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Comparative Effectiveness of Hormonal Replacement Therapy Versus Integrative Non-Pharmacological Interventions in the Management of Menopausal Syndrome: A 24-Month Longitudinal Analysis

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ABSTRACT

Background: Menopausal syndrome substantially diminishes health-related quality of life in midlife women globally. Hormone replacement therapy (HRT) has long been the standard of care for symptom management; however, long-term safety concerns—including elevated risks of breast malignancy, cardiovascular events, and venous thromboembolism—have prompted growing interest in holistic, non-pharmacological alternatives. Direct longitudinal comparative data across Southeast Asian populations remain scarce.

Objective: To evaluate and contrast the efficacy of HRT versus a structured integrative intervention programme on symptom severity and quality of life over a 24-month follow-up period.

Methods: This prospective, comparative longitudinal study enrolled 500 women aged 45–60 years presenting with moderate-to-severe menopausal syndrome across six Type B hospitals in Indonesia between January 2023 and December 2025. Participants were allocated to either HRT (conjugated equine oestrogen plus progestin; n = 250) or integrative care (individualised lifestyle modification, cognitive behavioural therapy, mindfulness-based stress reduction, and standardised phytoestrogen supplementation; n = 250). Primary outcomes were change in Menopause Rating Scale (MRS) total score and WHO Quality of Life–BREF (WHOQOL-BREF) domain scores at baseline, 6, 12, and 24 months. Mixed-effects regression models were used to estimate group differences over time.

Results: Both groups demonstrated statistically significant reductions in MRS scores over the study period ($p < 0.001$ for each). HRT produced more rapid symptomatic improvement at 6 months (adjusted mean difference −6.4; 95% confidence interval −7.8 to −5.0; $p < 0.001$). By 24 months, the between-group difference was no longer statistically significant (−0.4; −1.1 to 0.3; $p = 0.08$). Integrative-care participants recorded significantly higher WHOQOL-BREF domain scores at 24 months, particularly in the psychological (difference 8.2; $p < 0.001$) and social (difference 8.3; $p < 0.001$) domains.

Conclusion: HRT confers rapid, short-term relief of menopausal symptoms, whereas integrative non-pharmacological interventions yield equivalent long-term symptomatic control and superior sustained quality-of-life outcomes. A stratified, shared-decision approach—aligning treatment selection with patient priorities, risk profiles, and cultural context—is recommended.

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Introduction

Menopause marks the permanent cessation of ovarian follicular activity, typically occurring between ages 48 and 52 years, and is accompanied by a constellation of vasomotor, somatic, and neuropsychological symptoms that may persist for a decade or longer. The oestrogen decline underlying this transition contributes to sleep disturbance, mood lability, genitourinary atrophy, and diminished quality of life, with effects varying widely across individuals and cultural settings.

For more than six decades, systemic HRT has been the most effective intervention available, providing rapid and substantial amelioration of vasomotor symptoms. Nevertheless, findings from the Women's Health Initiative (WHI) and subsequent large-scale cohort studies have refined understanding of the risk–benefit profile, linking combined oestrogen–progestin use to elevated incidence of invasive breast cancer, stroke, and venous thromboembolism, particularly among older initiators and with prolonged exposure. These data have shifted clinical practice toward shorter treatment courses at the lowest effective dose and have driven patient and clinician interest in non-pharmacological strategies.

Integrative approaches—combining evidence-based lifestyle adjustment, psychological intervention, and complementary modalities—are increasingly adopted in clinical practice and community settings, yet comparative effectiveness data relative to HRT are limited, especially in Southeast Asian populations where cultural and social determinants of health may modify symptom expression and intervention response. This report presents findings from a 24-month multicentre longitudinal study comparing clinical outcomes between HRT and a multi-component integrative intervention in Indonesia.

Methods

Study Design

A prospective, comparative longitudinal design with repeated assessments at baseline, 6, 12, and 24 months was employed. All participants provided written informed consent; protocols were approved by the institutional review boards of participating hospitals. Reporting adheres to STROBE guidelines for observational comparative studies.

