Υπέρταση στις γυναίκες

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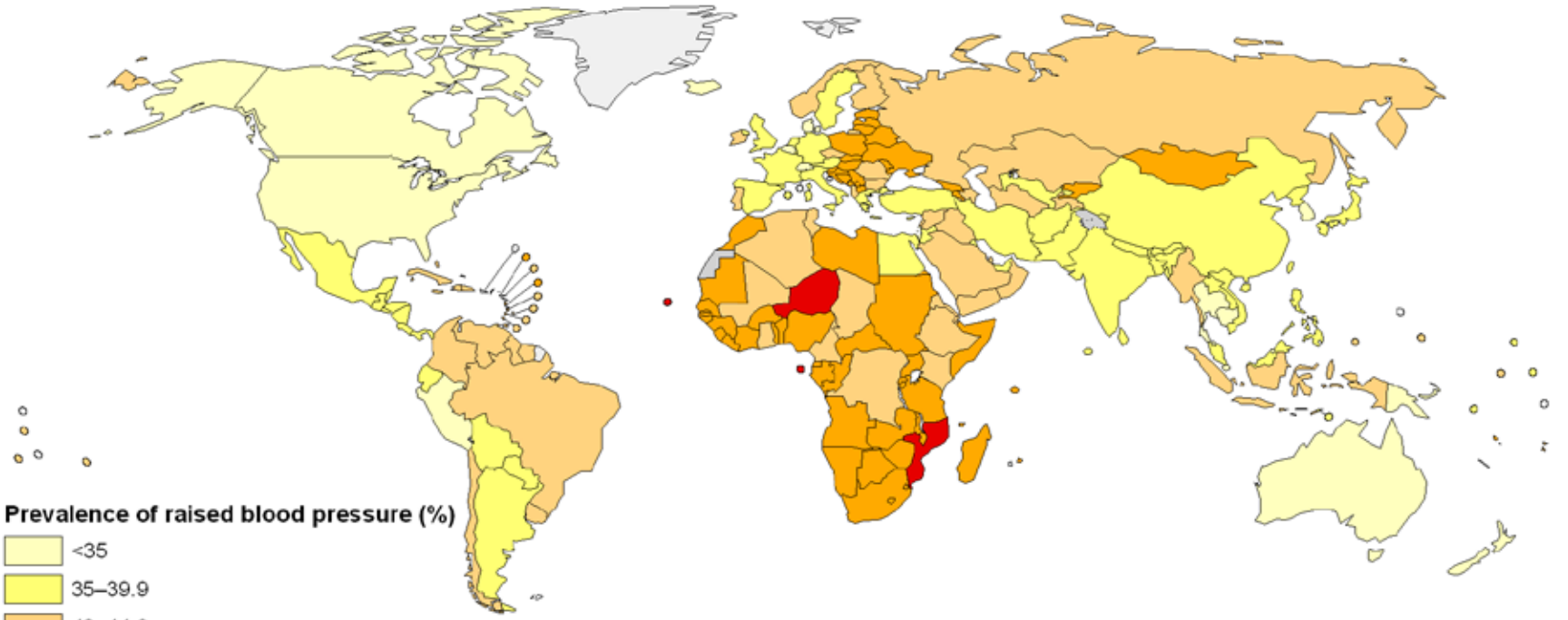
Cardiovascular disease is the Europe's No. 1 killer

- Main cause of disease
  More than 4.3 million deaths/year
- 48% of all deaths
  - Coronary heart disease – most common cause of death in Europe (1.9 million deaths/year)
  - Stroke – more than 500,000 deaths/year
- Cost to EU estimated at €192 billion/year

Prevalence of raised blood pressure*, ages 25+, age standardized
Both sexes, 2008



