HYPERTENSIVE DISORDERS IN PREGNANCY

What we Know?

What we need to know?

What is the role of cardiologist?

We must be an effective member of

Cardio-obstetric Team.

Dr Toufan , professor of cardiology , Echocardiologist ,FASE

OUTLINE

- Introduction
- Epidemiology
- Hypertensive Disorder
- Chronic Hypertension
- Gestational Hypertension
- Preeclampsia/Eclampsia
- Chronic HTN superimposed with preeclampsia
- Pathogenesis
- Risk factors
- Investigations
- Management

INTRODUCTION

- Commonest medical disorders diagnosed by obstetrician
- Spectrum of severity ranges mild to severe
- There is controversy and lack of clarity about mild to moderate HDP

EPIDEMIOLOGY

- Most common medical complications, affecting 5–10% of pregnancies worldwide.
- Leading cause of maternal death globally Complicate about 2-10%of pregnancies

  Estimated 50.000-60.000 preeclampsia related deaths worldwide
- Major cause of maternal, fetal, and neonatal morbidity and mortality.
- Incidence 7X higher in developing countries than in developed countries

EPIDEMIOLOGY

- Hypertensive disorders of pregnancy :
- Chronic hypertension: (1%–2% of pregnancies) onset before pregnancy or 20 weeks(+/- complicated with superimposed preeclampsia)
- Gestational hypertension: (5%–6% of pregnancies) onset from 20 weeks
- Preeclampsia: (2%–4% of pregnancies) onset from 20 weeks diagnosed when: maternal systemic end-organ dysfunction (most commonly proteinuria) and/or evidence of fetoplacental dysfunction (eg, fetal growth restriction).

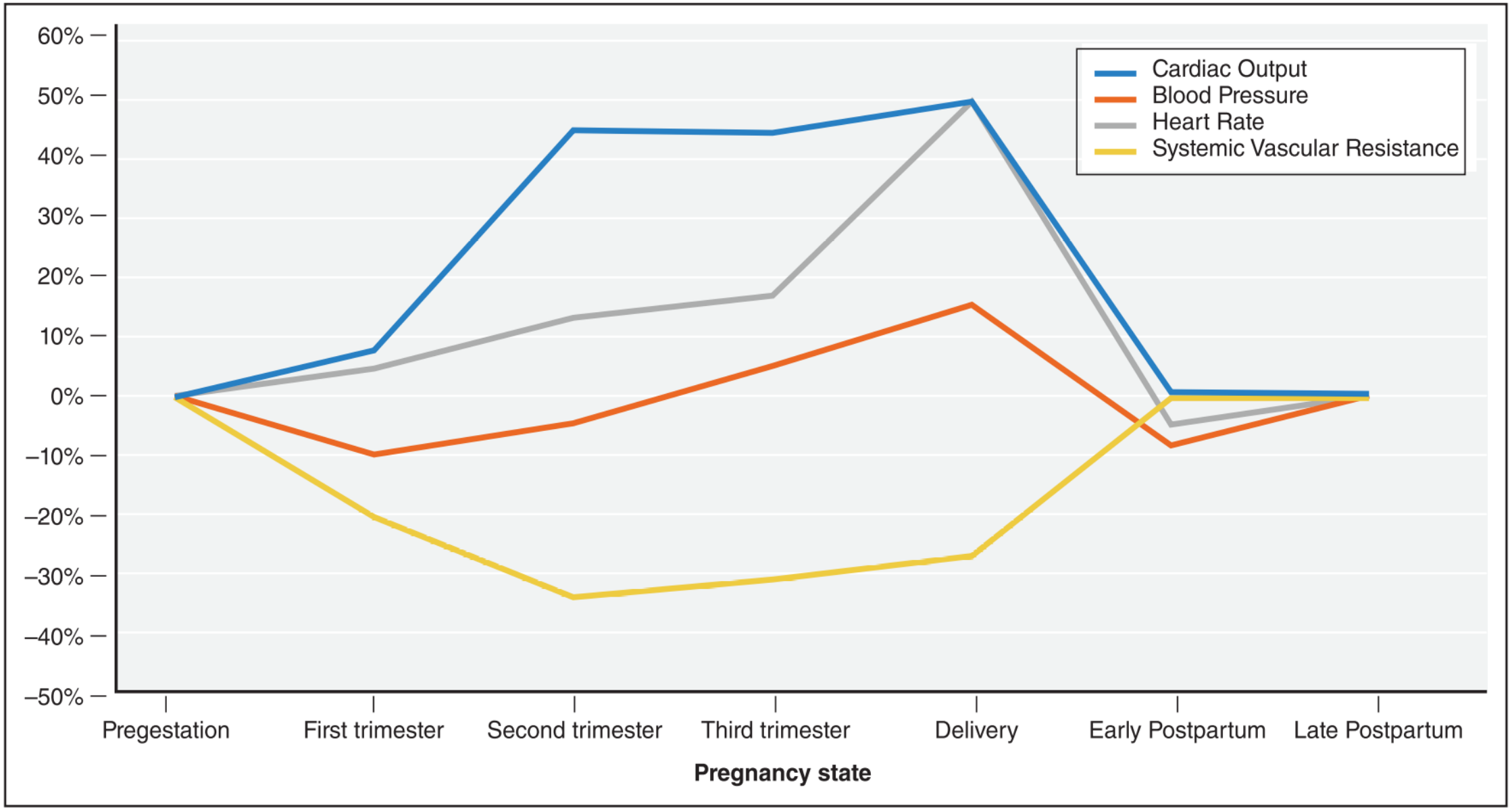


Figure 2. Physiological changes during pregnancy, including variation in cardiac output, blood pressure, and heart rate.[4,7]

Table 2. APOs and Associations With Mortality and CVD Outcomes

Pregnancy outcome/ reproductive risk factors	Outcome association	Strength of Evidence*
Hypertensive disorders of pregnancy (preeclampsia, gestational hypertension)	↑ Atherosclerotic CVD (including coronary heart disease, peripheral vascular disease, and ischemic stroke)	A
	↑ Hemorrhagic stroke	B
	↑ Heart failure	B
GD	↑ Atherosclerotic CVD	A
Preterm delivery	↑ Atherosclerotic CVD	A
SGA	↑ Atherosclerotic CVD	A
Large for gestational age	↑ Atherosclerotic CVD	B
Placental abruption	↑ Atherosclerotic CVD	A
Miscarriages/stillbirths	↑ Atherosclerotic CVD	A

APO indicates adverse pregnancy outcome; CVD, cardiovascular disease; GD, gestational diabetes; and SGA, small for gestational age.

