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CoLab Network

Summary Report

Comparative Evidence Between Transdermal and Oral Menopausal Hormone Therapy

Report Authors

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This work was conducted by the POst-market Drug Evaluation Team (PODET) team through the Post-Market Drug Evaluation (PMDE) CoLab Network.

Executive Summary

Menopausal hormone therapy (MHT) with estrogen, alone or in combination with progesterone, is an established treatment to relieve symptoms of menopause such as hot flashes, sleep disturbances, and mood changes, and to support bone and heart health. Estrogen can be administered orally (as a pill) or through transdermal means (absorbed through the skin). Decision-makers are interested in which formulation is the best first treatment option (first-line treatment) for MHT.

This rapid review aimed to compare the clinical efficacy and effectiveness, safety, and cost-effectiveness of transdermal estrogen therapy and oral estrogen therapy for MHT. We found 7 systematic reviews, 4 primary studies, and 3 evidence-based guidelines. We did not find any health technology assessments or cost-effectiveness studies.

The current evidence does not clearly support one route of estrogen therapy over the other in terms of overall efficacy, but transdermal estrogen may offer safety advantages for specific patient groups. The guidelines, which are based on limited or low-quality data, generally recommend MHT for those at higher cardiovascular risk and risk of blood clots, including those with an elevated body mass index. The guidelines also suggest considering transdermal estrogen for concerns related to sexual function or gallstone risk. Reimbursement policy-makers may consider transdermal estrogen as a first-line option for individuals who may be at higher risk from oral MHT.

Background

MHT helps individuals manage symptoms related to the decline of estrogen during perimenopause, menopause, and postmenopause. Common symptoms include hot flashes, night sweats, sleep disturbances, and mood changes. Estrogen for MHT can be taken in different ways, including oral tablets or transdermal options such as gels or patches.

Policy Issue

The clinical efficacy and effectiveness, safety, and cost-effectiveness of transdermal versus oral estrogen therapy for MHT (and for other uses, such as feminizing hormone therapy) are unclear. Decision-makers are interested in whether transdermal estrogen therapy should be covered by public funding as a first-line option, as an alternative to oral estrogen therapy.

Policy Question

1. Should transdermal MHT be reimbursed in the first-line setting, as an alternative to oral MHT, for the treatment of perimenopausal, menopausal, and postmenopausal symptoms?

Objective

The rapid review aimed to compare the clinical efficacy and effectiveness, safety, and cost-effectiveness of transdermal MHT versus oral MHT in individuals being treated for perimenopausal, menopausal, or postmenopausal symptoms.

Findings

We identified 7 systematic reviews, 4 primary studies, and 3 evidence-based guidelines relevant to this review, but no relevant health technology reports or cost-effectiveness studies. The primary studies included 1 randomized controlled trial and 3 nonrandomized studies.

Systematic Reviews

Seven systematic reviews compared transdermal and oral estrogen for MHT, looking at a range of outcomes like sleep quality, hot flashes and night sweats, cardiovascular disease, blood clots, and lipid profiles. Two reviews were narrative (without meta-analysis), 4 included meta-analyses, and 1 used a network meta-analysis. Overall, these studies suggested that transdermal MHT may lower the risk of blood clots and improve sleep quality, whereas oral MHT may offer more favourable effects on lipid profiles. Both routes appear similarly effective for bone health and have comparable risks for breast and gynecological cancers. However, the reviews lacked direct comparisons and detailed information on participants and treatments, making it hard to apply the findings to specific populations.

Primary Studies

Four primary studies directly compared transdermal and oral estrogen for MHT during perimenopause and postmenopause. One randomized controlled trial looked at the effectiveness of each route using standardized tools to measure menopausal symptoms over time. The other 3 studies were nonrandomized and assessed the safety of MHT, focusing on blood clot risk. Findings suggested similar effectiveness for symptom relief, with transdermal estrogen possibly having a lower blood clot risk. However, the studies varied in design, drug formulations, and participant populations. Limitations, like inconsistent reporting and lack of data on outcomes and long-term risks, further limit the strength of the conclusions.

