Mount Hood Osteoarthritis Challenge 2025

Draft Instructions- 1 May 2025

This challenge aims to assess the performance of different simulation models in predicting outcomes of interventions for osteoarthritis.

Challenge 1: Reference Simulation – STEP 9 Trial (Overall Population)
To enable model simulations to be compared across time and across different models, we ask groups to undertake a reference simulation based on the overall population of the STEP 9 trial. Existing models that have been updated (in any way) or new simulation models should undertake this reference simulation.

- Data Source: The STEP 9 trial (Lin et al., 2024, *N Engl J Med*; [insert DOI link: https://www.nejm.org/doi/full/10.1056/NEJMoa2403664]). Details on population below.
- Simulation Task: Participants should simulate the progression of knee osteoarthritis, including Quality-Adjusted Life Years, Kellgren-Lawrence osteoarthritis scores and body mass index (BMI) for a virtual cohort representative of the STEP 9 participants at baseline.
- Reporting Metrics:
    - Body mass index (percentage change)
    - Kellgren-Lawrence osteoarthritis (proportion of population with a KL 3 or 4)
    - Joint replacement
    - Life expectancy
    - Quality-adjusted life years
- Purpose: This reference simulation will serve as a benchmark for comparing model outputs and assessing model validity against observed data in a well-conducted trial of a relevant population receiving a standard intervention.

Challenge 2: Simulating Clinical Outcomes of Semaglutide Intervention in People with Osteoarthritis and Obesity
This challenge asks participants to simulate the lifetime outcomes of semaglutide (2.4 mg once weekly) compared to the control intervention (counseling on physical activity and a reduced-calorie diet) in a population with osteoarthritis and obesity, mirroring the STEP 9 trial participants (meaning simulate the reference population for patients that do and do not receive the weight reduction).

- Intervention: Semaglutide (2.4 mg once weekly subcutaneous injection) in addition to counseling on physical activity and a reduced-calorie diet which results in a 13.7% reduction in weight at 1 year after the start of the model. All other effects are assumed to function through weight loss (i.e., the change in

WOMAC score is due to a reduction in weight, not a direct effect of the medication). As seen in the control group in the trial, we will assume that the average WOMAC score will reduce by 27.5 in year 1.

- Comparator: Counseling on physical activity and a reduced-calorie diet (as per the STEP 9 control arm) which results in a 3.2% reduction in weight at 1 year after the start of the model. As seen in the control group in the trial, we will assume that the average WOMAC score will reduce by 27.5 in year 1.
- Time Horizon: Lifetime.
- Target Population: A virtual cohort with baseline characteristics matching the participants in the STEP 9 trial (mean age, mean BMI, mean WOMAC pain score, percentage of women, etc.).
- Outcomes of Interest (in each trial arm):
    - Progression of knee osteoarthritis (e.g., changes in WOMAC pain).
    - Incidence of relevant comorbidities (if your model allows).
    - Lifetime prevalence of total knee replacement
    - Quality-Adjusted Life Years (QALYs).
    - Life Years (LYs).

For now, focusing on Challenges 1 and 2 based on the STEP 9 trial data provides a strong and relevant framework for your osteoarthritis modeling project.

Model inputs for Challenge: Part 1 – Reference Simulation

Patient Baseline Characteristics (Challenge: Part 1) To allow for consistent comparisons across all models, baseline patient characteristics should follow the values as listed in Table 1. Any other baseline patient characteristics that your model may require can be sourced from publicly available literature (but please document this including sources in “Baseline Characteristics” tab in the accompanying Excel spreadsheet).

Utility Values: Please make a table the reports all utility weights used. Please detail how the model handles multiple events (additive, minimum, etc).

Challenge Part 1: simulation

Step 1: Run a simulation using the baseline risk factors from Table 1 (BMI and WOMAC pain) held constant over the lifetime simulation.

Extract the results and enter input values in a transparent manner in the accompanying Excel workbook in the tab labeled “Time paths & Outcomes” (modify the workbook to fit your outcomes, if necessary, but please try to preserve the basic structure). Do not forget to include traces (risk factor time paths) for input values of all the above risk factors, rates (or counts) of all major health states in the model (e.g., joint replacement, etc.), and life expectancy. For microsimulation models, please ensure that the number of replications is sufficient to generate stable results. Report how many replications were used.

Step 2: Trial replication simulation of treatment effects

Re-run the simulation with the intervention and the control arm that captures initial and permanent reductions in common risk factors from time paths modeled in Step 1 based on the Step 9 trial. For both the comparison group and the intervention group, the WOMAC score was reduced by 27.5 in the first post-baseline cycle. Reductions from these interventions should only be applied to post-baseline cycles and baseline values should remain unchanged.

- Control Weight Change from Baseline: 3.2 percentage points
- Intervention Weight Change from Baseline: 13.7 percentage

Extract the results and add to the accompanying Excel workbook (in tab labelled “Time paths & Outcomes”. Report outcomes and inputs in a transparent manner. Do not forget to include traces (numerical or curves) for input values of all the above risk factors; cumulative rates (or counts) of all major health states in the model (e.g. MI; stroke; renal failure, etc.), QALYS and life expectancy.

Step 3: Reference simulation of common treatment effects when risk-factor time-paths are NOT held constant

The simulation in step 1 does not capture the drift that can occur in many risk factors over time eg. the gradual increase in SBP. To understand what impact change in risk factors may have on incremental benefits the second component of this challenge is to redo the simulations outlined in step 2 using the actual risk factor time paths or assumptions regularly used in your model. Please assume that treatment effects are permanent vertical displacements from the trajectories without intervention time-paths.

Extract the results and add to the accompanying Excel workbook (in tab labelled “Time paths & Outcomes”. Report outcomes and inputs in a transparent manner. Do not forget to include traces (numerical or curves) for input values of all the above risk factors; cumulative rates (or counts) of all major health states in the model, QALYs and life expectancy.

Table 1. Population Characteristics

Characteristic	Total (N=407)
Age - yr	56 ± 10
Female sex - no. (%)	332 (81.6)
Race or ethnic group - no. (%)	
White	248 (60.9)
Asian	22 (5.4)
Black	31 (7.6)
American Indian or Alaska Native	48 (11.8)
Other	58 (14.3)
Body-mass index	
Mean	40.3 ± 7.2
Distribution - no. (%)	
<30	1 (0.2)
30 to <35	99 (24.3)
35 to <40	140 (34.4)
>=40	167 (41.0)
WOMAC pain score	70.9 ± 16.0
Coexisting conditions - no. (%)	
Cardiovascular disease	21 (5.2)