Hypertension
Clinical Overview

Brian Halstater, MD
Sea Pines Conference, July 2017

Goals and Objectives

By the end of the session, participants should be able to:

• Recall current blood pressure goals
• Interpret blood pressure readings based on clinical presentation
• Choose anti-hypertensive medication(s) based on most current guidelines
Overview

• Goals and Objectives
• HTN review
• Guidelines
  – USPSTF
  – JNC 7
  – JNC 8
  – 3 additional studies
• Conclusion
• Questions

HTN Review

HTN is a major risk factor for:
• Heart Disease (CAD)
• Stroke (CVA)
• Heart Failure (CHF)
• Renal Failure (RF)

https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_bloodpressure.htm
HTN Review

Americans:

- ~ 1 in 3 (75 M) have HTN
- ~ 1 in 3 have pre-HTN
- 54% with HTN have BP under control
- In 2014 ~ 1,100 deaths / day → 410,000 / yr
- Costs → $48.6 B / yr

https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_bloodpressure.htm

HTN in US
U.S. Preventive Services Task Force

Final Recommendation Statement
High Blood Pressure in Adults: Screening

Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or of the U.S. Department of Health and Human Services.

Recommendation Summary

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
<th>Grade (What’s This?)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults aged 18 years or older</td>
<td>The USPSTF recommends screening for high blood pressure in adults aged 18 years or older. The USPSTF recommends obtaining measurements outside of the clinical setting for diagnostic confirmation before starting treatment (see the Clinical Considerations section).</td>
<td>A</td>
</tr>
</tbody>
</table>

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USPSTF for BP Readings

Measurements *outside the clinical setting* before starting treatment

- **Office** – 2 seated BP at least 5 min apart; able to monitor over time
- **But** – **15-30%** may have lower BP at home than in office
- **Ambulatory cuffs** – measure every 20-30 min of normal life

USPSTF – HTN

- Screen either annually or every 3-5 years
  - 3-5 years for:
    - Ages 18-39 with no RF
    - BP under 130/80
  - Annually for:
    - 40 and over
    - Any age with RF
      - High normal BP (130-139/85-89)
      - BMI over 25
      - African American

Risk Factors for CAD

- HTN
- Tobacco use
- Obesity
- Physical inactivity
- Dyslipidemia
- Diabetes
- Microalbuminuria
- Age
  - > 55 men
  - > 65 women
- FHx of premature CVD
Consider Secondary Causes

- Sleep Apnea
- Drug-induced
- Renal disease
- Primary Aldosteronism
- Chronic Steroid Use/ Cushing’s

Note - In the absence of clinical signs to suggest possible secondary hypertension in adults, indications for further evaluation include resistant hypertension and early, late, or rapid onset of high blood pressure. AAFP review article on HTN
http://www.aafp.org/afp/2010/1215/p1471.html

Clues for Secondary HTN

- Aortic Coarctation
  - Arm:Leg SBP difference > 20
  - Delayed/ absent femoral pulses
  - Murmur
- Renal Artery Stenosis
  - ↑ Cr of 0.5-1 mg/ dL after ACE-I or ARB initiation
  - Renal bruit

http://www.aafp.org/afp/2010/1215/p1471.html
Clues for Secondary HTN

• Thyroid disorder
  – Bradycardia or tachycardia
  – Cold or heat intolerance
  – GI motility (constipation/ diarrhea)
  – Menstrual irregularity

• Sleep Apnea
  – Apneic during sleep
  – Daytime somnolence
  – Loud snoring
  – Neck diameter (>17” men; >15” in women)

http://www.aafp.org/afp/2010/1215/p1471.html
http://emedicine.medscape.com/article/295807-overview

Clues for Secondary HTN

• Aldosteronism
  – ↓ K

• Pheochromocytoma
  – Flushing
  – Headaches
  – Labile HTN
  – Orthostatic Hypotension
  – Sweating
  – Syncope

http://www.aafp.org/afp/2010/1215/p1471.html
Clues for Secondary HTN

• Cushing's
  – Buffalo hump
  – Central obesity
  – Moon facies
  – Striae (violet)

