Pharmocogenetics, Clinical Avatars and Predictions of Personalized Medicine

Progress on a 2009 ARRA EUREKA Award
Method and model development
Exploratory simulations and analysis
Preliminary results

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cbmi

National Library of Medicine
Nov 2009

Harvard Medical School

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A Biomedical Informatics Perspective:

- A Few Preliminaries
  - 'Square peg in a round hole'
  - Modified approach to 'translational' research
  - Platform for translational research
- Method and Clinical Avatars
- Tools and Preliminary Results

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Square Peg – Round Hole

Pharmacogenetic POC

- Anticoagulant drug with narrow therapeutic window
- Used in wide array of conditions → diverse patient population
- Individualized prescription
- Requires careful patient monitoring
  - Patient's International Normalized Ratio (INR) instrumental in maintaining therapeutic Warfarin dose
  - Genetic markers used to determine which patients are predisposed to slower or faster than 'normal' Warfarin absorption rates

Background

- Highly effective and commonly prescribed anticoagulant
  - 2 million warfarin users annually
  - 30 Million prescriptions annually
- One of the most common causes of serious adverse drug reaction (ADR)
- CYP2C9 and VKORC1 genotypes account for up to 60% of the variability in dose recommendations
  - Over 50% of dose variance attributed to personal health profile factors including genetic, gender, age, ethnicity, race, weight/height, and current drug regimen factors
  - Nomograph modifications emerging – Currently seven actively recruiting studies registered in clinicaltrials.gov (Florida, Intermountain, Hadassah, National Taiwan, Creighton, Brigham and Womens, Marshfield)
  - Brian Gage, Wash U., indicates as few as 40 patients can be used to modify algorithm (warfarindosing.org), personal communication with Matt Tector.
- *If all warfarin patients' dosage adjusted to genotype*:
  - 85,000 bleeding events avoided
  - 17,000 strokes avoided
  - Results in $1.1 Billion health care costs savings
    - AEI-Brookings Study: Health Care Savings from Personalizing Medicine Using Genetic Testing: The Case of Warfarin

Pharmacogenomic Labeling

FDA News

FOR IMMEDIATE RELEASE
August 16, 2007

Media Inquiries:
Karen Riley, 301-827-6242
Consumer Inquiries:
888-INFO-FDA

FDA Approves Updated Warfarin (Coumadin) Prescribing Information

New Genetic Information May Help Providers Improve Initial Dosing Estimates of the Anticoagulant for Individual Patients

The U.S. Food and Drug Administration announced today the approval of updated labeling for the widely used blood-thinning drug, Coumadin, to explain that people's genetic makeup may influence how they respond to the drug.

Manufacturers of warfarin, the generic version of Coumadin, are to add similar information to their products' labeling, FDA said.

The labeling change highlights the opportunity for healthcare providers to use genetic tests to improve their initial estimate of what is a reasonable warfarin dose for individual patients. Testing may help optimize the use of warfarin and lower the risk of bleeding complications from the drug.

These labeling updates are based on an analysis of recent studies that found people respond to the drug differently based, in part, on whether they have variations of certain genes.

FDA estimates that 2 million persons start taking warfarin in the United States every year to prevent blood clots, heart attacks and stroke. Warfarin is a difficult drug to use because the optimal dose varies and depends on many risk factors including a patient's diet, age, and the use of other medications.

Patients who take a dose larger than they can tolerate are at risk of life-threatening bleeding. Those who receive too low a dose are at risk of equally dangerous blood clots. Dosing is particularly important at the beginning of therapy, when problems in adjusting the dose can lead to complications such as bleeding.

Warfarin is the second most common drug – after insulin –implicated in emergency room visits for adverse drug events.

Physicians and other health care professionals who prescribe warfarin regularly check to see if the drug is working properly by ordering a test called the PT or prothrombin time that evaluates the blood's ability to clot properly. The results are measured in seconds and compared with the expected value in healthy people, known as the International Normalized Ratio or INR.

"Today's approved labeling change is one step in our commitment to personalized medicine. By using modern science to get the right drug in the right dose for the right patient, FDA will further enhance the safety and effectiveness of the medicines Americans depend on," said Commissioner of Food and Drugs Andrew C. von Eschenbach, M.D.

The FDA's "personalized medicine" initiative makes use of pharmacogenomics—the science that predicts a response to drugs based upon a person's genetic makeup. This effort supports the personalized health program spearheaded by Health and Human Services Secretary Mike Leavitt.

A person's genes "encode" enzymes and differences in the sequence of a gene can cause differences in enzyme activity or sensitivity. That is why different people process the same drug differently.

One-third of patients receiving warfarin metabolize it quite differently than expected. Research has shown that some of the unexpected response to warfarin depends on a patient's variants of the genes CYP2C9 and VKORC1.

"Although genetic testing can currently identify who has these genetic variants, more studies are needed to explore the precise starting dose for these patients," said Larry Lesko, Ph.D., director of the FDA's Office of Clinical Pharmacology. "FDA has been working with other government agencies and organizations to develop such studies under the auspices of our three-year-old Critical Path Initiative, which addresses the challenges of moving promising medical products from discovery to patient use."

FDA's Critical Path Initiative has funded a research project with the University of Utah and the Critical Path Institute of Tucson, Ariz., to develop genetically based instructions for warfarin dosing. The Initiative has also facilitated meetings and planning with the National Heart, Lung and Blood Institute for a clinical trial that will study warfarin dosing based on genetic test information and is helping to pay for another clinical study being conducted by Harvard Partners that will derive personalized warfarin dosing algorithms for patients new to the drug.

The dosage and administration of warfarin must be individualized for each patient according to the particular patient's PT/INR response to the drug. The specific dose recommendations are described in the warfarin product labeling, along with the new information regarding the impact of genetic information upon the initial dose and the response to warfarin. Ongoing warfarin therapy should be guided by continued INR monitoring.

Bristol-Myers Squibb Co. of Princeton, N.J., is the manufacturer of Coumadin.

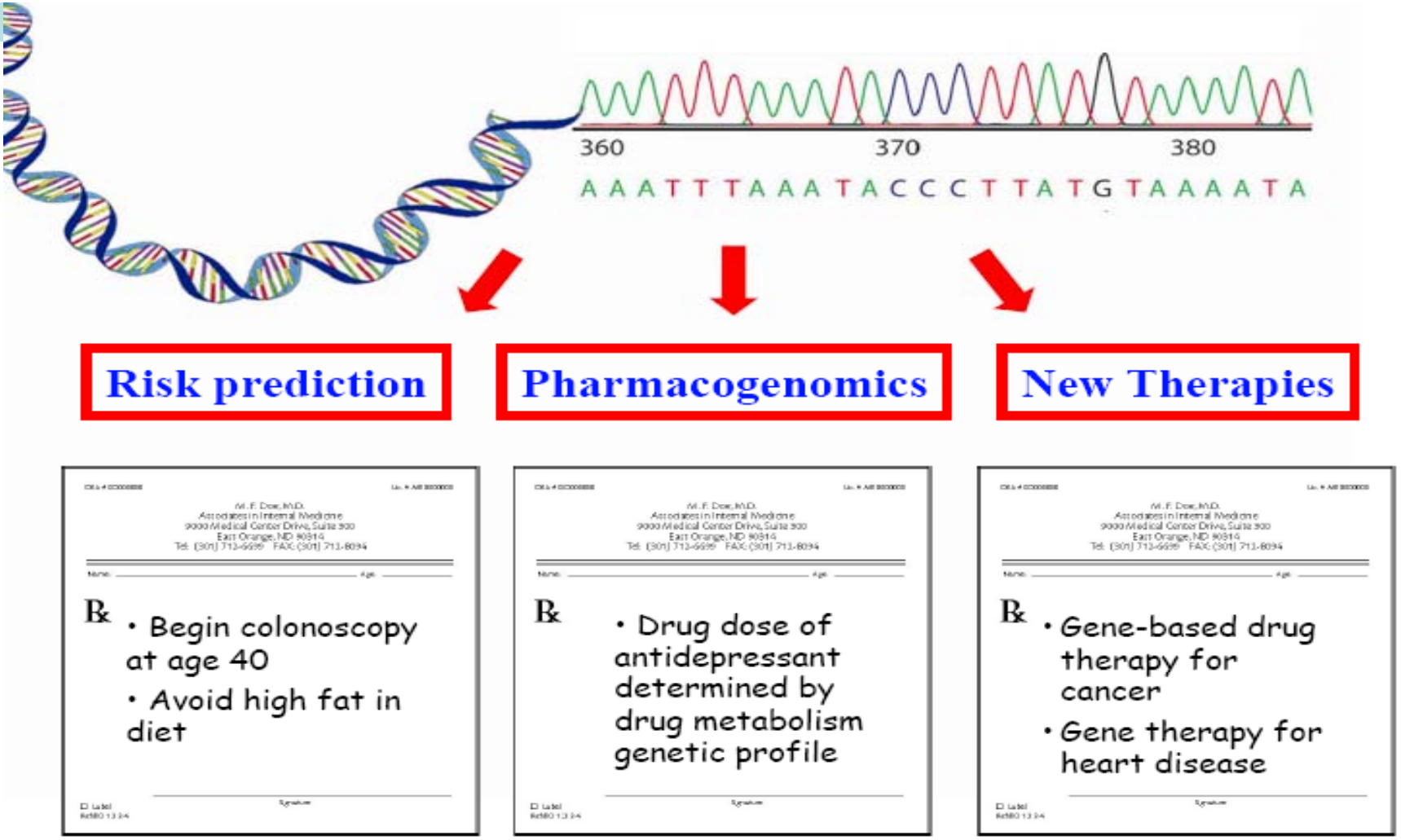
For more information see New Labeling Information for Warfarin.

August 16, 2007 – "In Milestone, FDA Pushes Genetic Tests Tied to Drug … warfarin's label will carry new information describing the role of genetics in dosing. The label will say that a lower initial warfarin dose 'should be considered for patients with certain genetic variations.'"

- *The Wall Street Journal*

"This information will benefit patients because it will describe why patients with a variation in the CYP2C9 and/or VKORC1 genes may need a lower warfarin dose than patients with the usual forms of these genes."

- *U.S. Food and Drug Administration*



From - Personalized Medicine – How the Human Genome Era Will Usher in a Healthcare Revolution
Francis S. Collins, M.D., Ph.D., Director, NHGRI February 10, 2005

POINTONE®

Congestive Heart Failure - Care Management Report

07/17/2006 **Provider: Dr. Wen Morrison**

Emily Robards
123 West Main Street, Any City, WI 12345
Phone: 123-456-7890

Alert	**Patient Status**	**Standard of Care**
Evaluate appropriate warfarin dosage. Patient at increased risk to warfarin complications	**CYP2C9*2 HET** **CYP2C9*3 HET**	Today's Algorithm: Patient's estimated initial warfarin dose: **?.? mg / day**

Pharmacogenetic Summary: Warfarin Translational Study

No associated genotyping data available for this subject.