54% of strokes and 47% of IHD attributable to untreated hypertension

* SBP ≥140 and/or DBP ≥90 or using medication to lower blood pressure

Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

Blood Pressure and CAD/Stroke Mortality

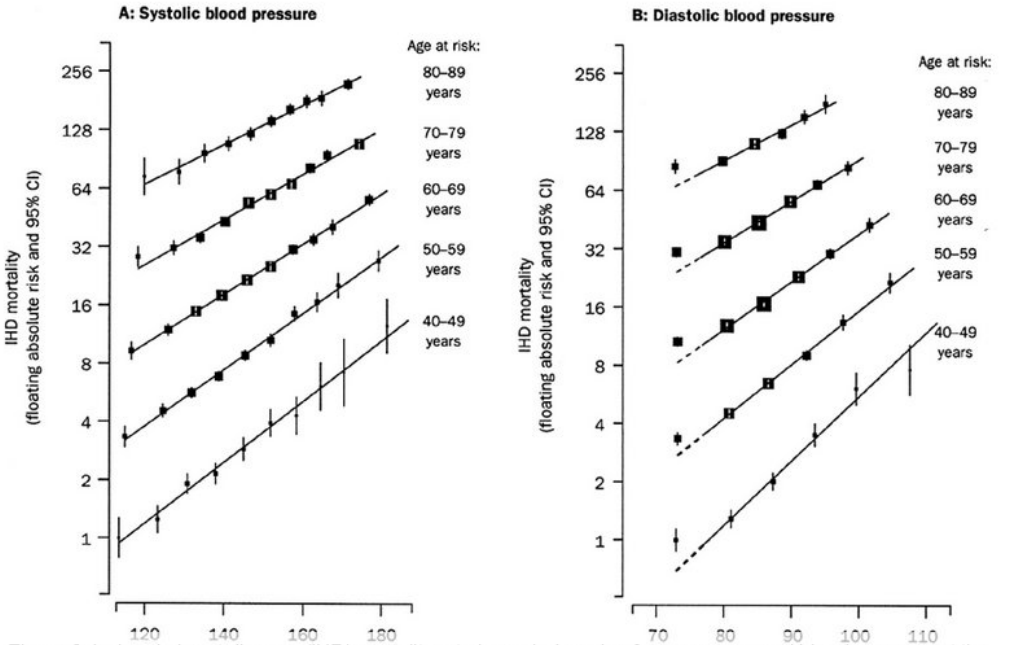
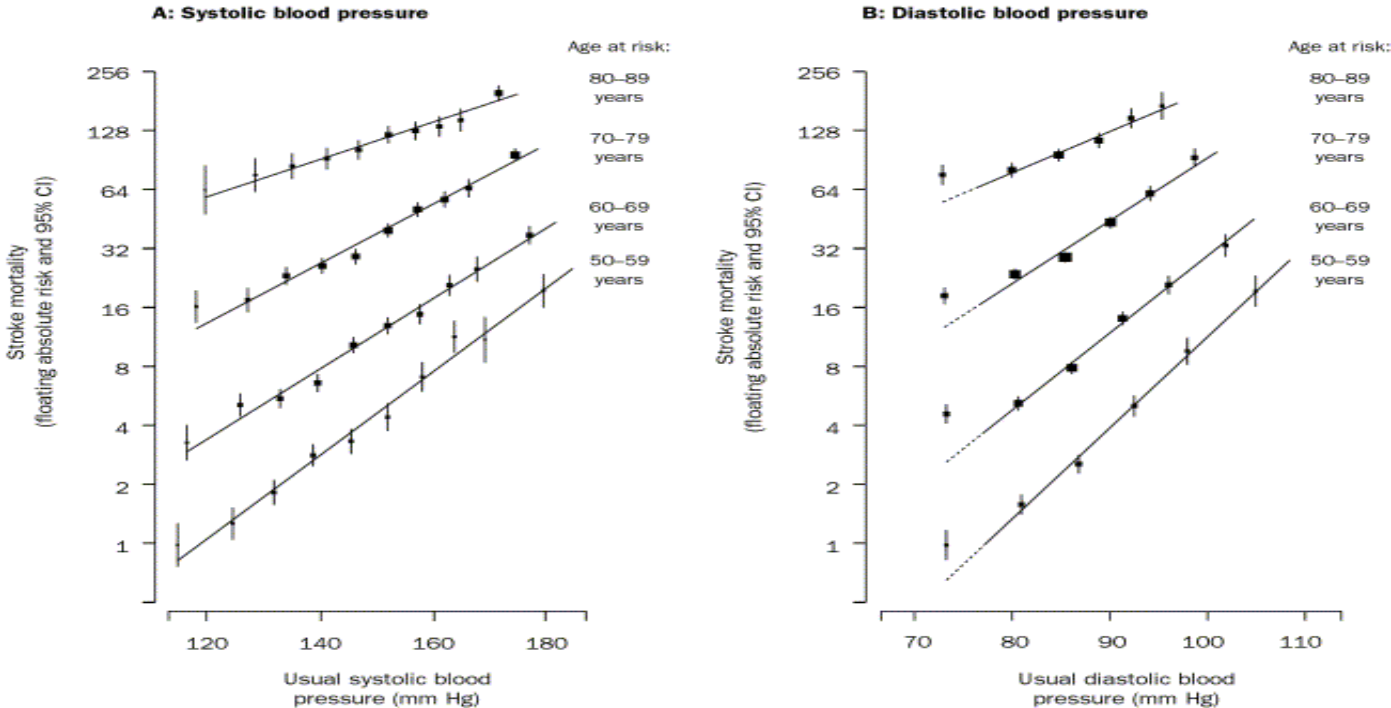
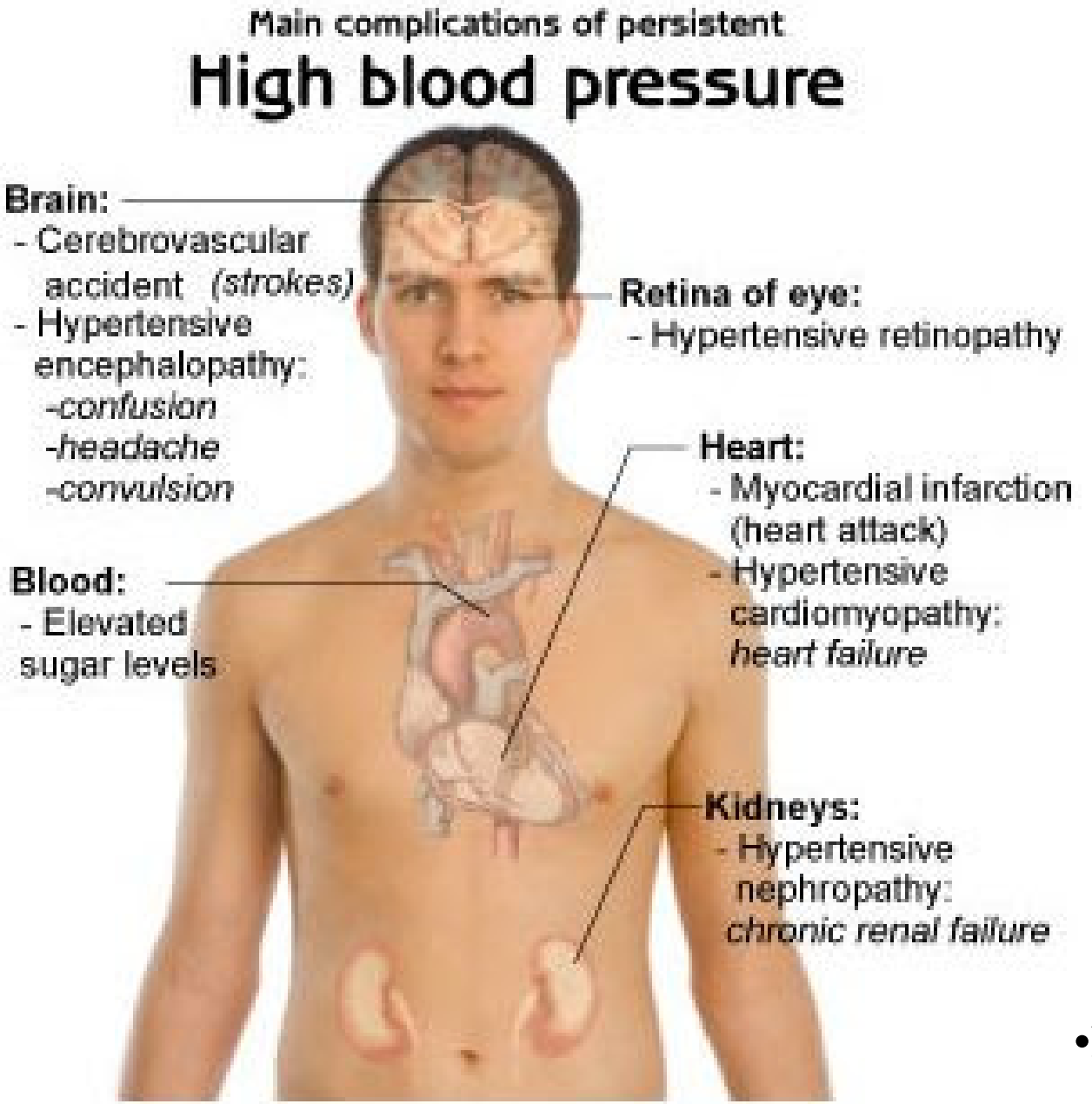


Figure 9. Ischemic heart disease (IHD) mortality rate in each decade of age versus usual blood pressure at the start of that decade. Source: Reprinted with permission from Elsevier (The Lancet, 2002;360:1903–1913).