http://www.aafp.org/afp/2010/1215/p1471.html

Medications - Causes

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>COMMON EXAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrogen</td>
<td>Oral contraceptives</td>
</tr>
<tr>
<td>Herbal</td>
<td>Ephedra, ginseng, ma huang</td>
</tr>
<tr>
<td>Illicit</td>
<td>Amphetamines, cocaine</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory</td>
<td>Cyclooxygenase-2 inhibitors, ibuprofen, naproxen (Naprosyn)</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>Buspirone (Buspar), carbamazepine (Tegretol), clozapine (Clozaril), fluoxetine (Prozac), lithium, tricyclic antidepressants</td>
</tr>
<tr>
<td>Steroid</td>
<td>Methylprednisolone (Depo-Medrol), prednisone</td>
</tr>
<tr>
<td>Sympathomimetic</td>
<td>Decongestants, diet pills</td>
</tr>
</tbody>
</table>

http://www.aafp.org/afp/2010/1215/p1471.html
Secondary Causes by Age

• Birth – 12y (70-85%) and 12-18y (10-15%)
  – Renal disease
  – Aortic Coartation

• 19-39y (5%)
  – Thyroid
  – Fibromuscular dysplasia (RAS)
  – Renal disease

http://www.aafp.org/afp/2010/1215/p1471.html

Secondary Causes by Age

• 40-64y (8-12%)
  – Aldosteronism
  – Thyroid disease
  – OSA
  – Cushing’s
  – Pheochromocytoma

• 65y and older (17%)
  – RAS (atherosclerotic)
  – RF
  – Thyroid disease (hypo)

http://www.aafp.org/afp/2010/1215/p1471.html
End Organ Damage

- Heart
  - LVH
  - MI/ Angina
  - CHF
- Brain
  - CVA
  - Stroke
- Renal
  - Chronic Renal Disease
- Vascular
  - Peripheral Artery Disease
- Ophthalmologic
  - Retinopathy

HTN – Physical Exam

- Vitals
  - Weight, Height, BMI
- General - Habitus
- Eyes – fundi
- Neck – Bruits, thyroid, neck size
- CV – PMI, Murmur, rhythm
- Pulm – wheezing, rales
- Ab – Masses, bruits
- Ext – Pulses, bruits, perfusion, edema
- Neuro – focality
Testing

• EKG – LVH, BBB, prior MI
• UA – protein, casts
• Glucose – DM, IGT
• Hct - Anemia
• K, Ca, GFR – aldosterone, hyperparathyroidism, renal insufficiency

Cardiovascular Risk Assessment

• Many tools available
  – [www.cvriskcalculator.com](http://www.cvriskcalculator.com) incorporates the JNC 8 and USPSTF aspirin guidelines
  • Not if prior MI/ CVA
  • Not validated if under 40
  • Provides guidelines for what to do for lipids/ aspirin
  – 10 year calculation for MI, CV death, CVA
Cardiovascular Risk Assessment

• Examplar:


• Tells us (in addition to 10 year risk):
  – ASA – yea/ nay
  – Statin – Yea (and what level)/ nay
  – BP tx – at goal/ not at goal
Heart Risk Calculator – 1/2

On the basis of your age and calculated risk for heart disease or stroke over 15%, the AHA/ACC guidelines suggest you start taking aspirin 3 mg every day if you are at increased risk for bleeding and are willing to take it every day for at least 10 years.

Based on your age and race, your blood pressure is poorly controlled, and you should include lifestyle interventions and consider starting a thiazide diuretic or calcium-channel blocker.

Demography

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>55</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
</tr>
<tr>
<td>Race</td>
<td>African-American</td>
</tr>
</tbody>
</table>

Cholesterol

<table>
<thead>
<tr>
<th>Value</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>200</td>
</tr>
<tr>
<td>HDL</td>
<td>65</td>
</tr>
</tbody>
</table>

Blood pressure

<table>
<thead>
<tr>
<th>Value</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic</td>
<td>145</td>
</tr>
<tr>
<td>Diastolic</td>
<td>88</td>
</tr>
</tbody>
</table>

Risk factors

<table>
<thead>
<tr>
<th>Factors</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>no</td>
</tr>
<tr>
<td>Smoking</td>
<td>yes</td>
</tr>
</tbody>
</table>

