

Improving Health During the Menopausal Transition: Findings from the Pathways to Prevention

Program

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Key Points

What evidence is needed to improve symptom management, treatment, and delivery of care for the menopausal transition? An independent panel of scientists convened as a part of the National Institutes of Health's Pathways to Prevention program to provide recommendations for future research. Complex, longitudinal, pragmatic, implementation-focused research that uses multiple data sources is needed to provide a more accurate and representative understanding of which treatment combinations work, for whom, and in which settings.

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Abstract

Importance: The menopausal transition has implications that extend well beyond reproductive aging and encompass cardiometabolic, genitourinary, neurocognitive, and musculoskeletal health. In the absence of evidence-based guidelines and access to effective treatments, women increasingly seek information and treatment from nontraditional sources based on limited evidence, contributing to fragmented and potentially harmful care. Untreated or poorly treated menopause symptoms are costly for the individual, community, and society.

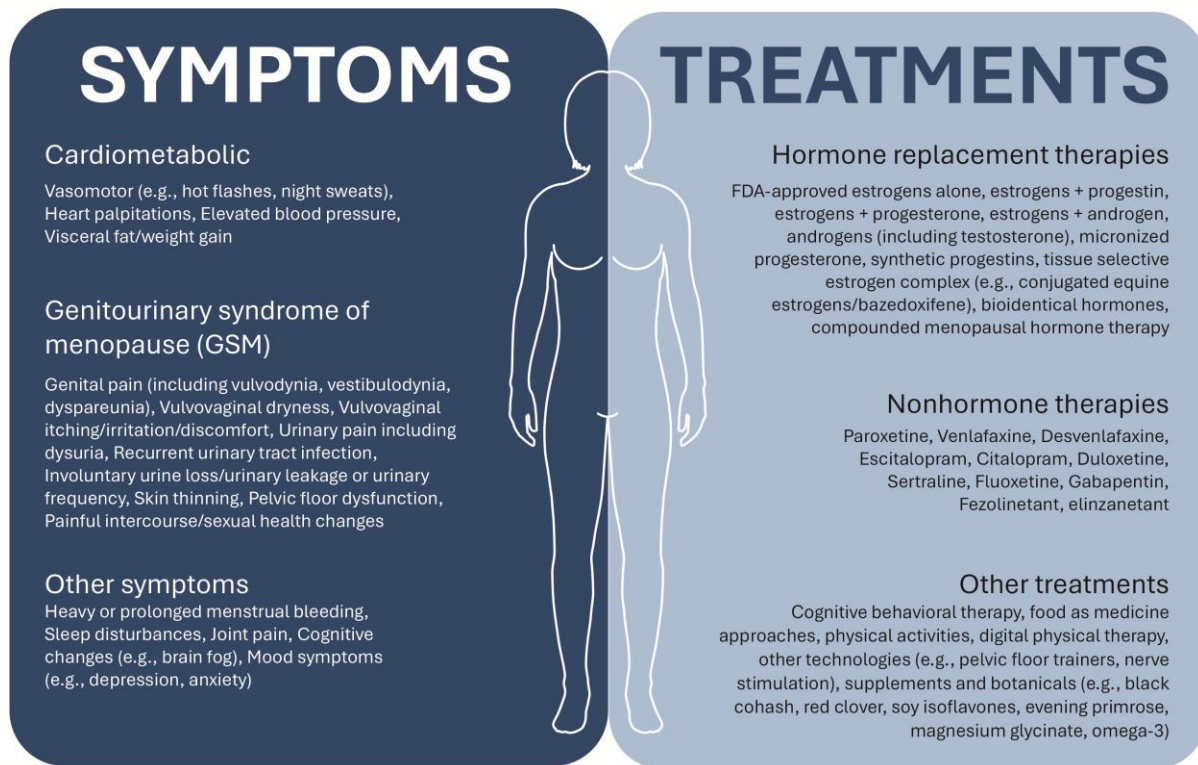
Observations: As a part of the National Institutes of Health (NIH) Pathways to Prevention (P2P) program, an independent panel of volunteers from multiple disciplines participated in a three-day workshop to review presentations of findings and experiences of researchers and advocates, including a commissioned systematic evidence review. The panel offers recommendations for future research.