Utilization Status

# CHF Hospital Stays (past 12 months) :	0	# Hospital Stays (past 12 months) :	0
# CHF ER Visits (past 12 months) :	0	# ER Visits (past 12 months) :	0
# Outpatient Visits (past 12 months) :	5	# Comorbid Conditions :	5

Past Medical History

Arrhythmias
Atrial Fibrillation and Flutter
Hypertension
Arrhythmias or Blocks - Ventricular
Depression
Thyroid Disease

Wisconsin Demonstration Project:

Optimized Warfarin Dosing with Genetic-Based Predictive Dose Algorithms

Aurora Health Care Patient Totals

Electronic data available for over 3,000,000 patients

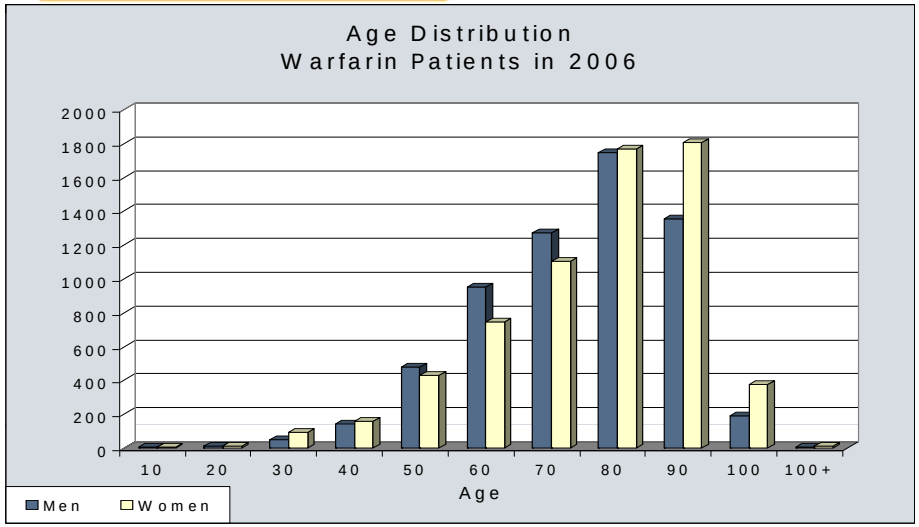
Warfarin Usage

Aurora Warfarin Usage Summary				
	2006		2007	
# of Patients by:	Actual	Est.	Actual (YTD)	Est.*
Warfarin Usage		➢ 25,000		➢ 30,000
Warfarin Usage & Stroke		➢ 1,500		➢ 2,000
Warfarin Usage & Thrombotic Event		➢ 3,000		➢ 4,000
Evidence of Warfarin Usage & INR > 3.0		➢ 10,000	Not Available	

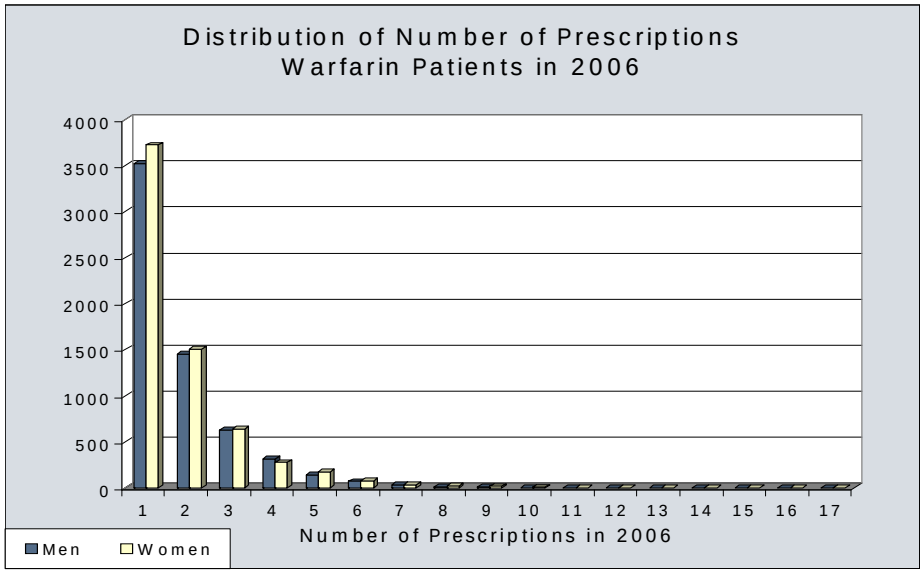
Estimated values extrapolated based on analysis of sampled data.
* 2007 Actual values through Aug. Est. values adjust for entire year.

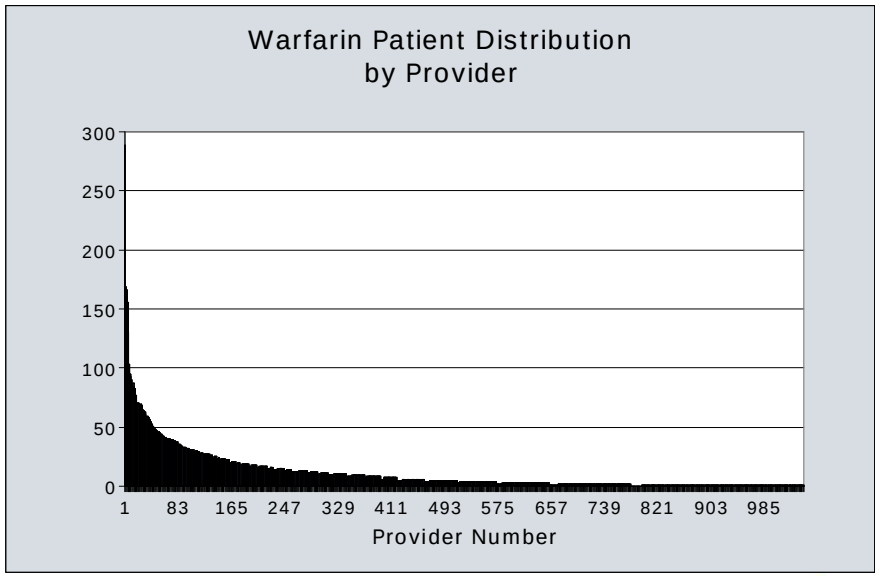
WISCONSIN
Warfarin Collaboration

Distribution of Warfarin Patients



- Gender matched age distribution
- Difficult to capture longitudinal complexity of dosing (analysis ongoing)
- 49% of patients seen by 100 Physicians
- High percentage of patients related to orthopedics
- Orthopedics focus in early rollout





Aurora Health Care

POINTONE

Wisconsin Demonstration Project:

Optimized Warfarin Dosing with Genetic-Based Predictive Dose Algorithms

Project was **not** approved:

- Healthcare practice remained skeptical – insufficient evidence that gene testing and algorithms were sufficiently valuable

- Educational issues with healthcare staff – what are genotypes?

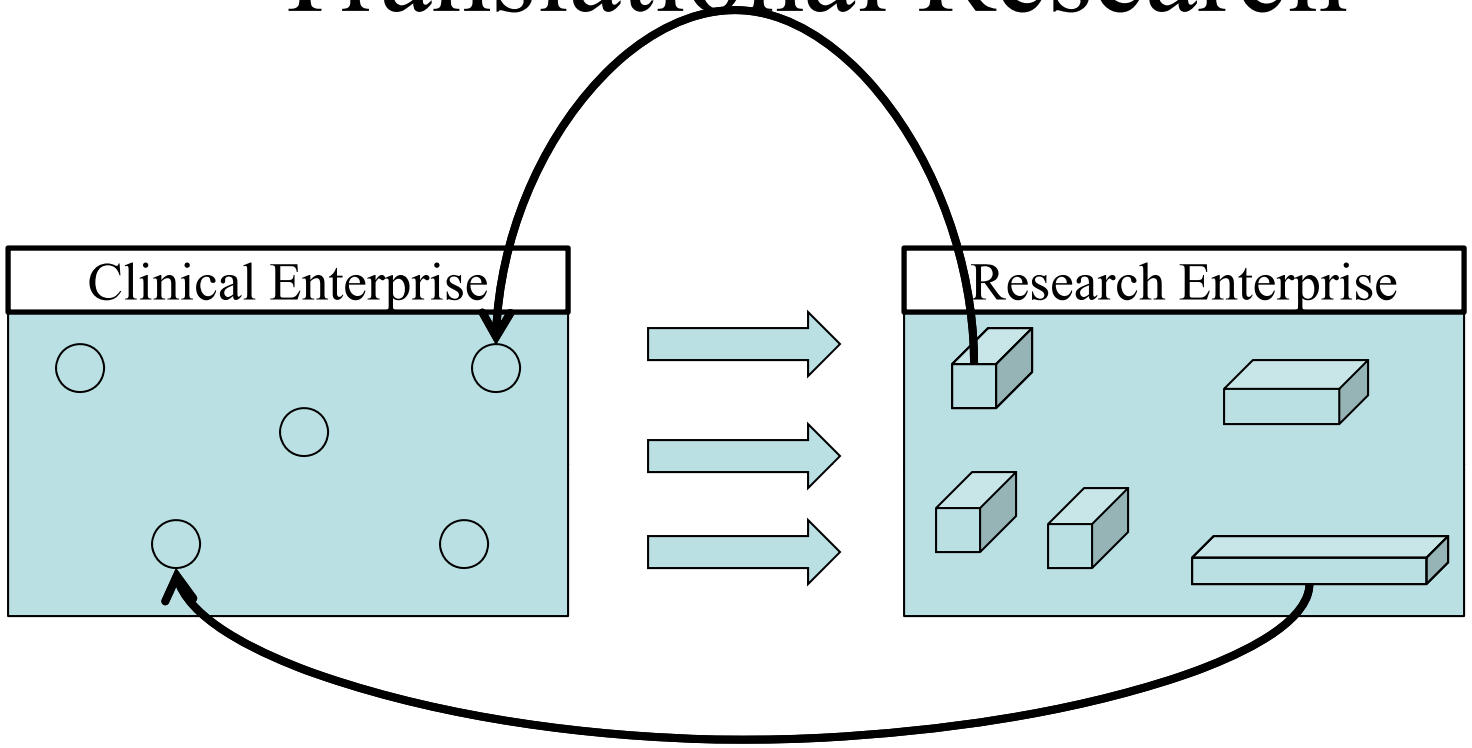
- Technology was premature and 'square peg' like compared to best practice devices.

- Access to and quality of EMR data problems.

