Welcome!

Please be seated by 8:45 AM

To follow slides on your laptop:
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Clinical Effectiveness and Decision Science

PCORI Advisory Panel Meeting

November 8th, 2019

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Housekeeping

- **Today's webinar is open to the public and is being recorded.**
  - Meeting materials can be found on the PCORI website www.pcori.org:
    - Meetings & Events → Advisory Panel Meetings → *Advisory Panel on Clinical Effectiveness and Decision Science Fall 2019 Meeting*
  - Comments may be submitted via chat; no public comment period is scheduled.
- Please remember to **speak loudly** and **clearly into a microphone**.
- State your name and affiliation when you speak.
- Please avoid technical language in your discussion.

Conflict of Interest Statement

Disclosures of conflicts of interest of members of this Committee are publicly available on PCORI's website and are required to be updated annually. Members of this Committee are also reminded to update conflict of interest disclosures if the information has changed by contacting your staff representative.

If this Committee will deliberate or take action on a manner that presents a conflict of interest for you, please inform the Chair so we can discuss how to address the issue. If you have questions about conflict of interest disclosures or recusals relating to you or others, please contact your staff representative.

Welcome & Introductions

Bridget Gaglio, PhD, MPH
Senior Program Officer, CEDS
Patient-Centered Outcomes Research Institute

Welcome from PCORI

Bridget Gaglio, PhD, MPH
Senior Program Officer

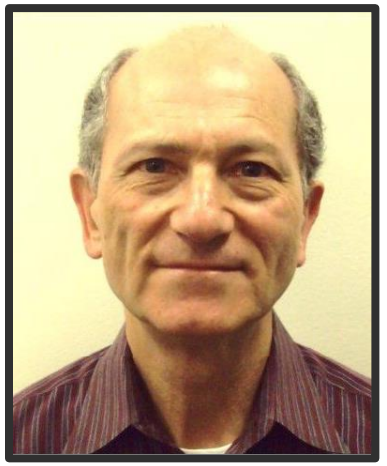
Department: Clinical Effectiveness and Decision Science

Facilitates research initiatives aimed at improving communication and dissemination of evidence-based information among patients and their healthcare providers. Program Officer panel manager for the CEDS Advisory Panel and lead Program Officer point of contact for the Communication and Dissemination Research PCORI Funding Announcement.

CEDS Panel Chair and Co-Chair

Cornell Wright, MPA
Executive Director, NC Office of Minority Health Disparities
NC Department of Health and Human Services
Representation: Policy Makers
CEDS Advisory Panel Chair

Lawrence Goldberg, MD
Psychiatrist Surveyor, The Joint Commission
Representation: Clinician
CEDS Advisory Panel Co-Chair



CEDS Panel Members

Nancy Blake, PhD, RN, NEA-BC, CCRN

Eric Cannon, PharmD, FAMCP

Neela Goswami, MD, MPH

Lawrence Goldberg, MD (Co-Chair)

Melissa Hicks

Kate Houghton, MPA

Robin Karlin, MS

Nancy White, DPT

Felix Fernandez, MD, MSc

Rafael Alfonso-Cristancho, MD, MSc, PhD

Zeeshan Butt, PhD

Helen Osborne, M.Ed., OTR/L

Ruth M. Parker, MD, MACP

Andrew Rosenberg, JD, MP

Sandi W. Smith, PhD

David Webster, MD, MBA

Maureen White, MD, MS, MBA

Cornell Wright, MPA (Chair)

Jeff Hersh, MD, PhD

Michael Schneider, DC, PhD

Susan Lin, ScD, OTR/L, FAOTA

Overview of Agenda & Activities

Cornell Wright, MPA
Lawrence Goldberg, MD

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Agenda

Time	Duration	Activity
9:00 AM	(30 min)	**Overview of PCORI Portfolio: Women's Health Topics**
9:30 AM	(45 min)	**Presentation + Q&A: Cardiovascular Disease in Women**
10:15 AM	(15 min)	**BREAK**
10:30 AM	(75 min)	**Panel Discussion: Cardiovascular Disease in Women**
11:45 AM	(15 min)	**Acknowledgements and Recognition**
12:00 PM	(60 min)	**LUNCH**
1:00 PM	(45 min)	**Presentation + Q&A: Health Implications in Menopause**
1:45 PM	(60 min)	**Panel Discussion: Health Implications in Menopause**
2:45 PM	(15 min)	**BREAK**
3:00 PM	(60 min)	**Global Discussion of Topics**
4:00 PM	(60 min)	**PCORI Reauthorization Update**
4:30 PM	(30 min)	**Wrap up/Closing**
4:45 PM	(15 min)	**Adjourn**

Overview of PCORI Portfolio

Women's Health

Bridget Gaglio, PhD, MPH

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History – Inclusion of Women in Clinical Trials

- **1977 – Food and Drug Administration (FDA)**
  - Issued a guideline banning most women of "childbearing potential" from participating in clinical research studies.

- **1983 – Health and Human Services (HHS)**
  - First task force on women's health, which led to a shift away from the FDA's approach.

- **1985 - Report of the Public Health Service Task Force on Women's Health Issues**
  - Encouraged reexamining current policies, National Institutes of Health (NIH) and the FDA both issued new guidelines to encourage more inclusion of women in studies.

History – Inclusion of Women in Clinical Trials

- **1993 - FDA issued new guideline**
  - This guideline formally rescinded the 1977 policy that banned most women from participating in studies.

- **1993 – United States Congress**
  - To ensure that the policies for inclusion were firmly implemented by NIH, Congress made what had previously been policy into law, through a section in the NIH Revitalization Act of 1993.

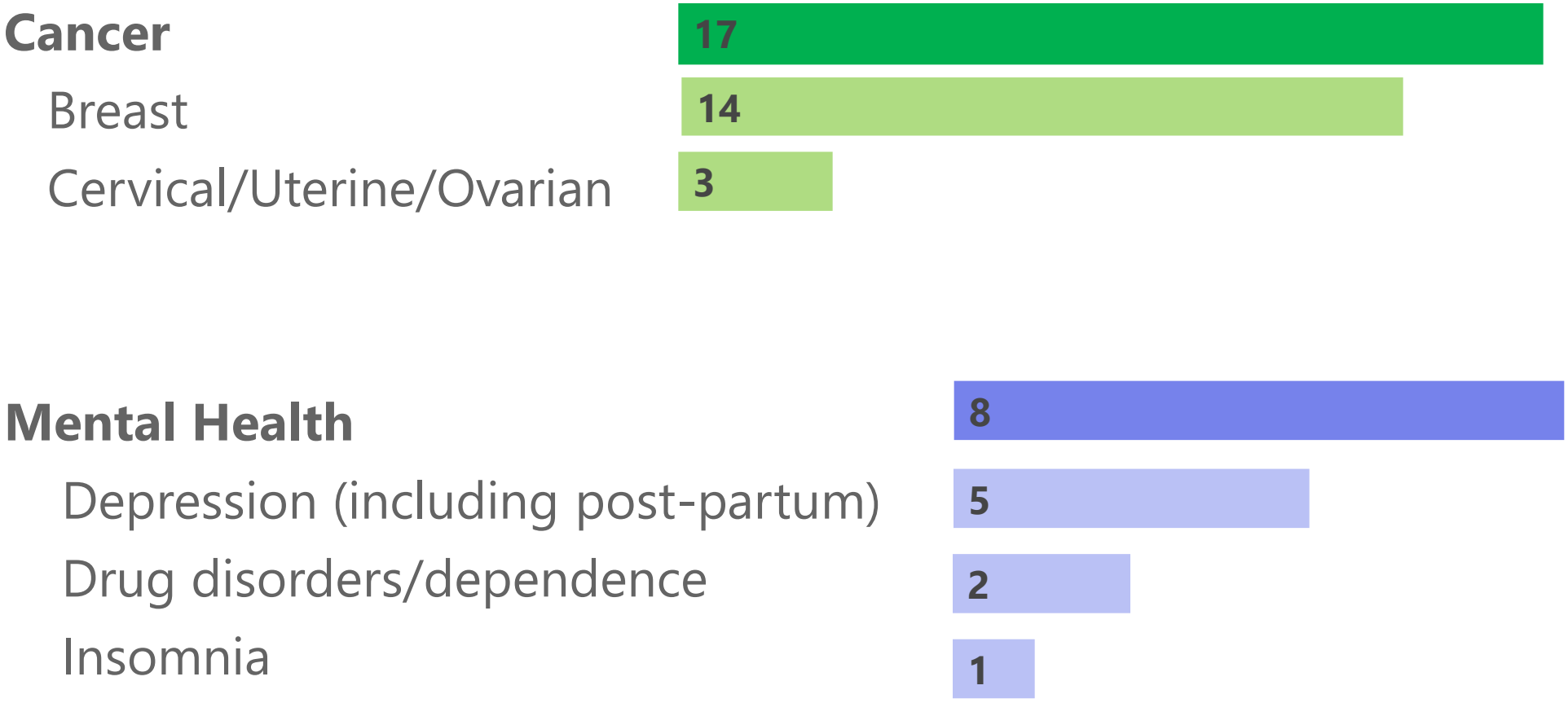
Current Research Policy and Guidelines

- **NIH Policy and Guidelines**
  - The NIH is mandated by the Public Health Service Act sec. 492B, 42 U.S.C. sec. 289a-2 to ensure the inclusion of women and minority groups in all NIH-funded clinical research in a manner that is appropriate to the scientific question under study.
  - The primary goal of this law is to ensure that research findings can be generalizable to the entire population and requires clinical trials to be designed to provide information about differences by sex/gender, race and/or ethnicity.
  - More information about the policy for Inclusion of Women and Minorities in NIH-funded research can be found here.

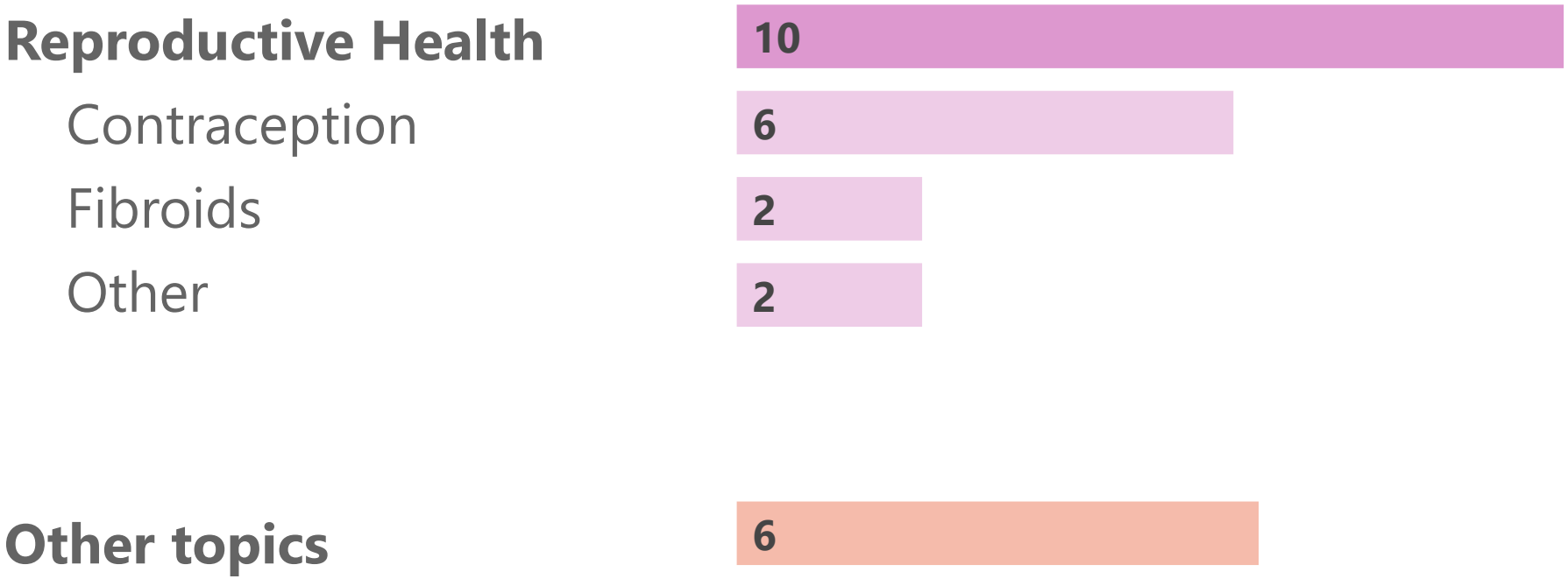
- **PCORI Policy and Guidelines**
  - Follows NIH policy.

