

# Hypertension in pregnancy

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# Hypertension in pregnancy

- Most common medical problem in pregnancy
- Complicates about 10% of pregnancies:
  - 1-5% of preexisting hypertension
  - 5-6% of gestational hypertension
  - 1-4% of preeclampsia

# Hypertensive disorders in pregnancy:

a major cause of

- maternal
- fetal
- neonatal *morbidity and mortality*

# **Classification of hypertension in pregnancy**

- **pre-existing hypertension**
- **gestational hypertension**
- **pre-existing hypertension plus superimposed gestational hypertension with proteinuria**
- **antenatally unclassifiable hypertension**

# Pre-existing hypertension

- 1-5% of pregnancies
- BP > 140/90 mmHg *predates pregnancy or develops before 20 weeks* of gestation
- In most cases, hypertension *persists more than 42 days post partum*, it may be associated with proteinuria

# Gestational hypertension

Pregnancy-induced hypertension with or without proteinuria

Hypertension develops *after 20 weeks' gestation*, in most cases, *it resolves within 42 days post partum*

*Poor organ perfusion*

# Cardiovascular changes in pregnancy

Parameter	$\Delta$	Timing
SBP	↓ 4-6 mmHg	All bottom at 20-24 wks, then rise gradually to pre-pregnancy values at term
DBP	↓ 8-15 mmHg	
MAP	↓ 6-10 mmHg	
HR	↑ 12-18 BPM	Early 2nd trimester, then stable
SV	↑ 10-30%	Early 2nd trimester, then stable
CO	↑ 33-45%	Peaks in early 2nd trimester, then until term

# Pre-existing hypertension plus superimposed gestational hypertension with proteinuria

Further worsening of BP and *protein excretion > 3 g/day* in 24-hour urine collection *after 20 weeks' gestation*

Previous terminology “**chronic hypertension with superimposed pre-eclampsia**”

# **Antenatally unclassifiable hypertension**

**Hypertension with or without systemic  
manifestation**

**BP *first recorded after 20 weeks' gestation,*  
re-assessment necessary at or after 42 days  
post partum**

# Pre-eclampsia

Gestational hypertension associated with *significant proteinuria*

- 300 mg/l or
- 500 mg/24 h or
- dipstick 2+ or more

*Poor organ perfusion*

# Risk factors for developing pre-eclampsia

- Nulliparity
- Multiple pregnancy
- Family history of pre-eclampsia
- Chronic hypertension
- Diabetes
- Increased insulin resistance
- Increased body mass index

# **Risk factors for developing pre-eclampsia**

- **Hypercoagulability (inherited thrombophilia)**
- **Renal disease even without significant impairment**
- **Low socioeconomic status**
- **Antiphospholipid syndrome (acquired thrombophilia)**
- **Previous pre-eclampsia**
- **Hydatidiform mole**
- **Black race**

# Antiplatelet drugs for prevention of pre-eclampsia and its consequences: systematic review

Lelia Duley, David Henderson-Smart, Marian Knight, James King

**39 trials; 30 563 women**

- **15% RR of pre-eclampsia**
- **8% RR preterm birth**
- **14% RR fetal or neonatal death**

# Prevention of Preeclampsia and Intrauterine Growth Restriction With Aspirin Started in Early Pregnancy

*A Meta-Analysis*

*Emmanuel Bujold, MD, MSc, Stéphanie Roberge, MSc, Yves Lacasse, MD, MSc, Marc Bureau, MD, François Audibert, MD, MSc, Sylvie Marcoux, MD, PhD, Jean-Claude Forest, MD, PhD, and Yves Giguère, MD, PhD*

**27 studies; 11 348 women**

- **53% RR of pre-eclampsia**
- **56% RR IUGR**



*National Institute for  
Health and Clinical Excellence*

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## **Hypertension in pregnancy**

**The management of hypertensive disorders  
during pregnancy**

**NICE clinical guideline 107**

Developed by the National Collaborating Centre for Women's and Children's Health

# NICE Clinical Guidelines 107

## Antiplatelet agents

Advise women at **high risk of pre-eclampsia** and those with  $\geq 1$  moderate risk factor for pre-eclampsia to take **75 mg of ASA** daily from 12 weeks until the birth of the baby

### High risk

- Hypertensive disease during a previous pregnancy
- CKD
- Autoimmune disease such as SLE or antiphospholipid syndrome
- Type 1 or Type 2 diabetes
- Chronic hypertension

# NICE Clinical Guidelines 107

## Antiplatelet agents

Advise women at high risk of pre-eclampsia and those with  $\geq 1$  moderate risk factor for pre-eclampsia to take 75 mg of ASA daily from 12 weeks until the birth of the baby

### Moderate risk

- First pregnancy
- Age  $\geq 40$  years
- Pregnancy interval of more than 10 years
- BMI  $\geq 35$  kg/m<sup>2</sup>
- Family history of pre-eclampsia
- Multiple pregnancy

# Management of hypertension in pregnancy

depends on

- BP levels
- gestational age
- associated maternal and fetal risk factors

# Non-pharmacologic management

- SBP 140-149 mmHg or  
DBP 90-99 mmHg
- ↓ activity, bed rest (left lateral position)

**AVOID** : weight reduction and salt restriction

# Principles for treatment of mild-to-moderate hypertension in pregnancy

The benefits of antihypertensive therapy for mild-to-moderately elevated BP in pregnancy ( $\leq 160/110$  mmHg), either chronic or pregnancy-induced, have not been demonstrated in clinical trials.