- A level of patient reluctance

- Cost

Translational Research

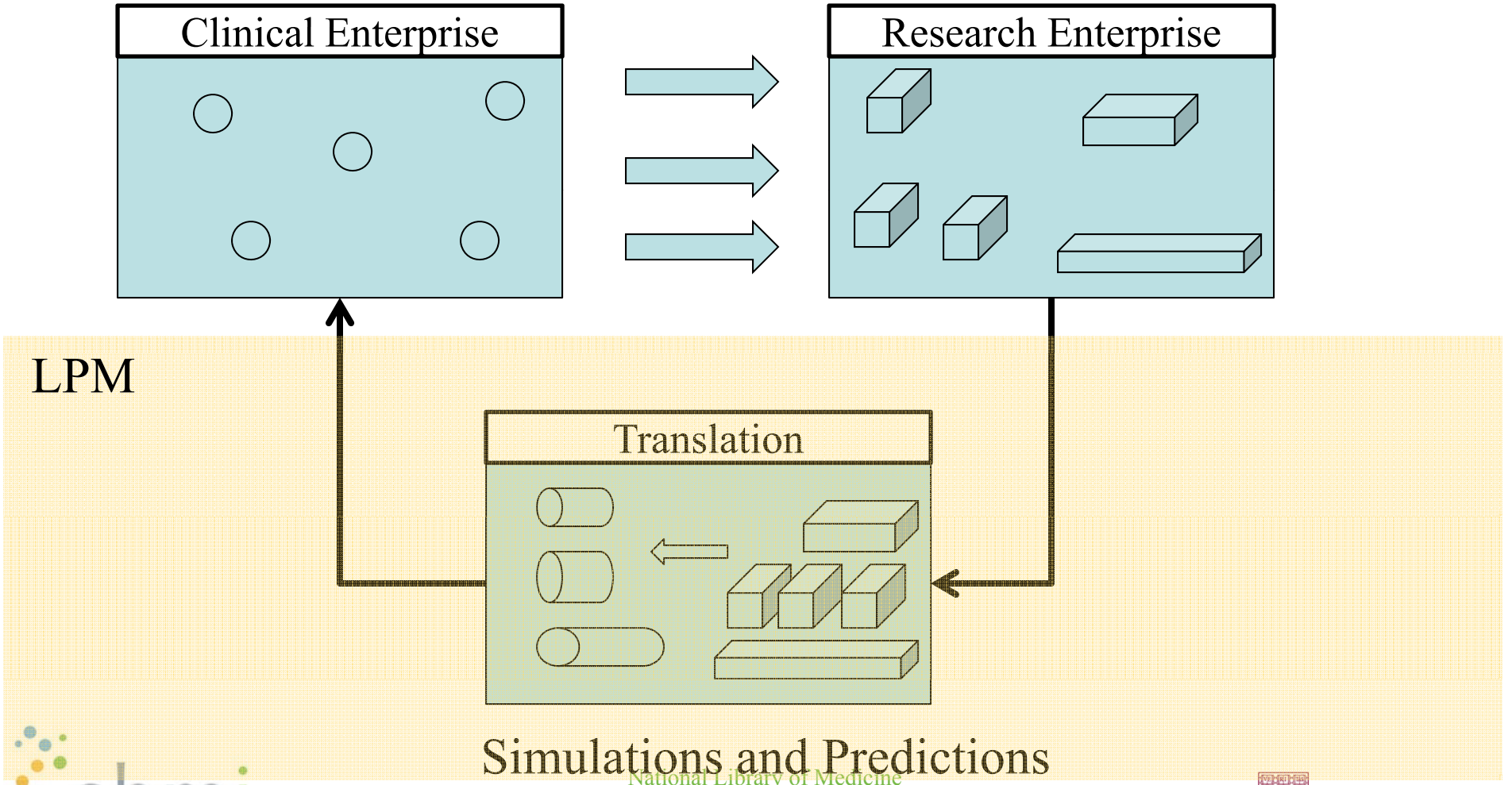


Round holes arise in clinical setting

Square Pegs derived from basic research

Translation emerges from Commercial R&D and Regulatory Approval process followed by clinical implementation

Translational Research



Platform for Translational Research

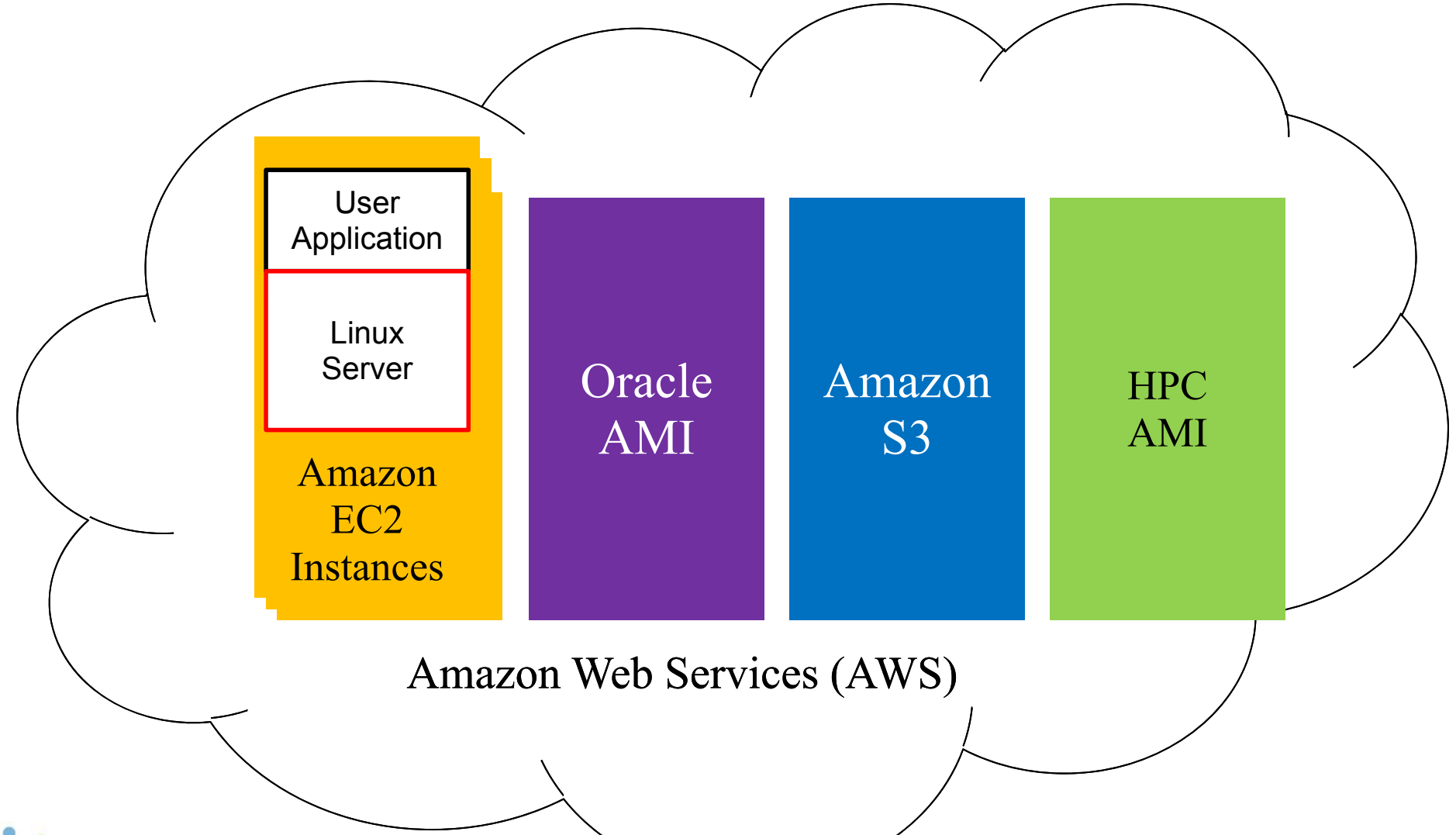
Objective: Create low cost, low administrative footprint Computational Center under typical "academic" and current technical and resource constraints:

- Tremendous Project diversity (scientific, complexity and computationally)
- Multiple project sites
- Multiple US and non-US collaborative project teams
- Diversity of IT experience
- Varying levels of project team access/ resource control
- Limited Resources: Time, AWS services, Administration

Focus: Research objective

IT issues are considered distractions.

Cloud Computing



Experiment: Spring of 09

lpm.hms.harvard.edu/palaver

Participants in the 'Clouded Translational Research' seminar will conduct a series of exercises in biomedical discovery and translational science using cloud computing technology. Participants represent Harvard, Children's Hospital of Boston, Brigham and Women's Hospital, Beth Israel Hospital, Mass General, the Broad Institute, two University of Wisconsin campuses (Madison and Milwaukee) and the Tokyo Medical and Dental University and will learn about and implement databases, analysis tools and web application development environments using the Amazon cloud computing environment – AWS (aws.amazon.com/).

pa·lav·er

lpm.hms.harvard.edu/palaver

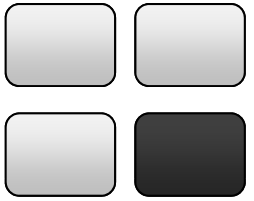
/pə lævər, - lɑvər/ noun

1. long parley usually between persons of different cultures or levels of sophistication
2. conference, discussion
3. idle talk
4. misleading or beguiling speech

LPM Project Breakdown/ Categories

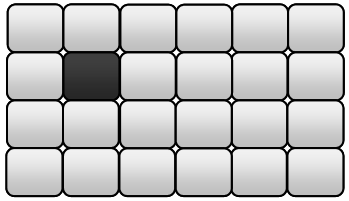
LPM Inelastic

- Clinical Avatars Project Development
- i2b2 AMI Development
- Clinicalpedia



LPM Managed Elastic

- Clinical Avatars Web Deployment
- i2b2 Federated Queries
- NGS RNA Algorithm Testing



LPM Elastic

- RoundUp
- SNP/Array/proteomic pipelines
- NGS Individualized Whole Genome Mapping