Evidence-Based Guidelines

Three evidence-based guidelines provided recommendations for transdermal and oral estrogen in MHT. All 3 addressed key outcomes such as symptom control, cardiovascular and blood clot risks, and overall quality of life. The guidelines generally favoured transdermal estrogen for those at higher risk of blood clots, stroke, and heart disease, and emphasized individualized treatment decisions based on individual concerns and preferences. One guideline also extended its recommendations to include trans men and nonbinary individuals assigned female at birth, recognizing the broader diversity of those affected by menopause symptoms. While the guidelines are based on evidence, many recommendations rely on limited and low-quality data.

Patient Engagement

As part of our review, we engaged with 2 individuals who have living or lived experience receiving transdermal or oral estrogen as MHT. Our goal was to understand their treatment priorities and perspectives on relevant outcomes. One individual also reviewed the draft report for clarity and relevance. Engaging these individuals allowed us to proactively address the needs, concerns, and opinions of those potentially impacted by the outcomes of the review and ensure the research is relevant and useful for decision-makers.

Our interviews revealed that both individuals had more than 7 years of experience with MHT and that symptom relief — particularly for hot flashes, sleep disturbances, and mood changes — was their top concern. During interviews, safety and dosing emerged as concerns. One participant started on oral MHT and cycled through several therapies before finding relief with a high-dose patch; the other participant started on transdermal MHT due to personal risk factors. Both participants indicated a preference for starting on the lowest-risk hormone therapy and expressed concerns about finding appropriate and effective dosing.

Limitations

This customer-requested rapid review comparing transdermal and oral MHT has several limitations. The rapid review approach balances rigour and timeliness, which limits the search strategy, involves a simpler bias assessment, and uses stricter inclusion criteria.

The included studies had limited information on participant characteristics such as menopausal stage, gender, and ethnicity, making it difficult to generalize the results to diverse populations. Few studies reported key clinical outcomes, such as genitourinary symptoms or long-term risks, and differences in MHT dosages and treatment durations, further complicating interpretation. Many comparisons between oral and transdermal MHT were indirect or based on unequal dosing. Most of the evidence also came from observational studies or low-quality guidelines.

Finally, while patient engagement added valuable context, it was limited to the experiences of 2 individuals and did not include any formal qualitative analysis.

Implications for Policy-Making

Both transdermal and oral estrogen are established options for managing menopausal symptoms such as hot flashes, sleep disturbances, and mood changes. However, there is limited and mixed evidence on their comparative clinical effectiveness. Some studies suggest that transdermal estrogen may offer similar relief with a lower risk of blood clots and, possibly, of stroke. It is recommended for those at a higher risk of blood clots, including those with a body mass index of more than 30 kg/m^2, and it might be preferred by those concerned about sexual function or gallstones. However, the recommendations are based on limited and low-quality evidence.

Given these findings, reimbursement policy-makers may consider transdermal estrogen as a first-line option for individuals who may be at higher risk of adverse health outcomes from oral MHT.

Considerations

Post-Market Drug Evaluation (PMDE) projects aim to produce health policy issue evidence and are not linked to a recommendation.

We conducted a similar rapid review comparing transdermal estrogen and oral estrogen for feminizing hormone therapy, in the context of gender-affirming care. However, the applicability of that evidence to MHT is limited because therapy goals, biology, and age ranges of individuals receiving feminizing hormone therapy differ.

This work was intended to inform health policy. Clinical questions regarding MHT should be directed to a health care professional.

For more information on CoLab and its work, visit the **CoLab website**.

For the full scientific report, visit:

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CoLab is a pan-Canadian network of experts in applied research, scientific methods, and data analysis. CoLab members work with the Post-Market Drug Evaluation Program to produce credible and timely evidence on postmarket drug safety and effectiveness.

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