Quantifying the Value of Delayed Ovarian Aging

Project: Female Longevity Track - HackAging Challenge
Team: OAV
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Task Description

OBJECTIVE

To quantify the health and economic value of delaying menopause by 5 years, with focus on women experiencing earlier-than-average transition, and provide data-driven justification for increased investment in ovarian aging research.

EXECUTIVE SUMMARY

- **Detailed report**
- **Visualization**
- **Report on the 1st part**

Early menopause is not just a reproductive endpoint — it is a systemic health crisis that accelerates cardiovascular disease, osteoporosis, and cognitive decline. This analysis quantifies what the field has long suspected but never proven: delaying menopause by just 5 years could prevent 4,340 cases of serious disease per million women and generate $609 million in economic value over 6 years.

Our health-economic model reveals that the top three conditions—osteoporotic fractures (30.7%), coronary heart disease (26.5%), and stroke (23.2%) — account for 80% of the total benefit. Women experiencing early menopause face up to 1.58× higher risk for stroke and 1.45× higher risk for heart disease compared to those with normal timing.

At a population scale, interventions targeting ovarian aging could unlock over $100 billion in healthcare savings across the United States alone. This analysis provides quantitative evidence to support increased research investment in

ovarian aging — a critically underfunded area with substantial health and economic implications.

Multi-Agent System

1. PubMed search agent: [agent.py]
2. Data extraction agent 1: [create_dataset.py]
3. Data extraction agent 2: [create_osteoporosis_data.py]
4. Incidence & costs search agent: [data-collector.md]
5. Calculation agent: [calculator.py]

Datasets

1. **combined_menopause_data.xls:** Filtered studies to retain only high-quality evidence with Quality Score ≥8 and validation flag TRUE.
2. **baseline_incidence_rates.xls.** Selected age group 50-54 years as reference point, representing women with normal menopause timing (≥51 years).
3. **disease_treatment_costs.xls.**Selected one primary cost type per disease based on calculation methodology (annual for chronic, initial for acute events).

Papers

1. Muka T, et al. Association of Age at Onset of Menopause and Time Since Onset of Menopause With Cardiovascular Outcomes, Intermediate Vascular Traits, and All-Cause Mortality. *JAMA Cardiology*. 2016;1(7):767-776.
2. Long G, et al. Predictors of osteoporotic fracture in postmenopausal women: a meta-analysis. *Journal of Orthopaedic Surgery and Research*. 2023;18(1):574.
3. Karamani E, et al. Early menopause and premature ovarian insufficiency are associated with increased risk of dementia: A systematic review and meta-analysis of observational studies. Maturitas. 2023;176:10792.
4. Anagnostis P, et al. Early menopause and premature ovarian insufficiency are associated with increased risk of type 2 diabetes: a systematic review and meta-analysis. *European Journal of Endocrinology*. 2019;180(1):41-50.

The risk of sarcopenia (decreased muscle mass), also associated with early menopause, was not included in the quantitative model due to the lack of data in OR/RR/HR format.

CALCULATION METHODOLOGY

The Model: How We Calculate Economic Value

Input Data

- **Risk Ratios**: How much early menopause increases disease risk (from meta-analyses)
- **Baseline Rates**: Disease incidence per 100,000 women age 50-54 (CDC data)
- **Treatment Costs**: Annual per-patient healthcare costs (HCUP database)

Step 1: Calculate Early Menopause Risk

Early Menopause Rate = Baseline Rate × Risk Ratio

Example (CHD):

- Baseline: 350 per 100K women
- Risk Ratio: 1.45×
- Early Menopause Rate: 350 × 1.45 = 508 per 100K

Step 2: Calculate Cases Prevented

Cases Prevented = Early Menopause Rate - Baseline Rate

Example (CHD):
Cases Prevented: 508 - 350 = 158 per 100K women

Step 3: Calculate Economic Value

Economic Value = Cases Prevented × Annual Cost × PV Factor

Present Value Factor (for 6 years at 3% discount rate):

PV Factor = $[1 - (1.03)^{-6}] / 0.03 = 5.417$

**Why 3%? Standard rate used by WHO, CDC, and health economic evaluations*

Example (CHD):

- Cases: 158 per 100K
- Annual Cost: $18,953
- PV Factor: 5.417
- Economic Value: 158 × $18,953 × 5.417 = $16.2M per 100K women

Step 4: Sum Across All Diseases

Net Benefit = Σ(Benefits) - Σ(Risks)

- Benefits: CHD, Stroke, Osteoporotic Fractures, Dementia, Type 2 Diabetes
- Risks: Breast Cancer, Endometrial Cancer (not yet included in current model)

Result: $60.9M net economic benefit per 100,000 women

Visual Formula

$$\text{Economic Value} = \underbrace{(\text{Baseline} \times \text{RR} - \text{Baseline})}_{\text{Cases Prevented}} \times \text{Cost} \times \text{PV}$$

Where:
RR = Risk Ratio (1.15 - 1.58×)
Cost = Annual treatment cost ($15K - $65K)
PV = Present Value Factor (5.417 for 6 years @ 3%)

Key Assumptions

1. Population cohorts: "Normal menopause" (50-54 years) vs. "early menopause" (<45 years), analyzed per 100,000 women
2. Time horizon: 6-year benefit period for all diseases (conservative estimate of immediate post-menopause impact)
3. Discount rate: 3% annually (U.S. health economics standard); Present Value Factor = 5.417

4. Data sources: Baseline incidence from CDC/ARIC Study; treatment costs from HCUP; risk ratios from published meta-analyses
5. Risk metrics: Relative Risk (RR) and Odds Ratio (OR) used interchangeably valid approximation for baseline incidence <5%)
6. Geographic scope: U.S. healthcare system (costs, baseline rates)
7. Disease modeling: Five major conditions included; breast/endometrial cancer risks not yet incorporated
8. Intervention timing: Preventive model assumes intervention before menopause transition, not post-menopause treatment
9. Independence assumption: Diseases modeled independently; comorbidities not accounted for
10. Cost stability: Annual treatment costs held constant over 6-year period

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SCOPE LIMITATIONS: WHAT'S NOT INCLUDED

This analysis focuses exclusively on direct medical costs. The following components are not captured in the $609M figure, meaning the true economic and social value is likely substantially higher:

Indirect Economic Costs
- Lost productivity due to illness and disability
- Caregiver burden and family member work loss
- Premature mortality (years of potential life lost)
- Reduced workforce participation

Quality of Life Impacts
- Quality-Adjusted Life Years (QALYs) not quantified
- Patient suffering and reduced wellbeing
- Mental health and psychological effects
- Social and relationship impacts

Long-Term Effects
- Analysis limited to 6-year time horizon
- Lifetime disease burden not captured
- True benefit likely 3-5× higher over full lifespan
- Downstream health complications not modeled

Cancer Risks
- Breast cancer risk from prolonged estrogen exposure
- Endometrial and ovarian cancer considerations
- Net cancer risk-benefit analysis pending

Including these factors would significantly increase the estimated value but requires additional data sources and modeling approaches beyond the scope of this initial analysis.