Heart:

•Aortic Aneurysms

•Atrial fibrillation

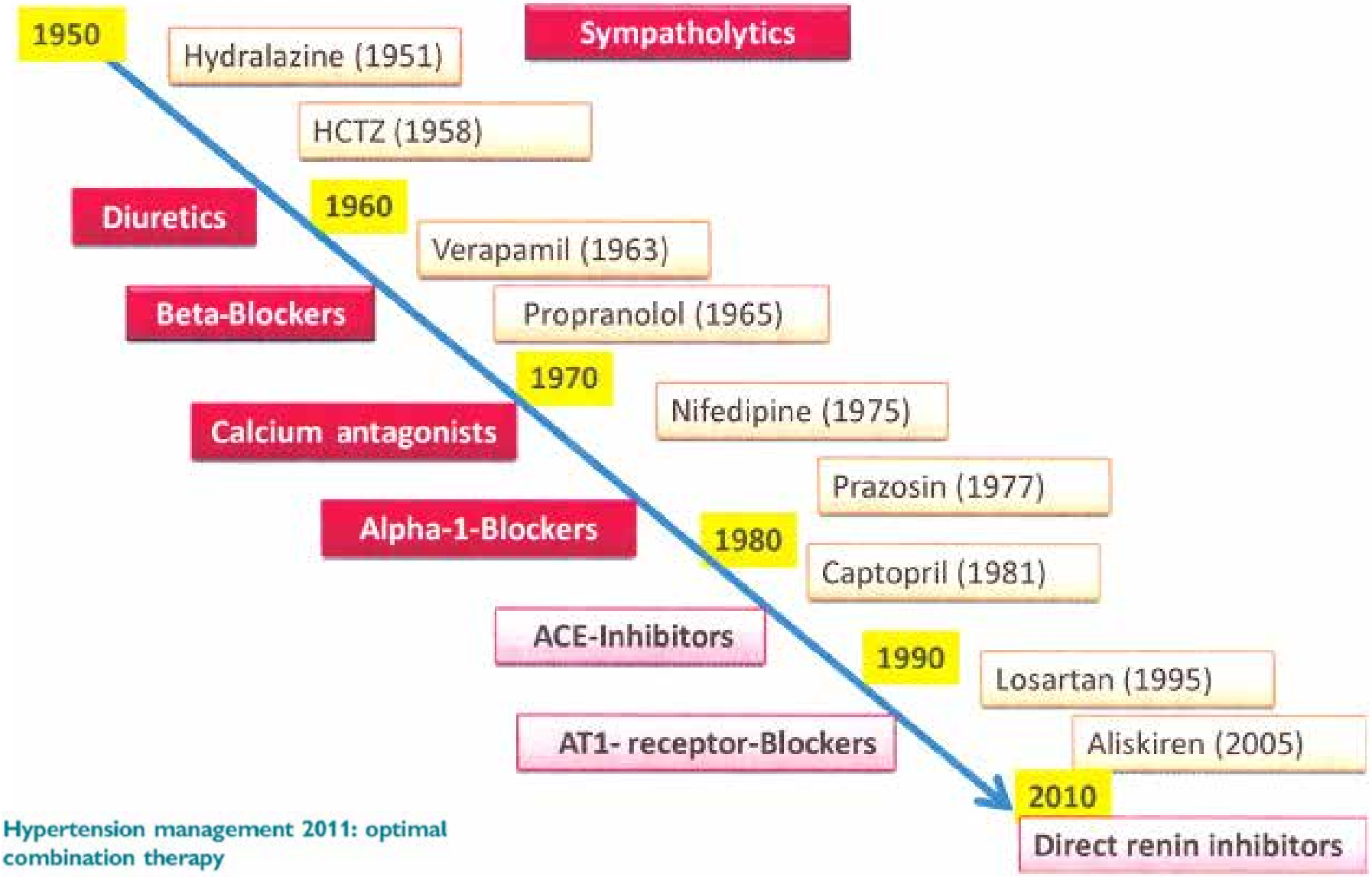
Arteries:

•Peripheral artery disease

• Sexual dysfunction

The history of antihypertensives

Reserpine, Pentolinium, Guanethidine, Methyl dopa (1950—1960), Clonidine (1980)



Hypertension management 2011: optimal combination therapy

Peter S. Sever[1]* and Franz H. Messerli[2]