- Less risk of developing severe hypertension
- No difference in outcome of preeclampsia, neonatal death, pre-term birth
- No difference in small-for-gestational-age babies

## **BP thresholds for drug treatment initiation in pregnancy**

<b>Country</b>	<b>BP threshold (mmHg)</b>	<b>BP goal (mmHg)</b>
<b>USA</b>	160/105	not set
<b>Canada</b>	140/90	80-90 for DBP
<b>Australia</b>	160/90	$\geq 110$ SBP
<b>Germany</b>	160/100	140-160/90

# Thresholds for drug treatment initiation

*BP > 140/90 mmHg in women*

- with gestational hypertension without proteinuria or
- pre-existing hypertension before 28 weeks' gestation or
- gestational hypertension and proteinuria or symptoms at any time or
- pre-existing hypertension and TOD or
- pre-existing hypertension and superimposed gestational hypertension

*BP > 150/95 mmHg*

- In all other circumstances

*methyldopa, labetalol, calcium antagonists, and beta-blockers*

**AVOID: ACE inhibitors, AIIA, diuretics**

*magnesium sulfate: eclampsia, treatment and prevention of seizures*

## Articles

# Fall in mean arterial pressure and fetal growth restriction in pregnancy hypertension: a meta-analysis

*P von Dadelszen, M P Ornstein, S B Bull, A G Logan, G Koren, L A Magee*

Treatment-induced falls in maternal BP may adversely affect fetal growth. **Given the small maternal benefits that are likely to be derived from therapy, new data are urgently needed to elucidate the relative maternal and fetal benefits and risks of oral antihypertensive drug treatment of mild-to-moderate pregnancy hypertension.**

# Definitions of Pregnancy Drug Classifications

## Category

- A.** Careful tests in humans have shown no harm.
- B.** Animal studies showed some harm, but well-designed studies in humans showed no harm, or animal studies did not show any harm and there are no good studies in humans.
- C.** Animal studies show some harm and there are no good studies in humans, or no human or animal studies have been done.
- D.** Human studies show some risk.
- X.** There is strong evidence that the drug causes birth defects, either in humans or in animals.

# Emergency management of hypertension in pregnancy

- SBP  $\geq$  170 or DBP  $\geq$  110 mmHg

~~hydrochlorazine~~, labetalol, methyldopa or nifedipine  
nicardipine, sodium nitroprusside (risk of fatal  
cyanide poisoning with prolonged treatment),  
nitroglycerin

# Hydralazine for treatment of severe hypertension in pregnancy: meta-analysis

Laura A Magee, Chris Cham, Elizabeth J Waterman, Arne Ohlsson, Peter von Dadelszen

## Abstract

**Objective** To review outcomes in randomised controlled trials comparing hydralazine against other antihypertensives for severe hypertension in pregnancy.

**Study design** Meta-analysis of randomised controlled trials (published between 1966 and September 2002) of short acting antihypertensives for severe hypertension in pregnancy. Independent data abstraction by two reviewers. Data were entered into RevMan software for analysis (fixed effects model, relative risk and 95% confidence interval); in a secondary analysis, risk difference was also calculated.

**Results** Of 21 trials (893 women), eight compared hydralazine with nifedipine and five with labetalol. Hydralazine was associated with a trend towards less persistent severe hypertension than labetalol (relative risk 0.29 (95% confidence interval 0.08 to 1.04); two trials), but more severe hypertension than nifedipine or isradipine (1.41 (0.95 to 2.09); four trials); there was significant heterogeneity in outcome between trials and differences in methodological quality. Hydralazine was associated with more maternal hypotension (3.29 (1.50 to 7.13); 13 trials); more caesarean sections (1.30 (1.08 to 1.59); 14 trials); more placental abruption (4.17 (1.19 to 14.28); five trials); more maternal oliguria (4.00 (1.22 to 12.50); three trials); more adverse effects on fetal heart rate (2.04

# **Antihypertensive drugs used in pregnancy**

**Women with pre-existing hypertension are advised to continue their current medication except for ACE inhibitors, AIIA and direct renin inhibitors**

# Why is RAS important in pregnancy?

- Regulation of renal hemodynamics  
(by maintaining GFR and urine production under conditions of low renal perfusion pressure, which are characteristic of the fetal and neonatal periods)
- Regulation of umbilical and placental circulation
- Regulation of fetal BP
- Kidney development (growth factors)
- Angiogenesis (angiotensin II)
- Regulation of fetal renal growth, function and development (ACE gene)

# Administration of AT<sub>1</sub>-blockers in pregnancy

- Fetal arterial hypotension
- Decreased glomerular perfusion pressure
- Impaired renal tubular development
- Reduced fetal urine output, oligohydramnios
  - Sequelae: limb contractures
  - pulmonary hypoplasia
  - cranio-facial deformation and neonatal anuria
- Decreased placental and umbilical perfusion:
  - intrauterine growth restriction
- Action on skull bones angiogenesis:
  - impaired ossification processes

*Critical period: second trimester !!*

# Maternal exposure to AT<sub>1</sub>-blockers

## Critical period: second trimester

**5 cases of fetal death and 1 case of neonatal death on Day 4 postpartum, with persisting anuria; exposure in early pregnancy, oligohydramnion.**

- Saji H, Yamanaka M, Hagiwara A, Ijiri R. Losartan and fetal toxic effects. *Lancet* 2001;357:363.
- Martinovic J, Benachi A, Laurent N, Daika-Dahmane F, Gubler MC. Fetal toxic effects and angiotensin-II receptor antagonists. *Lancet* 2001;358:241-8.
- Briggs GG, Nageotte MP. Fatal fetal outcome with the combined use of valsartan and atenolol. *Ann Pharmacoth* 2001;35:859-61.

# Major Congenital Malformations after First-Trimester Exposure to ACE Inhibitors

William O. Cooper, M.D., M.P.H., Sonia Hernandez-Diaz, M.D., Dr.P.H.,  
Patrick G. Arbogast, Ph.D., Judith A. Dudley, B.S., Shannon Dyer, B.S.,  
Patricia S. Gideon, R.N., Kathi Hall, B.S., and Wayne A. Ray, Ph.D.

