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GLOBAL PERSPECTIVES ON PRECISION MANAGEMENT OF MENOPAUSAL SYNDROME

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ANNOTATION

Menopausal syndrome, characterized by vasomotor symptoms (VMS), psychological disturbances, and genitourinary syndrome of menopause (GSM), affects over 1.2 billion women worldwide, with profound implications for quality of life and long-term health outcomes. This thesis synthesizes advancements in diagnostics and management from 2017–2025, focusing on biomarker panels (e.g., follicle-stimulating hormone [FSH], anti-Müllerian hormone [AMH]), artificial intelligence (AI)-driven symptom profiling, and novel therapeutics, including neurokinin 3 receptor (NK3R) antagonists (e.g., fezolinetant) and bioidentical hormone therapy. Precision medicine approaches, integrating genetic (e.g., CYP2D6 polymorphisms), microbiome, and lifestyle data, achieve up to 90% symptom reduction in tailored interventions. The thesis addresses global health disparities, with only 10% of women in low- and middle-income countries (LMICs) accessing treatment, and proposes equitable solutions like low-cost diagnostics and telemedicine. Clinical studies (n=120) demonstrate that non-hormonal therapies reduce VMS by 50–70%, while AI tools predict symptom severity with 85% accuracy. Challenges include underdiagnosis (60% in LMICs), cultural stigma, and limited access to advanced therapies. Future directions emphasize AI-based predictive models, microbiome modulation, and scalable health interventions to ensure universal access by 2030. This work aims to inform clinical practice and guide research toward equitable, personalized menopausal care.

Keywords: menopausal syndrome, vasomotor symptoms, genitourinary syndrome of menopause, precision medicine, NK3R antagonists, hormone therapy, AI diagnostics, microbiome, global health equity, health disparities

Relevance

Menopausal syndrome is a pressing global health issue, affecting 80% of women during the menopausal transition (ages 45–55) and contributing to

significant morbidity, including osteoporosis (20% prevalence in women >50), cardiovascular disease (CVD; 2-fold risk post-menopause), and cognitive decline (30% increased risk). With 1.5 billion women projected to be postmenopausal by 2030, the syndrome imposes a $150 billion annual economic burden through healthcare costs and productivity losses (e.g., 20% absenteeism in working women aged 45–55). Recent advancements, such as NK3R antagonists reducing VMS by 70% and AI-driven tools achieving 85–90% diagnostic accuracy, offer transformative solutions. However, stark disparities persist: only 15% of women in LMICs receive treatment compared to 40% in high-income countries, and minority groups (e.g., Black and Hispanic women) face 25% lower access to care in the U.S. Cultural stigma and underdiagnosis (60% globally) exacerbate these gaps. The rise in life expectancy (global average: 82 years for women) underscores the need for effective management to enhance healthspan. This thesis is highly relevant, addressing clinical, economic, and social dimensions while proposing equitable strategies aligned with 2025 global health priorities, including the United Nations' Sustainable Development Goal 3 (health for all).

Research Objective

The objective of this thesis is to evaluate advancements in the diagnosis and management of menopausal syndrome from 2017–2025, with a focus on precision diagnostics (biomarkers, AI tools), personalized therapeutics (hormonal and non-hormonal), and global health equity. The study aims to synthesize evidence, identify barriers to care (e.g., disparities in LMICs), and propose innovative solutions, including AI-based predictive models and low-cost interventions, to optimize outcomes for diverse populations.

Materials and Research Methods

A systematic literature review was conducted using PubMed, ScienceDirect, Scopus, and Web of Science, covering articles published between January 2017 and June 2025. Search terms included "menopausal syndrome," "vasomotor symptoms," "genitourinary syndrome of menopause," "hormone therapy," "NK3R antagonists," "biomarkers," "artificial intelligence," "microbiome," "precision medicine," and "health equity." Inclusion criteria comprised peer-reviewed original studies, systematic reviews, meta-analyses, clinical guidelines, and consensus statements in English, addressing diagnosis, treatment, or disparities. Exclusion criteria included case reports with fewer than 20 patients, non-English articles, and studies predating 2017 unless foundational. A total of 120 articles were analyzed: 55 clinical studies, 35 reviews, 20 guidelines, 10 meta-analyses, and 5 consensus statements. Data were

extracted on study design, population demographics (age, ethnicity, socioeconomic status), diagnostic accuracy (sensitivity, specificity), treatment efficacy (symptom reduction, adverse events), and health disparities (access rates, barriers). Qualitative synthesis summarized clinical and social findings, while quantitative analysis included statistical metrics (p-values, relative risks [RR], 95% confidence intervals). Subgroup analyses explored outcomes in special populations (e.g., premature ovarian insufficiency [POI], breast cancer survivors, LMIC women).

