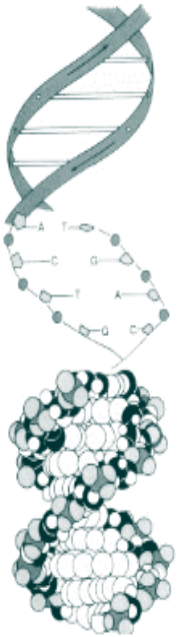


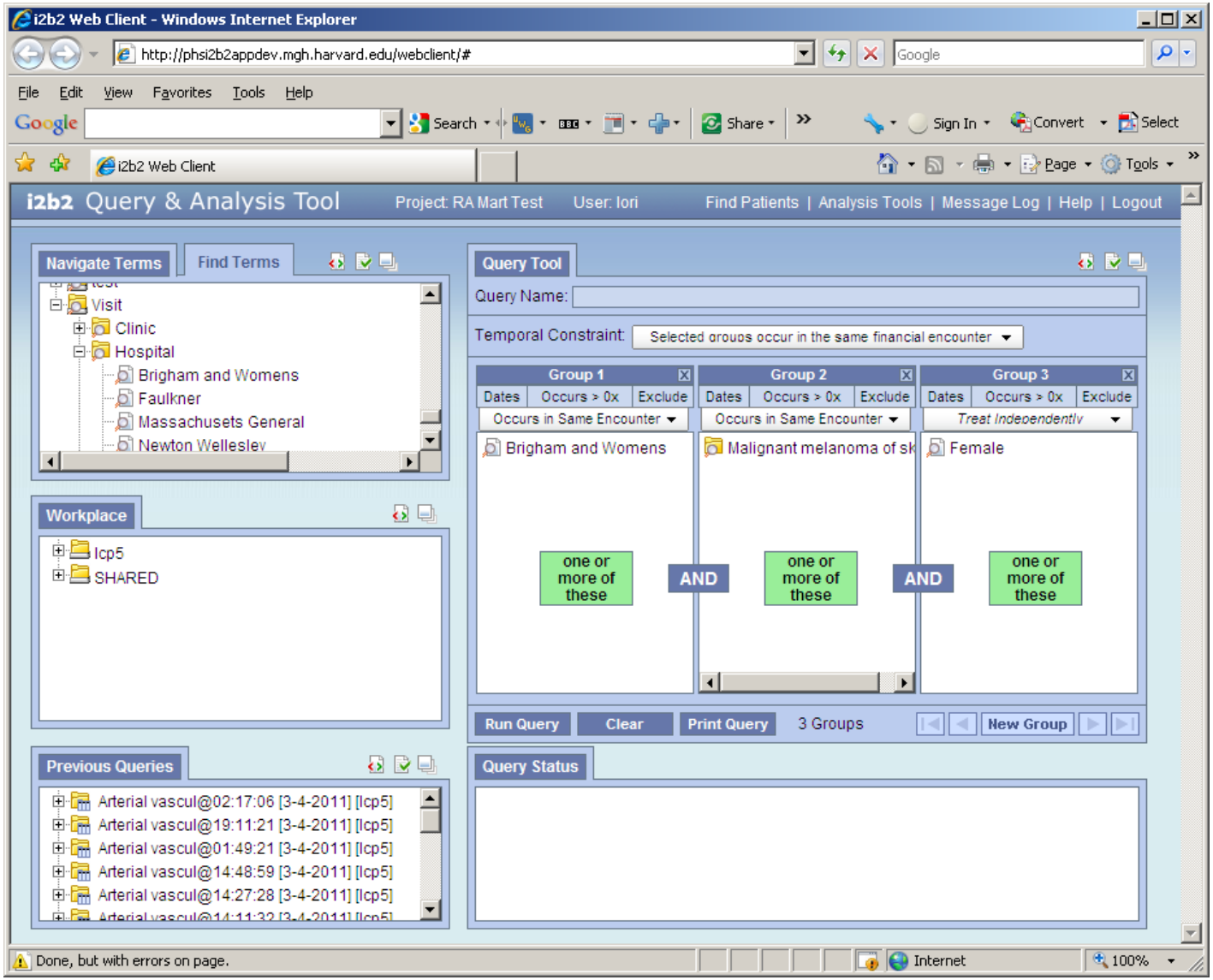
Improving EHR Data Quality with Automated Phenotyping

