The Reference Model for Chronic Disease Progression

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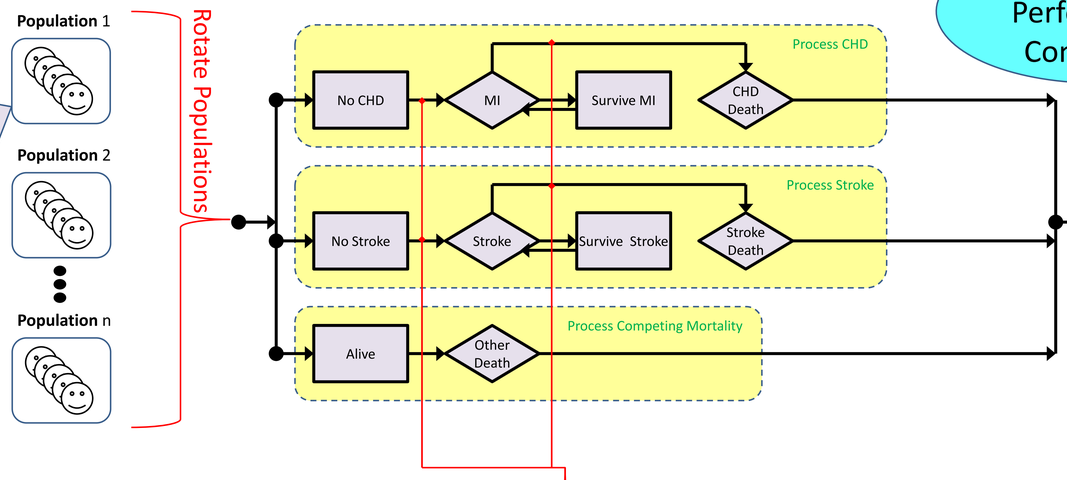
In a Nutshell
Competitive Disease Forecast
A League of Disease Models/Consumers Report

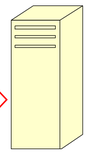
- Prototype utilizing computing power to model chronic disease progression
- Built from literature references and hence the name
- Designed to serve as a reference for new equations and populations

Discussion Points:
- Competition & High Performance Computing
- Open Source & Free Software
- Reproducibility and Code Sharing
- Test Driven Development of Models
- Quality Assurance
- Using Information from clinicaltrials.gov

