

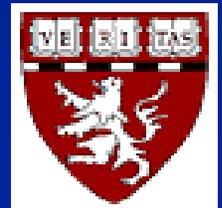
Preeclampsia and Future Risk of Cardiovascular Disease

Ellen W. Seely, M.D.

**Director of Clinical Research
Endocrinology, Diabetes and
Hypertension Division**

Brigham and Women's Hospital

**Professor of Medicine
Harvard Medical School
Boston, Massachusetts**



Case

54 yo woman presents to you to discuss her risk factors for cardiovascular disease.

PMH: menopause age 50, was on HRT for 2 years

FH: father had CABG age 65

SH: non smoker

Exam: BP 120/80 P 72 BMI 27

NI exam

BUN 14 mg/dl Cr 0.7 mg/dl FBS 90 mg/dl

TC 201 mg/dl HDL 40 mg/dl cLDL 120 mg/dl

Triglycerides 150 mg/dl

What other past history do you want to know?

Risk Factors for CVD In Women

- Hypertension
- Hyperlipidemia
- Diabetes
- Obesity
- Cigarette smoking
- Physical inactivity
- Family history
- Menopause
- Hormonal contraceptives
- Conjugated estrogen
- Reproductive life complicated by:*
 - Polycystic ovarian syndrome*
 - Gestational diabetes*
 - Preeclampsia*

Preeclampsia

- Affects 3 - 5% of pregnancies
- A leading cause of fetal/maternal morbidity and mortality in the U.S.
- Definition: Rise in BP >140/90 after 20 wks gestation in a previously normotensive woman with proteinuria
- Etiology unknown
- Multisystem disorder

Manifestations of Preeclampsia-Maternal

- Multisystem disorder affecting mother and fetus/offspring
- Characterized by endothelial damage
- Maternal manifestations:
 - Hypertension
 - Proteinuria > 300 mg/dy
 - Acute renal failure
 - HELLP syndrome (hemolysis, elevated liver tests and low platelets)
 - Disseminated intravascular coagulation
 - May progress to eclampsia (seizures)

Manifestations of Preeclampsia- Fetus/Offspring

- IUGR
- Prematurity
- Increased risk hypertension (adolescence)

Prevention of Preeclampsia

Despite known risk factors, NO treatments have been demonstrated to reduce the risk of preeclampsia

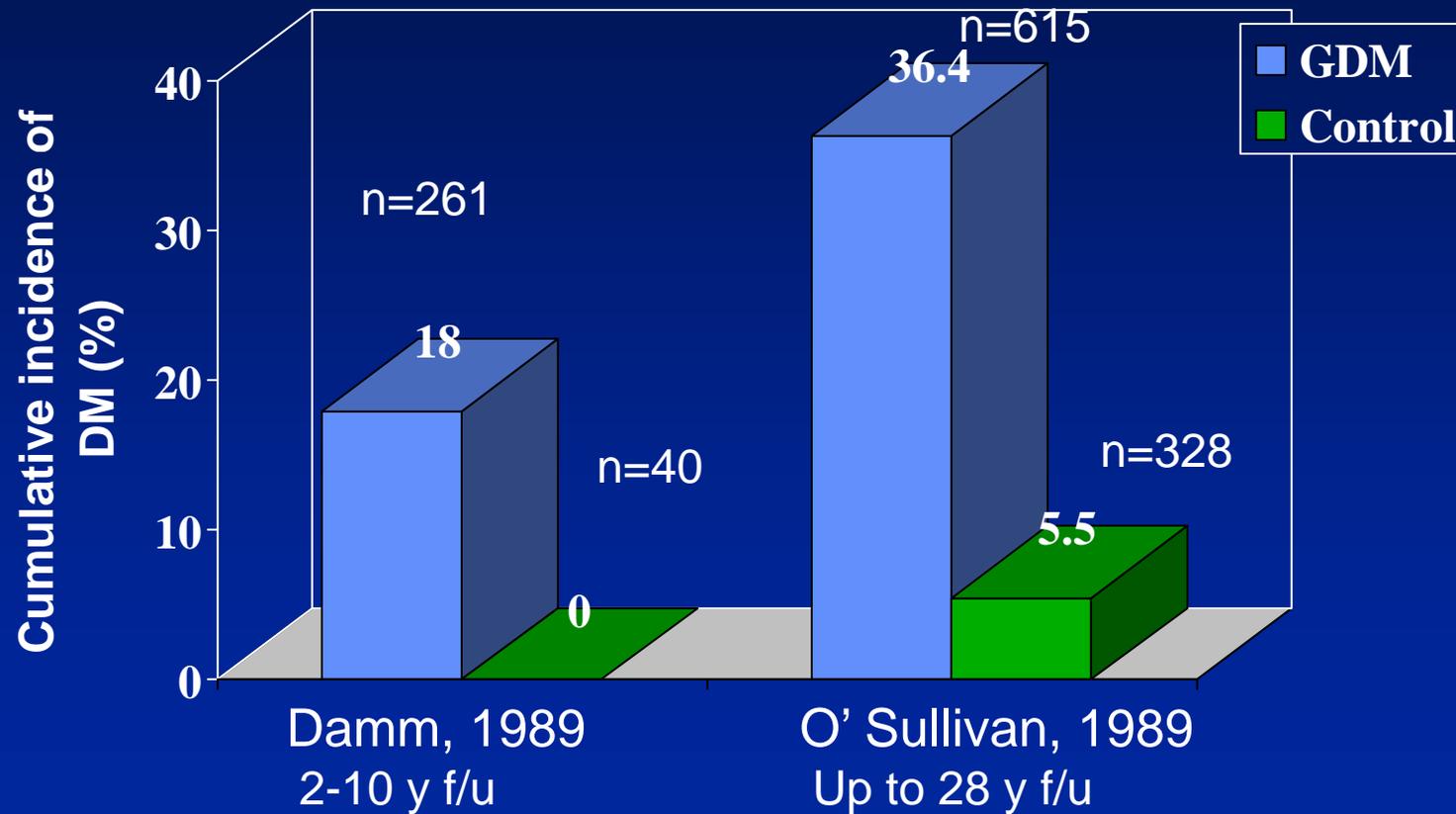
- Low dose aspirin
- Calcium
- Antioxidants vitamin E and C

