



REFRAMING MIDLIFE AS A CRITICAL WINDOW FOR WOMEN'S HEALTH

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Session Objectives:

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- Frame midlife as a distinct and heterogeneous phase of women's health.
 - Discuss the relationship between reproductive aging, chronological aging, and disease risk.
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Establish midlife as a critical window for long-term health and research.

- Priority questions for research, clinical care, and action

Midlife is a distinct and heterogeneous phase of women's health

- ▶ Midlife, roughly ages 40-65, (maybe 70 or 80 for healthy aging women) is increasingly recognized as a distinct, critical, and highly heterogeneous developmental phase.
- ▶ It is characterized by complex interactions between ovarian aging (the menopause transition), chronological aging, and overlapping psychosocial stressors.
- ▶ Resulting in widely varying symptom experiences and disease risks across different populations

Difference between chronological aging and biological aging

- ▶ **Chronological** Aging: Passage of time from birth measured in years.
 - ▶ Chronological aging is linear, cannot be accelerated or delayed.
- ▶ **Biological aging**, physiological or functional age, refers to the age of cells and relates to a decline in their function.
 - ▶ Varies between individuals of the same chronological age.
 - ▶ More accurate measure of age and may be better predictor of health.
 - ▶ Pace of biological aging can be faster or slower than chronological aging- resulting in an **age gap** difference between ages.
 - ▶ **Age gap** may help explain the considerable variation in the health and appearance of individuals of same chronological age.
- ▶ Lifestyle choice of smoking accelerates a person's biological age
- ▶ Regular exercise may help to slow the biological aging process.

Significance of Reproductive Aging?

“Every woman is going to experience it.”

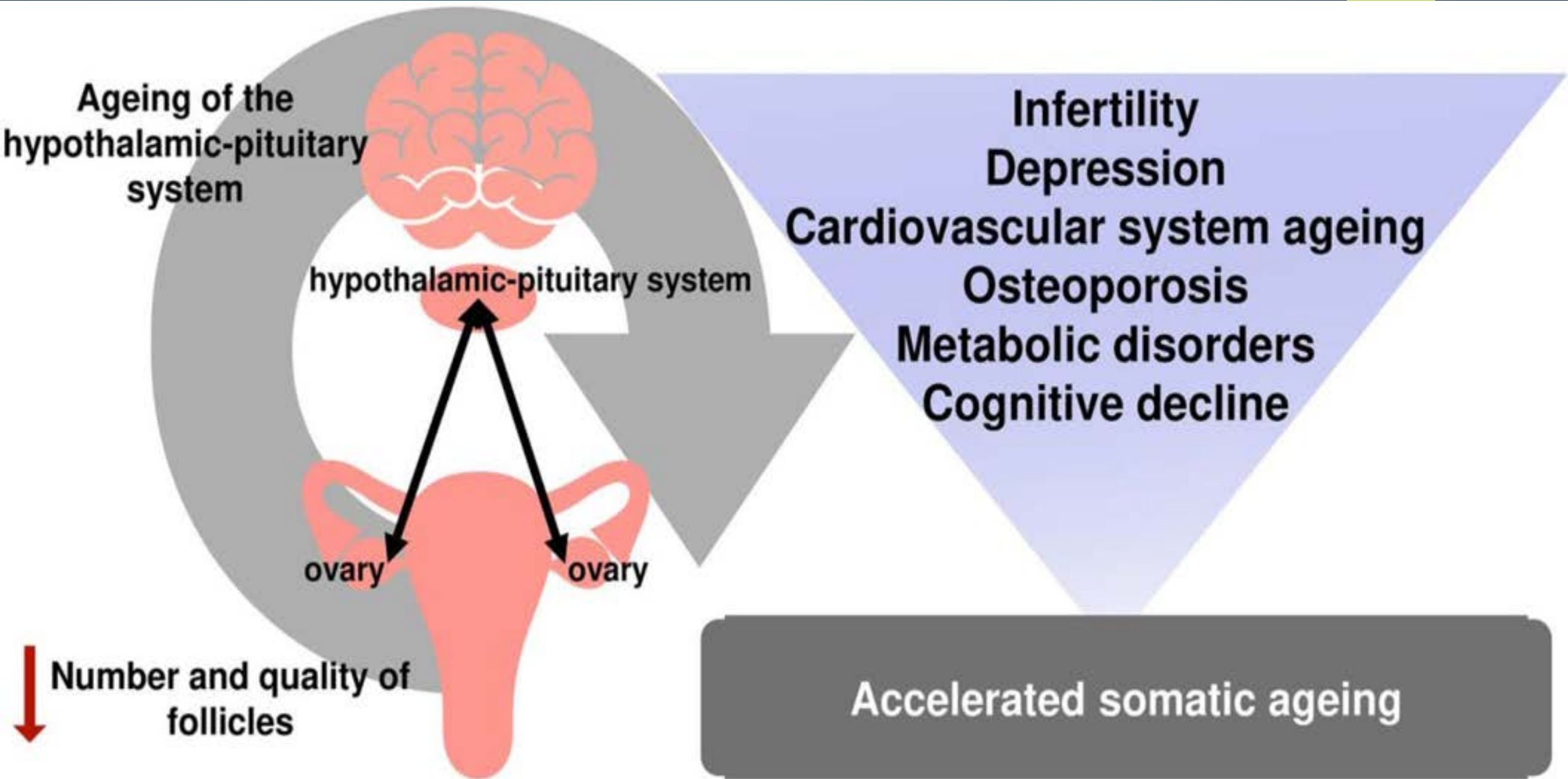
- ▶ **Reproductive aging as “pacemaker” setting tempo for whole body’s aging.**
 - ▶ Female reproductive aging has consequences for women’s health.
 - ▶ How does ovarian physiology change with age?
 - ▶ What measures, signatures, and sources of signals spur ovaries to age
- ▶ Improving women’s health after menopause requires looking beyond extending fertility or preventing the loss of follicles as women enter their 30’s and 40’s.
- ▶ Understanding molecules involved in reproductive aging could lead to diagnostics to **extend women’s “health span,”** the healthy portion of life
- ▶ **How do we preserve the ovaries health-promoting function?**