Shawn Murphy MD, Ph.D.
Partners Healthcare and Harvard Medical School
October 10th, 2019

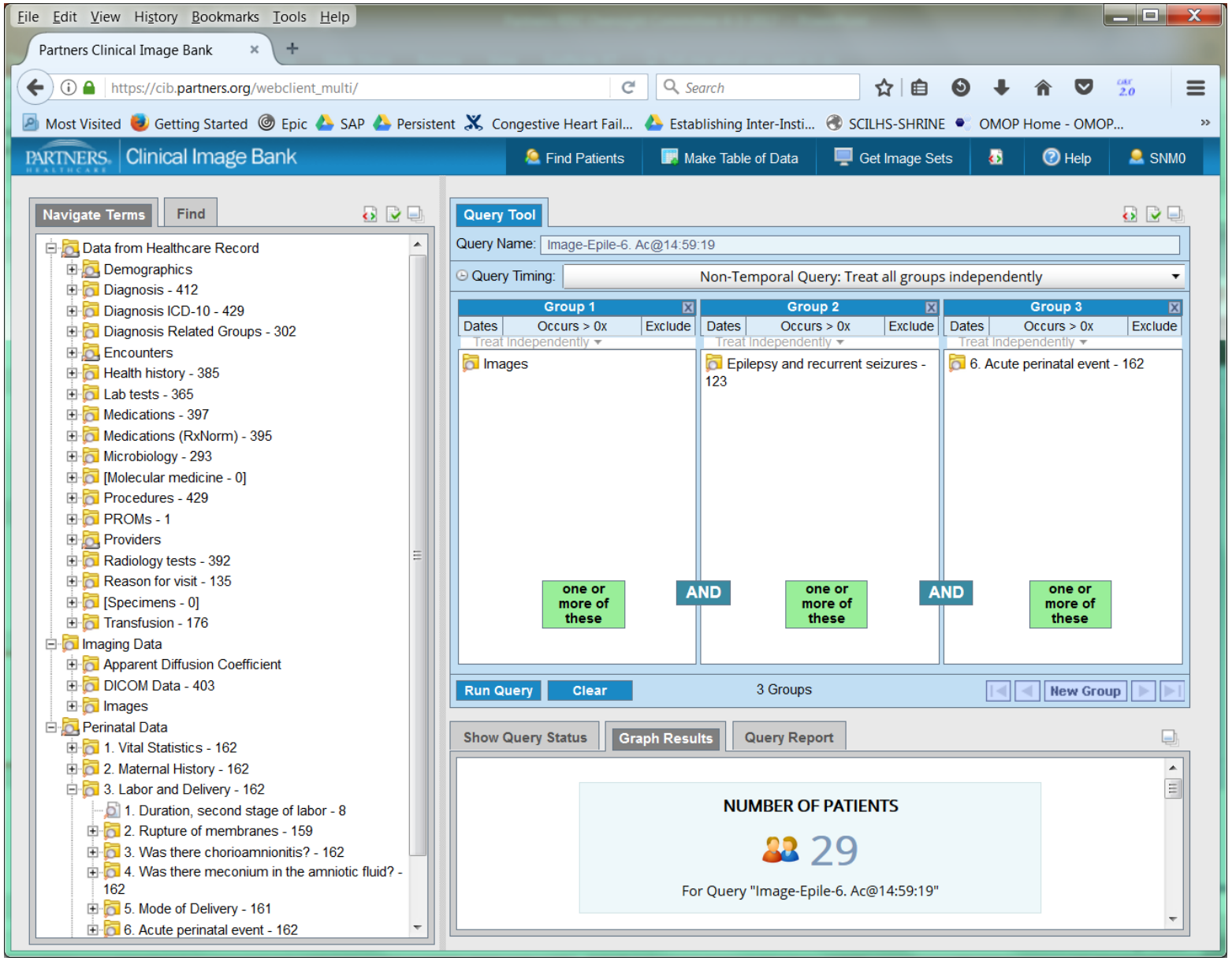
Integration strategy from “Informatics for Integrating Biology and the Bedside (i2b2)” sponsored by the National Institutes of Health, what is it?

