• Review the new hypertension guidelines
• Create an evidence-based medication regimen to treat hypertension for primary and secondary prevention
• Identify potential issues in HTN management
  • Resistant HTN
  • Adverse drug reactions
  • Drug-drug interactions

• CVD is the leading cause of death for men and women
• Lifetime Risk after age of 40
  • Men: 49%
  • Women: 32%
• Coronary heart disease comprises more than half of the CVD events

• US: 33.0% (78 million) of adults have HTN
• Current control rates (<140/90) at 46.5%
• Treatment associated with reductions in
  • Stroke – 35 to 40%
  • Myocardial infarction – 20 to 25%
  • Heart failure – >50%
• Achieving a sustained 12 mmHg reduction in SBP over 10 years prevents 1 death
  • CVD → NNT = 9
  • Stage 1 HTN → NNT = 11
• Seated quietly for 5” with feet on the floor and arms supported
• Use appropriate size cuff
• At least 2 measurements should be done
• BP readings and goals should be provided to patient

• Pre-hypertension
  • SBP 120-139 mmHg and DBP 80-89 mmHg
  • No drug therapy indicated in most cases
• Stage I hypertension
  • SBP 140-159 mmHg and DBP 90-99 mmHg
• Stage II hypertension
  • SBP ≥ 160 mmHg and DBP ≥ 100 mmHg

AC is a 50 year old man with diabetes who is s/p MI (3 months ago)
• His BP is 155/85 mmHg, HR is 80 bpm.
• He has been adherent to his lisinopril-HCTZ 20/25 mg/day.
• What is his BP goal?
  A. <130/80
  B. <140/80
  C. <140/90
  D. <150/90

• Depends who you ask…
  • Per ADA, his BP goal is <140/80 since he has diabetes
  • Per other BP guidelines, his goal is <140/90

JNC 7 – last NHLBI sanctioned guideline
JNC 8 – Not sanctioned/endorsed by any group
American Society of Hypertension / International Society of Hypertension
• ACC/AHA/CDC Science Advisory
• ADA – for patients with diabetes
• KDIGO – for patients with CKD
• ACC/AHA Secondary Prevention – for patients with CVD
• Sanctioned HTN guideline expected in 2015

• Each set of these guidelines was independently developed. They used different methodologies and criteria for reaching their conclusions and varied in how comprehensive their recommendations were.
• All acknowledged that many key questions remained unanswered and called for greater research.
Areas of agreement - 140/90 for both goal and threshold

- Individuals younger than 60
- Individuals with diabetes
- Individuals with chronic kidney disease (CKD) without significant proteinuria

- Controversial
- Unable to reach unanimity on the recommendation of a goal SBP of lower than 150mm Hg.
- Some members recommended continuing the JNC 7 SBP goal of lower than 140mmHg for individuals older than 60 years based on expert opinion.
- These members concluded that the evidence was insufficient to raise the SBP target from lower than 140 to lower than 150 mm Hg in high-risk groups, such as black persons, those with CVD including diabetes, and those with multiple risk factors.

- The panel agreed that more research is needed to identify optimal goals of SBP for patients with high BP.

Only other grade A (strong) recommendation
- Other 7 recommendations are outlined in the next few slides regarding BP goals and treatment recommendations

Biggest area of diversion is between 60 and 79 years old.
- There is more general agreement for those individuals 80 years old and older, particularly if they are fragile, that the treatment goal should be 150/90 rather than 140/90.
- This includes the expert opinion that if an individual is doing well on treatment there is no compelling reason to reduce the intensity of treatment at a specific age.
- Other guidelines (Canadian, UK and ESH/ESC) all support the 150/90 goal for those 80 years old and older.
The American Heart Association and the American College of Cardiology released four cardiovascular treatment guidelines for healthcare providers in November, and next year they will be updating their high blood pressure guidelines as well. The new report that was published in JAMA... will be taken into consideration for those guidelines, which will be the national standard for treating hypertension.

Until then, the AHA/ACC recognize the most recent hypertension guidelines, published in 2004 by the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, as the national standard.