Why Midlife and ages 40-60 are considered a Critical Window

- ▶ Midlife years between 40–60 is most critical window for determining long-term health
- ▶ During this period, foundational biological and neurological shifts occur
 - ▶ Establish a pivotal foundation to either prevent or accelerate chronic conditions like cognitive decline, dementia, bone loss, and cardiovascular disease in later life
- ▶ **Research identifies this stage as a "make or break" period for lifelong health**
- ▶ **Neurological shifts:** Large-scale studies reveal brain aging is nonlinear, with functional network destabilization beginning around age 44.
 - ▶ Interventions during this "metabolic stress" window can successfully stabilize neurons before significant decline takes hold
- ▶ **Systemic aging:** Research shows the body undergoes rapid waves of alterations in inflammatory and hormonal pathways, heightening vulnerability to systemic diseases
- ▶ **The menopausal transition: For women, the convergence of hormonal, metabolic, and vascular shifts increases lifetime risk of CVD, osteoporosis, stroke and dementia.**

Midlife is not a time of decline, but a crucial intervention window to mitigate chronic health conditions and promote long-term longevity.

- ▶ Incorporate preventive health care and shared decision making
- ▶ Build awareness about midlife health concerns
- ▶ Recognize risk factors
- ▶ Evaluate stress effects on aging (epigenetics)
- ▶ Address barriers to accessing providers and treatments across specialties