See Supplemental Table 1 for specific studies and references.

*Strength of Evidence A indicates multiple consistent cohort studies, meta-analyses of such studies, or both. Strength of Evidence B indicates fewer available studies or inconsistencies in the evidence.

BP Measurement

- Sitting position (or the left lateral recumbent during labour)
- Appropriately-sized arm cuff at heart level and using Korotkoff V for diastolic BP (DBP).
- Mercury sphygmomanometers :

gold standard for BP measurement in pregnancy

BP Measurement

- Automatic devices tend to under-record the true BP and are unreliable in severe pre-eclampsia.
- Therefore, only devices validated according to recognized protocols should be used in pregnancy

BP Measurement

- **ABPM** superior to routine BP measurement for the prediction of pregnancy outcome.
- Devices used for **ABPM** are technically more accurate than those used for office or home BP measurement.
- **ABPM** avoids unnecessary treatment of white-coat hypertension, **useful** in the management of high-risk pregnant women with hypertension and those with diabetic or hypertensive nephropathy

Home blood pressure monitoring (HBPM)

- Is Highly REC because:
- Is Convenient,Help to Diagnose White coat HTN
- (vs. clinic BP) values are more closely associated with adverse outcomes
- Promotes both antihypertensive medication compliance and BP control
- Pregnancy during the coronavirus disease 2019 (COVID-19), given the widespread implementation of this method of self-monitoring, used to achieve social distancing.

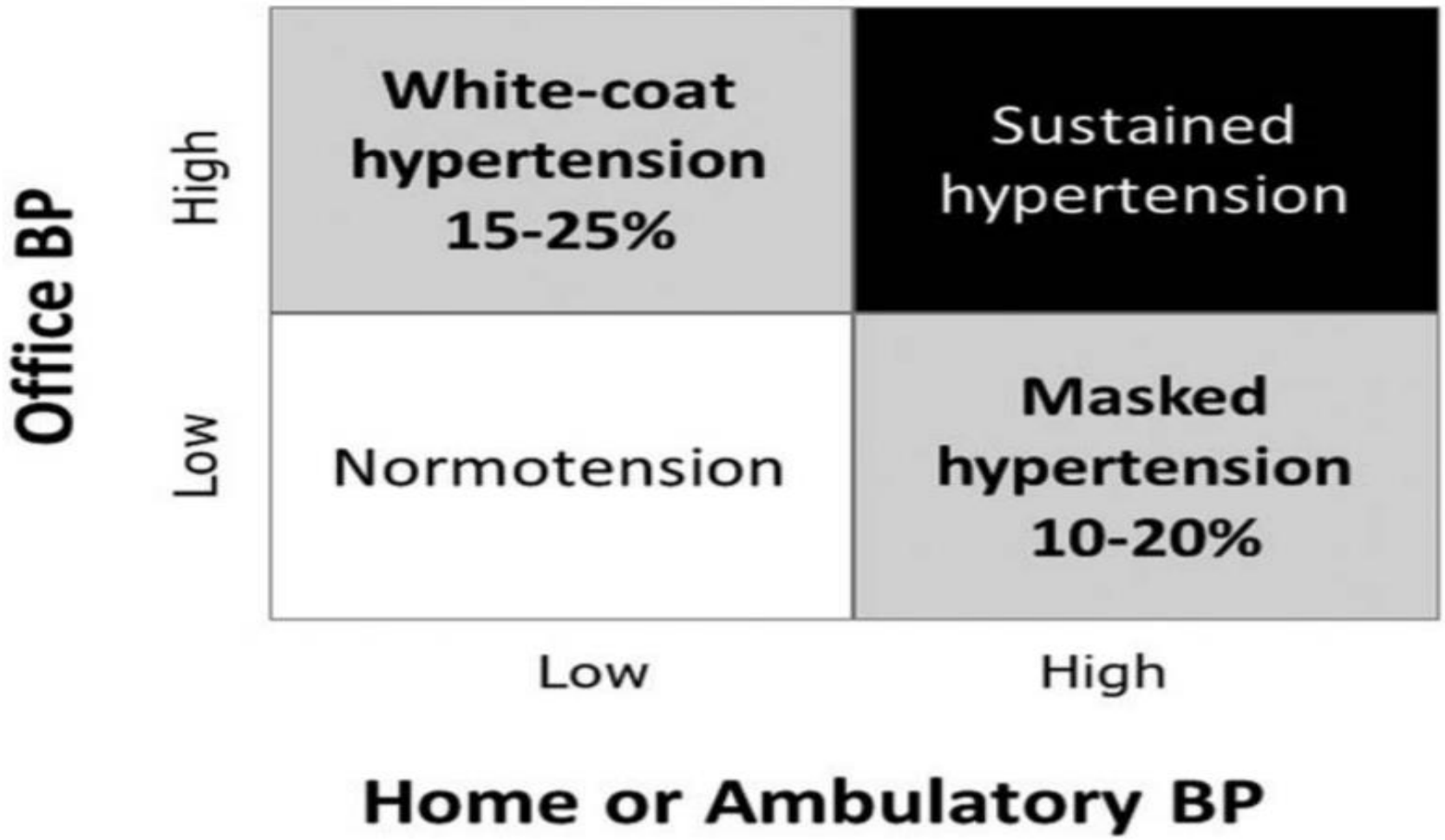


FIGURE 1 Classification of patients attending BP clinics according to their office and out-of-office BP measurements.

