Clinical Validation Protocol

Build 295 · R12 amendment · November 13, 2026

This public amendment records the current synthetic control design and its verification status. It supplements the historical working master protocol v1.4.3, which is available separately through controlled distribution. The amendment records changes made after exploratory replay and provides guidance for future confirmatory work.

Current model input roster

Behavioral (8): Steps, Dietary Fiber, Total Sugar, Na/K Ratio, Sleep Onset, Energy Ratio, Alcohol, and Light Exposure.

Functional (6): HRV, Resting Heart Rate, VO_2 Max, Total Sleep, Walking Speed, and Cardio Recovery.

Cardiometabolic (3): systolic blood pressure, fasting glucose, and BMI.

Sodium and potassium are source measurements for Na/K Ratio. Dietary, active, and resting energy are source measurements for Energy Ratio. Total Carbohydrates and Meditation are outside the scored roster. Sleep Onset measures night-to-night clock-time variability.

Verification boundary

Synthetic controls enter through the ordinary Demo attachment and exercise shared computation and display. Synthetic REC reconciliation is separate from physiological observations. The simulations support software verification. Independent clinical and prognostic validation remain research workstreams.

Synthetic control design

Directional controls use a 50-day baseline and 1,000 daily observations. Fresh clinical specimens occur on days 1, 400, and 800. Distinguish carried values and freshness from a new draw.

Stable Reference uses seeded background variability without a directional intervention.

Cardiometabolic Decline stages worsening activity and nutrition ahead of later functional and cardiometabolic changes.

Alcohol + Sleep stages sustained alcohol exposure, less regular and shorter sleep, lower HRV, and a later modest MCV response.

Reduced Activity models deconditioning with relatively stable diet.

Aerobic Conditioning increases activity and aerobic performance while dietary intake remains stable. The later blood-pressure response is small.

Optimal Fitness combines stronger conditioning with improved diet and sleep.

Cardio Reset progressively reverses the modeled cardiometabolic burden.

Evidence and qualification

In a three-profile simulator audit, both clinical clocks moved in the intended direction at both intervals for all Optimal Fitness profiles and two Cardio Reset profiles. Neither Aerobic Conditioning nor Reduced Activity showed stepwise agreement in both clocks across both intervals in any profile. Report the clocks alongside their measured analytes. Installed import, persistence, freshness, and rendered verification remain open.

Future confirmatory replay should freeze the candidate version, input and reference artifacts, expected bands, and acceptance criteria before execution.

Scientific references

Cardiometabolic Decline and Reset

AHA cardiovascular-kidney-metabolic health advisory · PMID 37807924

AHA scientific statement · PMID 37807920

EnRicH randomized trial · PMID 34347008

ADAG average glucose and A1c study · PMCID PMC2742903

Alcohol + Sleep

Evening alcohol and nocturnal autonomic function · PMCID PMC7819834

Alcohol and sleep evidence synthesis · PMID 39631226

Long-term alcohol exposure and red-cell indices · PMID 16581347

Sleep restriction and insulin resistance · PMCID PMC10733650

Aerobic Conditioning, Optimal Fitness and Reduced Activity

DREW randomized aerobic training trial · PMID 17507344

Aerobic training and cardiac autonomic regulation · PMID 19299682

Time course of endurance detraining · PMID 6511559

Clinical clocks

Klemera and Doubal · PMID 16318865

Levine et al. · PMID 29676998

These sources inform the direction of selected biological responses. The scenario amplitudes and timing are synthetic assumptions.