## RESULTS

Infants with only first-trimester exposure to ACE inhibitors had an increased risk of major congenital malformations (risk ratio, 2.71; 95 percent confidence interval, 1.72 to 4.27) as compared with infants who had no exposure to antihypertensive medications. In contrast, fetal exposure to other antihypertensive medications during only the first trimester did not confer an increased risk (risk ratio, 0.66; 95 percent confidence interval, 0.25 to 1.75). Infants exposed to ACE inhibitors were at increased risk for malformations of the cardiovascular system (risk ratio, 3.72; 95 percent confidence interval, 1.89 to 7.30) and the central nervous system (risk ratio, 4.39; 95 percent confidence interval, 1.37 to 14.02).

*N Engl J Med 2006;354:2443-2451*

# Antihypertensive drugs used in pregnancy

*Central alfa  
agonists*

**Methyldopa** is the **drug of choice**.

*Beta-blockers*

**Atenolol** and **metoprolol** appear to be safe and effective in late pregnancy.

*Alfa-/beta-  
blockers*

**Labetalol** has comparable efficacy with methyldopa, in case of severe hypertension, it could be given intravenously.

# Atenolol in essential hypertension during pregnancy

Lucy Butters, Susan Kennedy, Peter C Rubin

## Abstract

**Objective**—To determine the effect of atenolol on the outcome of pregnancy in women with essential hypertension.

**Design**—Prospective, randomised, double blind, placebo controlled study.

**Setting**—Hospital clinic.

**Patients**—33 Women with mild essential hypertension (systolic blood pressure 140-170 mm Hg or diastolic pressure 90-110 mm Hg on two occasions at least 24 hours apart) consecutively referred to two obstetric medical clinics. Four patients in the placebo group were withdrawn from the study: control of blood pressure was inadequate in two, one developed breathlessness, and one changed her mind about participating. The mean gestation in the 29 remaining women on entry to the study was 15.9 weeks.

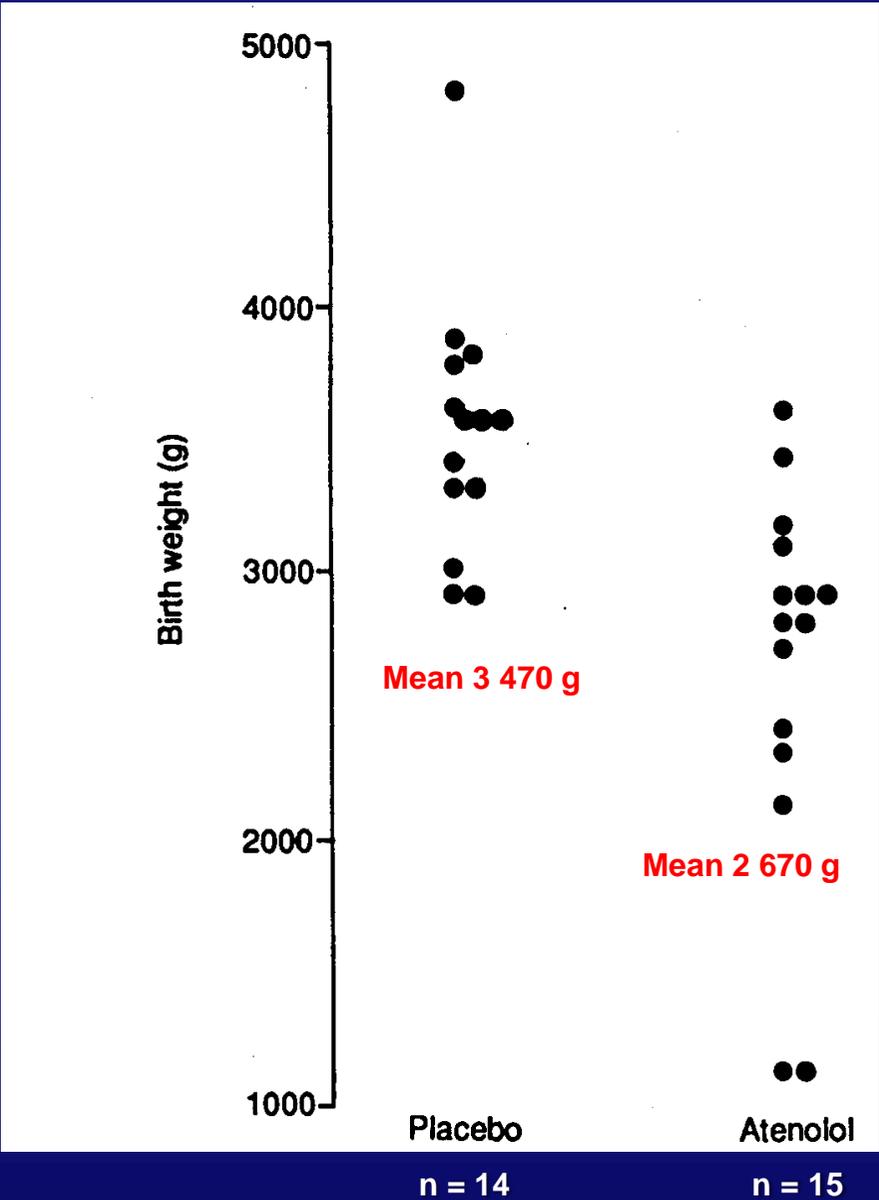
**Main outcome measures**—Blood pressure and birth weight.

**Intervention**—14 Women received placebo. 15 Women received atenolol 50 mg daily initially, increasing until either the blood pressure was <140/90 mm Hg or a dose of 200 µg daily was reached.

**Results**—The mean blood pressure on entry was 148/86 mm Hg in the group given atenolol and 144/86 mm Hg in the group given placebo. During treatment the mean diastolic pressure was significantly reduced by atenolol compared with placebo (to 74 v 81 mm Hg; difference in means (95% confidence interval) 7.0 (2.9 to 10.0) mm Hg) but the effect on systolic pressure was marginal (132 v 136 mm Hg; 4.0 (–1.4 to 8.6) mm Hg). Babies in the atenolol group had a significantly lower birth weight than those in the placebo group (2620 g v 3530 g; 910 (440 to 1380) g).

**Conclusion**—Atenolol given from the end of the first trimester in patients with mild hypertension is associated with intrauterine growth retardation. When taken in conjunction with the results of a previous study in which methyldopa was given these findings indicate that benefit is unlikely to result from treating mild essential hypertension in pregnancy.