Conclusions and Relevance: Complex, longitudinal, pragmatic, implementation-focused research that uses multiple data sources is needed to provide a more accurate and representative understanding of which treatment combinations work, for whom, and in which settings. This requires the development of standardized definitions of menopause stages, validated measures and assessment tools that capture the full range of menopause symptoms, and study designs that evaluate overlapping symptom trajectories rather than isolated symptoms.

Introduction

The menopausal transition is a dynamic, multifaceted physiologic process with implications that extend well beyond reproductive aging to encompass cardiometabolic, genitourinary, neurocognitive, and musculoskeletal health. This transition is characterized by the end of ovarian follicular activity, which leads to hormonal shifts that in turn produce a constellation of physiologic changes (e.g., adverse cardiometabolic remodeling, including visceral adiposity, insulin resistance, lipid changes, arterial stiffening, and endothelial dysfunction) that correlate with vasomotor symptoms (e.g., hot flashes, night sweats), genitourinary symptoms, sleep disruptions, mood changes, brain fog, joint pains, and adverse long-term health effects (1,2). **Figure 1** shows the wide variety of symptoms women experience during the menopausal transition and the treatment types that have been explored to manage those symptoms. The enormous range, variability, and interrelatedness of menopause physiology and symptoms, among other factors, has complicated research on the menopausal transition, clinical guideline development, and in turn, effective clinical care. Indeed, the costs of untreated or poorly treated menopause symptoms based on missed days from work alone are estimated at \$1.8 billion a year (3). In the absence of evidence-based guidelines and access to effective treatments in traditional health care settings, women increasingly seek information and treatment from nontraditional sources in the growing menopause marketplace. These sources are often based on limited evidence, further contributing to fragmented and potentially harmful care (4).

Figure 1: Menopausal Transition: Key Definitions, Symptoms, and Treatments



The menopausal transition, including perimenopause and early postmenopause, is the physiologic process leading to the final menstrual period, typically occurring between ages 45 and 55 years, with early postmenopause extending 5 to 8 years.

In this context, it is critical to examine the state of current evidence on the menopausal transition and what is needed to improve symptom management, treatment, and delivery of care going forward. Most of what we currently know about the effectiveness of interventions in menopause comes from National Institutes of Health (NIH)–supported studies (e.g., Women’s Health Initiative, Study of Women’s Health Across the Nation (SWAN), MS Brain Health Initiative), as well as from reviews by NIH (5), the Agency for Healthcare Research and Quality (AHRQ) (6–8), and the National Academies of Sciences, Engineering, and Medicine (9, 10). This evidence is largely focused on older White women, on menopause and postmenopause (rather than perimenopause), and on hormonal treatments rather than the broader range of nonhormonal treatments and supportive strategies (e.g., nutrition and physical activity) that women may use. A holistic approach to research and clinical care is essential to capture

overlapping symptom trajectories during the menopausal transition and their cumulative effects on health and quality of life.