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

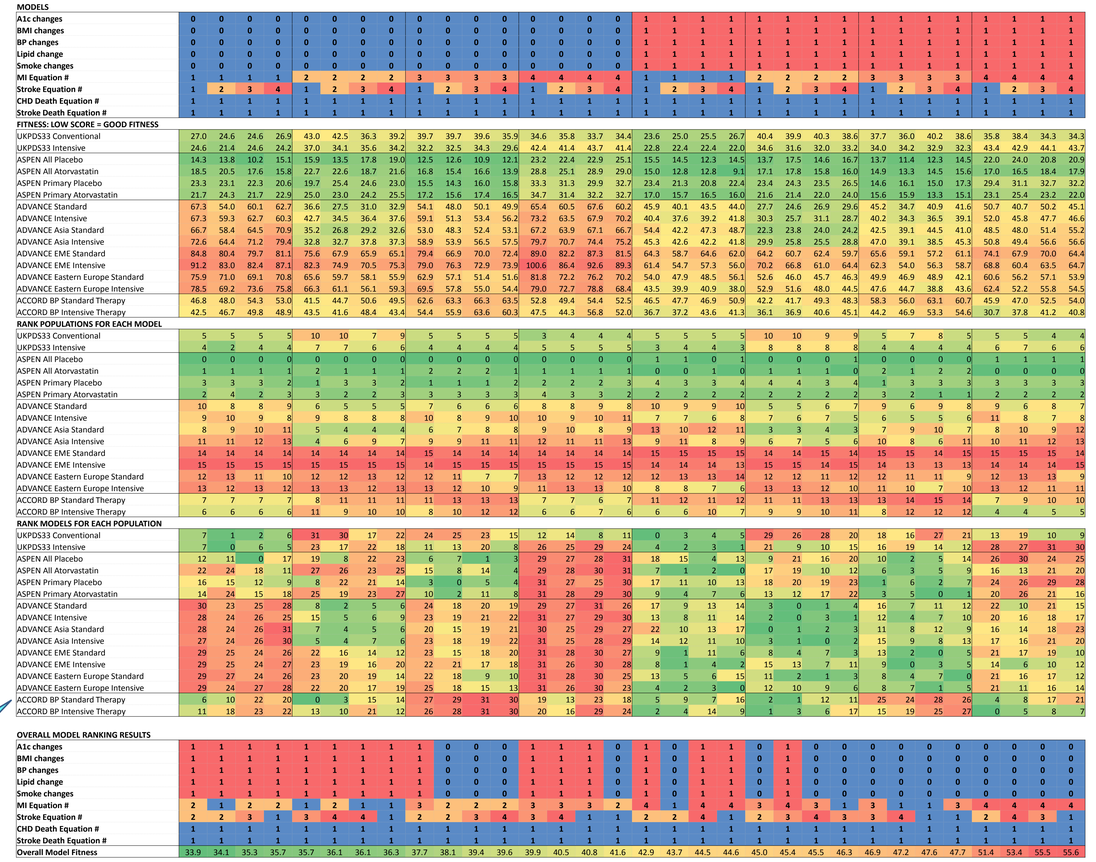


High Performance Computing



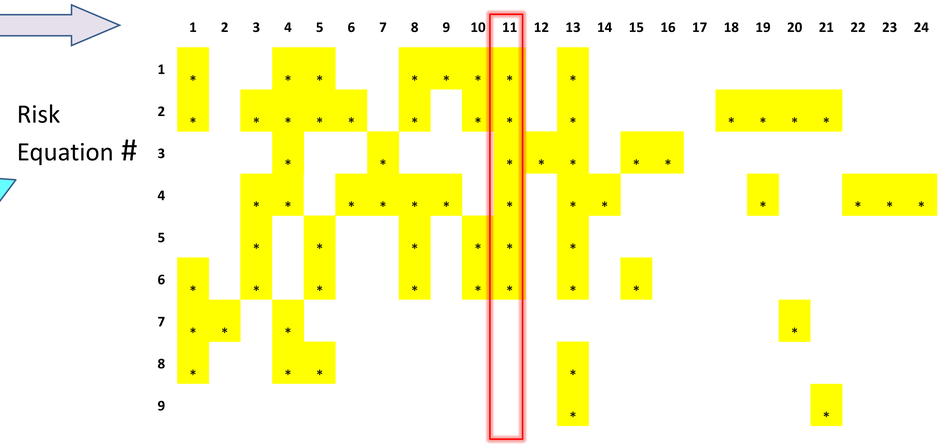
Death

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



MODELS																															
A1c changes	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
BMI changes	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
BP changes	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Lipid change	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Smoke changes	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
MI Equation #	1	1	1	1	2	2	2	2	3	3	3	3	4	4	4	4	1	1	1	1	2	2	2	2	3	3	3	3	4	4	4	4
Stroke Equation #	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
CHD Death Equation #	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Stroke Death Equation #	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
FITNESS: LOW SCORE = GOOD FITNESS																															
UKPDS33 Conventional	27.0	24.6	24.6	26.9	43.0	42.5	36.3	39.2	39.7	39.7	39.6	35.9	34.6	35.8	33.7	34.4	23.6	25.0	25.5	26.7	40.4	39.9	40.3	38.6	37.7	36.0	40.2	38.6	35.8	38.4	34.3	34.3
UKPDS33 Intensive	24.6	21.4	24.6	24.2	37.0	34.1	35.6	34.2	32.2	32.5	34.3	29.6	42.4	41.4	43.7	41.4	22.8	22.4	22.4	22.0	34.6	31.6	32.0	33.2	34.0	34.2	32.9	32.3	43.4	42.9	44.1	43.7
ASPEN All Placebo	14.3	13.8	10.2	15.1	15.9	13.5	17.8	19.0	12.5	12.6	10.9	12.1	23.2	22.4	22.9	25.1	15.5	14.5	12.3	14.5	13.7	17.5	14.6	16.7	13.7	11.4	12.3	14.5	22.0	24.0	20.8	20.9
ASPEN All Atorvastatin	18.5	20.5	17.6	15.8	22.7	22.6	18.7	21.6	16.8	15.4	16.6	13.9	28.8	25.1	28.9	29.0	15.0	12.8	12.8	9.1	17.1	17.8	15.8	16.0	14.9	13.3	14.5	15.6	17.0	16.5	18.4	17.9
ASPEN Primary Placebo	23.3	23.1	22.3	20.6	19.7	25.4	24.6	23.0	15.5	14.3	16.0	15.8	33.3	31.3	29.9	32.7	23.4	21.3	20.8	22.4	23.4	24.3	23.5	26.5	14.6	16.1	15.0	17.3	29.4	31.1	32.7	32.2
ASPEN Primary Atorvastatin	21.7	24.3	21.7	22.9	25.0	23.0	24.2	25.5	17.2	15.6	17.4	16.5	34.7	31.4	32.2	32.7	17.0	15.7	16.5	16.0	21.6	21.4	22.0	24.0	15.6	15.9	13.3	15.1	23.1	25.4	23.2	22.0
ADVANCE Standard	67.3	54.0	60.1	62.7	36.6	27.5	31.0	32.9	54.1	48.0	50.1	49.9	65.4	60.5	67.6	60.2	45.9	40.1	43.5	44.0	27.7	24.6	26.9	29.6	45.2	34.7	40.9	41.6	50.7	40.7	50.2	45.1
