Hypertenze u žen reprodukčního věku

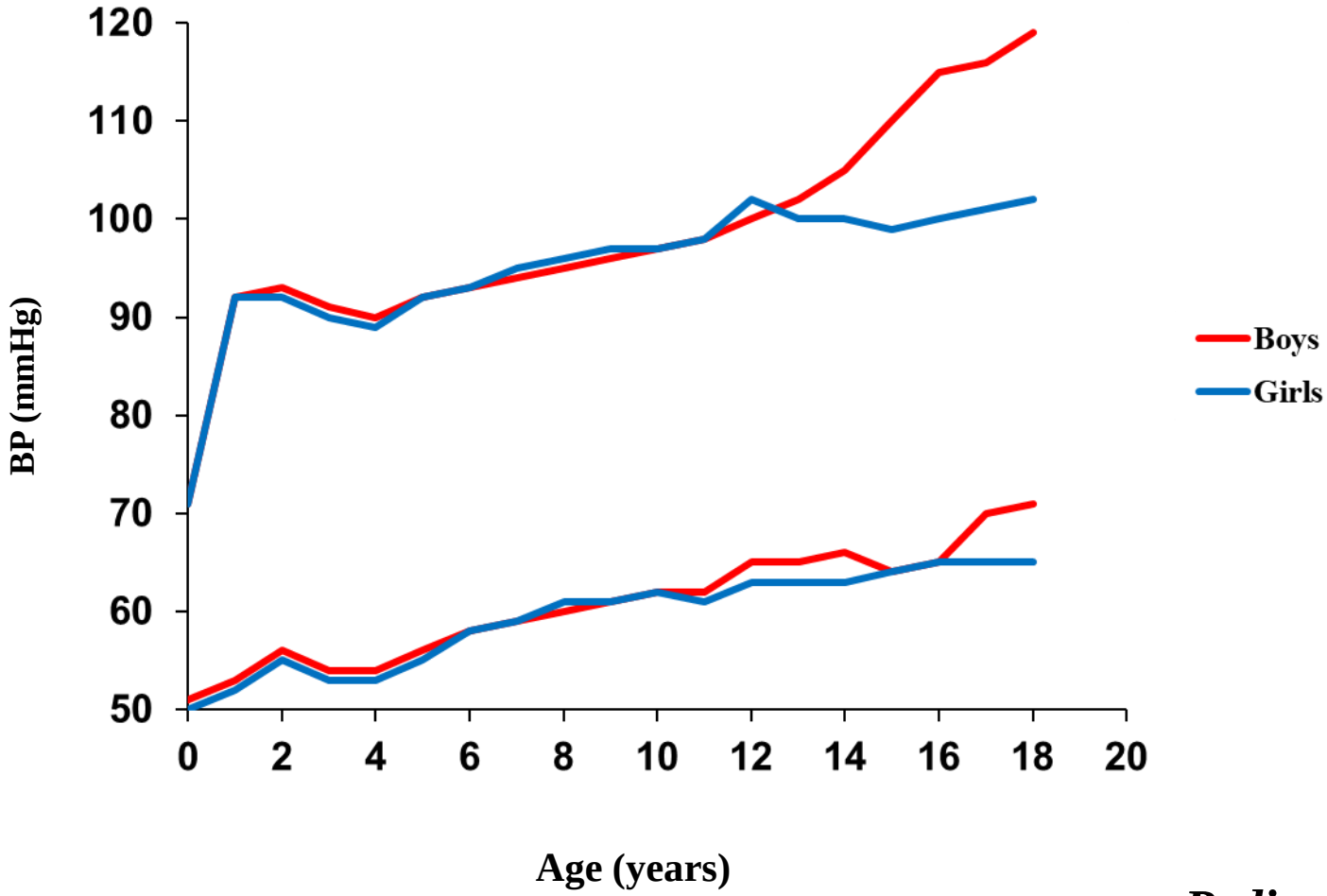
Renata Cífková

Centrum kardiovaskulární prevence 1. LF UK a FTN
II. interní klinika 1. LF UK a VFN
Praha

- **Epidemiologie hypertenze**
- **Prekoncepční poradenství**
- **Perorální antikoncepce**
- **Asistovaná reprodukce**

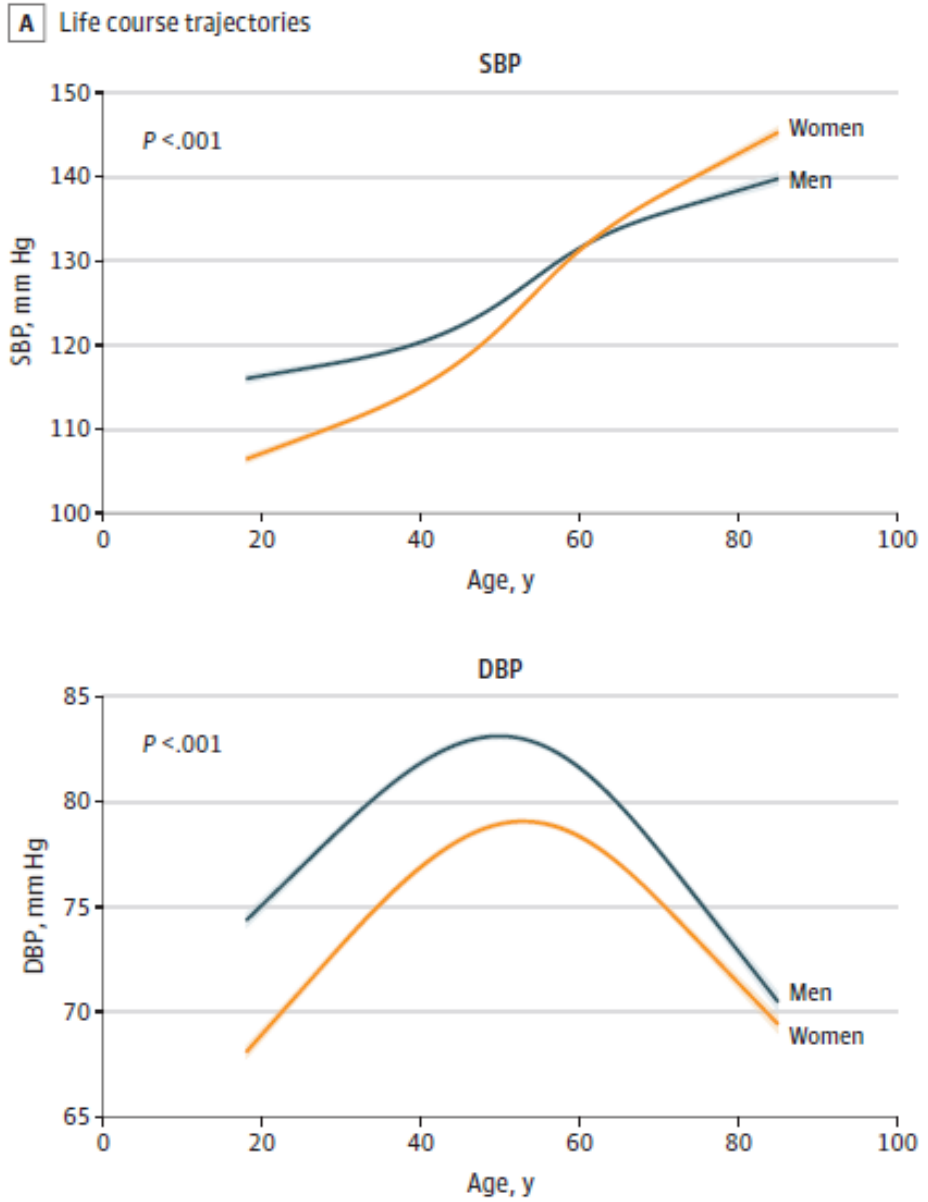
- **Epidemiologie hypertenze**
- **Prekoncepční poradenství**
- ~~Hypertenze v těhotenství~~
- **Perorální antikoncepce**
- **Asistovaná reprodukce**