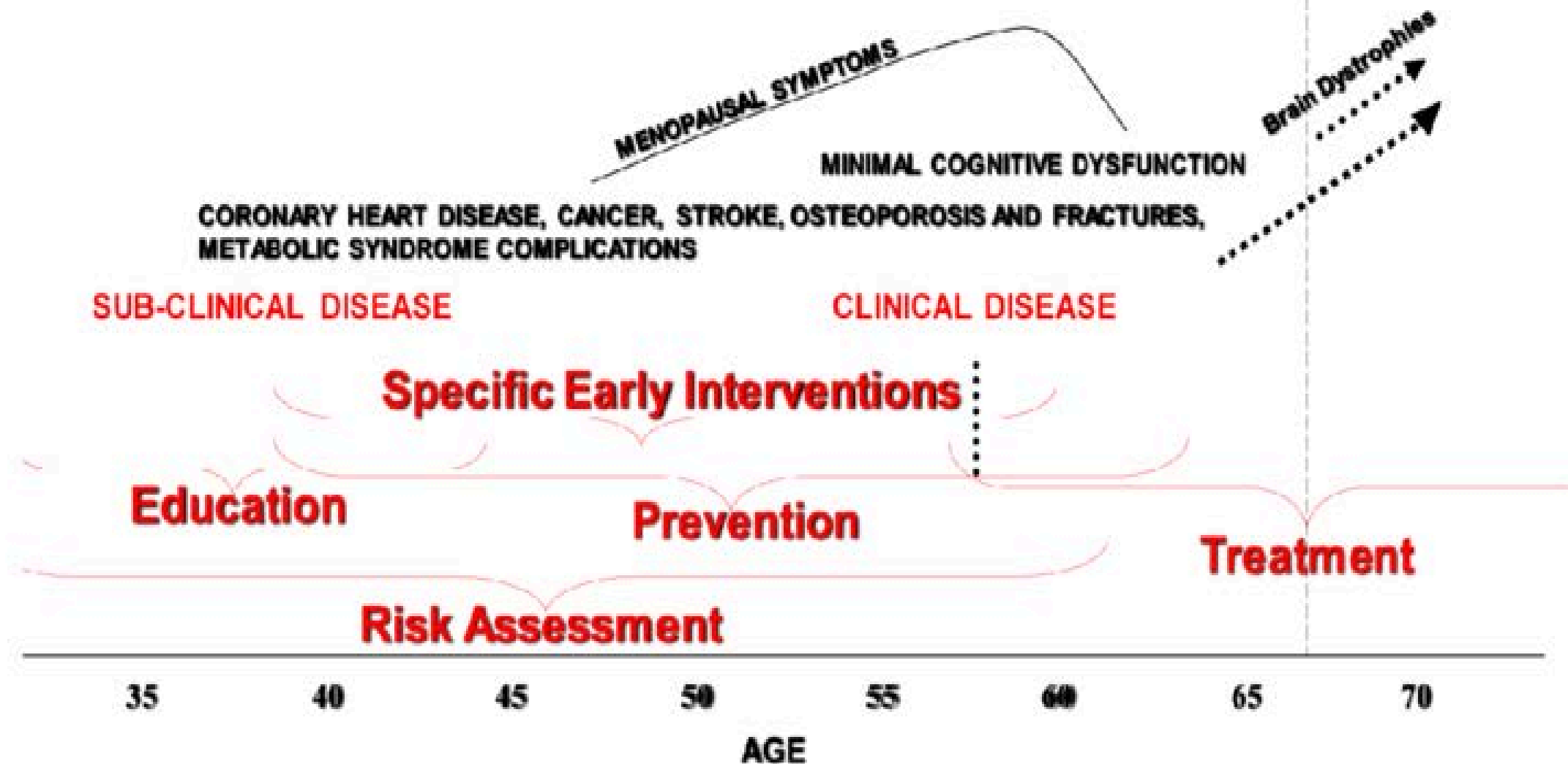


PERIMENOPAUSE

MENOPAUSE

POSTMENOPAUSE / GERIATRICS

Midlife Health Care needs to includes all of these timepoints



The Heterogeneous Experience of Midlife

- ▶ **Symptom Variations:** The rate and magnitude of reproductive hormone decline vary by factors such as baseline body weight and ethnicity
- ▶ **Psychosocial Stressors:** Midlife women frequently occupy the "sandwich generation," simultaneously balancing careers, caregiving for children, and tending to aging parents. These evolving social and professional roles can significantly impact overall well-being.
- ▶ **Disparities in Care:** The burden of midlife conditions and access to care are not distributed equally. Systemic reviews—such as those published in The Lancet Obstetrics, Gynecology, & Women's Health—highlight that Black women and women with lower socioeconomic status disproportionately face fragmented care and limited access to evidence-based treatments

Psychological

- Mood swings
- Anxiety/irritability
- Low mood
- Overwhelmed
- Loss of confidence

Reproductive & Other

- Vaginal dryness
- Reduced libido
- Urinary changes
- Headaches/fatigue
- Dry eyes/tinnitus
- Burning mouth