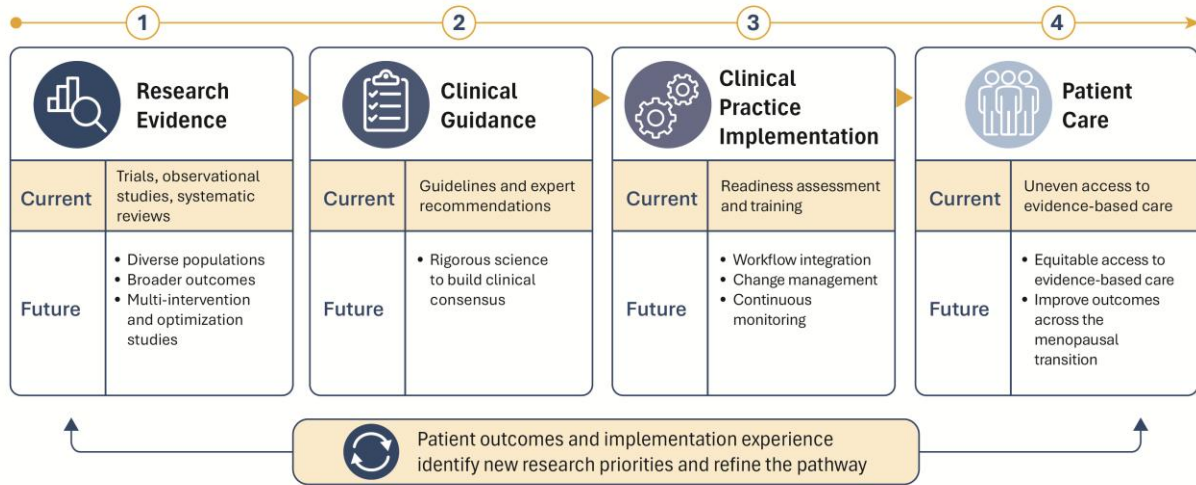
To address this complex issue, an in-depth evaluation of existing science and an assessment of research needs was co-sponsored by the NIH's National Institute on Aging, National Cancer Institute, National Heart, Lung, and Blood Institute, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institute of Mental Health, the Office of Research on Women's Health, and the Office of Disease Prevention. The initiative included a systematic evidence review (SER) conducted by the Research Triangle Institute International-University of North Carolina Evidence-based Practice Center, under contract to the AHRQ. In April 2026, the NIH convened a Pathways to Prevention workshop entitled "Advancing Research to Improve Health During the Menopausal Transition" (11). The 3-day workshop included summary presentations of the evidence review and presentations from invited experts in various domains of menopause research and care. An independent panel of scientists assessed the evidence review and workshop proceedings, then drafted a report reflecting their key findings and recommendations. Prior to publication, the report was posted for public comment.

Conceptual Framework for Translating Menopause Research into Care

Given the complexity of the menopause transition and the limited evidence focused specifically on perimenopause and early menopause, the panel developed a conceptual framework to guide its recommendations. **Figure 2** depicts the translational pathway from research evidence to clinical guidance, practice implementation, and patient care. Gaps in the evidence base contribute to clinician uncertainty, inconsistent clinical guidance, and fragmented care. In turn, many women seek information, support, and treatment outside traditional health care settings, where marketplace solutions may have limited supporting evidence and may increase susceptibility to misinformation. This cycle underscores the need for implementation-ready evidence that can support clinical decision-

making, improve access to evidence-informed care, and guide women and clinicians through the menopause transition.

Figure 2: Translating Menopausal Transition Research into Care From Research Evidence to Better Care



Two multipart key questions (KQs) guided the evidence review, workshop, and panel recommendations (**Table 1**). Note that we use the term “women” throughout the report to refer to biological female individuals (assigned female at birth).

Assessment of Evidence by Key Question

Key Question 1: What is the effectiveness, comparative effectiveness, and harms of treatments for menopausal symptoms in perimenopausal and early postmenopausal women?

What is known

Overall, the SER found limited evidence to guide treatment of menopausal symptoms in perimenopausal and early postmenopausal women. Low or very low certainty evidence suggests that selected hormone replacement therapies, including estrogen with or without progestogen, may provide moderate benefit for vasomotor symptoms. Evidence also suggests some benefit for estrogen combined with progestogen for genitourinary symptoms and joint pain, whereas comparisons of estrogen plus

115 progestogen versus estrogen alone show no difference for vasomotor symptoms. Comparison of
116 micronized progesterone to medroxyprogesterone acetate shows no benefit for vasomotor symptoms,
117 mood, or quality of life, although some evidence suggests benefit for heavy or prolonged menstrual
118 bleeding (12).