Mean SBP and DBP of boys and girls from birth to 18 years, USA



Pediatrics 1987;79:1-25

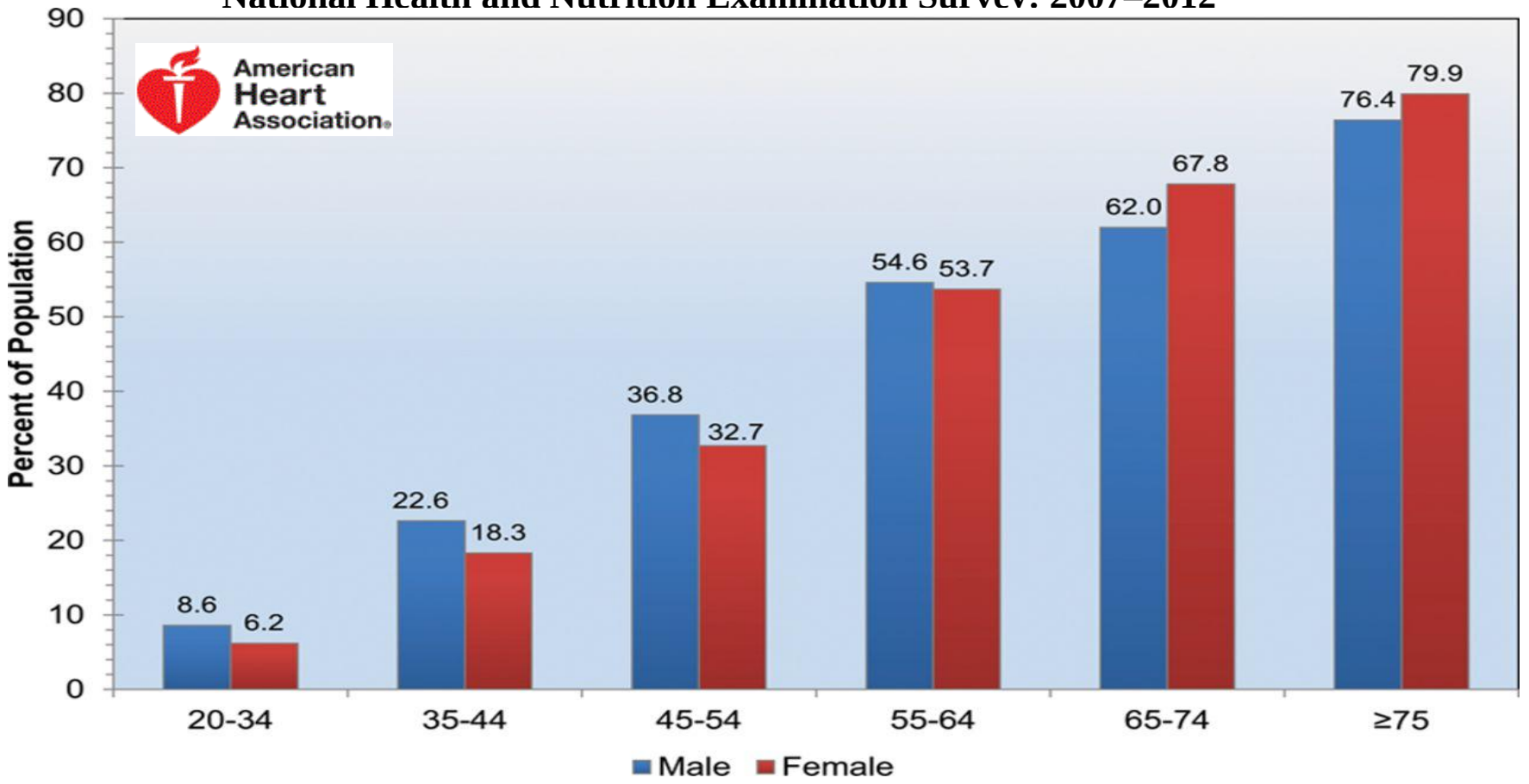
Sex specific trajectories of BP



JAMA Cardiology 2020;5:255-262

Prevalence of high BP in adults ≥20 years of age by age and sex

National Health and Nutrition Examination Survey: 2007–2012



Population Group	Prevalence, 2012, Age ≥20 y	Mortality,* 2013, All Ages	Hospital Discharges, 2010, All Ages
Both sexes	80 000 000 (32.6%)	71 942	488 000
Males	38 300 000 (33.5%)	33 563 (46.7%)†	216 000
Females	41 700 000 (31.7%)	38 379 (53.3%)†	272 000

Circulation. 2016;133:e38-e360

OPEN ACCESS Freely available online

PLoS one

Hypertension in Women of Reproductive Age in the United States: NHANES 1999-2008

Brian T. Bateman[1]*, Kate M. Shaw[2], Elena V. Kuklina[2], William M. Callaghan[3], Ellen W. Seely[4], Sonia Hernández-Díaz[5]