Definition of hypertension in pregnancy

- According to Working Group ,Blood pressure ≥140/90 mm of Hg
  - ≥30 mm of Hg or more in SBP.
  - ≥15 mm of Hg or more in DBP.
- Systolic BP>=140 mmHg and/or DBP >=90 mmHg
- Mildly elevated (140–159/ 90–109 mmHg)
- Severely elevated(>=160/110 mmHg)
- Based only on office (or in-hospital)

Diagnosis of HTN

- Severe hypertension : systolic BP ≥160 mmHg or a diastolic BP ≥110 mmHg, based on the average of at least two measurements, taken within 15 minutes at most, using the same arm.
- White-coat hypertension is defined as an office BP ≥140/90 , but a normal out-of-office BP, most commonly defined as most as <135/85mmHg
- Masked hypertension is defined as a normal office BP, but one that is elevated out-of-office(>=135/85)
- Transient hypertension is typically seen in the office setting, and resolves with repeated BP measurement

Preeclampsia is important because:

- women with preeclampsia have a 71% increased risk of **CVD mortality**
- 2.5-fold increased risk of **coronary artery disease**
- 4-fold increased risk of **Heart failure** compared with normal cohorts

Pregnancy Induced HTN
Possible Mechanism of action

H

- Abnormal Cytotrophoblast Invasion
- Decreased Uterine Placental Blood Flow

T

- Placental Ischemia
- Placental release cytokine factors

N

- Endothelial Dysfunction
- ET↑ TBX↑ PGI2↓ NO↓ AGT II sensitivity↑
- Renal Pressure Natriuresis ↓

Risk Factors

Maternal causes:

- Obesity
- Primiparity
- Mother age<20 />40
- Past H/O HTN,RD,DM
- Adolescent pregnancy
- Chronic HTN
- New Paternity
- Thrombophilia
- Having a donated kidney

Pregnancy:

- Previous preeclampsia
- Multiple gestation(twins/triplets)

Placental abnormalities:

- HyperPlacentosis
- Placental Ischemia/Family history

Family History

- FH of preeclampsia
- African American race

classification of hypertension in pregnancy

- Pre-existing hypertension
- Gestational hypertension
- Pre-eclampsia
- Pre-existing hypertension plus superimposed gestational hypertension with proteinuria
- Antenatally unclassifiable hypertension

Pre-existing hypertension

- Precedes pregnancy or develops **before** 20 weeks of gestation.
- It usually persists for more than 42 days post-partum and may be associated with proteinuria

Gestational hypertension

- Develops after 20 weeks of gestation and usually resolves within 42 days post-partum.

Pre-eclampsia

- GH with significant proteinuria (>0.3 g/24 h or ACR >_30 mg/mmol).
- Occurs more frequently during the first pregnancy
- Often associated with foetal growth restriction due to placental insufficiency and is a common cause of prematurity.
- Only cure is delivery
- As proteinuria may be a late manifestation of preeclampsia, it should be suspected when de novo hypertension is accompanied by headache, visual disturbances, abdominal pain, or abnormal laboratory tests, specifically low platelets and/or abnormal liver function.

Life threatening complication of Pre-Eclampsia:

→Eclampsia

→ HELLP

(hemolysis, elevated liver enzymes, low platelets) syndrome:

Immediate treatment and delivery required

High risk of pre-eclampsia

- Hypertensive disease during a previous pregnancy
- Chronic kidney disease
- Autoimmune disease such as systemic lupus erythematosus or antiphospholipid syndrome
- Type 1 or type 2 diabetes
- Chronic hypertension

Moderate risk of pre-eclampsia

- More than one of the following risk factors:
- First pregnancy
- Age 40 years or older
- Pregnancy interval of more than 10 years
- BMI of >_35 kg/m2 at first visit
- Family history of pre-eclampsia
- Multiple pregnancy.

Pre-existing hypertension plus superimposed gestational hypertension with proteinuria

Antenatally unclassifiable hypertension

- When BP is first recorded after 20 weeks of gestation and hypertension is diagnosed; re-assessment is necessary after 42 days post-partum

Investigations

- Full Blood count
- Serum Cr/Uric Acid
- LFT
- Dipstick>=1+ / ACR(<30mg/mmol)/24hr urine protein(>0.2gr/day→ close monitoring)
- Obstetric scans(may be considered)
- Umbilical artery Doppler (may be considered)

Investigation /Cardiology consult

What should we note at first visit of pregnant woman

- Be part of Cardio-obstetric team
- Preconception planning, all medications should be reviewed to ensure safety during pregnancy
- Cardiovascular consequence of GH

(Dissection : Coronary/Aorta ,PPCMP ,CAD)

- Screening for CV complication caused by pre-existing HTN
- Post partum monitoring/Future CV risk/Contraception

Management of hypertension in pregnancy

- **Non-pharmacological management(minimal effect):**

Regular exercise during pregnancy may improve vascular function and prevent preeclampsia

Advised to avoid a weight gain of more than 6.8 kg(mostly in obese women)

Diet

Management of hypertension in pregnancy

- **Pharmacologic treatment of Mild-Moderate HTN:**

European Guidelines: initiation of drug treatment in all women

-BP 150/95 mmHg and / >140/90 mmHg in women with:

-GH(with or without proteinuria)

-Pre-existing hypertension with the superimposition of gestational hypertension

-Hypertension with subclinical organ damage or symptoms at any time during pregnancy.

Antihypertensives safe in pregnancy

Drug	Starting dose	Maximum dose
Methyldopa	250 mg TDS/QID	4 g / day
Labetalol	100 mg BD	2400 mg/ day
Nifedipine	10 mg BD	120 mg / day
Thiazide diuretic	12.5 mg BD	50 mg/day

Management of hypertension in pregnancy

▣ Pharmacological management(severe HTN):

SBP >_170 mmHg or DBP >_110 mmHg in a pregnant woman an <u>emergency, and hospitalization is indicated</u>

IV labetalol, oral methyldopa, or nifedipine

IV hydralazine is no longer the drug of choice as its use is associated with more perinatal adverse effects than other drugs(still commonly used)

IV Urapidil(centrally acting antihypertensive that blocks peripheral α_1-adrenoceptors) with cautious

Labetalol Hydrochloride

- Oral ; Initial dose; 100mg twice daily then titrate up to 400 twice daily
- IV; 50 mg stat(1 minute then repeat every 5min)
- Infusion ; start with 20mg/hr then titrate 160mg/hr
- Pregnancy category :C

Hydralazine

- 5-10 mg IV/IM initially, Then 5-10 mg q20-30min PRN, OR 0.5-10 mg/hr IV infusion
- No longer the drug of choice

  However, is still commonly used when other treatment regimens have failed to achieve adequate BP control.
- Pregnancy category :C

Management of hypertension in pregnancy

- **Pharmacological management(severe HTN):**
- **Sodium nitroprusside:** **only as the drug of last choice**

  risk of fetal cyanide poisoning

  Category : C
- **Nitroglycerin** :**Drug of choice when pre-eclampsia with pulmonary oedema**

  given as an IV infusion of 5 µg/min, and gradually increased every 3–5 min to a maximum dose of 100 µg /min.

