

Network Hypertension Algorithm

Content Review and Approval: This document is subject to review, revision, and (re)approval by the Clinical Integration and Oversight Committee (CIOC) annually and following updates to evidence based practice guidelines

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Disclaimer: This algorithm is neither a substitute for professional judgment nor intended to account for all possible precautions, contraindications, or clinical scenarios. Please consult additional references where necessary (e.g. pregnancy).

Last updated: Sept. 11th, 2014

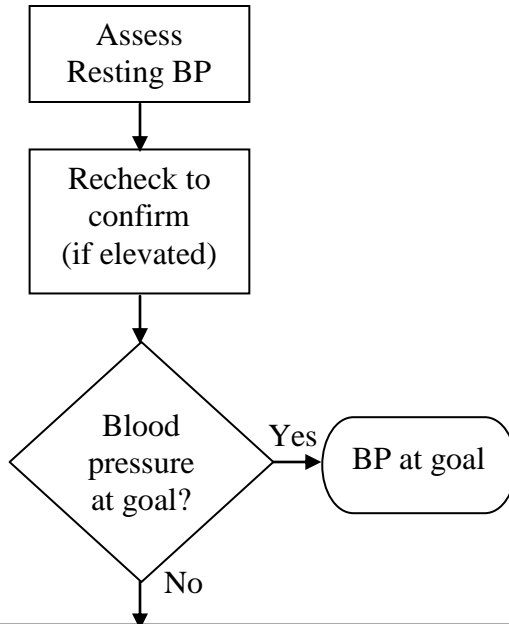
Network Hypertension Algorithm

Target population: All adults with hypertension

Therapeutic targets: Under age 60: < 140/90

Age 60 and up: < 150/90 (and less than 140/90 if DM or CKD)

Tip: BP control determined by the *most recent BP* during the measurement year (*HEDIS*)



Preferred BP Med Classes (Uncomplicated HTN)

1st, 2nd, and 3rd line options

- ACE or ARB
- Calcium channel blocker (CCB)
- Thiazide diuretic

 - B-blocker: 1st line if systolic HF or MI/CAD

Preferred 4th line options

- Aldosterone antagonist
- Beta blocker

See Decision Support for discussion of additional drugs

Preferred Meds in Each Class

ACE:
Lisinopril

ARB:
Irbesartan, Valsartan, Losartan

Calcium channel blockers (CCB):
Amlodipine, Diltiazem

Thiazide diuretics:
Chlorthalidone, HCTZ

B-blockers:
Carvedilol, Bisoprolol, Metoprolol

Increased Potency/Efficacy

ARB:
Irbesartan & Valsartan > Losartan

Diuretic:
Chlorthalidone > HCTZ

B-blocker:
Once daily: Bisoprolol > Atenolol
Twice daily: Carvedilol > Metoprolol

Intensify Treatment
(In addition to physical activity and the DASH diet)

If on monotherapy:

- Add a second drug from a different class
- Increase dose of current drug if no dose limiting factor(s)
- Change to a more potent drug in a currently used class

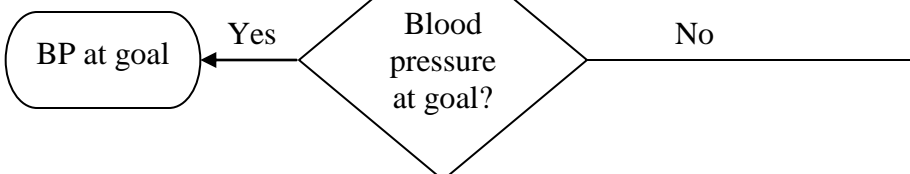
If on dual therapy:

- Increase dose of current drug(s) if no dose limiting factor(s)
- Change to a more potent drug in a currently used class
- Add a third drug from a different class

If on triple therapy:

- Increase doses of current drug(s) if no dose limiting factor(s)
- Change to more potent drug(s) in a currently used class
- Add a fourth drug from a different class (resistant HTN)

Recheck BP in 2-4 weeks
Recheck within 1 week if SBP 160+ or DBP 100+



Supplemental BP Goals & Tips

<u>Population</u>	<u>BP Target (optional)</u>
Diabetes	< 140/80
Diabetes	< 130/80 for the following
<ul style="list-style-type: none">• Age < 65, and/or• High risk of stroke, and/or• CKD with micro-/macro- albuminuria	
Heart failure	< 130/80 (and consider \leq 120/80)

Elderly: For patients 65 and older...