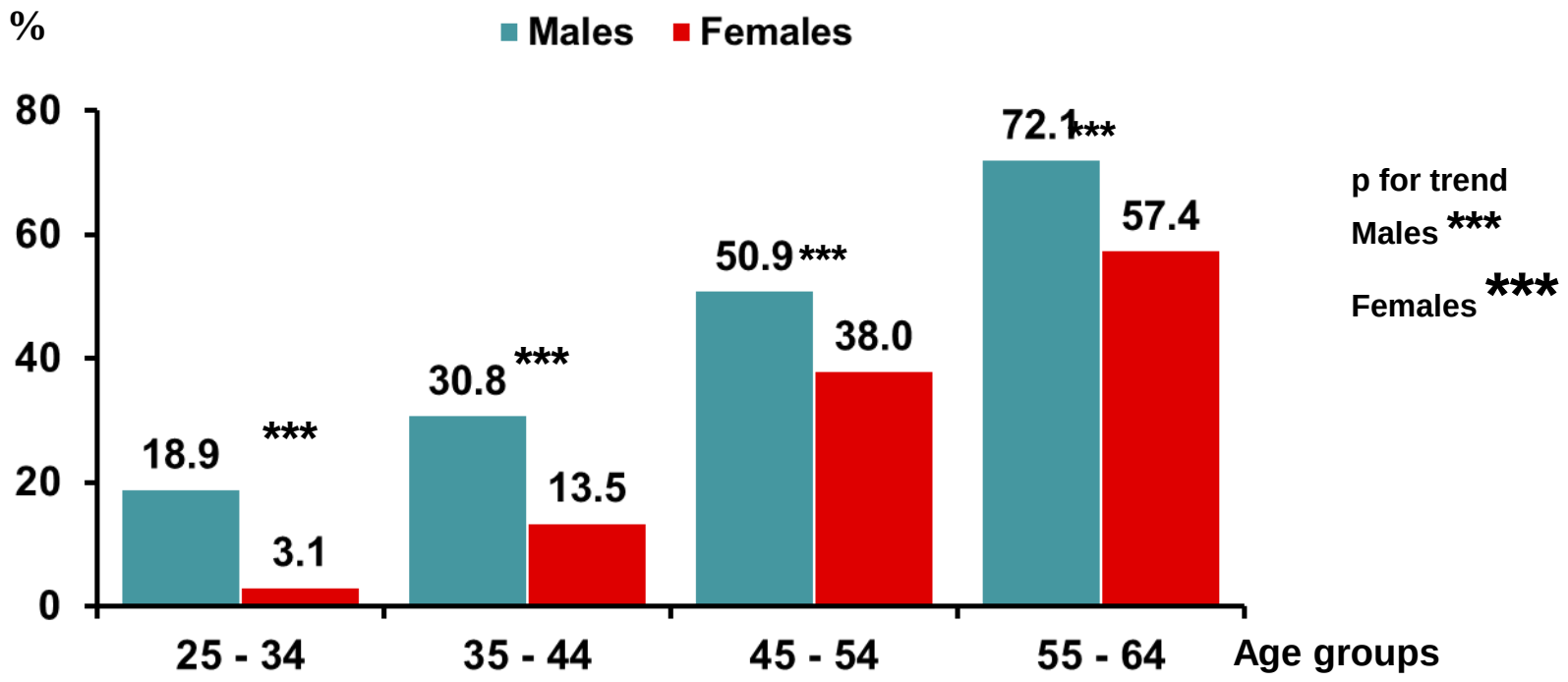
1 Division of Obstetric Anesthesia, Department of Anesthesia, Critical Care, and Pain Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, United States of America, 2 Division for Heart Disease and Stroke Prevention, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America, 3 Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America, 4 Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, United States of America, 5 Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts, United States of America

- **Methods:** NHANES 1999 – 2008
- **Population:** 5,521 women aged 20 – 44 yrs
- **Conclusion:** Hypertension occurs in about 8% of women of reproductive age

PLoS ONE 7(4): e36171 doi:10.1371/journal.pone.0036171

Prevalence of hypertension by age groups

Czech Republic, 2015-2018



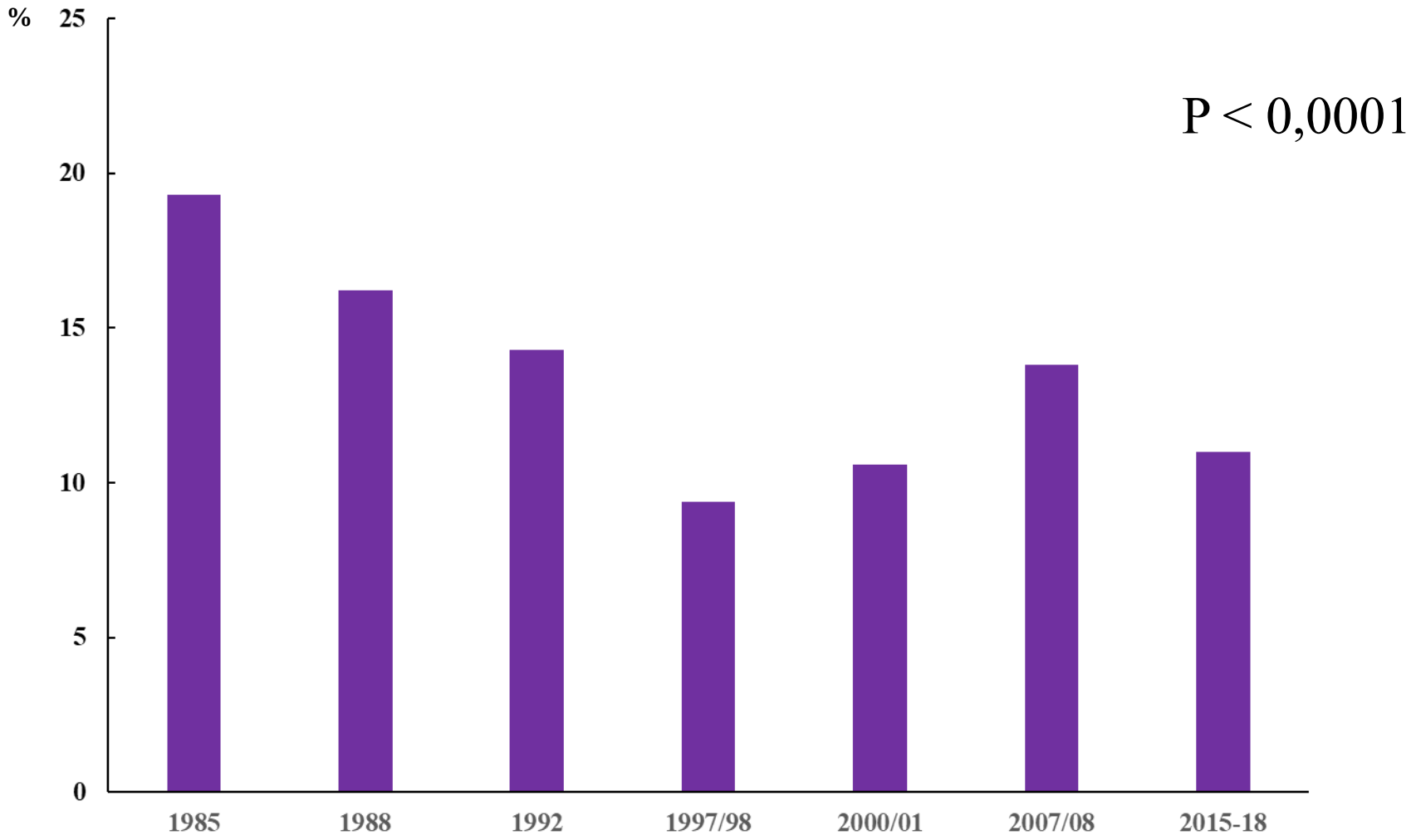
Cífková et al., Cor Vasa 2020;62:6–15

Východisko

- **Ženy reprodukčního věku nebyly zařazovány do klinických studií, omezené informace pocházejí z dostupných epidemiologických studií**