# Birth weights of babies in atenolol and placebo groups



## Effect of Atenolol on Birth Weight

Gregory Y.H. Lip, MD, Michèle Beevers, SRN, David Churchill, MD, Lara M. Shaffer, MB, and D. Gareth Beevers, MD

**A** previous small, prospective study from Glasgow reported that babies born to women treated with atenolol in early pregnancy had significantly lower birth weights than those in the placebo group.<sup>1</sup> Beta blockers, while safe in the third trimester of pregnancy, are also considered to cause significant growth restriction when used for longer periods.<sup>2</sup> An antenatal hypertension clinic has been in operation at City Hospital, Birmingham since 1980, where pregnant women with hypertension undergo careful follow-up jointly by an obstetrician and a physician with a special interest in hypertension. Patients were referred to the clinic by obstetricians and general practitioners on the basis of previous hypertension, or raised blood pressures detected for the first time in pregnancy. In many, the blood pressure decreased with no therapy, and where possible antihypertensive drugs were discontinued. After the Glasgow study,<sup>1</sup> the use of atenolol in early pregnancy was discontinued and an audit was conducted of birth weights in relation to drug therapy.

...

We conducted an analysis of our own prospectively gathered and computerized database of all women attending our clinic between 1980 and 1995. Information on demographic data, presenting blood pressures, drug therapies, pregnancy complications, and pregnancy outcome were recorded. The mean

termine significant predictors for birth weights. A  $p$  value  $<0.05$  was considered statistically significant.

We reviewed data from the antenatal records of 398 consecutive pregnancies (137 white, 103 black, 158 Asian women; mean age  $30 \pm 6$  years) attending our antenatal hypertension clinic between 1980 and 1995. Two hundred thirty-five women were not taking any therapy during the first 20 weeks of pregnancy, whereas atenolol was taken by 76 women, labetalol by 7, other  $\beta$  blockers by 12, calcium antagonists by 22, diuretics by 26, methyldopa by 17, and angiotensin-converting enzyme inhibitors by 7 women; 18 women were taking multiple drug combinations.

Blood pressures during antihypertensive therapy are summarized in Table I. When compared with untreated cases, there was a trend toward higher mean systolic (1-way ANOVA,  $p = 0.064$ ) and diastolic blood pressures ( $p < 0.001$ ) in the first 20 weeks of pregnancy among women who were taking antihypertensive drugs (Table I). There were no significant differences in mean gestation period for each patient subgroup of treated and untreated women (1-way ANOVA,  $p = \text{NS}$ ).

Mean birth weights, median placental weights, and ponderal index are also summarized in Table I. Babies born to women taking atenolol were significantly lighter (1-way ANOVA,  $F = 5.3$ ,  $p < 0.001$ )

## **Effect of Atenolol on Birth Weight**

Gregory Y.H. Lip, MD, Michèle Beevers, SRN, David Churchill, MD, Lara M. Shaffer, MB,  
and D. Gareth Beevers, MD

In conclusion, this survey suggests that atenolol use may be detrimental in early pregnancy and provides confirmatory data with previous small prospective randomized trials. Our findings suggest that **atenolol should be avoided in women who are trying to conceive or who are in the early stages of pregnancy.**

# Stroke and Severe Preeclampsia and Eclampsia: A Paradigm Shift Focusing on Systolic Blood Pressure

James N. Martin Jr, MD, Brad D. Thigpen, DO, Robert C. Moore, MD, Carl H. Rose, MD, Julie Cushman, RN, and Warren May, PhD

## **Conclusion:**

**A paradigm shift is needed toward considering antihypertensive therapy for severely preeclamptic and eclamptic patients when SBP reaches or exceeds 155-160 mmHg.**

# Trends in Pregnancy Hospitalizations That Included a Stroke in the United States From 1994 to 2007

## Reasons for Concern?

Elena V. Kuklina, MD, PhD; Xin Tong, MPH; Pooja Bansil, MPH;  
Mary G. George, MD, MSPH; William M. Callaghan, MD, MPH

**Background and Purpose**—Stroke is an important contributor to maternal morbidity and mortality, but there are no recent data on trends in pregnancy-related hospitalizations that have involved a stroke. This report describes stroke hospitalizations for women in the antenatal, delivery, and postpartum periods from 1994 to 1995 to 2006 to 2007 and analyzes the changes in these hospitalizations over time.

**Methods**—Hospital discharge data were obtained from the Nationwide Inpatient Sample, developed as part of the Healthcare Cost and Utilization Project sponsored by the Agency for Healthcare Research and Quality. Pregnancy-related hospitalizations with stroke were identified according to the International Classification of Diseases, Ninth Revision. All statistical analyses accounted for the complex sampling design of the data source.

**Results**—Between 1994 to 1995 and 2006 to 2007, the rate of any stroke (subarachnoid hemorrhage, intracerebral hemorrhage, ischemic stroke, transient ischemic attack, cerebral venous thrombosis, or unspecified) among antenatal hospitalizations increased by 47% (from 0.15 to 0.22 per 1000 deliveries) and among postpartum hospitalizations by 83% (from 0.12 to 0.22 per 1000 deliveries) while remaining unchanged at 0.27 for delivery hospitalizations. In 2006 to 2007, ≈32% and 53% of antenatal and postpartum hospitalizations with stroke, respectively, had concurrent hypertensive disorders or heart disease. Changes in the prevalence of these 2 conditions from 1994 to 1995 to 2006 to 2007 explained almost all of the increase in postpartum hospitalizations with stroke during the same period.

**Conclusions**—Our results have demonstrated an increasing trend in the rate of pregnancy-related hospitalizations with stroke in the United States, especially during the postpartum period, from 1994 to 1995 to 2006 to 2007.

# Antihypertensive drugs used in pregnancy

## *Diuretics*

Diuretics are recommended for chronic hypertension if prescribed before gestation or if patients appear to be salt-sensitive. They are not recommended in pre-eclampsia.