European Heart Journal Advance Access published June 22, 2011

Εκτίμηση καρδιαγγειακού κινδύνου

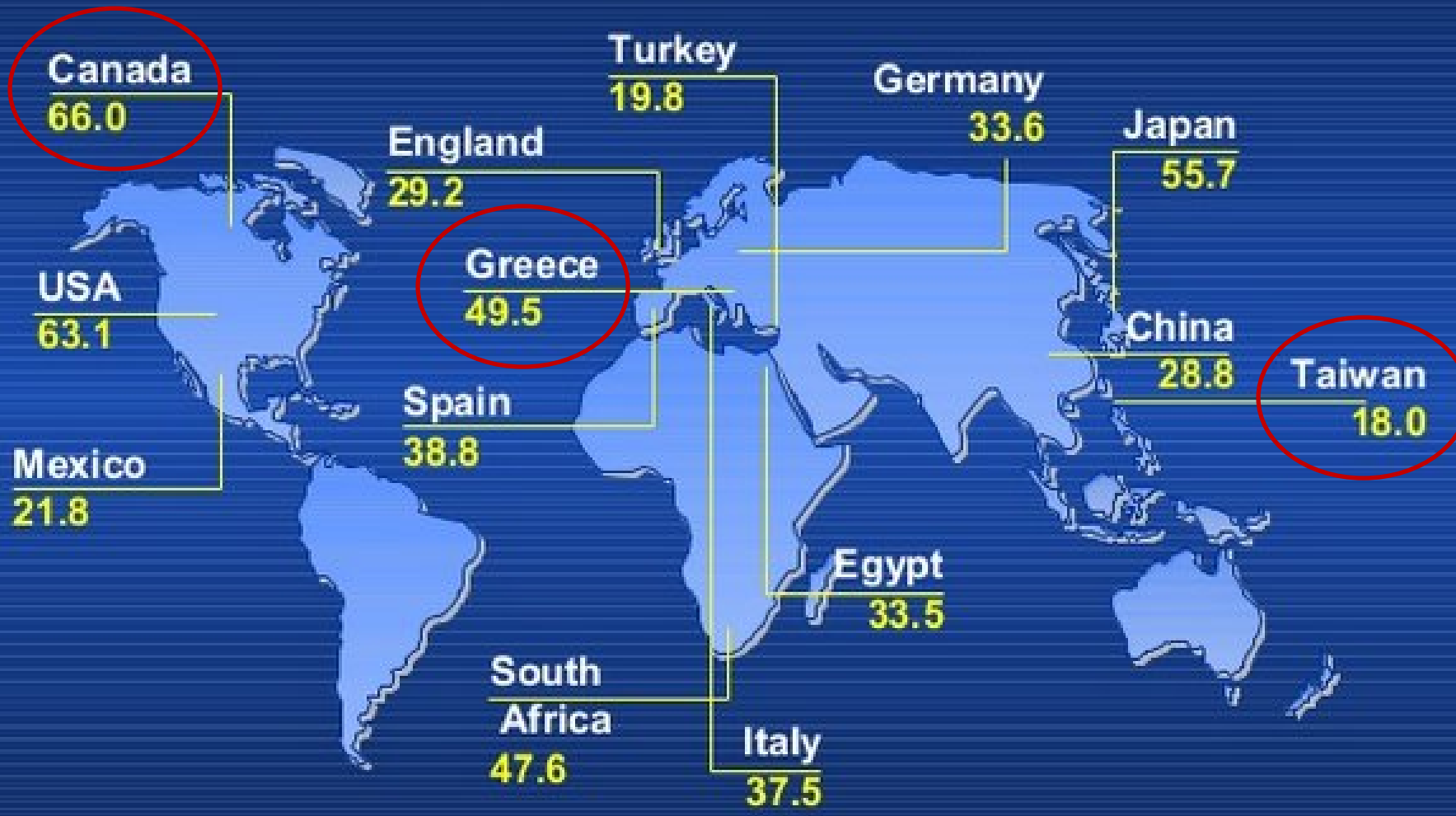
Other risk factors, asymptomatic organ damage or disease	Blood pressure (mmHg)			
	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP ≥180 or DBP ≥110
No other RF		Low risk	Moderate risk	High risk
1–2 RF	Low risk	Moderate risk	Moderate to high risk	High risk
≥3 RF	Low to moderate risk	Moderate to high risk	High risk	High risk
OD, CKD stage 3 or diabetes	Moderate to high risk	High risk	High risk	High to very high risk
Symptomatic CVD, CKD stage ≥ 4 or diabetes with OD/RFs	Very high risk	Very high risk	Very high risk	Very high risk

BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; DBP = diastolic blood pressure; HT = hypertension; OD = organ damage; RF = risk factor; SBP = systolic blood pressure.

FIGURE 1 Stratification of total CV risk in categories of low, moderate, high and very high risk according to SBP and DBP and prevalence of RFs, asymptomatic OD, diabetes, CKD stage or symptomatic CVD. Subjects with a high normal office but a raised out-of-office BP (masked hypertension) have a CV risk in the hypertension range. Subjects with a high office BP but normal out-of-office BP (white-coat hypertension), particularly if there is no diabetes, OD, CVD or CKD, have lower risk than sustained hypertension for the same office BP.

2013 ESH/ESC Guidelines for the management of arterial hypertension

Worldwide blood pressure control in treated hypertensive patients



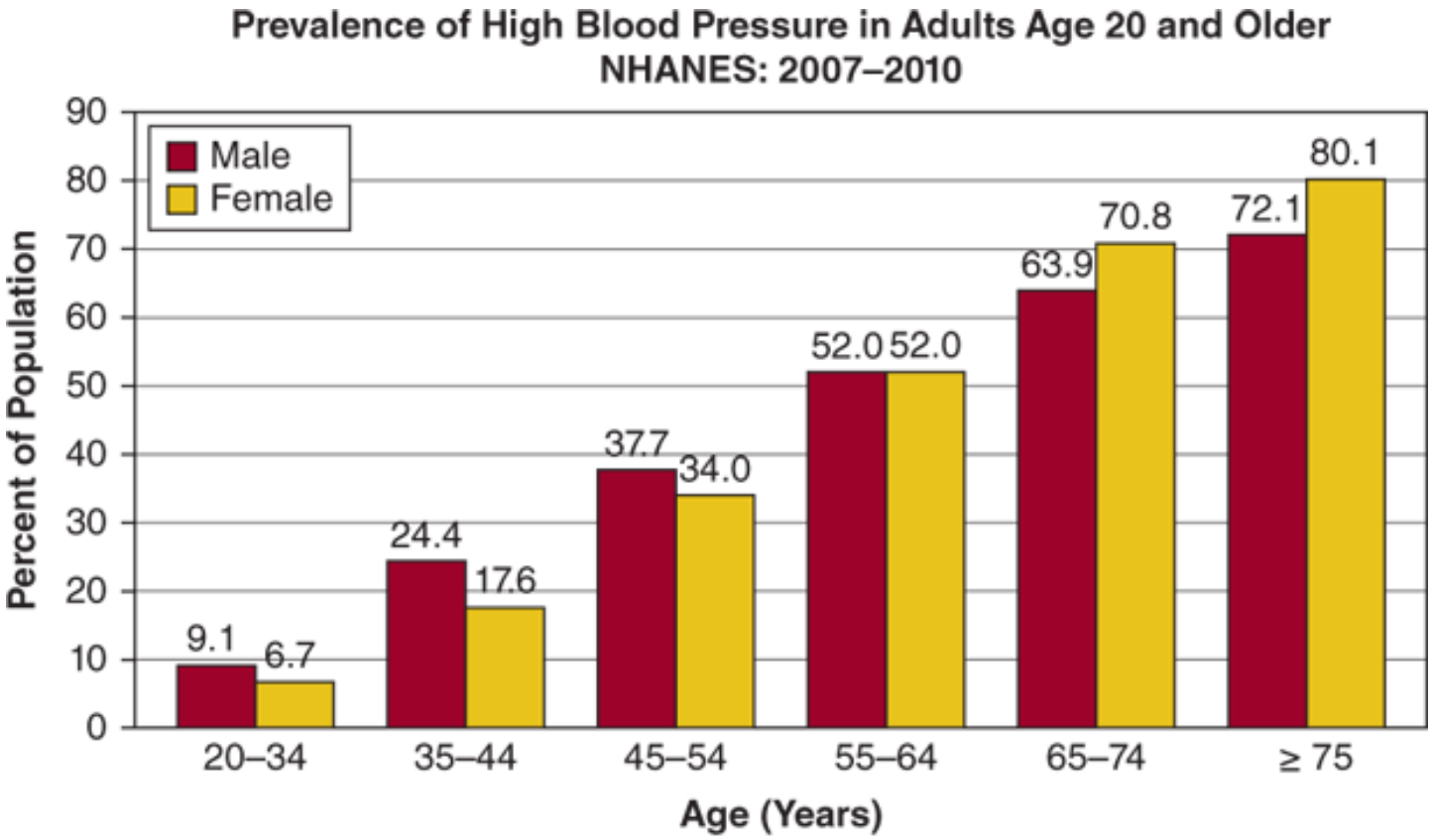
Updated from Kearney et al. *J Hypertens* 2004;22:11–9