- Diet modification
  - DASH diet → reduce SBP by 8 – 14 mmHg
  - Na restriction → reduce SBP by 2 – 8 mmHg
- Weight reduction
  - For every 10kg loss → reduce SBP by 5 – 20 mmHg
- Exercise regularly
  - 30 min/day → reduce SBP by 4 – 9 mmHg
- Alcohol moderation
  - Limit 2 drinks/day (1 for women) → reduce SBP by 2 – 4 mmHg

- ACE inhibitors
- ARBs
- Renin inhibitor
- Beta blockers
- Diuretics
  - Thiazide
  - Loops
  - Potassium sparing
- Calcium channel blockers
  - Dihydramipride
  - NonDihydrympidine

- Alpha-1 blockers
- Aldosterone receptor blockers
- Central alpha-2 agonists
- Vasodilators

| JNC 7 | Initial therapy | Thiazide diuretic or CCB, ACE inhibitor or ARB, beta blocker |
| JNC 8 | Initial therapy | Thiazide-type diuretic, or CCB, ACE inhibitor or ARB |
| ASH/ISH | Initial therapy | Thiazide diuretic, or CCB, ACE inhibitor or ARB |
| ACC/AHA HTN | Initial therapy | Thiazide diuretic |

| JNC 1 | Initial therapy | Two drug therapy: Thiazide plus CCB, ACE inhibitor or ARB |
| JNC 8 | Initial therapy | Two drug therapy: Thiazide plus CCB, ACE inhibitor or ARB |
| ASH/ISH | Initial therapy | Three drug therapy: Thiazide plus CCB, ACE inhibitor or ARB |
| ACC/AHA HTN | Initial therapy | Three drug therapy: Thiazide plus CCB, ACE inhibitor or ARB |

- African American
- Non-African American
- ≥ 60 years
A.M. is a 32-year-old woman with type 1 diabetes and HTN. She and her husband have decided to have children.

Her current medication regimen is as follows: ramipril 10 mg daily and insulin as directed.

Her vital signs today include BP 128/73 mm Hg, repeat 129/76 mm Hg; HR 82 beats/minute; height 5’6”; weight 155 lb; and body mass index (BMI) 25.

Which one of the following medication changes, if any, needs to be made?
1. No change in therapy is warranted at this time.
2. Discontinue ramipril and replace with labetolol.
3. Discontinue all antihypertensive therapy.

- Examples: lisinopril, enalapril, ramipril
- Evidence –
  - HOPE
  - EUROPA
  - PEACE
  - PROGRESS
  - ANBP-2
- Contraindications
  - Bilateral renal artery stenosis
  - Pregnancy
  - Angioedema
- Important adverse drug reactions
  - Increasing serum creatinine (up to 30% acceptable)
  - Hyperkalemia
  - Angioedema
  - Cough
- Dosing and monitoring
  - Consider avoiding in women during childbearing years
  - Monitor Scr and K 7 to 10 days after initiation or titration
A 60-year-old man with diabetes is new to your clinic.

- Today, his BP is 145/78 mm Hg, with repeat of 141/73 mm Hg. His HR is 80 beats/minute.
- He reports intolerance to two different ACEIs because of cough. He is currently taking metformin 850 mg 3 times/day, glipizide 10 mg 2 times/day, HCTZ 25 mg daily, and omeprazole as needed.
- Laboratory results reveal Cr 1.5 (CrCl [IBW] = 54 mL/minute), A1c 6.8%, K 4.0, and microalbumin/ Cr 98.2. His BMI is 31.6.

Which one of the following options is the best way to address his elevated BP?

1. No further treatment is needed.
2. Start amlodipine 2.5 mg daily.
3. Start losartan 25 mg daily.
4. Start atenolol 25 mg daily.

If he had ACE inhibitor induced angioedema, would you pick losartan next?

1. Yes
2. No

Examples: losartan, valsartan, candesartan

Evidence – LIFE, VAJANT

Clinical utilization
- Recommended as first line, but generally reserved for patients with ACEI intolerances
- Concomitant medical conditions (after ACE inhibitors)
  - Heart failure
  - Diabetes
  - Chronic kidney disease

Contraindications
- Bilateral renal artery stenosis
- Pregnancy
- Angioedema

Important adverse drug reactions
- Increasing serum creatinine
- Hyperkalemia
- Angioedema

Dosing and monitoring
- Consider avoiding in women during childbearing years
- Monitor Scr and K 7 to 10 days after initiation or titration

Aliikiren (Tekturna) – no clinical outcomes data

Contraindications
- Pregnancy
- Use in combo with ACEI or ARB (ALTITUDE– increased risk of stroke, renal complications, hyperkalemia)

Important adverse drug reactions
- Angioedema
- Hyperkalemia

Clinical Utilization - very limited

Dosing and monitoring
- Consider avoiding in women during childbearing years
- High fat meal decrease absorption
AC is a 50-year-old man with diabetes who is s/p MI (3 months ago).
- His BP is 155/85 mmHg, HR is 80 bpm.
- He has been adherent to his lisinopril-HCTZ 20/25 mg/day.
- What’s the next best step to control his HTN?
  A. Add amlodipine 5 mg/day
  B. Add metoprolol 25 mg BID
  C. Add losartan 50 mg/day
  D. Add furosemide 20 mg BID

A beta blocker would be the next best choice because he is s/p MI.
A dihydropyridine CCB is likely to be the next choice since he is African-American.
Losartan is not recommended since he is on lisinopril.
Furosemide is likely not needed since he is on HCTZ.