## *Direct vasodilators*

**Hydralazine** is no longer the parenteral drug of choice; perinatal adverse effects.

# Antihypertensive drugs used in pregnancy

*Calcium-  
channel blockers*

Oral nifedipine or i.v. isradipine could be given in hypertensive emergencies. Potential synergism with magnesium sulfate may induce hypotension.

*ACE inhibitors,  
AIIA,  
direct renin inhibitors*

**Fetal abnormalities** including death can be caused and these drugs should not be used in pregnancy.

# Breast-feeding

- Does not increase BP in nursing mothers
- All antihypertensive agents taken by the nursing mother are excreted into breast milk; however, most of them are present at very low concentrations, except for propranolol and nifedipine concentrations, which are similar to maternal plasma

# COMMENTARY

## Hypertension in Pregnancy: A Potential Window into Long-Term Cardiovascular Risk in Women

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Hypertensive disorders of pregnancy affect approximately 6–8% of pregnancies and are the second leading cause of maternal mortality in the United States. They are also a leading cause of maternal and neonatal morbidity (1). Despite the frequency of these disorders, their cause is unknown and their treatment is inadequate. Hypertension in pregnancy is a gender specific condition by definition. As with many other disorders that affect women, hypertension in pregnancy involves the overlap of the fields of internal medicine and obstetrics. Whereas most essential hypertension is managed by internists, when a pregnant woman is hypertensive, the care of the hypertension is managed primarily by obstetricians. This leads to an interesting potential duality in the focus and approach of each specialty. In general, hypertension in pregnancy has been viewed as an obstetrical disorder and has not been an area of investigation for most internists. For the obstetrician, the disorder is one of pregnancy itself, and the focus is on the outcome of the individual pregnancy. On the other hand, for the internist an emerging focus is on the potential implications of hyperten-

and resolving postpartum. Preeclampsia differs from gestational hypertension due to its multisystem involvement as proteinuria as described below. When a woman with preexisting hypertension develops an exacerbation of hypertension during pregnancy accompanied by proteinuria or other systemic signs, this is termed hypertension superimposed preeclampsia.

### *Diagnosis and clinical course*

When a woman presents with hypertension in pregnancy the first step is to establish whether it is of new onset or preexisting. With more women delaying child bearing to later ages, pregnancies are occurring more frequently at an age when women have already developed essential hypertension. Essential hypertension carries with it an excellent prognosis in pregnancy unless superimposed preeclampsia develops. Two major areas of difference in management between hypertension during pregnancy *vs.* hypertension outside of pregnancy are in the choice of antihypertensive agents and the goal of treatment.

# Pre-eclampsia and risk of cardiovascular disease and cancer in later life: systematic review and meta-analysis

Leanne Bellamy, medical student,<sup>1</sup> Juan-Pablo Casas, clinical lecturer,<sup>2</sup> Aroon D Hingorani, reader,<sup>3</sup> David J Williams, consultant obstetric physician<sup>4</sup>

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## ABSTRACT

**Objective** To quantify the risk of future cardiovascular diseases, cancer, and mortality after pre-eclampsia.

**Design** Systematic review and meta-analysis.

**Data sources** Embase and Medline without language restrictions, including papers published between 1960 and December 2006, and hand searching of reference lists of relevant articles and reviews for additional reports.

**Review methods** Prospective and retrospective cohort studies were included, providing a dataset of 3 488 160 women, with 198 252 affected by pre-eclampsia (exposure group) and 29 495 episodes of cardiovascular disease and cancer (study outcomes).

**Results** After pre-eclampsia women have an increased risk of vascular disease. The relative risks (95% confidence intervals) for hypertension were 3.70 (2.70 to 5.05) after 14.1 years weighted mean follow-up, for ischaemic heart disease 2.16 (1.86 to 2.52) after 11.7 years, for stroke 1.81 (1.45 to 2.27) after 10.4 years, and for venous thromboembolism 1.79 (1.37 to 2.33) after 4.7 years. No increase in risk of any cancer was found (0.96, 0.73 to 1.27), including breast cancer (1.04, 0.78 to 1.39) 17 years after pre-eclampsia. Overall mortality after pre-eclampsia was increased: 1.49 (1.05 to 2.14) after 14.5 years.

**Conclusions** A history of pre-eclampsia should be considered when evaluating risk of cardiovascular

and some are also features of the “metabolic syndrome” a “risk factor” for cardiovascular disease.<sup>10</sup> It is possible that pre-eclampsia increases risk of later cardiovascular disease,<sup>11</sup> either because of a shared cause or because subclinical vascular damage occurs during pre-eclampsia.

If a history of pre-eclampsia exerts an independent risk for future cardiovascular disease it may increase the risk of cardiovascular disease in mid-life in affected women, which would render them eligible for preventive therapies at an earlier age than usual. To investigate the association between pre-eclampsia and atherosclerosis in later life we carried out a systematic review and meta-analysis of studies that had estimated the risk of arterial and venous diseases after pre-eclampsia. We also evaluated the risk of future cancer after pre-eclampsia, in particular breast cancer, one of the commonest causes of death in middle aged women.<sup>13,14</sup> Finally we investigated mortality from any cause after a pregnancy affected by pre-eclampsia.

## METHODS

We searched Medline and Embase with no language restrictions up to December 2006. Additional eligible studies were sought by a hand search of reference lists from primary articles and relevant reviews. (See [bmj.com](http://bmj.com) for search terms and combinations).