Compliance
with antihypertensive therapy

- Compliance equal to 25-85% depending on series with a 53% as a mean value

- Risk factors for **non-compliance**:

1. young age
2. female sex
3. single persons
4. **comorbidities**
5. **cost for medications**
6. drug class-side effects
7. lack of symptoms
8. **ineffective consultation**



During early adulthood mean systolic BP is higher in men than women, but the subsequent rate of rise in BP is steeper for women than men. Prevalence and severity of hypertension increase markedly with advancing age in women, such **that a higher percentage of women than men have high BP after 65 years**

Hypertension in women

Eduardo Pimenta

Hypertension Research (2012) 35, 148–152

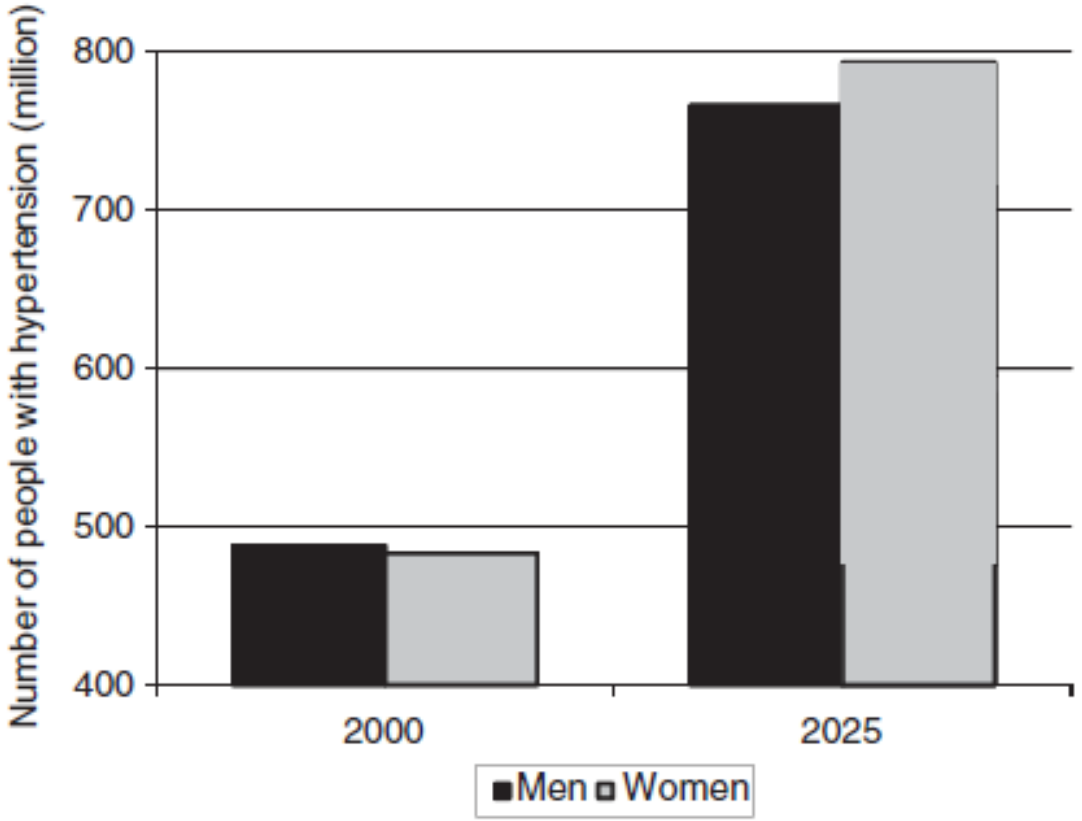


Figure 1 Number of men and women with hypertension in 2000 and 2025. (Data from Kearney *et al.*[6])

Aging of world population by 2025 and longer life expectancies in women than in men are possibly related to the greater increases in the prevalence of hypertension among women.

Hypertension in women

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Hypertension Research (2012) 35, 148–152

Data from the Framingham Heart Study showed **gender differences in BP control rates** and in the pattern of antihypertensive medications prescribed. An **age-related decrease in BP control rates** were more pronounced in women than in men. Among the oldest participants with hypertension, only 23% of women (vs. 38% of men) were controlled to BP ≤140/90 mmHg.

Treatment **with thiazide diuretics** was also **more frequent** among women than men (38 vs. 23%, respectively) while **ACE-I** prescription **less common**. It is unknown whether the age-related decline in BP control among women is related to **true treatment resistance because of biological factors or to inappropriate therapeutic choices in the clinical setting (drug selection, inadequate intensity of treatment, lack of compliance).**

Lloyd-Jones DM, Evans JC, Levy D. Hypertension in adults across the age spectrum: current outcomes and control in the community. JAMA 2005; 294: 466–472.