- Software for explicitly organizing and transforming person-oriented clinical data to a way that is optimized for clinical genomics research
  - Allows integration of clinical data, trials data, and genotypic data
- A portable and extensible application framework
  - Software is built in a modular pattern that allows additions without disturbing core parts
  - Available as open source at https://www.i2b2.org

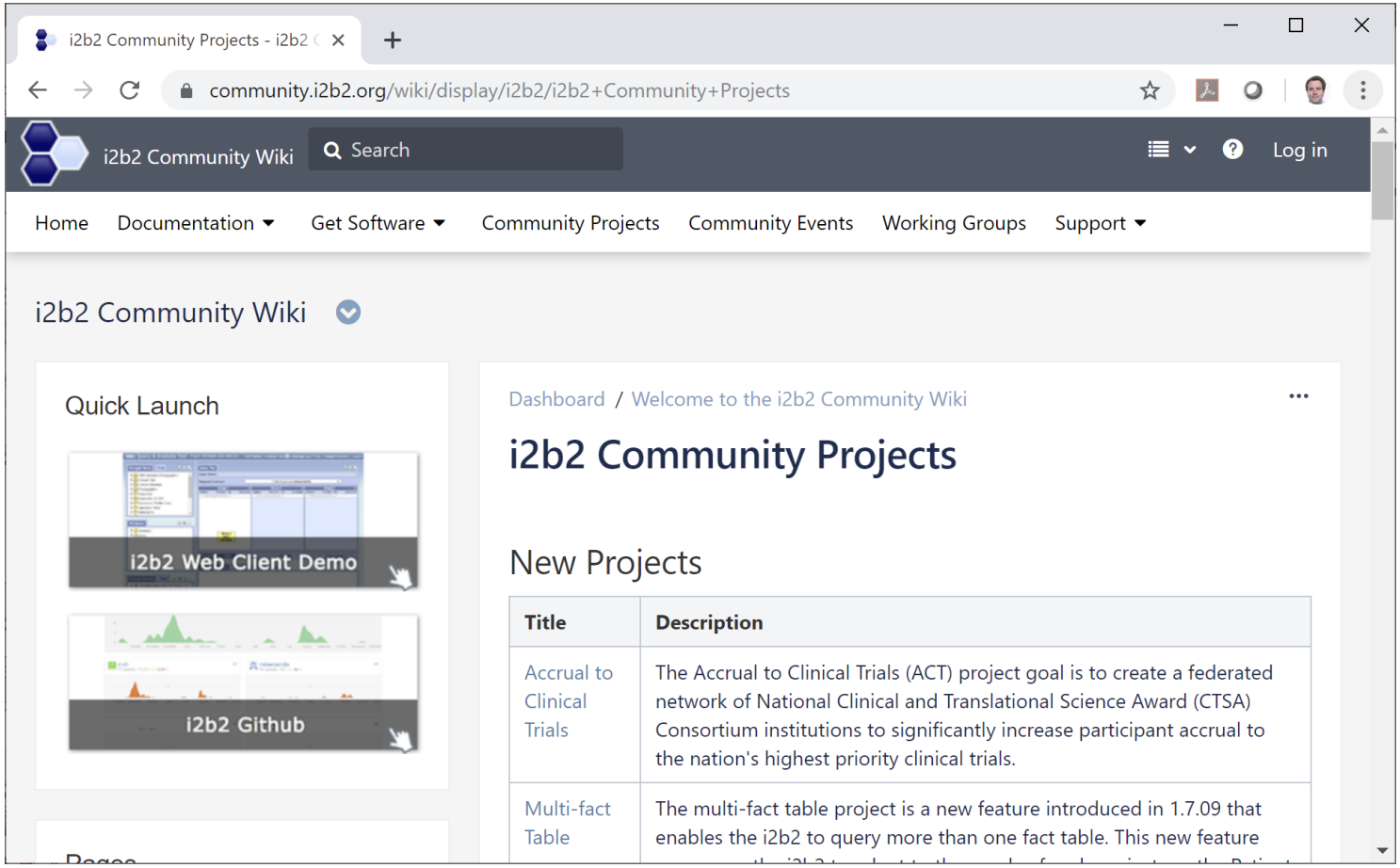
Interogation can occur through i2b2 web client