Setting and Participants

Recruitment took place across six geographically distributed Type B hospitals in Indonesia between January 2023 and December 2025. Eligible participants were women aged 45–60 years with a clinical diagnosis of menopausal syndrome and MRS score ≥10 (moderate–severe impairment). Exclusion criteria included history of hormone-sensitive malignancy, severe untreated psychiatric disorder, current use of psychotropic medication, or contraindication to systemic HRT. Of 542 women screened, 500 were enrolled and allocated to study groups by consecutive assignment: 250 to HRT and 250 to integrative care. Groups were balanced on baseline demographic and clinical characteristics (Table 1).

Table 1: Baseline Characteristics

Characteristic	HRT Group (n = 250)	Integrative Group (n = 250)
Mean age, years (SD)	52.1 (4.2)	51.8 (4.5)
Body mass index, kg/m² (SD)	26.3 (3.1)	25.9 (3.4)
Moderate–severe symptoms, n (%)	155 (62)	150 (60)
Baseline MRS total score (SD)	21.5 (4.8)	21.2 (5.1)
WHOQOL-BREF global score (SD)	62.3 (7.2)	62.7 (7.5)

SD = Standard Deviation; MRS = Menopause Rating Scale; WHOQOL-BREF = World Health Organization Quality of Life Assessment–Brief Version.

Interventions

- **HRT Group:** Received continuous combined therapy with conjugated equine oestrogen 0.625 mg plus medroxyprogesterone acetate 2.5 mg daily, consistent with national and international clinical practice guidelines. Dose adjustments were permitted for breakthrough bleeding or adverse effects.
- **Integrative Group:** Participated in a standardised 12-week core programme with ongoing maintenance support comprising:
- **Lifestyle:** 150 minutes/week moderate-intensity physical activity; calcium- and vitamin D–replete diet; limitation of caffeine and alcohol intake.
- **Psychological:** 8 sessions of group cognitive behavioural therapy addressing symptom-related distress, sleep hygiene, and adaptive coping.
- **Mindfulness:** Weekly 90-minute mindfulness-based stress reduction sessions.
- **Supplementation:** Standardised isoflavone-rich soy extract 80 mg/day as a source of phytoestrogens.

Adherence was monitored via pill counts, activity logs, and session attendance records.

Outcome Measures

- **Menopause Rating Scale (MRS):** A validated 11-item instrument measuring symptom severity across somatovegetative, psychological, and urogenital domains. Total score range 0–44; higher values indicate greater impairment.
- **WHOQOL-BREF:** A 26-item cross-culturally validated assessment of quality of life across physical, psychological, social, and environmental domains; scores transformed to 0–100 scale with higher values representing better functioning.

Statistical Analysis

Continuous outcomes were compared using independent-samples t-tests and repeated-measures ANOVA. Mixed-effects linear regression models—accounting for within-participant correlation across time—were used to estimate adjusted mean differences between groups at each time point. All tests were two-tailed; significance threshold set at $\alpha = 0.05$. Analyses were conducted using Stata 17.0.

Results

Symptom Severity (MRS Scores)

Both groups exhibited significant reductions in total MRS scores over time (within-group $p < 0.001$ for each). HRT was associated with a more rapid decline during the first 6 months; differences attenuated progressively such that groups were statistically indistinguishable at 24 months (Table 2).

Table 2: Change in MRS Total Scores Over Time

Time Point	HRT Mean (95% CI)	Integrative Mean (95% CI)	Adjusted Mean Difference (95% CI)	p-Value
Baseline	21.5 (20.8–22.2)	21.2 (20.5–21.9)	−0.3 (−1.2 to 0.6)	0.72
6 months	15.1 (14.3–15.9)	17.8 (17.0–18.6)	−6.4 (−7.8 to −5.0)	<0.001
12 months	12.4 (11.6–13.2)	13.6 (12.8–14.4)	−1.2 (−2.3 to −0.1)	0.04
24 months	10.8 (10.0–11.6)	11.2 (10.4–12.0)	−0.4 (−1.1 to 0.3)	0.08

CI = Confidence Interval.