119 The SER did not identify evidence of benefit of hormone therapy for mood, cognition, sleep, or
120 quality of life, and evidence on harms was limited for the outcomes and populations studied (e.g., heavy
121 or prolonged menstrual bleeding, coronary heart disease, cancer, serious adverse event, or death) (12).
122 The discussion regarding hormone therapy in women with elevated breast cancer risk or a history of
123 breast cancer was complex. Workshop presenters emphasized that breast cancer survivors, BRCA1/2
124 carriers without a personal history of breast cancer, and women at elevated risk for breast cancer
125 require distinct risk-benefit considerations. Presenters also discussed tissue-selective estrogen
126 complexes, including conjugated estrogens/bazedoxifene, as a potential alternative to estrogen-
127 progestogen therapy for selected women with a uterus and higher breast cancer risk, but emphasized
128 that comparative-effectiveness and safety evidence remains limited (11, 12, 16).

129 Nonhormone therapies (e.g., tissue-selective estrogen complex, gabapentin, and Food and Drug
130 Administration [FDA] approved neurokinin antagonists (i.e., fezolinetant and elinzanetant) show some
131 moderate benefit for vasomotor symptoms and quality of life (13). Evidence limited to postmenopausal
132 women suggests potential benefit from cognitive behavioral therapy (CBT) and, to a lesser extent, from
133 estrogen to reduce sleep interruptions (14). For genitourinary and sexual health symptoms, vaginal
134 estrogen, vaginal dehydroepiandrosterone, oral ospemifene, and moisturizers have evidence of efficacy,
135 whereas energy-based devices do not (6). A randomized trial of a smartphone-delivered program using
136 CBT, mindfulness, and physical activity components reduced hot-flash distress and improved depressive
137 symptoms and sleep (15).

What is not known

Evidence is limited on the effectiveness and harms of hormonal and nonhormonal therapies for menopausal symptoms among women with elevated breast cancer risk or history of hormone-sensitive cancer and on treatment approaches for heavy or prolonged menstrual bleeding. Comparative effectiveness data are also limited for nonhormonal therapies on coronary heart disease and adverse events. When combination hormone therapy was compared to tissue-selective estrogen complexes, there was no evidence of benefit for joint pain. Workshop speakers emphasized gaps in understanding how menopause symptoms interrelate, including whether treating sleep disruption can improve mood and cognition. Little information is available on weight gain as a menopause symptom or consideration for the effects of new classes of anti-obesity medications (e.g., glucagon-like peptide-1 [GLP-1], glucose-dependent insulintropic polypeptide [GIP], and glucagon receptor agonists) on menopause symptoms. These findings underscore an important mismatch between the evidence base and clinical practice and show why implementation-ready evidence is needed. The strongest evidence remains concentrated around vasomotor symptoms, whereas patients commonly present with overlapping symptom clusters that include sleep disruption, mood symptoms, genitourinary and sexual health symptoms, heavy or prolonged bleeding, cognitive symptoms, joint pain, and changes in weight or body composition. Current studies do not yet provide sufficient guidance on which treatment or combination of treatments to use across menopause stages, risk profiles, or care settings. These gaps contribute to clinician uncertainty, inconsistent counseling, and patient reliance on treatments or information sources outside traditional care settings.

Key Question 1a: Do the effectiveness, comparative effectiveness, and harms of treatment vary by dose, delivery mode, formulations, or duration of treatment?

What is known

The SER found low or very low-certainty evidence on whether treatment effects vary by dose or delivery mode and no evidence on variation by formulation or duration (12). Workshop presenters highlighted studies suggesting that standard-dose systemic menopausal hormone therapy (e.g., estrogen/progestogen or progestogen-only) may have comparably high efficacy in reducing vasomotor symptoms across formulations and delivery modes (16). However, evidence is mixed on whether higher estrogen has greater benefit. Transdermal and oral estrogen were reported to have similar efficacy in improving sleep (12).

Workshop presentations raised clinically relevant safety considerations. Higher estrogen doses may be associated with a higher overall risk of harm, and oral estrogen, compared to transdermal estrogen, has a higher cardiovascular risk (11). For progestogen alone, breast cancer risk varies by dose and delivery mode (16). There is weak evidence that longer duration of hormone treatment is associated with greater cardiovascular and other risks, though anecdotally, clinicians generally recommend durations of 5 or fewer years. Compounded hormones and pellets do not have guaranteed quality, purity, or dosing consistency (10). For vaginal estrogen, various formulations have similar efficacy and risks, and the low-dose vaginal estrogen ring and tablet do not raise systemic blood levels, although vaginal cream may (17, 18).