  Category :B2/C
- **If IV access has not been stablished Immediate release Nifedipine**

Anti-convulsant drug therapy- in severe pre-eclampsia

Magnesium Sulphate

- **4 gm (20 ml of 20% solu.) I.V. within 3-5 mins.**
- **5 gm (10 ml of 50% solu.) deep I.M. in each buttock with 1 ml of 1% of xylocaine**

If recurrent fits after 30 min of loading dose- repeat 2 gm 20% (4 ml drug with 6 ml NS) slow in 5 min

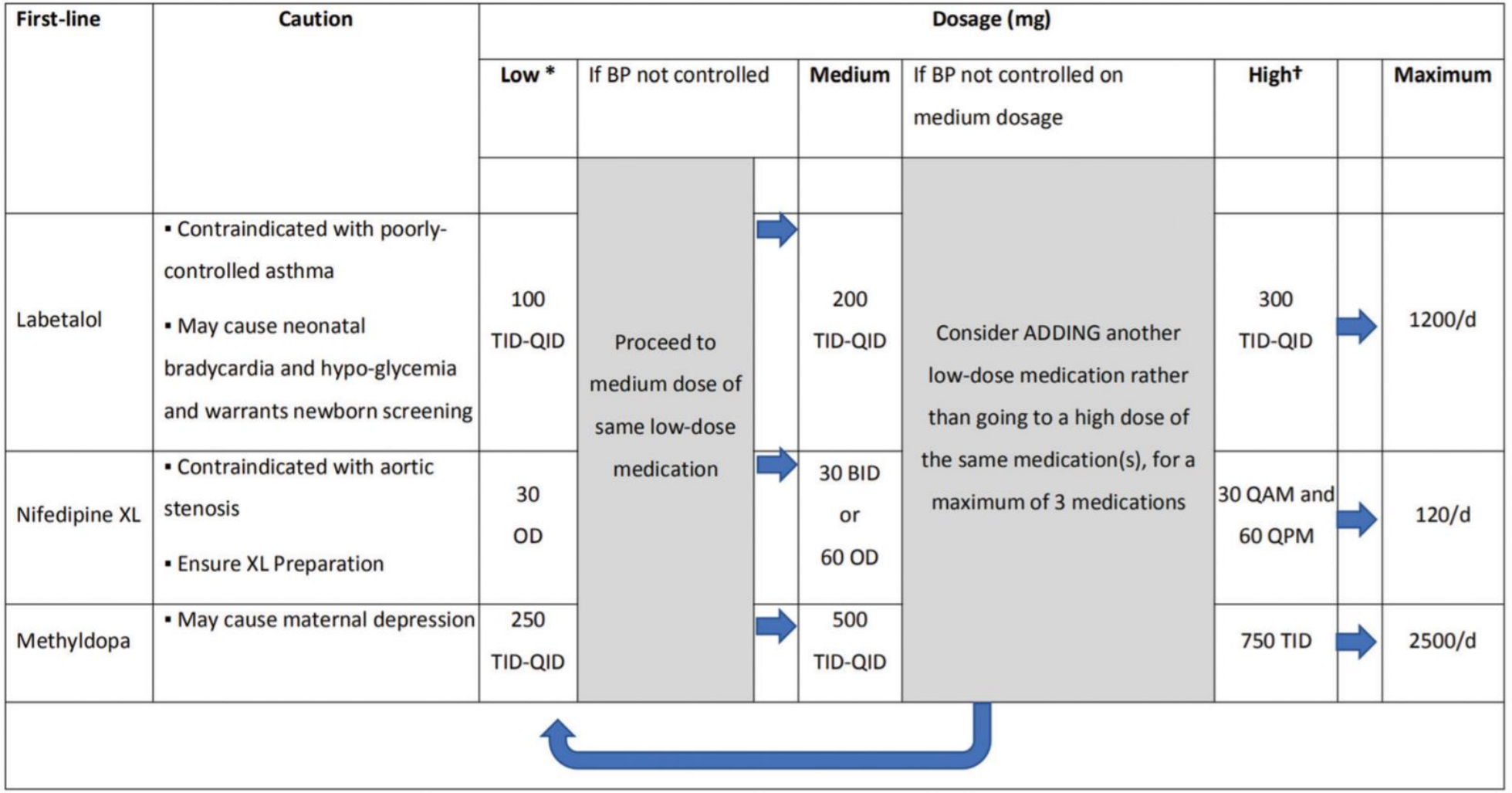
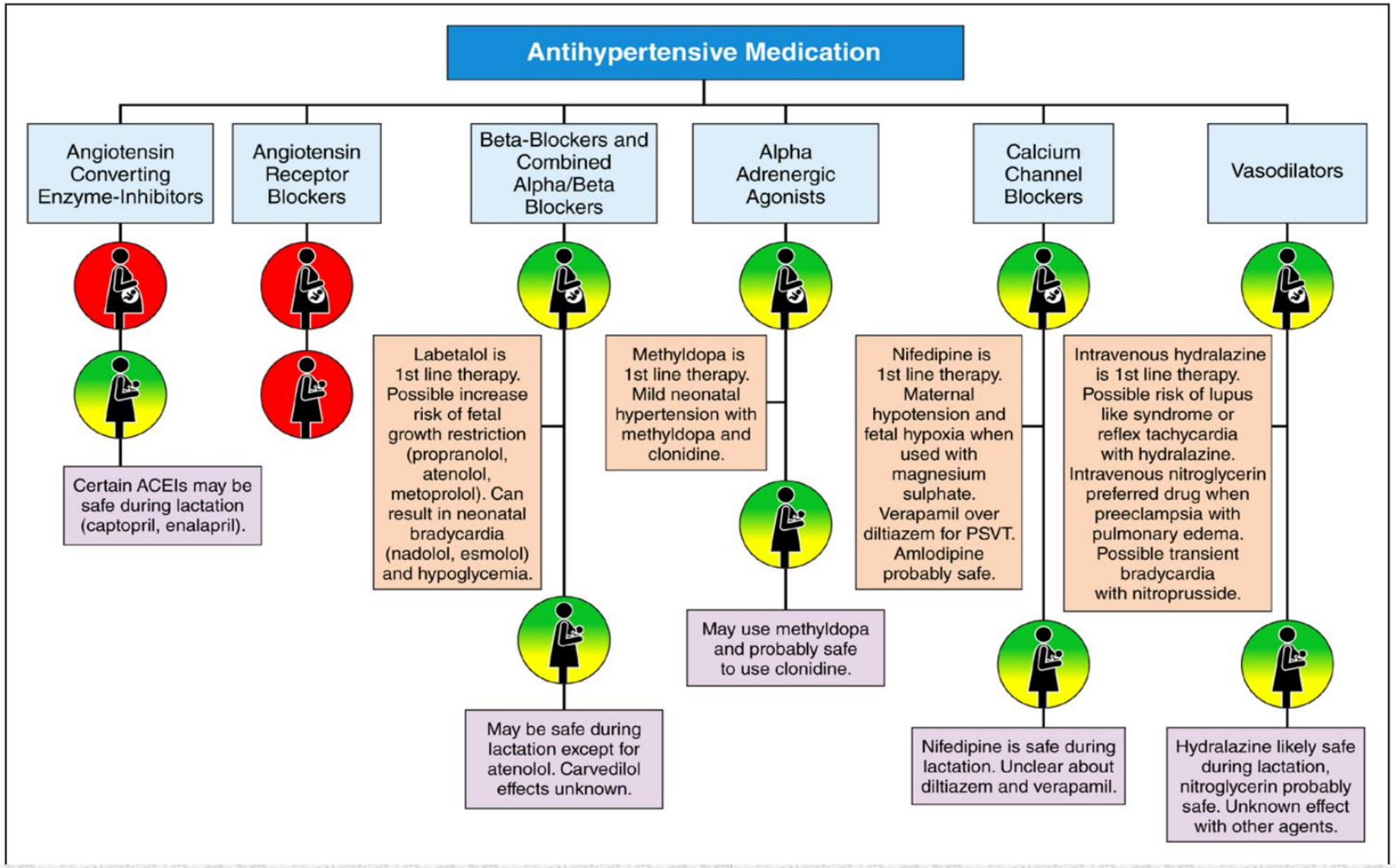