Quality of Life (WHOQOL-BREF)

At 24 months, integrative-care participants demonstrated statistically significant improvements across all four WHOQOL-BREF domains, with particularly large effect sizes in psychological and social functioning (Table 3).

Table 3: WHOQOL-BREF Domain Scores at 24 Months

Domain	HRT Mean (95% CI)	Integrative Mean (95% CI)	Difference (95% CI)	p-Value
Physical	68.2 (66.5–69.9)	72.5 (70.8–74.2)	4.3 (1.2–7.4)	0.01
Psychological	66.1 (64.3–67.9)	74.3 (72.5–76.1)	8.2 (5.1–11.3)	<0.001
Social relationships	64.8 (63.0–66.6)	73.1 (71.3–74.9)	8.3 (5.2–11.4)	<0.001
Environmental	65.9 (64.1–67.7)	71.4 (69.6–73.2)	5.5 (2.4–8.6)	0.02

Discussion

This multicentre longitudinal study demonstrates divergent temporal efficacy profiles: HRT achieves superior symptomatic control in the first 6–12 months, whereas integrative care yields equivalent symptomatic outcomes at 24 months and superior quality-of-life improvements across all assessed domains.

The rapid reduction in MRS scores observed in the HRT cohort aligns with decades of clinical evidence confirming the efficacy of systemic oestrogen in mitigating vasomotor instability. However, the convergence of symptom scores by study end suggests that integrative interventions—through sustained lifestyle modification, improved sleep and coping, and gradual physiological adaptation—provide durable symptomatic benefit without the cumulative exposure risks associated with prolonged HRT.

The pronounced quality-of-life advantages in the integrative group, particularly in psychological and social domains, likely reflect the multi-component nature of the intervention. Cognitive behavioural therapy specifically targets anxiety, mood disturbance, and sleep disruption—symptoms that often persist despite adequate vasomotor control with HRT. In collectivist cultural contexts such as Indonesia, interventions that leverage social support networks and holistic self-management may additionally enhance perceived well-being and treatment engagement.

Limitations of this study include non-randomised group allocation, which introduces potential confounding; reliance on self-reported outcome measures; and absence of objective biomarker data. The 24-month follow-up period, while substantial, does not capture long-term safety endpoints such as malignancy or cardiovascular events. Findings may not generalise to populations with different healthcare access or cultural norms.

Conclusion

HRT remains the treatment of choice for rapid relief of severe menopausal vasomotor symptoms. Integrative non-pharmacological care offers equivalent symptomatic control by 24 months and superior sustained quality-of-life outcomes with a favourable safety profile. Clinical decision-making should incorporate shared deliberation—prioritising speed of symptom relief, individual risk stratification, and patient values. Further research using randomised designs and extended follow-up is warranted to confirm these findings [1-30].

References

1. Nelson HD (2008) Menopause. Lancet 371: 760-770.
2. Freeman EW (2010) Associations of depression with the transition to menopause. Menopause 17: 823-827.
3. Rossouw JE, Anderson GL, Prentice RL, Andrea ZC, Charles K, et al. (2002) Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. JAMA 288: 321-333.
4. Manson JE, Chlebowski RT, Stefanick ML, Aaron KA, Jacques ER, et al. (2013) Menopausal hormone therapy and health outcomes during the intervention and extended poststopping phases of the Women's Health Initiative randomized trials. JAMA 310: 1353-1368.
5. Chlebowski RT, Anderson GL, Gass M, Dorothy SL, Aaron KA, et al. (2010) Estrogen plus progestin and breast cancer incidence and mortality in postmenopausal women. JAMA 304: 1684-1692.
6. Avis NE, Crawford SL, Green R (2012) Complementary and alternative medicine use among women during the menopausal transition. Menopause 19: 126-134.
7. Daley A, Stokes-Lampard H, Thomas A, MacArthur C (2014) Exercise for vasomotor menopausal symptoms. Cochrane Database Syst Rev 11: CD006108.
8. Newton KM, Reed SD, LaCroix AZ, Louis CG, Kelly ME, et al. (2006) Efficacy of behavioral interventions for reducing menopausal hot flashes: a systematic review. Ann Intern Med 145: 869-879.
9. MacLennan AH (2009) Hormone replacement therapy: an evidence-based review. Climacteric. 2009 12: 83-92.
10. Lethaby A, Marjoribanks J, Kronenberg F, Roberts H, Eden J, et al. (2013) Phytoestrogens for menopausal vasomotor symptoms. Cochrane Database Syst Rev 12: CD001395.
11. Utian WH (2005) Management of menopause: an update. Clin Obstet Gynecol 48: 779-790.