Prevalence hypertenze u žen reprodukčního věku

Czech MONICA and post-MONICA

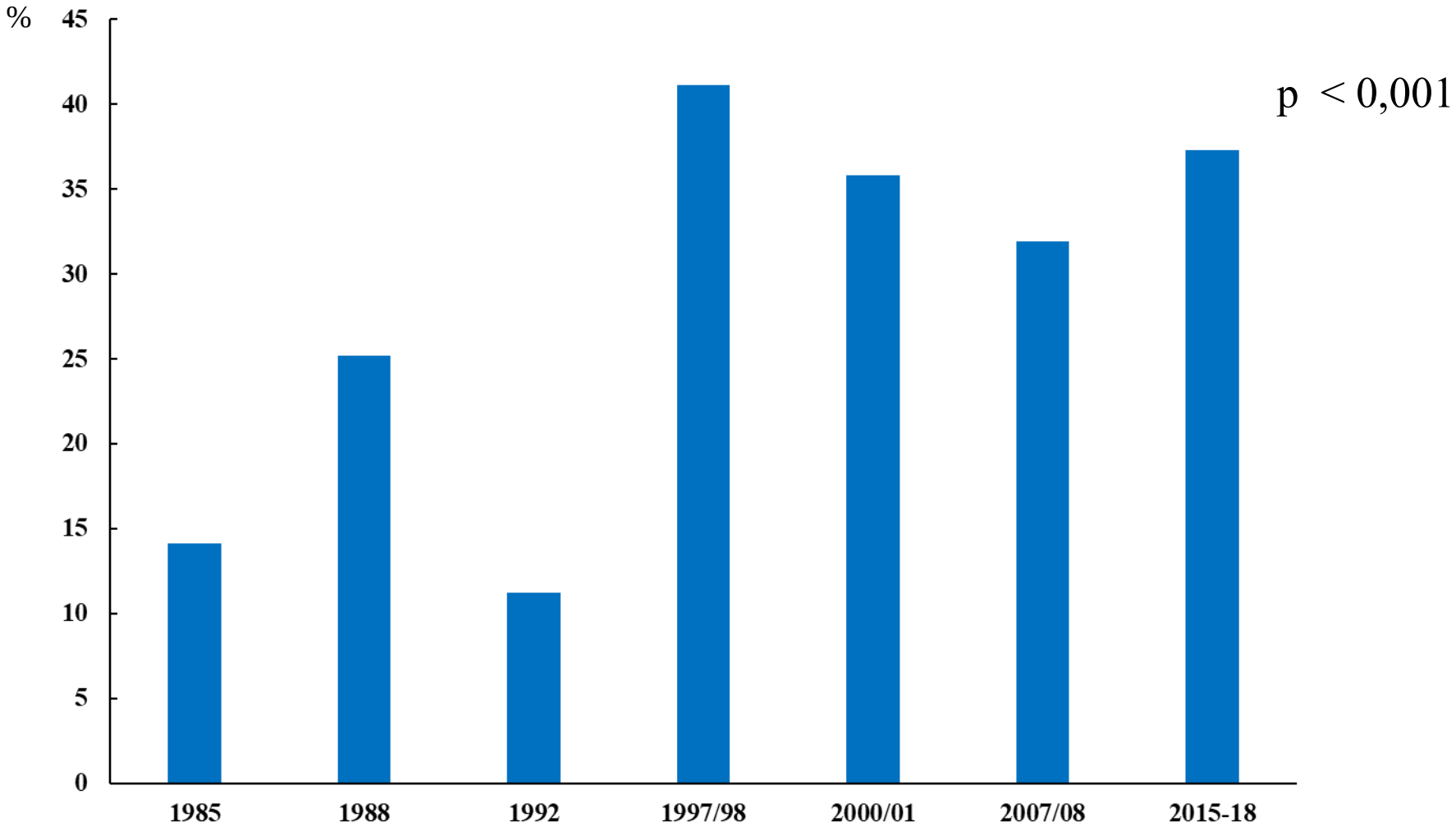


Znalost hypertenze u žen reprodukčního věku

Czech MONICA and post-MONICA

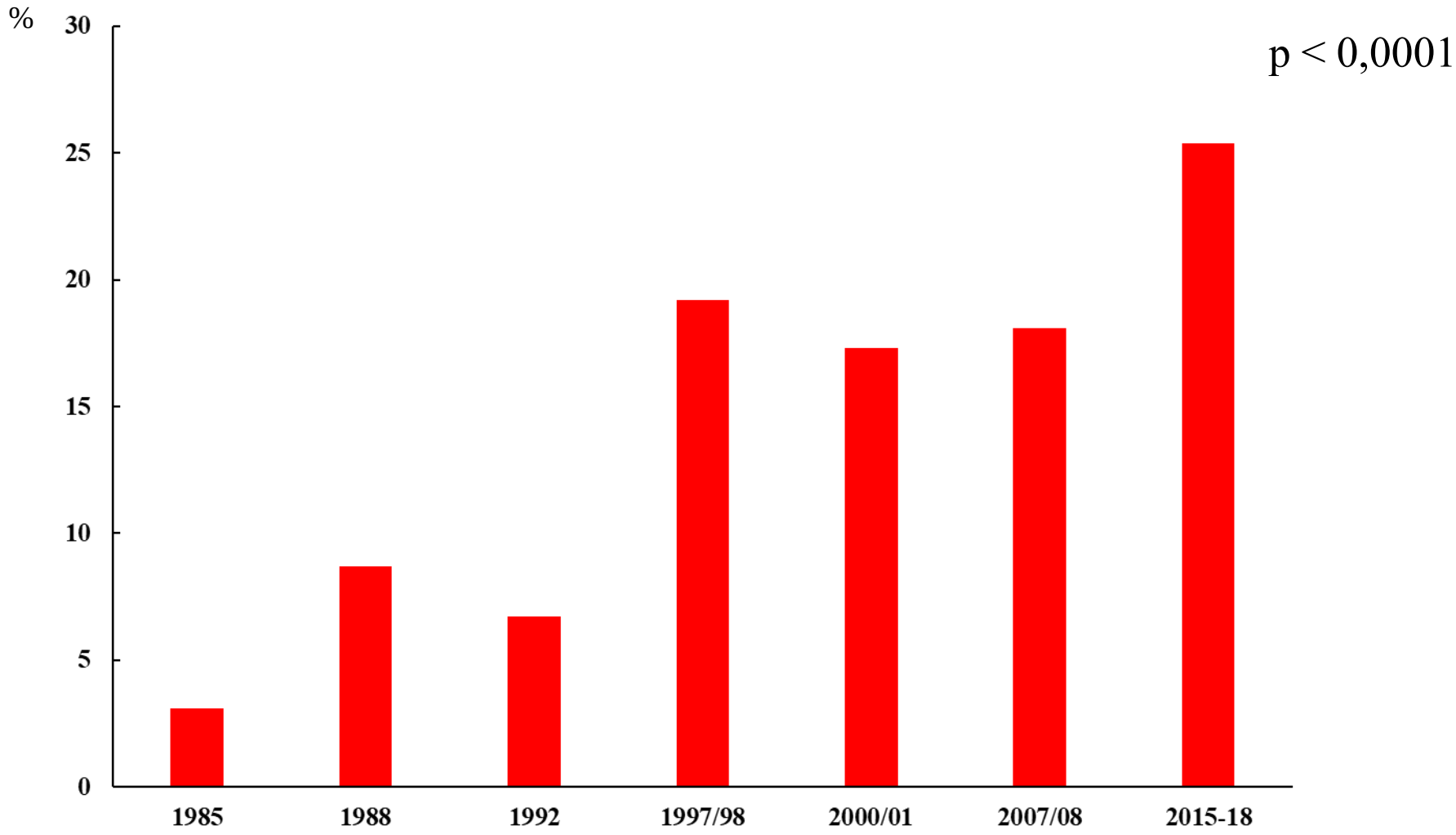
Léčba hypertenze u žen reprodukčního věku