- 1) Use caution with DBP < 70
- 2) Lowering diastolic pressure < 60-65 may increase cardiovascular events
- 3) **See "Elderly and Othostatics" on page 3**

For isolated systolic hypertension (SBP > 140, DBP < 90):

Thiazide diuretics and **calcium channel blockers**

lower systolic pressure more so than diastolic

Compelling Indications

ACE or ARB:

- Diabetes w/ microalbuminuria
- Systolic heart failure

B-blockers:

- CAD
- Systolic heart failure

Alpha blockers: Benign prostatic hypertrophy

Lifestyle Measures

Routine physical activity/exercise and the DASH diet are recommended for **all patients**

DASH diet principles include:

Low sodium intake:

- Avoid the salt shaker (tip: sea salt is not really healthier)
- Avoid salty snacks, canned soups, ramen noodles, and boxed meals

Plenty of fruits, vegetables, low fat dairy, and whole grains (high fiber, Mg⁺⁺, Ca⁺⁺, and K⁺)

End result: Well balanced nutrition that's low in sodium and fat – and high in heart healthy foods

Exercise & Activity: [The American Heart Association](#) currently recommends the following

At least 30 minutes of **moderate intensity aerobic activity** *at least* 5 days per week (total of 150 minutes or more)

OR

At least 25 minutes of **vigorous aerobic activity** *at least* 3 days per week (total of 75 minutes) (or a combination of moderate and vigorous)

AND

Moderate to high intensity muscle strengthening activity *at least* 2 or more days per week for additional health benefits

Lifestyle changes and goal setting: It's recommended that each patient encounter include at least 1 discussion point that incorporates goal setting and a plan to achieve it

Tip: Many patients will fail to adopt an exercise routine unless a plan is made that incorporates which activity (or activities) they will pursue, duration of activity, and a schedule that works (days & times)

Hypertension Management Pearls

Elderly (age 65+) and Orthostatics: Prior to treatment or increasing BP meds, check sitting and standing blood pressure to assess for orthostatic hypotension to prevent medication adverse reactions

Orthostatic hypotension: ≥ 20 mmHg drop in SBP or ≥ 10 mmHG drop in DBP on standing

Monotherapy considerations for special populations

Note: The suggested 1st line medications (listed below) are for uncomplicated hypertension based on known response/efficacy in certain populations. For patients with complicating factors, drug selection should be tailored according to their compelling indications/comorbid diagnoses.

- African American: **CCBs** and **thiazide diuretics** are the most effective monotherapy options

ACE/ARB note: Less effective as monotherapy in African Americans but still appealing for combination therapy. Can be as effective as in Caucasians – *WHEN combined with a thiazide or calcium channel blocker*

- Younger patients (age < 65 years): Consider **ACE/ARB** for initial monotherapy (a **CCB** or **thiazide diuretic** would also be a reasonable option)
 - Elderly (65 years+): **Thiazide diuretics** and **CCBs** lower systolic pressure more so than diastolic – an advantage in treating isolated systolic hypertension (most common in the elderly)
-

Adding a second drug: Utilizing two antihypertensives is often more effective and therefore preferable vs. monotherapy in the following circumstances.

Therapy naïve: Baseline BP ≥ 20 mmHG above systolic or ≥ 10 mmHG above diastolic goal

On treatment: But uncontrolled on a moderate to high dose of a single agent

Renal function & Electrolyte Monitoring: ACEs, ARBs, diuretics, and spironolactone can affect renal function and electrolyte balance – sometimes dramatically (especially in the elderly and patients with renal insufficiency).

