

**50 Summers of Computer Simulation
(Panel)
Seasons of Disease Modeling**

**Jacob Barhak
Austin, Texas**

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Disease Modeling Time Table

Season	Modeling Focus
1980s+	Markov Models
1995-2004	Risk equations
2000s	Microsimulation & Discrete Event Simulation
2010s	High Performance Computing
2015+	Model and Data Exchange Standards

1980s+ : Markov Models

- Examples:
 - Leff et. Al An LP planning model for a mental health community support system. Management Science
 - JR Beck, SG Pauker - The Markov process in medical prognosis. Medical decision making, Vol. 3 No. 4 , 1983



1995-2004 : Risk Equations

- Examples:
 - Framingham:
 - Wilson P. W. F., D'Agostino R. B., Levy D., Belanger A. M., Silbershatz H. and Kannel W. B. 1998, "Prediction of Coronary Heart Disease Using Risk Factor Categories". Circulation Vol. 97 pp. 1837-1847
 - UKPDS:
 - Stevens R., Kothari V., Adler A., Stratton I., The UKPDS risk engine: a model for the risk of coronary heart disease in type II diabetes UKPDS 56, Clinical Science 2001; 101 671–679
 - V. Kothari, R.J. Stevens, A.I. Adler, I.M. Stratton, S.E. Manley, H.A. Neil, R.R. Holman, Risk of stroke in type 2 diabetes estimated by the UK Prospective Diabetes Study risk engine (UKPDS 60). Stroke 33:1776-1781, 2002. <https://dx.doi.org/10.1161/01.STR.0000020091.07144.C7>

$$P_{Sick} = P_{01} = f(\text{Age}, \text{BP}, \text{Smoke}, \dots, \text{Time})$$

2000s : Microsimulation & Discrete Event Simulation

Examples:

$$P_{Sick} = P_{01} = f(\text{Age}, \text{BP}, \text{Smoke}, \dots, \text{Time})$$



- Microsimulation:

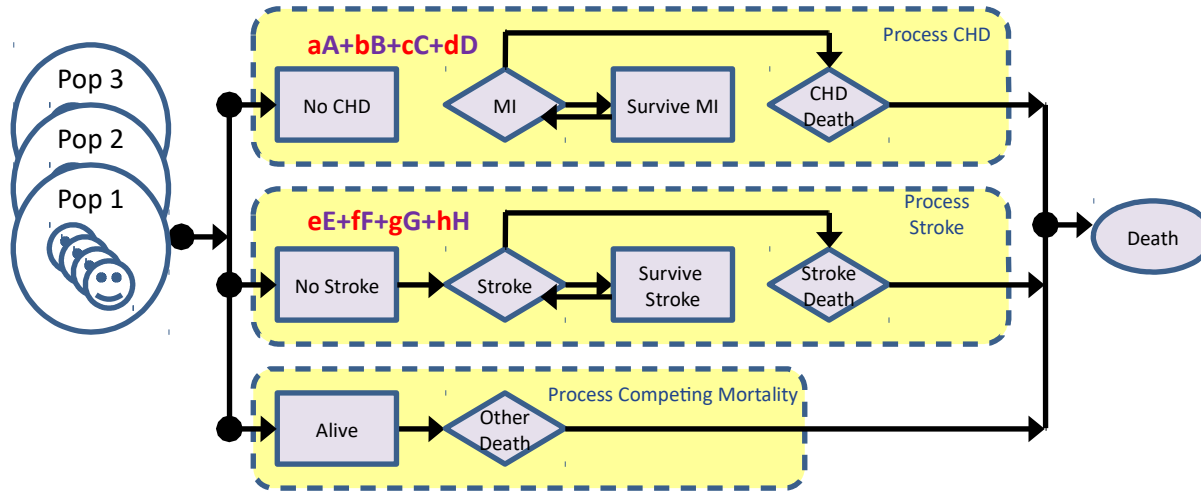
- Clarke P.M., Gray A.M., Briggs A., Farmer A.J., Fenn P., Stevens R.J., Matthews D. R., Stratton I. M., Holman R. R., & UK Prospective Diabetes Study (UKPDS) Group. 2004. A model to estimate the lifetime health outcomes of patients with type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model (UKPDS no. 68). Diabetologia, Vol. 47(10), pp. 1747-59. <http://dx.doi.org/10.1007/s00125-004-1527-z>

