# CHAPTER 8
# Hypertension

Worldwide, hypertension is a leading cause of preventable end-organ disease. This is true even in rural sub-Saharan Africa, a setting with high levels of physical activity and malnutrition and low levels of obesity and tobacco use.[1] There are no national prevalence studies on hypertension in rural Rwanda, but there are numerous studies of adults in other rural areas of sub-Saharan Africa. These studies show a pattern of low prevalence but severe hypertension, often in isolation from other metabolic risk factors. For example, a study in rural Gambia during the mid-1990s found 6.8% of surveyed participants over the age of 15 had a blood pressure greater than 160/95 mmHg.[2] Roughly half of these cases had systolic blood pressures greater than 180 mmHg. Almost 80% had no other metabolic risk factor. Almost 18% of the population had blood pressures greater than 140/90 mmHg. Other surveys from the past 30 years have produced similar findings.[3,4] As in industrialized countries, most hypertension in sub-Saharan Africa is likely due to essential hypertension.

The Framingham Heart Study began during the 1950s, prior to the widespread use of effective antihypertensives. Back then, 11% of women between the ages of 45 and 75 had blood pressures greater than 180/110 mmHg.[5] By the 1980s, this prevalence had declined to 0.9%. Data from sites like rural Gambia suggest that as much as 2% of the population over age 15 currently has untreated systolic blood pressures greater than 180 mmHg.[2] So far, in Rwanda, we have focused on the chronic care of patients in this category who present to district hospitals. This approach has the advantage of treating first those people most likely to have negative cardiovascular outcomes and establishing good systems on a small scale prior to expanding case-finding.

However, passive case-finding misses most asymptomatic patients, patients whose untreated hypertension leaves them vulnerable to end-organ disease. More active case-finding would involve opportunistic screening for hypertension as part of acute care at the health-center level. This approach raises the controversial question of what level of hypertension necessitates treatment.

Blood pressure is a continuous risk factor and interacts with other variables such as age, tobacco exposure, and lipid and glucose levels. For this reason, many have advocated medication treatment thresholds based not on a single risk factor, but on wider criteria: the patient's

absolute risk for a combination of cardiovascular events.[6,7] As we have discussed, most people with high blood pressure in rural sub-Saharan settings have no risk factors for cardiovascular disease beyond their hypertension. Most absolute risk models would calculate the risk of a cardiovascular event for such people at less than 10% over a 5-year period even at very high blood pressures. However, it is unclear how well these models predict the outcomes associated with isolated hypertension at levels above 160/95 mmHg, particularly in sub-Saharan Africa. International hypertension guidelines that embrace the absolute risk approaches have made the caveat that patients with persistent blood pressures above 170/100 mmHg (New Zealand) or 160/95 mmHg (WHO) should receive pharmacologic treatment regardless of their calculated risk.[8,9] Another factor not often included in standard treatment models is the cost to the patient. Facility-based chronic care for hypertension is expensive for patients, especially in rural areas. They must pay for transport to the clinic and also, in most health systems, for the costs of their care. Our protocols offer one attempt to balance the risks associated with untreated hypertension and the significant cost of treatment to patients and society. This approach treats all patients with confirmed blood pressures greater than or equal to 160/95 mmHg. Patients with lower levels of blood pressure are treated only if they also have diabetes, renal failure, or two or more other cardiovascular risk factors, such as advanced age (greater than 65), current tobacco use, or obesity. Given the relatively low risk of developing end-organ damage from mild, lone hypertension and the large health care and direct patient costs of chronic medical therapy, we have adopted a policy of watchful waiting for this group of patients. We believe reducing the facility-based component of care for lower-risk hypertension offers one way of reducing costs and making this intervention more accessible. We have not yet explored an intervention for low-risk hypertension at the community level in rural Rwanda. The reason for this is because community health workers are currently burdened with a host of different tasks, and because the short-term risks for these patients are probably small.

Provision of hypertension treatment at first-level facilities close to patient homes also reduces health system and out-of-pocket costs. Most hypertension is relatively simple to diagnose and treat once a system of chronic care has been established. In Rwanda, most hypertension is managed at the health-center level. At this level, nurses with a basic level of training treat simple NCDs as well as HIV and TB in integrated chronic care clinics. These clinics tend to be closer to patients' homes and cost less to run than those at district level. Patients with severe levels of hypertension are referred to the district hospital or district-level NCD clinic for more specialized treatment.

In some settings, combination tablets (polypills) currently under development may offer another means of reducing treatment costs and increasing compliance, particularly among patients who have previously suffered a myocardial infarction.[10] These combination tablets often mix a hypertension agent with other medications such as aspirin and HMG-CoA reductase inhibitors (statins) to reduce the risk of vascular events among hypertensives. However, non-ischemic events, such as heart failure, renal failure, and hemorrhagic stroke, constitute the primary risks faced by hypertensive patients in settings such as rural Rwanda.[11] For this reason, we do not advocate the routine use of these combination or adjuvant therapies for most hypertensives in our setting. Rather, we reserve the use of aspirin for hypertensive patients with diabetes. Currently, we do not recommend adding statins to the Rwandan formulary for rural facilities because of the low incidence of vascular events.

## 8.1 Clinic and Community-Based Hypertension Screening

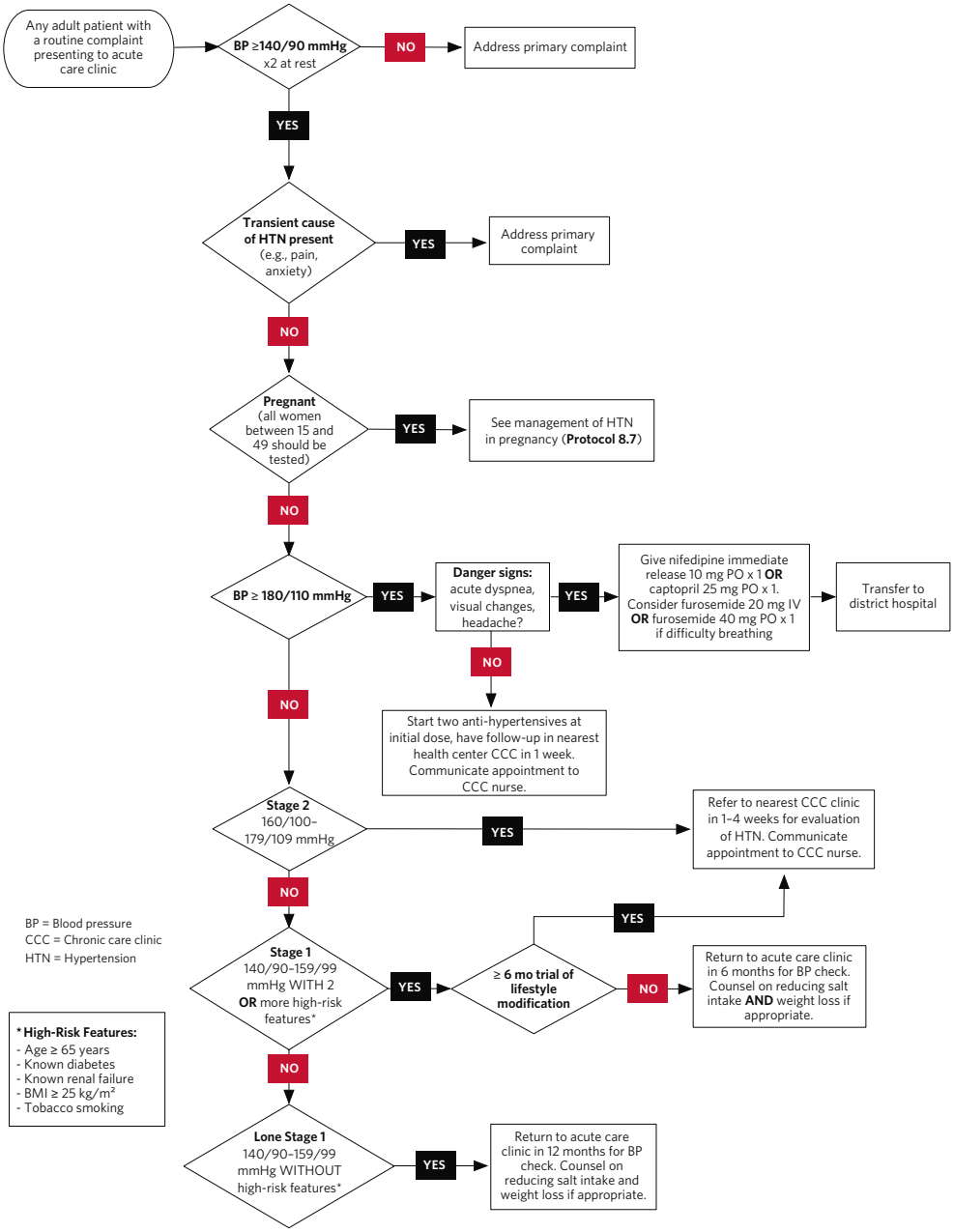
In rural Rwanda, hypertension, HIV, and streptococcal pharyngitis constitute the main drivers of cardiovascular risk. Blood pressure screening in asymptomatic individuals can help identify people with hypertension before they develop end-organ complications. Of course, screening will identify a spectrum of high- and low-risk patients. A strong chronic care system and risk-stratification protocols are needed to avoid overwhelming the fragile health infrastructure with patients who have low levels of hypertension that confer little risk of end-organ disease. Our goal in screening is to identify high-risk individuals who would not otherwise seek treatment before complications arise.

Potential occasions for screening include opportunistic blood pressure measurement at acute care or outpatient department clinics and systematic blood pressure measurement by health workers in the community. In resource-poor settings, lack of equipment, training, and time can pose barriers to implementation of routine blood pressure measurement at any level of the health care system. Given the competing demands on community health workers, we have focused initially on screening at the health-center level. We do this in the context of acute care protocols for the Integrated Management of Adult and Adolescent Illness.[12] At PIH-supported health centers, we encourage practitioners to measure the vital signs, including blood pressure, of everyone over the age of 15 who presents with a routine complaint. We use validated automatic blood pressure machines and we keep manual cuffs available in case the machine malfunctions. Batteries or electricity can power the machines. Accurate measurements require training in appropriate cuff sizes and the procurement of machines compatible with small, regular, and large adult cuffs.