Figure 3. Suggested dose titration of antihypertensive therapy for non-urgent control of hypertension in pregnancy (modified from Magee LA *et al.*[85]). *Starting doses are higher than generally recommended for adults given more rapid clearance in pregnancy. †When a medication is at high (or maximum) dosage, consider using a different medication to treat any severe hypertension that may develop). BID: Twice/day; BP: Blood pressure; d: Day; OD: Once/day; QAM: Every morning; QID: Four times/day; QPM: Every evening; TID: Three times/day; XL: Extended release.

Drags		Caution	T 0 min	T 30 min	T 60 min	T 90 min	T 120 min	T 150 min	T 180 min
Labetalol	Oral	▪ Contra-indicated with uncontrolled asthma or heart failure ▪ May cause neonatal bradycardia and neonatal hypoglycemia and warrants newborn screening	200 mg	-	200 mg	-	200mg	-	Use alternative from a different drug class†
	IV intermittent		10-20 mg	20-40 mg‡	40-80 mg	40-80 mg	40-80 mg	40-80 mg§	
	IV infusion		0.5-2 mg/min	→	→	→	→	→†	
Nifedipine (oral capsule - swallow whole, do NOT bite)		▪ May cause maternal headache and tachycardia	10 mg	10 mg	-	10 mg	-	10 mg	
Methyldopa (oral)		▪ Onset of action may be delayed	1000 mg	-	-	-	-		
Hydralazine (IV)		▪ May increase risk of maternal hypotension, and maternal and fetal tachycardia	5 mg	5-10 mg	5-10 mg¶	5-10 mg¶			

Figure 4. Suggested dose titration of antihypertensive therapy for urgent control of hypertension in pregnancy* (modified from Magee LA *et al.*[86]). *When severe hypertension has resolved, switch to routine oral medication. †If nifedipine or hydralazine were the initial drug used, choose oral labetalol or oral methyldopa as the alternative. ‡Double the initial dose of labetalol IV. §Do not exceed the maximum dose of IV labetalol, which is 300 mg total in a treatment course. ¶Do not exceed the maximum dose of IV hydralazine of 20 mg. IV: Intravenous; T: Time; →: Carry on without change.


Antihypertensive Medication
Angiotensin Converting Enzyme-Inhibitors
Angiotensin Receptor Blockers
Beta-Blockers and Combined Alpha/Beta Blockers
Alpha Adrenergic Agonists
Calcium Channel Blockers
Vasodilators
Certain ACEIs may be safe during lactation (captopril, enalapril).
Labetalol is 1st line therapy. Possible increase risk of fetal growth restriction (propranolol, atenolol, metoprolol). Can result in neonatal bradycardia (nadolol, esmolol) and hypoglycemia.
May be safe during lactation except for atenolol. Carvedilol effects unknown.
Methyldopa is 1st line therapy. Mild neonatal hypertension with methyldopa and clonidine.
May use methyldopa and probably safe to use clonidine.
Nifedipine is 1st line therapy. Maternal hypotension and fetal hypoxia when used with magnesium sulphate. Verapamil over diltiazem for PSVT. Amlodipine probably safe.
Nifedipine is safe during lactation. Unclear about diltiazem and verapamil.
Intravenous hydralazine is 1st line therapy. Possible risk of lupus like syndrome or reflex tachycardia with hydralazine. Intravenous nitroglycerin preferred drug when preeclampsia with pulmonary edema. Possible transient bradycardia with nitroprusside.
Hydralazine likely safe during lactation, nitroglycerin probably safe. Unknown effect with other agents.