Hypertension in women

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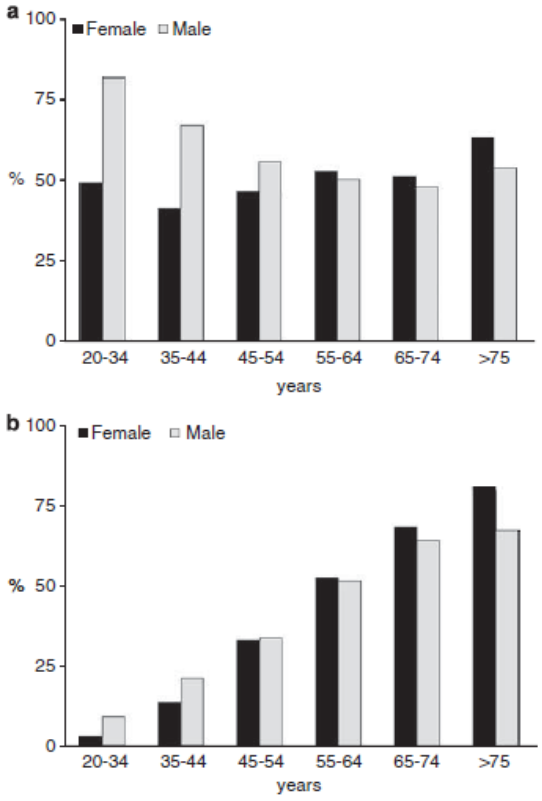
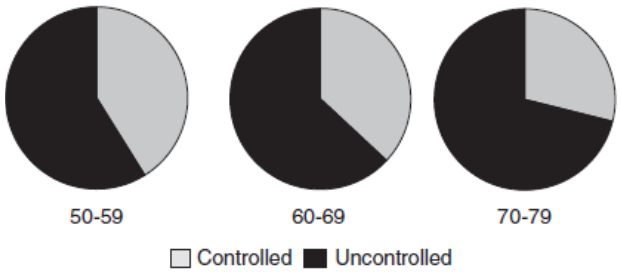


Figure 1 HTN control and prevalence among persons 20 years of age and over: United States, selected years 1988–1994 through 2005–2008. (**a**) Uncontrolled HTN among persons with diagnosed HTN. Uncontrolled HTN is defined as measured systolic BP of at least 140 mm Hg or diastolic BP of at least 90 mm Hg, among those with measured high BP or reporting taking antihypertensive medication. (**b**) Prevalence of HTN. HTN is defined



gure 2 Blood pressure control rates in women according to age. (Data om Wassertheil-Smoller *et al.*[26])

<u>Hypertension control</u> in women remains **poor**, especially among **elderly women.**

Rates of uncontrolled hypertension were positively related with age with only **29% of hypertensive women aged 70–79 years having clinic BP <140/90mmHg**.

An increased prevalence of **concomitant CV factors**, including central obesity, elevated total cholesterol and low HDL-C levels are likely to contribute to poor BP control in elderly women.

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Gender Differences in Hypertension: Myths and Reality

Michael Doumas · Vasilios Papademetriou · Charles Faselis · Peter Kokkinos

Curr Hypertens Rep (2013) 15:321–330

Pathophysiology

- Protective effects of estrogens before menopause in women
- Progesterone promotes and estradiol attenuates sympathetic activity
- Sexual dimorphism in salt sensitivity
- Attenuation of endothelin-1 effects in women

Estrogen induces vasodilatation, prevents vascular remodeling processes, inhibits vascular response to injury, provides reno-protection and decreases basal sympathetic tone.

Progesterone induces endothelium-dependent vascular relaxation.

Gender Differences in Hypertension: Myths and Reality

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Target organ damage

- Lower prevalence of left ventricular hypertrophy in women
- Higher prevalence of heart failure with preserved ejection fraction in women

Hypertension-induced left ventricular hypertrophy is different in female and male patients, since **hypertensive women are more likely to develop concentric hypertrophy** while eccentric hypertrophy is more common among men.

Arterial stiffness becomes more pronounced in postmenopausal women than men, leading to greater pulsatile afterload and subsequent diastolic dysfunction.

Carotid plaques are more common in hypertensive men than women.

Hypertension in women

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Hypertension Research (2012) 35, 148–152

Fibromuscular dysplasia, a nonatherosclerotic noninflammatory vascular disease that can affect renal arteries and cause renovascular hypertension, primarily affects women aged from age 20 to 60, but can also affects men and children.

Primary aldosteronism (PA), once considered being a rare condition has been demonstrated to be much more prevalent than previously thought and is probably the commonest cause of secondary hypertension. **The prevalence of PA is similar in men and women**, but **estrogen and progesterone can affect aldosterone and renin levels and, consequently, can interfere with the investigation of PA**. Screening with aldosterone–renin ratio can be affected by the phase of menstrual cycle and by different forms of contraception.

Pregnancy

Hypertension in women

Eduardo Pimenta

Hypertension Research (2012) 35, 148–152

During early **pregnancy**, significant plasma volume expansion is common and frequently associated with a decrease in systemic vascular resistance, which leads to an increased cardiac output as well as a **fall in mean arterial pressure**. In women with mild pre-existing HTN these changes **can obscure an early diagnosis of HTN**. Pregnancy-associated HTN affects about 10% of all pregnancies.

Preeclampsia, which is a pregnancy-specific syndrome of exaggerated vasoconstriction and reduced organ perfusion, must be differentiated from **pre-existing chronic hypertension** as the former can threaten the lives of both mother and fetus, and requires specialized care.

Preeclampsia places women at **long-term risk for CV diseases** and that careful follow-up and aggressive preventive strategies are recommended.

Hypertension in women

Eduardo Pimenta

Hypertension Research (2012) 35, 148–152

Combined oral contraceptives (COCs) induce **small increases in BP** in the entire population of users and has been associated with a **small excess risk of CV disease** among women, especially in those with hypertension.

Hypertension is two to three times more common among women taking oral COCs, especially in those **obese and at advanced age**, than in those not taking these medications.

Modern preparations that contain **lower doses (<30 mg) of estrogen** can also lead to development of hypertension and can precipitate accelerated or malignant hypertension.

Environmental characteristics (pre-existing pregnancy-induced hypertension, occult renal disease, obesity, middle age (>35 years) and duration of COC use) as well as **genetic characteristics** (family history of hypertension, increase susceptibility to COC-induced hypertension).

Controlled prospective studies have consistently demonstrated **a return of BP** to pretreatment levels **within 3 months of discontinuing COCs**.

Progestin-only contraceptives are a better choice for women with established hypertension.

Hypertension in women

Eduardo Pimenta

Hypertension Research (2012) 35, 148–152

The effect of **menopause** on BP is controversial and confounded by the effects of aging and clustering of other CV risk factors, such as body weight, LV hypertrophy and lipid levels.

After adjustment for age and body mass index, **the prevalence** of hypertension in **postmenopausal women is at least two fold and** steeper **that in premenopausal women.**

Changes in BP after menopause seem to be related with alterations in estrogen and progesterone levels.

Both hormones have a significant impact on **renal salt handling**. While the BP response of premenopausal normotensive women is insensitive to dietary salt intake, BP in postmenopausal women becomes salt sensitive.