Best Practice Cloud Management

AWS/RightScale Main Account

Project Deployment

Server Configuration

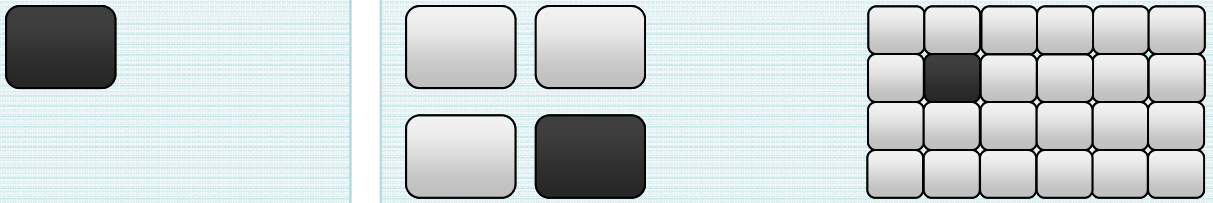
SSH Key Pair

RightScale Sub Account

Project Deployment

Server Configuration

RightScale SSH

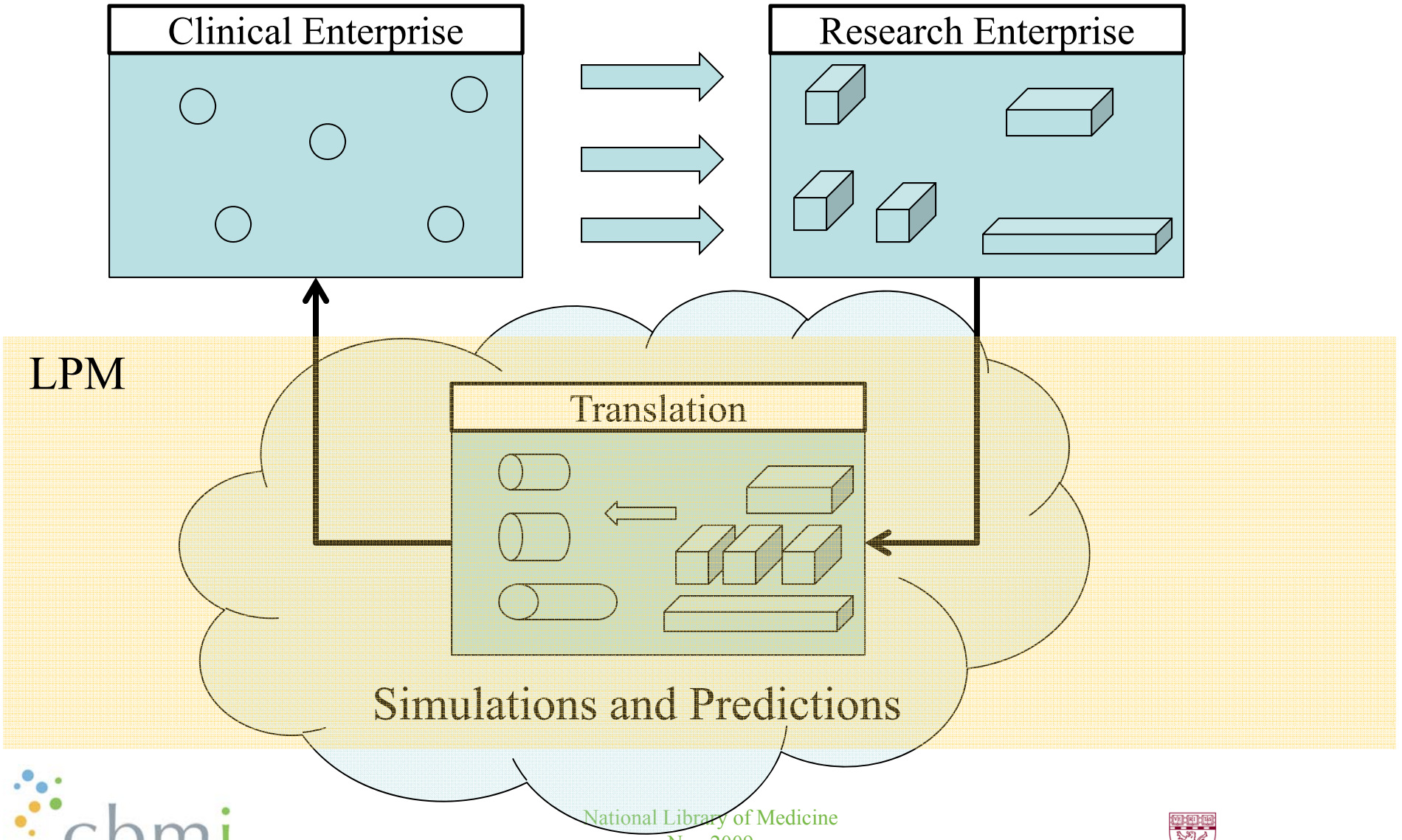


Inelastic *Managed Elastic* *Elastic*

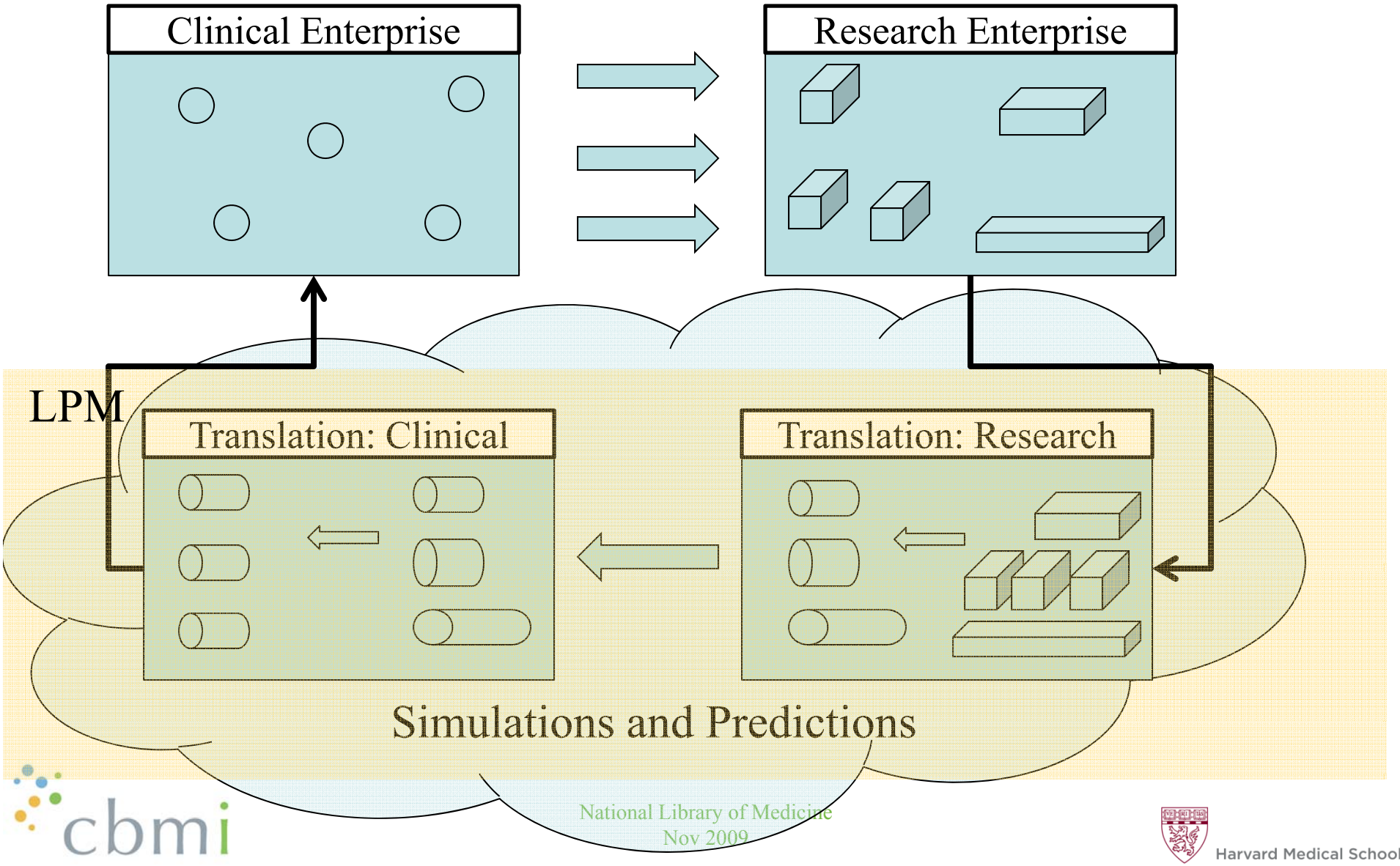
Best Practice Components

- Method to ‘break down’ and categorize projects
- Process to allocate and monitor resources
- Scripts to control applications
  - Shutdown
  - ’cold’ storage (AMI)
  - GITHUB: basecode, database, data, shutdown/startup
  - ‘hot’ start
- Method for coordinating project tasks/activity
- Methods (evolving) for porting ‘highly’ elastic applications.