- Discrete Event:

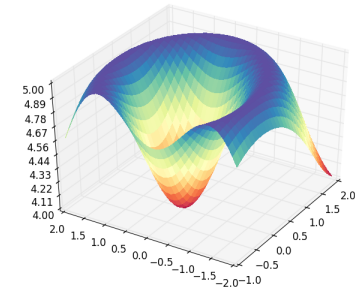
$$\text{TimeEvent}(\text{Sick}) = f(\text{Age}, \text{BP}, \text{Smoke}, \dots, \text{Time})$$

- David M. Eddy, Leonard Schlessinger, Validation of the Archimedes Diabetes Model, Diabetes Care 2003 Nov; 26(11): 3102-3110. <https://doi.org/10.2337/diacare.26.11.3102>
- Schlessinger L., Eddy D.M., Archimedes: a new model for simulating health care systems: the mathematical formulation, Journal of Biomedical Informatics 2002, 35 37-50, [http://dx.doi.org/10.1016/S1532-0464\(02\)00006-0](http://dx.doi.org/10.1016/S1532-0464(02)00006-0)

2010 : High Performance Computing



Eq EH	E	E	E	E	...
Eq AD	A	B	C	D	...
Pop 1	4	6	2	1	...
Pop 2	2	4	6	1	...
Pop 3	2	3	9	2	...
...



- **The Reference Model for Disease Progression**

- The Reference Model for Disease Progression. Online: <https://simtk.org/projects/therefmodel/>
- J. Barhak, The Reference Model: A Decade of Healthcare Predictive Analytics with Python, PyTexas 2017, Nov 18-19, 2017, Galvanize, Austin TX. Video: https://youtu.be/Pj_N4izLmsl