Examples: metoprolol, carvedilol, labetalol
Mechanism of action – selective (β₁) and nonselective (β₁ and β₂) receptor antagonism
Evidence – AHA/ACC guidelines since 1980s
Clinical utilization
- Concomitant medical conditions
  - Heart failure
  - CHF
  - Diabetes
  - No longer listed as first-line therapy if none of the above concomitant conditions present

Contraindications (relative)
- SA or AV node dysfunction
- Hypotension
- Decompensated heart failure
- Severe bronchospastic disease
Important adverse drug reactions
- Bradycardia
- Heart block
- Bronchospasm
- Exercise intolerance
- Sexual dysfunction
Dosing and monitoring
- Monitor heart rate regularly

A 65-year-old woman with progressing renal insufficiency presents.
- Today, her BP is 128/65 mm Hg, with repeat of 127/66 mm Hg.
- She is currently taking HCTZ 25 mg daily, amlodipine 5 mg daily, and a multivitamin daily.
- Today, laboratory results reveal Cr 2.3 (CrCl [IBW] = 22.8 mL/minute), K 3.9, and Na 133. Her BMI is 21.9.

What changes, if any, should be made to her medication regimen?
1. Discontinue HCTZ and amlodipine.
2. Discontinue HCTZ only.
3. Discontinue amlodipine only.
4. No change in her current regimen is warranted.
• Examples: HCTZ, chlorothalidone, metolazone
• Evidence – ALLHAT, SHEP, MRC
• Clinical utilization
  • First line anti-hypertensive
  • Enhances the efficacy of multi-drug regimens
  • Affordable

• Contraindications - Anuria
• Important adverse drug reactions
  • Electrolyte abnormalities (hypokalemia, hyponatremia)
  • Hyperuricemia
• Dosing and monitoring
  • Ineffective for patients with GFR <30 ml/min
  • Monitor Scr, Na and K 7 to 10 days after initiation or titration

• Examples: furosemide, bumetanide, torsemide, ethacrynic acid
• Clinical utilization
  • Utilize BID dosing for HTN
  • Useful in patients with HF and/or CKD
  • Approximate dose equivalence:
    • Furosemide 40 mg =
    • Bumetanide 1 mg =
    • Torsemide 10 mg =
    • Ethacrynic acid 50 mg

• Contraindications – anuria
• Important adverse drug reactions
  • Electrolyte abnormalities (Na, K, Mg)
  • Dehydration
• Dosing and monitoring
  • Monitor Scr, Na and K 7 to 10 days after initiation or titration

• Examples: triamterene, amiloride
• Clinical utilization
  • Typically used with thiazide diuretic for potassium balance
• Contraindications – anuria, hyperkalemia, severe renal or hepatic disease
• Important adverse drug reactions - hyperkalemia
• Dosing and monitoring
  • Avoid in patients with Clcr <10 ml/min
  • Monitor Scr and K 7 to 10 days after initiation or titration

• Examples: amlodipine, felodipine, nifedipine
• Evidence – ACCOMPLISH, ASCOT, VALUE
• Clinical utilization
  • First line anti-hypertensive
  • Potent BP lowering
  • Improves anginal symptoms
• Important adverse drug reactions – peripheral edema
• Dosing and monitoring – start at low dose for elderly patients
• Diltiazem and verapamil
• Evidence – CONVINCE, INVEST, NORDIL
• Clinical utilization – useful in patients with atrial fibrillation or angina

• Contraindications
  • Heart block
  • Sick sinus syndrome
• Important adverse drug reactions
  • Bradycardia
  • Heart block
  • Constipation
• Dosing and monitoring
  • Potent CYP450 inhibitor (potentially serious drug-drug interactions – e.g. some statins, ranolazine)
  • Do not use with concomitant systolic HF

• Definition: failure to reach BP goal with full doses of appropriate three drug regimen that includes diuretic
• Rule out:
  • Improper BP measurement
  • Medication nonadherence
  • Excessive Na intake
  • Drug-induced/drug-exacerbated
  • Identifiable concomitant disease