Recommendations for the management of hypertension

Recommendations	Class[a]	Level[b]
Low-dose aspirin (100–150 mg daily) is recommended in women at high or moderate risk of pre-eclampsia from week 12 to weeks 36–37.[343,344]	I	A
In women with gestational hypertension or pre-existing hypertension superimposed by gestational hypertension, or with hypertension and subclinical organ damage or symptoms, initiation of drug treatment is recommended at SBP >140 mmHg or DBP >90 mmHg.[185] In all other cases, initiation of drug treatment is recommended if SBP ≥150 mmHg or DBP ≥95 mmHg.[348,375]	I	C
SBP ≥170 mmHg or DBP ≥110 mmHg in a pregnant woman is an emergency, and hospitalization is recommended.	I	C
Methyldopa (B), labetalol (C), and calcium antagonists (C) are recommended for the treatment of hypertension in pregnancy.[51,379,389]	I	B (methyldopa) C (labetalol and calcium antagonists)
In women with gestational hypertension or mild pre-eclampsia, delivery is recommended at 37 weeks.[383]	I	B
It is recommended to expedite delivery in pre-eclampsia and with adverse conditions such as visual disturbances or haemostatic disorders.	I	C
In pre-eclampsia associated with pulmonary oedema, nitroglycerin given as an intravenous infusion is recommended.[361]	I	C
In severe hypertension, drug treatment with intravenous labetalol, or oral methyldopa or nifedipine, is recommended.[51]	I	C
Limitation of weight gain to <6.8 kg should be considered in obese women.[377]	IIa	C
ACE inhibitors, ARBs, or direct renin inhibitors are not recommended.[51,185,361]	III	C

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BP = blood pressure; DBP = diastolic blood pressure; SBP = systolic blood pressure.
[a]Class of recommendation.
[b]Level of evidence.

Prevention of hypertension and pre-eclampsia

- 100–150 mg of aspirin daily from week 12 to weeks 36
- Calcium supplementation (1.5–2 g/day, orally) is recommended for the prevention of pre-eclampsia in women with low dietary intake of calcium(600mg/day)
- Vitamins C and E do not decrease pre-eclampsia risk; on the contrary, they are more frequently associated with a low birth weight

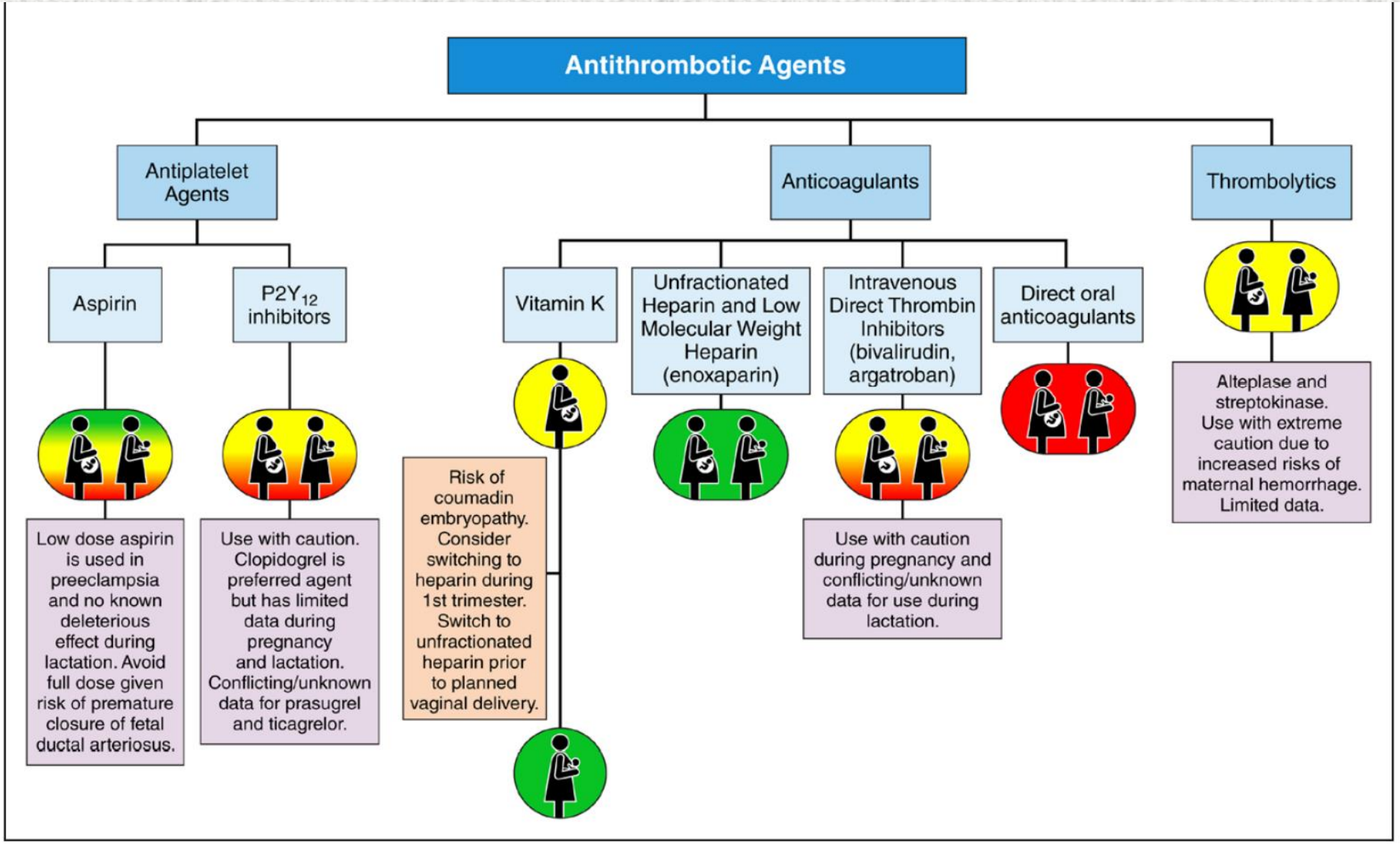


Figure 3. Antihypertensive medications and anticoagulants used during pregnancy.[3,5,9–12]
Boxes with various shades: Red shows contraindicated medications; yellow, use-with-caution medications; and green, relatively safe medications. ACEI indicates angiotensin-converting enzyme inhibitor; and PSVT, paroxysmal supraventricular tachycardia.

Risk factors /complications

- **Maternal risks**: Placental abruption, stroke, multiple organ failure, and disseminated intravascular coagulation

- **Fetal risks include**: High-risk of intrauterine growth retardation (25% of cases of preeclampsia), pre-maturity (27% of cases of pre-eclampsia), and intrauterine death (4% of cases of pre-eclampsia).