What is not known

Evidence remains insufficient to determine optimal dosing, delivery mode, formulation, or duration for most menopause treatments, especially nonhormonal pharmacologic and nonpharmacologic treatments, treatments for specific nonvasomotor symptoms, combinations of treatments for symptom clusters, and treatment selections in the context of comorbidities (12). The lack

of practical evidence on dosing, formulation, delivery, and duration contributes directly to clinician uncertainty and creates space for nonstandard or marketplace treatments that may not be supported by adequate evidence.

Key Question 1b: Do the effectiveness, comparative effectiveness, and harms of treatment vary by timing and type of menopause (early, average; iatrogenic, natural)?

What is known

The SER found very limited evidence concerning how treatment outcomes vary by timing or type of menopause, particularly because few studies focused on perimenopausal women (12). Workshop presenters highlighted that most studies include age as a proxy for type or stage of menopause, even though age at onset of menopause varies greatly (19, 20). Workshop presenters noted that hormone therapies may be most beneficial in reducing risk for cardiovascular disease, osteoporosis, and muscle loss when initiated before age 60 or within 10 years of menopause onset (16). Presenters noted that absolute risks of systemic estrogen and estrogen/progestogen are lower for appropriately selected younger or recently menopausal women (21). Limited evidence also suggests that systemic estrogen may have benefit as a treatment for depression in perimenopause but not in postmenopause (22).

What is not known

The lack of clear definitions for type or stage of menopause hinders the ability to conduct subgroup analyses among women at different stages of the menopause transition. There is almost no evidence on whether treatment efficacy varies by timing of menopause, except for one study suggesting no difference or benefit of progestogen on vasomotor symptoms (12). Without standardized staging and timing measures, clinicians must often rely on age-based approximations rather than evidence that reflects a patient's menopausal stage, symptom trajectory, and risk profile. This gap limits the development of stage-specific guidance and contributes to the uncertainty and variability in care described in the conceptual framework.

Key Question 1c: Do the effectiveness, comparative effectiveness, and harms of treatment vary by individual- or system-level factors?

What is known

The SER found no evidence on menopausal treatment efficacy or harms by individual- or system-level factors (12). However, presenters shared studies suggesting that safety and efficacy profiles of menopausal treatment are influenced by a range of individual characteristics, including age, age at menopause onset, menopause type (e.g., spontaneous vs. iatrogenic), symptom burden or severity, body composition, contraceptive needs, comorbidities (e.g., diabetes, cardiovascular disease, cancer, osteoporosis, endometriosis, polycystic ovary syndrome), and medical or surgical history (2, 23, 24). Presenters offered findings suggesting that clinical decision-making requires balancing symptom relief against potential harms of treatment for women with specific individual characteristics, such as hormone therapy for women with elevated breast cancer risk (12). Potential harms also vary by baseline cardiovascular and oncologic risk profile.

Presenters highlighted disparities in outcomes by race and ethnicity (25, 26). For example, SWAN found that Black, Hispanic, and multiracial women receiving hormone replacement therapy experience more frequent, severe, and longer-lasting vasomotor symptoms and lower quality of life compared to White women (27). Presenters also shared findings showing cumulative exposure to psychological trauma and chronic stress can amplify cardiometabolic risks, accelerate cognitive aging, and worsen vasomotor, sleep, and mood symptoms (28, 29). Presenters shared findings indicating cultural differences in the reporting of menopause symptoms (30). They also noted efforts to standardize symptom monitoring through wearable devices, including biometric tracking and symptom decoders (31), while acknowledging systemic barriers to accessing such technologies.

What is not known

A scarcity of research exists on the complex array of individual- and system-level factors that may affect the effectiveness of menopause treatment, due in part to the lack of heterogeneity in study populations (12). For example, neither the SER nor the presentations included subgroup analyses for patients who may be at high risk for adverse treatment effects, such as those with early oophorectomy, gender transition, hormone-sensitive cancers, or obesity (12). It is also unknown how treatment varies by system-level factors, such as social determinants of health, access to and quality of care, and treatment uptake.