However, the effects of natural estrogen and progesterone appear to be different from the synthetic preparations. Increased angiotensinogen generation has been proposed as a potential mechanism that links estrogen therapy to HTN.

Hypertension in women

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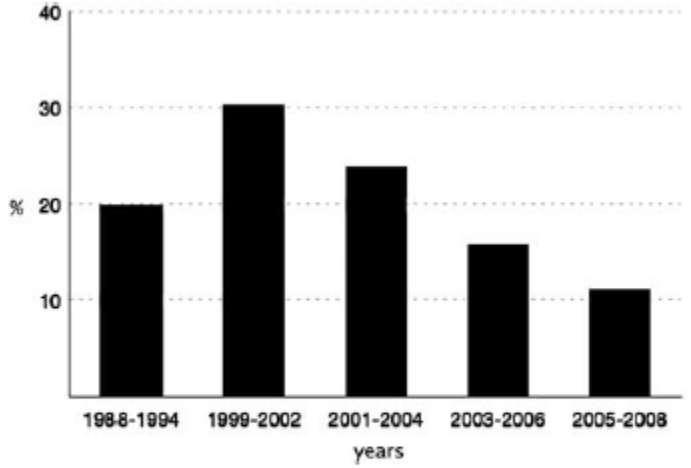

Figure 3 Sex hormone use in the past month, among women aged 45–64 years: United States, selected years 1988–1994 through 2005–2008. Primary indications for use were as contraceptives or for menopause and hot flashes. The data are based on a sample of the civilian non-institutionalized population. Source: CDC/NCHS, National Health and Nutrition Examination Survey. Available from: http://www.cdc.gov/nchs/hus.htm (accessed 24 June 2011).

Conflicting results have been reported by studies that evaluated the effects of **hormone replacement therapy (HRT)** on BP. Differences in patient populations studied, methods of measuring BP, hormone preparations and routes of administration partially explain the discrepancy between the studies.

Minimal BP effects in normotensive women have been showed in most studies. HRT induces, if any, small changes in BP and should not preclude HRT use in either normotensive or hypertensive women. Nevertheless, **all hypertensive women treated with HRT should have their BP measured** initially and then at 3–6-month intervals depending on the difficulty of control.

Complications

CARDIOLOGY

Relationship of Baseline Major Risk Factors to Coronary and All-Cause Mortality, and to Longevity: Findings from Long-Term Follow-Up of Chicago Cohorts

Stamler J.[a] · Dyer A.R.[a] · Shekelle R.B.[b] · Neaton J.[c] · Stamler R.[a]

In the **Chicago Heart Association cohort**, which was conducted in the 1960s and 1970s, **high BP was the most common major risk factor in women** and independently **increased the risk of CHD mortality** (RR 3.17)

Listening to the sound of silence between men and women

Akiko Sakata, Masaki Mogi, Masaharu Ito and Masatsugu Horiuchi

Hypertension Research (2010) **33**, 668–669; doi:10.1038/hr.2010.96; published online 10 June 2010

Most epidemiological studies have shown that **men have a higher stroke incidence than women**. Such a gender difference in stroke incidence might be caused by the beneficial effects of **estrogen** on the brain in **premenopausal women.**

- In animal models, estrogen appeared to protect against ischemic brain damage (endothelium/neurons)
- Stroke incidence was increased in postmenopausal women whose serum estradiol level was the same/ less than the level in men.
- Estrogen treatment after menopause increases the risk of stroke and venous thromboembolic disease.

Therefore, the effect of estrogen is not a simple answer for explaining the gender difference in stroke incidence.

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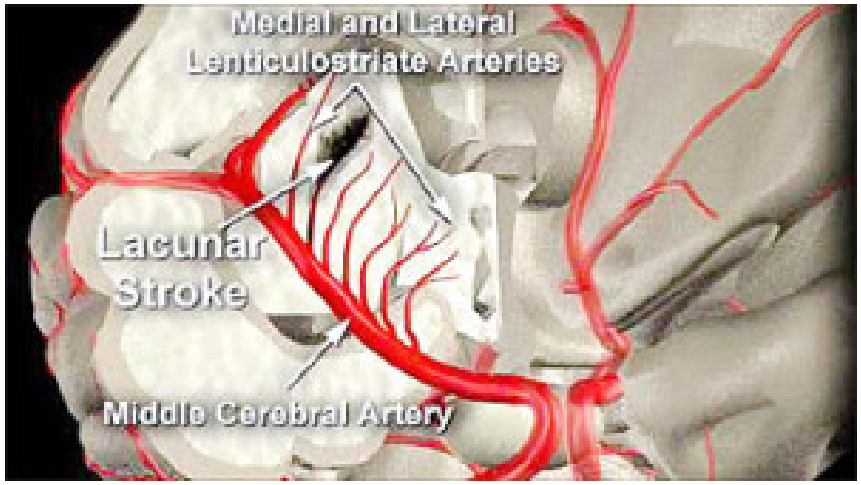
The rates of ischemic stroke were reduced in both men and women owing to **better management of hypertension for the past 40 years;** however, there was a dramatic change in stroke subtypes. Women suffer more from lacunar infarctions and less from atherothrombotic infarctions compared to men.



Interestingly, in women more Silent Brain Infarctions (x3 risk for clinical stroke) appear in brain imaging than in men.

* Hypertens Res 2010; 33:748–752.

Gender Differences in Hypertension: Myths and Reality

Michael Doumas · Vasilios Papademetriou · Charles Faselis · Peter Kokkinos

Curr Hypertens Rep (2013) 15:321–330

Males have a faster decline of renal function with age than females; however, **this gender association is reversed in older age** and postmenopausal women experience a more rapid deterioration of renal function than male individuals.

Natural estrogen seems to exert beneficial actions on renal function.

Contradictory findings exist regarding the **impact of gender on the prevalence of chronic kidney disease**. The prevalence of chronic kidney disease in women was found lower, similar, or higher than in men in different population cohorts.

Women compared to men with incident hypertension were significantly **less likely to suffer from myocardial infarction and stroke** or die from any cause, while **they were significantly more likely to develop chronic kidney disease.**

J Hypertens. 2013;31:271–7.

Treatment

Management of hypertension in women

Niels Engberding and Nanette K Wenger

Hypertension Research (2012) 35, 251–260

Early clinical trials of treating mild-to-moderate HTN were primarily conducted on **a middle-aged male population**, and most decisions regarding hypertensive treatment for women **prior to the 1990s** were based on data obtained from these trials.