Czech MONICA and post-MONICA



Kontrola hypertenze (< 140/90) u žen reprodukčního věku

Czech MONICA and post-MONICA



Prekoncepční poradenství

- **ACE inhibitory, AT1 blokátory a přímé inhibitory reninu by neměly být předepisovány ženám, které jsou schopny početí a nemají spolehlivou antikoncepci**

Prekoncepční poradenství

- **ACE inhibitory, AT1 blokátory a přímé inhibitory reninu by neměly být předepisovány ženám, které jsou schopny početí a nemají spolehlivou antikoncepci**

- **ACE inhibitory, AT1 blokátor a přímé inhibitory reninu jsou přísně kontraindikovány v těhotenství**

Prekoncepční poradenství

- **Beta-blokátory mohou navodit bradykardii plodu, růstovou retardaci a hypoglykémii, jsou méně účinné než blokátory kalciových kanálů**

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.

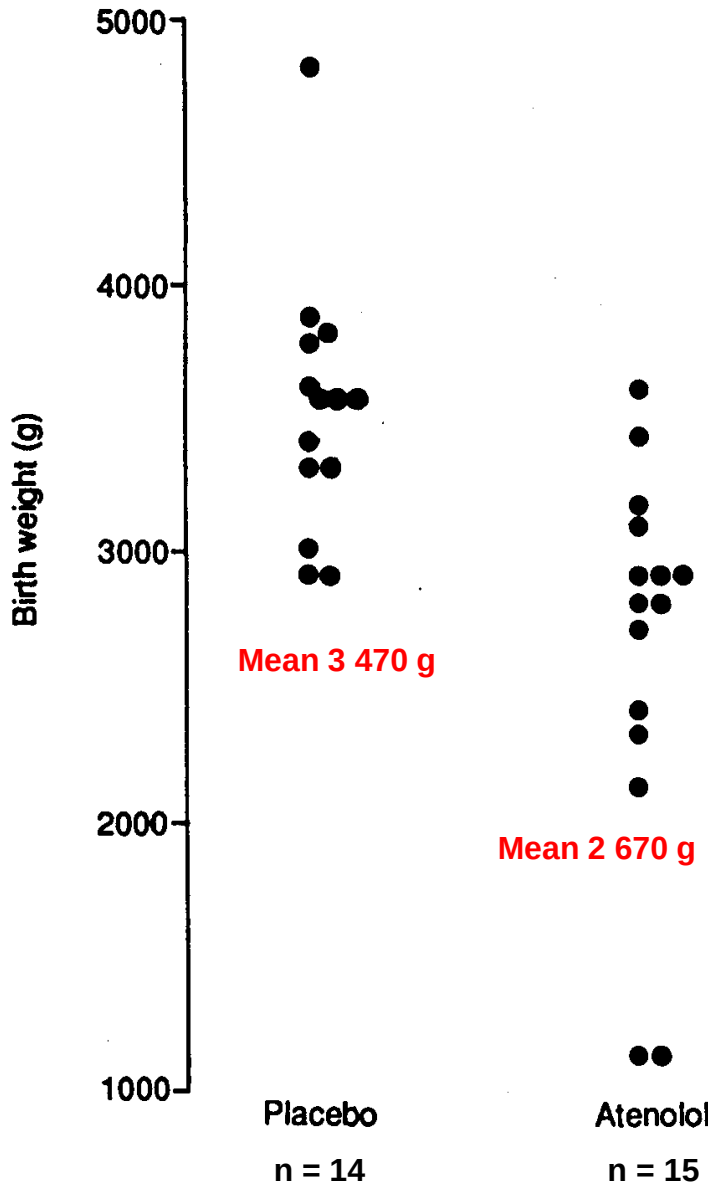
Intervention—14 Women received placebo. 15 Women received atenolol 50 mg daily initially, increasing until either the blood pressure was <140/90 mm Hg or a dose of 200 μg daily was reached.

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.

BMJ 1990;301:587-9

Birth weights of babies in atenolol and placebo groups



BMJ 1990;301:587-9

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.[1] Beta blockers, while safe in the third trimester of pregnancy, are also considered to cause significant growth restriction when used for longer periods.[2] 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,[1] 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 ± 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, labetolol by 7, other β 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 = 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.