Ongoing vitamin D studies...

Preeclampsia-Treatment

- Only “cure” is delivery
 - Resolves postpartum
- but:
- *May predict future cardiovascular disease*

Gestational Diabetes: Future Risk of T2DM



Preeclampsia and Future CVD

- Hypertension
- Cardiovascular disease
- Renal Disease

Preeclampsia: Future Hypertension

Investigators: Adams and MacGillivray 1960

Methods: 149 women with chart diagnosis of preeclampsia (1938-1943) with follow-up (1958-1960) compared with 185 women with NT pregnancy and 197 nulliparous women

Preeclampsia: Long Term BP Sequelae

%SBP>140 %DBP>90
mmHg

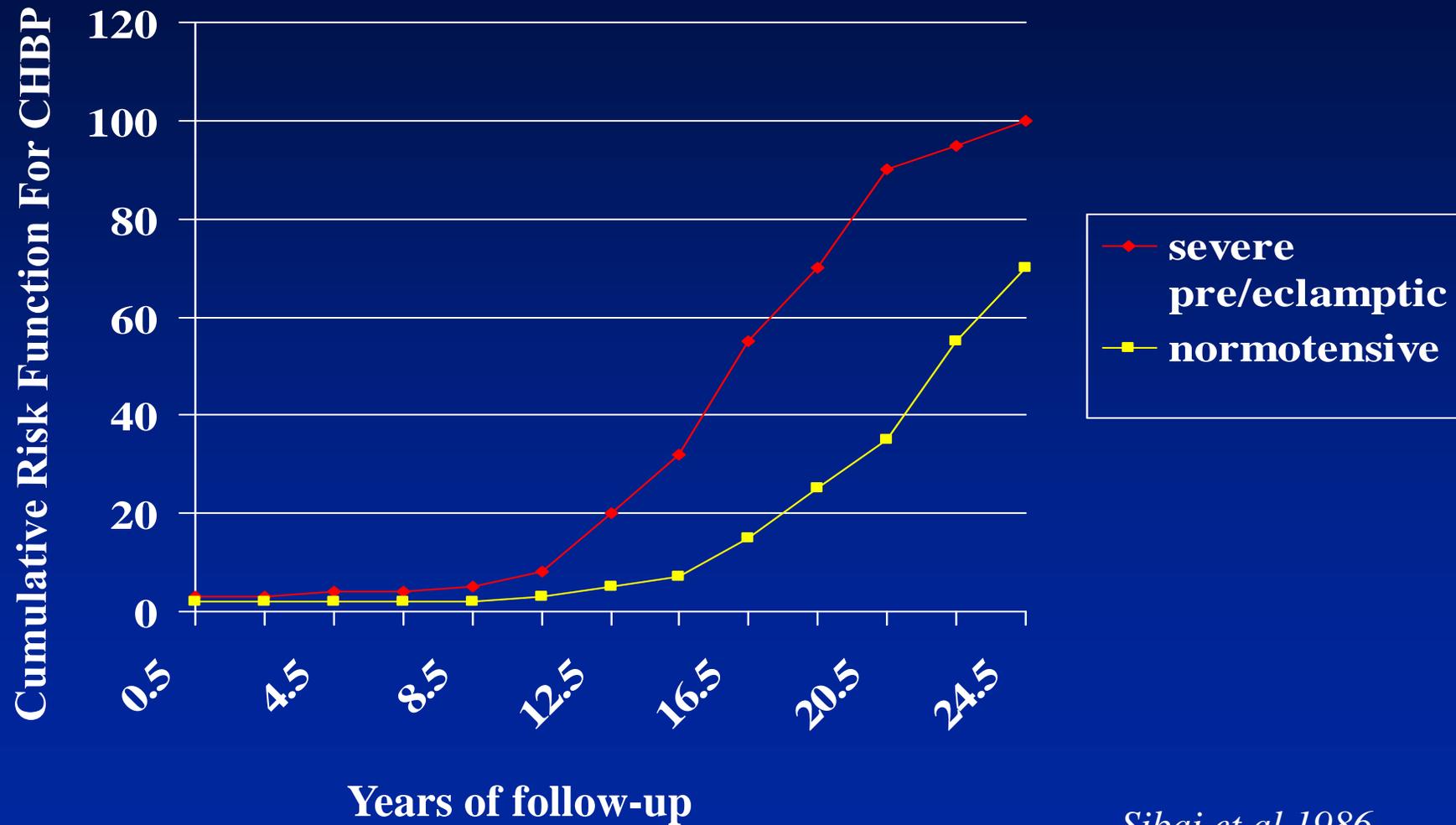
Preeclampsia	58	60
NT in preg	26	21
Nulliparous	41	35

