THE REFERENCE MODEL SCORES FITNESS OF MODELS AND POPULATIONS

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In a Nutshell

Competitive Disease Forecast

A League of Disease Models/Consumers Report

ABSTRACT

OBJECTIVES:
To figure out what disease models equations/hypothesis work best on what populations.

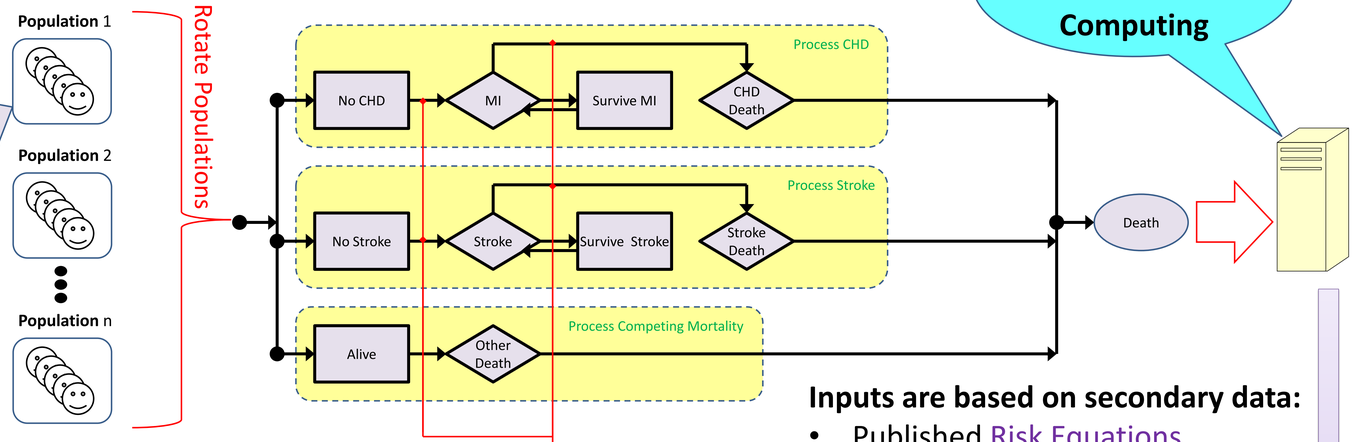
METHODS:
1) Extraction of multiple published disease models/risk equations for cardiovascular disease and multiple diabetic population distributions and outcomes. The populations used were UKPDS, ASPEN, ADVANCE, ACCORD, NDR, KP.
2) Implementation of these components and systematic cross validation of models against populations using micro-simulation and relying on computing power.
3) Defining a fitness score to convert multiple outcome differences into a single number.
4) Defining different queries with weights to rank model / population fitness.

The methods avoid using individual data and rely on more accessible summary data.

RESULTS:
The fitness score matrix uses color coding and ranking to visually demonstrate the fitness between 6/34 populations/cohorts and 64 combinations of published risk equations and hypotheses. The results show that different combinations of risk equations behave differently on different population cohorts. For each query, the system ranks the models. Models that implement the following two corrections generally behaved better:
1) Temporal correction for treatment improvement
2) Biomarker change introduced in the first year.

CONCLUSIONS:
1) Modelers should talk in terms of best fitting model rather than best model since in many cases, the best model changes according to specifics of the query.
2) Disease modelers who develop risk equations should add a temporal correction term within their risk equations to prevent model outdating.
3) The fitness score function allows comparing behavior of different populations using a similar metric and provides a visual explanation of current understanding of disease progression.

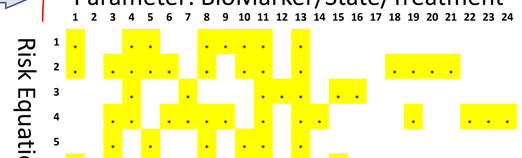
Population Characteristics:
Age, Male, Race, SBP, DBP, A1c, Smoke, BMI, HDL, LDL, Trig, TC, ACR, Lipid Ratio, Age At Diagnosis Of Diabetes, AF, Survive Stroke, Survive MI, MicroAlbuminuria, MacroAlbuminuria, Diabetes Type 2, Treated for Hypertension, Family History CHD, Rheumatoid Arthritis, Townsend Index, A1c Change, BMI Change, DBP Change, SBP Change, HDL Change, LDL Change, Trig Change, TC Change, Smoke Change, Year