PCORI Women's Health Portfolio

Portfolio by Health Topic [n=41]



Portfolio by Health Topic [n=41]



Studies along the Care Continuum

Why Focus on Women's Health?

- In every organ system, there are diseases that are unique to women, more common in women than in men, or characterized by differences in disease course to men.
  - Asthma, iron deficiency, osteoporosis, rheumatoid arthritis, depression, coronary microvascular disease, rosacea, multiple sclerosis, irritable bowel syndrome, urinary tract infection, and age-related macular degeneration are more common in women than in men.
  - Women have higher rates of adverse drug reactions than do men.
  - Pregnancy affects the course of numerous diseases.

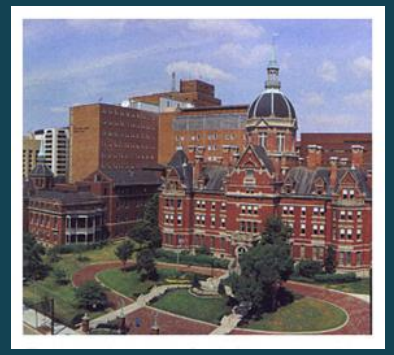
Leading up to Today's Meeting

- CEDS Advisory Panel members were surveyed back in September on topics for consideration.
- A list of 13 health topics were sent out for voting. This was based on current health statistics, reviews of the literature, and gaps in the PCORI portfolio.
- Panelists were asked to rate the top three from the list.
- Top three were:
  1. Cardiovascular disease
  2. Maternal mortality*
  3. Health issues related to menopause

Questions

Cardiovascular Disease in Women

Presentation + Q&A



Pamela Ouyang, MBBS, MD
Professor of Medicine
Deputy Director, Institute for Clinical and Translational Research
Johns Hopkins University SOM

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Conflicts

- Funding:
  - NIH
  - AHA
  - Cordex
- No conflicts related to information presented

Areas of Discussion

- Women vs. Men
  - Sex and gender differences
    - Differences in risk factors
    - Differences in view of disease, medications and procedures
- Under-diagnosis and under-treatment
  - Patient level
  - Health care provider/system level
- Trajectory of risk across lifespan
  - Changing priorities
  - Impact of care systems

Sex and Gender

- **Sex** : biological differences between females and males, including chromosomes, sex organs, and endogenous hormonal profiles.
- **Gender** : social construct and enacted roles and behaviors, which occurs in a historical and cultural context, and varies across societies and over time.

Sex And Gender Influences on Health and Disease

SEX DIFFERENCES

Genetics:
Transcription, expression, transmission

Sex Hormone levels and effects

Epigenetics

Expression of receptors, enzymes, binding proteins etc.

Anatomical differences

Metabolism

GENDER DIFFERENCES

Personal and societal perception of roles in workforce, family, etc.

Personal and societal perception and coping strategies with health/disease

Differences in disease attribution by patient and physician.

Nonmedical factors altering access to health care

CVD in Men and Women

	MEN	WOMEN
Cause of death in US	1 of 2 die of CVD	1 of 3 die of CVD
Average age at MI	60 yrs.	70 yrs.
Pathology findings in myocardial infarction	Plaque rupture	Plaque erosion or non occlusive coronary disease, spontaneous coronary artery dissection
Cardiac cause of chest pain	Obstructive CAD, ? microvascular	Obstructive CAD, vasospasm, microvascular disease
Heart failure (HF)	HF reduced EF	HF preserved EF, stress cardiomyopathy
Hypertension	Greater prevalence in women when age > 65 y	
QT duration	Longer QTc in women vs men	
Atrial Fibrillation	Women have higher stroke risk	

Female Sex and CVD Risk Factors and Conditions

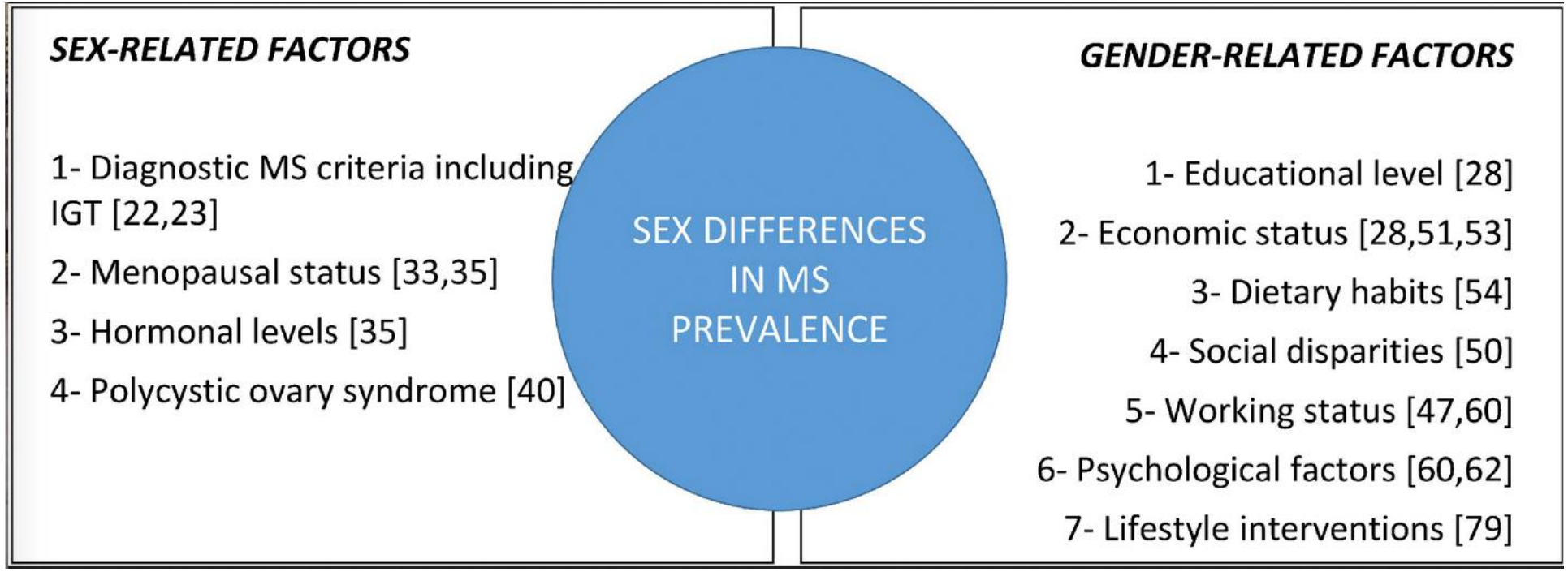
Female Specific Risk Factors	Female Specific Heart Disease
Adverse pregnancy outcomes (gestational hypertension, pre-eclampsia, gestational DM, pre-term delivery, small for gestational age)	Peripartum cardiomyopathy
Female Predominant Risk Factor	**Female-Predominant Heart Disease**
Auto-immune disease (SLE, RA)	Spontaneous coronary artery dissection
Breast cancer therapies	Stress CM/Takostubo
	MINOCA (MI with nonobstructive CAD)
	Coronary microvascular dysfunction
	Coronary vasospasm
	HFpEF
	Pulmonary hypertension
	POTS

Prevalence of Risk Factors Differ in Women and Men

- Obesity
- Inactivity
- Hypertension
- Metabolic syndrome: various definitions
  - NCEP ATP III : 3 of following:
    - Insulin resistance,
    - WC >40 inch (M), > 35 (F),
    - TG $\geq$ 150
    - HDL < 40 (M) or < 50 (F),
    - HTN (> 130 SBP or >85 DBP)

Sex and Gender-Related Factors Associated with Prevalence of MetSyn

Pucci G et al. Pharmacol Res 2017:120:34



Impact of Ischemic Heart Disease Risk Factors Differ in Women and Men

- Diabetes
- Hypertension
- Smoking

Association Between Risk Factors and Incident MI
Adjusted Women-to-Men Hazard Ratios

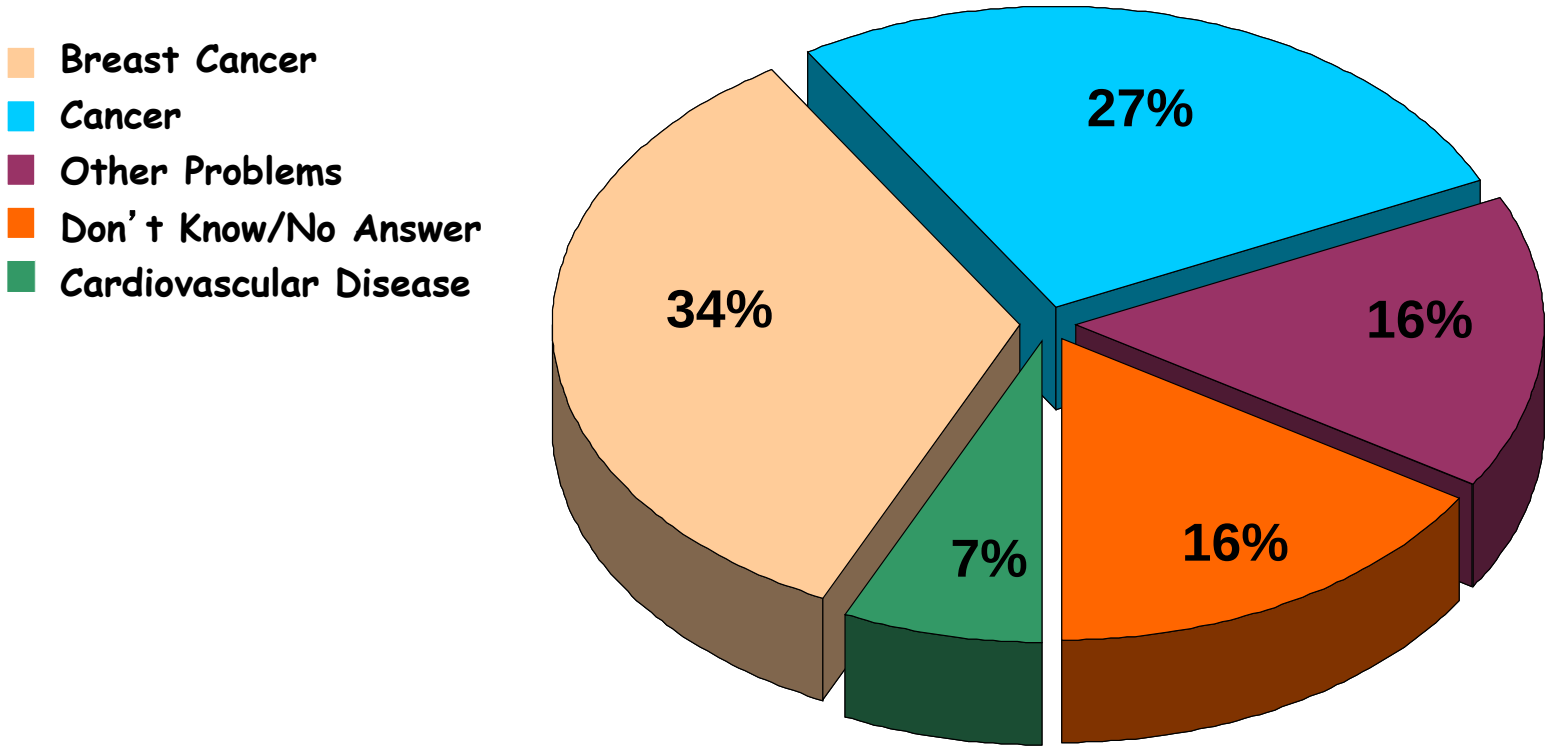
Risk Factor	Ratio of HR (95% CI)
Hypertension	
Elevated BP vs No HTN	1.83 (1.33 to 2.52)
Stage 1 HTN vs No HTN	1.45 (1.12 to 1.88)
Stage 2 HTN vs No HTN	1.46 (1.15 to 1.93)
By **Smoking Intensity**	
1-9 cig/day vs never	1.23 (0.80 to 1.90)
10-19 cig/day vs never	1.42 (1.11 to 1.83)
≥ 20 cig/day vs never	2.01 (1.57 to 2.57)
Diabetes	
Type 1 vs no DM	2.91 (1.56 to 5.45)
Type 2 vs no DM	1.47 (1.16 to 1.87)