A more or less intensive facility-based screening approach may be appropriate in other settings. A more resource-intensive strategy would be to hire an extra clerk to measure vital signs on all patients and to triage accordingly. A less intensive strategy would be to only measure blood pressure of patients above a certain age (e.g., 40). In some resource-poor settings, community-based screening may be an appropriate adjunct to clinic-based blood pressure measurement. This screening could take place at churches or schools. The utility of community-based screening depends in part on how often adults visit health facilities, or whether they visit them at all. As mentioned above, competing demands for services at the community level may make active detection strategies a lower priority in some contexts. **PROTOCOL 8.1** outlines an approach for this initial screening process.

As mentioned above, hypertension is both very common and relatively simple to treat. Most hypertension patients can be treated at the health-center level. However, the subject becomes more complex when one considers all the diseases encompassed by the diagnosis of hypertension. At low levels of blood pressure elevation, risk to the patient is very low and required treatment is accordingly minimal. At higher levels, hypertension becomes a rapidly deadly disease, requiring very aggressive treatment. In between, there is a range of more and less severe presentations. This heterogeneity results in what may appear to be complex protocols to explain treatment of a simple problem. However, this approach, we believe, represents our best attempt to appropriately tailor treatment according to risk while avoiding unnecessary testing or referrals.

## PROTOCOL 8.1 Initial Screening and Management of Hypertension in Adults in Acute Consultation Clinics




In this chapter we give detailed explanations of the reasoning behind each of the protocols for hypertension.

### 8.1.1 Evaluation of Blood Pressure in Acute Care Clinics

Acute care clinicians should check the blood pressure of any adult (≥ 15 years) patient presenting with a routine complaint. We discuss evaluation of blood pressure in children in **SECTION 8.6**. If the blood pressure measures less than 140/90 mmHg, the clinician proceeds with the visit as usual. If the blood pressure measures ≥ 140/90 mmHg, the clinician rechecks the blood pressure, making sure that the patient is at rest and that the cuff size is appropriate.

If both measurements are greater than or equal to 140/90 mmHg, the clinician looks for and addresses any identifiable transient cause of hypertension (e.g., pain or anxiety).

Female patients between age 15 and 49 are tested for pregnancy. For management of hypertension in pregnancy, see **PROTOCOL 8.7** and **SECTION 8.9**.

The clinician then evaluates the patient's level of hypertension and treats accordingly.

### 8.1.2 Identification and Treatment of Emergency Conditions in Acute Consultation

Patients with symptomatic stage 3 hypertension (≥ 180/110 mmHg) receive fast-acting anti-hypertensive therapy (**TABLE 8.4**) and are transferred to the district hospital for inpatient management (see **SECTION 8.4**).

### 8.1.3 Treatment of Asymptomatic Hypertension by Disease Classification

Asymptomatic stage 3 hypertension patients are started on two anti-hypertensives and given a follow-up appointment in the nearest health center integrated chronic care clinic within the next week. **SECTION 8.3** discusses our rationale for drug choices, and **TABLE 8.2** and **TABLE 8.3** outline initial antihypertensive treatment for stable patients.

In all cases of referral to the health center integrated chronic care clinic, the acute care clinician must communicate the referral to the chronic care clinician, either through a shared written patient log book and/or through the electronic medical record system.

#### 8.1.3.1 Stage 2 Hypertension (160/100–179/109 mmHg)

Patients with stage 2 hypertension (160/100–180/110 mmHg) are not started on any medications in the acute setting. They are referred to the nearest health center integrated chronic care clinic in a non-urgent fashion. This approach ensures confirmation of the diagnosis prior to initiation of therapy in patients at low risk for short-term complications.

#### 8.1.3.2 Stage 1 Hypertension (140/90–159/99) with High-Risk Features

Patients with stage 1 hypertension are evaluated for high-risk features that may warrant more aggressive treatment of blood pressure. High-risk features include known diabetes or renal failure, overweight (BMI ≥ 25 kg/m2), tobacco use, or age greater than 65 (**TABLE 8.1**). Clinicians already routinely measure height and weight and use a chart to find the corresponding BMI for all patients as part of adult malnutrition screening in acute care. In addition, patients are asked about tobacco use and previous diagnosis of diabetes. Information on prior diagnoses can often be obtained from the patient-carried medical record.

Each risk factor earns a patient a certain number of points. Risk factors such as diabetes and renal failure confer more risk than the other risk factors and are weighted more heavily. Patients with 2 or more points are considered high risk and are treated more aggressively.

**TABLE 8.1 High-Risk Features in Hypertension**

| High-risk feature | Points |
|---|---|
| Diagnosis of diabetes | 2 |
| Diagnosis of renal failure (creatinine ≥ 100 μmol/L (1.1 mg/dL)) | 2 |
| Age ≥ 65 years | 1 |
| BMI ≥ 25 kg/m2 | 1 |
| Tobacco smoking | 1 |
| *A total of 2 or more points is considered high risk and warrants more aggressive treatment.* | |

Patients with stage 1 hypertension (140/90–159/99 mmHg) who have two or more high-risk features are counseled on reducing salt intake and, if appropriate, on the benefits of weight loss. They are asked to return to acute care in six months. If still hypertensive after a six-month trial of lifestyle modification, the patient is referred to the nearest integrated chronic care clinic within 1 to 4 weeks. The clinician does not initiate anti-hypertensive therapy in the acute care setting.

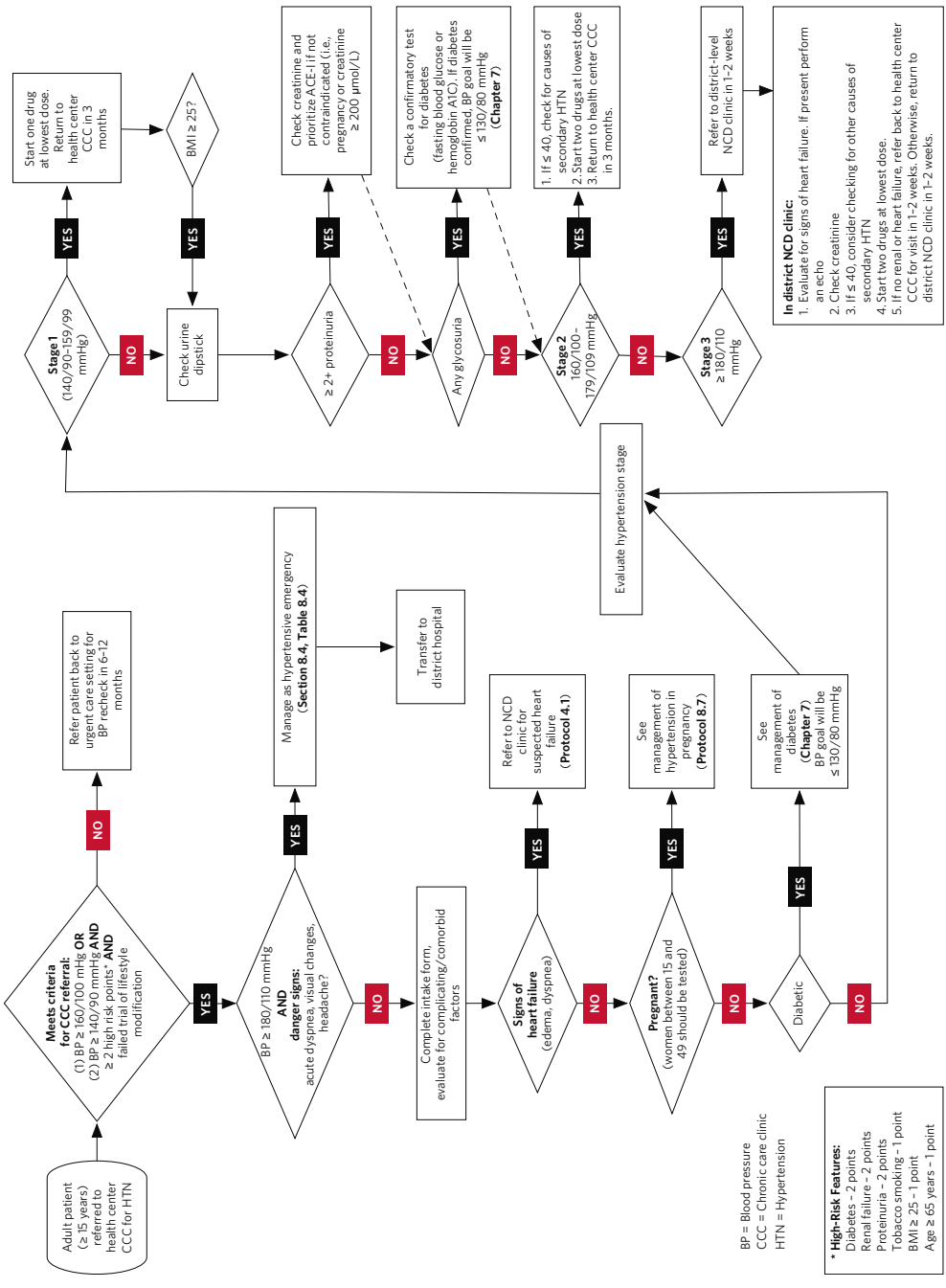
#### 8.1.3.3 Low-Risk Stage 1 Hypertension

Patients with stage 1 hypertension and fewer than two risk points are at low risk of complications from their hypertension. For this reason, we advocate delaying pharmacologic treatment and/or referral to integrated chronic care clinics for these patients. These patients are counseled to avoid added salt and instructed to return to the acute care clinic in one year for a repeat blood pressure measurement. Patients with a BMI ≥ 25 are also counseled on the benefits of weight loss.

## 8.2 Initial Management of Newly Referred Adult Hypertension Cases in Health Center Integrated Chronic Care Clinics

**PROTOCOL 8.2** outlines the initial management of newly referred hypertension cases in integrated chronic care clinics.

### PROTOCOL 8.2 Initial Management of Newly Referred Adult Hypertension Cases in Health Center Integrated Chronic Care Clinics



Adult patients referred to the integrated chronic care clinic for elevated blood pressure first undergo confirmation of hypertension. If the patient has a blood pressure < 140/90 mmHg, the patient is reassured and dismissed from the clinic.

If the patient has confirmed hypertension, clinicians further classify patients into levels of risk and initiate therapy accordingly. Only patients who have a blood pressure ≥ 160/100 mmHg confirmed on two separate visits, or who have a blood pressure between 140/90 and 159/99 mmHg with two or more high-risk features (**TABLE 8.1**) despite a 6-month trial of salt reduction and/or weight loss, if indicated, should enroll in an integrated chronic care clinic for pharmacologic treatment. Others should be referred back to the acute care clinic for repeat blood pressure measurement in 6–12 months.