Running a Query

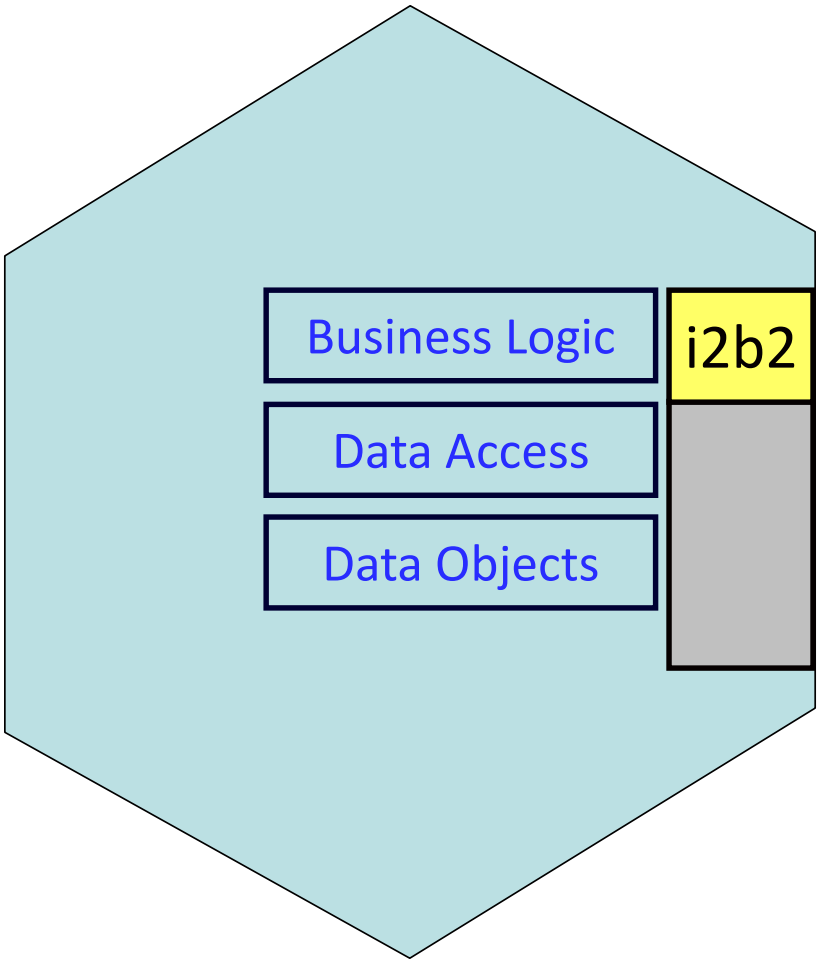


I2b2 Community Software Modules contributed as “Cells”