These patients – or those who take a combination of drugs that affect the kidneys/electrolytes – may require lab assessment (e.g. basic metabolic panel/BMP) within a matter of days following the start of the aforementioned meds (and a repeat assessment may be indicated soon after).

Note: If the serum creatinine rises by 50% or more (vs. baseline) after starting ACE/ARB therapy, it may indicate the presence of renal artery stenosis and additional workup may be needed. If/when deemed safe to restart ACE/ARB therapy, a decreased dose should be considered.

Resistant hypertension & aldosterone: Elevated aldosterone is a relatively common contributor to resistant hypertension, making spironolactone a consideration for patients not responding to other agents (so long as they don't have contraindications).

Antihypertensive Initiation and Titration

ACE inhibitors

<u>Agent</u>	<u>Starting Dose</u>	<u>If BP not at goal</u>	<u>Max Dose</u>
Lisinopril			
General	10 mg/day	Double monthly	80 mg/day*
Elderly/CKD	2.5 to 5 mg/day	Double monthly	
Heart failure	5 mg/day	Double q2-4 weeks†	

* Consider titrating or adding another medication before increasing above 40 mg/day (80 mg/day offers limited added efficacy but does increase side effect/toxicity risk)

† Maximum recommended dose = 40 mg/day for systolic heart failure

Recommended lab monitoring:

Elderly/CKD (GFR < 60): Consider checking a BMP in the weeks following the start of therapy

Precautions:

Acute renal failure: Consider holding ACE therapy if creatinine increases by 50% or more from baseline; this can indicate the presence of renal artery stenosis with further workup possibly indicated. Consider dose reduction if/when resumed and monitor closely.

ACE inhibitor cough: Estimates vary, but cough may occur in up to 10-20% of patients who take an ACE, and around 3.5% of patients who take lisinopril – which is comparatively lower than the estimated incidence attributed to enalapril (as high as 15%), and ramipril (as high as 12%).

Cough characteristics: dry/nonproductive, persistent throughout the day (and night), and usually resolves within days of stopping the ACE-I (but can take weeks in rare instances)

Management: Consider changing to an ARB, especially if compelling conditions present (e.g. diabetes, systolic heart failure)

Chronic kidney disease (GFR < 60): Use with caution and monitor carefully in stage III CKD, especially IIIb (GFR 30-44 ml/min). Discuss w/ physician before initiating or increasing in stage IV-V CKD (GFR < 30); may be potentially more dangerous than beneficial.

Hyperkalemia: Combining 3 or more drugs that promote potassium retention (e.g. ACE + Maxzide + Spironolactone) is not recommended. Caution is advised when combining 2 such drugs.

Elderly patients and/or CKD (GFR < 60):

- Consider rechecking a BMP within the month following initiation or dose increase – especially if combined with diuretic therapy or other potentially nephrotoxic drugs
- Avoid combining NSAIDs with ACE or ARB therapy in this population

Angiotensin Receptor Blockers (ARBs)

<i>Agent</i>	<i>Starting Dose</i>	<i>If BP not at goal</i>	<i>Max Dose</i>
Irbesartan (preferred generic ARB)			
General	150 mg/day	Double monthly	300 mg/day
Elderly/CKD	75 mg/day	Double monthly	
Valsartan			
General	160 mg/day	Double monthly	320 mg/day
Elderly/CKD	80 mg/day	Double monthly	
Heart failure	40 mg BID	Double every 2-4 weeks	
<i>Note: Generic Valsartan <u>without</u> HCTZ will be available late summer 2014, but will initially be tier 2 on most health plans due to higher cost (prior authorization may apply)</i>			
Losartan			
General	50 mg/day	Double monthly	100 mg/day*
Elderly/CKD	25mg/day	Double monthly	
<i>* Note: Dividing losartan into BID dosing may be more effective than once daily dosing</i>			

Recommended lab monitoring:

Elderly/CKD (GFR < 60): Consider checking a BMP in the weeks following the start of therapy

Precautions:

Acute renal failure: Consider holding ARB therapy if creatinine increases by 50% or more from baseline; this can indicate the presence of renal artery stenosis with further workup possibly indicated. Consider dose reduction if/when resumed and monitor closely.