Elizabeth R C Millett et al. BMJ 2018;363:bmj.k4247

Patient and Health Care Issues

- Patient level
  - Recognition of risk
  - Likelihood to seek treatment
  - Adherence to medications
  - Concern about adverse side effects
- Health Care Level
  - Recognition of risk
  - Prescription of guideline therapies
  - Less aggressive care – intervention, meds

Women's Perceptions of Their Greatest Health Problems



Adapted from Mosca et al. *Arch Fam Med.* 2000;9:506-515.

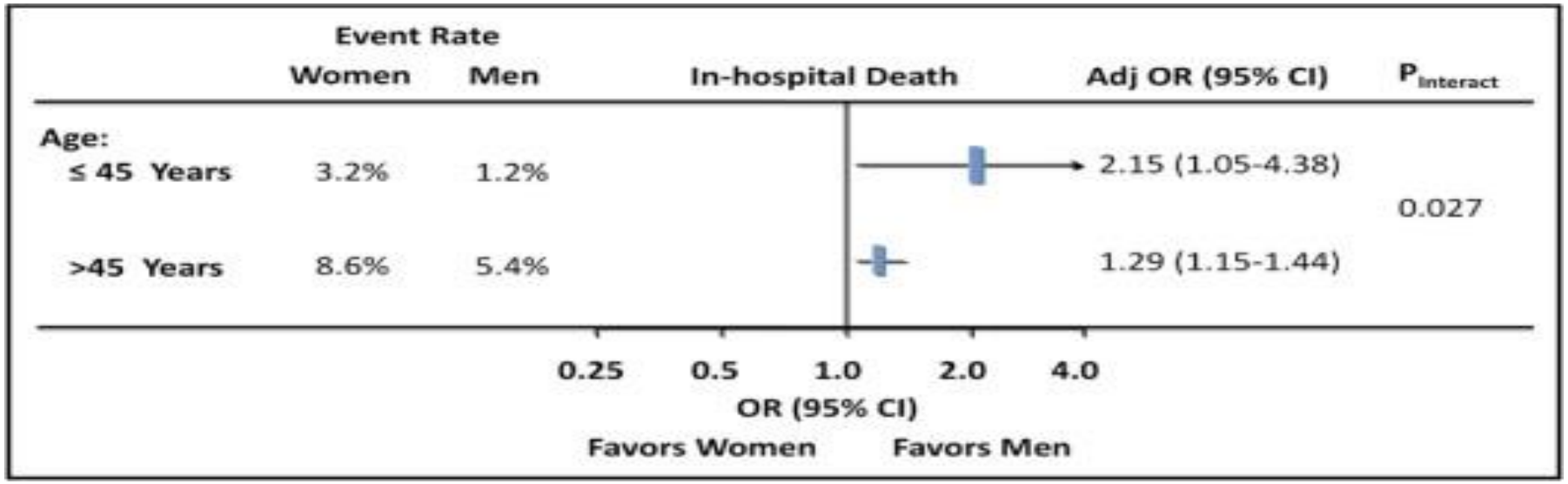
Gender Related Factors Impacting Care

In a cohort of **STEMI** patients presenting to a large metropolitan region, after multivariable adjustment, female gender was associated with both patient and system delay

- **Time from Sx to 1st medical contact**
  - **34% (27-min) increase in time**
- **Time from medical contact to reperfusion therapy**
  - **23% (or 13-min) increase in time**

Sex disparities in MI mortality

Women after STEMI have higher mortality than men, particularly younger women



31,544 patients presenting with ST-segment elevation myocardial infarction who were enrolled in the American Heart Association's Get With the Guidelines Coronary Artery Disease registry

Bangalore et al. Age and Gender Differences in Quality of Care and Outcomes for Patients with ST-segment Elevation Myocardial Infarction. The American Journal of Medicine 2012.

Gender Disparities in Pharmacologic Treatment post MI

ACE/ARB, β-blockers, and statins

- After Myocardial Infarction (MI), women were less likely to
  - Be initiated on preventive pharmacotherapies
  - Be adherent to treatment (defined as >80%)
  - Be on Optimal Medical Therapy 1 year after discharge
  - **Disparity greatest for younger women age 20-54 years**

(analyses were adjusted for age, race, income, pre-MI medication use, type of MI, and comorbidities)

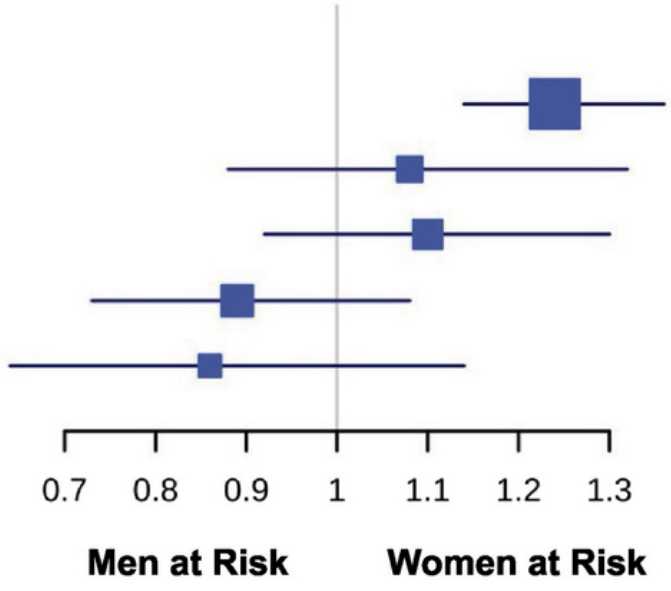
Smolina K et al. Sex Disparities in Post-Acute Myocardial Infarction Pharmacologic Treatment Initiation and Adherence, Circ Cardiovasc Qual Outcomes. 2015 Nov;8(6):586-92. doi: 10.1161/CIRCOUTCOMES.115.001987.

Sex Differences in Atrial Fibrillation

- Risk increases with age, hypertension, coronary disease
- Complications differ in men and women
- Initial studies of anticoagulation did not include enough women to evaluate treatments by sex/gender
- Outcomes from procedures (ablation)

Sex Differences in Outcomes in AF

Outcome	HR	95% CI		I2
Stroke	1.24	1.14	1.36	55.96
TEE	1.08	0.88	1.32	83.39
Major Bleeding	1.10	0.92	1.3	69.21
CV Death	0.89	0.73	1.08	0.00
All-Cause Death	0.86	0.64	1.14	91.98



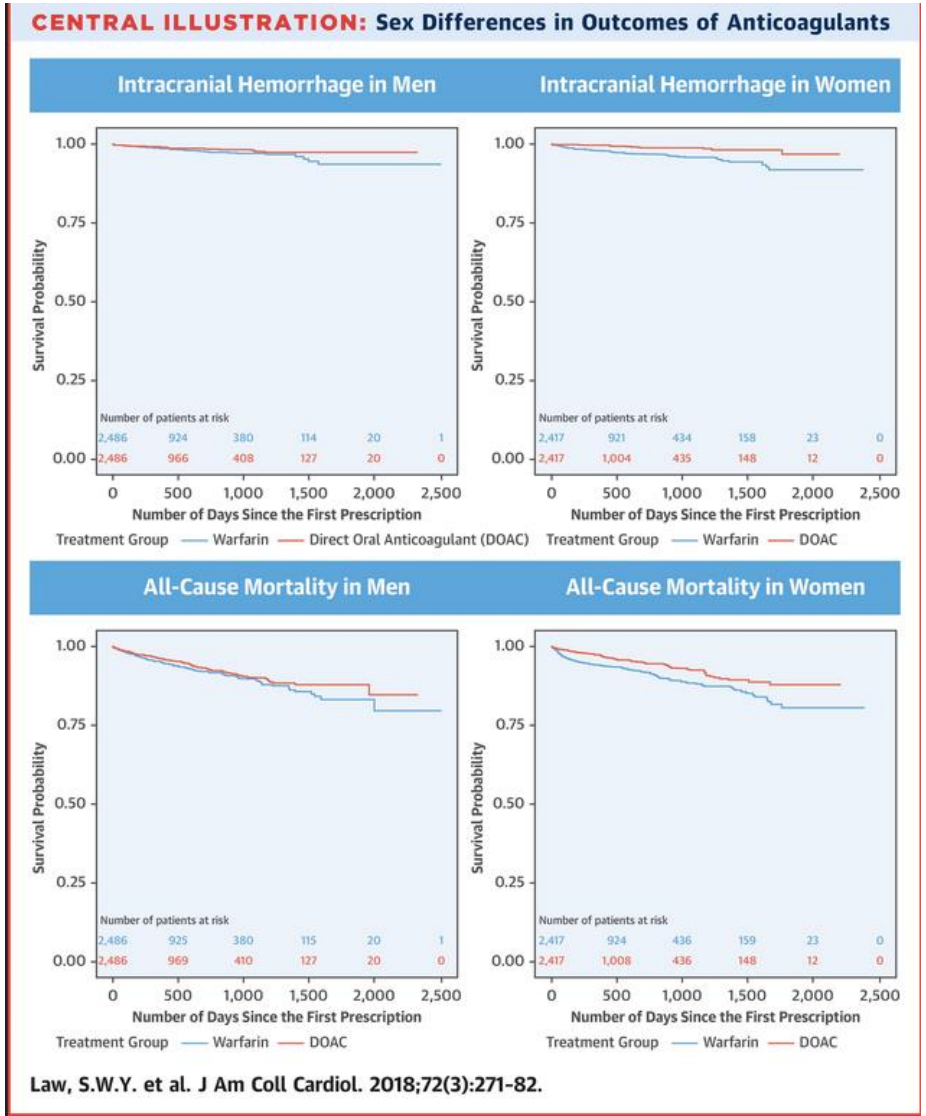
Marzona I et al. Internat J Cardiol 2018;269:182