### 8.2.1 Identification and Treatment of Emergency Conditions in the Health Center Integrated Chronic Care Clinic

Patients with stage 3 hypertension (≥ 180/110 mmHg) should be evaluated for symptoms of hypertensive emergency. Those with signs of end-organ effects from the elevated blood pressure (e.g., acute dyspnea, headache, or visual changes) should receive fast-acting anti-hypertensive therapy (**TABLE 8.4**) and are transferred to the district hospital for inpatient management. See **SECTION 8.4** for management guidelines for hypertensive emergency.

### 8.2.2 Evaluation for Comorbid Conditions in the Health Center Integrated Chronic Care Clinic

If the patient shows no signs of hypertensive emergency, the chronic care clinician proceeds with the standardized intake form (**APPENDIX D**), which includes information on the presence of complicating or co-morbid factors. This intake process should take approximately five minutes.

Initial patient history and physical exam may reveal signs of heart failure, including increased respiratory rate and peripheral edema. As mentioned earlier, patients with an acute elevation in blood pressure can develop symptoms of heart failure. These patients should be treated according to the guidelines for management of hypertensive emergency (**SECTION 8.4**). However, some patients who have high blood pressure will have chronic heart failure as a result of long-standing hypertension (hypertensive heart disease). Patients with symptoms of chronic heart failure such as chronic dyspnea and edema should be evaluated as suspected heart failure patients (see **CHAPTER 4**).Women between the ages of 15–49 are tested for pregnancy, and pregnant patients are managed according to **PROTOCOL 8.7**.

Patients with known diabetes are at much greater risk of complications from hypertension and will warrant more aggressive treatment. We initiate anti-hypertensive medications in these patients at a blood pressure of ≥ 130/90 mmHg. See **CHAPTER 7** for further detail on management of diabetic patients.

### 8.2.3 Evaluation of Hypertension Stage in the Health Center Integrated Chronic Care Clinic

After assessing for comorbid/complicating factors and evidence of hypertensive emergency, patients are classified according to hypertension severity. Patients with higher degrees of hypertension and/or comorbid factors receive more aggressive treatment according to the high-risk, point-based system above (**TABLE 8.1**). **TABLE 8.2** outlines the initial treatment strategy based on risk and hypertension category. **SECTION 8.3** and **TABLE 8.3** outline a step-by-step approach to antihypertensive medication selection.

#### 8.2.3.1 Treatment of Higher-Risk Stage 1 Hypertension in the Health Center Integrated Chronic Care Clinic

Patients with higher-risk stage 1 hypertension (BP 140/90–159/99 mmHg and ≥ 2 high risk points; see **TABLE 8.1**) who have failed a six-month trial of lifestyle modification should be started on one antihypertensive at the starting dose (**TABLE 8.3**). Patients with diabetes or renal failure will also fall into this category. These patients should follow up at the health center chronic care clinic for a blood pressure check and medication dose titration in three months.

#### 8.2.3.2 Evaluation of Proteinuria in Stage 2 and Stage 3 Hypertension in the Health Center Integrated Chronic Care Clinic

Patients with stage 2 or greater hypertension (BP ≥ 160/100 mmHg) are at increased risk of developing renal failure. The presence of renal failure in these patients will change treatment strategies. For this reason, we advocate checking a urine dipstick for proteinuria as a rough marker of renal dysfunction. Patients with greater than 2+ proteinuria should be referred to the district hosptial to have their creatinine checked. Patients with a creatinine less than 200 μmol/L and proteinuria should be started on an ACE inhibitor as first-line therapy for its established renal protective effects.

#### 8.2.3.3 Evaluation of Glycosuria in Stage 2 and Stage 3 Hypertension or Overweight Patients in the Health Center Integrated Chronic Care Clinic

Patients with hypertension and overweight are at increased risk for diabetes. Those who are found to have any glucose on their urine dipstick should receive confirmatory testing with either a fasting glucose or a hemoglobin A1C. Patients confirmed to have diabetes should be managed

according to the diabetes guidelines in **CHAPTER 7**. They will also have a lower goal blood pressure of ≤ 130/90 mmHg.

#### 8.2.3.4 Treatment of Stage 2 Hypertension in the Health Center Integrated Chronic Care Clinic

Patients with stage 2 hypertension (BP 160/100–179/109) should be started on two antihypertensives at starting doses (**TABLE 8.3**)**.** Two drugs are started because this level of hypertension is usually not controlled with one agent alone. These patients should follow up in 3 months at the health center chronic care clinic.

#### 8.2.3.5 Treatment of Asymptomatic Stage 3 Hypertension in the Health Center Integrated Chronic Care Clinic

Patients with asymptomatic stage 3 hypertension should likewise be started on two-drug therapy at starting doses (**TABLE 8.3**). Given their degree of hypertension, these patients are at high risk of complications, such as heart and renal failure. They should all be referred to the district level NCD clinic for further evaluation urgently, within 1–2 weeks.

In the district NCD clinic, patients should be re-evaluated for signs of heart failure. Patients with any such signs or symptoms likely have hypertensive heart disease and should have an echocardiograph performed (see **CHAPTER 4** and **PROTOCOL 4.1** for diagnosis of heart failure).

All patients should have creatinine levels checked. Patients under 40 who have a normal creatinine should have other causes of secondary hypertension investigated (**PROTOCOL 8.3**).

Patients should be started on two anti-hypertensive medications at the lowest dose. Patients without evidence of heart or renal failure may be referred back to the health center chronic care clinic for ongoing management. There they should continue to be followed closely with follow-up visits every 1–2 weeks until their treatment is stabilized. Patients with evidence of heart or renal failure or those who have secondary hypertension will require continued follow-up at the district-level NCD clinic.

**TABLE 8.2 Initiation of Hypertension Treatment According to Stage and Risk Factors**

| Stage | Blood pressure range | Treatment | Clinic follow-up |
|---|---|---|---|
| Stage 1<br>**AND**<br>≤ 1 high risk point (TABLE 8.1) | 140/90–159/99 mmHg | Do not start medications.<br>Counsel on salt intake and weight loss if indicated. | 12 months in acute care |
| Stage 1<br>**AND**<br>≥ 2 high risk points (TABLE 8.1)<br>**AND**<br>No trial of lifestyle modification | 140/90–159/99 mmHg | Do not start medications.<br>Counsel on salt intake and weight loss if indicated. | 6 months in acute care |
| Stage 1<br>**AND**<br>≥ 2 high risk points (TABLE 8.1)<br>**AND**<br>Failed 6-month trial of lifestyle modification | 140/90–159/99 mmHg | Start first-line medication at lowest dose | 3 months in health center integrated chronic care clinic |
| Stage 2 | 160/100–179/109 mmHg | Start first- and second-line medications at lowest dose | 3 months in health center integrated chronic care clinic |
| Stage 3<br>**WITHOUT**<br>Danger signs* | ≥ 180/110+ mmHg | Start first- and second-line medications at lowest dose | 1–2 weeks in district level NCD clinic |
| Stage 3<br>**WITH**<br>Danger signs* | ≥ 180/110+ mmHg | Initiate therapy listed in TABLE 8.4. Transfer to district hospital for inpatient management | |

* Danger signs include acute dyspnea, visual changes, headaches.

## 8.3 Recommended Hypertension Medications and Dosing

TABLE 8.3 shows the usual order in which medications should be started for hypertension management in adults. This order was chosen based on safety, side-effect profile, cost, and ease of dosing. Just as some of these factors (such as cost) vary between countries, so may the ordering of preferred anti-hypertensive medications in different settings. APPENDIX B lists our cost estimates for each medication.

In the presence of some comorbid conditions, such as proteinuria, renal failure, and pregnancy, different medications may be preferred. These exceptions are noted in the text below and in TABLE 8.5, TABLE 8.6, and TABLE 8.15.

**First-line agents.** For most patients, hydrochlorothiazide is the best medication to start initially. It is extraordinarily cheap, taken only once

a day, and the incidence of clinically significant side effects such as hypokalemia are low. However, in some circumstances, such as pregnancy, renal failure, or diabetes, a different medication should be used first (see **TABLE 8.5**, **TABLE 8.6**, **and TABLE 8.15**).

**Second-line agents.** When a patient's dose of the first-line medication has been maximized without achieving adequate blood pressure control, another medication must be started. For most patients, this will be an indication for starting a calcium-channel blocker (such as amlodipine or nifedipine). Patients with stage 2 or 3 hypertension will likely need at least 2 medications to achieve blood pressure control. In these situations, patients should be initiated on the starting dose of both the first- and second-line agents at their first visit.

**Third-line agents.** In many patients, two medications even at their maximum dose may not be enough to achieve blood pressure control. This is particularly true for patients with stage 3 hypertension. ACE inhibitors (lisinopril or captopril) are the preferred third-line agent after the maximum dose of hydrochlorthiazide and amlodipine have been reached. ACE inhibitors are contraindicated in pregnancy and renal failure (creatinine ≥ 200 μmol/L).

**Fourth-line agents.** Some patients may have hypertension that is particularly resistant to blood pressure medications. Four medications for hypertension may be needed. In general, atenolol is the fourth-line antihypertensive of choice. Although it is inexpensive, the effectiveness of atenolol in reducing central blood pressure and preventing adverse cardiovascular outcomes has been called into question.[13]

**Fifth-line agents.** These medications should rarely be used for hypertension management in the absence of a specific indication. Although effective, methyldopa and hydralazine require multiple doses per day and cost significantly more than other available medication. Paradoxically, these medications are frequently the most available in resource-poor settings due to their safety in pregnancy (see **SECTION 8.9**).