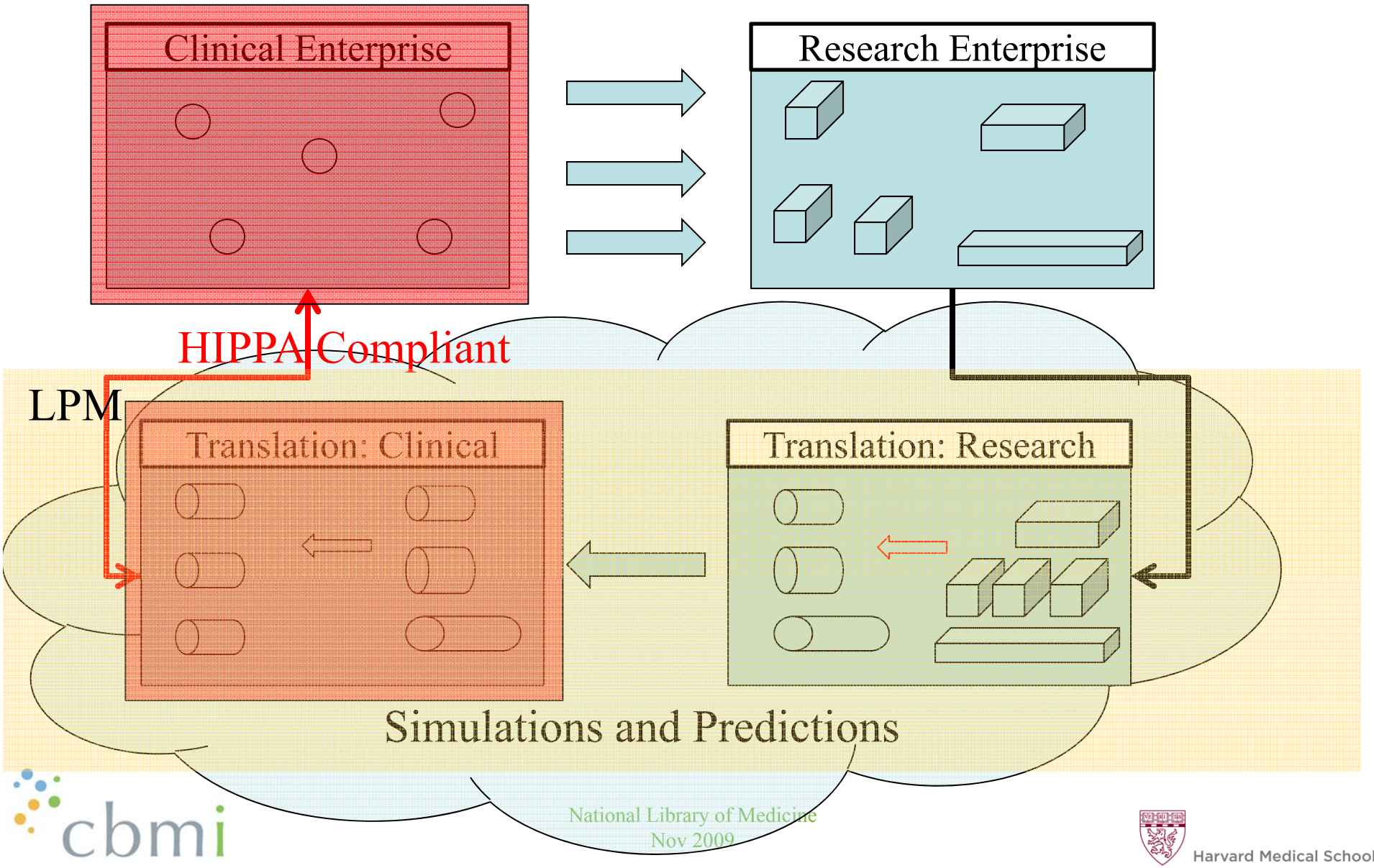
Clouded Translational Research



Clouded Translational Research



Clouded Translational Research



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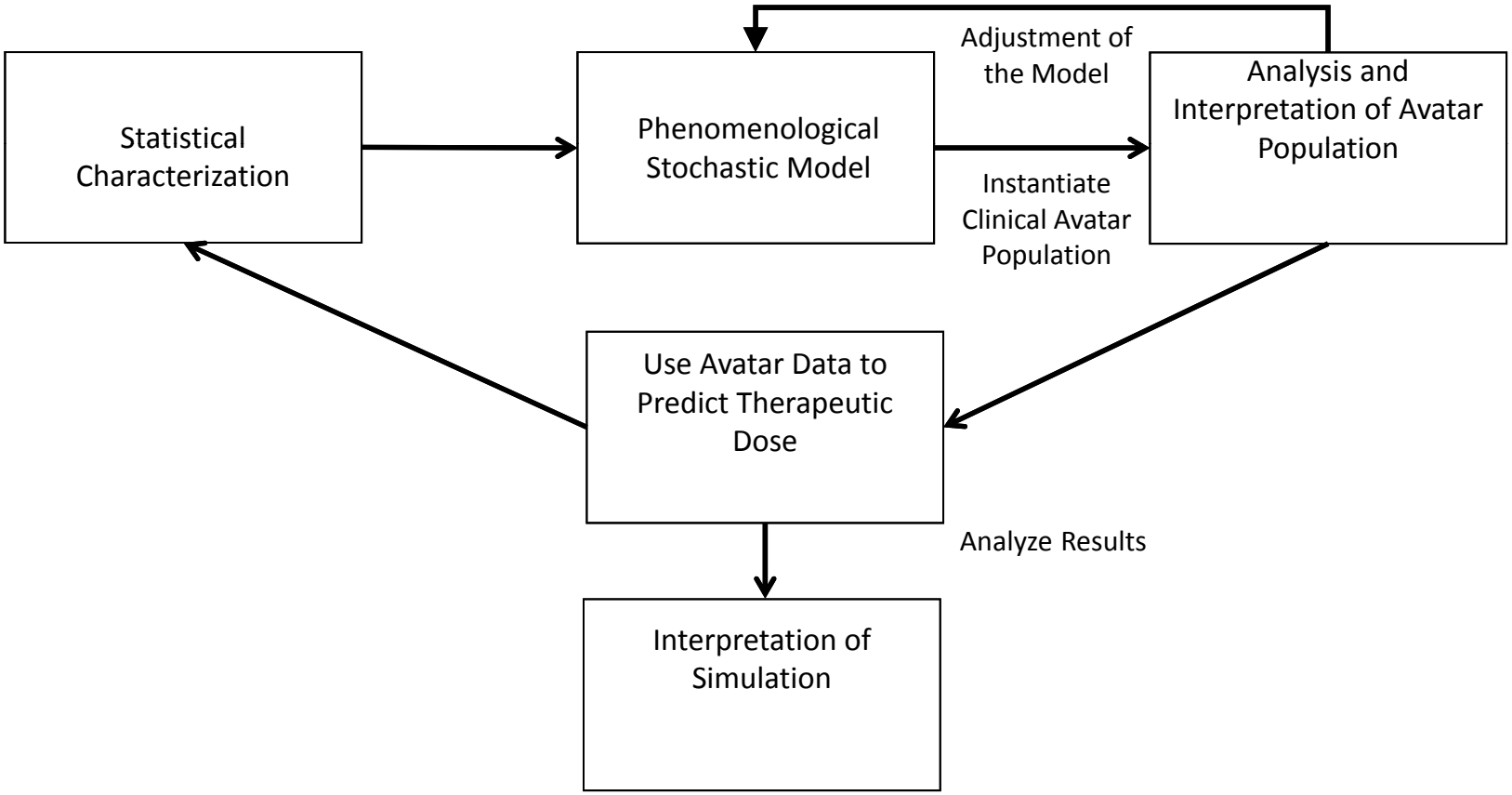
Warfarin Pharmacogenetic Modeling Method: V 1.0



Algorithms – Gage Model

Dose = exp[0.9751 − 0.3238 × v(y) + (0.4317 × BSA) - 0.4008 × c_3(y) − (0.00745 × age) − 0.2066 × c_2(y) + (0.2029 × target INR) − (0.2538 x Amiodarone use) + (0.0922 × Smokes) - (0.0901 × African-American race) + (0.0664 × DVT/PE)]

v(y) = { 0 if VKORC1 -1639 genotype = G/G
{ 1 if VKORC1 -1639 genotype = G/A
{ 2 if VKORC1 -1639 genotype = A/A

c_2(y) = { 0 if CYP2C9*2 genotype = C/C
{ 1 if CYP2C9*2 genotype = C/T
{ 2 if CYP2C9*2 genotype = T/T

c_3(y) = { 0 if CYP2C9*3 genotype = A/A
{ 1 if CYP2C9*3 genotype = A/C
{ 2 if CYP2C9*3 genotype = C/C

Amiodarone use:
1 if taking, 0 otherwise

African-American race:
1 if AA, 0 otherwise

Smokes: 1 if yes

DVT/PE: 1 if present

Gage B, Eby C, Johnson J, Deych E, Rieder M, Ridker P, et al. Use of Pharmacogenetic and Clinical Factors to Predict the Therapeutic Dose of Warfarin. Clin.Pharmacol.Ther. 2008 Feb 27.

Algorithms – Anderson Model

$$\text{Dose} = 1.64 + \exp[3.984 + c(x) + v(x) + g(x) - \text{age}*(0.009) + \text{weight}*(0.003)]$$

$$c(x) = \begin{cases} 0 & \text{if genotype = CYP2C9*1/*1} \\ -0.197 & \text{if genotype = CYP2C9*1/*2} \\ -0.360 & \text{if genotype = CYP2C9*1/*3} \\ -0.947 & \text{if genotype = CYP2C9*2/*3} \\ -0.265 & \text{if genotype = CYP2C9*2/*2} \\ -1.892 & \text{if genotype = CYP2C9*3/*3} \end{cases}$$

$$v(x) = \begin{cases} 0 & \text{if VKORC1 1173 genotype = C/C} \\ -0.304 & \text{if VKORC1 1173 genotype = C/T} \\ -0.569 & \text{if VKORC1 1173 genotype = T/T} \end{cases}$$

$$g(x) = \begin{cases} 0 & \text{if gender = female} \\ 0.094 & \text{if gender = male} \end{cases}$$

1. Anderson JL, Horne BD, Stevens SM, Grove AS, Barton S, Nicholas ZP, et al. Randomized trial of genotype-guided versus standard warfarin dosing in patients initiating oral anticoagulation. Circulation 2007 Nov 27;116(22):2563-2570.

Clinical Avatars (Model data set structure)

Variable(s)	Parameters
Age	18 to 24 (21.1%), 25 to 44 (30.3%), 45 to 64 (21.9%), 65 to 94 (26.7%)
Gender	Male {< 18 (51.26%), 18 to 24 (51.11%), 25 to 44 (50.06%), 45 to 64 (48.65%), 65 and over (41.18%)}; Female {< 18 (48.74%), 18 to 24 (48.89%), 25 to 44 (49.94%), 45 to 64 (51.35%), 65 and over (58.82%)}
Race	White (75.1%), African American (12.3%), Native American (0.9%), Asian (3.6%), Pacific Islander (0.1%), Other (5.5%), Unknown (2.5%)
Height	Mean: 69.2", St.D: 6.6", Min : 56.0", Max: 82.4"
Weight	Mean: 189.8 lb, St.D: 59.1 lb, Min: 71.6 lb, Max : 308.0 lb
Smoker	White - 20%; African American - 21%; Native American - 35%; Asian / Pacific Islander - 11%; Other - 23%
Amiodarone	Y - 55%, N - 45%
DVT	Y - 26.8% N - 73.2%
VKORC1	A/A - 65%, A/B - 20%, B/B - 15%
CYP2C9	*1/*1 - 64.3%, *1/*2 - 18%, *1/*3 - 11.7% , *2/*2 - 2% , *2/*3 - 2.1% , *3/*3 - 0.25%

The clinical avatar population and the resulting variables and statistical distributions.

Simulated Patient Populations

- Created to reflect actual population-wide and individual demographic, clinical, and laboratory characterizations
- Rapid simulation analysis of a wide selection of patient population scenarios
- Simulations produce predictive evidence
- Evidence suggests most informative studies/trials.

Clinical Avatars

Human

PHI	First Name: Ozzy Last Name: Osborne
Physical	Height: 6’ Weight: 160
Genetic	CYP2C9: *1/*1 VKORC1: A/A

Avatar

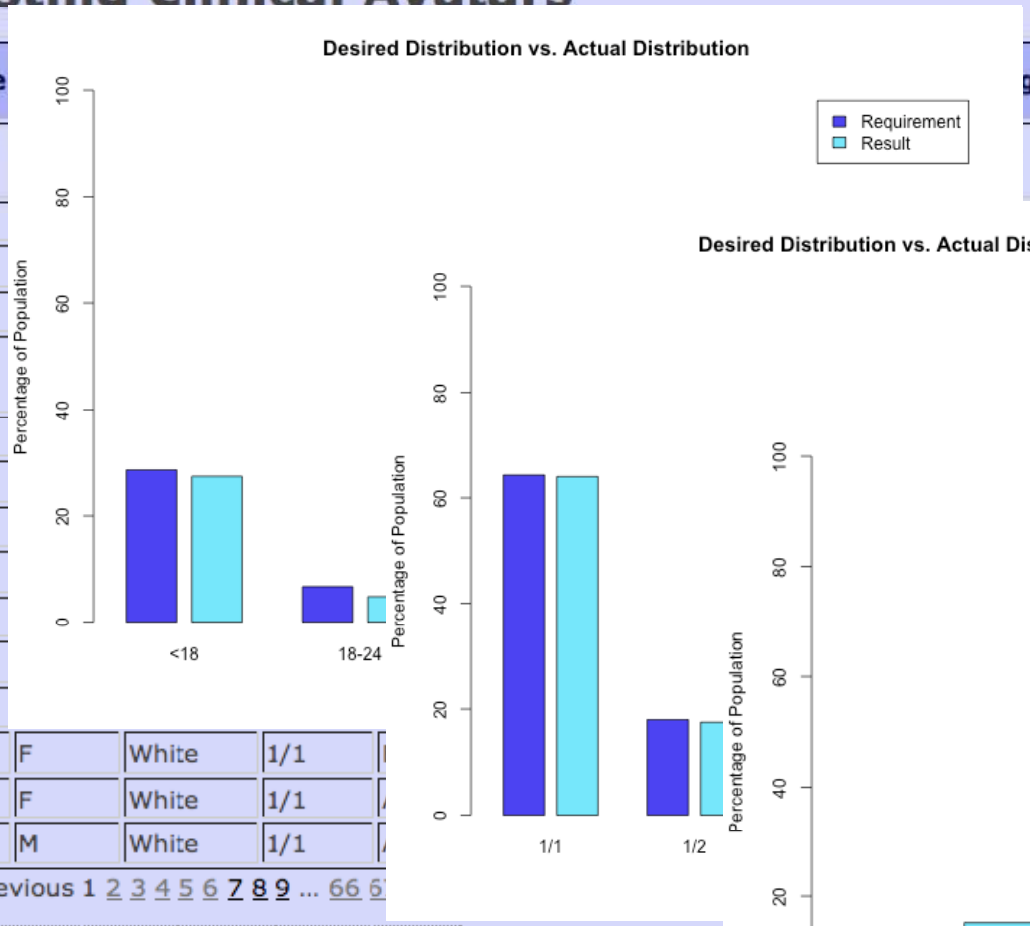
PHI	First Name: Animal Last Name: House
Physical	Height: 6’ 6” Weight: 180
Genetic	CYP2C9: *3/*3 VKORC1: A/B