## AHA Guideline

# Effectiveness-Based Guidelines for the Prevention of Cardiovascular Disease in Women—2011 Update

## A Guideline From the American Heart Association

### EXECUTIVE WRITING COMMITTEE

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- **Pregnancy provides a unique opportunity to estimate a woman's lifetime risk**
- **Preeclampsia may be an early indicator of CVD risk**

**When  
to Treat Hypertension  
in Pregnancy**

- 1. There is general consensus severe hypertension in pregnancy ( $\geq 160/110$  mmHg) should be treated by antihypertensive drugs**
- 2. However, there is no evidence drug treatment of mild-to-moderate hypertension in pregnancy is beneficial (no difference in outcome of preeclampsia, neonatal death, pre-term birth, small-for-gestational-age babies)**
- 3. Limitations in study design (small number of participants, no longitudinal outcome)**

**How  
to Treat Hypertension  
in Pregnancy**

# Conclusions

- In *non-severe hypertension*, oral methyldopa, labetalol, calcium antagonists, and (less frequently) beta-blockers are drugs of choice
- In pre-eclampsia with pulmonary edema, nitroglycerin is the drug of choice, diuretic therapy is inappropriate because plasma volume is reduced
- As *emergency*, intravenous labetalol, oral methyldopa, and oral nifedipine are indicated. *Intravenous hydralazine is no longer the drug of choice* because of an excess of perinatal adverse effects

# **ASA in the prevention of pre-eclampsia**

- **ASA (75 mg daily) is recommended in the prevention of pre-eclampsia in women at high or moderate risk of pre-eclampsia from 12 weeks of gestation until delivery**



## ESC Guidelines on the management of cardiovascular diseases during pregnancy

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

Endorsed by the European Society of Gynecology (ESG), the Association for European Paediatric Cardiology (AEPC), and the German Society for Gender Medicine (DGesGM)

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# Maternal antihypertensive medications usually compatible with breastfeeding

**Captopril**

**Diltiazem**

**Enalapril**

**Hydralazine**

**Hydrochlorothiazide**

**Labetalol**

**Methyldopa**

**Minoxidil**

**Nadolol**

**Nifedipine**

**Oxprenolol**

**Propranolol**

**Spiro lactone**

**Timolol**

**Verapamil**

# **Maternal antihypertensive medications usually compatible with breastfeeding**

- **Diuretics (furosemide, hydrochlorothiazide, and spironolactone) may reduce milk production.**
- **Metoprolol is classified as compatible with breastfeeding, although it is concentrated in human milk.**
- **Acebutolol and atenolol should not be used in nursing mothers.**

*Pediatrics 2001;108:776-789*

# Conclusions

- *I.v. infusion of sodium nitroprusside* is useful *in hypertensive crisis*, but prolonged administration should be avoided
- Calcium supplementation, fish oil, and low-dose aspirin are not recommended. However, *low-dose aspirin may be used prophylactically in women with a history of an early onset of pre-eclampsia*

**A 28-year-old primipara with no history of hypertension whose BP was normal in the first half of pregnancy, is referred to you at 26 weeks of gestation with BP 140-150/90-95 mmHg, she has no symptoms**

**Urinalysis: dipstick +**

**What would be your classification of hypertension in this patient?**

- 1. Pre-existing hypertension**
- 2. Gestational hypertension**
- 3. Pre-eclampsia**

**Primipara, 28 years old, no history of hypertension, normal BP in the first half of pregnancy, with BP 140-150/90-95 mmHg at 26 weeks of gestation; urinalysis: dipstick +**

**What would be your suggested management of hypertension?**

- 1. Methyldopa 200 mg t.i.d.**
- 2. Salt restriction**
- 3. Reduction in daily activities**
- 4. Atenolol 50 mg b.i.d.**

**Visit 4 weeks later (i.e., week 30 of gestation)**

**Primipara, 28 years old, no history of hypertension, normal BP in the first half of pregnancy, with BP 140-150/90-95 mmHg at 30 weeks of gestation, no symptoms**

**Which is the most important test you need for further evaluation?**

- 1. Blood count**
- 2. Liver tests**
- 3. Urinalysis**
- 4. EKG**

**Primipara, 28 years old, no history of hypertension, normal BP in the first half of pregnancy, with BP 140-150/90-95 mmHg at 30 weeks of gestation, no symptoms**

**Urinalysis: dipstick ++**

**What would you suggest as the next step?**

- 1. Initiate drug treatment immediately**
- 2. Quantify proteinuria**
- 3. ABPM**
- 4. ABPM + quantify proteinuria**

**Primipara, 28 years old, no history of hypertension, normal BP in the first half of pregnancy, with BP 140-150/90-95 mmHg at 30 weeks of gestation**

**24-h urine collection: 0.355 g protein**

**ABPM: mean daytime BP 138/91 mmHg  
mean nighttime BP 128/82 mmHg**

**What would you suggest as the next step?**

- 1. Wait and watch; schedule the next visit in 2 weeks**
- 2. Initiate methyldopa 250 mg b.i.d.**
- 3. Initiate nifedipine SR 20 mg b.i.d.**

# WHO definition of hypertension in pregnancy

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1. SBP  $\geq$  140 mmHg or DBP  $\geq$  90 mmHg
2. Rise in SBP  $\geq$  25 mmHg or rise in DBP  $\geq$  15 mmHg compared to pre-pregnancy values or those in the first trimester

# **2007 ESH-ESC Guidelines**

## **Measurement of BP**

- **Mercury sphygmomanometer**
- **Phase V to be recorded**

# Lack of reproducibility in pregnancy of Korotkoff phase IV as measured by mercury sphygmomanometry

*Andrew Shennan, Manish Gupta, Aidan Halligan, David J Taylor, Michael de Swiet*

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## **Summary**

**Background** Since hypertensive disorders of pregnancy are common, blood pressure is frequently measured in all pregnant women. Many authorities recommend that Korotkoff phase IV (K4, muffling of sound) is taken as the diastolic identification point measured on mercury sphygmomanometry in pregnancy because of reports that phase V (K5, disappearance of sound) is at or near to zero cuff pressure in some pregnant women. We compared the identification and reproducibility of K4 and K5 by observers unaware of each other's results.