**TABLE 8.3 Recommended Hypertension Medications and Dosing for Most Adult Patients**

| First-line drug | Starting dose | Increase dose by | Maximum dose | Notes |
|---|---|---|---|---|
| **Hydrochlorothiazide** | 12.5 mg 1x/day | 12.5 mg 1x/day | 25 mg 1x/day | Can cause hypokalemia<br>Not effective in the setting of severe renal failure (creatinine ≥ 300 µmol/L) |
| **Second-line drug** | **Starting dose** | **Increase dose by** | **Maximum dose** | **Notes** |
| **Amlodipine** | 5 mg 1x/day | 5 mg 1x/day | 10 mg 1x/day | Can cause lower-extremity edema |
| **Third-line drug** | **Starting Dose** | **Increase dose by** | **Maximum dose** | **Notes** |
| **Lisinopril** | 5 mg 1x/day | 5 mg 1x/day | 20 mg 1x/day | Contraindicated in pregnancy and renal failure (creatinine ≥ 200 µmol/L)<br>Can cause cough |
| **Captopril** | 12.5 mg 3x/day | 12.5 mg 3x/day | 50 mg 3x/day | |
| **Fourth-line drug** | **Starting dose** | **Increase dose by** | **Maximum dose** | **Notes** |
| **Atenolol** | 25 mg 1x/day | 25 mg 1x/day | 50 mg 1x/day | Contraindicated if heart rate ≤ 55 bpm<br>Use with caution in renal failure, since atenolol is renally cleared |
| **Fifth-line drug** | **Starting dose** | **Increase dose by** | **Maximum dose** | **Notes** |
| **Hydralazine** | 25 mg 3x/day | 25 mg 3x/day | 50 mg 3x/day | Safe in pregnancy<br>Headache common side effect of hydralazine |
| **Methyldopa** | 250 mg 2x/day | 250 mg 2x/day | 500 mg 2x/day | Safe in pregnancy |

## 8.4 Recognition and Management of Hypertensive Emergency in Adults

Acute rises in blood pressure can result in end-organ damage in a matter of hours. These hypertensive emergencies usually occur at blood pressures above 180 mmHg systolic or 110 mmHg diastolic. Signs of a hypertensive emergency include headache and blurred vision caused by increased intracranial pressure, dyspnea caused by an acute stiffening of the heart and back-up of fluid into the lungs, and hematuria or flank pain caused by injury to the kidneys.

Patients reporting such symptoms with blood pressures of 180/110 mmHg or greater should be treated immediately with medications to lower their blood pressure by approximately 25% in the first hour.

Because the body adjusts to hypertension over time, lowering blood pressure too rapidly can decrease blood flow to the brain and cause clinical deterioration. **TABLE 8.4** lists medications recommended for acute management of hypertensive emergency.

All patients with suspected hypertensive emergency should be transferred to the nearest district hospital for inpatient management.

**TABLE 8.4 Recommended Medications for Management of Hypertensive Emergency (Adult Dosing)**

| Medication | Dosing | Notes |
|---|---|---|
| **Nifedipine** (immediate release) | 10 mg orally | |
| **Captopril** | 25 mg orally | Contraindicated in pregnancy and renal failure (Cr ≥ 200 μmol/L) |
| **Hydralazine** | 25 mg orally | |
| **Furosemide** | 40 mg orally or 20 mg IV | If evidence of pulmonary congestion |

## 8.5 Renal Dysfunction in Hypertension

Hypertension and renal dysfunction often coexist. When the kidneys no longer work well enough to dispose of excess fluid, blood pressure may increase. Hypertension may also lead to renal failure by putting increased stress on the kidney's filtering system. Controlling blood pressure with antihypertensives can slow the progression of renal disease. However, certain medications are either dangerous or no longer work well in the setting of renal failure, as explained below.

**TABLE 8.5 Hypertension Medications and Dosing in Setting of Proteinuria or Mild Renal Failure (CKD 1-3, Creatinine 100–199 µmol/L)**

| First-line drug | Starting dose | Increase dose by | Maximum dose | Notes |
|---|---|---|---|---|
| **Lisinopril** | 5 mg 1x/day | 5 mg 1x/day | 20 mg 1x/day | Contraindicated in pregnancy and renal failure (creatinine ≥ 200 µmol/L)<br>Can cause cough |
| **Captopril** | 12.5 mg 3x/day | 12.5 mg 3x/day | 50 mg 3x/day | |
| **Second-line drug** | **Starting dose** | **Increase dose by** | **Maximum dose** | **Notes** |
| **Hydrochlorothiazide** | 12.5 mg 1x/day | 12.5 mg 1x/day | 25 mg 1x/day | Can cause hypokalemia<br>Not effective in the setting of severe renal failure (creatinine ≥ 300 µmol/L) |
| **Third-line drug** | **Starting dose** | **Increase dose by** | **Maximum dose** | **Notes** |
| **Amlodipine** | 5 mg 1x/day | 5 mg 1x/day | 10 mg 1x/day | Can cause lower-extremity edema |
| **Fourth-line drug** | **Starting dose** | **Increase dose by** | **Maximum dose** | **Notes** |
| **Atenolol** | 25 mg 1x/day | 25 mg 1x/day | 50 mg 1x/day | Contraindicated if heart rate ≤ 55 bpm<br>Use with caution in renal failure as is renally cleared |
| **Fifth-line drug** | **Starting dose** | **Increase dose by** | **Maximum dose** | **Notes** |
| **Hydralazine** | 25 mg 3x/day | 25 mg 3x/day | 50 mg 3x/day | Safe in pregnancy. Headache common side effect |
| **Methyldopa** | 250 mg 2x/day | 250 mg 2x/day | 500 mg 2x/day | Safe in pregnancy |

### 8.5.1 Proteinuria or Mild to Moderate Renal Failure (Creatinine between 100–199 µmol/L)

Proteinuria is an early sign of renal dysfunction. Mild to moderate renal failure (chronic kidney disease stages 1 through 3) is typically present at creatinine levels between 100 and 199 µmol/L in adults. ACE inhibitors help decrease proteinuria and prevent further renal damage in this setting. ACE inhibitors should be started as the first-line agent in all patients with proteinuria or mild to moderate renal failure unless contraindications are present. Contraindications include a creatinine level ≥ 200 µmol/L (≥ 2.3 mg/dL) and pregnancy.

**TABLE 8.6 Recommended Hypertension Medications and Dosing in Setting of Severe Renal Failure (Creatinine ≥ 200 µmol/L)**

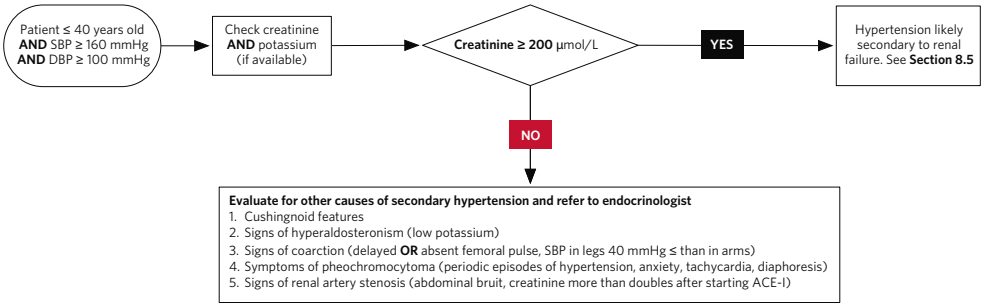
| First-line drug | | Starting dose | Increase dose by | Maximum dose | Notes |
|---|---|---|---|---|---|
| If Cr < 300 µmol/L | **Hydrochlorothiazide** | 12.5 mg 1x/day | 12.5 mg 1x/day | 25 mg 1x/day | Can cause hypokalemia |
| If Cr ≥ 300 µmol/L | **Furosemide** | 20 mg 1x/day | 20 mg 1x/day | 40 mg 1x/day | |
| **Second-line drug** | | **Starting dose** | **Increase dose by** | **Maximum dose** | **Notes** |
| **Amlodipine** | | 5 mg 1x/day | 5 mg 1x/day | 10 mg 1x/day | Can cause lower-extremity edema |
| **Third-line drug** | | **Starting dose** | **Increase dose by** | **Maximum dose** | **Notes** |
| **Atenolol** | | 25 mg 1x/day | 25 mg 1x/day | 100 mg 1x/day | Contraindicated if heart rate ≤ 55 bpm<br>Use with caution in renal failure |
| **Fourth-line drug** | | **Starting dose** | **Increase dose by** | **Maximum dose** | **Notes** |
| **Hydralazine** | | 25 mg 3x/day | 25 mg 3x/day | 50 mg 3x/day | Safe in pregnancy<br>Headache common side effect |
| **Methyldopa** | | 250 mg 2x/day | 250 mg 2x/day | 500 mg 2x/day | Safe in pregnancy |

If a patient is found to have a severely elevated creatinine ≥ 200 µmol/L (≥ 2.3 mg/dL), hydrochlorothiazide should still be the first-line agent. However, in the case of even more severe renal dysfunction (creatinine ≥ 300 µmol/L or 3.4 mg/dL), hydrochlorothiazide loses its efficacy. In this scenario, a loop diuretic (furosemide) should be substituted as the first-line agent. Calcium-channel blockers (amlodipine and nifedipine) are also safe in renal failure, and should be the next choice. Atenolol can also be used, but the dose should not exceed 50 mg/day in these patients. This is because atenolol is excreted by the kidneys. ACE inhibitors and spironolactone should be avoided due to the risk of hyperkalemia. Because these patients are at risk for multiple complications, they should be followed at the level of the district hospital.

## 8.6 Evaluation and Management of Hypertension in Patients ≥ 15

Most essential hypertension will occur in patients over the age of 40. If a patient presents with moderate to severe hypertension at a younger age, secondary causes of hypertension are more likely to be a cause (see **TABLE 8.7**). **PROTOCOL 8.3** outlines a diagnostic approach to patients between the ages of 15 and 40. **SECTION 8.8** discusses an approach to hypertension in children younger than 15.

### PROTOCOL 8.3 Initial Diagnosis and Management of Suspected Secondary Hypertension in Adults (age ≥ 15)




Renal failure, often due to chronic glomerulonephritis, is by far the most common reason for secondary hypertension in settings such as rural Africa. Therefore, adult patients who are under 40 years of age with blood pressure over 160 mmHg systolic or 100 mmHg diastolic should be referred to a health facility where creatinine can be checked. If creatinine is normal, the patient should be evaluated for other signs or symptoms suggestive of a secondary cause of hypertension, and referred accordingly. While investigating the secondary cause of hypertension, treatment may be initiated according to the protocol for hypertension (see **PROTOCOL 8.2**).