http://localhost:3000/

take screenshot in

Most Visited | Latest Headlines | Rails | R | Git | Email | LPM | Decision Trees | Harvard | AWS

Listing Clinical Avatars



Age				ght	Amiodarone	Gage Dose	Anderson Dose	WSI			
86					N	2.3	2.9	0.547852	Show	Edit	Destroy
36								0.35013	Show	Edit	Destroy
14								0.350399	Show	Edit	Destroy
17								0.191282	Show	Edit	Destroy
13											estroy
29											estroy
37											estroy
14											estroy
27											estroy
72											estroy
52											estroy
42											estroy
16	F	White	1/1								estroy
15	F	White	1/1								estroy
16	M	White	1/1								estroy

« Previous 1 2 3 4 5 6 7 8 9 ... 66 6

Generate Avatar Population/Doses/Charts

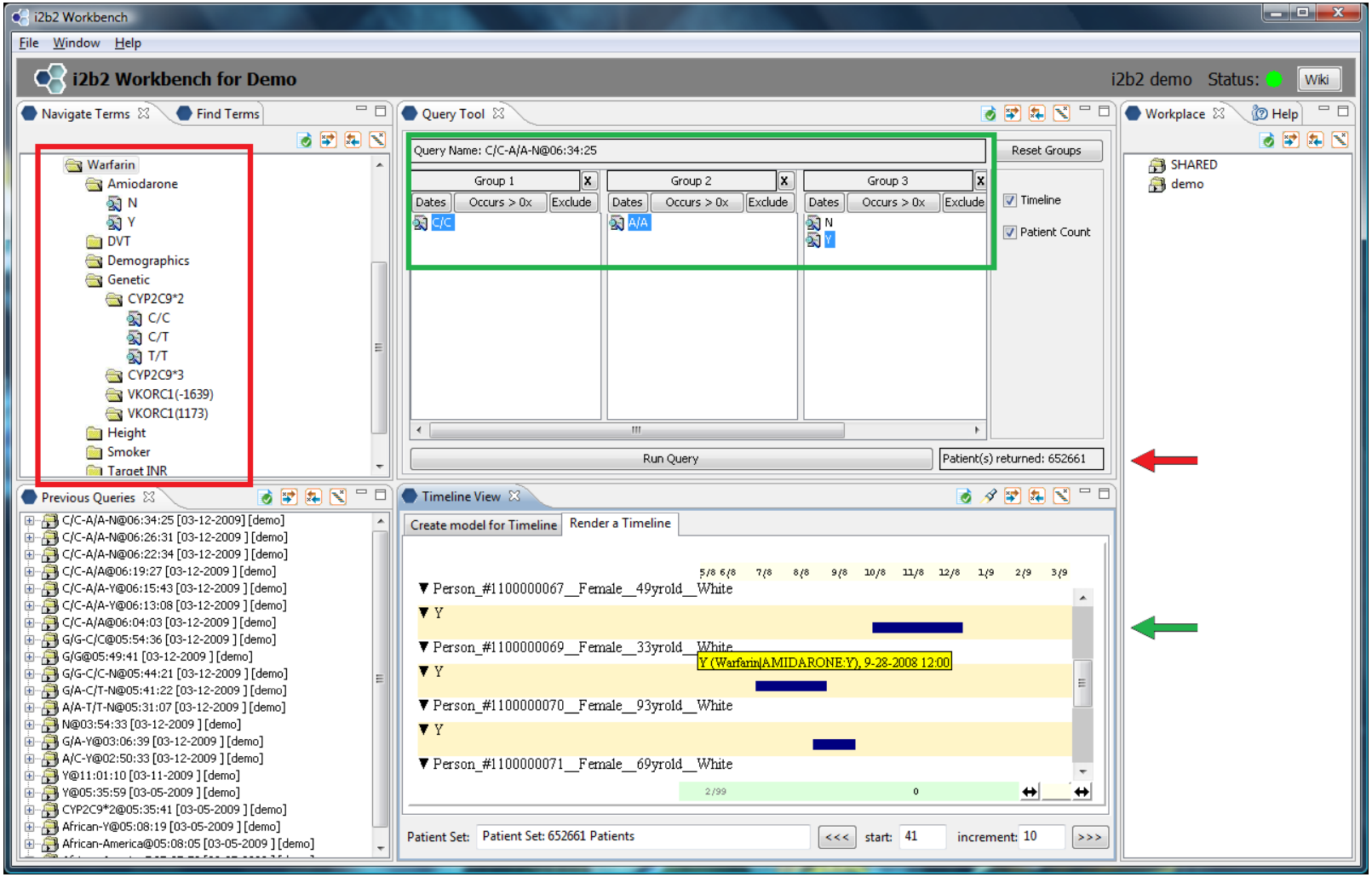
Charts

Import Avatars

R Statistics

LPM Homepage

The i2b2 use Map.



. **i2b2 workbench screenshot with:**

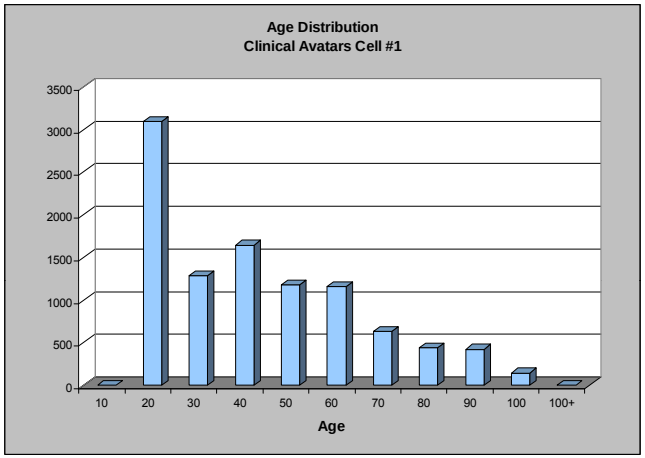
Warfarin specialty-focused ontology (top left, red box).

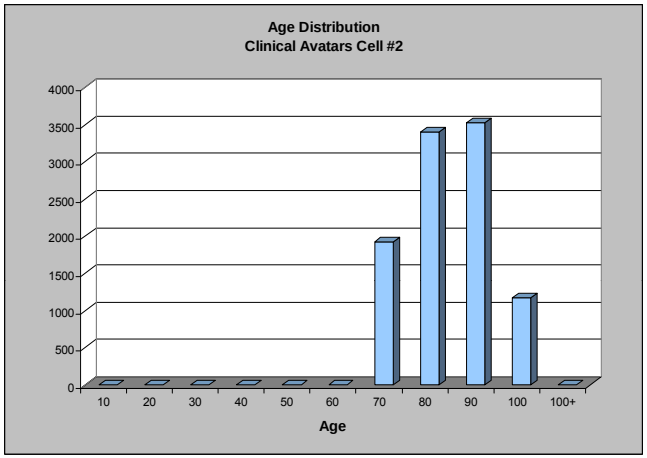
Query including genetic criteria (top middle, green box).

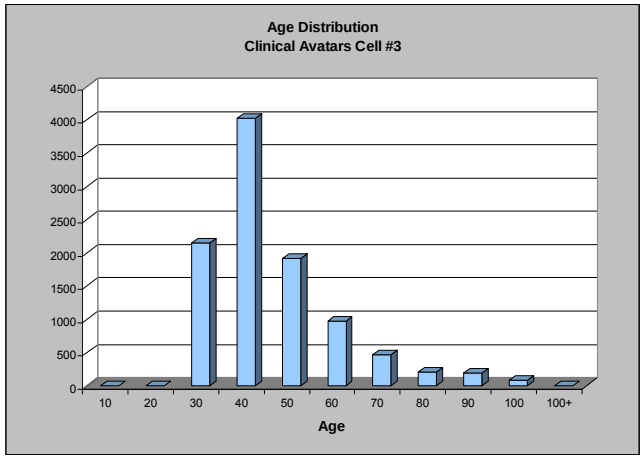
Number of patient 'avatars' (middle right, red arrow).

Selection of avatars that meet the criteria and one avatar's amiodarone usage timeframe (bottom center, green arrow).

Three Age Structured CA Populations (I2B2 SHRINE Test)







Clinical avatar populations were simulated for three i2b2 cells, each with a population of 10,000 avatars

Each cell contains different distributions of Age (blue columns), Gender, Race, Genotype, BMI, Smoker, Amiodarone Use, etc.