Within the **last two decades, women have been included in major outcome trials of antihypertensive treatment,** which have generally shown comparable benefit in both women and men.

Therefore, treatment recommendations remain the same for women and men.

Sex-related differences in pharmacokinetics and pharmacodynamics of anti-hypertensive drugs

Koichi Ueno[1,2] and Hiromi Sato[1]

Hypertension Research (2012) 35, 245–250

Pharmacokinetics is a term that describes the kinetics of the processes undergone by drugs in the body. It comprises main four steps: absorption, distribution, metabolism and clearance (Cl) from the body.

Distribution: **Women have a higher percent body fat than men, which can affect the volume of distribution of certain drugs**.

Metabolism: **Sex-specific differences in activities** of cytochrome P450 (CYP), transporters, uridine diphosphate glucuronosyltransferase enzymes, and renal excretion will result in differences in Cl.

Clearance: **Renal Cl of unchanged drugs is decreased in women because of a lower rate of glomerular filtration**.

However, clinically significant differences in therapeutic response resulting from sex-specific disparities in pharmacokinetics seem to be rare.

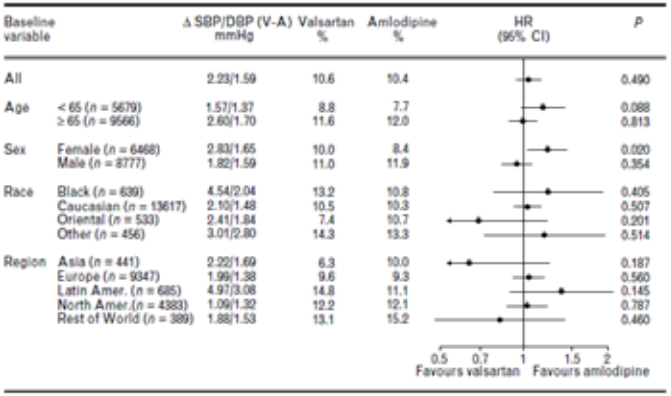
It is important to take into account body weight and age, as well as co-morbidity in determining the appropriate drug regimen for both men and women.

Hypertension in women

Eduardo Pimenta

Hypertension Research (2012) 35, 148–152

Fig. 2



Primary endpoint (composite cardiac mortality and morbidity) in various subgroups of patients subdivided by demographic characteristics. Number of patients in each subgroup in parentheses. The other columns indicate (from left to right): systolic blood pressure (SBP) and diastolic blood pressure (DBP) mean differences between valsartan-based and amlodipine-based treatments [ΔSBP/DBP (V−A)] (positive values indicate a greater blood pressure reduction by amlodipine-based treatment); percentages of patients with a first event in the valsartan and amlodipine groups; hazard ratios (HR) with 95% confidence intervals (CI), and *P* values. Cox regression models.

Gender differences in both benefit and adverse effects of treatment.

In the VALUE study, **women**, but not men, **assigned to valsartan-based treatment presented a relative increased risk of the primary endpoint of cardiac mortality and morbidity compared with those who received amlodipine-based treatment.** Furthermore, the trend toward less congestive heart failure with valsartan-based treatment was not statistically significant in women.

The ALLHAT Trial **showed a slightly greater BP response to amlodipine compared with lisinopril in women**, and this finding was associated with a **more pronounced reduction in stroke**.

In the LIFE study despite similar BP reduction **fewer events occurred in women than in men.**

Hypertension in women

Eduardo Pimenta

Hypertension Research (2012) 35, 148–152

The Blood Pressure Lowering Treatment Trialists Collaboration reviewed 31 randomized trials that included 87 349 women and 103 268 men.

Despite baseline BP levels were slightly higher among women than men, there was no evidence that women and men present different levels of protection from BP lowering regarding :

- total major CV events (stroke, coronary heart disease events, heart failure and other CV death).
- specific events as coronary heart disease, heart failure, CV death or total mortality.

Treatment regimens based on **calcium antagonists** conferred **marginally greater protection** than regimens based on **angiotensin-converting enzyme inhibitors** in **women** compared with men.

Treatment with **beta blockers or diuretics** showed **similar benefit to other drug** classes **for either gender**.

Lancet 2014; (384) : p591–598

Adverse events

Epidemiologic population studies have suggested that **lowering BP, while reducing risks of stroke and vascular complications, might increase mortality or adverse events among the elderly** (>80 years of age). These observations were particularly striking **in older men**. After adjustment for baseline BP, a decrease in diastolic pressure of >5mmHg was associated with higher all-cause mortality.

In women, a decrease in either diastolic or systolic BP **was not associated with poorer survival.**

Lancet 1999; 353:793-96

Hypertension in women

Eduardo Pimenta

Hypertension Research (2012) 35, 148–152

Biochemical responses to drugs appear to be gender dependent.

Ø Angiotensin-converting enzyme inhibitor–induced **cough** is two to three times more common in women than in men. ACE-I and ARBs are contraindicated in women with family plan.

Ø Women are more likely to complain of calcium channel blocker-related **peripheral edema** and minoxidil-induced **hirsutism**.

Ø Women are more likely to develop **hyponatremi**a or **hypokalemia** and men more likely to develop **gout** in response to diuretic therapy. However, HCTZ are particularly useful in elderly women, because their use was associated with decreased risk of hip fracture probably by reduction of urinary calcium loss.

Ø **Sexual dysfunction** related to antihypertensive therapy, which is more commonly discussed with men than women, **seems to be a problem in women as well as in men**. This effect is most often associated with centrally acting agents, b-blockers and thiazide diuretics, whereas angiotensin receptor blocker therapy may improve these symptoms.

High Blood Pressure and Women

Updated:Jan 29,2018

Pregnancy and other factors can elevate the risk of HBP among women

One common misconception is that high blood pressure (HBP or hypertension) rarely affects women. However, nearly half of all adults with high blood pressure are women. And at 65 and older, women are more likely than men

Conclusions (1)

- Prevalence of hypertension is expected to increase more in women than men in the future.

- HTN awareness and treatment are higher in women than in men while the proportion of patients treated and controlled was higher in men than in women. It is suggested: a. raising HTN awareness and treatment for men, whereas b. controlling HTN in women.

Conclusions (2)

- Development of hypertension with COCs can occur and, usually, it resolves with withdrawal of the COC.

- Although the BP effects of menopause or HRT remain controversial, subsequent hypertension importantly contributes to CV morbidity and mortality in women.

- Antihypertensive treatments have comparable benefits in both women and men, but additional analyses/trials have demonstrated gender differences in both benefit/adverse effects of treatment.