https://community.i2b2.org/wiki/display/i2b2/i2b2+Community+Projects

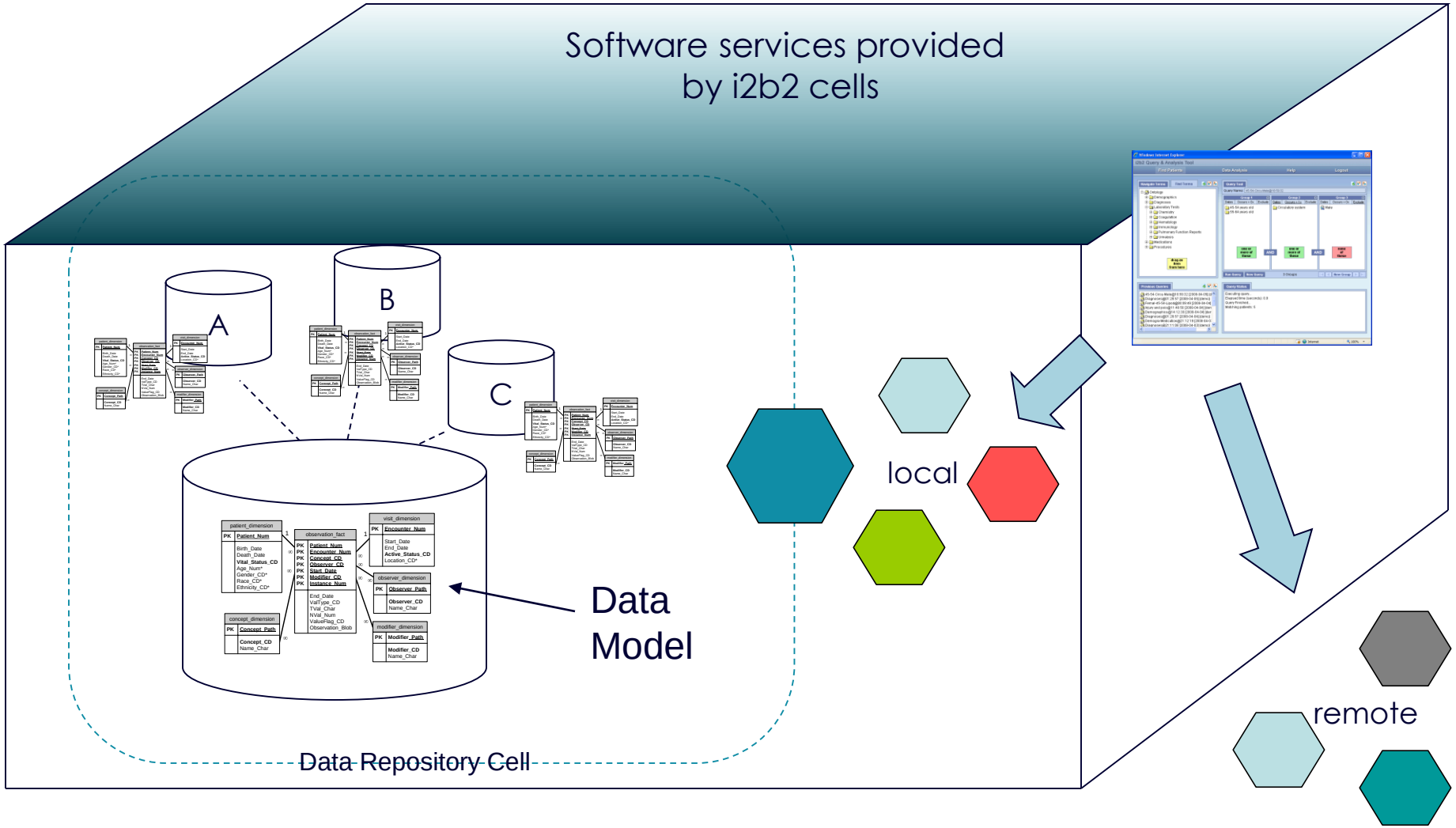
i2b2 Cell: The Canonical Software Module