Adams and MacGillivray 1961

Preeclampsia and Future Hypertension

- **Investigators: Sibai et al. 1986**
- **Study population: 406 women with severe preeclampsia, 409 matched women with NT pregnancy**
- **BP follow-up: 2-24 yrs**

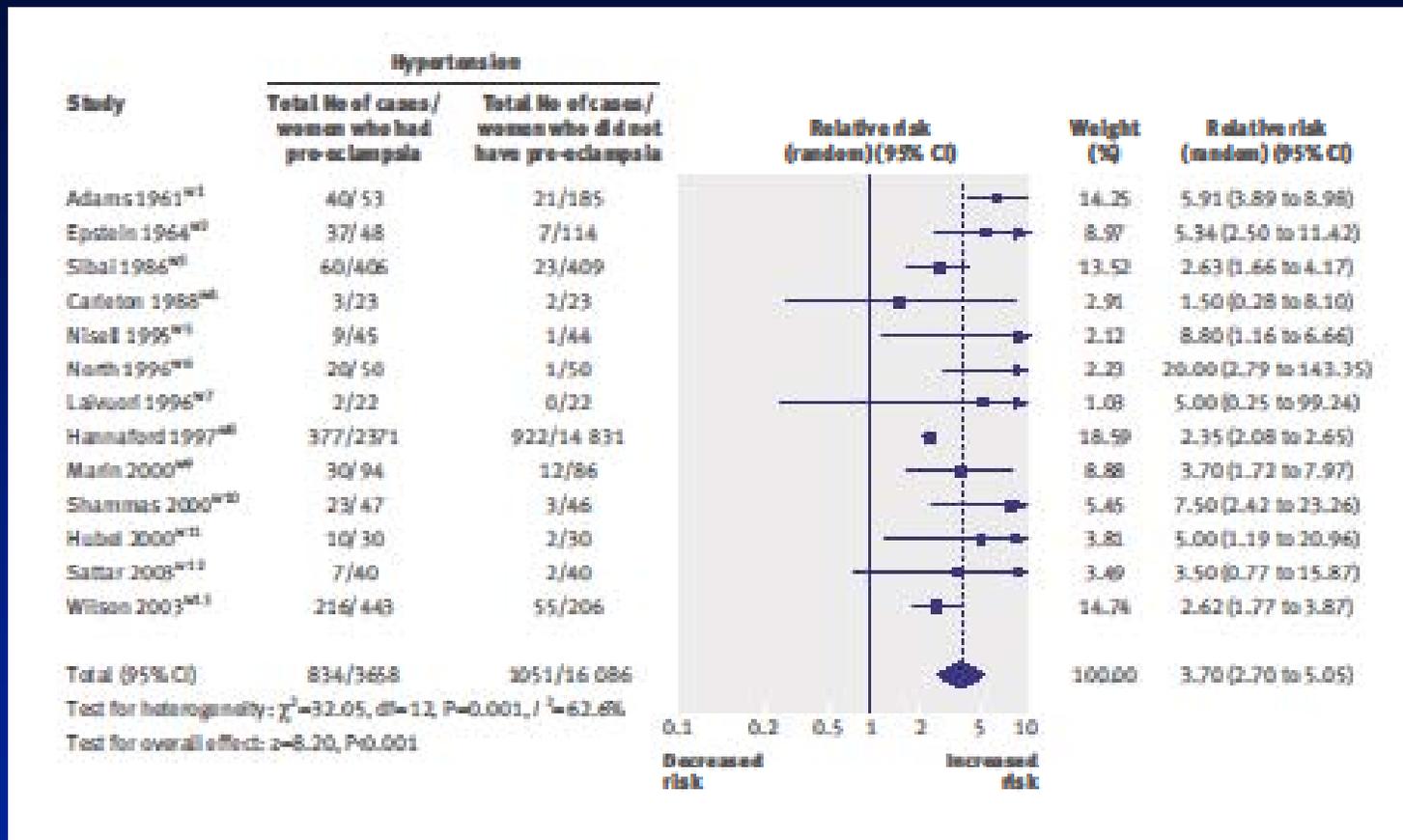
Long-term Risk of Hypertension



Sibai et al. 1986

Preeclampsia and Future Hypertension: Meta-analysis

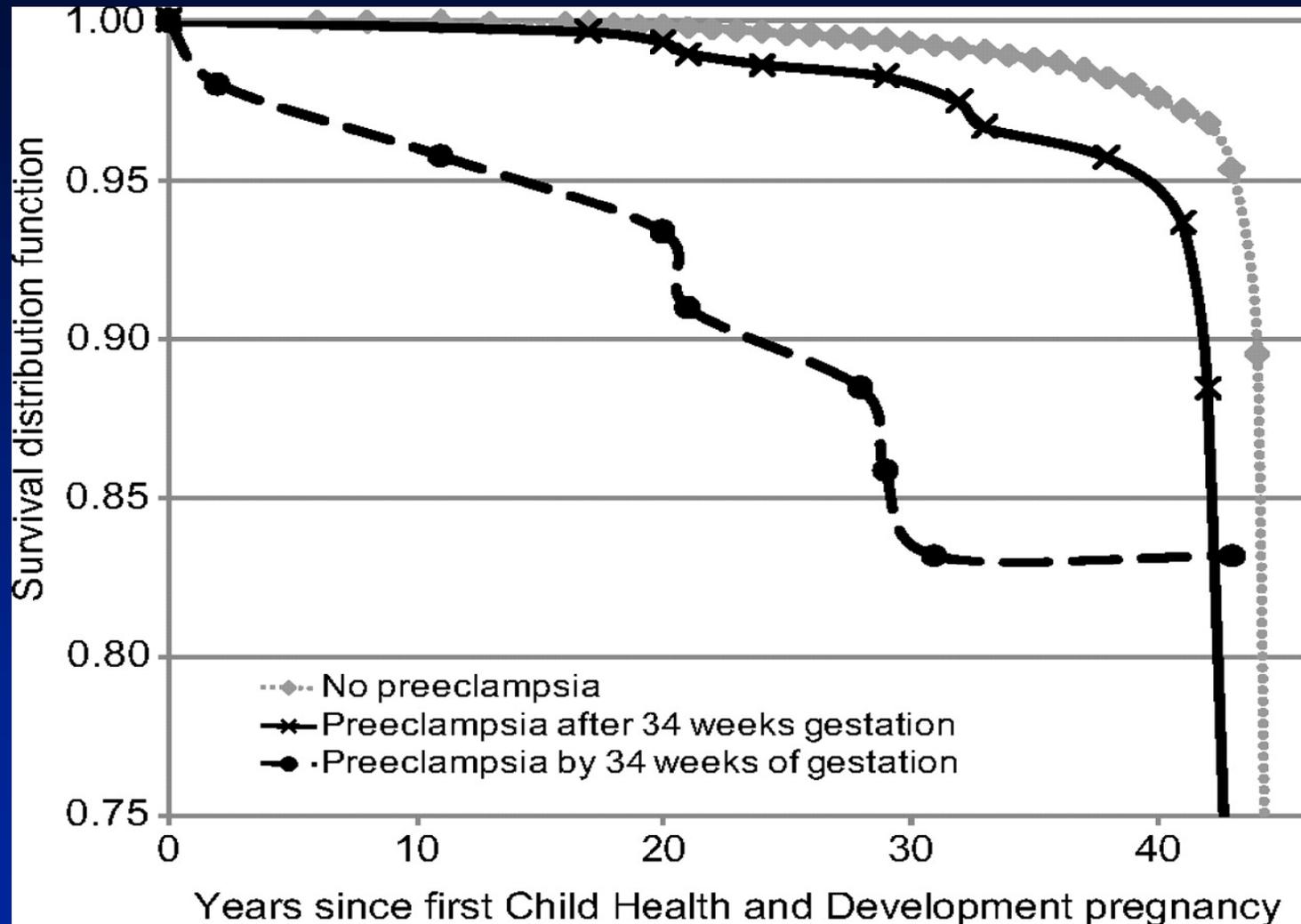
Bellamy et al.
BMJ 2007



13 studies including over 20, 000 women; mean adjusted f/u 14. 1 years
 relative risk for hypertension 3.7 (2.7-5.1)

* Majority of these studies did not adjust for BMI

Preeclampsia and Future CVD Death



Mongraw-Chaffin, M. L. et al. 2010

Hypertension



Possible Explanations for the Association of Preeclampsia with Future CVD

Three views:

- Is pregnancy a stress test that unmasks CV risk?

OR

- Does preeclampsia cause vascular damage increasing risk for CVD?