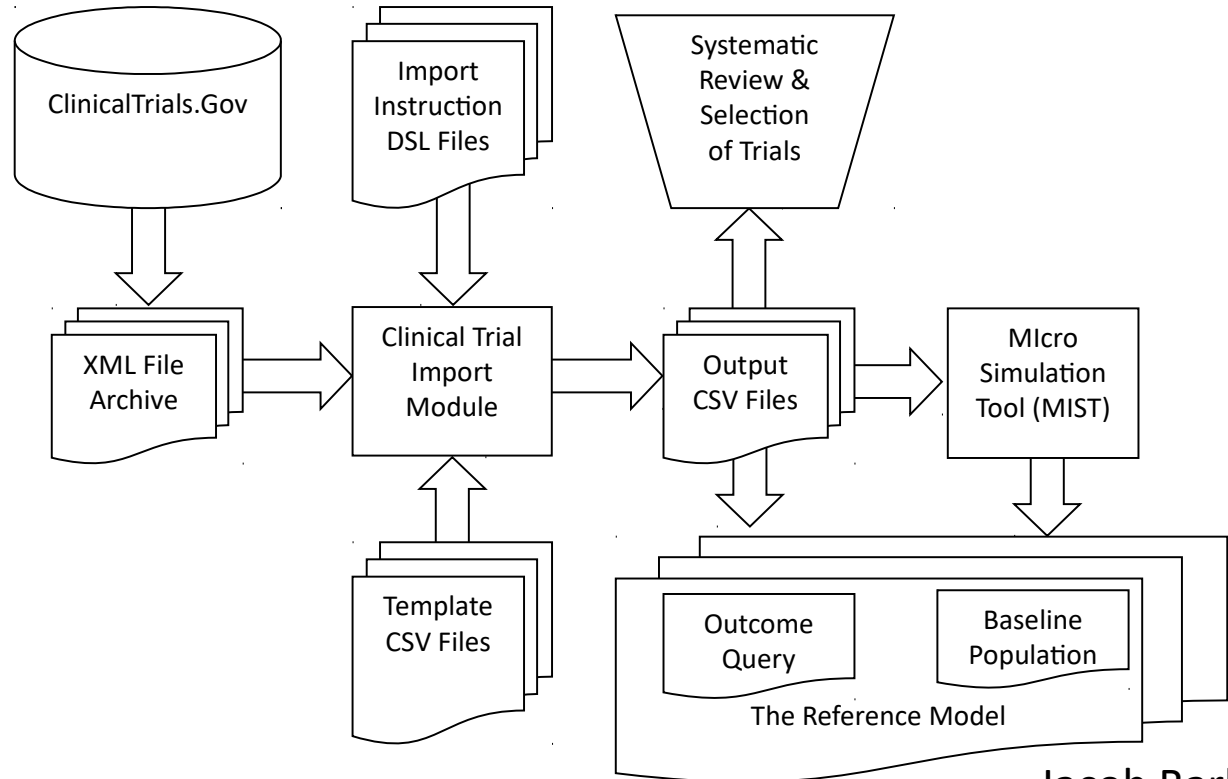
2015+ : Data Exchange

Importing Data from ClinicalTrials.Gov

- Systematic Review

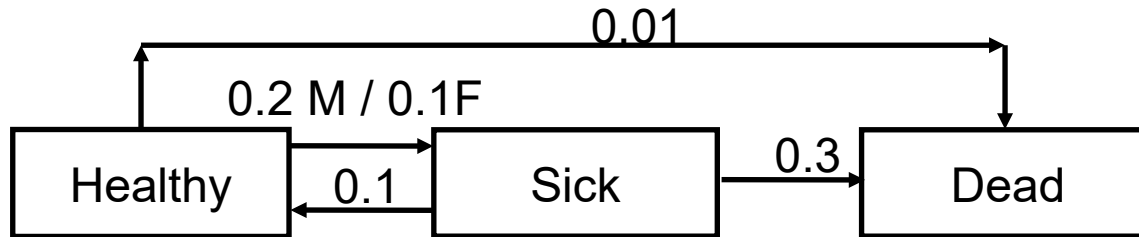
- Import Populations

- Import Outcomes



2015+ : Exchange Standards for Disease Models

SBML / PharmML



- Healthy to Dead: 0.01.
- Healthy to Sick: 0.2 for Male, 0.1 for Female.
- Sick to Healthy: 0.1.
- Sick to Dead: 0.3.

- Initial conditions: Healthy = (50 Male, 50 Female), Sick = (0,0) and Dead = (0,0).
- Output requested: How many men / women are in each disease state for each of the first 10 years?
- Implementation available through GitHub in:
 - MIST : <https://github.com/Jacob-Barhak/SharingDiseaseModels/blob/master/Example3.zip>
 - Tellurium : <https://github.com/Jacob-Barhak/SharingDiseaseModels/blob/master/Example3.py>
 - Rule Bender : <https://github.com/Jacob-Barhak/SharingDiseaseModels/blob/master/Example3.bngl>
 - PharmML : https://github.com/Jacob-Barhak/SharingDiseaseModels/blob/master/categorical_MARKOV3.xml
 - SBML : <https://github.com/Jacob-Barhak/SharingDiseaseModels/blob/master/Example3.xml>

Slide from Joint work
L. Smith, M. J. Swat, J. Barhak
“Sharing Formats for Disease Models”
SummerSim 2016

2015+ : SBML/PharmML Basics

- XML based exchange formats
 - SBML = Stands for Systems Biology Markup Language
 - Supported by 290 tools
 - Extensions are possible through packages
 - Used by 8460 models in BioModels.net
 - Web Site: http://sbml.org/Main_Page
 - PharmML = Pharmacometrics Markup Language
 - Developed by the Drug Disease Model Resources (DDMoRe) consortium
 - Newer format tailored towards specific medical models
 - Web Site: <http://www.pharmml.org/>

Questions?

Jacob Barhak

<http://sites.google.com/site/jacobbarhak/>