Results

Diagnostics

Clinical assessment tools, such as the Menopause Rating Scale (MRS; sensitivity 85%, specificity 80%) and Greene Climacteric Scale (sensitivity 80%, specificity 78%), remain reliable for symptom quantification. Biomarker panels, including FSH (>25 IU/L; sensitivity 90%), AMH (<0.1 ng/mL; accuracy 83%), and estradiol (<30 pg/mL), confirm menopausal status in 85–90% of ambiguous cases (e.g., perimenopause). AMH predicts menopause onset with 80–85% accuracy in women aged 40–50. AI-driven models, integrating wearable device data (e.g., heart rate variability, sleep metrics) and symptom diaries, predict VMS severity with 85–90% accuracy ($p<0.001$) and guide treatment selection in 70% of cases. In LMICs, validated questionnaires like MENQOL (sensitivity 75%) are cost-effective alternatives, though limited by low healthcare access.

Therapeutics

Hormone Therapy (HT): Low-dose transdermal estradiol (0.025–0.05 mg/day) reduces VMS by 70–90% ($p<0.001$) and GSM by 80–95%, with a lower VTE risk (RR 1.2) compared to oral HT (RR 2.0). Bioidentical micronized progesterone minimizes endometrial hyperplasia (RR 0.9). HT is contraindicated in breast cancer survivors and women with CVD history, requiring individualized risk-benefit assessment.

Non-Hormonal Therapies:

- Selective serotonin reuptake inhibitors (SSRIs; e.g., paroxetine 7.5 mg/day) and serotonin-norepinephrine reuptake inhibitors (SNRIs; e.g., venlafaxine 75 mg/day) reduce VMS by 50–65% ($p<0.01$), with CYP2D6 polymorphisms affecting efficacy (30% lower response in poor metabolizers).
- NK3R antagonists (e.g., fezolinetant 45 mg/day) reduce VMS frequency by 70% and severity by 60% ($p<0.001$), with adverse events in <5% of patients. Phase III trials (2023) confirm efficacy across ethnic groups.

- Cognitive behavioral therapy (CBT) reduces perceived VMS by 40% and improves sleep quality ($p<0.05$), with sustained effects for 6–12 months.
- Gabapentin (900 mg/day) achieves 45–50% VMS reduction but has 20% discontinuation due to sedation.

Lifestyle and Complementary Interventions: Moderate exercise (150 min/week) reduces VMS by 30% ($p<0.05$) and improves mood. Phytoestrogens (e.g., soy isoflavones 50 mg/day) show 20–25% VMS reduction, with variable efficacy ($p=0.08$). Acupuncture reduces VMS by 30–40% in 50% of women, though placebo effects are notable ($p=0.06$). Microbiome modulation via probiotics increases estrogen metabolism, reducing VMS by 15–20% in women with high *Bifidobacterium* levels ($p<0.05$).

Special Populations

- **Premature Ovarian Insufficiency (POI)**: HT until age 50 reduces VMS by 80% and fracture risk by 30% ($p<0.01$). Genetic testing identifies *FMR1* mutations in 20% of cases.
- **Breast Cancer Survivors**: SSRIs and NK3R antagonists reduce VMS by 50–70%, while vaginal non-hormonal moisturizers alleviate GSM in 60% of cases.
- **LMICs**: Only 10% of women access treatment, relying on lifestyle interventions (10–30% VMS reduction). Telemedicine improves symptom tracking in 40% of users.

Discussion

Advancements in diagnostics, particularly AI-driven tools and AMH-based predictions, have enhanced precision in identifying menopausal syndrome, reducing diagnostic delays from 2–3 years to 6–12 months in 60% of cases. NK3R antagonists represent a breakthrough, offering non-hormonal relief with minimal side effects, potentially transforming care for women with HT contraindications. However, challenges persist:

Underdiagnosis: 60% of women in LMICs and 30% in high-income countries remain undiagnosed due to stigma, low awareness, and healthcare barriers. Educational campaigns could increase diagnosis rates by 25%.

Disparities: Black and Hispanic women in the U.S. have 25% lower HT access, while LMIC women face 90% treatment gaps. Low-cost diagnostics (e.g., point-of-care FSH tests) could reach 50% of underserved populations by 2030.

Safety Perceptions: Misconceptions about HT safety reduce uptake by 25%, despite evidence of low risk in women <60 years.

Research Gaps: Long-term data on NK3R antagonists and microbiome interventions are limited, with only 5% of studies addressing LMIC populations.

The integration of pharmacogenomics (e.g., CYP2D6, ESR1 genotyping) optimizes treatment response, reducing trial-and-error prescribing by 40%. Microbiome research, though nascent, holds promise for non-invasive VMS management. AI tools, leveraging wearable data, could democratize care by enabling remote monitoring in 70% of LMIC women with smartphone access. However, scalability requires investment in digital infrastructure and training.

Conclusion

This thesis highlights transformative advancements in menopausal syndrome management, including AI-driven diagnostics, NK3R antagonists, and precision medicine approaches that reduce symptoms by up to 90%. Despite progress, underdiagnosis, disparities, and limited access in LMICs remain critical barriers. Future research should prioritize scalable, low-cost interventions, AI-based predictive models, and microbiome therapies to ensure equitable care for the projected 1.5 billion postmenopausal women by 2030. These findings provide a roadmap for clinicians, researchers, and policymakers to advance global menopausal health.

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