Am J Cardiol 1997;79:1436-1438

Prekoncepční poradenství

- **Beta-blokátory mohou navodit bradykardii plodu, růstovou retardaci a hypoglykémii, jsou méně účinné než blokátory kalciových kanálů**

- **Beta-blokátor a jeho dávka by měly být pečlivě voleny**
  - **nepříznivější data jsou pro labetalol**
  - **vyhnout se podávání atenololu**

Prekoncepční poradenství

- **Vyloučit sekundární hypertenzi**

Etiologie hypertenze u mladých žen

- **esenciální**
- **stenóza renální tepny**

  fibromuskulární dysplázie

  M:Ž = 1:8

BMJ

BMJ 2014;348:g2301 doi: 10.1136/bmj.g2301 (Published 15 April 2014)

RESEARCH

Chronic hypertension and pregnancy outcomes: systematic review and meta-analysis

OPEN ACCESS

Kate Bramham *clinical research fellow*, Bethany Parnell *medical student*, Catherine Nelson-Piercy *professor of obstetric medicine*, Paul T Seed *senior lecturer in medical statistics*, Lucilla Poston *professor of Women's Health*, Lucy C Chappell *clinical senior lecturer in maternal and fetal medicine*

Division of Women's Health, Women's Health Academic Centre, King's College London and King's Health Partners, St Thomas' Hospital, London SE1 7EH, United Kingdom

- **55 eligible studies, 795 221 pregnancies**

BMJ 2014;348:g2301 doi: 10.1136/bmj.g2301

Chronic hypertension and pregnancy outcomes: systematic review and meta-analysis

Women with chronic hypertension had high pooled incidences of

- superimposed pre-eclampsia (25.9%; 95% CI 21.0% - 31.5 %)
- caesarean section (41.4%; CI 35.5% - 47.7%)
- preterm delivery <37 weeks' gestation (28.1% ; CI 22.6 - 34.4%),
- birth weight <2500 g (16.9%; CI 13.1% - 21.5%)
- neonatal unit admission (20.5%, CI 15.7% - 26.4%)
- perinatal death (4.0%; CI 2.9% to 5.4%)

BMJ 2014;348:g2301 doi: 10.1136/bmj.g2301

Prevence preeklampsie

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 of IUGR**

Obstet Gynecol 2010;116:402-14

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 17, 2017 VOL. 377 NO. 7

Aspirin versus Placebo in Pregnancies at High Risk for Preterm Preeclampsia

Daniel L. Rolnik, M.D., David Wright, Ph.D., Liona C. Poon, M.D., Neil O'Gorman, M.D., Argyro Syngelaki, Ph.D., Catalina de Paco Matallana, M.D., Ranjit Akolekar, M.D., Simona Cicero, M.D., Deepa Janga, M.D., Mandeep Singh, M.D., Francisca S. Molina, M.D., Nicola Persico, M.D., Jacques C. Jani, M.D., Walter Plasencia, M.D., George Papaioannou, M.D., Kinneret Tenenbaum-Gavish, M.D., Hamutal Meiri, Ph.D., Sveinbjorn Gizurarson, Ph.D., Kate Maclagan, Ph.D., and Kypros H. Nicolaides, M.D.

- **multicenter, double-blind, placebo-controlled trial**
- **1776 women, singleton pregnancies at high risk for preterm preeclampsia**
- **ASA 150 mg vs. placebo**

The NEW ENGLAND JOURNAL of MEDICINE

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Conclusions

Treatment with low-dose aspirin in women at high risk for preterm preeclampsia resulted in a lower incidence of this diagnosis than placebo.

Prevention of pre-eclampsia

Advise women at high risk of pre-eclampsia to take 100-150 mg of ASA daily (at bedtime) preferably before 16 weeks and ideally from weeks 11 to 36 of gestation

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**
- Assisted reproductive therapy in the current pregnancy

Perorální antikoncepce a TK

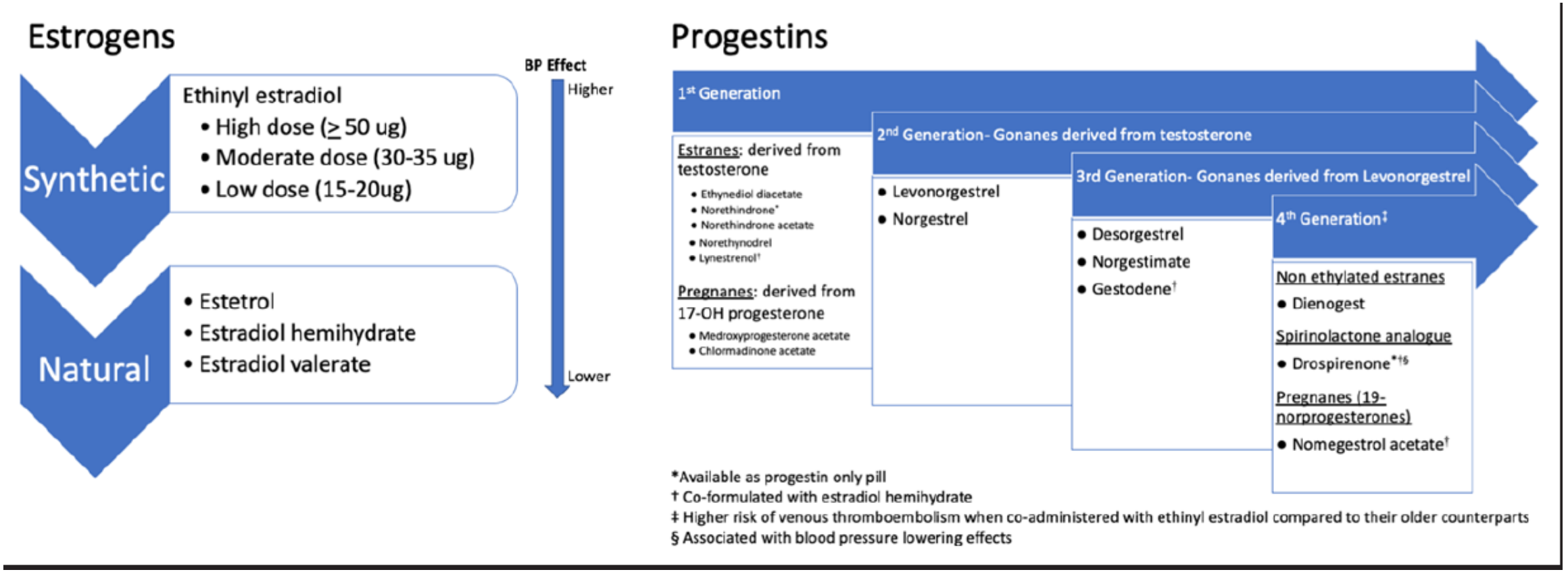
Oral Contraceptives and Hypertension

James W. Woods

Oral contraceptives result in a *mild elevation of BP* in most women and overt *hypertension in about 5%.* Both estrogen and progestogen are responsible for the BP effect, but the mechanism is as yet unknown. The *risk of cardiovascular complications* is found primarily in women *over 35 years* of age and in those *who smoke.* Preparations with an estrogen content of 30µg and a progestogen content of 1mg or less appear to be safe.