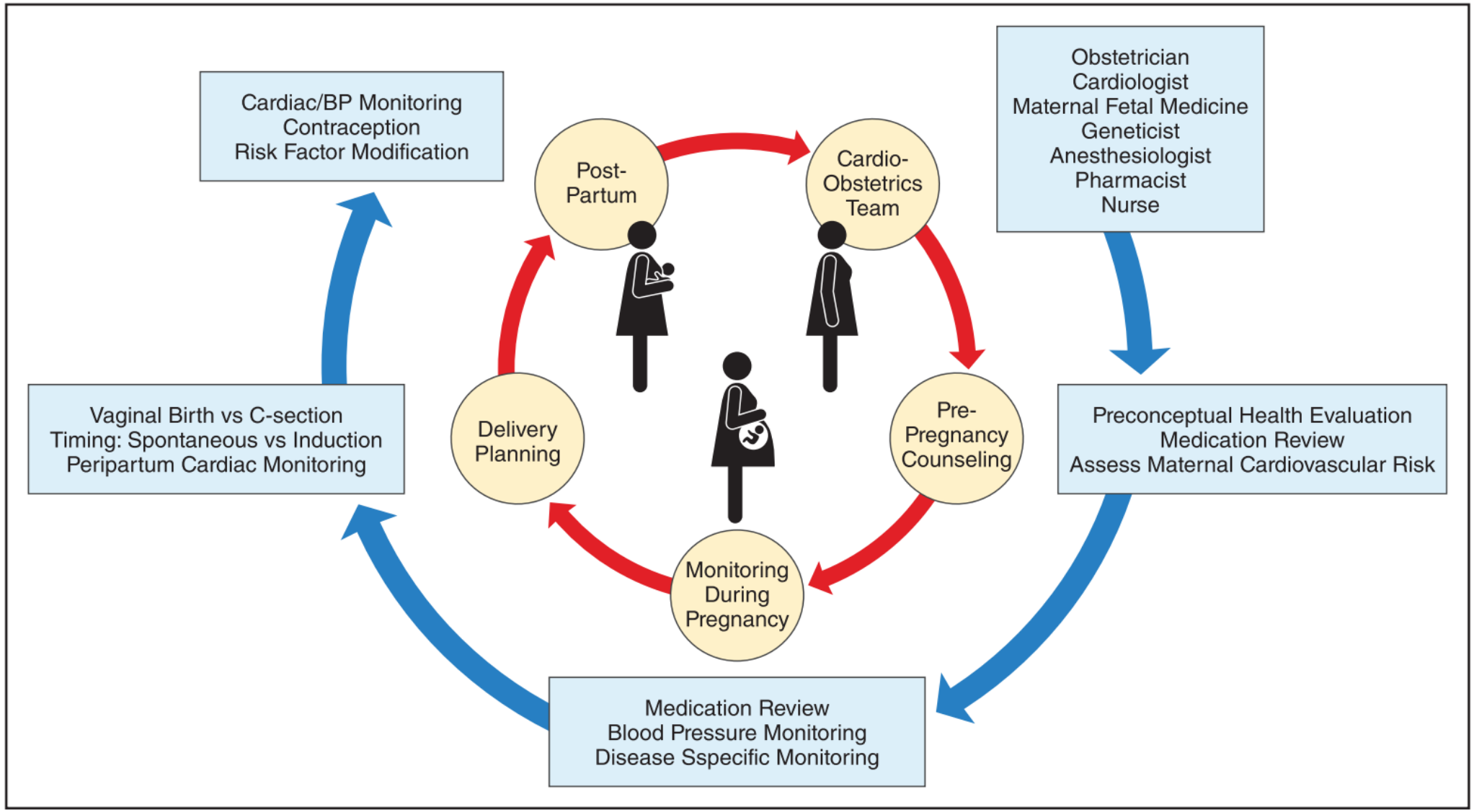


Figure 1. Cardio-obstetrics team in the management of women before pregnancy, during pregnancy, and postpartum.
BP indicates blood pressure.

Prognosis after Delivery

- Post Partum BP(↑first week)/150/90 persistent HTN
- Hypertension & Lactation(same drug concentration of Propranolol and Nifedipine in Breast milk like maternal plasma)
- Risk of Recurrency of HTN in subsequent pregnancy(The earlier the onset of hypertension in the first pregnancy, the higher the risk of recurrence in a subsequent pregnancy.

Long-term cardiovascular consequences of gestational hypertension

- Gestational hypertension or pre-eclampsia:

↑ risk of HTN, stroke, and IHD in later adult life.

- Lifestyle modifications

- Annual visits to a primary care physician to check BP and metabolic factors are recommended
- Fertility treatment