ADVANCE Intensive	67.3	59.3	62.7	60.3	42.7	34.5	36.4	37.6	59.1	51.3	53.4	56.2	73.2	63.5	67.9	70.2	40.4	37.6	39.2	41.8	30.3	25.7	31.1	28.7	40.2	34.3	36.5	39.1	52.0	45.8	47.7	46.6
ADVANCE Asia Standard	66.7	58.4	64.5	70.9	35.2	26.8	29.2	32.6	53.0	48.3	52.4	53.1	67.2	63.9	67.1	66.7	54.4	42.2	47.3	48.7	22.3	23.8	24.0	24.2	42.5	39.1	44.5	41.0	48.5	48.0	51.4	55.2
ADVANCE Asia Intensive	72.6	64.4	71.2	79.4	32.8	32.7	37.8	37.3	58.9	53.9	56.5	57.5	79.7	70.7	74.4	75.2	45.3	42.6	42.2	41.8	29.9	25.8	25.5	28.8	47.0	39.1	38.5	45.3	50.8	49.4	56.6	56.6
ADVANCE EME Standard	84.8	80.4	79.7	81.1	75.6	67.9	65.9	65.1	79.4	66.9	70.0	72.4	89.0	82.2	87.3	81.5	64.3	58.7	64.6	62.0	64.2	60.7	62.4	59.7	65.6	59.1	57.2	61.1	74.1	67.9	70.0	64.4
ADVANCE EME Intensive	91.2	83.0	82.4	87.1	82.3	74.9	70.5	75.3	79.0	76.3	72.9	73.9	100.6	86.4	92.6	89.3	61.4	54.7	57.3	56.0	70.2	66.8	61.0	64.4	62.3	54.0	56.3	58.7	68.8	60.4	63.5	64.7
ADVANCE Eastern Europe Standard	75.9	71.0	69.1	70.8	65.6	59.7	58.1	55.9	62.9	57.1	51.4	51.6	81.8	72.2	76.2	70.2	54.0	47.9	48.5	56.1	52.6	46.0	45.7	46.3	49.9	46.9	48.9	42.1	60.6	56.2	57.1	53.9
ADVANCE Eastern Europe Intensive	78.5	69.2	73.6	75.8	66.3	61.1	56.1	59.3	69.5	57.8	55.0	54.4	79.0	72.7	78.8	68.4	43.5	39.9	40.9	38.0	52.9	51.6	48.0	44.5	47.6	44.7	38.8	43.6	62.4	52.2	55.8	54.5
ACCORD BP Standard Therapy	46.8	48.0	54.3	53.0	41.5	44.7	50.6	49.5	62.6	63.3	66.3	63.5	52.8	49.4	54.4	52.5	46.5	47.7	46.9	50.9	42.2	41.7	49.3	48.3	58.3	56.0	63.1	60.7	45.9	47.0	52.5	54.0
ACCORD BP Intensive Therapy	42.5	46.7	49.8	48.9	43.5	41.6	48.4	43.4	54.4	55.9	63.6	60.3	47.5	44.3	56.8	52.0	36.7	37.2	43.6	41.3	36.9	40.6	45.1	44.2	46.9	53.3	54.6	30.7	37.8	41.2	40.8	
RANK POPULATIONS FOR EACH MODEL																																
UKPDS33 Conventional	5	5	5	5	10	10	7	9	5	5	5	5	3	4	4	4	5	5	5	5	10	10	9	9	5	7	8	5	5	5	4	4
UKPDS33 Intensive	4	2	4	4	7	7	6	6	4	4	4	4	5	5	5	5	3	4	4	3	8	8	8	8	4	4	4	4	6	7	6	6
ASPEN All Placebo	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	1	0	0	0	1	0	0	0	0	1	1	1	1
ASPEN All Atorvastatin	1	1	1	1	2	1	1	1	2	2	2	1	1	1	1	1	0	0	1	0	1	1	1	0	2	1	2	2	0	0	0	0
ASPEN Primary Placebo	3	3	3	2	1	3	3	2	1	1	1	2	2	2	2	3	4	3	3	4	4	4	3	4	1	3	3	3	3	3	3	3
ASPEN Primary Atorvastatin	2	4	2	3	3	2	2	3	3	3	3	3	4	3	3	2	2	2	2	2	2	2	2	2	3	2	1	1	2	2	2	2
ADVANCE Standard	10	8	8	9	6	5	5	5	7	6	6	6	8	8	9	8	10	9	9	10	5	5	6	7	9	9	6	9	8	9	6	8