Physical

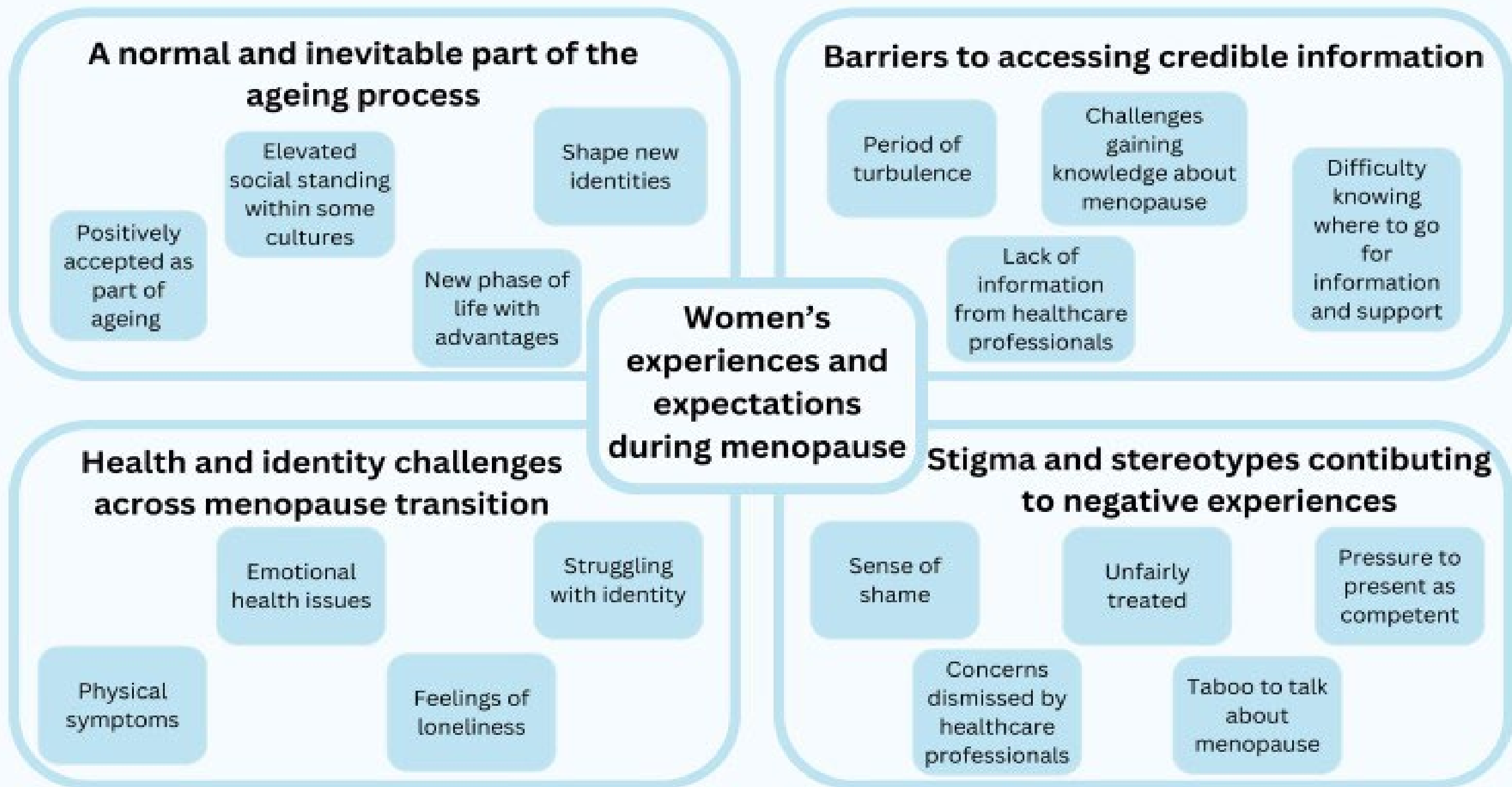
- Hot flashes & night sweats
- Sleep disturbances
- Weight changes
- Joint/muscle pain
- Heart palpitations
- Hair thinning

Cognitive

- "Brain fog"
- Memory lapses
- Concentration difficulties
- Word-finding problems

Symptoms
vary by
individual

2024/03/SWHR-Menopause-Toolkit-2
-Understanding-Menopause.pdf



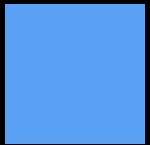
SHARED DECISION-MAKING IN CLINICAL ENCOUNTERS



Given multitude of biological and social influences on health and the unique needs and roles of women during midlife, HCP need time and patience to actively engage women in their health care decisions.