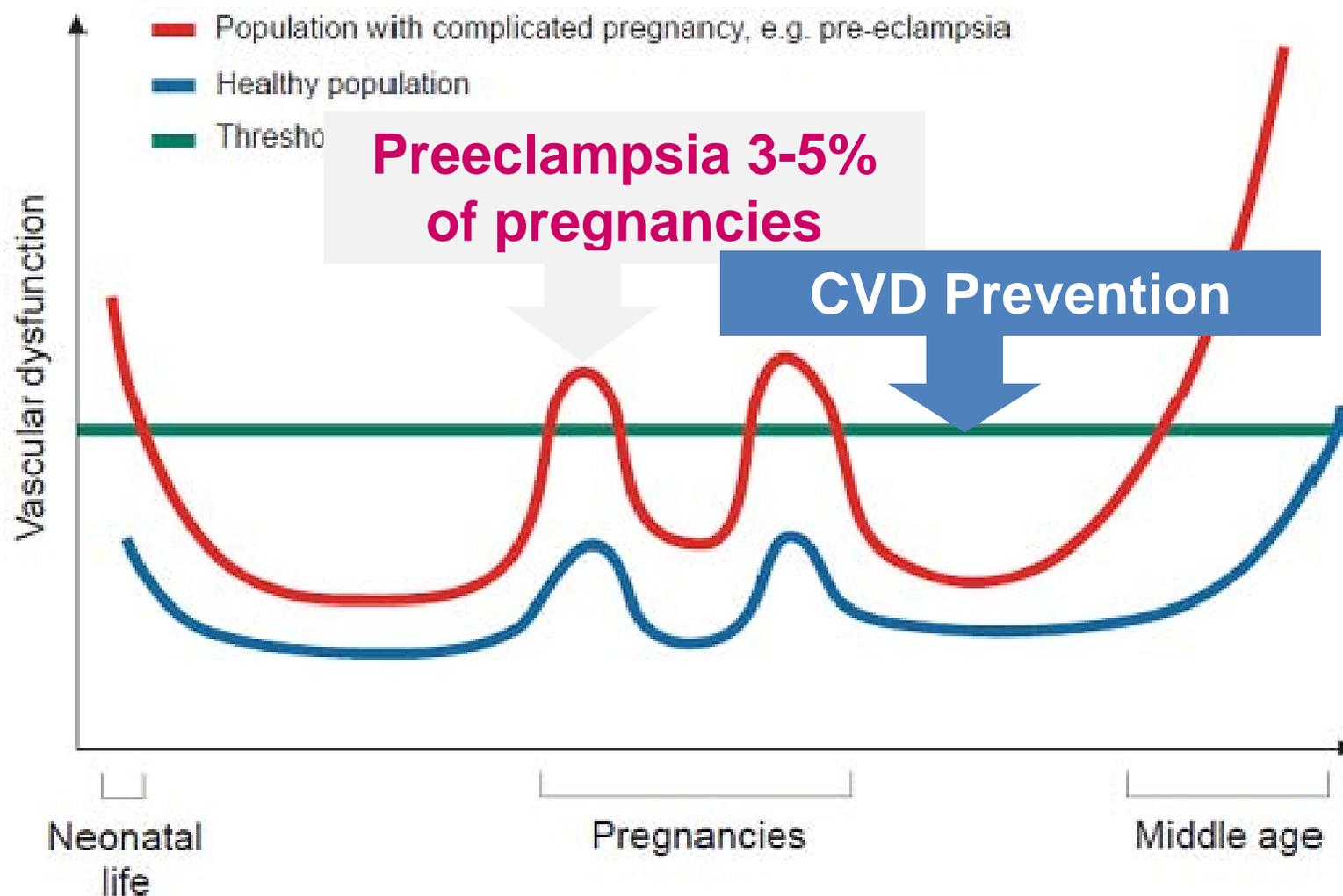
OR

- a combination of the 2?

Shared Risk Factors for BOTH Preeclampsia & CVD

- Endothelial dysfunction
- Obesity
- Insulin resistance/diabetes
- Hypertension
- Dyslipidemia