ADVANCE Intensive	9	10	9	8	9	8	8	8	10	8	9	10	10	9	10	11	7	7	6	8	7	6	7	5	6	5	5	6	11	8	7	7
ADVANCE Asia Standard	8	9	10	11	5	4	4	4	6	7	8	8	9	10	8	9	13	10	12	11	3	3	4	3	7	9	10	7	8	10	9	8
ADVANCE Asia Intensive	11	11	12	13	4	6	9	7	9	9	11	11	12	11	11	13	9	11	8	9	6	7	5	6	10	8	6	11	10	11	12	13
ADVANCE EME Standard	14	14	14	14	14	14	14	14	15	14	14	14	14	14	14	14	15	15	15	15	14	14	15	14	15	15	14	15	15	15	15	15
ADVANCE EME Intensive	15	15	15	15	15	15	15	15	14	15	15	15	15	15	15	15	14	14	14	13	15	15	14	15	14	13	13	13	14	14	14	15
ADVANCE Eastern Europe Standard	12	13	11	10	12	12	13	12	12	11	7	13	12	12	12	12	12	13	13	14	12	12	11	12	12	11	11	9	12	13	13	9
ADVANCE Eastern Europe Intensive	13	12	13	12	13	13	12	13	13	12	10	9	11	13	13	10	8	8	7	6	13	13	12	10	11	10	7	10	13	12	11	11
ACCORD BP Standard Therapy	7	7	7	7	8	11	11	11	11	13	13	13	7	7	6	7	11	12	11	12	11	11	13	13	13	14	15	14	7	9	10	10
ACCORD BP Intensive Therapy	6	6	6	6	11	9	10	10	8	10	12	12	6	6	7	6	6	6	10	7	9	9	10	11	8	12	12	12	4	4	5	5
RANK MODELS FOR EACH POPULATION																																
UKPDS33 Conventional	7	1	2	6	31	30	17	22	24	25	23	15	12	14	8	11	0	3	4	5	29	26	28	20	18	16	27	21	13	19	10	9
UKPDS33 Intensive	7	0	6	5	23	17	22	18	11	13	20	8	26	25	29	24	4	2	3	1	21	9	10	15	16	19	14	12	28	27	31	30
ASPEN All Placebo	12	11	8	17	19	8	22	23	6	7	3	9	29	27	28	31	18	15	4	13	9	21	19	10	12	6	3	5	9	16	13	20
ASPEN All Atorvastatin	22	24	18	11	27	26	23	25	15	8	14	4	29	28	30	31	7	1	2	0	17	19	10	12	6	3	5	9	16	13	21	20
ASPEN Primary Placebo	16	15	12	9	8	22	21	14	3	0	5	4	31	27	25	30	17	11	10	13	18	20	19	23	1	6	2	7	24	26	29	28
ASPEN Primary Atorvastatin	14	24	15	18	25	19	23	27	10	2	11	8	31	28	29	30	9	4	7	6	13	12	17	22	3	5	0	1	20	26	21	16
ADVANCE Standard	30	23	25	28	8	2	5	6	24	18	20	19	29	27	31	26	17	9	13	14	3	0	1	4	16	7	11	12	22	10	21	15
ADVANCE Intensive	28	24	26	25	15	5	6	9	23	19	21	22	31	27	29	30	13	8	11	14	2	0	3	1	12	4	7	10	20	16	18	17
ADVANCE Asia Standard	28	24	26	31	9	4	7	6	20	15	19	21	30	25	29	27	22	10	13	17	0	1	2	3	11	8	12	9	16	14	18	23
ADVANCE Asia Intensive	27	24	26	30	5	4	7	6	23	18	19	22	31	25	28	29	14	12	11	10	3	1	0	2	15	9	8	13	17	16	21	20
ADVANCE EME Standard	29	25	24	26	22	16	14	12	23	15	18	20	31	28	30	27	9	1	11	6	8	4	7	3	13	2	0	5	21	17	19	10
ADVANCE EME Intensive	29	25	24	27	23	19	16	20	22	21	17	18	31	26	30	28	8	1	4	2	15	13	7	11	9	0	3	5	14	6	10	12
