Predicting Future Cardiovascular Adverse Events at Population Scale Using a Real-World Data Foundation Model: Implications for Clinical Trial and Launch Planning

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Background

Cardiovascular (CV) adverse events – including myocardial infarction (MI), stroke, heart failure, atrial fibrillation, coronary artery disease (CAD), and coronary revascularization – are critical safety endpoints in clinical trials and pharmacovigilance.

Population-level prediction from **real-world data (RWD)** could enable sponsors to characterize CV risk, improve trial feasibility, and support safety planning.

Objectives

To evaluate **PhenOM**, a foundation model trained on billions of longitudinal patient records, for predicting major adverse cardiovascular events (MACE) in a US real-world population.

Methods

- **Data source:** OM1 Real World Data Cloud, a de-identified US longitudinal dataset encompassing more than 370 million patients
- **Model:** PhenOM generates patient-level risk scores from full longitudinal event sequences
- **Outcomes:** seven new-onset CV events – acute MI, ischemic stroke, hemorrhagic stroke, heart failure, atrial fibrillation, CAD, and coronary revascularization – each with a 12-month prediction horizon
- **Evaluation:** AUROC, calibration slope, and lift at the top 10%, 1%, and 0.1% risk thresholds following TRIPOD+AI[1]
- **Subgroups:** performance stratified by age cohort and US census region

Results

- **Discrimination:** robust across all seven outcomes, with AUROCs from 0.73 (hemorrhagic stroke) to 0.87 (heart failure); median 0.79 (Figure 2)
- **Calibration:** slopes close to 1.0, indicating well-calibrated absolute risk estimates
- **Enrichment:** at the top 1% risk threshold, lift ranged from 8-fold (CAD) to 15-fold (revascularization) above baseline (Figure 3)
- **Consistency:** performance was consistent across census regions and age strata (18–64 and 65+ years)
- **Implication:** results support reductions in sample size and monitoring burden for trial safety planning

0.79
Median AUROC
range 0.73–0.87

≈1.0
Calibration slope
well-calibrated risk

8–15×
Lift at top 1%
vs. baseline

Figure 1. Study design

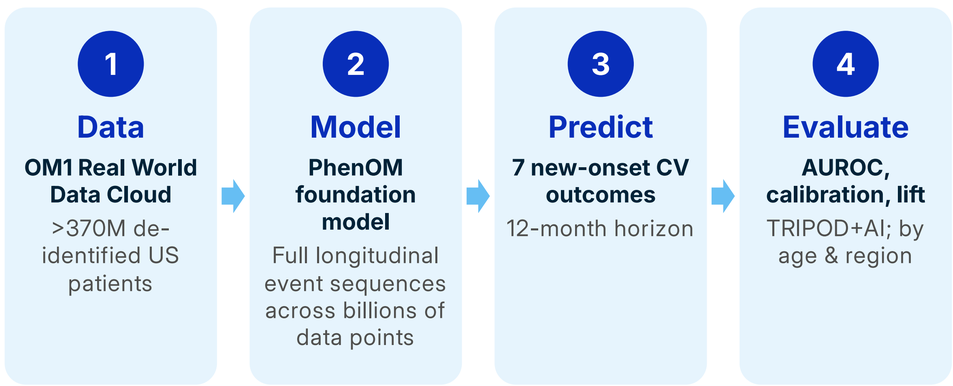
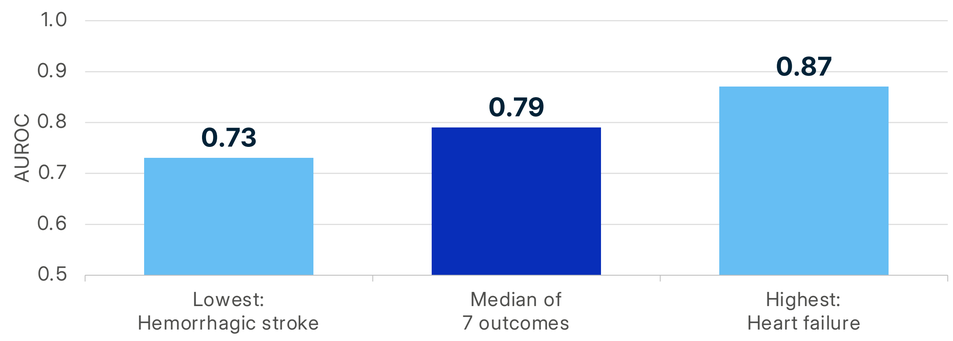
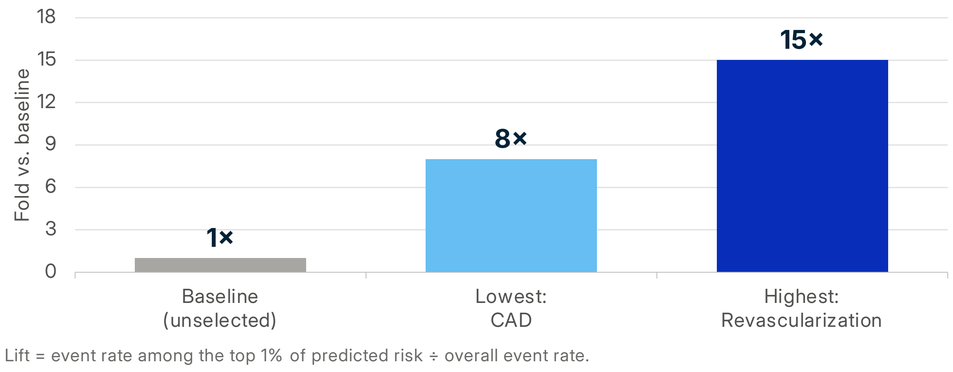


Figure 2. Discrimination (AUROC) across the seven CV outcomes



Axis starts at 0.5 (no discrimination). AUROC, area under the receiver operating characteristic curve.

Figure 3. Lift at the top 1% risk threshold



Lift = event rate among the top 1% of predicted risk ÷ overall event rate.

Table 1. Applications for trial and launch planning

Application	How PhenOM supports it
Pre-trial CV risk characterization	Population-scale, calibrated estimates of expected CV event risk
High-risk subgroup identification	Targeted safety monitoring; lower utilization & monitoring burden
Model-guided enrichment	High lift at narrow thresholds supports smaller sample sizes
Background event rate estimation	Expected event rates for external comparator arms
Pharmacovigilance population sizing	Sizing at-risk populations for launch readiness

Conclusions

- PhenOM predicted seven new-onset CV adverse events from RWD with clinically meaningful discrimination (median AUROC 0.79) and well-calibrated risk
- High lift at narrow risk thresholds (8× to 15× at the top 1%) enables substantial enrichment of high-risk populations
- A scalable, RWD-based complement to traditional approaches for trial planning, safety monitoring, and launch readiness

Conference
Presented at ISPOR Europe 2026, 8–11 November 2026, Vienna, Austria

Reference
1. Collins GS, et al. TRIPOD+AI statement: updated guidance for reporting clinical prediction models that use regression or machine learning methods. BMJ. 2024;385:e078378.

Abbreviations
AUROC, area under the receiver operating characteristic curve; CAD, coronary artery disease; CV, cardiovascular; MACE, major adverse cardiovascular events; MI, myocardial infarction; RWD, real-world data.