Sex Differences in Outcomes of Anticoagulation in AF

Law SWY et al. JACC 2018;72:271

DOAC

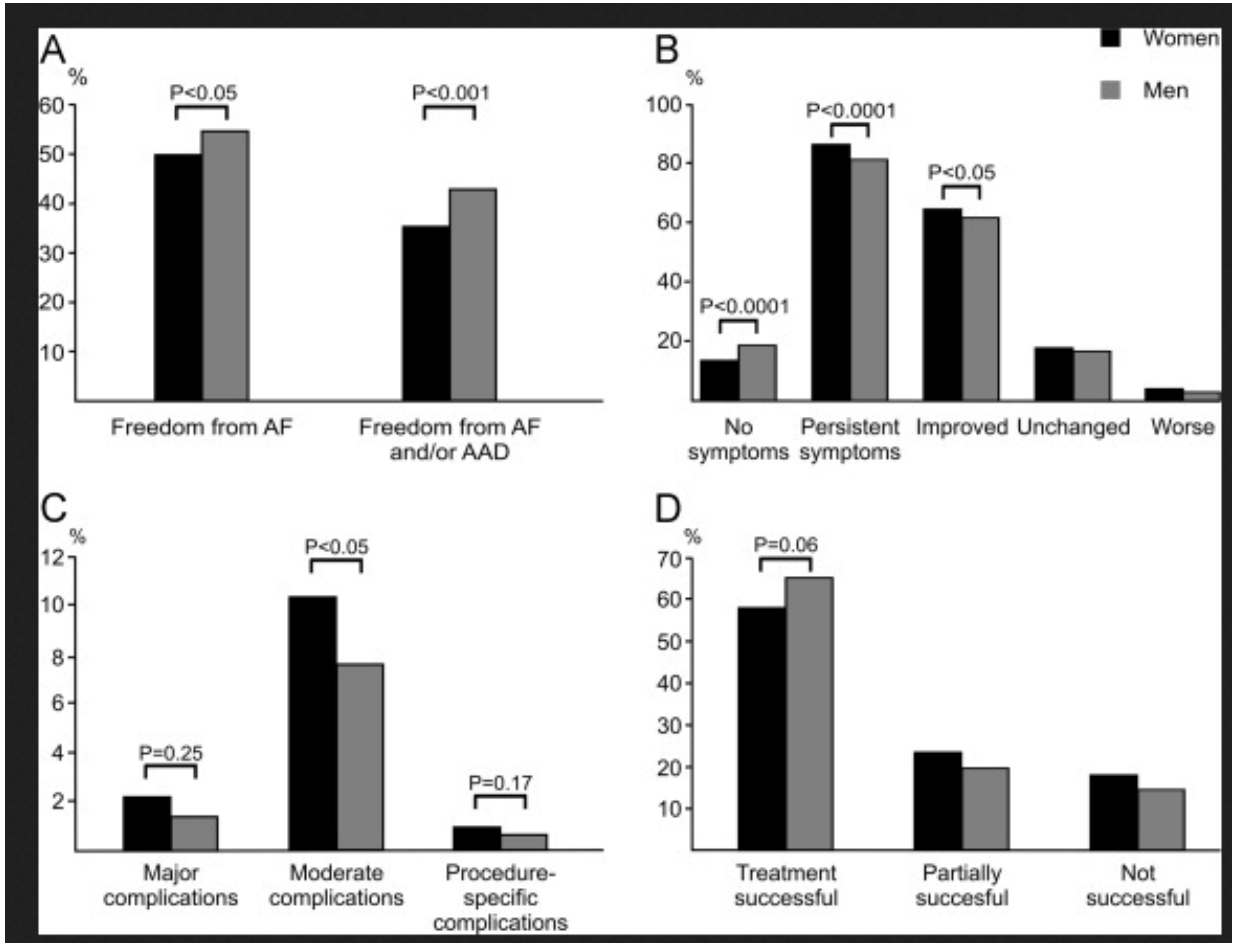
Warfarin



Sex Differences in Outcomes After AF Ablation

Women

Men

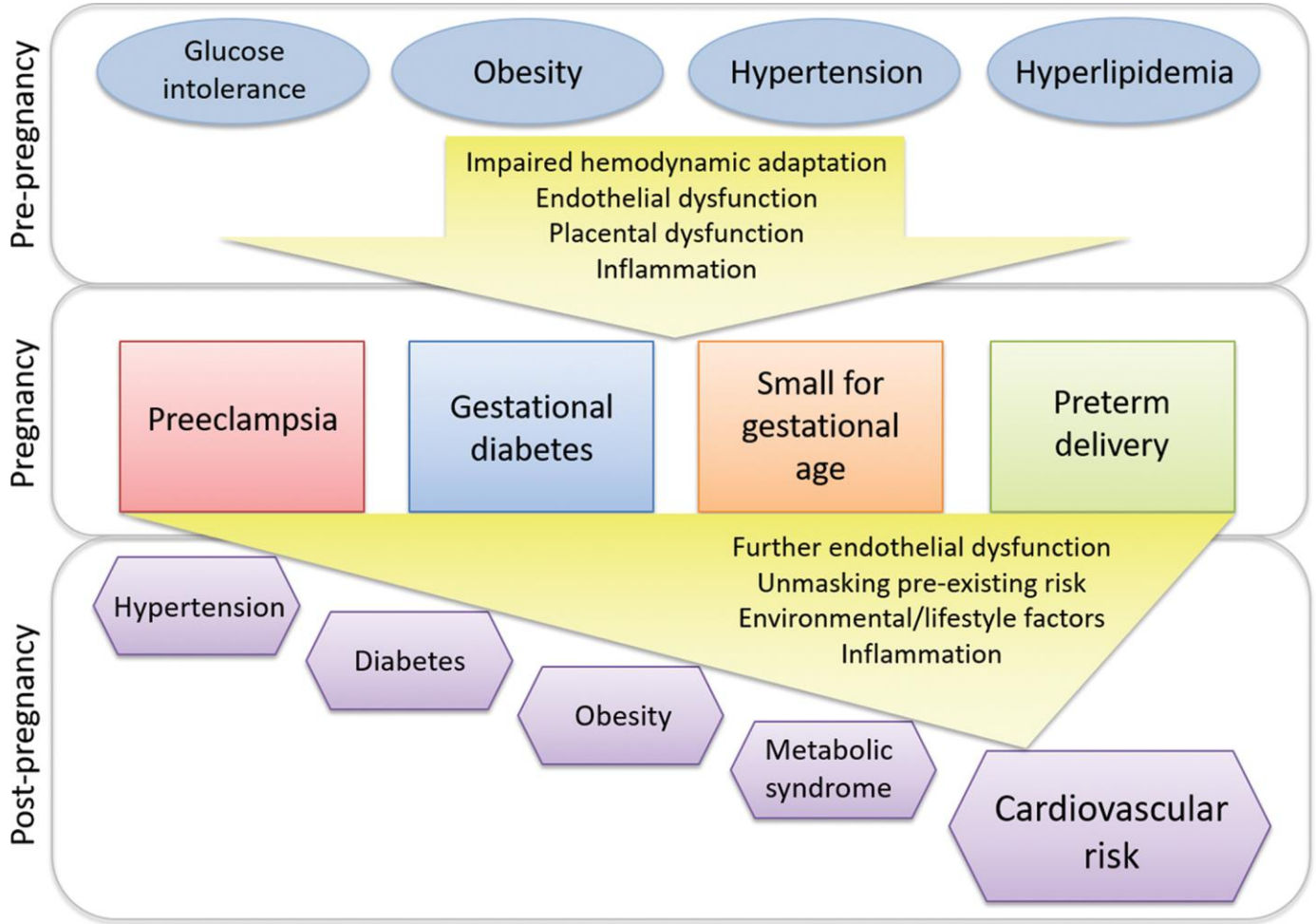


Zylla MM. Heart Rhythm 2016;13:1837

CV Risk Factors Specific to Women

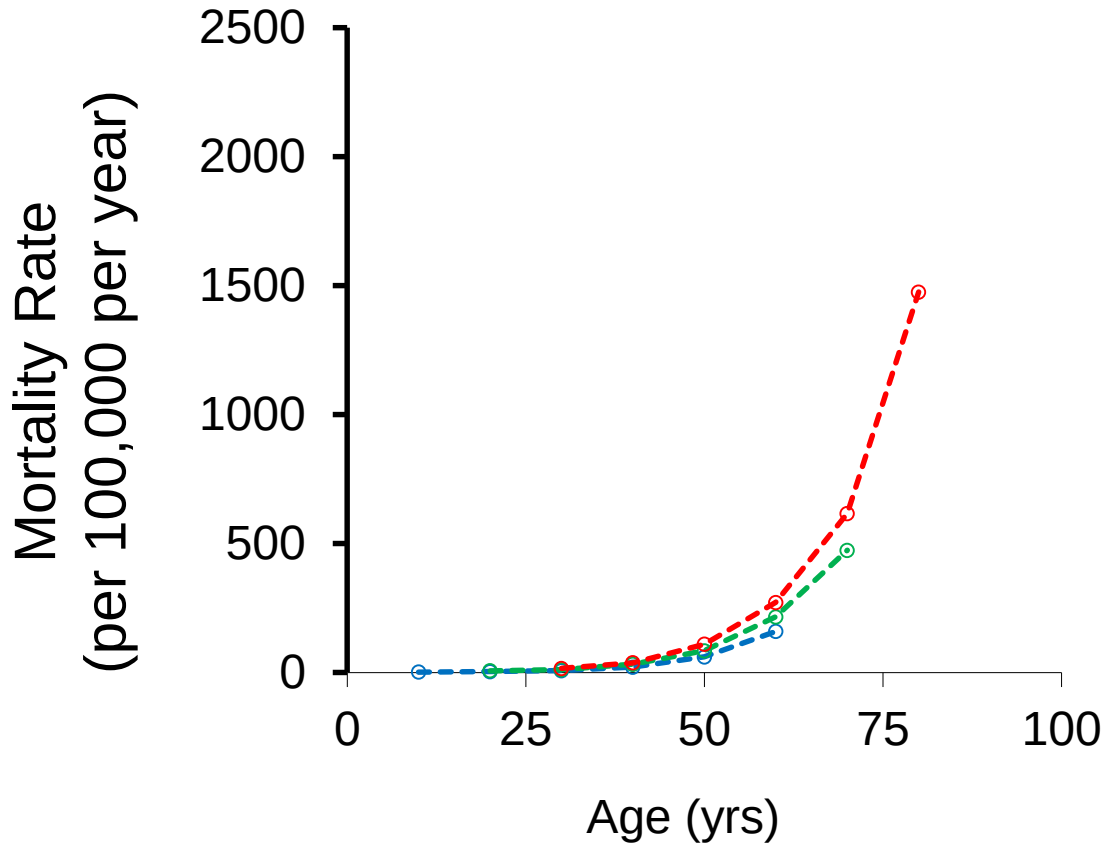
- Adverse pregnancy outcomes
  - Confer risk that may not be evident for decade(s)
  - Women need to be informed of associated risk
  - Management should focus on lifestyle changes and monitoring of risk (blood pressure, diabetes, obesity)
  - Changing health care providers across lifespan can result in failure to continue monitoring
- Menopause