## **Introduction**

Hypertensive disorders affect more than 10% of pregnant women.<sup>1</sup> Measurement of blood pressure is essential for diagnosis and management of these disorders and is therefore one of the commonest tests done in pregnancy. Most definitions and clinical decisions are based on the diastolic blood pressure,<sup>2-4</sup> and the majority of measurements are made by mercury sphygmomanometry. This technique relies on the auscultation of Korotkoff sounds over the brachial artery heard distal to a deflating cuff.<sup>5</sup> In 1907 Ettinger described a muffling of sound (a transformation of a clear sound to a dull tone) during this

*Lancet 1996;347:139-42*

# **ABPM in pregnancy**

- **White-coat hypertension**
- **Early prediction of pre-eclampsia**
- **Prognosis in late pregnancy**

# Devices evaluated in pregnancy

Device	Type	AAMI	BHS	Recommendation
Diestronic Profilomat	Aus	Pass	B/C	no
Tycos QuietTrak	Aus	Fail	B/B	no
Tycos QuietTrak	Aus	-	A/A	yes
SpaceLab 90207	Osc	Pass	B/B	yes
SpaceLab 90207	Osc	Pass	A/C	no
SpaceLab 90207	Osc	Pass	B/C	no

# Devices evaluated in pre-eclampsia

<b>Device</b>	<b>Type</b>	<b>AAMI</b>	<b>BHS</b>	<b>Recommendation</b>
<b>Tycos QuietTrak</b>	<b>Aus</b>	<b>Fail</b>	<b>D/D</b>	<b>no</b>
<b>SpaceLab 90207</b>	<b>Osc</b>	<b>Fail</b>	<b>D/D</b>	<b>no</b>
<b>SpaceLab 90207</b>	<b>Osc</b>	<b>Pass</b>	<b>C/C</b>	<b>no</b>

# Hypertensive encephalopathy

1-2% of untreated essential hypertension  
SBP > 250 or DBP > 150 mmHg

## Treatment

- ↓ Mean BP by no more than 15-25% towards DBP 100-110 mmHg
- Drug of choice: *sodium nitroprusside*
- Other drugs: *nitroglycerin, nifedipine, labetalol*

# Antiplatelet drugs for prevention of pre-eclampsia and its consequences: systematic review

Lelia Duley, David Henderson-Smart, Marian Knight, James King

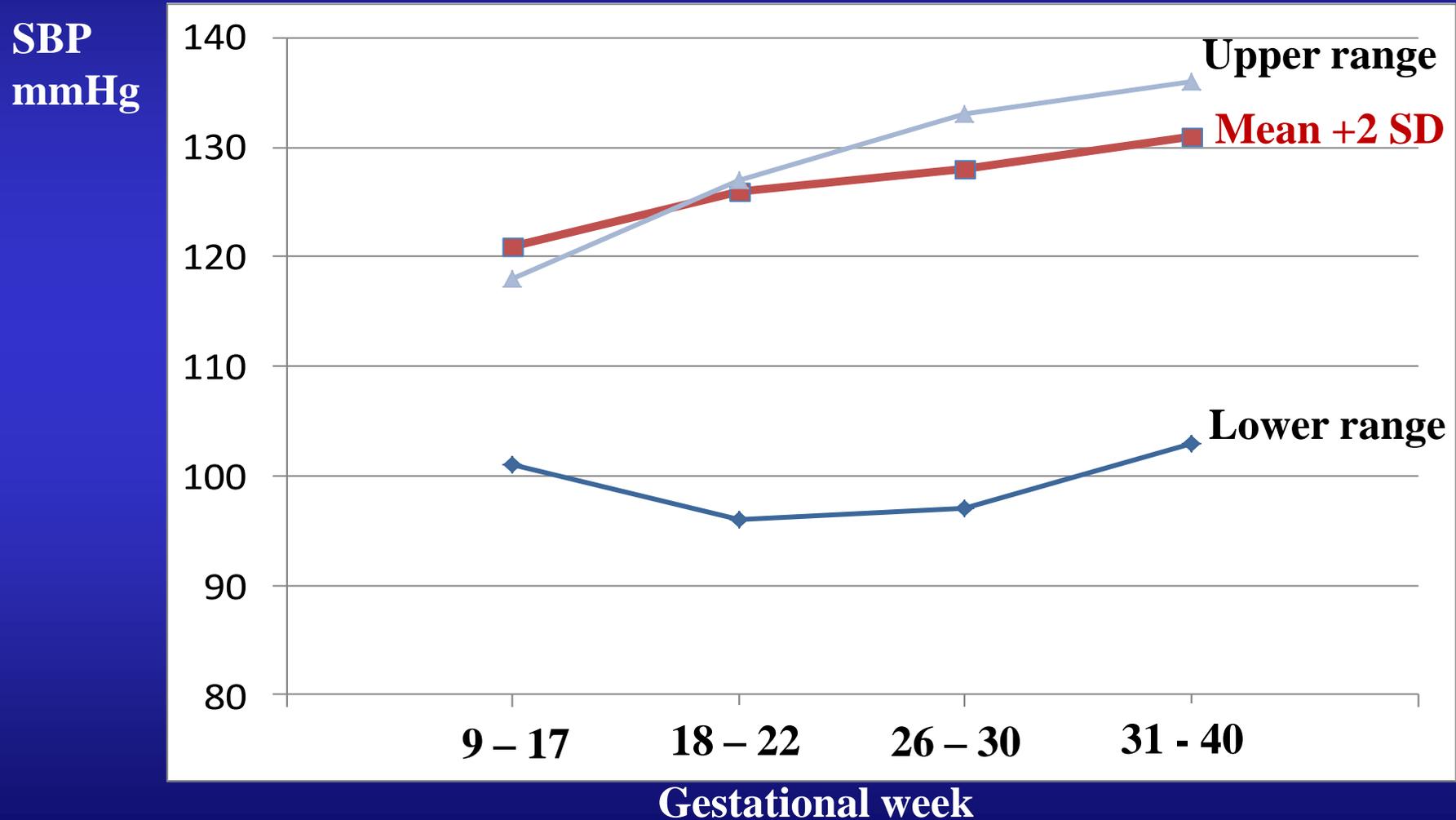
**39 trials; 30 563 women**

- **15% RR of pre-eclampsia**
- **8% RR preterm birth**
- **14% RR fetal or neonatal death**