Collaborative discussions about treatment options, hormone therapy or nonhormone options, and potential risks and benefits.



Aim for treatment plans that align patient preferences, values, and needs with health system capacity.



Healthcare policy solutions to support these efforts and provisions for increased access and coverage for medical appointments, treatments, and specialty care.

Clinical markers

**FSH
AMH**

FMR1

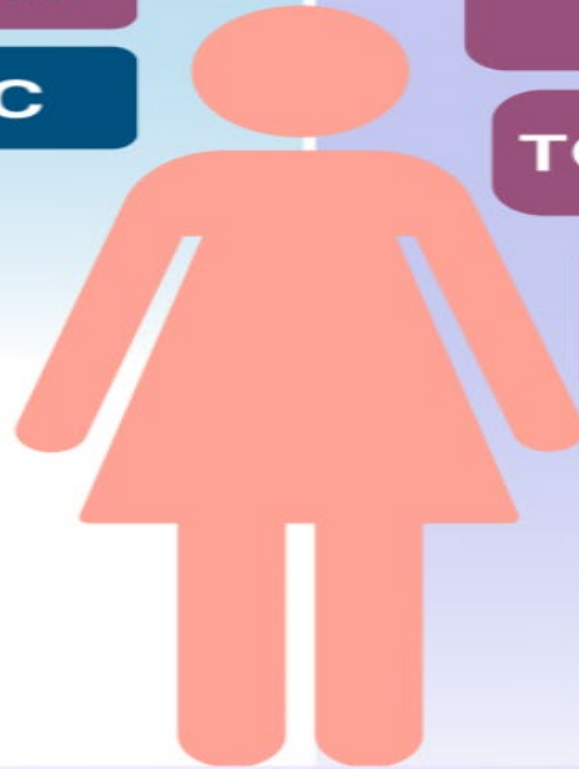
AFC

Biochemical

Molecular

Instrumental

Other



Potential markers

**Homologous recombination
and meiosis pathway**

TGFβ, DNA damage pathways

**mRNA transcription and
translation pathways**

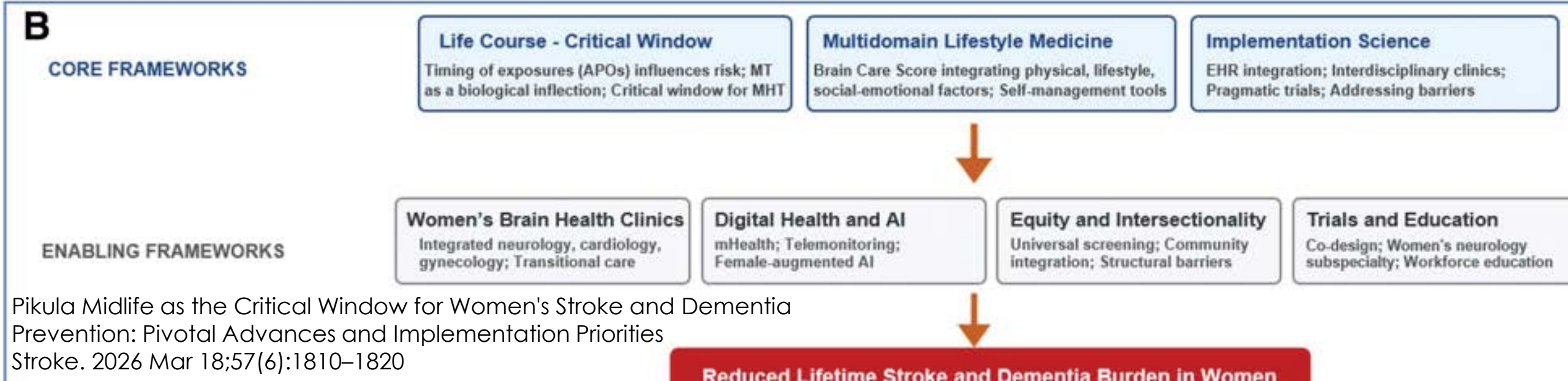
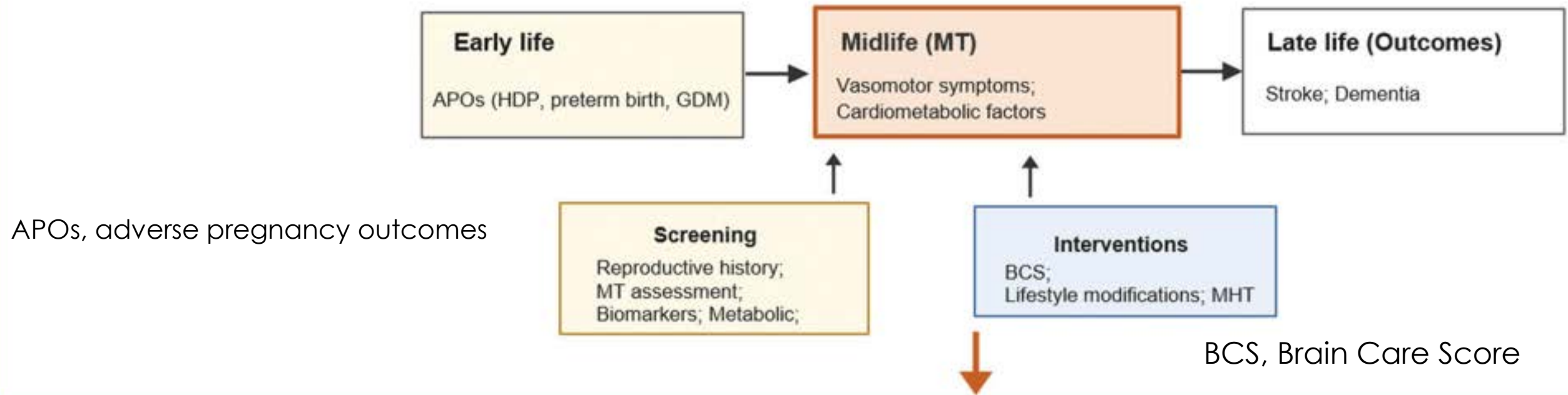
**Mitochondrial
dysfunction**