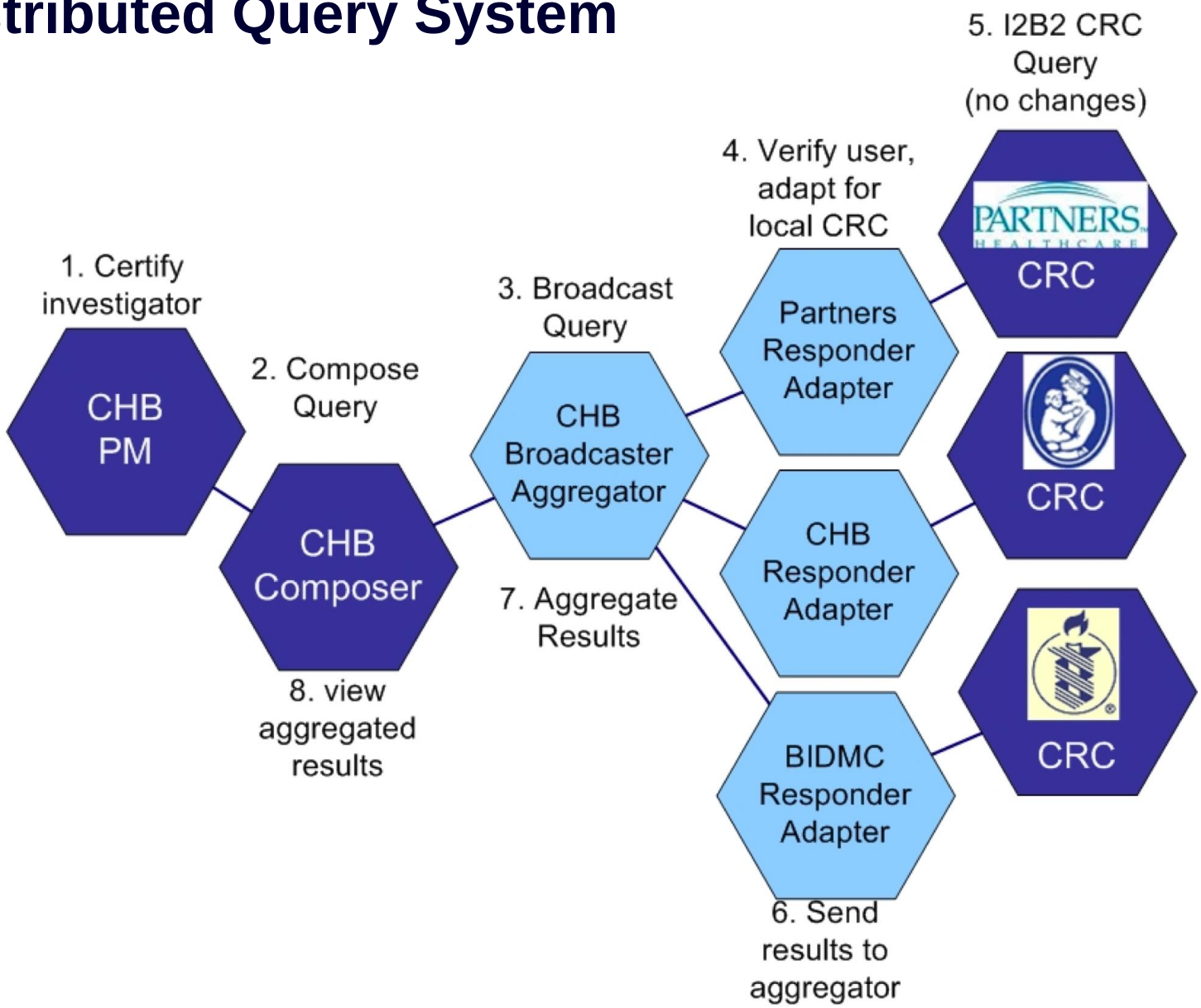
HTTP XML

(minimum: RESTful)

