<th>Condition</th>
<th>Class/Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;140/90</td>
<td>CAD</td>
<td>IIa/B</td>
</tr>
<tr>
<td></td>
<td>ACS</td>
<td>IIa/C</td>
</tr>
<tr>
<td></td>
<td>HF</td>
<td>IIa/B</td>
</tr>
<tr>
<td></td>
<td>CAD</td>
<td>IIb/B</td>
</tr>
<tr>
<td>&lt;130/80</td>
<td>Post-myocardial infarction, stroke or TIA, carotid artery disease, PAD, AAA</td>
<td>IIb/B</td>
</tr>
</tbody>
</table>

Abbreviations:
- **AAA**: Abdominal Aortic Aneurysm
- **ACS**: Acute Coronary Syndrome
- **CAD**: Coronary Artery Disease
- **HF**: Heart Failure
- **PAD**: Peripheral Arterial Disease
- **TIA**: Transient Ischemic Attack

Reference: Circulation 2015;131:e435-e470
Pharmacological Treatment of Hypertension in the Management of Ischemic Heart Disease

<table>
<thead>
<tr>
<th></th>
<th>ACEI or ARB</th>
<th>Diuretic</th>
<th>β-Blocker</th>
<th>Non-DHP CCB</th>
<th>DHP CCB</th>
<th>Nitrates</th>
<th>Aldosterone Antagonist</th>
<th>Hydralazine/Isosorbide Dinitrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable Angina</td>
<td>1*</td>
<td>1†</td>
<td>1</td>
<td>2‡</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>ACS</td>
<td>1*</td>
<td>1†</td>
<td>1§</td>
<td>2‡</td>
<td>2</td>
<td>2</td>
<td>2‖</td>
<td></td>
</tr>
<tr>
<td>HF</td>
<td>1</td>
<td>1†</td>
<td>1‖</td>
<td>2</td>
<td>1‖</td>
<td>2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ACEI indicates angiotensin-converting enzyme inhibitor; ACS, acute coronary syndrome; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; DHP, dihydropyridine; HF, heart failure; 1, drug of choice; and 2, “add-on,” alternative drug, or special indications.

* Especially if prior myocardial infarction, left ventricular systolic dysfunction, diabetes mellitus, or proteinuric chronic kidney disease is present.

† Chlorthalidone is preferred. Loop diuretic should be used in the presence of HF (New York Heart Association class III or IV) or chronic kidney disease with glomerular filtration rate <30 mL·min⁻¹·1.73 m⁻². Caution should be exercised in HF with preserved ejection fraction.

‡ If β-blocker is contraindicated, a non-DHP CCB can be substituted, but not if left ventricular dysfunction or HF is present. Caution should be exercised if combining a non-DHP CCB with a β-blocker.
The <140/90-mm Hg BP target is reasonable for the secondary prevention of cardiovascular events in patients with hypertension and CAD (Class IIa; Level of Evidence B).

A lower target BP (<130/80 mm Hg) may be appropriate in some individuals with CAD, previous MI, stroke or transient ischemic attack, or CAD risk equivalents (carotid artery disease, PAD, abdominal aortic aneurysm) (Class IIb; Level of Evidence B).

In patients with an elevated DBP and CAD with evidence of myocardial ischemia, the BP should be lowered slowly, and caution is advised in inducing decreases in DBP to <60 mm Hg in any patient with diabetes mellitus or who is >60 years of age. In older hypertensive individuals with wide pulse pressures, lowering SBP may cause very low DBP values (<60 mm Hg). This should alert the clinician to assess carefully any untoward signs or symptoms, especially those resulting from myocardial ischemia (Class IIa; Level of Evidence C).
Special Populations

Treatment of Hypertension in Patients With Heart Failure
### Recommendation for Prevention

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B-R</td>
<td>In patients at increased risk, stage A HF, the optimal blood pressure in those with hypertension should be less than 130/80 mm Hg.(^{189-193})</td>
<td><strong>NEW:</strong> Recommendation reflects new RCT data.</td>
</tr>
</tbody>
</table>

See Online Data Supplements E and F.

A large RCT demonstrated that in those with increased cardiovascular risk (defined as age >75 years, established vascular disease, chronic renal disease, or a Framingham Risk Score >15%), control of blood pressure to a goal systolic pressure of <120 mm Hg, as determined by blood pressure assessment as per research protocol, was associated with a significant reduction in the incidence of HE\(^{193}\) and an overall decrease in cardiovascular death. Blood pressure measurements as generally taken in the office setting are typically 5 to 10 mm Hg higher than research measurements; thus, the goal of <130/80 mm Hg is an approximation of the target blood pressure in conventional practice. **Targeting a significant reduction in systolic blood pressure in those at increased risk for cardiovascular disease is a novel strategy to prevent HF.**
# Recommendation for Hypertension in Stage HFrEF

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendation</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>C-EO</td>
<td>Patients with HFrEF and hypertension should be prescribed GDMT titrated to attain systolic blood pressure less than 130 mm Hg.¹⁹¹</td>
<td>NEW: Recommendation has been adapted from recent clinical trial data but not specifically tested per se in a randomized trial of patients with HF.</td>
</tr>
</tbody>
</table>

Clinical trials evaluating goal blood pressure reduction and optimal blood pressure-lowering agents in the setting of HFrEF and concomitant hypertension have not been done. However, it is apparent that in those patients at higher risk, blood pressure lowering is associated with fewer adverse cardiovascular events. GDMT for HFrEF with agents known to lower blood pressure should consider a goal blood pressure reduction consistent with a threshold now associated with improved clinical outcomes but not yet proven by RCTs in a population with HF.
Recommendation for Hypertension in Stage HFpEF

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendation</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>C-LD</td>
<td><strong>Patients with HFpEF and persistent hypertension after management of volume overload should be prescribed GDMT titrated to attain systolic blood pressure less than 130 mm Hg.</strong>&lt;sup&gt;9,167,169,170,195-199&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>

NEW: New target goal blood pressure based on updated interpretation of recent clinical trial data.

The use of nitrates in the setting of HFpEF is associated with a signal of harm and, in most situations, should be avoided. For many common antihypertensive agents, including alpha blockers, beta blockers, and calcium channel blockers, there are limited data to guide the choice of antihypertensive therapy in the setting of HFpEF.<sup>172</sup> Nevertheless, RAAS inhibition with ACE inhibitor, ARB (especially mineralocorticoid receptor antagonists), and possibly ARNI would represent the preferred choice. A shared decision-making discussion with the patient influenced by physician judgment should drive the ultimate choice of antihypertensive agents.
Conclusion

- Evidence based data concludes the use of antihypertensive treatment with indapamide (sustained release), with or without perindopril, is beneficial for hypertensive persons ≤ 80 years of age.