Chronic kidney disease (GFR < 60): Use with caution and monitor carefully in stage III CKD, especially IIIb (GFR 30-44 ml/min). Discuss w/ physician before initiating or increasing in stage IV-V CKD (GFR < 30); may be potentially more dangerous than beneficial.

Hyperkalemia: Combining 3 or more drugs that promote potassium retention (e.g. ACE + Maxzide + Spironolactone) is not recommended. Caution is advised when combining 2 such drugs.

Elderly patients and/or CKD (GFR < 60):

- Consider rechecking a BMP within the month following initiation or dose increase – especially if combined with diuretic therapy or other potentially nephrotoxic drugs
- Avoid combining NSAIDs with ACE or ARB therapy in this population

Calcium Channel Blockers (CCBs)

<i>Agent</i>	<i>Starting Dose</i>	<i>If BP not at goal</i>	<i>Max Dose</i>
Amlodipine			
General	5 mg/day	Double monthly	10 mg/day
Elderly/liver dx	2.5 mg/day	Double monthly	
Diltiazem (preferred if a CCB is required for rate control in A. fib)			
General	120-240 mg/day	↑ by 60-120 mg monthly	540 mg/day
Elderly	90-120 mg/day	↑ by 30-60 mg monthly	

Precautions

Bradycardia: Diltiazem (and Verapamil)

- Check for pulse < 55 bpm prior to starting/titrating
- Discuss with physician prior to starting if on a B-blocker

Drug interactions: Amlodipine, diltiazem, and verapamil inhibit CYP3A4 and are prone to significant interactions with commonly used drugs (e.g. simvastatin and lovastatin) which may require dose limitations or alternative therapy. Consult up to date drug interaction reference(s) or pharmacist to assess.

Peripheral edema: A common and sometimes problematic side effect of CCBs that is *not* generally due to excess fluid accumulation. CCB induced edema is caused by a hemodynamic imbalance where – due to arterial vasodilation – the blood flow to the lower extremities exceeds the venous return (CCBs don't increase venous dilation/capacitance).

Since excess fluid is not the cause of this type of edema, attempts to diurese are often unsuccessful. Starting/titrating agents that result in venous dilation (e.g. ACE or ARB) and thereby resolve the hemodynamic imbalance tends to be the more reliably effective option.

Systolic heart failure: Avoid diltiazem and verapamil

Thiazide Diuretics

<i>Agent</i>	<i>Starting Dose</i>	<i>If BP not at goal</i>	<i>Max Dose</i>
Chlorthalidone (preferred thiazide for resistant hypertension)			
General	12.5-25 mg/day	↑ by 12.5-25 mg monthly	100 mg/day*
Elderly	12.5-25 mg/day	↑ by 12.5-25 mg monthly	
CKD	<i>DO NOT USE W/ CRCL < 30 ML/MIN (INEFFECTIVE)</i>		

* Doses of 25 mg/day or less do not seem to increase electrolyte disturbances in comparison to HCTZ (see Precautions)

Hydrochlorothiazide (HCTZ)

General	12.5-25 mg/day	Double monthly	50 mg/day
Elderly	12.5-25 mg/day	↑ by 12.5 mg monthly	
CKD	<i>DO NOT USE W/ CRCL < 30 ML/MIN (INEFFECTIVE)</i>		

Potency Comparison

Chlorthalidone 12.5 mg ~ HCTZ 25 mg
Chlorthalidone 25 mg ~ HCTZ 50 mg

Recommended lab monitoring:

General:	Recheck BMP within 1 month of starting therapy/increasing dose
Elderly/CKD (GFR < 60):	Recheck BMP within 3-7 days of starting therapy

Precautions

Chlorthalidone dosing: Doses up to 25 mg/day (equivalent to ~ HCTZ 50 mg/day) don't seem to exaggerate electrolyte disturbances in comparison to HCTZ. Higher doses (50-100 mg/day), however, may increase this risk and require closer supervision.