These gaps limit the ability to translate evidence into risk-stratified, culturally responsive, and personalized care. Without evidence that reflects the diversity of menopausal experiences and care settings, clinicians must extrapolate from narrow study populations, which contributes to uncertainty, variable counseling, and inequitable access to evidence-informed treatment.

Key Question 2a: What is the impact of individual-level factors on the receipt of treatment for perimenopausal and early postmenopausal women with symptoms?

What is known

The SER and presentations highlighted that treatment experiences are shaped by race and ethnicity, education, literacy levels, and socioeconomic factors (11, 12). Broader literature similarly suggests disparities in menopause care by race and ethnicity, geography, and income, with higher treatment discontinuation among racial and ethnic minority populations and lower-income groups. Numerous studies demonstrated that individual-level factors, such as mistrust of clinicians and institutions and stigma, affect the receipt of menopause treatment (12). One study found that Black women were less likely to receive hormone therapy and more likely to receive compounded bioidentical hormone therapy (32).

The lack of clinical guidelines and inconsistent access to evidence-informed care have contributed to the rapid growth of digital health and social media platforms as major sources of menopause-related health information. These platforms shape patient perceptions, expectations, help-seeking behaviors, and treatment decision-making. Misinformation on these platforms may affect individuals' receipt of effective treatments. For example, compounded bioidentical hormone therapy continues to be marketed as innovative despite absent efficacy data (10, 12) and no FDA evidence that it is safer or more effective than FDA-approved products (33). Warnings about manipulative techniques, corrective explanations, and evaluative-thinking prompts are promising tools to reduce menopause misinformation online (10).

What is not known

There is a lack of information on the impact of individual-level factors on help-seeking and the receipt of and adherence to menopause treatment. This includes understanding the impact of trauma on seeking and receiving care as well as best practices for integrating trauma-informed approaches into routine menopause care (12). Evidence is also limited on which communication strategies, digital literacy interventions, and culturally tailored resources improve access to evidence-informed menopause care across diverse populations.

These gaps reinforce the translational challenges described in the conceptual framework. When trusted guidance and accessible care are limited, women may rely on informal, commercial, or digital sources of variable quality. Research is needed not only to identify effective treatments, but also to understand how individual-level factors shape whether women seek, receive, trust, and continue evidence-informed care.

Key Question 2b: What is the impact of system-level factors on the receipt of treatment for perimenopausal and early postmenopausal women with symptoms?

What is known

The SER and presentations identified system-level factors that affect the receipt of menopause treatment, including insurance and formulary barriers, out-of-pocket costs, limited specialty menopause training for clinicians, practice variation, digital health misinformation, and limited access to culturally relevant information (11, 12). These factors influence whether women can access evidence-informed counseling and treatment in the traditional health care setting.

What is not known

There is limited research available to support system- and organizational-level policies and procedures that promote the receipt of menopause treatment (12). Work is needed to develop standardized approaches and assessment tools that capture the full range of menopause symptoms, establish risk profiles, provide decision-support, and integrate these approaches into routine workflows (34). More research is needed on how health systems can most effectively enable evidence-based menopause care—for example, through change management, clinician training, workflows, and financial and technological infrastructure (11).

These gaps highlight the implementation component of the conceptual framework. Even when evidence-informed treatments are available, women may not receive them unless health systems have the workflows, decision-support tools, reimbursement structures, and trained clinicians needed to deliver menopause care effectively.

Conclusions

The menopausal transition is a universal yet highly heterogeneous experience with important short- and long-term implications for health, functioning, and quality of life. Decades of NIH-supported studies have established evidence supporting systemic hormone therapy for vasomotor symptoms,

particularly among women early in the menopausal transition, and emerging pharmacologic and nonpharmacologic therapies have expanded treatment options. However, evidence remains limited for many clinically important symptoms and outcomes, including symptom clusters, long-term safety, chronic disease prevention, and treatment effectiveness across diverse populations. Variation in experiences of menopause and treatment outcomes by geography, race and ethnicity, socioeconomic status, access to care, and social determinants of health reinforces the need for actionable and relevant evidence.