Complicated Pregnancy as a Window into Future CVD Health

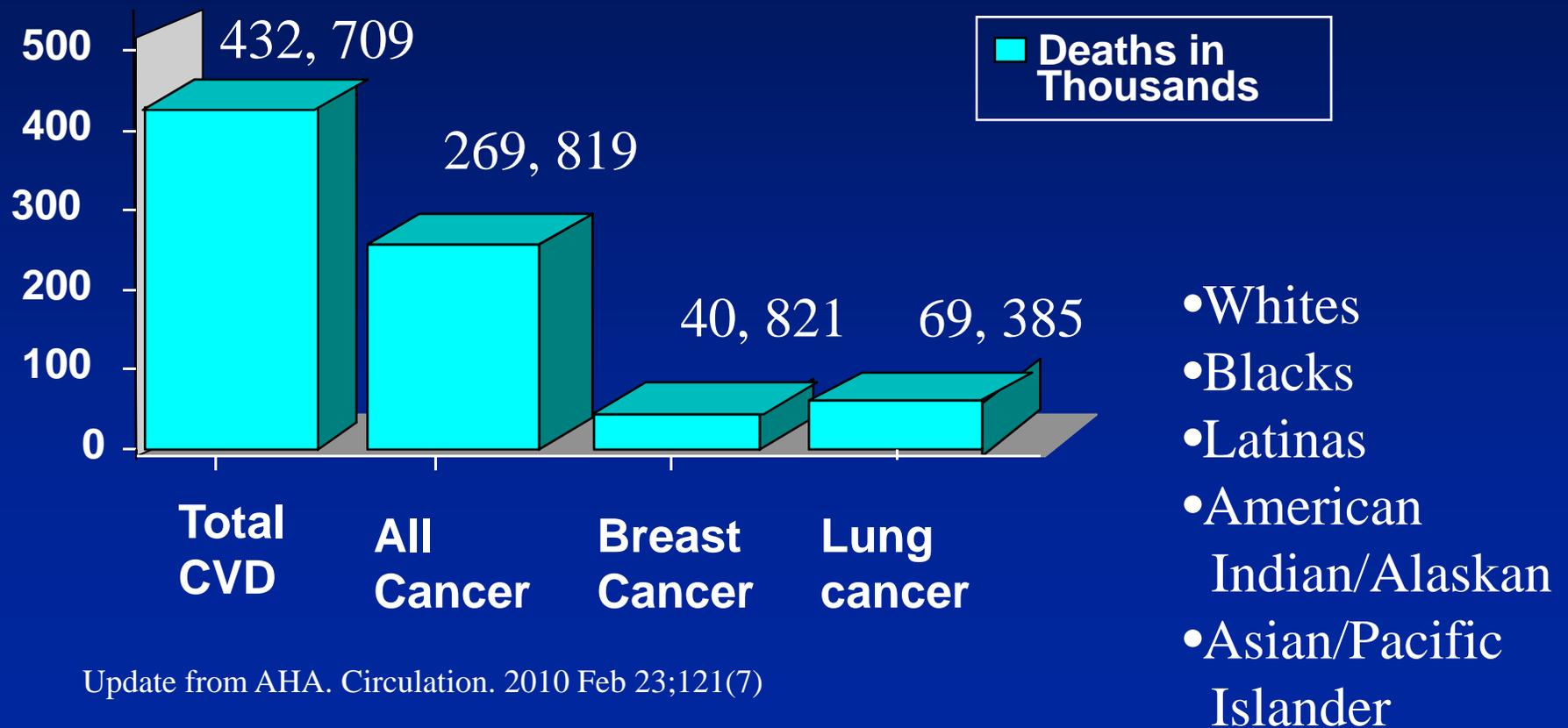


adapted with permission from Sattar N & Greer I, *BMJ* 2002;325:157-160

Breathing Life Into the Lifecourse Approach: Pregnancy History and Cardiovascular Disease in Women

Rich-Edwards JW, McElrath TF, Karumanchi SA, Seely EW *Hypertension*. 2010;56:331

LEADING CAUSES OF DEATH FOR ALL U.S. WOMEN 2006



Can the risk for future CVD be modified?

Evidence-Based Guidelines for Cardiovascular Disease Prevention in Women: 2007 Update

- Lifestyle intervention
 - Smoking cessation
 - Physical activity
 - Weight reduction to BMI < 25
- Risk Factor Reduction
 - treatment of BP, lipids, diabetes

Evidence-Based Guidelines for Cardiovascular Disease Prevention in Women: 2007 Update

Journal of the American College of Cardiology 2007
49, 1230-1250

Breathing Life Into the Lifecourse Approach: Pregnancy History and Cardiovascular Disease in Women
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TABLE 1. Classification of CVD Risk in Women

Risk Status	Criteria
High risk	<ul style="list-style-type: none"> Established coronary heart disease Cerebrovascular disease Peripheral arterial disease Abdominal aortic aneurysm End-stage or chronic renal disease Diabetes mellitus 10-Year Framingham global risk >20%*
At risk	<ul style="list-style-type: none"> ≥1 major risk factors for CVD, including: <ul style="list-style-type: none"> Cigarette smoking Poor diet Physical inactivity Obesity, especially central adiposity Family history of premature CVD (CVD at <55 years of age in male relative and <65 years of age in female relative) Hypertension Dyslipidemia Evidence of subclinical vascular disease (eg, coronary calcification) Metabolic syndrome Poor exercise capacity on treadmill test and/or abnormal heart rate recovery after stopping exercise
Optimal risk	Framingham global risk <10% and a healthy lifestyle, with no risk factors

Complicated Pregnancy

Reproductive Life Complications and Future CVD Risk-Summary

Reproductive life cardiometabolic complications- PCOS, GDM and Preeclampsia- offer a window into future CVD risk in women for the potential targeting of affected women for CVD risk modification to prevent morbidity and mortality from CVD

Recommendations for Future Directions

- Clinical

- Obtaining a history of reproductive complications should be routine part of every patient history
- Electronic medical records should link pregnancy and primary care records
- Internists should obtain training in obstetrics and obstetricians continue to obtain training in medicine

- Research

- Interdisciplinary teams of population, clinical and basic scientists

Thank you

Risk Factors for Preeclampsia

- Extremes of age
- Multiple gestations
- Family history
- Preexisting hypertension
- Diabetes mellitus
- Renal disease
- Connective tissue disease
- Obesity