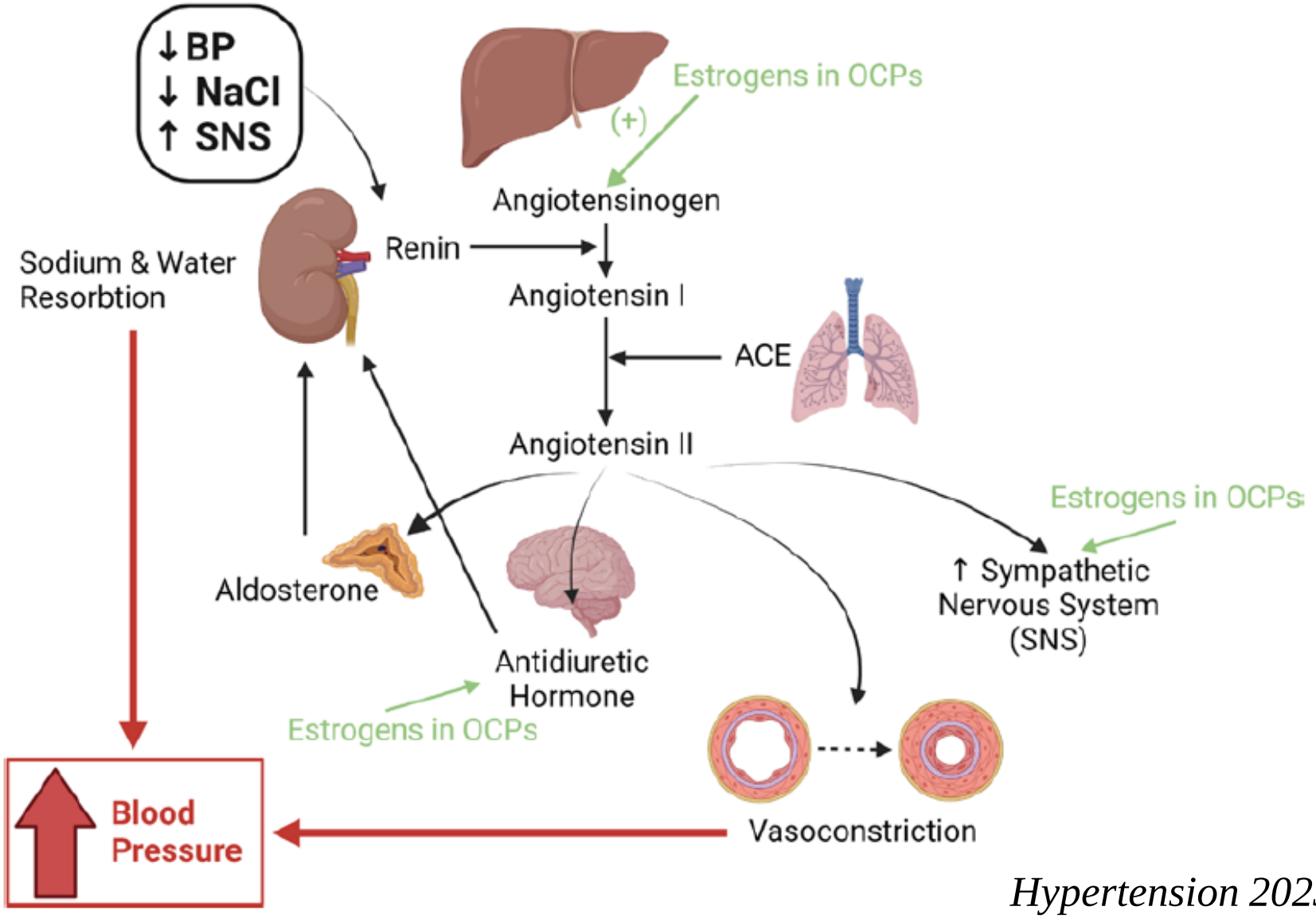
Hypertension 11 (Suppl II): II-11-II-15, 1998

Estrogens and progestins used in OC pills



Hypertension 2023;80:924-935

Estrogeny v perorálních kontraceptivech a TK



Hypertension 2023;80:924-935

Perorální antikoncepce

- ***Perorální antikonceptiva obsahující estrogen způsobují mírný vzestup TK u většiny žen.***

- **Incidence hypertenze je nižší u přípravků obsahujících pouze 30-35µg estrogenu a syntetický progesteron.**

- ***Hypertenze je ve většině případů mírná*** **a TK se normalizuje u více než 50% žen po vysazení perorální antikoncepce.**

- **U malého počtu žen se může vyvinou závažná hypertenze s možností rychlé akcelerace do maligní fáze → ireverzibilní poškození ledvin.**

RR for hypertension by OC Use
NHS II (1989-1993)

Hypertension	Never	OC use Past	OC use Current
Cases, n	211	1,193	163
RR, adj. for age	1.0	1.1 (0.9-1.2)	1.5 (1.2-1.8)
RR, adj. for age and BMI	1.0	1.2 (1.0-1.4)	1.8 (1.5-2.3)
RR, multiple adj.	1.0	1.2 (1.0-1.4)	1.8 (1.5-2.3)

Circulation 1996;483-489

Doporučení pro užívání perorální antikoncepce

- **Nepředepisovat:** - **ženám kuřačkám > 35 let**
  - **SLE**
  - **TEN v anamnéze**

- **Předepisovat s opatrností:**
  - **ženám s migrenózními bolestmi hlavy**

Doporučení pro perorální antikoncepci
2023 ESH Guidelines

- **Initiation of low-dose COC can be advised in normotensive women without CV complications or additional RF after careful BP monitoring – to be repeated every 3-6 months.**
- **In newly diagnosed women with grade 1 hypertension or treated and controlled hypertension, COC may be considered if no other method is appropriate.**
- **Newly diagnosed women with higher hypertension grades or treated but not controlled or with a history or at high risk of CVD should not receive estrogen-based OC.**

Metody asistované reprodukce

Received: 12 May 2016 | Revised: 7 July 2016 | Accepted: 23 July 2016
DOI: 10.1111/jch.12945

ORIGINAL PAPER

WILEY

Risk of hypertensive disorders in pregnancy following assisted reproductive technology: overview and meta-analysis

Costas Thomopoulos MD[1] | George Salamalekis MD[2] | Konstantinos Kintis MD[3] | Iliana Andrianopoulou BDN[1] | Helena Michalopoulou MD[1] | George Skalis MD[1] | Stefanos Archontakis MD[1] | Ourania Argyri MD[1] | Costas Tsioufis MD[3] | Thomas K. Makris MD[1] | Emmanuel Salamalekis MD[2]

- **66 longitudinal studies**; 7 038 029 pregnancies
  203 375 following any ART
- **Conclusions:** All outcomes independent of gestation order were increased following any invasive ART: GH +79% (95% CI, 24%–157%)
  PE +75% (95% CI, 50%– 103%)
  PHD +54% (95% CI, 39%–70%)