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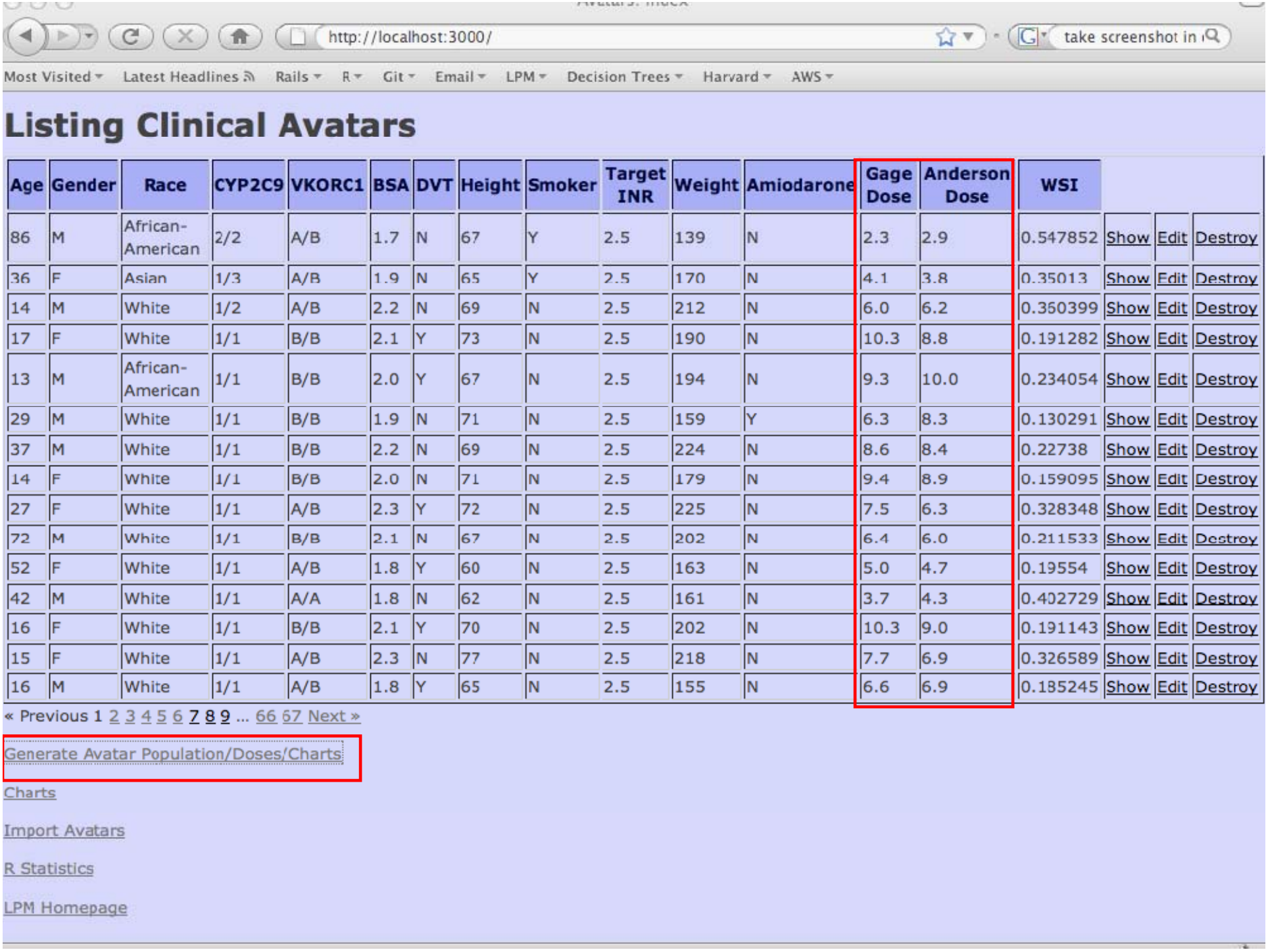


Listing Clinical Avatars

Age	Gender	Race	CYP2C9	VKORC1	BSA	DVT	Height	Smoker	Target INR	Weight	Amiodarone	Gage Dose	Anderson Dose	WSI			
86	M	African-American	2/2	A/B	1.7	N	67	Y	2.5	139	N	2.3	2.9	0.547852	Show	Edit	Destroy
36	F	Asian	1/3	A/B	1.9	N	65	Y	2.5	170	N	4.1	3.8	0.35013	Show	Edit	Destroy
14	M	White	1/2	A/B	2.2	N	69	N	2.5	212	N	6.0	6.2	0.350399	Show	Edit	Destroy
17	F	White	1/1	B/B	2.1	Y	73	N	2.5	190	N	10.3	8.8	0.191282	Show	Edit	Destroy
13	M	African-American	1/1	B/B	2.0	Y	67	N	2.5	194	N	9.3	10.0	0.234054	Show	Edit	Destroy
29	M	White	1/1	B/B	1.9	N	71	N	2.5	159	Y	6.3	8.3	0.130291	Show	Edit	Destroy
37	M	White	1/1	B/B	2.2	N	69	N	2.5	224	N	8.6	8.4	0.22738	Show	Edit	Destroy
14	F	White	1/1	B/B	2.0	N	71	N	2.5	179	N	9.4	8.9	0.159095	Show	Edit	Destroy
27	F	White	1/1	A/B	2.3	Y	72	N	2.5	225	N	7.5	6.3	0.328348	Show	Edit	Destroy
72	M	White	1/1	B/B	2.1	N	67	N	2.5	202	N	6.4	6.0	0.211533	Show	Edit	Destroy
52	F	White	1/1	A/B	1.8	Y	60	N	2.5	163	N	5.0	4.7	0.19554	Show	Edit	Destroy
42	M	White	1/1	A/A	1.8	N	62	N	2.5	161	N	3.7	4.3	0.402729	Show	Edit	Destroy
16	F	White	1/1	B/B	2.1	Y	70	N	2.5	202	N	10.3	9.0	0.191143	Show	Edit	Destroy
15	F	White	1/1	A/B	2.3	N	77	N	2.5	218	N	7.7	6.9	0.326589	Show	Edit	Destroy
16	M	White	1/1	A/B	1.8	Y	65	N	2.5	155	N	6.6	6.9	0.185245	Show	Edit	Destroy

« Previous 1 2 3 4 5 6 7 8 9 ... 66 67 Next »