Advancing the evidence base requires the development of standardized definitions of menopause stages, validated measures and assessment tools that capture the full range of menopause symptoms, and study designs that evaluate overlapping symptom trajectories rather than isolated symptoms. The panel's recommendations in **Table 1** emphasize the need to move from evidence gaps to implementation-ready research and care. **Table 2** identifies the research domains and components needed to comprehensively inform the evidence base. While research is underway, efforts should be taken to build clinical consensus on best practices for perimenopause and early post menopause. Recent clinical guidance illustrates that available evidence can be translated into practical recommendations while research continues, but United States–focused implementation studies and guidance are still needed (35). Primary care and general gynecological care are important frontline settings for menopause care. Complex, longitudinal, pragmatic, implementation-focused studies that use multiple data sources are needed to provide a more accurate and representative understanding of which treatment combinations work, for whom, and in which settings. We urgently need trustworthy, evidence-informed, culturally responsive, and accessible approaches to care. The panel's recommendations call for a coordinated research agenda that links biological mechanisms, symptom trajectories, comparative effectiveness, implementation, and equity to help close the gap between evidence generation and meaningful improvements in menopause care.

Table 1: Key Recommendations for Future Research

Key Questions Guiding the Systematic Evidence Review and Workshop	Recommendations
KQ 1: What are the effectiveness, comparative effectiveness, and harms of treatments for menopausal symptoms in perimenopausal and early postmenopausal women?	Establish a standardized approach, measures, and assessment tools to capture the full range of symptoms shown in Figure 1 and combinations of symptom clusters.
	Conduct large-scale, longer-term (>1 year) multicenter, cohort, comparative effectiveness trials to examine the positive and adverse effects of the array of menopause treatments on a broad range of symptoms and symptom clusters for perimenopausal and early postmenopausal women.
	Assess the impact of new classes of anti-obesity medications on menopausal transition symptoms.
KQ 1a: Do the effectiveness, comparative effectiveness, and harms of treatment vary by dose, delivery mode, formulation, or duration of treatment?	Use the full range of data sources and study designs outlined in Figure 4 (for example, large-scale comparative effectiveness trials and observational studies using real-world data and quasi-experimental designs) to determine optimal dosing, delivery mode, formulation, and duration of pharmacologic and nonpharmacologic treatments.
	Establish standardized treatment doses, modes, formulations, and durations to enable rigorous comparison.
KQ 1b: Do the effectiveness, comparative effectiveness, and harms of treatment vary by timing and type of menopause (early, average, iatrogenic, natural)?	Create standardized definitions, measures, and assessment tools to capture the types and stages of menopause.
	Conduct subgroup analyses based on types and stages of menopause and timing of menopause treatment.

327 **Table 1: Key Recommendations for Future Research (continued)**
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Key Questions Guiding the Systematic Evidence Review and Workshop	Recommendations
KQ 1c: Do the effectiveness, comparative effectiveness, and harms of treatment vary by individual- or system-level factors?	Support intentional recruitment (and oversampling) of geographically and socioeconomically diverse populations, as well as culturally informed study designs, to provide a more representative profile of symptom burden and the effectiveness of menopause treatments.
	Establish a standardized approach, measures, and assessment tools to capture individual characteristics that may impact treatment effectiveness (e.g., age of menopause onset, menopause type (e.g., spontaneous vs. iatrogenic), symptom burden or severity, body composition, contraceptive needs, comorbidities (e.g., diabetes, cardiovascular disease, cancer, osteoporosis, endometriosis, polycystic ovary syndrome), and medical/surgical history.
	Triangulate data from multiple sources (e.g., patient-reported outcome measure surveys, electronic health records, administrative data, data collected from wearable devices) to establish profiles for patients at different levels of risk.
	Develop and use tools (e.g., risk assessment, shared decision-making, calculators) that support shared decision-making and personalizing suggested treatments, doses, modes, formulations, and durations.
	Identify the organizational, workflow, and system-level factors that facilitate or hinder health care systems' implementation of risk-stratified, personalized care models linking patient characteristics and symptom clusters to evidence-informed treatment recommendations.