Adverse Pregnancy Outcomes and Future CV Disease



CHD Mortality Rates in US Women by Age

Vaidya D, et al. BMJ 2011;343:d5170



Birth Cohorts: 1915-1924 1925-1934 1935-1944

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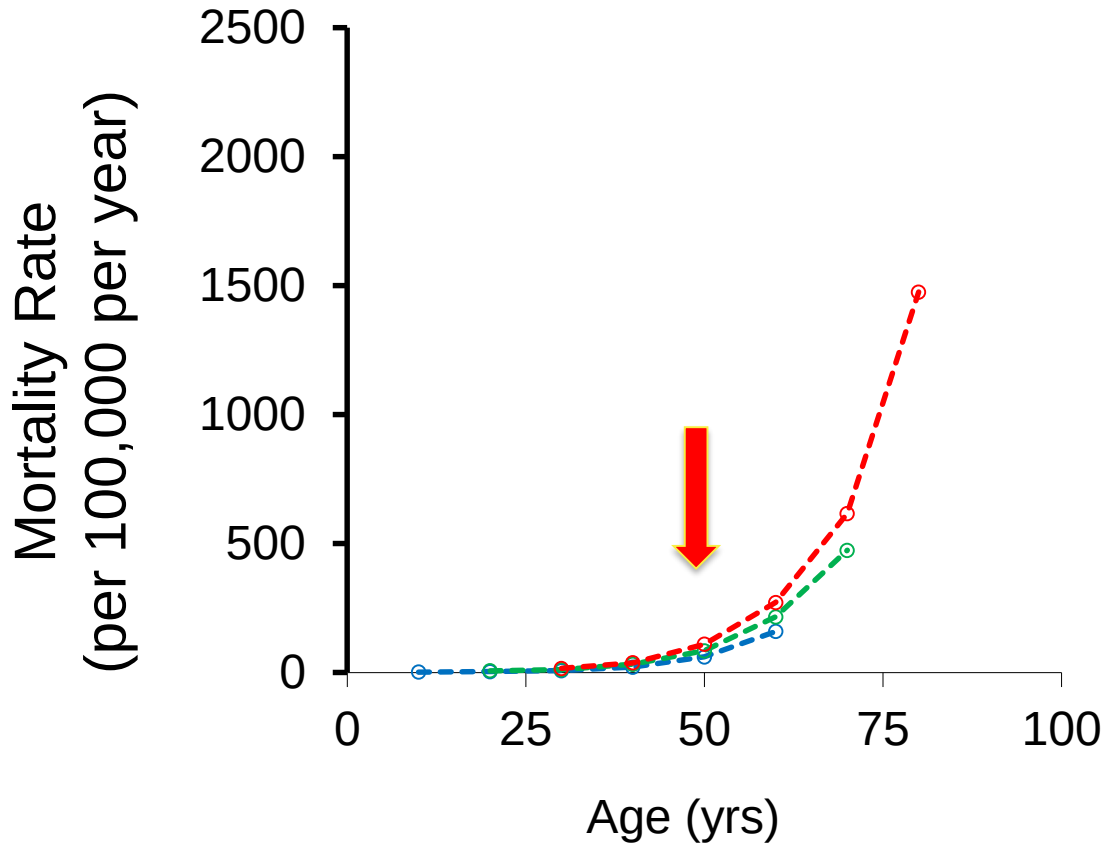
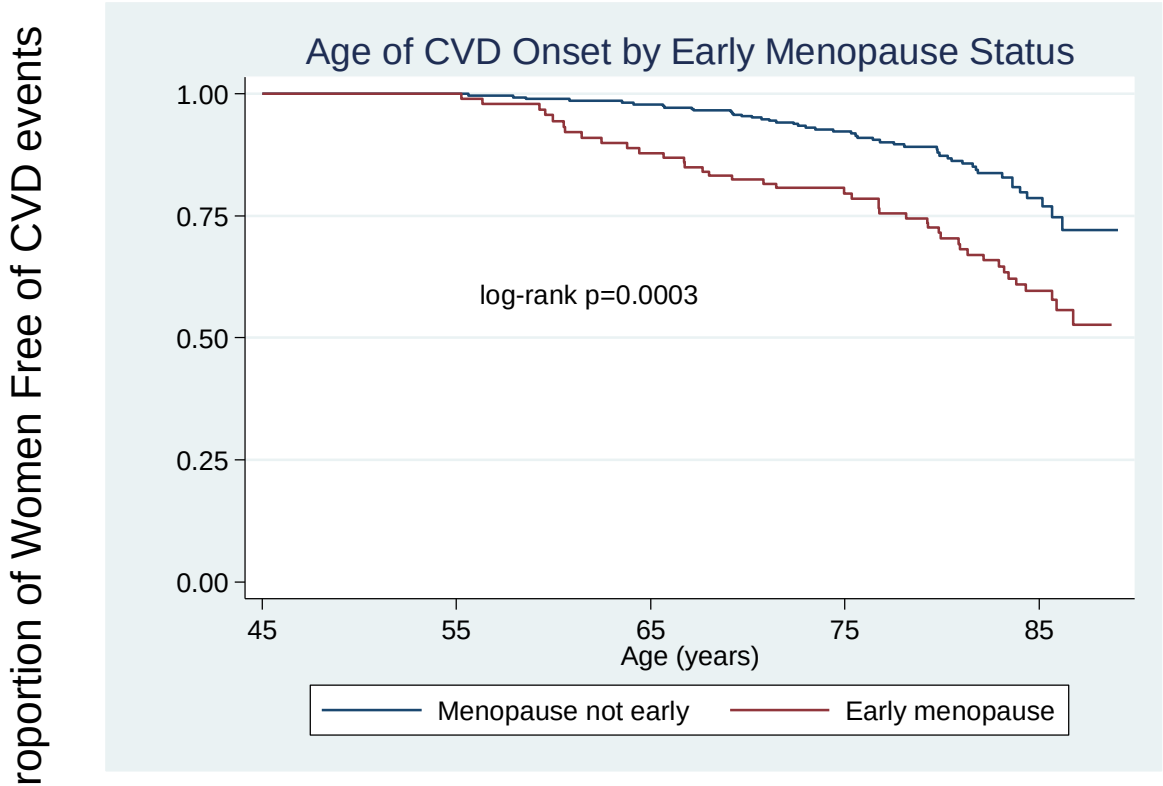


Birth Cohorts: 1915-1924 1925-1934 1935-1944

Association between early menopause (natural/surgical <age 46y) and incident CVD: MESA



N=2509
postmenopausal F

CVD events: MI, SCD, Angina, Stroke, CVD death

The increased risk for CVD events in early menopause group (HR 2.11 [1.34-3.32] persisted after adjustment for race/ethnicity, risk factors (smoking, HTN, Chol, HDL-C, diabetes) and menopause type.

Wellons M, et al. Menopause. 2012 Oct;19(10):1081-7.

Effect of Menopausal Hormone Therapy on CVD Risk

- Women's Health Initiative

- Largest trial of HT in postmenopausal women
  - No reduction in CVD risk in women randomized to
    - combined CEE/MPA (n=16,608)
    - CEE alone (n=10,739)
  - Increase in stroke with CEE

What do we know about women's perceptions

- Recognizing risk
- Understanding medications
- Limited participation in trials

Factors impacting understanding prescribed medications

Bosch-Lenders et al Age and Ageing 2016;45:402

- 754 older men and women (73 y old) taking 5 + meds were interviewed
- Average daily intake of 9 prescribed drugs
- Only 15% able to recall indication for each of the drugs
- Less likely if
  - Taking many meds (≥ 10 vs ≤ 5 ; OR 0.05)
  - Age 80y or more (80+ y vs 60-69 y; OR 0.46)
  - Male sex (OR 0.53)
- More able if living with a partner (OR 2.11)

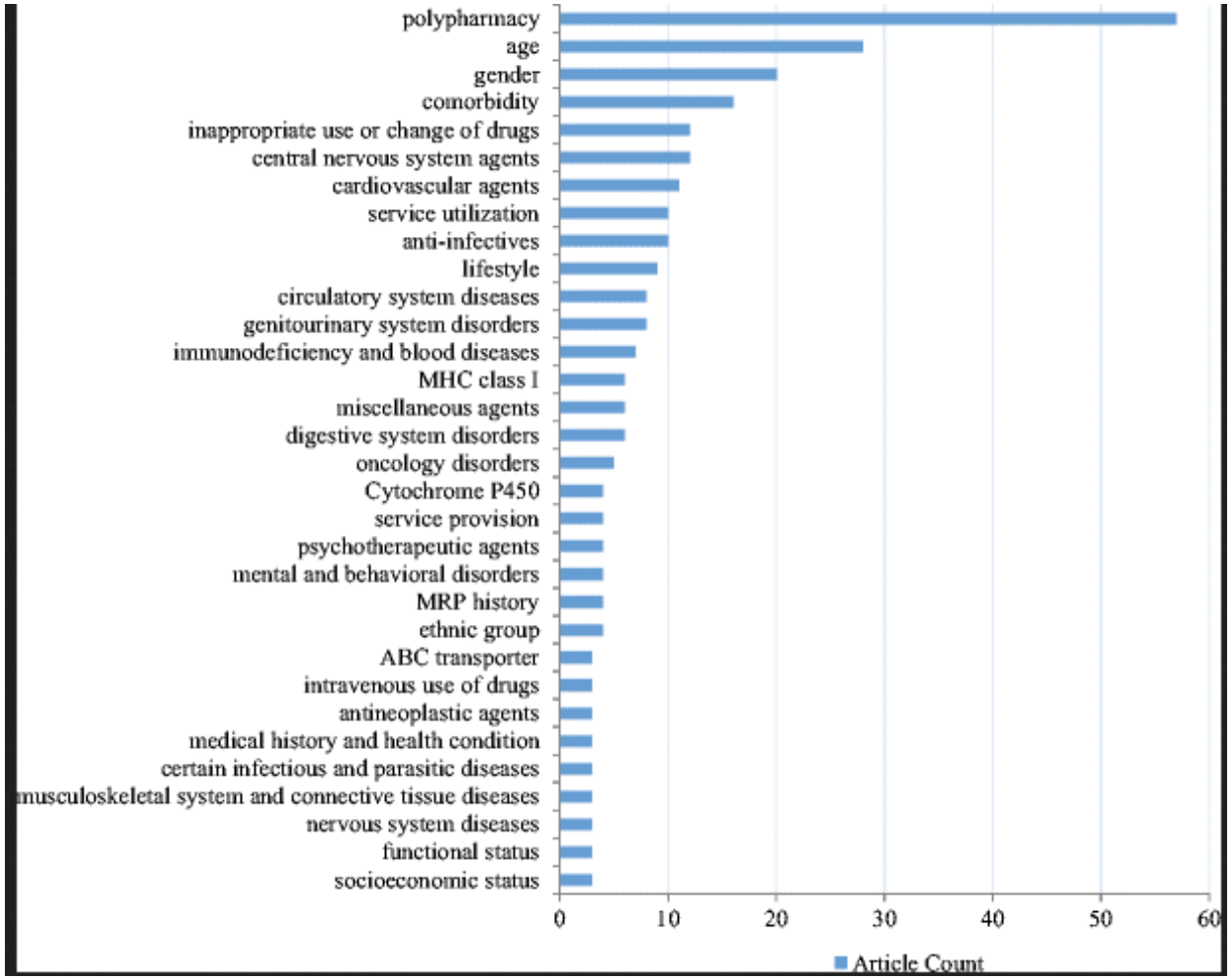
Sex and Gender related issues affecting optimal therapy