# Conclusions

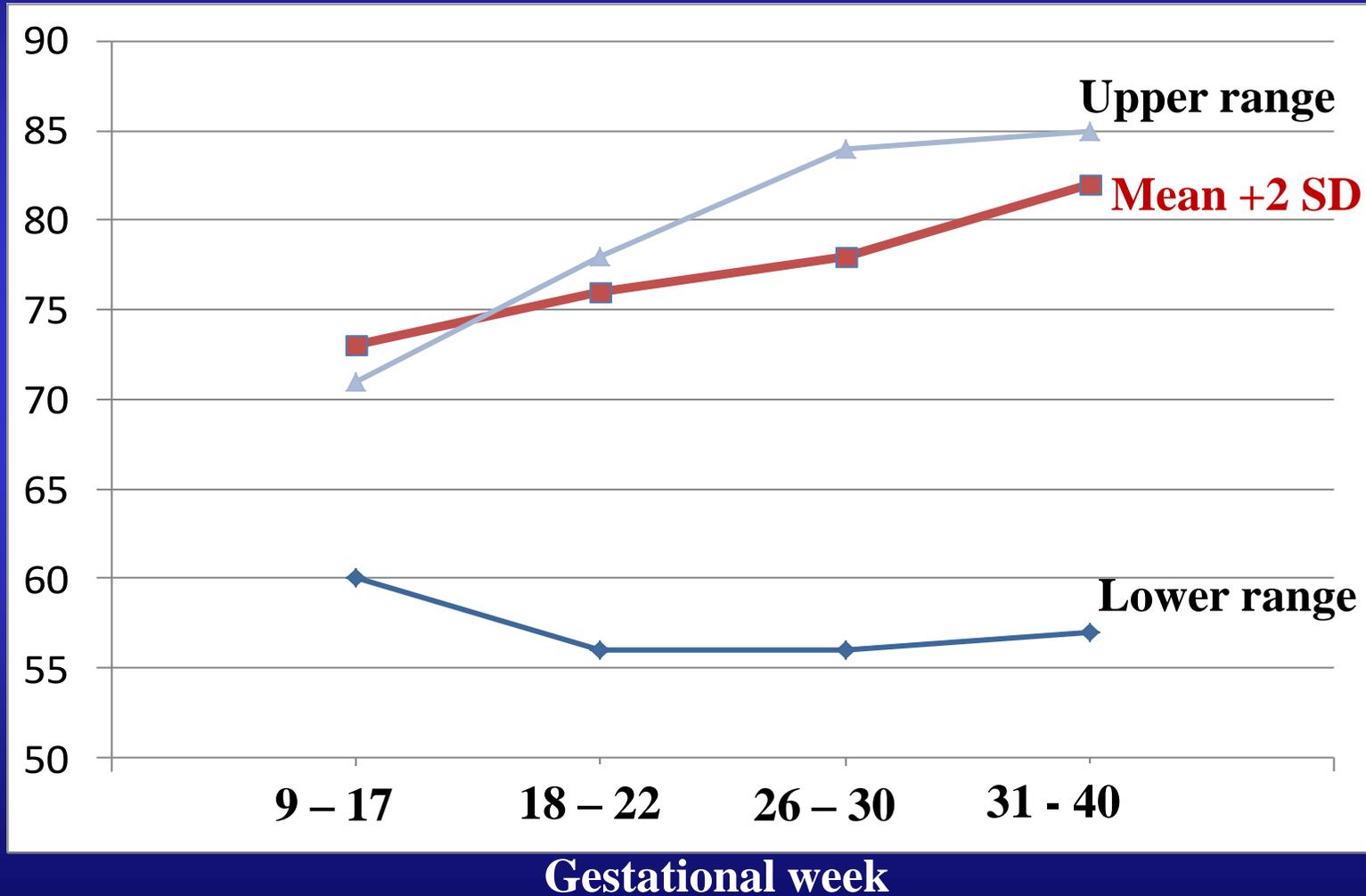
- *Korotkoff Phase V is now recommended for the measurement of DBP in pregnancy* with Phase IV being indicated only if Korotkoff sounds persist at cuff pressures approaching 0 mmHg
- *Non-pharmacological management* should be considered for pregnant women with **SBP 140-149 mmHg or DBP 90-95 mmHg**
- In *gestational hypertension* with or without proteinuria, *drug treatment* is indicated at **BP levels  $\geq$  140/90 mmHg**

# Ambulatory blood pressure values according to gestational age



# Ambulatory blood pressure values according to gestational age

DBP  
mmHg



## Guideline

# European Society of Hypertension Position Paper on Ambulatory Blood Pressure Monitoring

Eoin O'Brien\*, Gianfranco Parati\*, George Stergiou\*, Roland Asmar, Laurie Beilin, Grzegorz Bilo, Denis Clement, Alejandro de la Sierra, Peter de Leeuw, Eamon Dolan, Robert Fagard, John Graves, Geoffrey A. Head, Yutaka Imai, Kazuomi Kario, Empar Lurbe, Jean-Michel Mallion, Giuseppe Mancia, Thomas Mengden, Martin Myers, Gbenga Ogedegbe, Takayoshi Ohkubo, Stefano Omboni, Paolo Palatini, Josep Redon, Luis M. Ruilope, Andrew Shennan, Jan A. Staessen, Gert vanMontfrans, Paolo Verdecchia, Bernard Waeber, Jiguang Wang, Alberto Zanchetti, Yuqing Zhang, on behalf of the European Society of Hypertension Working Group on Blood Pressure Monitoring\*\*

Ambulatory blood pressure monitoring (ABPM) is being used increasingly in both clinical practice and hypertension research. Although there are many guidelines that emphasize the indications for ABPM, there is no comprehensive guideline dealing with all aspects of the technique. It was agreed at a consensus meeting on ABPM

**Keywords:** ambulatory blood pressure monitoring, clinic blood pressure measurement, clinical indications, guidelines, home blood pressure measurement, recommendations, research application