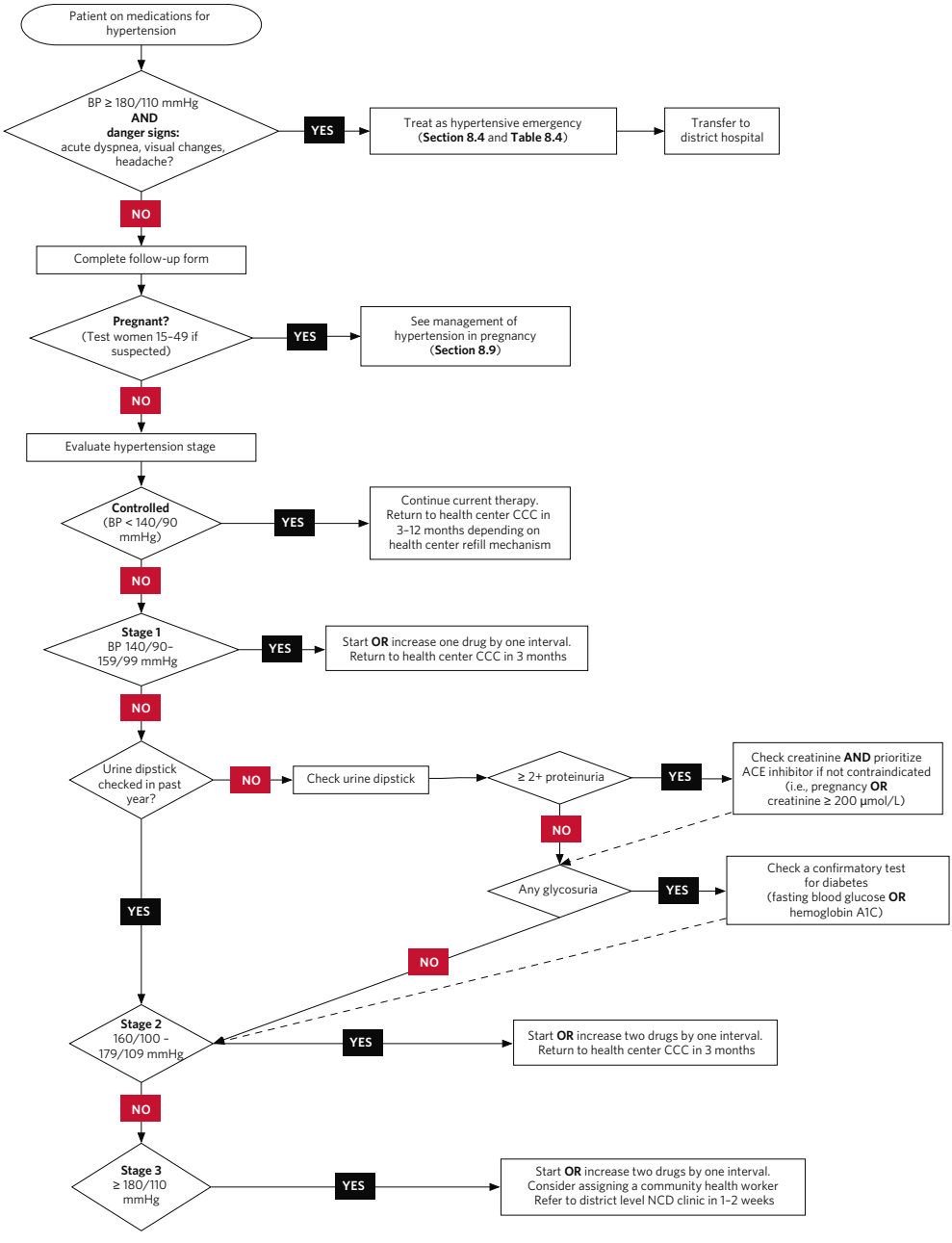
**TABLE 8.7 Causes of Secondary Hypertension**

| Cause | Findings | Management |
|---|---|---|
| **Renal failure** | Elevated creatinine (≥ 200 µmol/L or 2x normal creatinine for age in children) | See **SECTION 8.5** for adults and **SECTION 8.8.4** for children |
| **Cushing's syndrome (hypercortisolism)** | Truncal obesity, round face, extremity wasting, hypokalemia | Refer to tertiary referral center for endocrinology consultation |
| **Hyperaldosteronism** | Hypokalemia | Refer to tertiary referral center for endocrinology consultation |
| **Pheochromocytoma** | Periodic episodes of hypertension, anxiety, tachycardia, diaphoresis | Refer to tertiary referral center for endocrinology consultation |
| **Coarctation** | Delayed or absent femoral pulse; SBP in legs 40 mmHg ≤ than SBP in arms | Refer to tertiary referral center for echocardiography and cardiology consultation |
| **Renal artery stenosis** | Abdominal bruit; creatinine more than doubles after starting ACE inhibitor | Refer to tertiary referral center for renal ultrasound and nephrology consultation |

## 8.7 Follow-Up Treatment for Hypertension in Adults

**PROTOCOL 8.4** outlines an approach to ongoing management of adult patients who are followed in the chronic care clinics for hypertension.

### PROTOCOL 8.4 Follow-Up Visit for Chronic Hypertension in Adults at Health Center Integrated Chronic Care Clinic




BP = Blood pressure
CCC = Chronic care clinic

On return visits, the clinician should re-evaluate the patient, first for signs of hypertensive emergency, and then for any change in complicating or comorbid factors. The clinician should then review the effectiveness and appropriateness of the current medication regimen.

### 8.7.1 Management of Well-Controlled Hypertension on Follow-Up

Patients with well-controlled hypertension should have their current regimen continued. These patients do not need to be seen in the clinic very often. However, it may be difficult for the pharmacy to give patients multi-month supplies of medication without causing stock-outs. Therefore, the time between clinic visits will depend mostly on the dispensing capacity of the pharmacy and the refill policy of the health center.

### 8.7.2 Follow-Up of Stage 1 Hypertension

For patients with stage 1 hypertension (between 140/90 and 159/99 mmHg), the blood pressure medication should be increased by one interval (see **TABLE 8.3**).

### 8.7.3 Follow-Up of Stage 2 Hypertension

Patients with stage 2 hypertension (between 160/100 and 179/109 mmHg) should have two medications started or increased by one interval (see **TABLE 8.3**). Patients in this category should have a urine dipstick checked once a year. Patients with proteinuria and a creatinine level < 200 µmol/L should have an ACE inhibitor started as part of their regimen. Patients with any glycosuria should undergo a confirmatory test for diabetes, such as a hemoglobin A1C or a fasting glucose finger-stick.

### 8.7.4 Follow-Up of Stage 3 Hypertension

Patients with stage 3 hypertension (≥ 180/110 mmHg) should also have two medications started or increased by one interval (see **TABLE 8.3**). Patients in this category should also have a urine dipstick checked once a year, and patients with proteinuria should have an ACE inhibitor started as part of their regimen. Patients with any glycosuria should undergo a confirmatory test for diabetes, such as a hemoglobin A1C or a fasting glucose finger-stick. In addition, patients in this category need closer follow-up and should be given an appointment within 1–2 weeks. Some of these patients may benefit from a community health worker to provide support and ensure good medication adherence.

## 8.8 Diagnosis and Management of Hypertension in Children (Age < 15)

Hypertension in children (defined here as ≥ 95th percentile systolic or diastolic blood pressure for age) is rare, but when present often signals serious disease. Most hypertension in children is due to secondary causes (see **TABLE 8.7**). The most common secondary cause is renal failure.

### 8.8.1 Initial Diagnosis of Hypertension in Children

**PROTOCOL 8.5** outlines an approach to the initial management of pediatric patients found to have hypertension. Blood pressure is not routinely measured on all children presenting to health-center acute care clinics. Children only need to have blood pressure checked if there are signs or symptoms that are concerning for either elevated or low blood pressure. These should include any child presenting to the health center with edema or complaints about changes in urine color. Children who have new onset seizures or are ill-appearing should also have their blood pressure checked. Health centers must be stocked with functioning pediatric cuffs. In cases in which a pediatric cuff is not available, clinicians should use the small adult cuff (the standard cuff for a low BMI population) as a thigh cuff. Appropriate cuff size is when 100% of the bladder of the cuff wraps around the circumference of the arm. When in doubt, choose the larger cuff size, as too small a cuff will give falsely high BP readings. Table 8.8 lists blood pressure percentiles for age for children (< 15 years). This information is also listed in **APPENDIX E**. We define hypertension in a child as a systolic or diastolic blood pressure ≥ 95th percentile for age.