- Biological Variables
  - Differences in pharmacology
  - Pregnancy
  - Menopause
- Limited data in clinical trials
- Interaction with other clinical conditions that differ by sex
  - Depression
  - Breast cancer therapy

Factors Associated with Adverse Drug Events

Adverse Drug Events:
Categories:
- Patient- related
- Disease- related
Medication – related

Median prevalence of ADE – 19.5%



Zhou L et al. Eur J Clin Pharmacol 2018;74:389

Factors Associated with Adverse Drug Events

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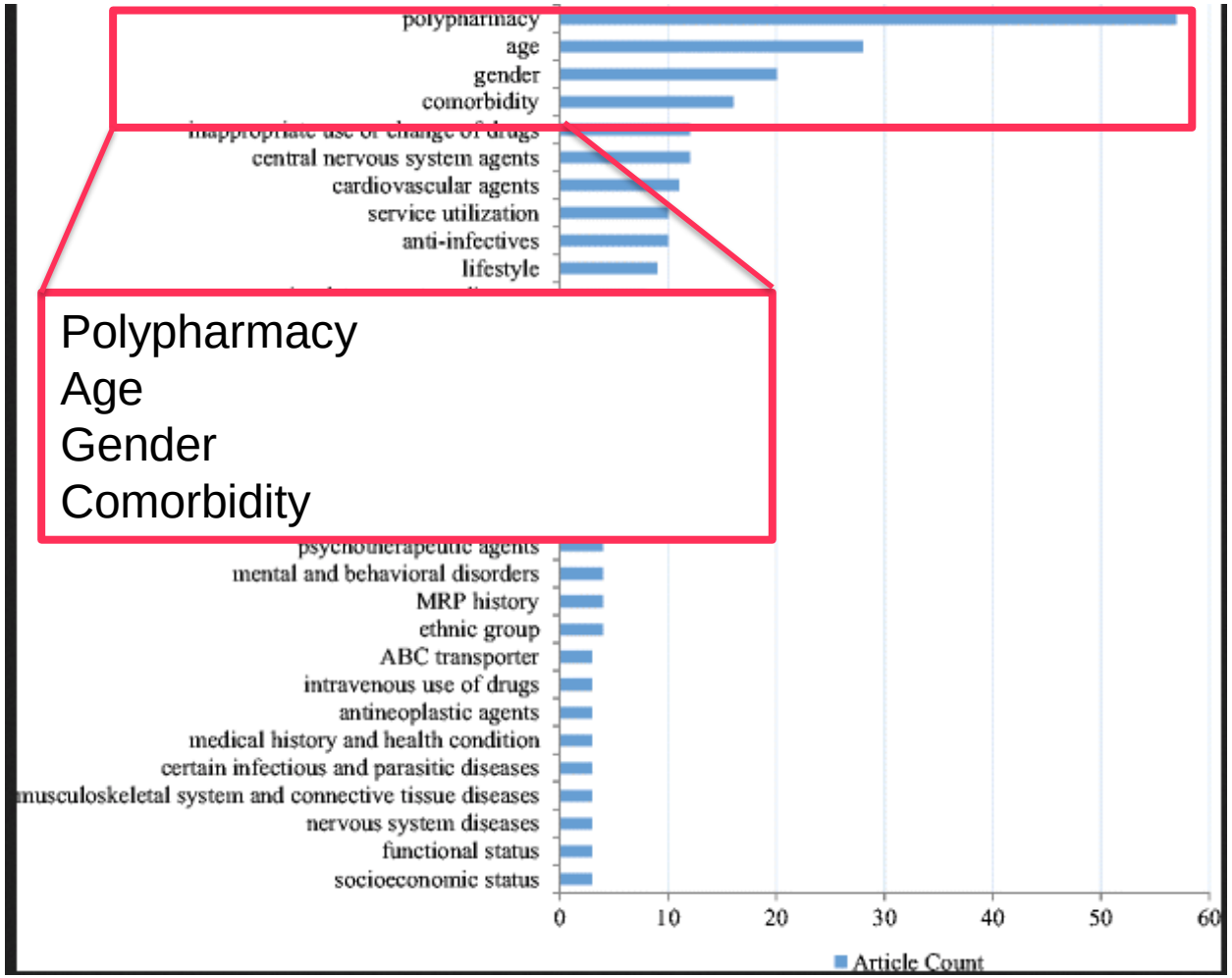

Zhou L et al. Eur J Clin Pharmacol 2018;74:389

Research Questions

- What do women understand about their CV disease risk
  - This will differ by age, race/ethnicity, comorbidities
  - How best to reach different demographic groups
- How best to inform/educate women and health care providers about risk factors, assessment of disease, and effectiveness of medications/procedures in women
- Several female specific or female predominant diseases (SCAD, stress CM, adverse pregnancy outcomes) are uncommon and our understanding of the pathophysiology/optimal management etc. is limited.
  - Need collaborative/registry research to gather sufficient numbers to answer important questions.
- Why is it difficult to get women to participate in clinical research?
- How best to implement lifestyle changes that will be persistent

THANK YOU

?

BREAK

10:15 – 10:30 AM

Up Next: Panel Discussion on Cardiovascular Disease in Women

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Panel Discussion

Cardiovascular Disease in Women

Pamela Ouyang, MBBS, MD
Mellanie Hills
Alayna Effron, EdD

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Panel Discussants
Topic: Cardiovascular Disease in Women

Pamela Ouyang, MBBS, MD
Professor of Medicine
Deputy Director, Institute for Clinical and Translational Research at Johns Hopkins University SOM

Mellanie True Hills
Founder and CEO at StopAfib.org

Alayna Effron, Ed.D, MSc., C.H.E.S.
Director of Development for HealthyWomen

Acknowledgements and Recognition

Advisory Panel Terms Ending Fall 2019

Bridget Gaglio, PHD, MPH

Amanda Barbeau, MPH
Program Associate, CEDS

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Thank you for your service!

- Nancy White, DPT
- Jeff Hersh, MD, PhD
- Felix Fernandez, MD, MSc
- Michael Schneider, DC, PhD
- Rafael Alfonso-Cristancho, MD, MSc, PhD
- Susan Lin, ScD, OTR/L, FAOTA
- Zeeshan Butt, PhD

LUNCH

12:00 – 1:00 PM

Up Next: Health Implications of Menopause

Health Implications of Menopause

Presentation + Q&A

JoAnn V. Pinkerton, MD
Professor of Obstetrics and Gynecology
Director, Midlife Health
University of Virginia Health System
North American Menopause Society,
Executive Director Emeritus and Past President

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Demographics of menopause

- About 37.5 million women reaching or at menopause
- Life Expectancy average for women in 2016
  - approximately 81 for white and Hispanic populations
  - 75 for black population
- By 2050, approx. 47 million women aged 45 to 64 years
- Women spend 1/3 to ½ of their lives after menopause

(Arias E, Xy J.National Vital Statistics Reports Volume 68, Number 7June 24, 2019United States Life Tables, 2017 https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_07-508.pdf. Accessed 9-1-19
US Census. 2017 National Population Projections Tables https://www.census.gov/data/tables/2017/demo/popproj/2017-summary-tables.html. Accessed 9-1-19

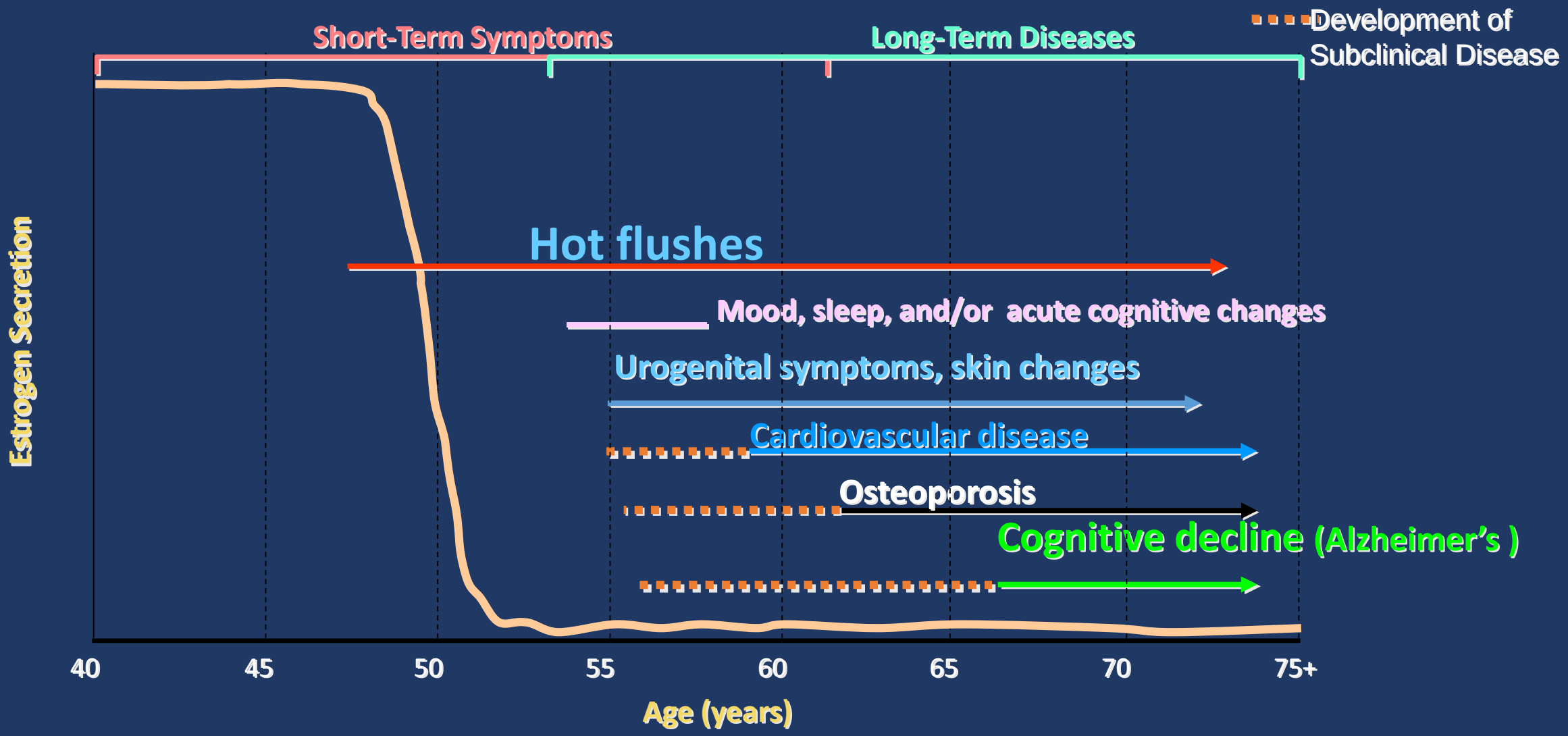
Menopause Matters

- In the US, 1.3 million women become menopausal each year.
- It typically begins between the ages of 51 and 52.
- 5% of women experience early menopause between ages 40 and 45
- 1% of women experience premature menopause before age 40, due to permanent ovarian failure; may be associated with sex chromosome abnormalities
- Menopause may be due to chemotherapy or surgical removal of ovaries or medications.

What is Menopause?