CLINICAL STATEMENTS AND GUIDELINES

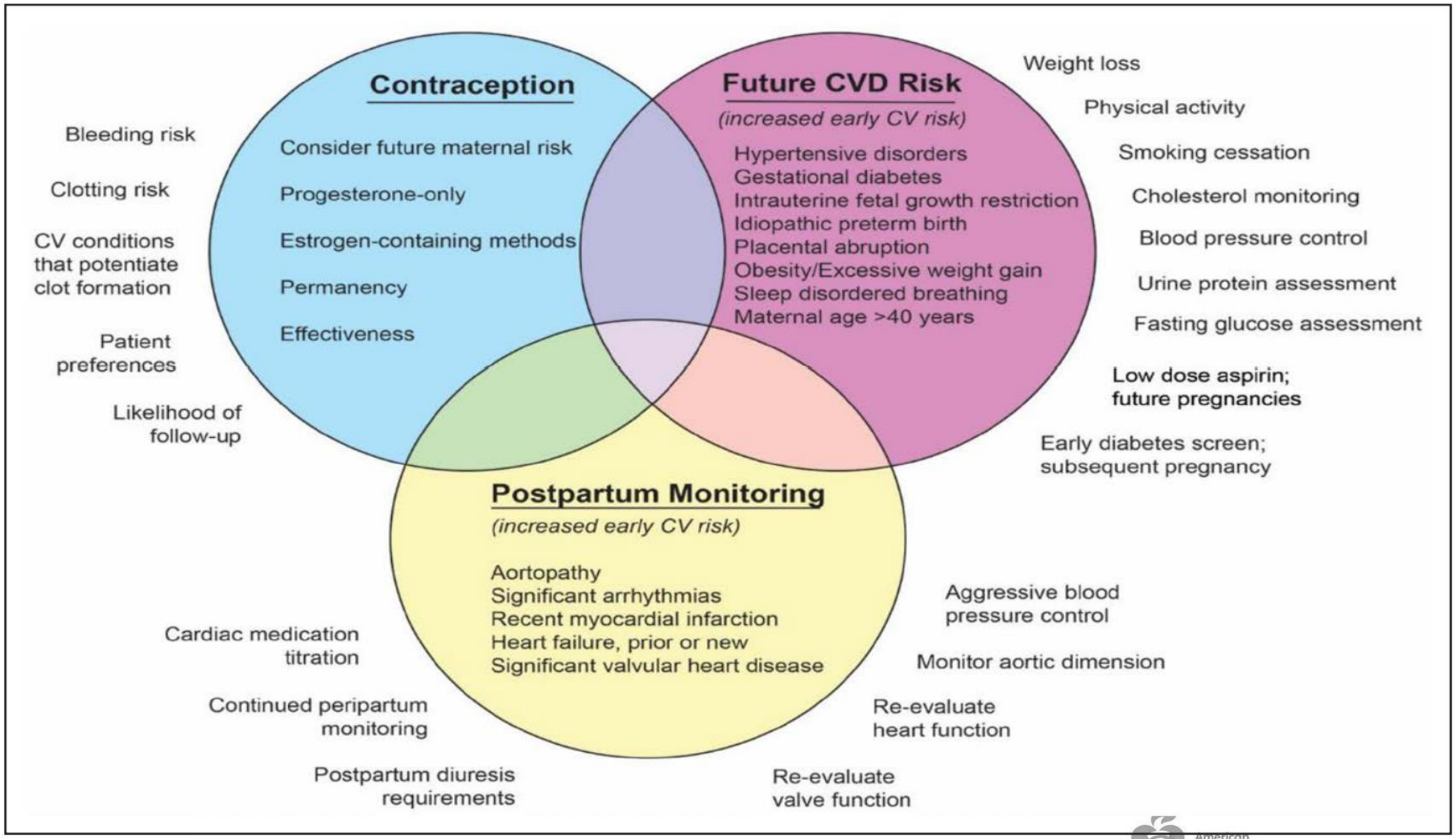


Figure 5. Postdelivery follow-up and late cardiovascular (CV) risk.
CVD indicates cardiovascular disease.

Table 2. Approach to Contraceptive Use in Women With CVD

Condition	Subcondition	IUD	Implant	DMPA	POP	CHC
DVT/PE	Remote, not receiving anticoagulation	R	R	R	R	U
	Acute	R	R	R	R	U
	History, receiving ≥3 mo of anticoagulation	R	R	R	R	U
	Family history (first-degree relative)	R	R	R	R	R
High blood pressure in pregnancy	History in prior pregnancy	R	R	R	R	R
Hypertension	Controlled	R	R	R	R	U
	SBP >140–159 mm Hg, DBP >90–99 mm Hg	R	R	R	R	U
	SBP >160 mm Hg, DBP >100 mm Hg	R	R	U	R	U
	Vascular disease	R	R	U	R	U
IHD	Current	Variable depending on whether IHD is present before vs after contraception. Copper IUD safe. For progesterone-IUD, implants, DMPA, and POP, risk likely outweighs benefit. CHC should be avoided.				
Multiple cardiovascular risk factors	Tobacco, diabetes mellitus, hypertension, older age, dyslipidemia	R	R	U	R	U
PPCM	Normal/mild systolic dysfunction	R	R	R	R	U
	Moderate to severe systolic dysfunction	R	R	R	R	U
Valvular heart disease	Uncomplicated	R	R	R	R	R
	Complicated*	R	R	R	R	U

CHC indicates combined hormonal contraception; CVD, cardiovascular disease; DMPA, depot medroxyprogesterone acetate; DBP, diastolic blood pressure; DVT, deep venous thrombosis; IHD, ischemic heart disease; IUD, intrauterine device; PE, pulmonary embolism; POP, progestin-only pill; PPCM, peripartum cardiomyopathy; R, reasonable (benefit outweighs risk); SBP, systolic blood pressure; and U, unreasonable (risk outweighs benefit).

*Defined as a condition that places the woman at an increased risk as a result of pregnancy.

Adapted from Curtis et al.[141]

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2020 International Society of Hypertension Global Hypertension Practice Guidelines

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Table of Contents

Section 1: Introduction

Context and Purpose of This Guideline

Statement of Remit

To align with its mission to reduce the global burden of raised blood pressure (BP), the International Society of Hypertension (ISH) has developed worldwide practice guidelines for the management of hypertension in adults, aged 18 years and older.

The ISH Guidelines Committee extracted evidence-based content presented in recently published extensively reviewed guidelines and tailored ESSENTIAL and OPTIMAL standards of care in a practical format that is easy-to-use particularly in low, but also in high resource settings – by clinicians, but also nurses and community health workers, as appropriate. Although distinction between low and high resource settings often refers to high (HIC) and low- and middle-income countries (LMIC), it is well established that in HIC there are areas with low resource settings, and vice versa.

Herein optimal care refers to evidence-based standard of care articulated in recent guidelines[1,2] and summarized here, whereas ESSENTIAL standards recognize that OPTIMAL standards would not always be possible. Hence essential standards refer to minimum standards of care. To allow specification of essential standards of care for low resource settings, the Committee was often confronted with the limitation or absence in clinical evidence, and thus applied expert opinion.

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ESC European Society of Cardiology

European Heart Journal (2018) **39**, 3165–3241
doi:10.1093/eurheartj/ehy340

ESC GUIDELINES

2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy

The Task Force for the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC)

Endorsed by: the International Society of Gender Medicine (IGM), the German Institute of Gender in Medicine (DGesGM), the European Society of Anaesthesiology (ESA), and the European Society of Gynecology (ESG)

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Circulation

AHA SCIENTIFIC STATEMENT

Cardiovascular Considerations in Caring for Pregnant Patients

A Scientific Statement From the American Heart Association

ABSTRACT: Cardio-obstetrics has emerged as an important multidisciplinary field that requires a team approach to the management of cardiovascular disease during pregnancy. Cardiac conditions during pregnancy include hypertensive disorders, hypercholesterolemia, myocardial infarction, cardiomyopathies, arrhythmias, valvular disease, thromboembolic disease, aortic disease, and cerebrovascular diseases. Cardiovascular disease is the primary cause of pregnancy-related mortality in the United States. Advancing maternal age and preexisting comorbid

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Summary of maternal-fetal interaction and the effect of position