**PROTOCOL 8.5 Initial Diagnosis and Management of Hypertension in Children in the Acute Care Clinic**

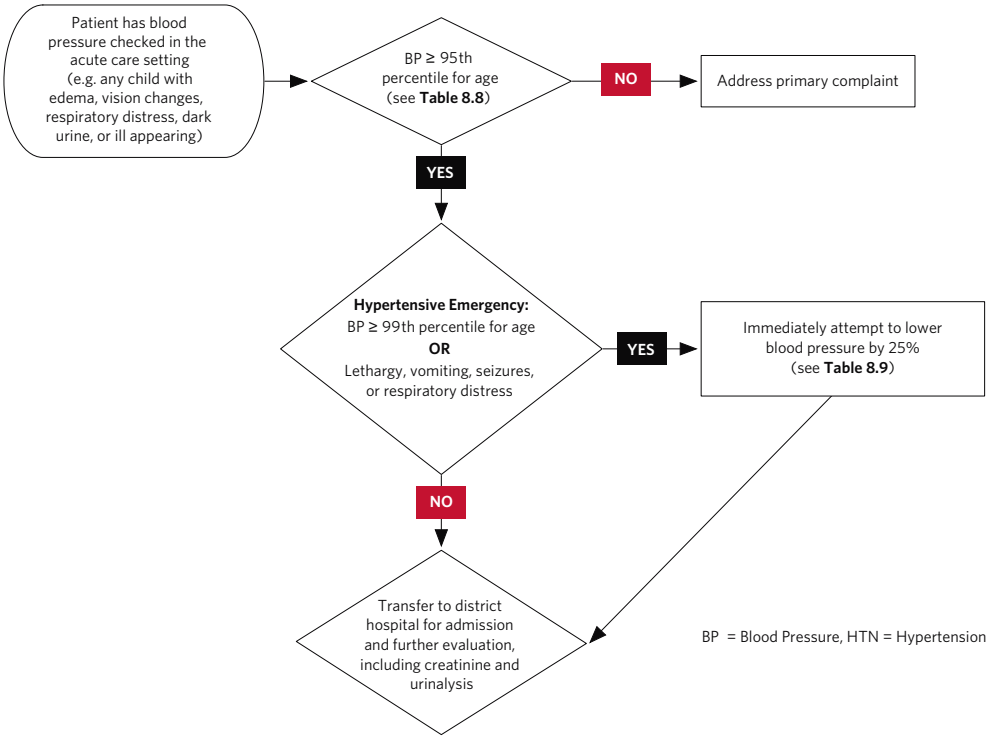


**TABLE 8.8 Blood pressure ranges for children**

| Age (year) | | Blood pressure percentile (mmHg) (for 25th percentile of height) | | | |
|---|---|---|---|---|---|
| | | 50th percentile | 90th percentile | 95th percentile | 99th percentile |
| 1 | Systolic | 83 | 97 | 101 | 108 |
| | Diastolic | 36 | 51 | 55 | 63 |
| 2 | Systolic | 87 | 100 | 104 | 111 |
| | Diastolic | 41 | 56 | 60 | 68 |
| 3 | Systolic | 89 | 103 | 107 | 114 |
| | Diastolic | 45 | 60 | 64 | 72 |
| 4 | Systolic | 91 | 105 | 109 | 116 |
| | Diastolic | 49 | 64 | 68 | 76 |
| 5 | Systolic | 93 | 106 | 110 | 118 |
| | Diastolic | 52 | 67 | 71 | 79 |
| 6 | Systolic | 94 | 108 | 112 | 119 |
| | Diastolic | 54 | 69 | 73 | 81 |
| 7 | Systolic | 95 | 109 | 113 | 120 |
| | Diastolic | 56 | 71 | 75 | 83 |
| 8 | Systolic | 97 | 110 | 114 | 122 |
| | Diastolic | 58 | 72 | 77 | 85 |
| 9 | Systolic | 98 | 112 | 116 | 123 |
| | Diastolic | 59 | 74 | 78 | 86 |
| 10 | Systolic | 100 | 114 | 117 | 125 |
| | Diastolic | 60 | 74 | 79 | 86 |
| 11 | Systolic | 102 | 115 | 119 | 127 |
| | Diastolic | 60 | 75 | 79 | 87 |
| 12 | Systolic | 104 | 118 | 122 | 129 |
| | Diastolic | 61 | 75 | 80 | 88 |
| 13 | Systolic | 106 | 120 | 124 | 131 |
| | Diastolic | 61 | 76 | 80 | 88 |
| 14 | Systolic | 109 | 123 | 127 | 134 |
| | Diastolic | 62 | 77 | 81 | 89 |
| 15 | Systolic | 112 | 125 | 129 | 136 |
| | Diastolic | 63 | 78 | 82 | 90 |

### 8.8.2 Recognition and Management of Hypertensive Emergency in Children

Patients with a very high blood pressure (≥ 99th percentile for age) and/or signs of severe end-organ damage, such as lethargy, severe headaches or vision changes, seizures or respiratory distress, should have their blood pressure lowered by 25% if possible while transport is being arranged. **TABLE 8.9** lists medications and dosing to acutely reduce blood pressure in pediatric patients. As in adults, dropping blood pressure too quickly can be very dangerous. If correct dosing is not available for smaller children, the clinician should focus on fast transfer and avoid over-medication.

**TABLE 8.9 Recommended Medications and Dosing for Pediatric Patients For Hypertensive Emergency (BP ≥ 99th percentile or ≥ 95th percentile with symptoms)**

| | < 10 kg | 10 kg | 15 kg | 20 kg | 30 kg | ≥ 40 kg |
|---|---|---|---|---|---|---|
| **Hydralazine** 50 mg tablet | See mg/kg dosing* | See mg/kg dosing* | See mg/kg dosing* | 12.5 mg ¼ tab x 1 | 12.5 mg ¼ tab x 1 | 25 mg ½ tab x 1 |
| **Initial dose:** 0.5 mg/kg/dose. **Maximum dose:** 25 mg/dose. | | | | | | |
| **Nifedipine** 10 mg tablet | See mg/kg dosing* | 2.5 mg ¼ tab x 1 | 5 mg ½ tab x 1 | 10 mg 1 tab x 1 | 10 mg 1 tab x 1 | 10 mg 1 tab x 1 |
| **Initial dose:** 0.25-0.5 mg/kg/dose. **Maximum dose**: 10 mg/dose. | | | | | | |
| **Captopril** 25 mg tablet | See mg/kg dosing* | 6.25 mg ¼ tab x 1 | 6.25 mg ¼ tab x 1 | 12.5 mg ½ tab x 1 | 12.5 mg ½ tab x 1 | 25 mg 1 tab x 1 |
| **Initial dose:** 0.3–0.5 mg/kg/dose. **Maximum dose:** 3 mg/kg/dose. | | | | | | |

* Note that dosing medications for small children may require crushing pills and diluting. This should only be done under the supervision of an experienced clinician.

### 8.8.3 Initial Management of Children with Hypertension

Children with newly diagnosed hypertension (≥ the 95th percentile for age) who are not in a hypertensive crisis do not need their blood pressure acutely decreased before being admitted to the hospital. However, these children should still be hospitalized for an evaluation of the cause of the hypertension and initiation of treatment.

In the inpatient setting, renal function should be evaluated with a creatinine and urinalysis. Most children will be found to have signs of renal dysfunction due to post-streptococcal glomerulonephritis, nephrotic syndrome, or untreated severe urinary tract infection. If renal function is normal, other causes of secondary hypertension should be investigated. These secondary causes are similar to those seen in young adults with hypertension (see **TABLE 8.7**).

### 8.8.4 Follow-Up of Children with Hypertension

After discharge, children should follow up in the district NCD clinic within 1–2 weeks for blood pressure evaluation and medication adjustment (see **PROTOCOL 8.6**).

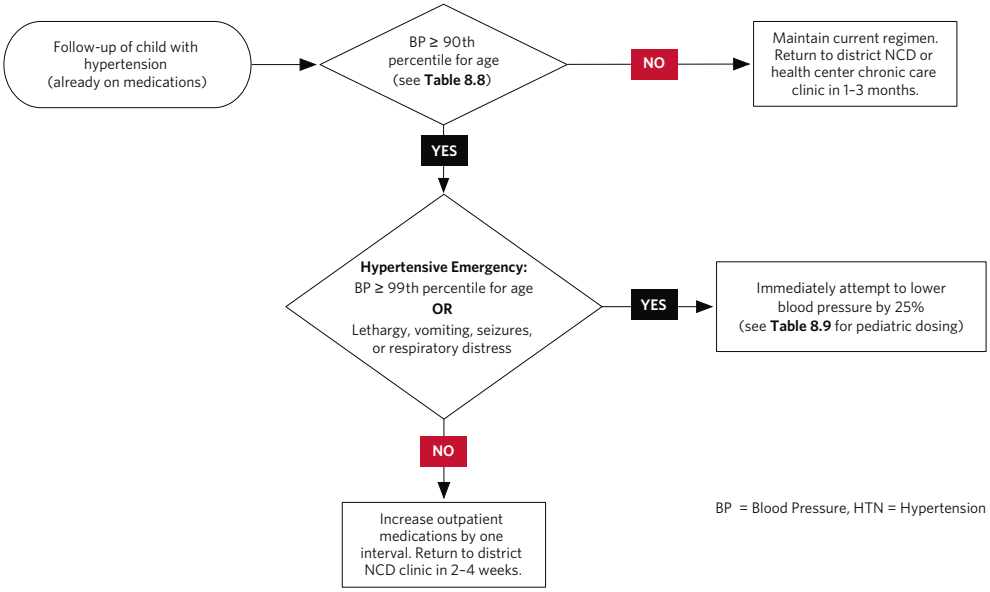
On a follow-up visit, the child should be evaluated for level of blood pressure as well as signs and symptoms of organ dysfunction. If there has been a change in clinical status, creatinine should be checked, if available. Children and their family members should be asked about medication adherence. Some children may benefit from a community health worker if adherence is a problem.

Children who have well-controlled blood pressure (< 90th percentile for age) should be kept on their current regimen. Care for these children may be transferred to the health-center level for at least some of their visits if this is more convenient for the patient and family. As a general rule, these children should be seen every 1–3 months at the health center and 2 times per year in the district NCD clinic. Children with difficult-to-control blood pressure or renal failure should continue to be followed primarily at the district hospital, where electrolytes can be monitored.

If the patient has a persistently elevated blood pressure and signs or symptoms of a hypertensive emergency, the child should be managed as described above (**SECTION 8.8.2**, **TABLE 8.9**) and re-hospitalized.

Children with mildly to moderately elevated blood pressure (≥ 90th percentile for age) despite good adherence to their medication regimen should have their antihypertensive medication dosing increased (see **TABLE 8.10**). As with adults, one medication should be increased until either the maximum dose is reached or side effects are encountered. At this point, a second agent should be added. Children should have follow-up visits every 2–4 weeks in the district NCD clinic until blood pressure is controlled.

## PROTOCOL 8.6 Outpatient Follow-Up of Children with Hypertension




## TABLE 8.10 Recommended Medications and Dosing for Pediatric Patients with Chronic Hypertension (BP ≥ 95th percentile)

| First-line drug | | | | | | |
|---|---|---|---|---|---|---|
| **Starting doses** | **≤ 10 kg** | **10 kg** | **15 kg** | **20 kg** | **30 kg** | **≥ 40 kg** |
| **Hydrochlorothiazide** 25 mg tablet | See mg/kg dosing* | 12.5 mg ½ tab daily | 12.5 mg ½ tab daily | 25 mg 1 tab daily | 25 mg 1 tab daily | 25 mg 1 tab daily |
| **Initial dose:** 1 mg/kg/day as one daily dose. **Maximum dose:** 3 mg/kg/day as one daily dose, up to 25 mg/day. **Notes:** May cause hypokalemia. Doses higher than 25 mg increase risk of hypokalemia without much additional blood pressure control. Use with caution in newborns, as they are more sensitive to electrolyte shifts. Should be stopped if progressive renal failure occurs. | | | | | | |
| **Second-line drug** | | | | | | |
| **Starting doses** | **≤ 10 kg** | **10 kg** | **15 kg** | **20 kg** | **30 kg** | **≥ 40 kg** |
| **Amlodipine** 10 mg tablet | See mg/kg dosing* | 2.5 mg ¼ tab daily | 2.5 mg ¼ tab daily | 2.5–5 mg ¼–½ tab daily | 2.5–5 mg ¼–½ tab daily | 5–10 mg ½–1 tab daily |
| **Initial dose:** 0.1 mg/kg/day. **Maximum dose:** 10 mg once daily. **Notes:** Not well studied in children less than 6 years of age. | | | | | | |