Aging clocks

**CHOOSING A STRATEGY: reproduction, hormone
therapy start, preventing age-related diseases**

A

Midlife as Critical Window for Women's Stroke and Dementia Prevention



Ready for Implementation Prevention Components	Emerging
APO screening (2024 AHA/ASA Class I) MT status assessment Cardiometabolic status hsCRP and Lp(a) measurement in midlife Early, personalized MHT for women without contraindications Lifestyle interventions	Integration of reproductive history into EHR Digital tools for MT symptom tracking RNA-based Lp(a)-lowering therapies Neuroimaging markers (WMH trajectories, PET phenotypes)
Stroke. 2026 Mar 18;57(6):1810–1820	

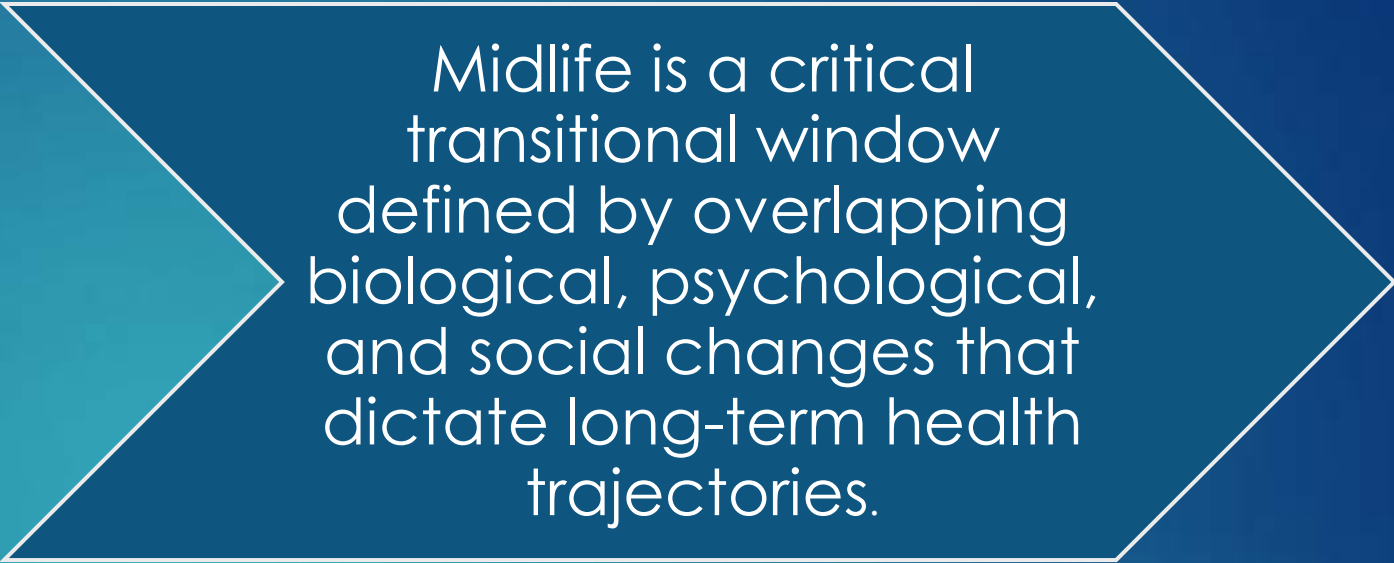
Why Menopause Matters for Health



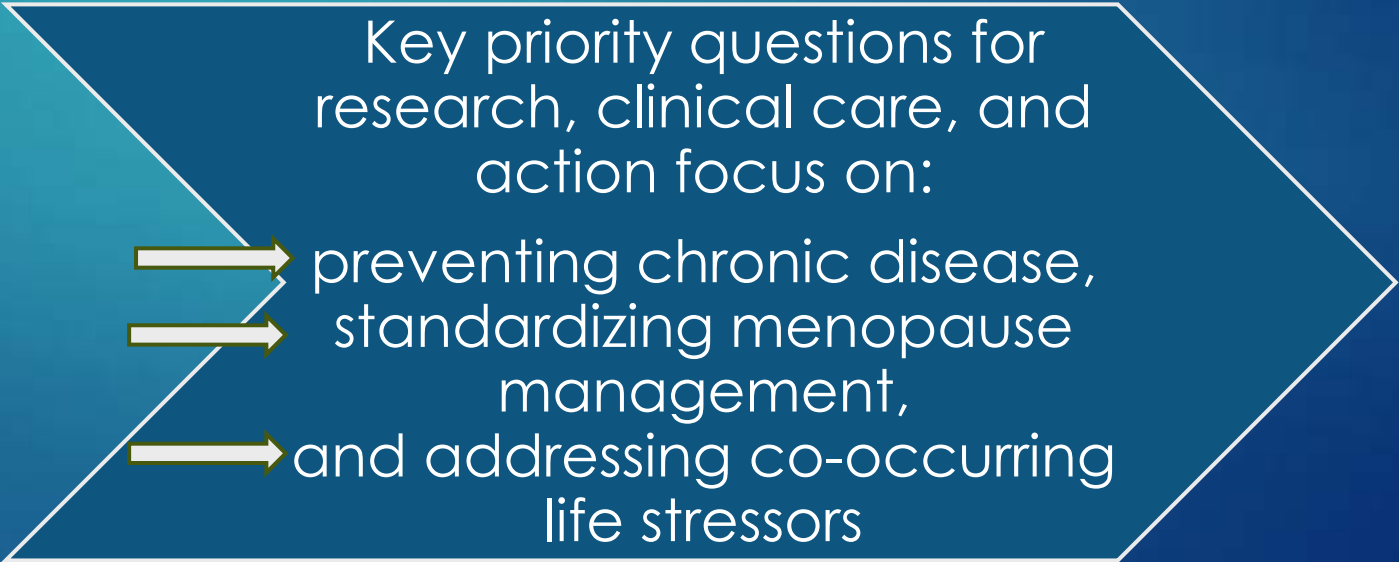
- ▶ Menopause is a critical window for prevention and care
- ▶ Linked to an increased risk:
 - ▶ Heart disease
 - ▶ Genitourinary conditions
 - ▶ Osteoporosis (bone)
 - ▶ Cognition and mental health changes (brain and mood)



Menopause is a
life stage,
not a disease



Midlife is a critical transitional window defined by overlapping biological, psychological, and social changes that dictate long-term health trajectories.