- Menopause is the permanent cessation of menses for 12 months resulting from estrogen deficiency
- The median age of menopause is 51.
- Most women experience hot flashes, night sweats and sleep disruption
- Menopause affects many other areas of the body such as bone, urogenital, mood and cognition, and cardiovascular.
- Women spend up to one-third of their lives in post-menopause

Estrogen Loss and Manifestations of Health Risks Over Time



Health Consequences of Menopause

- Heart Disease- Before age 55, women have a lower risk of heart disease than men.
- Stroke- Risk for stroke doubles every decade after age 55
- Osteoporosis-Less estrogen leads to bone loss and fracture risk
- Urinary Incontinence- 50% pm women difficulty holding their urine
- Mood and Depression-Depression and anxiety increase as women traverse the menopause; most vulnerable women are those without any prior episodes.
- Cognitive Changes- Loss of estrogen associated with deficits in verbal and working memory. Almost 3/4 of women have sense of memory loss

Santoro N, Menopausal Symptoms and Their Management. *Endocrinol Metab Clin North Am*. 2015;44(3):497–515.

Menopausal symptoms & signs

Classic symptoms:

- Change in menstrual cycle pattern (during perimenopause)
- Vasomotor symptoms (hot flashes & night sweats)
- Vulvovaginal symptoms, dyspareunia
- Sleep disturbances
- *Other symptoms :*
- Cognitive concerns (memory, concentration)
- Psychological symptoms (depression, anxiety, moodiness)

➢ No one universal menopausal syndrome

Avis et al *Am J Med* 2005;118 Suppl 12B:37-46; NIH *Ann Intern Med* 2005;142:1003-13

Quotes from menopausal women

“Not sleeping, memory loss, angriness and frustration, pains all over my body and hot flashes at least 15 times a day. If I was a dog, I’m sure I would be put down.”

“It's time to stop grouping up and complaining about all our estrogen deficient symptoms and demand real answers and plenty of estrogen.”
— Marie Hoag MBA

- **Can you imagine a world where 1 in 10 MEN felt pain during sex?**
- They would literally run through the streets setting things on fire and bemoaning the tragedy that their lives have become.

“Osteoporosis is not an inevitable part of ageing; it is preventable. So it is vital that all of us, of all ages, start taking care of our bones now, before it is too late.”

Camilla Parker Bowles

“I thought menopause was going to be a breeze”

- Hot flashes- 6-8 hot flashes a day
- 1 to 2 soaking night sweats per week
- Early morning awakening, can’t go back 3-4 times/week
- Emotional lability
- Fatigue
- Decreased concentration
- Mental fog
- Vaginal dryness/ pain with intercourse
- Reduced sexual satisfaction
- Urinary urgency

Women's Health Initiative study 2002

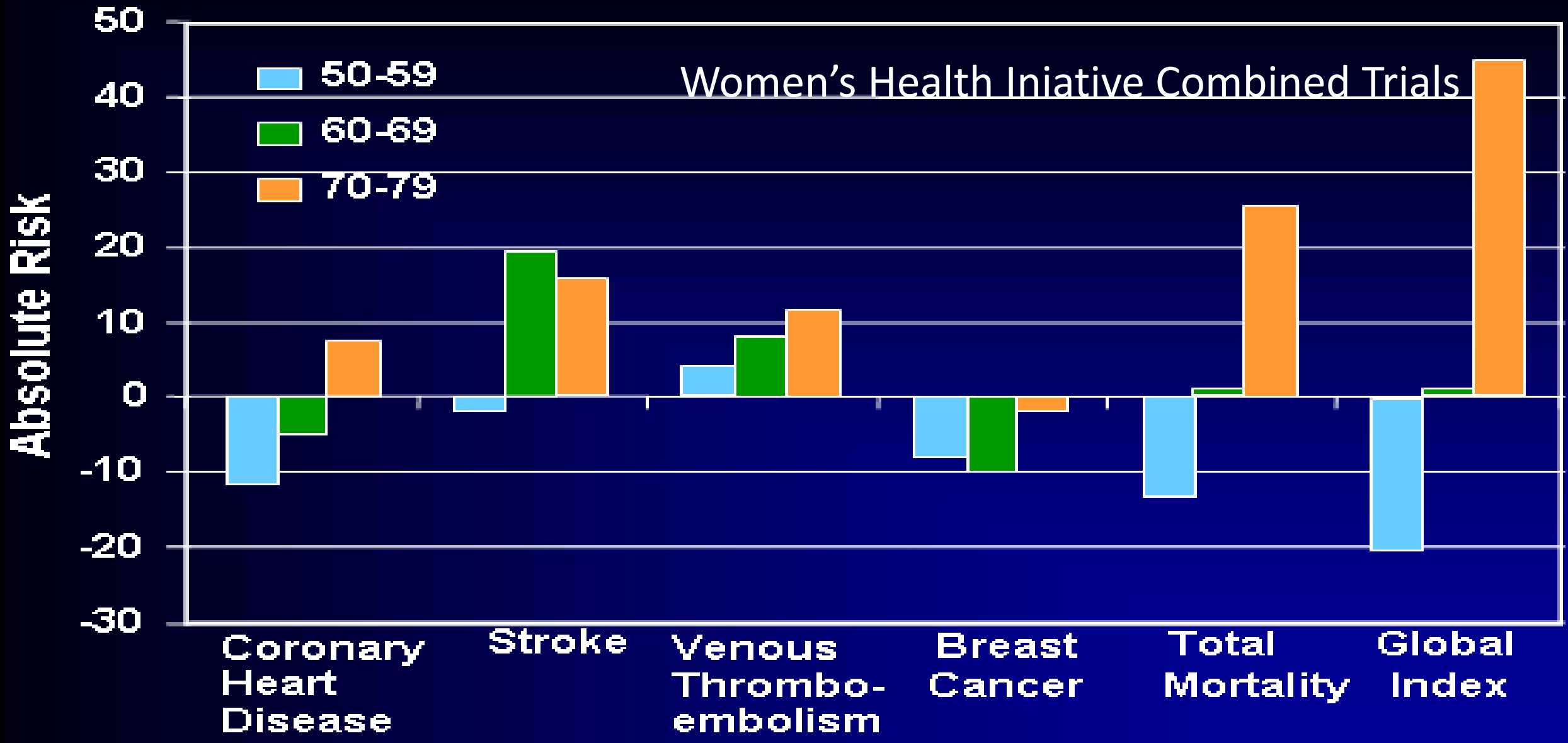
Breast cancer

Heart disease

Stroke

Probable Dementia

Fear has been driving the conversation about hormone therapy



Writing Group for the Women's Health Initiative Investigators. *JAMA* 2004;291:1701-1712.
Rossouw et al. *JAMA* 2007;297:1465-1477.

HT and HEART (CHD): 'Timing Hypothesis'

- If initiated **early** in the menopausal transition, HT does not increase CHD risk
  - HT may reduce morbidity/mortality risk if initiated early
- **'Early':** Age 50-59 years, or < 10 years after menopause onset

- HT increases CHD risk if initiated later
  - If initiated >10 years after menopause, an increase in (CHD) events seen
  - Findings congruent with human and non-human primate data

- Consider individual patient's risk for CVD, stroke, VTE when starting HT
- HT not recommended for primary prevention of CVD- USPSTF 2017

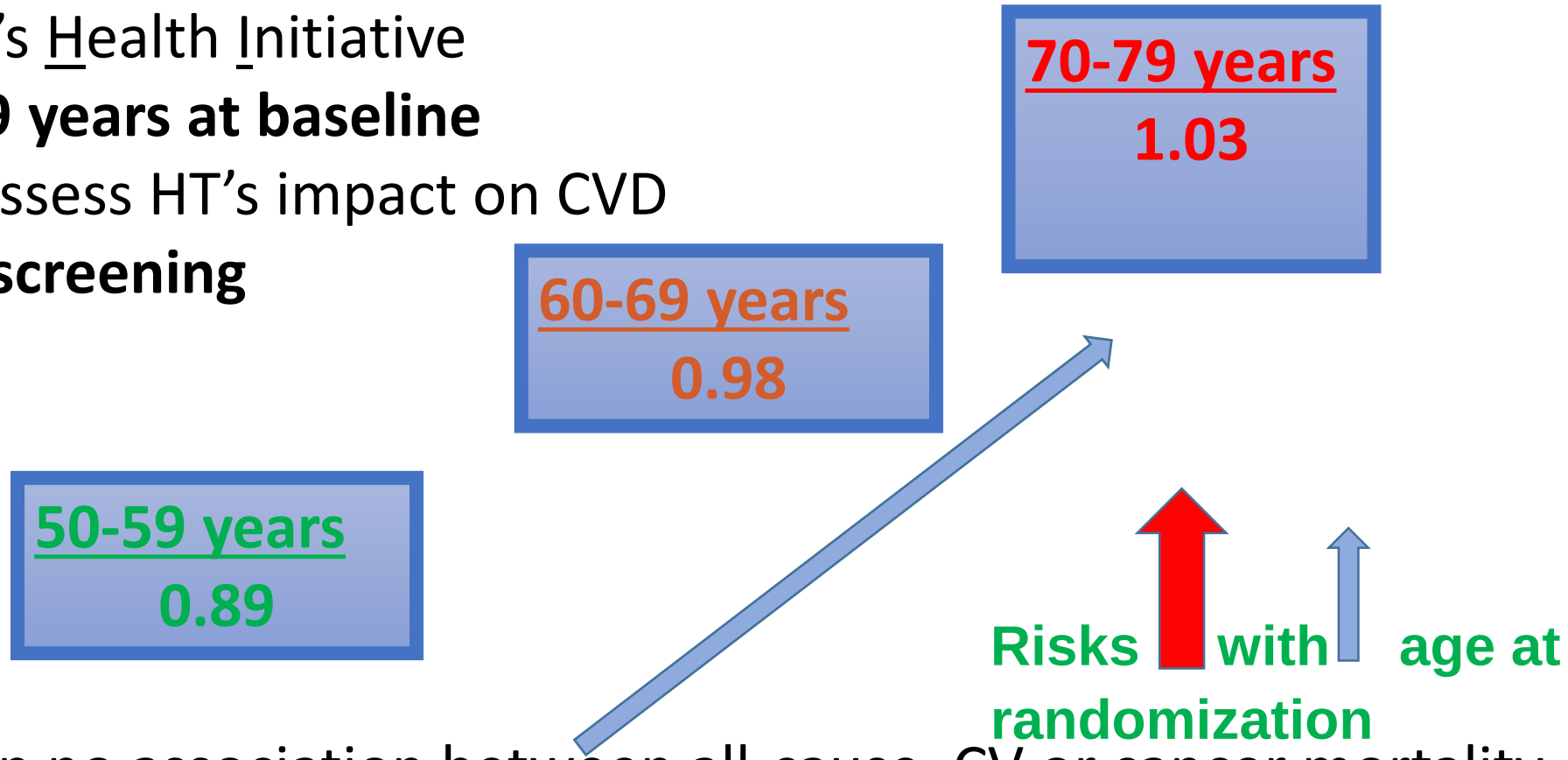
J Hsia, et al. Arch Int Med 2006
JE Manson et al. N Eng J Med 2007
Stram DO, et al. Menopause 2011
MA Allison, JE Manson. Editorial. Menopause 2011
JE Rossouw et al. JAMA 2007 Manson JAMA 2013, 2017
S Toh, et al. Annals Int Med 2010 USPSTF 2017
HN Hodis, et al. Circulation 2014
P Tuomikoski, et al. Obstet Gynecol 2014

The timing hypothesis refers to initiation,

not continuation, of hormone therapy…

All-cause Pooled (EPT+ET) Mortality Hazard Ratios at 18 Years Cumulative f/u by Age at Randomization

WHI: Women's Health Initiative
Women **50-79 years at baseline**
Designed to assess HT's impact on CVD
Mean age at screening
63-64 years



18 yr follow up no association between all-cause, CV or cancer mortality.
Women ages 50-59, reduction in all cause mortality but did not meet statistical significance.