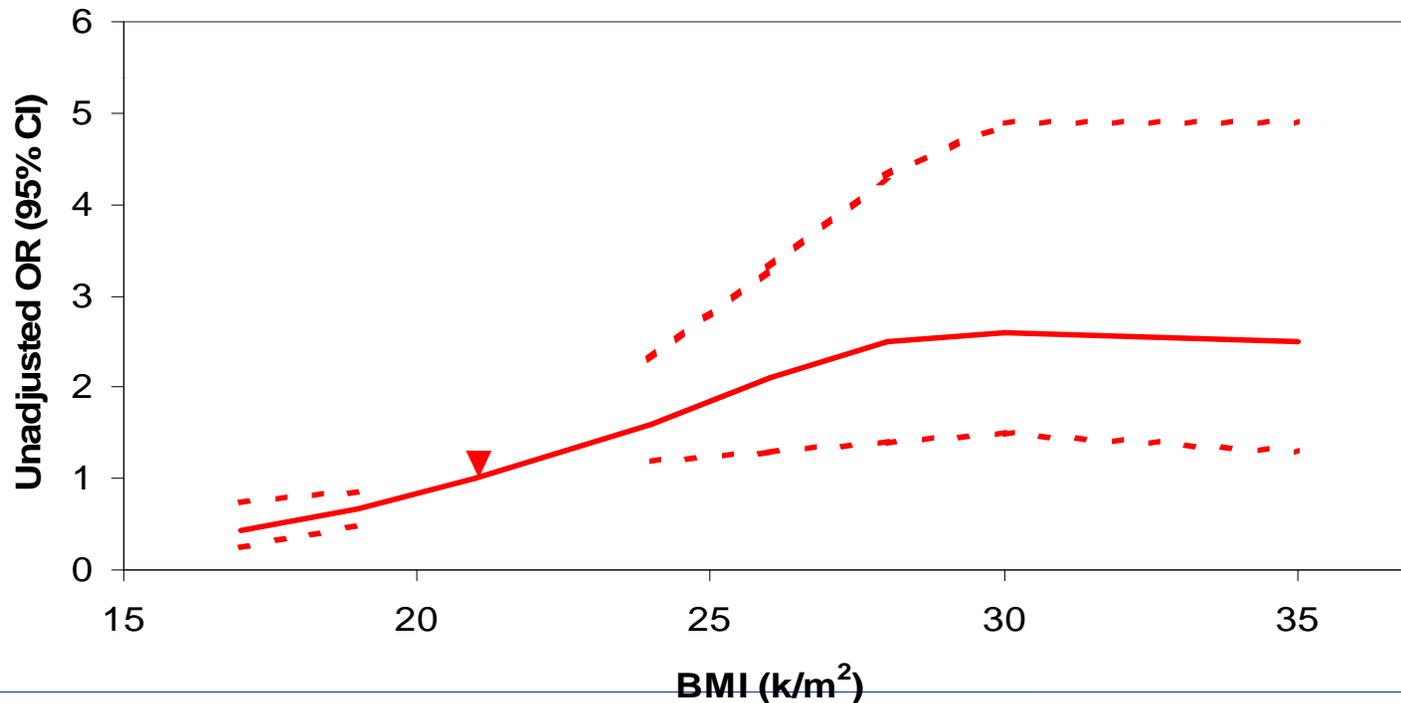
Chronic Hypertension and Preeclampsia Rates

• General population	4-5%
• Preexisting hypertension	25 %
< 4 y duration	22%
≥ 4 y duration	31%
DBP <100 mm Hg	24%
DBP 100-110 mm Hg	42%

Based on BP at visit regardless of antihypertensive Rx

Risk of PE according to BMI

Association between prepregnancy body mass index (BMI) and the risk of preeclampsia (n=1179)