High Performance Computing

Rotate equation/ hypothesis variations

Parameter: BioMarker/State/Treatment



Inputs are based on secondary data:
- Published Risk Equations
- Published Clinical Trials: i.e. no real individual data
- Other publications

Potentially access more populations and cover more phenomena

Hypothesis 1:
Biomarker Change:

Example From Table 1 in:
ADVANCE Collaborative Group, Intensive Blood Glucose Control and Vascular Outcomes in Patients with Type 2 Diabetes, NEJM, 2008 Jun 12;358(24):2560-72. doi:10.1056/NEJMoa0802987. Epub 2008 Jun 6.

	Baseline	End of Trial
A1c	7.48	7.24
BMI	28	28
DBP	80.5	74.3
SBP	145	137.9
HDL	1.25	1.25
LDL	3.11	2.65
Trig	1.64	1.59

Without Biomarker change, Use the baseline distribution in risk equation

With biomarker change, from 1st year use end of trial distribution in risk equation

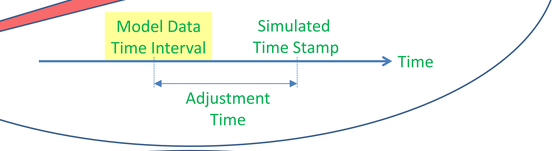
Outputs:
1. Clinical outcomes / Deaths
2. Costs / Quality of Life
3. Population / Equation / Hypothesis fitness

Best Model

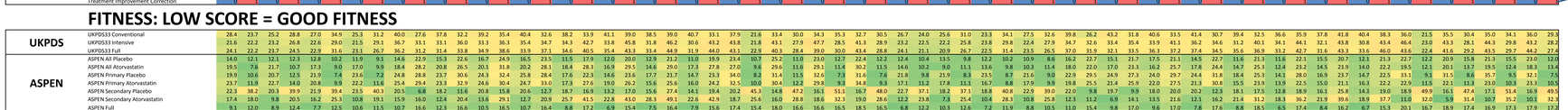
Hypothesis 2:
Temporal Correction for Treatment Improvement:
Each model variation was executed:

Without Temporal Treatment Correction

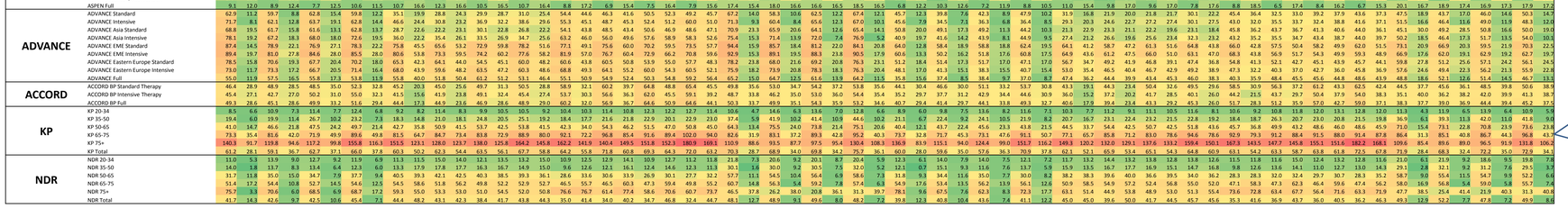
With Temporal Treatment Correction



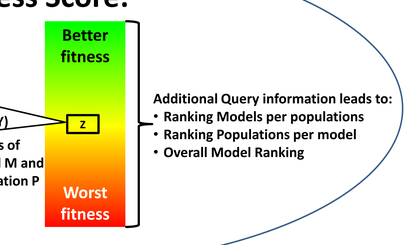
MODELS



FITNESS: LOW SCORE = GOOD FITNESS



Fitness Score:



Additional Query information leads to:
- Ranking Models per populations
- Ranking Populations per model
- Overall Model Ranking

OVERALL MODEL RANKING RESULTS

Best 20 models have temporal treatment correction !

Best Model

Temporal correction is a good idea!
It accounts for model outdating

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