Table 1: Key Recommendations for Future Research (continued)

Key Questions Guiding the Systematic Evidence Review and Workshop	Recommendations
KQ 2a: What is the impact of individual-level factors on the receipt of treatment for perimenopausal and early postmenopausal women with symptoms?	Conduct research to examine the impact of individual-level factors on the receipt of menopause treatment across diverse populations and reasons for declining treatment.
	Develop culturally tailored, broadly disseminated, menopause preparedness resources modeled on established puberty and pregnancy education frameworks to counter misinformation (e.g., social media, conventional media, digital health platforms through applications and web-based content).
	Implement digital health literacy interventions to help users access evidence-based and best practices and to distinguish professional from nonprofessional content.
	Apply decision-support tools (including risk profiles) to improve the receipt of and adherence to treatment across diverse populations.
	Establish clinical consensus on best practices for perimenopausal and early postmenopausal women while rigorous research is underway.
KQ 2b: What is the impact of system-level factors on the receipt of treatment for perimenopausal and early postmenopausal women with symptoms?	Test multilevel interventions that include clinician education, patient navigator models, community and workplace approaches, telemedicine, and the impact of FDA approvals.
	Enable primary care and women's health clinicians to provide high-quality menopause care (e.g., by developing AI-enabled decision support tools and culturally responsive clinician education).
	Develop processes to rapidly update and disseminate clinical practice guidelines as new evidence emerges. Determine how insurance benefit design and payment models can support delivery of evidence-based menopause care.

Table 2: Essential Research Domains and Components

Research Domains	Components
Data Sources	Primary data trials, registry, claims/administrative, electronic medical record, wearables, PROMs, linked sources
Study Design/Analytic Approach	Large-scale, longer-term (>1 year), multicenter, cohort, comparative effectiveness trials; secondary analyses of trial data
	Robust quasi-experimental methods (e.g., target trial emulation, regression discontinuity) to evaluate interventions in real-world settings
	Large-language models to extract key information from unstructured text
	Intervention optimization trials
Populations	Intentionally recruited/oversampled geographically and socioeconomically diverse populations
Tools, Treatments, Policies Studied	Systemic and topical hormonal treatments, nonhormonal pharmacologic treatments (including anti-obesity medications)
	Use standardized treatment types and dosing
	Wearable devices to capture symptoms
	Clinical decision support, personalized risk assessment tools and treatment decision aids, patient-facing educational tools, patient navigators, community and workplace interventions to improve menopause care
	Digital health literacy interventions and culturally tailored, broadly disseminated, menopause preparedness resources (modeled on established puberty and pregnancy education frameworks) to help users access evidence-based practices and counter misinformation
	Primary care/general gynecology care-based menopause care delivery interventions
	Nontraditional menopause care delivery models
	Impact of FDA decisions
Key Outcomes	Effectiveness of treatments for full range of individual and clustered symptoms (Figure 1) (e.g., vasomotor, genitourinary, sleep, mood, metabolic, cognitive, weight, including standardized patient-reported outcome measures) and adverse long-term health effects of menopause, tailored to a range of sociodemographic populations
	Treatment adherence
	Treatment adverse effects
	Patient experience
	Patient care burdens (e.g., health care contact days) Spending

Table 2: Essential Research Domains and Components (continued)

Research Domains	Components
Key Predictors and Modifiers of Outcomes	Treatment characteristics: dosing, delivery mode, formulation, duration
	Individual characteristics: pharmacogenomics; age at menopause onset, menopause stage (including perimenopausal, early-post-menopausal, using standardized definitions, measures, and assessment tools), menopause type (e.g., spontaneous vs. iatrogenic), menopause symptom burden/severity; comorbidities (e.g., diabetes, cardiovascular disease, cancer, osteoporosis, endometriosis, polyendocrine metabolic ovarian syndrome); medical/surgical history; age, race/ethnicity; body composition, contraceptive needs
	Health system characteristics: clinician, health system factors

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