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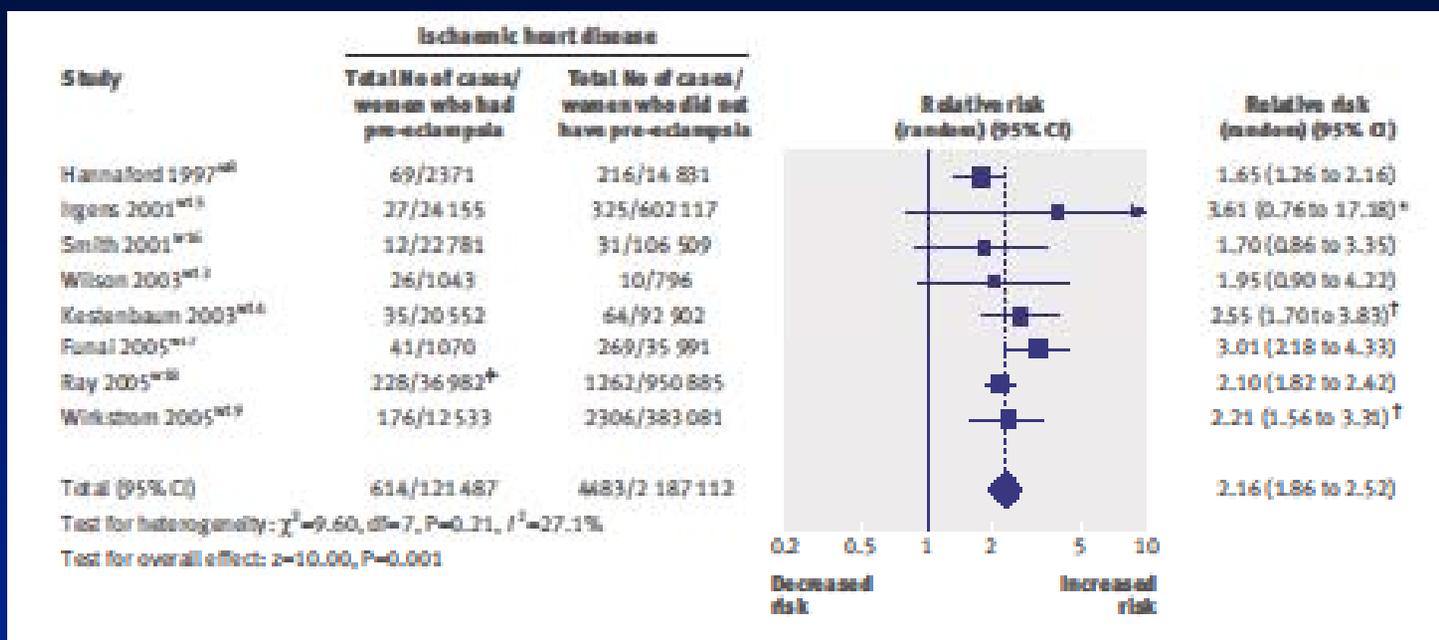
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Preeclampsia and Future Ischemic Heart Disease

Bellamy et al.
BMJ 2007

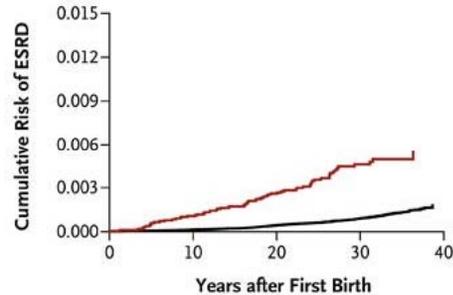


**8 studies including over 2 million women; mean adjusted f/u 11.7 years
 relative risk for IHD (fatal and non fatal) 2.2 (1.9-2.5)**

*** None of these studies adjusted for BMI**

Preeclampsia and Future Renal Disease

A After One Pregnancy



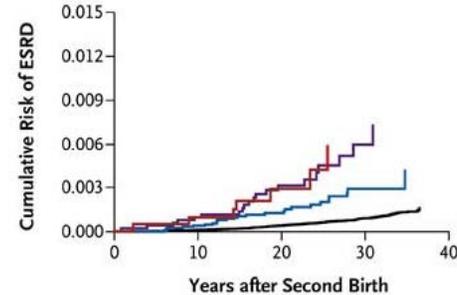
— Preeclampsia

No. at risk	11,511	18,565	12,048	4288	0
No. with ESRD	0	16	44	64	67

— No Preeclampsia

No. at risk	252,572	477,847	341,327	142,775	0
No. with ESRD	0	42	190	327	410

B After Two Pregnancies



— Preeclampsia in Both Pregnancies

No. at risk	1840	2241	1082	331	0
No. with ESRD	0	2	5	7	7

— Preeclampsia in the Second Pregnancy but Not in the First

No. at risk	4372	5602	3166	927	0
No. with ESRD	0	5	14	19	20

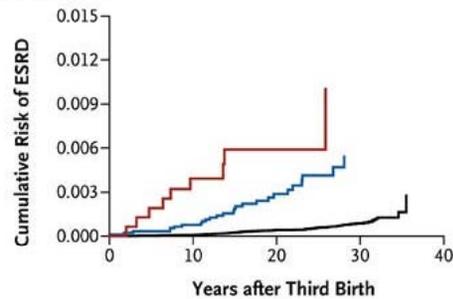
— Preeclampsia in the First Pregnancy but Not in the Second

No. at risk	9636	13,578	7650	3056	0
No. with ESRD	0	5	15	24	25

— No Preeclampsia

No. at risk	274,700	426,931	277,382	111,106	0
No. with ESRD	0	37	143	236	266

C After Three Pregnancies



— Preeclampsia in Two or More Pregnancies

No. at risk	1498	1359	516	102	0
No. with ESRD	0	6	8	9	9

— Preeclampsia in One Pregnancy

No. at risk	8708	8638	4020	974	0
No. with ESRD	0	7	20	26	26

— No Preeclampsia

No. at risk	151,346	166,165	86,389	23,000	0
No. with ESRD	0	14	56	76	84

Vikse BE et al.2008



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