On medication: no

http://www.cvriskcalculator.com/

Heart Risk Calculator – 2/2

Notes and further reading

- Moderate intensity statins may be atorvastatin 10 mg, pravastatin 40 mg, or simvastatin 20-40 mg. High intensity statins may be atorvastatin 40 mg-80 mg.
- AHA/ACC guidelines stress the importance of multiple modifications to lower cardiovascular disease risk in all patients. This includes eating a Healthy Diet, regular aerobic exercise, maintenance of desirable body weight and avoidance of tobacco products.
- Nephrologists and patients must engage in a discussion which considers addressing risk factors such as smoking and optimal weight, the potential for ASCVD risk reduction benefits, adverse medication effects, drug-drug interactions, and patient preferences for treatment.
- Additional factors may be considered to further treatment decisions making. These factors may include primary LDL-C greater than 190 mg/dL, or other evidence of ASCVD, family history of premature ASCVD with onset less than 55 years of age in a first-degree male relative or less than 65 years of age in a first-degree female relative, high-sensitivity C-reactive protein greater than 2 mg/L, CAC score greater than 500 Agatston units or greater than 75 percentile for age, sex, and ethnicity, ankle-brachial index score less than 0.9, or estimated lifetime risk of ASCVD.

http://www.cvriskcalculator.com/
### JNC 7 – Brief Review (1 slide)

<table>
<thead>
<tr>
<th>BP Classification</th>
<th>SBP</th>
<th>DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt; 120</td>
<td>AND &lt; 80</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120-139</td>
<td>or 80-89</td>
</tr>
<tr>
<td>Stage 1 HTN</td>
<td>140-159</td>
<td>or 90-99</td>
</tr>
<tr>
<td>Stage 2 HTN</td>
<td>&gt; 159</td>
<td>or &gt; 99</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>BP Classification - Treatment</th>
<th>Lifestyle modifications</th>
<th>Drugs – no compelling reason</th>
<th>Drugs – compelling reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Encourage</td>
<td>NI</td>
<td>NI</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>Yes</td>
<td>NI</td>
<td>Yes (CKD or DM goal is under 130/80)</td>
</tr>
<tr>
<td>Stage 1 HTN</td>
<td>Yes</td>
<td>Thiazide; consider other or combo</td>
<td>Yes for indication</td>
</tr>
<tr>
<td>Stage 2 HTN</td>
<td>Yes</td>
<td>2 drug combo</td>
<td>2 drug combo, with indication as well</td>
</tr>
</tbody>
</table>

### Lifestyle Modifications

- Lose weight
- Increase exercise
- Limit EtOH
- Smoking cessation
- Decrease salt (Na) intake
- Decrease saturated fat intake
Meta-Analyses of Lifestyle Interventions

https://www.ncbi.nlm.nih.gov/books/NBK83262/ Figure 4

JNC 8 – Newest Guidelines

Simplify after JNC 7

• There are 9 recommendations addressing 3 outcome driven clinical questions
• Race based
• Age based
• Disease based
• Guidelines – as always, clinical judgment is required

JNC 8 – Newest Guidelines

Panel of Experts, weighted evidence using SOR scale
A - Strong Recommendation
B - Moderate Recommendation
C - Weak Recommendation
D - Recommendation Against
E - Expert Opinion
N - No Recommendation For / Against

JNC 8 – Focus on 3 Clinical Questions

Q1 – In adults with hypertension, does initiating antihypertensive pharmacologic therapy at specific BP thresholds improve health outcomes?
JNC 8 – Focus on 3 Clinical Questions

Q2 – In adults with hypertension, does treatment with antihypertensive pharmacologic therapy to a specified BP goal lead to improvements in health outcomes?

JNC 8 – Focus on 3 Clinical Questions

Q3 – In adults with hypertension, do various antihypertensive drugs or drug classes differ in comparative benefits and harms on specific health outcomes?
JNC 8 – Recommendations

1–5 → address the first two questions
• threshold for BP treatment
• goal of BP treatment

6–8 → address the third question
• selection of antihypertensive drugs

9 → summary of strategies
• based on expert opinion for starting and adding antihypertensive drugs

JNC 8 – Recommendation 1

General Population and age over 59 y

• Start BP medication at:
  – SBP > 149 – or –
  – DBP > 90

• Treat to goal of:
  – SBP < 150 – and –
  – DBP < 90

• Grade A – strong recommendation
JNC 8 – Corollary Recommendation 1

*General Population* and age *over 59 y*

- Drug treatment for HTN achieves better than expected results (such as SBP <140)
- Well tolerated
- No effect on health/ QOL
→ No need to adjust therapy