| **Third-line drug** | | | | | | |
|---|---|---|---|---|---|---|
| **Starting doses** | **≤ 10 kg** | **10 kg** | **15 kg** | **20 kg** | **30 kg** | **≥ 40 kg** |
| **Lisinopril**<br>10 mg tablet | See mg/kg dosing* | See mg/kg dosing* | See mg/kg dosing* | 2.5–5 mg<br>¼–½ tab daily | 2.5–5 mg<br>¼–½ tab daily | 5–10 mg<br>½–1 tab daily |
| **Initial dose:** 0.07 mg/kg/day as one daily dose.<br>**Maximum dose:** 0.6 mg/kg/day or 20 mg as one daily dose.<br>**Notes:** Contraindicated in pregnancy and renal failure (creatinine ≥ 2x normal for age). Can cause cough. | | | | | | |
| **Captopril**<br>25 mg tablet | See mg/kg dosing* | 6.25 mg<br>¼ tab 2x/day | 6.25 mg<br>¼ tab 2x/day | 6.25–12.5 mg<br>¼–½ tab 2x/day | 6.25–12.5 mg<br>¼–½ tab 2x/day | 12.5–25 mg<br>½–1 tab 2x/day |
| **Initial dose:** 0.3–0.5 mg/kg/dose given 2 times/day.<br>**Maximum dose:** 6 mg/kg/day divided into 2 doses/day.<br>**Notes:** Contraindicated in pregnancy and renal failure (creatinine ≥ 2x normal for age). Can cause cough. | | | | | | |
| **Fourth-line drug** | | | | | | |
| **Starting doses** | **≤ 10 kg** | **10 kg** | **15 kg** | **20 kg** | **30 kg** | **≥ 40 kg** |
| **Atenolol**<br>50 mg tablet | See mg/kg dosing* | 12.5 mg<br>¼ tab daily | 12.5 mg<br>¼ tab daily | 12.5–25 mg<br>¼–½ tab daily | 25 mg<br>½ tab daily | 25–50 mg<br>½–1 tab daily |
| **Initial dose:** 0.5–1 mg/kg/day as one daily dose.<br>**Maximum dose:** 2 mg/kg/day as one daily dose, up to 100 mg/day.<br>**Notes:** Contraindicated if heart rate ≤ normal HR range for age. In renal failure, use half of normal recommended dose. | | | | | | |
| **Add if edema or Stage 4 chronic kidney disease (CKD 4)** | | | | | | |
| | **≤ 10 kg** | **10 kg** | **15 kg** | **20 kg** | **30 kg** | **≥ 40 kg** |
| **Furosemide**<br>40 mg tablet | See mg/kg dosing* | 10 mg<br>¼ tab daily | 10–20 mg<br>¼ tab daily | 20 mg<br>½ tab daily | 20–40 mg<br>½–1 tab daily | 20–80 mg<br>½–2 tabs daily |
| ***Oral***<br>**Initial dose:** 1–2 mg/kg/day as 1–2 doses. Do not start at more than 20 mg/dose.<br>**Maximum dose:** 4 mg/kg/dose given 2–4 times/day.<br>**Increase by:** 1 mg/kg/dose.<br>**Note:** Need to give higher dose range in renal failure. | | | | | | |

* Dosing medications for small children may require crushing pills and diluting. This should only be done under the supervision of an experienced clinician.

### 8.8.5 Management of Hypertension in Children with Renal Failure

The management strategy for children with both hypertension and renal failure is very similar to that in adults. As with adults, treatment of blood pressure with appropriate medication in children can slow the progression of renal disease. **CHAPTER 6** discusses the diagnosis and management of renal failure in greater detail.

**TABLE 8.11** lists medications in the order of preference in renal failure.

### TABLE 8.11 Recommended Hypertension Medications for Pediatric Patients with Renal Failure

| For CKD 1-3 (GFR ≥ 30, creatinine < 2x normal value for age)* | |
|---|---|
| **First-line drug** | Lisinopril or Captopril |
| **Second-line drug** | Hydrochlorothiazide |
| **Third-line drug** | Amlodipine |
| **Fourth-line drug** | Atenolol** |
| **For CKD 4 or 5 (GFR < 30, creatinine ≥ 2x normal value for age)*** | |
| **First-line drug** | Furosemide |
| **Second-line drug** | Amlodipine |
| **Third-line drug** | Atenolol** |

* See TABLE 8.10 for dosing.

** In renal failure, use half of normal recommended dose.

For mild to moderate renal dysfunction (proteinuria, creatinine < 2x normal value for age, CKD 1-3), an ACE inhibitor is recommended as a first-line agent in children. Medications should be increased incrementally to reach desired blood pressure (< 90th percentile for age) as described above. See TABLE 8.10 for medication dosing. Note that atenolol dosing is reduced in renal failure, as the medication is excreted through the kidneys. Dosing should be half of that used for children without renal failure.

ACE inhibitors are not safe for use in children with severe renal failure, defined here as a creatinine ≥ 2x normal value for age, roughly corresponding with a GFR < 30 (CKD 4-5). At this level of renal failure, the risks of hyperkalemia become too high to justify its use in our setting. TABLE 8.11 lists medications in order of preference in severe renal failure. Most of these children will need to be followed at the district-level health center for electrolyte and creatinine monitoring.

## 8.9 Hypertension in Pregnancy

Hypertensive disorders account for approximately 9% of total maternal mortality in Africa.[14] The management of these conditions is complicated by the fact that many common antihypertensives cause birth defects. Few clinical trials have investigated treatment of hypertension in pregnancy. As a result, there is significant disagreement on the subject, and most current guidelines rely on expert opinion rather than well-designed studies.

Hypertension in pregnancy can be pre-existing (chronic) or caused by the pregnancy itself.[15] In normal pregnancy, blood pressure tends to fall. In this context, blood pressures above 140 mmHg systolic or 90 diastolic are considered elevated; blood pressures greater than 160 mmHg systolic or 110 mmHg diastolic are considered severely elevated.[16]

**TABLE 8.12** outlines the categories of hypertensive disorders in pregnancy. Treatment of hypertension does not alter the course of hypertensive disorders of pregnancy, given that anti-hypertensive medications do not affect the underlying pathophysiology of the disease. The one proven benefit of treating blood pressure in pregnancy is stroke prevention.[16] Providing magnesium to patients with severe preeclampsia has been shown to decrease the risk of seizures.

Proteinuria is a defining feature of preeclampsia. The gold standard for signficant proteinuria is the presence of 300 mg of protein in urine collected over a 24-hour period. Random protein-to-creatinine measurements with a ratio ≥ 0.19 correlate well with 24-hour urine protein measurements ≥ 300 mg. However, these tests may be impractical for wide-scale use in settings without well-developed lab infrastructure. Urine dipsticks are quick and inexpensive, but they are less sensitive and specific in detecting significant protein excretion in patients with suspected preeclampsia. Specificity improves with more strongly positive dipstick results. WHO's Integrated Management of Pregnancy and Childbirth (IMPAC) guidelines recommend using 3+ proteinuria as a marker of severe proteinura, and 2+ proteinuria as the threshold for diagnosing significant proteinuria. In our protocols, we have adopted the same proteinuria thresholds.[17,18]

Definitions of hypertensive disorders in pregnancy also incorporate the gestational age of pregnancy. However, accurate pregnacy dating can be difficult in resource-poor settings. Ultrasound offers the best estimation of gestational age, and several studies have shown these measurements can be easily taught.[19] In settings in which an ultrasound is not available and last menstrual period is not accurately known, fundal height may be used as a proxy for gestational age.[20,21] Since most complications of hypertension in pregnancy occur at greater than 34 weeks of gestational age, using a convervative threshold of 20 cm fundal height (typically equivalent to 20 weeks gestational age) should guarantee acceptable sensitivity.

The choice of antihypertensives is limited in pregnancy by the known potential for birth defects with ACE inhibitors, and lack of safety data for most other agents except for methyldopa, hydralazine, and nifedipine. Recommended agents include those that have been shown to be safe

and effective. These are listed in order of preference in **TABLE 8.15**. ACE inhibitors are contraindicated in pregnancy.

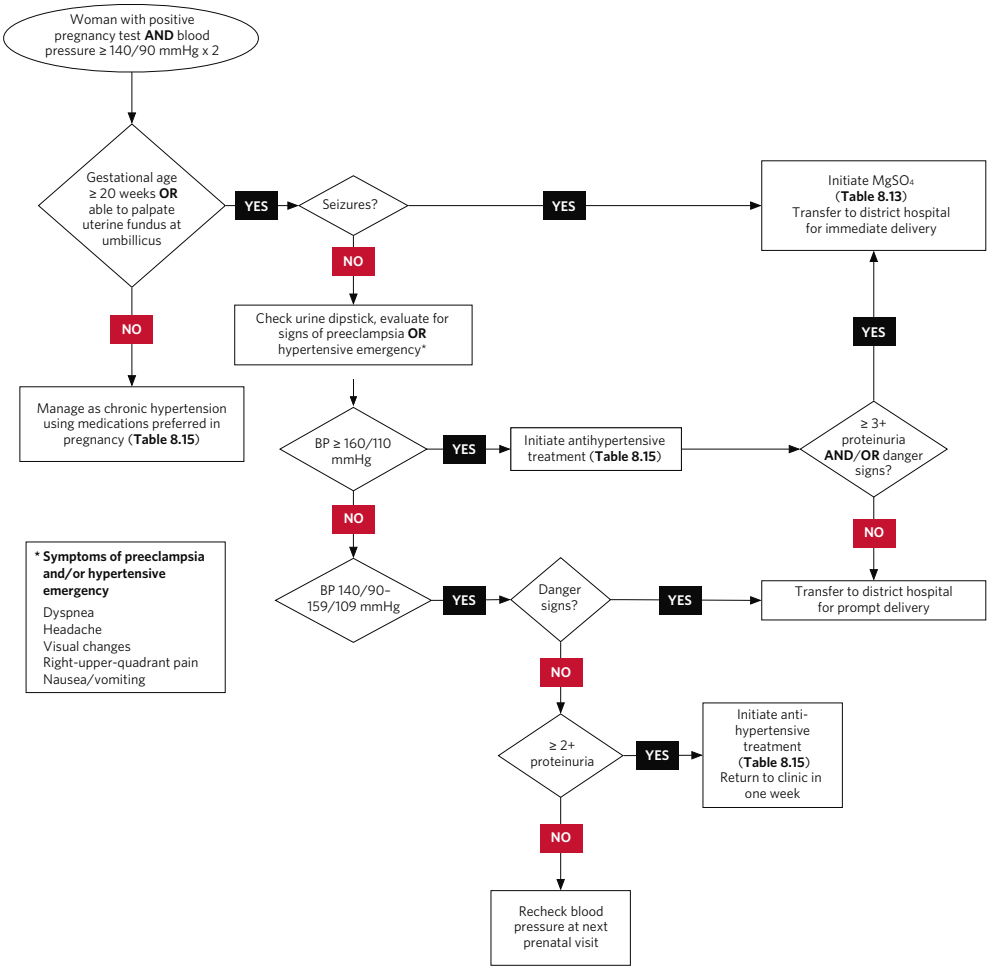
Traditionally, diastolic blood pressure has been used to guide treatment initiation in pregnancy, as it seems to better correlate with risk of developing seizures.[17] However, recent studies show that systolic blood pressure correlates better with risk of maternal stroke.[16] In our protocols, we have included both diastolic and systolic blood pressure as criteria for treatment initiation.