Key priority questions for research, clinical care, and action focus on:

- preventing chronic disease,
- standardizing menopause management,
- and addressing co-occurring life stressors

Priority Questions for Clinical CAre

- ▶ **Integrated Care:** Healthcare providers need to shift toward whole-person, age-friendly models of care prioritizing what matters most to the individual over symptom checklists?
- ▶ **Menopause & Hormone Therapy:** Personalized risks and benefits of menopausal hormone therapy (MHT), How to equip providers to be better equipped to evaluate eligibility
- ▶ **Mental Health Screening:** Are clinicians screening deeply enough to differentiate overlapping physical and mental health challenges— depression, serious psychological distress, and vasomotor symptoms (hot flashes)—not dismissing them as "a midlife crisis"
- ▶ **Preventative Baselines:** How to better utilize midlife as a critical window to screen and adjust metabolic biomarkers to prevent heart, bone, cognitive and physical disability in late life?
- ▶ Where are we going? Digital tools, integrated biomarkers, wearable devices?

Priority Questions for research

- ▶ **Cardiometabolic Trajectories:** How do early-life health markers (gestational diabetes) interact with midlife physiological changes to predict cardiovascular risk later in life?
- ▶ **Brain Health & Menopause:** What are the cellular mechanisms linking the menopausal transition with short- and long-term cognitive changes
- ▶ **Bone Health-** how to recognize risk factors and prevent osteoporosis?
- ▶ **Mental Health- Social Determinants:** increased risk of depression and anxiety
- ▶ **How do structural racism, historical trauma, and socioeconomic disparities** impact timing and symptom burden of midlife health challenges, particularly across diverse demographic groups?
- ▶ **Multimorbidity:** How can clinical studies move beyond single-disease frameworks to address the simultaneous management of multiple co-occurring midlife stressors and physical symptoms, metabolic changes, and mental and mood concerns (brain fog and Alzheimer's disease risk)

The Knowledge Gap and Medical Training deficit

- ▶ Many health care providers have received minimal menopause education
- ▶ Leads to dismissed symptoms, out of date information, or lack of familiarity beyond basic approaches.
- ▶ Specialty menopause clinics and practitioners with specific expertise exist but have been geographically limited, often private fees.
- ▶ Sharp increase in certified menopause specialists with little experience
 - ▶ Large numbers of women wanting to be seen to discuss options at all ages.
- ▶ Knowledge gap extends to women who know little about menopause transition, don't know what to expect, how to discern normal symptoms from medical concerns, and uncertainty about therapeutic options.
- ▶ Women often feel need to educate themselves (often using social media or influencers) rather than receiving proactive, evidence based guidance.

The Pathways to Prevention Workshop

“Advancing Research to Improve Health During the Menopausal Transition”

- ▶ One significant gap evident in the Workshop is the need for trained menopause providers.
- ▶ The **COMpetency in Menopause & Integrated Therapy (COMMIT) Challenge** focused on training clinicians.
- ▶ The intent of NIH-sponsored challenge is to recognize and advance existing, evidence-based, scalable curricula.

Reframing Midlife Health at UVA

- ▶ Clinical practice and research -multidisciplinary- we all see it differently- healthy aging starts at early perimenopause and continuing.
- ▶ Engage providers & researchers- internists, family practice, obgyn, neurology, endocrinology, urology, physical medicine, kinesiology
- ▶ Twice monthly Menopause Matters multidisciplinary zoom- 15 min on topic, then case discussions, recorded and archived
- ▶ Developing algorithms of who and where women can be seen and who needs menopause specialists for complex patients
- ▶ Professional symposium “Menopause is thriving at UVA”- bring all experts in one room on one day to learn from one another
- ▶ Community symposiums and webinars – take education to community

Moving toward Better Menopause Support

Improving menopause experiences requires changes

- Individual knowledge and self advocacy

- Health care provider education, best practices

- Research on biomarkers to prevent chronic disease

- Workplace policies and culture

- Broader cultural narratives- neither dismiss nor catastrophize

Our Challenge today and for the
National Academy

During this workshop, we will

- ▶ Assess the state of the science
- ▶ Identify key gaps in evidence and methodology
- ▶ Explore opportunities to advance a more integrated, coordinated, and actionable research agenda for midlife women's health
- ▶ Discuss misinformation and communication



Questions for this Workshop

- ▶ How do we disentangle reproductive and somatic aging?
- ▶ What changes signal poor outcomes/future disease vs. transient symptoms?
- ▶ When is intervention most effective and for whom?
- ▶ What would an integrated research and care model look like?
- ▶ What practice and policy changes do we need?