• Specific drugs
  • NSAIDs
  • Cocaine, amphetamines
  • Sympathomimetics
  • Oral contraceptives
  • Adrenal steroids
  • Cyclosporin or tacrolimus
  • Erythropoietin
  • Licitore
  • Dietary supplements

• Associated conditions
  • Obesity
  • Alcoholism
• Clinical inertia
  • Failure to initiate or titrate combination meds
  • Decision support and involving nurses and pharmacist clinicians can be helpful
• Identifiable causes of HTN

• Sleep apnea
• Drug induced or related causes
• Chronic kidney disease
• Primary aldosteronism
• Renovascular disease
• Chronic steroid therapy or Cushing’s syndrome
• Pheochromocytoma
• Coartation of the aorta
• Thyroid or parathyroid disease
A 58-year-old woman with CAD presents to clinic with her home blood pressure readings. She is currently taking HCTZ 25mg daily, lisinopril 40mg daily, amlodipine 10mg daily and metoprolol 25mg bid. She has tried terazosin, but had to discontinue it due to dizziness.

Today her blood pressure is 153/79, with repeat of 151/81. Her heart rate is 58 bpm.

Today, laboratory results reveal: Cr 1.2 (CrCl \((\text{ABW})\) = 51.8 ml/min), K 3.9, Na 142. Her BMI is 27.5. EF is 45%.

Which of the following changes, if any, would be the best intervention for this patient?

1. Start spironolactone 25mg daily
2. Stop her HCTZ and start spironolactone 25mg daily
3. Increase her metoprolol to 50mg bid
4. No change in her current regimen is warranted

**Spironolactone and eplerenone**

- **Clinical utilization**
  - Resistant hypertension
  - Patients with HF and HTN
  - Do not use if
    - K >5.0 mEq/L
    - CrCl <30 mL/min

**Contraindications**
- anuria, acute renal insufficiency, hyperkalemia
- Eplerenone CI'd in DM + microalbuminurea (↑ K') and concomitant K' supplements

- **Important adverse drug reactions**
  - Hyperkalemia
  - Gynecomastia with spironolactone

- **Dosing and monitoring**
  - Monitor Scr and K 7 to 10 days after initiation or titration

**Important adverse drug reactions – dizziness and orthostatic hypotension**

- Significant drug interactions: PDE-5 inhibitors (sildenafil (Viagra), vardenafil (Levitra), tadalafil (Cialis))
- Dosing and monitoring
  - Start very low dose and titrate slowly
  - Patients could consider taking first dose in bed

**Examples:** Clonidine, methyldopa

- Mechanism of action – stimulates \(\alpha_2\) receptors in brain which decreases sympathetic cardiac output and peripheral vascular resistance

- **Clinical utilization**
  - Clonidine
  - Resistant HTN
  - Hypertensive urgency
  - Methyldopa – use for HTN with pregnancy
• Important adverse drug reactions
  • Dizziness and orthostatic hypotension
  • Dry mouth
• Dosing and monitoring
  • Rebound HTN possible if withdrawn too quickly, especially if on concomitant beta blocker (except carvedilol) due to unopposed α stimulation
  • Avoid in patients with HF
• Examples: hydralazine, minoxidil
• Mechanism of action – smooth muscle relaxant in arteries
• Clinical utilization
  • Resistant HTN
  • HTN + HF – hydralazine
• Important adverse drug reactions
  • Fluid retention (use with diuretic)
  • Tachycardia (use with beta blocker)
  • Drug-induced lupus-like syndrome
• Dosing and monitoring – can dose BID to QID

• Beta blockers and verapamil/diltiazem for HTN (may see for atrial fibrillation)
• Beta blockers and clonidine
• Aliskiren and ACEi/ARB

• At least 2 drugs
  • Most patients will ultimately require 2 or more drugs
  • Add 2nd drug from another class when single drug at optimal doses fails to achieve goal
  • BP >20/10 mmHg above goal, consider starting with 2 drugs
• Follow-up
  • Monthly intervals until goal achieved; labs may be needed more frequently
  • Titrate to max doses first then add on meds until BP goal is achieved
  • More frequent visits may be necessary for Stage 2 HTN or if compelling indications
  • Fight the inertia: close enough isn’t good enough

• After a drought of new guidelines, it rained in 2013
• Many of the guidelines conflict
• The sanctioned, endorsed HTN guideline from ACC/AHA/ASH due in 2015 will likely provide more unified recommendations
• Start with first line HTN meds
  • Thiazide diuretics
  • CCB
  • ACE inhibitor or ARBs
  • Consider concomitant diseases
  • Close enough isn’t good enough