**TABLE 8.12 Hypertensive Disorders of Pregnancy**

| Classification | Definition | Risks | Role of antihypertensives |
|---|---|---|---|
| Chronic hypertension | BP ≥ 140/90 mmHg<br>**AND**<br>Diagnosis of hypertension prior to pregnancy or before 20 weeks of gestation | ≥ 20% will develop preeclampsia[22]<br>Placental abruption<br>Intrauterine growth retardation | Does not reduce the risk of developing preeclampsia<br>May reduce risk of maternal cerebral hemorrhage |
| Gestational hypertension | BP ≥ 140/90 mmHg<br>**AND**<br>Diagnoses or progression of hypertension after 20 weeks of gestation<br>**WITHOUT**<br>Significant proteinuria<br>Defined as ≥ 2+ on a urine dipstick | 50% will develop preeclampsia[23]<br>10% will develop severe preeclampsia | Does not reduce the risk of developing preeclampsia<br>May reduce risk of maternal cerebral hemorrhage |
| Preeclampsia | BP ≥ 140/90 mmHg<br>**AND**<br>Diagnosis or progression of hypertension after 20 weeks of gestation<br>**AND**<br>Significant proteinuria<br>Defined as ≥ 2+ on a urine dipstick | 25% will develop severe preeclampsia<br>Eclampsia (seizures)<br>Maternal stroke | Does not reduce the risk of developing severe preeclampsia<br>May reduce risk of maternal cerebral hemorrhage |
| Severe preeclampsia | Preeclampsia<br>**AND**<br>BP ≥ 160/110 mmHg<br>**OR**<br>≥ 3+ proteinuria<br>**OR**<br>Any symptom of end-organ damage (oliguria, right-upper-quadrant pain, severe persistent headache, cerebral hemorrhage, nausea, pulmonary edema, low platelets [≤ 100,000], severe intrauterine growth restriction, or transaminitis [≥ twice normal]) | Eclampsia (seizures)<br>Maternal stroke | Does not reduce the risk of developing severe preeclampsia<br>May reduce risk of maternal hemorrhage |

**PROTOCOL 8.7** outlines an algorithm for management of hypertension in pregnancy, defined as a confirmed blood pressure greater or equal to 140/90 mmHg on two separate occasions. At PIH-supported Rwanda MOH sites, prenatal providers manage hypertension in pregnancy; however, this may be a function appropriate for an integrated chronic care clinic in other settings.

## PROTOCOL 8.7 Management of Hypertension in Pregnancy




All women between the ages of 15 and 49 who present to either the acute care or the integrated chronic care clinic with hypertension are tested for pregnancy. Pregnant patients are referred to the prenatal clinic. Likewise, all pregnant women presenting for prenatal care should have their blood pressure measured at every visit.

### 8.9.1 Hypertension in Early Pregnancy (Chronic Hypertension)

Pregnancy-induced hypertension usually occurs in the third trimester. Therefore, patients with hypertension in the earlier stages of pregnancy likely have pre-exisiting hypertension. Here, we use a cut-off of less than 20 weeks gestational age and/or a fundal height less than 20 cm as the definition of early pregnancy. The management of these patients is similar to that of non-pregnant hypertensives, with the exception that different medications are preferred (see **TABLE 8.15**). These patients are at increased risk of developing preeclampsia and should be seen more frequently in the later stages of pregnancy.

### 8.9.2 Hypertension in Later Pregnacy (Gestational Hypertension and Preeclampsia)

Patients who develop hypertension, or whose hypertension progresses at greater than 20 weeks gestational age, are at higher risk of pre-eclampsia and eclampsia. **PROTOCOL 8.7** outlines an adaptation of the IMPAC algorithim for evaluation and treatment of these patients.[18]

### 8.9.3 Recognition and Management of Emergent Conditions

Patients who are actively seizing or have had seizures during late pregnancy should be immediately started on magnesium and transferred to the nearest district hospital for immediate delivery. See **TABLE 8.13** for loading and maintenance dosing.

**TABLE 8.13 Loading and Maintenance Dosing of Magnesium Sulfate in Eclampsia and Severe Preeclampsia (Adapted from IMPAC)[17,18]**

| |
|---|
| **Start with loading dose:**<br>Inject 4 grams (20 ml of 20% concentration) by IV over 20 minutes.<br>**AND**<br>Inject 5 grams (10 ml of 50% concentration) mixed with 1 ml of 1%–2% lidocaine IM in each buttock (for a total of 10 grams).<br>If unable to establish IV, give only IM dose as loading dose. |
| **If seizures recur after 15 minutes, give reloading dose:**<br>Inject 2 grams of 20% concentration IV over 5 minutes. |
| **Follow with maintenance dose:**<br>Inject 5 grams of 50% concentration IM mixed with 1 ml of 1%–2% lidocaine in alternate buttocks every four hours. |
| **Maximum total dose:**<br>40 g every 24 hours |
| **Side-effect monitoring:**<br>Monitor for respiratory depression (respiratory rate ≤ 16), loss of reflexes and decreased urinary output (≤ 100 ml/4 hrs). Injecting the magnesium too quickly increases the risk of respiratory or cardiac depression.<br>Stop the therapy if the respiratory rate falls below 16 per minute, patellar reflexes are absent, or urinary output is less than 100 mL over 4 hours.<br>For respiratory depression, give calcium gluconate 1 g IV (10 ml of 10% solution) over 10 minutes |
| **Other safety considerations**<br>Do not leave the patient by herself.<br>Place her on her left side.<br>Transfer immediately to district hospital unless delivery is imminent |

### 8.9.4 Screening for Preeclampsia

Patients with no history of seizure activity should be screened for preeclampsia with a urine dipstick and evaluation of symptoms of end-organ damage. These symptoms include right-upper-quadrant pain, headaches, visual changes (e.g., seeing spots), or lower-extremity edema.

### 8.9.5 Treatment of Preeclampsia According to Disease Classification

**Severe preeclampsia.** Severe preeclampsia is preeclampsia with a blood pressure ≥ 160/110 mmHg, or symptoms of end-organ damage, or greater than or equal to 3+ proteinuria. These patients should be started on antihypertensives and receive a loading dose of magnesium for seizure prophylaxsis, while being prepared for immediate transfer to the nearest district hospital for prompt delivery. Nifedipine is the fastest-acting antihypertensive that is safe in pregnancy. The second-line agent, methyldopa, has a longer onset of action (**TABLE 8.14**).

**Severe gestational hypertension.** Patients with severe hypertension (≥ 160/110 mmHg) without proteinuria or other signs of preeclampsia

should be started on antihypertensives and transferred to the nearest district hospital for admission (**TABLE 8.14**). Likewise, pregnant women with mild blood pressure elevation with any sign that could indicate preeclampsia (dyspnea, headache, vision changes, right-upper-quadrant pain, nausea, or vomiting) should be hospitalized for observation.

**TABLE 8.14 Recommended Medications for Management of Hypertension in Severe Preeclampsia**

| Medication | Dosing | Notes |
|---|---|---|
| **Nifedipine** (immediate release) | 10 mg orally | Fast acting |
| **Methyldopa** | 250 mg orally | Slower acting |

#### 8.9.5.1 Mild to Moderate Preeclampsia

Mild to moderate preeclampsia is defined by a blood pressure ≥ 140/90 but < 160/110 mmHg, and ≥ 2+ proteinuria and no signs or symptoms of severe preeclampsia. These patients should be started on antihypertensives and followed closely in the prenatal clinic (**TABLE 8.15**). If a woman is already on antihypertensives, she should have her medication dosage increased, with a goal blood pressure of 140–150/90–100 mmHg. Ideally, she will be admitted for observation for at least a 24-hour period and she should be given strict precautionary instructions to return to care immediately if she develops any of the symptoms of severe preeclampsia or has decreased fetal movement.

#### 8.9.5.2 Mild to Moderate Gestational Hypertension

Women with mild hypertension should not be started on medications. Patients already on medications should continue antihypertensive treatment with drugs appropriate for pregnancy.

**TABLE 8.15 Recommended Hypertension Medications and Dosing in Pregnancy**

| First-line drug | Starting dose | Increase dose by | Maximum dose | Notes |
|---|---|---|---|---|
| **Methyldopa** | 250 mg 2x/day | 250 mg 2x/day | 500 mg 2x/day | Best-proven safety in pregnancy, cheap, widely available |
| **Second-line drug** | **Starting dose** | **Increase dose by** | **Maximum dose** | **Notes** |
| **Nifedipine** (immediate release) | 10 mg 3x/day | 20 mg 3x/day | 60 mg 3x/day | Can cause lower-extremity edema |
| **Amlodipine** | 5 mg 1x/day | 5 mg 1x/day | 10 mg 1x/day | |
| **Third-line drug** | **Starting dose** | **Increase dose by** | **Maximum dose** | **Notes** |
| **Atenolol** | 25 mg 1x/day | 25 mg 1x/day | 100 mg 1x/day | Contraindicated if heart rate ≤ 55 bpm |
| **Fourth-line drug** | **Starting dose** | **Increase dose by** | **Maximum dose** | **Notes** |
| **Hydralazine** | 25 mg 3x/day | 25 mg 3x/day | 50 mg 3x/day | Headache common side effect.<br>Expensive, requires thrice-daily dosing |

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