Grade E – Expert opinion

JNC 8 – Recommendation 2

*General Population* and *age < 60*

- Start BP medication at:
  - DBP > 89
- Treat to goal of:
  - DBP < 90

Grade A (ages 30-59) and E (18-29)
JNC 8 – Recommendation 3

*General Population* and age < 60
• Start BP medication at:
  – SBP > 139
• Treat to goal of:
  – SBP < 140

Grade E

JNC 8 – Recommendation 4

Population with **CKD** and *age > 17*
• Start BP medication
  – SBP > 139 – or –
  – DBP > 89
• Treat to goal of:
  – SBP < 140 – and –
  – DBP < 90

Grade E
JNC 8 – Recommendation 5

Population with Diabetes and age > 17

• Start BP medication
  – SBP > 139 – or –
  – DBP > 89

• Treat to goal of:
  – SBP < 140 – and –
  – DBP < 90

Grade E

JNC 8 – Recommendation 6

General non-black population (including those with DM)

• Initial treatment should include:
  – Thiazide type diuretic (TZ)
  – Calcium Channel Blocker (CCB)
  – Angiotensin-Converting Enzyme Inhibitor (ACEI)
  – Angiotensin Receptor Blocker (ARB)

Grade B – Moderate Recommendation
JNC 8 – Recommendation 7

*General black population* (including those with DM)

- Initial treatment should include:
  - TZ
  - CCB

Grade B (general black population) and C Weak Recommendation (black patients with DM)

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JNC 8 – Recommendation 8

Population over age 17 with *CKD* – all patients *regardless of race or presence/ absence of DM*

- Initial or add on treatment should include an ACEI or ARB (to improve renal outcomes)

Grade B
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)

Reframe

The main objective of hypertension treatment is to attain and maintain goal BP. Treat for 1 month, if not at goal, adjust by one of two choices:

- Increase the dose of the initial drug
- Add a second drug from one of the classes in recommendation 6 (thiazide-type diuretic, CCB, ACEI, or ARB)

Continue to follow BP and modify until BP is at goal.
If not at goal with 2 drugs, add a third (and titrate) drug from rec 6
Do not use an ACEI and an ARB together
If goal BP cannot be reached using only the drugs in rec 6 (contraindication or the need to use more than 3 drugs) 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 complicated patients
Graphic on JNC 8 Goals 1/2

http://jamanetwork.com/data/Journals/JAMA/929741/jsc130010f1.png

Graphic on JNC 8 Goals 2/2

http://jamanetwork.com/data/Journals/JAMA/929741/jsc130010f1.png
SPRINT Study – After JNC 8

• Over 9000 patients, over 50y with SBP and elevated CVD risk, no DM
• Randomized to SBP of either < 120 or < 140
• Primary outcome, composite:
  – MI or other acute coronary syndromes
  – CVA
  – CHF
  – CV Death

SPRINT Study – Results

• Stopped early
  – Lower goal did much better than standard goal (under 120 better than 140)
  – 25% lower relative risk of primary outcome
  – Higher rate of adverse events however in lower goal group
  – Lower goal group needed 1 additional medication to reach goal
ACCORD BP Trial

Action to Control Cardiovascular Risk in Diabetes Blood Pressure Trial

- Looked at JNC 7 recommendation for lower BP is better for patients with DM
- Looked at goal BP below 120 SBP for CV events with high risk patients with DM
- Looking at BP lowering as a treatment strategy

ACCORD BP Trial

- 10,251 high risk patients with DM II
- Subset of 4,733 (47.7% women)
  - Intensive vs standard BP control
- DM II with GlyHg of 7.5 or more
- 40 y + with CVD or 55 y + with CV risk factors
ACCORD BP Trial

• Non-blinded
• Random assignment to 1 of 2 groups
  – Target SBP <120 (2,362)
  – Target SBP <140 (2,371)
• Clinical practice BP lowering was used
• Outcomes
  – $1^0$ - major CV event
  – $2^0$ – several

Groups – BP differences
**ACCORD BP Trial**

Only outcome improved with intensive therapy is fatal and non-fatal stroke

**Adverse Events**

More adverse events in the intensive therapy (SBP goal < 120) group when compared with the standard (SBP goal < 140) group
ACCORD BP Trial
Kaplan-Meier Graphs

Overall – SBP goal of < 120 show no reduction of major CV events compared with SBP goal < 140 for patients with DM at high risk for CV disease

BP Goal?

http://siegofitness.blogspot.com/2012/03/muscle-confusion-i-am-so-confused.html
HOT OFF THE PRESSES