ADVANCE Eastern Europe Standard	29	27	24	26	23	20	19	14	22	18	9	10	31	28	30	25	13	5	6	15	11	2	1	3	8	4	7	0	21	16	17	12
ADVANCE Eastern Europe Intensive	29	24	27	28	22	20	17	19	25	18	15	13	31	26	30	23	4	2	3	0	12	10	9	6	8	7	1	5	21	11	16	14
ACCORD BP Standard Therapy	6	10	22	20	0	3	15	14	27	29	31	30	19	13	23	18	5	9	7	16	2	1	12	11	25	24	28	26	4	8	17	21
ACCORD BP Intensive Therapy	11	18	23	22	13	10	21	12	26	28	31	30	20	16	29	24	2	4	14	9	1	3	6	17	15	19	25	27	0	5	8	7
OVERALL MODEL RANKING RESULTS																																
A1c changes	1	1	1	1	1	1	1	1	1	0	0	0	1	1	1	0	1	0	1	1	0	1	0	0	0	0	0	0	0	0	0	0
BMI changes	1	1	1	1	1	1	1	1	1	0	0	0	1	1	1	0	1	0	1	1	0	1	0	0	0	0	0	0	0	0	0	0
BP changes	1	1	1	1	1	1	1	1	1	0	0	0	1	1	1	0	1	0	1	1	0	1	0	0	0	0	0	0	0	0	0	0
Lipid change	1	1	1	1	1	1	1	1	1	0	0	0	1	1	1	0	1	0	1	1	0	1	0	0	0	0	0	0	0	0	0	0
Smoke changes	1	1	1	1	1	1	1	1	1	0	0	0	1	1	1	0	1	0	1	1	0	1	0	0	0	0	0	0	0	0	0	0
MI Equation #	2	1	2	2	1	2	1	1	3	2	2	2	3	3	3	2	4	1	4	4	3	4	3	1	3	1	1	3	4	4	4	4
Stroke Equation #	2	2	3	1	3	4	4	1	2	2	3	4	3	4	1	1	2	2	4	1	1	2	3	4	3	3	4	1	1	2	4	3	1
CHD Death Equation #	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Stroke Death Equation #	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Overall Model Fitness	33.9	34.1	35.3	35.7	35.7	36.1	36.1	36.3	37.7	38.1	39.4	39.6	39.9	40.5	40.8	41.6	42.9	43.7	44.5	44.6	45.0	45.4	45.5	46.3	46.9	47.2	47.6	47.7	51.4	53.4	55.5	55.6

Parameter: BioMarker/State/Treatment



Equations represent observed phenomena and can be combined with hypothesis

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

Allows the model to access more populations and cover more phenomena

Comparisons improve understanding of disease progression

References:
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- You Tube Video - The Reference Model for Disease Progression: Online: http://www.youtube.com/watch?v=7qxPSgINaD8
- J. Barhak, The Reference Model for Disease Progression. Poster presentation, SciPy 2012, Austin Tx, 18-19 July 2012. A paper version is currently under review for SciPy 2012 proceedings and can be accessed publically before publication online: https://github.com/Jacob-Barhak/scipy_proceedings/blob/2012/papers/Jacob_Barhak/TheReferenceModelSciPy2012.rst

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