Hypokalemia: Thiazides are potassium wasting if not combined with a potassium sparing component (e.g. Triamterene). If hypokalemia develops, consider changing to a combination product with a potassium sparing component (e.g. Triamterene/hydrochlorothiazide) or start a potassium supplement.

Hyperkalemia: Combining 3 or more drugs that promote potassium retention (e.g. ACE + Maxzide + Spironolactone) is not recommended. Caution is advised when combining 2 such drugs.

Elderly patients and/or CKD (GFR < 60):

- Consider rechecking a BMP within 1 week following initiation or dose increase – especially if combined with an ACE/ARB, other diuretics, NSAIDs, or other potentially nephrotoxic drugs

Beta Blockers

<i>Agent</i>	<i>Starting Dose</i>	<i>If BP not at goal</i>	<i>Max Dose</i>
Carvedilol (preferred B-blocker for most patients)			
General	6.25 mg BID	Double q2-4 weeks	25 mg BID*
Elderly	3.125 mg BID	Double q2-4 weeks	
Heart failure	3.125 mg BID	Double q2 weeks	
* Up to 50 mg BID may be used in patients weighing > 85 kg (monitor BP & pulses very closely)			
Metoprolol (preferred if a B-blocker is required for rate control in A. fib)			
Metoprolol <i>tartrate</i> (Lopressor - regular release tablets)			
General	25-50 mg BID	Double q2-4 weeks	400 mg/day*
Elderly	12.5-25 mg BID	Double q2-4 weeks	
Heart failure	<i>Metoprolol tartrate not recommended</i> (use carvedilol, bisoprolol, or Toprol XL)		
* Total daily doses > 200 mg are rarely needed (monitor BP and pulse very closely if > 200 mg)			
Metoprolol <i>succinate</i> (Toprol XL – extended release tablets)			
General	50-100 mg/day	Double q2-4 weeks	400 mg/day*
Elderly	25 mg/day	Double q2-4 weeks	
Heart failure	25 mg once daily**	Double q2 weeks	
* Total daily doses > 200 mg are rarely needed (monitor BP and pulse very closely if > 200 mg)			
** Consider starting metoprolol succinate at 12.5 mg/day for class III-IV heart failure; target/maximum recommended dose of 200 mg/day in systolic heart failure (titrate as tolerated)			
Bisoprolol (preferred once daily B-blocker)			
General	2.5-5 mg/day	Double q2-4 weeks	20 mg/day
Elderly	2.5 mg/day	Double q2-4 weeks	
Heart failure	1.25 mg once daily	Double q2 weeks	

Precautions

Bradycardia:

- Monitor for pulse < 55 bpm prior to starting/titrating
- Discuss with physician prior to starting for patients on diltiazem or verapamil

Asthma/COPD: Cardioselective agents that provide primarily B1 blockade (bisoprolol, metoprolol) may be less likely to affect pulmonary status. This selectivity fades with escalating doses.

PLEASE SEE NEXT PAGE FOR B-BLOCKER COMPARISON

Beta Blockers (Continued) - Comparison

B-blocker selection/comparison:

Key

- + = Advantage
- = Disadvantage

Carvedilol: Preferred due to efficacy in hypertension and heart failure coupled with pharmacokinetic and cost considerations

- + Regular release carvedilol has a longer half-life (6-10 hours) than regular release metoprolol tartrate (3-4 hours), making carvedilol the more reliably effective option for BID dosing
- + Carvedilol's more diverse mechanism of action (alpha-1 blockade and vasodilation) also contributes to increased comparative efficacy