Optimal Systolic Blood Pressure Target After SPRINT: Insights from a Network Meta-Analysis of Randomized Trials

Gripit Petchkouris, MD, MHA • Eric Topolski, MD • Jennifer Clausen, MD • Arthur Schwartzson, MD • Howard Winkler, MD
Division of Cardiology, New York University School of Medicine, New York, NY
Division of Cardiology, University of Rochester, Rochester, NY
Division of Cardiology, New York University School of Medicine, New York, NY

BACKGROUND: The optimal systolic blood pressure (SBP) target has been under debate. The recent SPRINT trial demonstrated significant benefits of SBP targets of 120 mm Hg or lower versus standard care. The current meta-analysis was performed to compare results among different SBP targets (120, 130, 140, 150, and 160 mm Hg) and to determine the optimal SBP target. This analysis included trials with a total of 68,780 patients in 9 studies, 6 of which were randomized trials comparing BP targets with a SBP target of 120 mm Hg or lower versus standard care. There was a significant decrease in total mortality with SBP targets of 120 mm Hg or lower compared with standard care (P = 0.01). In addition, the rate of CVD death and HF was lower with SBP targets of 120 mm Hg or lower compared with standard care (P = 0.04). There was a reduction in CVD death and HF with SBP targets of 120 mm Hg or lower compared with standard care (P = 0.04). There was a significant decrease in CVD death and HF with SBP targets of 120 mm Hg or lower compared with standard care (P = 0.04).

METHODS: A network meta-analysis was performed using a Bayesian network meta-analysis framework. The primary outcome was all-cause mortality, and the secondary outcomes were CVD death, HF, and adverse effects.

RESULTS: The network meta-analysis showed that SBP targets of 120 mm Hg or lower were associated with lower all-cause mortality, CVD death, and HF compared with standard care. The results were consistent across all prespecified subgroups.

CONCLUSION: The results of this network meta-analysis support the recent findings of SPRINT and provide additional evidence for the safety and efficacy of SBP targets of 120 mm Hg or lower. Further research is needed to evaluate the long-term benefits and risks of SBP targets of 120 mm Hg or lower.

http://www.amjmed.com/article/S0002-9343(17)30035-9/pdf

Meta-Analysis

• Randomized Clinical Trials
  – SBP targets (5 targets)
    • Under 160
    • Under 150
    • Under 140
    • Under 130
    • Under 120
  – CVA, MI, death (CV death), HF, adverse effects
Meta-Analysis

- 17 Trials
- 55,163 patients
- Mean of 3.7 years of follow up
- 204,103 patient – years of follow up
- Used SBP goal of < 160 as reference group

Key:
- < 120
- < 130
- < 140
- < 150
- < 160

X-axis → further from 0 is increased safety
Y-axis → Further from 0 is increased efficacy
Summary

• Treat patients over 60 with BP over 150/90 to under 150/90
• Treat patients under 60 with BP over 140/90 to under 140/90
• Any of 4 major classes is OK (TZ, CCB, ACEI or ARB), should include TZ
• Probably will need 2 medications

Summary

• If DM or CKD treat if over 140/90
  – If DM – use ACEI or ARB (regardless of race)
• If black – use TZ or CCB
• Titrate by increasing dose or adding 2nd agent to get to goal
• Encourage lifestyle changes
• Consider goal of under 130 systolic
Resources/ Additional Reading

JNC 7

JNC 8
- http://jamanetwork.com/journals/jama/fullarticle/1791497
- http://jamanetwork.com/journals/jama/fullarticle/1820434 (patient information)

JNC 8 Editorials
- http://jamanetwork.com/journals/jama/fullarticle/1791421
- http://jamanetwork.com/journals/jama/fullarticle/1791422
- http://jamanetwork.com/journals/jama/fullarticle/1791423
- http://jamanetwork.com/journals/jama/fullarticle/1887750 (letters to the editor and response)

CDC High Blood Pressure Fact Sheet
- https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_bloodpressure.htm

United States Preventive Services Task Force Final Recommendation Statement on High Blood Pressure in Adults: Screening

Secondary Hypertension
- http://www.aafp.org/afp/2010/1215/p1471.html - Overview from AAFP

Salt Restriction
- http://jamanetwork.com/journals/jama/fullarticle/1877204
Resources/ Additional Reading

mHealth

Other HTN articles

Acknowledgements

• Vanessa Solomon, DO for her assistance in developing this talk