J Clin Hypertens 2017; 19: 173–183

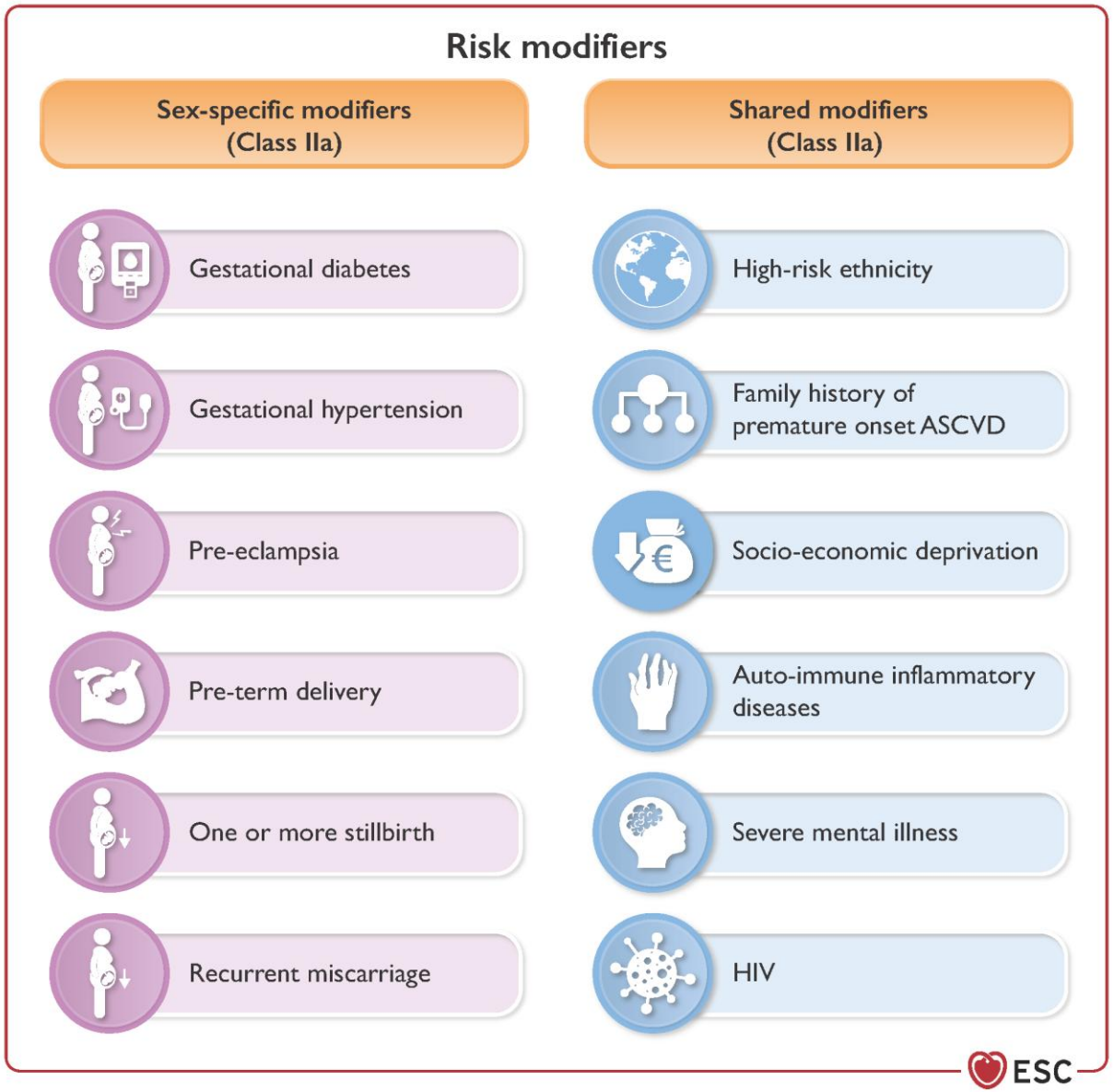
Modifikátory KV rizika specifická pro ženy

Doprovodná onemocnění zvyšující KV riziko

- poruchy spánku a OSA
- duševní choroby: anxieta, somatoformní (somatizační) poruchy, drogové závislosti, psychopatie, poruchy nálady, psychózy
- choroby vázané na pohlaví
  - choroby vázané na těhotenství (hypertenze v těhotenství, gestační DM, předčasný porod, opakované spontanní potraty)
  - neporodnické nemoci (sy polycystických ovarií, předčasná menopauza, sy předčasného ovariálního selhání)
  - erektilní dysfunkce

Figure 8

Cardiovascular disease risk modifers to consider for up-classification of risk



2024 ESC Guidelines for the management of elevated blood pressure and hypertension
(European Heart Journal; 2024 – doi: 10.1093/eurheartj/ehae178)

Premature ovarian insufficiency

Definition

Clinical syndrome defined by loss of ovarian activity before the age of 40

- Menstrual disturbance (amenorrhea/oligomenorrhea)
- -----↑ gonadotropins
- ↓ estradiol

Prevalence

- **Approx. 1 %** (ethnicity may affect the prevalence; higher in African Americans and Hispanics; lower in Chinese and Japanese populations)

Consequences of POI for the CV system

- Increased risk of CVD; women with POI should be advised to modify their risk factors

Recommendation

- Early HRT initiation is strongly recommended (despite lack of longitudinal outcome data) and should be continued until the average age of natural menopause

Human Reproduction 2016;31:926–937

Human Reproduction, Vol.31, No.5 pp. 926–937, 2016
Advanced Access publication on March 22, 2016 doi:10.1093/humrep/dew027

human reproduction

ESHRE PAGES

ESHRE Guideline: management of women with premature ovarian insufficiency†

The ESHRE Guideline Group on POI, L. Webber[1,*], M. Davies[1], R. Anderson[2], J. Bartlett[3], D. Braat[4], B. Cartwright[5], R. Cifkova[6], S. de Muinck Keizer-Schrama[7], E. Hogervorst[8], F. Janse[9], L. Liao[1], V. Vlaisavljevic[10], C. Zillikens[11], and N. Vermeulen[12]

Human Reproduction 2016;31:926–937

Závěry

- **Hypertenze postihuje 8-9% žen reprodukčního věku, 50% z nich jsou medikamentózně léčeny, proto je nutné prekoncepční poradenství**
- **Ženy s preexistující hypertenzí mají více komplikací v těhotenství včetně vysokého rizika rozvoje preeklampsie – prevence nízká dávka ASA.**
- ***Perorální antikonceptiva obsahující estrogen způsobují mírnou elevaci TK* u většiny žen. Hypertenze je většinou mírná a TK se normalizuje u více než 50% žen po vysazení perorální antikoncepce.**

Závěry

- **Ženy, které počnou metodou asistované reprodukce, mají zvýšené riziko rozvoje hypertenze v těhotenství.**

- **Asistovaná reprodukce navodila předčasné stárnutí cév u zdánlivě zdravých, mladých dospělých bez přítomnosti klasických KV RF.**