Metoprolol:

- Short half-life (3-4 hours) compromises the efficacy of BID regular release metoprolol (tartrate)
- + The most commonly used B-blocker status post MI
- + Provides better rate control in atrial fibrillation than carvedilol

Bisoprolol: A strong consideration for patients with cost and compliance issues

- + A longer half-life (7-15 hours) makes bisoprolol an effective once daily option
- + Substantial efficacy and outcomes data to support its use
- + Offers rate control (A. fib) superior to carvedilol

Bisoprolol availability:

- ❖ *Bisoprolol (Zebeta):* Available generically in 5 mg and 10 mg strengths
- ❖ *Bisoprolol-HCTZ combo (Ziac):* Available generically and on some discount programs

Atenolol:

- May be less effective than carvedilol, bisoprolol, or metoprolol w/ less supporting outcomes data
- Despite approval for once daily dosing, may not be effective for 24 hours

Aldosterone Antagonists

<i>Agent</i>	<i>Starting Dose</i>	<i>If BP not at goal</i>	<i>Max Dose</i>
Spirolactone			
General	25 mg once or twice daily	Double monthly	100 mg/day*
Elderly	12.5-25 mg/day	↑ by 12.5 to 25 mg monthly	

* Most patients will respond to 50-100 mg/day; higher doses may not be effective for most patients

Recommended lab monitoring:

BMP at baseline and then:

- Within 3-7 days after starting
- Monthly x 3 months
- Periodically thereafter

Especially when combined with other agents that affect renal function and electrolytes (and after dose increases)

Precautions

Contraindications:

Do not start Spirolactone if:

- K⁺ is 5 mEq/L or higher, OR
- GFR is < 30 ml/minute

Hyperkalemia: Combining 3 or more drugs that promote potassium retention (e.g. ACE + Maxzide + Spirolactone) is not recommended. Caution is advised when combining 2 such drugs.

Elderly patients and/or CKD (GFR < 60):

- Confirm no contraindications present before starting/titrating.
- Strongly consider rechecking BMP with 3-7 days after starting/increasing due to increased risk of renal and electrolyte disturbance – especially since most patients will already be on an ACE/ARB, diuretic, and possibly other nephrotoxic drugs

Other Antihypertensive Medication Notes

Aliskiren: Avoid combining with an ACE or ARB in diabetic patients – increased risk of toxicity without clinical benefit. Optimizing ACE or ARB therapy and either an ACE or ARB with other antihypertensive agents is recommended prior to consideration of changing to aliskiren.

Alpha blockers: Compelling use with BPH. Potential add on to preferred meds and classes for resistant hypertension.

Central acting alpha agonists (clonidine, guanfacine): Side effects limit utility (dry mouth, sedation, etc). Potential add on to preferred meds and classes for resistant hypertension.

HCTZ: In comparison to chlorthalidone or indapamide, HCTZ has less supporting evidence for cardiovascular risk reduction and improved mortality and may be less effective for BP reduction. This may be due to a shorter elimination half-life for HCTZ (6-12 hours) vs. chlorthalidone (40-60 hours) or indapamide (14-26 hours) and shorter duration of action.

Note: Chlorthalidone doses of 25 mg/day or less do not appear to cause more electrolyte disturbances or hyperglycemia in comparison to HCTZ (whereas higher doses may). Concomitant ACE/ARB therapy may also reduce hypokalemia potential.

Hydralazine: Can be effectively combined with nitrates for patients intolerant to ACE/ARB therapy for heart failure. Also a possible add-on to preferred antihypertensives if resistant.

Indapamide: A thiazide diuretic with efficacy and outcomes data superior to HCTZ (similar to chlorthalidone in that regard), and a viable alternative to patients not meeting BP goals on HCTZ.

Nitrates: Primary purpose remains antianginal therapy. Not generally used for hypertension management alone. Can be effectively combined with hydralazine for patients intolerant to ACE/ARB therapy for heart failure.