Generate Avatar Population/Doses/Charts

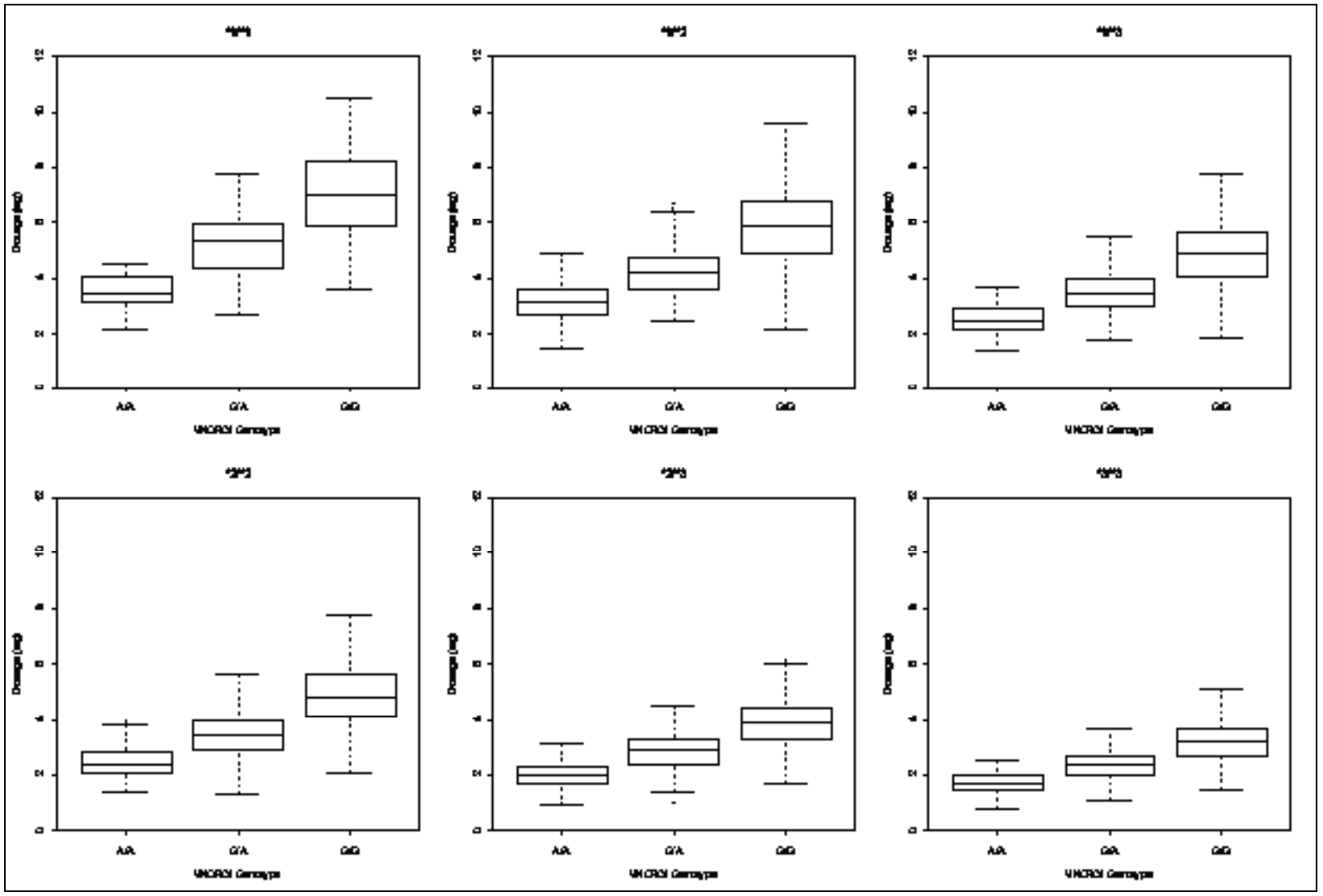
Charts

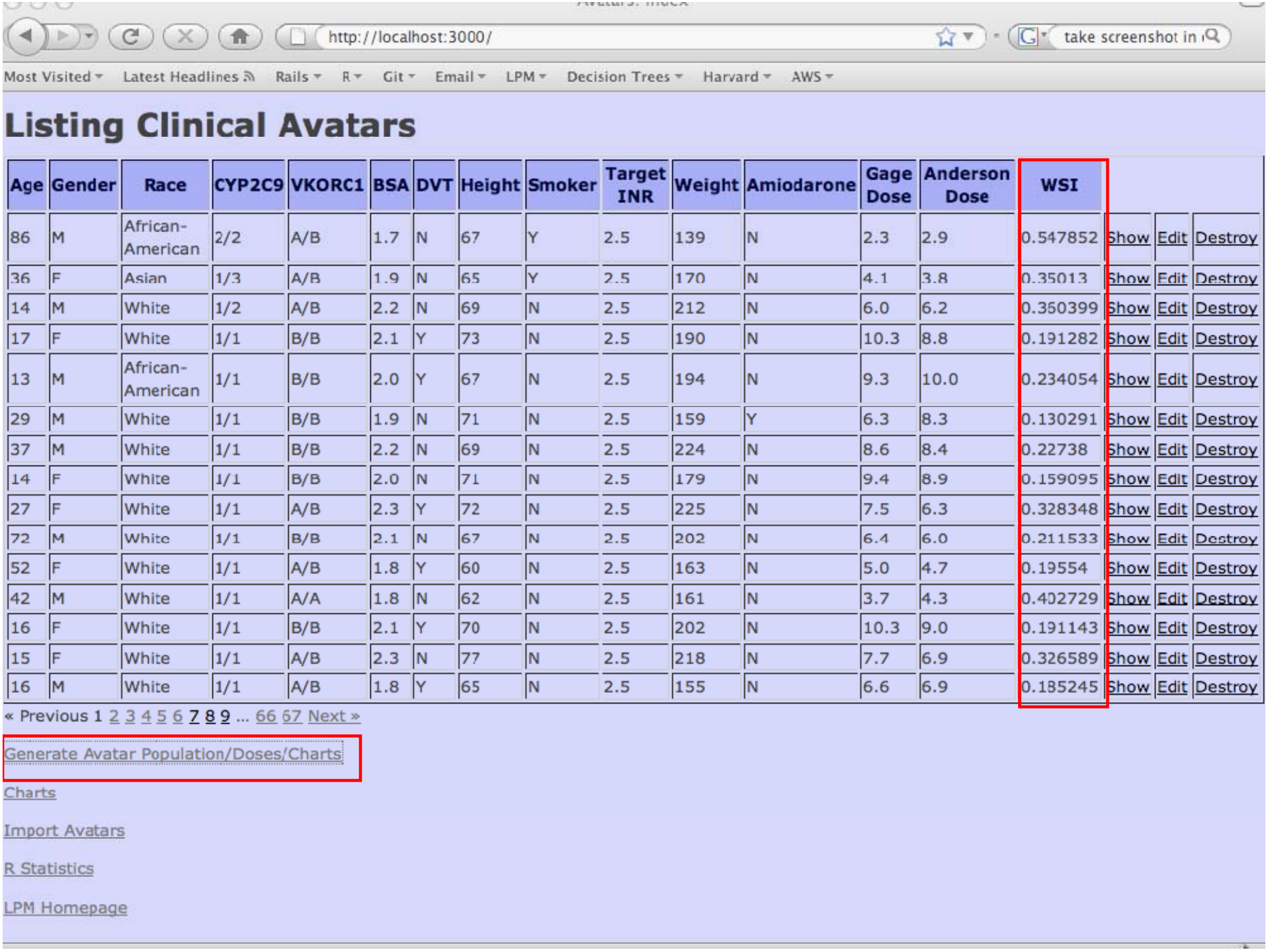
Import Avatars

R Statistics

LPM Homepage

Analysis of Change in Dose due to Genotypic Variation (Gage Model)





Listing Clinical Avatars

Age	Gender	Race	CYP2C9	VKORC1	BSA	DVT	Height	Smoker	Target INR	Weight	Amiodarone	Gage Dose	Anderson Dose	WSI			
86	M	African-American	2/2	A/B	1.7	N	67	Y	2.5	139	N	2.3	2.9	0.547852	Show	Edit	Destroy
36	F	Asian	1/3	A/B	1.9	N	65	Y	2.5	170	N	4.1	3.8	0.35013	Show	Edit	Destroy
14	M	White	1/2	A/B	2.2	N	69	N	2.5	212	N	6.0	6.2	0.350399	Show	Edit	Destroy
17	F	White	1/1	B/B	2.1	Y	73	N	2.5	190	N	10.3	8.8	0.191282	Show	Edit	Destroy
13	M	African-American	1/1	B/B	2.0	Y	67	N	2.5	194	N	9.3	10.0	0.234054	Show	Edit	Destroy
29	M	White	1/1	B/B	1.9	N	71	N	2.5	159	Y	6.3	8.3	0.130291	Show	Edit	Destroy
37	M	White	1/1	B/B	2.2	N	69	N	2.5	224	N	8.6	8.4	0.22738	Show	Edit	Destroy
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27	F	White	1/1	A/B	2.3	Y	72	N	2.5	225	N	7.5	6.3	0.328348	Show	Edit	Destroy
72	M	White	1/1	B/B	2.1	N	67	N	2.5	202	N	6.4	6.0	0.211533	Show	Edit	Destroy
52	F	White	1/1	A/B	1.8	Y	60	N	2.5	163	N	5.0	4.7	0.19554	Show	Edit	Destroy
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16	M	White	1/1	A/B	1.8	Y	65	N	2.5	155	N	6.6	6.9	0.185245	Show	Edit	Destroy

« Previous 1 2 3 4 5 6 7 8 9 ... 66 67 Next »

Generate Avatar Population/Doses/Charts

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Progress (Y1 Q1) and Next Steps

- LPM Warfarin Web App Available
- 1 - 100 Million clinical avatar populations and dosing simulations
- Platform supports clinical trial simulation, incidentalome testing, and exploration of metrics for clinical efficacy and outcome
- Exploration of Warfarin 'Sensitive' patients

Next Steps

- Improve C.A. population model
- Warfarin PK/PD incorporated into simulation model
- Extend C.A. data model to EMR format
- Consider and test design of clinical trials
- Consider comparative effectiveness simulations

Y1 Q1 Results

NLM Eureka, 1 R01 LM010130-01

All project personnel hired.

New Jobs	3.0
Saved Jobs	2.0

Project partially completed (<50%)

Peer reviewed results appeared in open source publication, Oct, 2009:

www.recovery.gov

Click on Massachusetts

Click on Congressional District 8

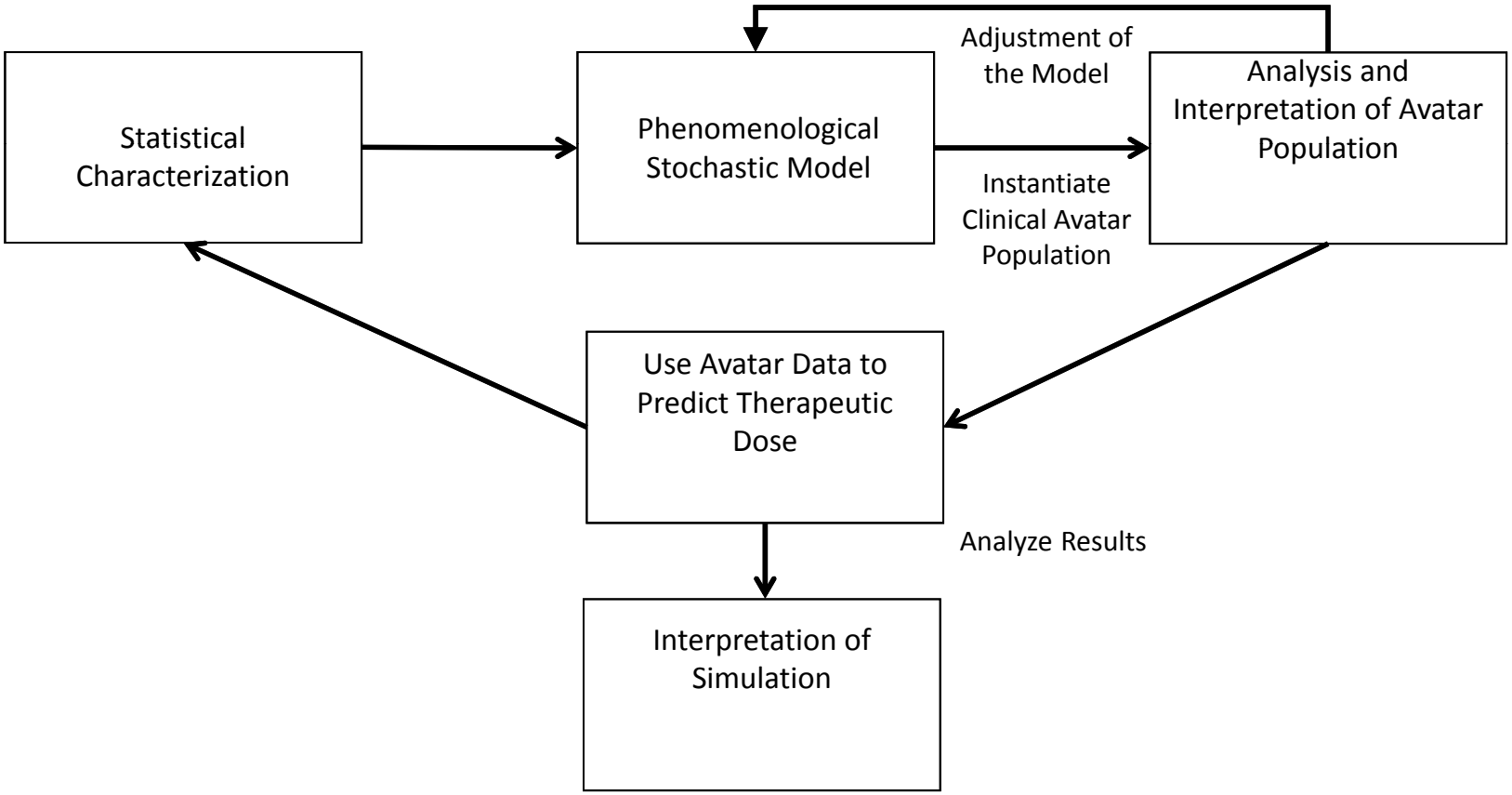
Click on Academic

Click on Harvard Medical School

Click on CBMI

Click on LPM

Warfarin Pharmacogenetic Modeling Method: V 1.+



Y1 Q2

- LPM Warfarin Web App Available
- 1 - 100 Million clinical avatar populations and dosing simulations
- Platform supports clinical trial simulation, incidentalome testing, and exploration of metrics for clinical efficacy and outcome
- Exploration of Warfarin 'Sensitive' patients

Next Steps

- **Improve C.A. population model**
- **Warfarin PK/PD incorporated into simulation model**
- **Extend C.A. data model to EMR format**
- Consider and test design of clinical trials
- Consider comparative effectiveness simulations

Program Milestones:

- Established Clouded Translational Research Platform
- Refined a TR Methodology
- Created Tools:
  - Clinical Avatar Simulator
  - Pharmacogenetic Predictive Modeling Simulator
- Pharmacogenetics Test Case: Warfarin Dosing
- Method and Clinical Avatars
- Preliminary Studies and Results

Wisconsin Demonstration Project:

Optimized Warfarin Dosing with Genetic-Based Predictive Dose Algorithms

Project was not approved:

- Healthcare practice remained skeptical – insufficient evidence that gene testing and algorithms were sufficiently valuable

- Educational issues with healthcare staff – what are genotypes?

- Technology was premature and 'square peg' like compared to best practice devices.

- Insufficient patient buy-in

- Access to and quality of EMR data problems.

- Cost

Francis Collins, Director, National Institutes of Health
Personalized Medicine in an Era of Health Care Reform
AAAS Symposium on Research and Policy
June, 2009, Washington D.C.

Personalized Medicine: Scientific and Policy Challenges:

1. Push sequencing technology to achieve wide availability of the $1000 genome within the next 5 years
2. Make sure that "meaningful use" in health IT includes genomic information
3. Identify additional environmental contributions to common disease
4. Implement a better system for oversight of genetic tests
5. Conduct rigorous PGx studies on multiple drugs
6. Widen the translational pipeline
7. Promote rigorous health economics research to assess value of personalized medicine
8. Develop a process to shorten dramatically the time from evidence generation to practice change

Acknowledgements

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