JE Manson, et al. JAMA October , 2013 & September 2017

Problem Number One

- Women need trusted information about menopause and hormone therapy
- Fear about use of hormone therapy prevents women from receiving safe and effective therapy

Time to take the fear out of the hormone therapy conversation

Despite published evidence from the WHI

suggesting hormone therapy is **relatively safe, viable solution for symptomatic menopausal women under age 60 or who are within 10 years postmenopause**,

the number of women being prescribed and using hormones continues to decline.

Clinical Questions :

- Risks and benefits of menopausal hormone therapy?
- Best candidates for use of menopausal hormone therapy?
- When should menopausal hormone therapy be stopped?
- When to consider extended use of hormone therapy?
- How is genitourinary syndrome of menopause treated?

Funding Priority 1

- Increase recognition, diagnosis, and treatment of menopausal symptoms (vasomotor, sleep, mood) with safe and effective pharmacologic and non-pharmacologic (ie. Behavioral) therapies
  - Among clinicians including learners
  - Among patients
  - Take fear out of the conversation and replace it with evidence based information
  - Increase access to accurate menopausal information
  - Support development and empirical evaluation of novel therapies
  - Incorporate trauma informed care for menopausal women

Problem Number 2
Osteoporosis More Common than Breast Cancer

- Women more at risk for developing osteoporosis than for developing breast cancer
- 10 million Americans have osteoporosis
- Number of hip fractures is increasing
- Risk Factors: early menopause, thin, Caucasian
- Eating disorders, steroids, gastric bypass

Osteoporotic bone

Funding Priority Number 2

- Increase prevention, diagnosis, and treatment of osteoporosis to prevent osteoporotic related fractures, morbidity and mortality
  - Among clinicians
  - Among patients
  - There is a 'Prevent the second fracture" but what about "prevent the first fracture"

Genitourinary symptoms

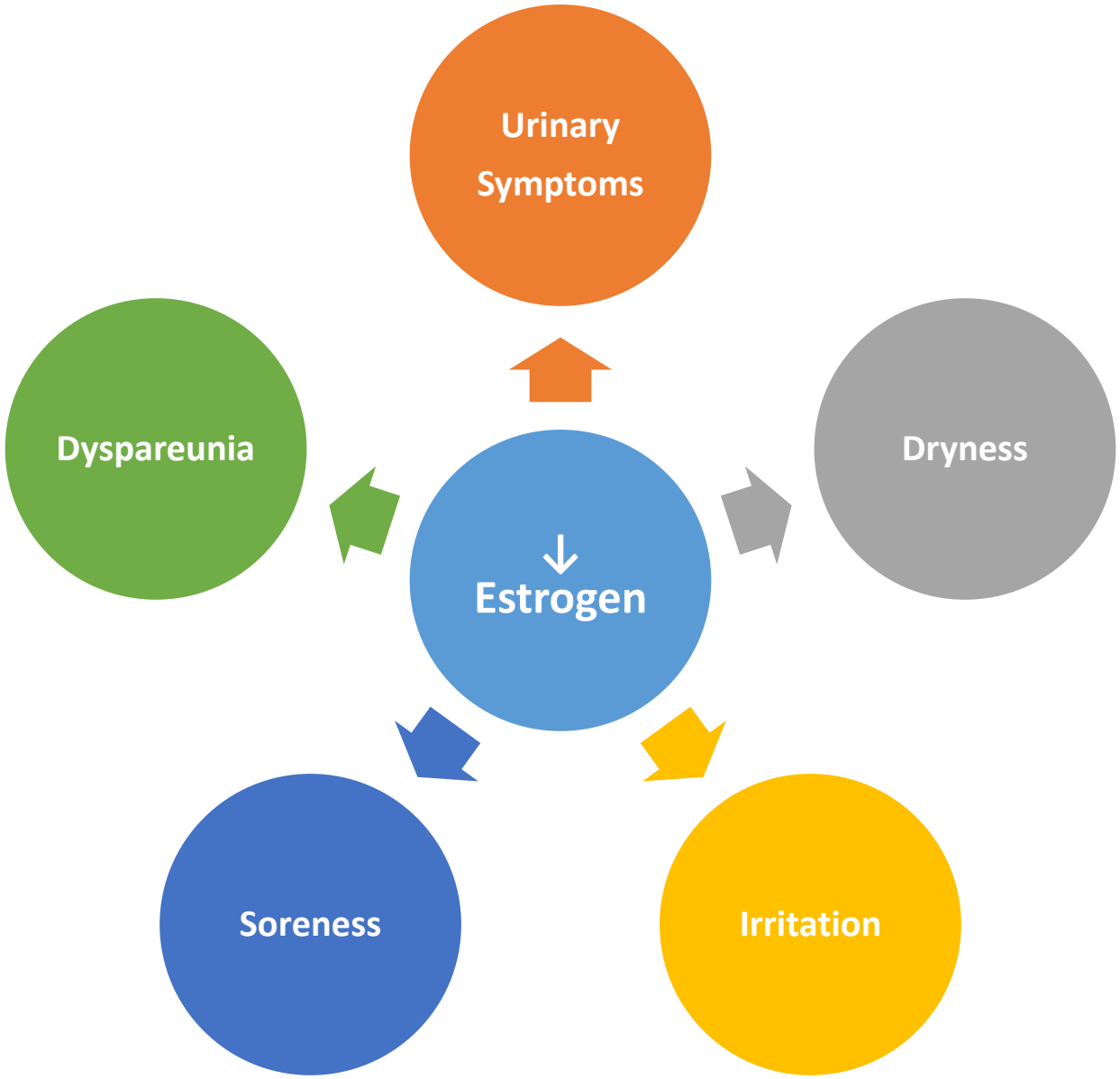
- Approximately 60% of women experience urogenital symptoms. These symptoms include vaginal atrophy, urethral atrophy, and sexual dysfunction (i.e., a decline in libido).
- Vaginal atrophy results in dryness, pruritus, and dyspareunia (painful intercourse).
- Urethral atrophy results in stress incontinence, frequency, urgency, and dysuria.

The Symptoms of VA can include

- Burning (urinating or not)
- Itching
- Dryness
- Vaginal irritation
- Painful intercourse (sex)
- Light bleeding after sex
- A clear or watery discharge
- Urgency with urination
- Urinary leakage
- Frequent bladder infections

As though hot flashes are not bad enough!

Symptoms of decreased estrogenization



Mac Bride et al. (2010)

Under- and Misdiagnosis

- Patients may not seek help due to embarrassment, lack of knowledge, or lack of access
- Patients may self-treat without prior diagnosis
- Unnecessary or inappropriate use of OTC preparations is common
- Clinicians may not ask about symptoms
- Clinicians may not evaluate correctly or misinterpret results

Problem number 3

- Only 25% of patients with the symptoms of genitourinary syndrome of menopause receive adequate therapy
- Both patients and providers are embarrassed to ask about this problem
- Increase conversation, diagnosis and treatment of genitourinary syndrome of menopause for both clinicians and women
- Determine safety of long term vaginal estrogen

Funding Priority 3

- Increase conversation, diagnosis and treatment of genitourinary syndrome of menopause for both clinicians and women

  - Among clinicians
  - Among patients

The Experts Agree About Hormone Therapy

- Benefits are likely to outweigh risks for symptomatic women who initiate HT when aged younger than 60 years and within 10 years of menopause with bothersome symptoms or elevated risk of fracture

The 2017 NAMS Hormone Therapy Position Statement published in July 2017 issue of *Menopause*

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The Experts Agree about who SHOULDN'T TAKE Hormone Therapy

- For women who initiate HT > than 10 or 20 years from menopause or 60 yrs or older, the benefit-risk ratio appears less favorable than for younger women
- Greater absolute risks
    - CHD, stroke, VTE, & dementia

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Treatment of Hot Flushes

Most effective	Effective	Possibly Effective	NOT effective or not indicated
Estrogen (85-95%)	**Venlafaxine** *(60-65%)* Progesterone Paroxetine Gabapentin	Clonidine Black Cohosh	Dong Quai SERMS(NI) Phytoestrogens (soy) Red Clover St John's Wort

Obstet Gynecol 2014 Jan;123(1); 202-216

Funding Priority 4

- Develop relevant and meaningful outcome measurements for patients for decision making
  - Hormone and non hormone therapy for menopausal symptoms
  - Behavioral approaches to managing menopausal symptoms
  - Medications to treat osteoporosis for women at elevated risk of fracture
  - Quick tool to diagnose depression in women approaching menopause
  - Tools to increase conversation about painful sex and genitourinary symptoms
  - Tools to incorporate trauma informed care for menopausal women

Funding Priorities

1. Increase recognition, diagnosis, and treatment of menopausal symptoms
    Need safe and effective pharmacologic and non-pharmacologic (ie. behavioral) therapies
2. Increase prevention, diagnosis, and treatment of osteoporosis to prevent osteoporotic related fractures, morbidity and mortality
3. Increase conversation, diagnosis and treatment of genitourinary syndrome of menopause for both clinicians and women and determine safety of long term vaginal estrogen

Funding Priority

4. Develop relevant and meaningful outcome measurements for patients for decision making about

- Therapies for menopausal symptoms-hormone and non hormone and behavioral approaches
- Risks and benefits of medications to treat osteoporosis for women at high risk of fracture to prevent fracture
- Depression in women approaching menopause
- Conversation about painful sex and genitourinary symptoms
- Incorporate trauma informed care for menopausal women

Possible studies

- Patient-centered strategy might assemble women who are long-term users of systemic HT and find out why they are using HT, and what their expectations and outcomes are
- Comparison of estrogen to new nonhormone therapy, neurokinens, to behavioral approaches
- Responses to gabapentin for nighttime hot flashes and correlation with blood levels.
- Role of HT in prevention of osteoporosis (not just prevention of fractures, but also prevention of osteoporosis as an important asymptomatic, preventable condition)
- Patient centered strategy on why fear of osteoporosis medications is greater than fear of fracture with morbidity and mortality from hip fractures and morbidity from vertebral and wrist fractures.
- Long term safety of vaginal hormone therapy (estradiol, DHEA,) compared to nonhormones
- Does the boxed warning affect women's use of vaginal estrogen therapy?

Health Implications of Menopause

Panel Discussion

JoAnn Pinkerton, MD
Alayna Effron, EdD

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Panel Discussants
Topic: Health Implications of Menopause

Dr. JoAnn Pinkerton, MD
Division Director of Midlife
Health Center at UVA Health

Alayna Effron, Ed.D, MSc., C.H.E.S.
Director of Development
for HealthyWomen

BREAK

2:45 – 3:00 PM

Up Next: Global Discussion

Global Discussion of Topics

CEDS Advisory Panel

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PCORI Reauthorization Update

Andrew Hu, MPP
Director, Public Policy and Government Relations
Patient-Centered Outcomes Research Institute

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Wrap Up/Closing

Cornell Wright, MPA
Lawrence Goldberg, MD

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Adjourn