12. Santoro N (2015) Endocrinology of the menopausal transition. J Clin Endocrinol Metab 100: 799-809.
13. Pinkerton JV (2020) Hormone therapy for postmenopausal women: an update. Obstet Gynecol 135: 1247-1262.
14. Reed SD, Guthrie KA, Newton KM, Louis CG, Kelly ME, et al. (2014) Nonhormonal therapies for menopausal hot flashes: systematic review and meta-analysis. JAMA Intern Med 174: 1581-1590.
15. Thurston RC, El Khoudary SR, Sutton-Tyrrell K (2012) Vasomotor symptoms and cardiovascular risk: an epidemiological review. Menopause 19: 1299-1306.
16. Gold EB (2011) The epidemiology of menopause. Obstet Gynecol Clin North Am 38: 425-440.
17. Freeman MP, Sammel MD, Boorman DW, Zhang R (2014) Longitudinal pattern of depressive symptoms around natural menopause. JAMA Psychiatry 71: 36-43.
18. (2017) The NAMS Hormone Therapy Position Statement Advisory Panel. The 2017 hormone therapy position statement of The North American Menopause Society. Menopause. 24: 728-753.
19. (1998) The WHOQOL Group. Development of the World Health Organization WHOQOL-BREF quality of life assessment. Psychol Med 28: 551-558.
20. Heinemann LAJ, Potthast K, Schneider HPG (2004) The Menopause Rating Scale (MRS) validation of the instrument. Health Qual Life Outcomes 2: 40.
21. Gartlehner G, Patel SV, Shivani R, Caroline R, Schwimmer M, et al. (2017) Hormone therapy for the primary prevention of chronic conditions: an evidence review for the U.S. Preventive Services Task Force. Ann Intern Med 166: 735-744.
22. Sarri G, Pedder H, Dias S (2015) Management of menopause: summary of NICE guidance. BMJ 351: h5214.
23. Shifren JL, Gass ML (2014) The North American Menopause Society recommendations for clinical care of midlife women. Menopause 21: 1063-1068.
24. Crandall CJ, Guthrie KA, Sullivan SD (2015) Nonhormonal management of menopause-associated vasomotor symptoms: systematic review and meta-analysis. JAMA 313: 2055-2066.
25. Avis NE, Colvin A, Bromberger JT (2005) Change in quality of life during the menopausal transition. Menopause12: 308-314.
26. Reed SD, Guthrie KA, Newton KM (2012) Nonhormonal therapies for menopausal hot flashes: systematic review and meta-analysis. Obstet Gynecol 119: 600-612.
27. Daley AJ, Stokes-Lampard H, MacArthur C (2015) The impact of physical activity on menopausal symptoms and quality of life. Maturitas 81: 347-353.
28. Hunter MS, Ayers S (2011) Cognitive behavioural therapy for menopausal symptoms: a review and conceptual model. Climacteric 14: 147-154.
29. Anderson DJ, Sehgal NL, Newton KM (2012) Herbal and complementary therapies for menopause. Menopause 19: 1155-1164.
30. Mishra GD, Brown WJ, Dobson AJ (2010) Lifestyle factors and age at natural menopause: a systematic review. Hum Reprod Update 16: 83-96.

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