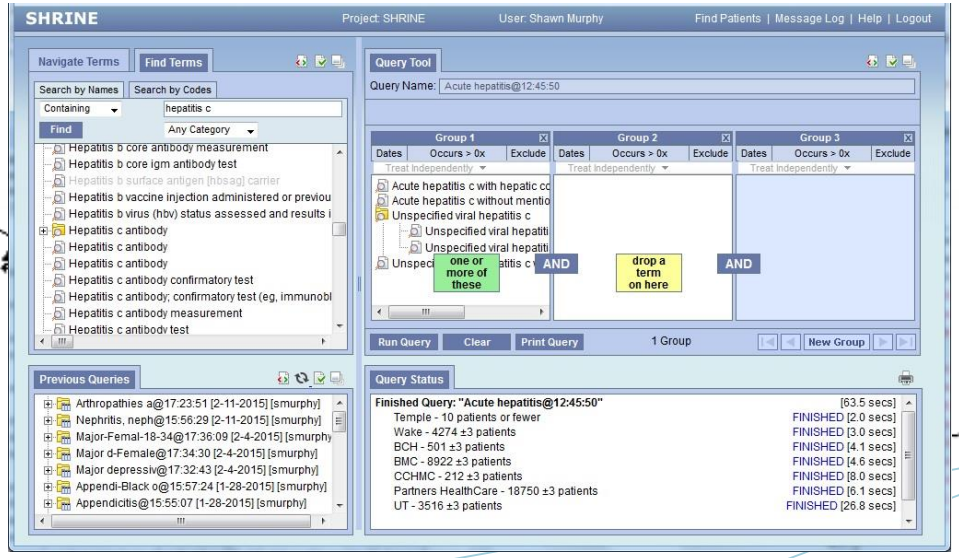
An i2b2 Environment is built from i2b2 Cells



Distributed Query System



Federated Queries



Partners HealthCare System

Boston Children's Hospital

BIDMC

Boston Health Net (BMC and Community Health Centers)

Columbia U. Medical Center and New York Presbyterian Hospital

University of California, Davis

Washington University in St. Louis

Wake Forest Baptist Medical Center

Morehouse/Grady/RCMI

U Texas Health Science Center/Houston

Implementations

CTSA's

- Boston University
- Case Western Reserve University (*including Cleveland Clinic*)
- Children's National Medical Center (GWU), Washington D.C.
- Duke University
- Emory University (*including Morehouse School of Medicine and Georgia Tech*)
- Harvard University (*including Beth Israel Deaconness Medical Center, Brigham and Women's Hospital, Children's Hospital Boston, Dana Farber Cancer Center, Joslin Diabetes Center, Massachusetts General Hospital*)
- Medical University of South Carolina
- Medical College of Wisconsin
- Oregon Health & Science University
- Penn State MIlton S. Hershey Medical Center
- Tufts University
- University of Alabama at Birmingham
- University of Arkansas for Medical Sciences
- University of California Davis
- University of California, Irvine
- University of California, Los Angeles*
- University of California, San Diego*
- University of California San Francisco
- University of Chicago
- University of Cincinnati (including *Cinncinati Children's Hospital Medical Center*)
- University of Colorado Denver (including *Children's Hospital Colorado*)
- University of Florida
- University of Kansas Medical Center
- University of Kentucky Research Foundation
- University of Massachusetts Medical School, Worcester
- University of Michigan
- University of Pennsylvania (including *Children's Hospital of Philadelphia*)
- University of Pittsburgh (including their *Cancer Institute*)
- University of Rochester School of Medicine and Dentistry
- University of Texas Health Sciences Center at Houston
- University of Texas Health Sciences Center at San Antonio
- University of Texas Medical Branch (Galveston)
- University of Texas Southwestern Medical Center at Dallas
- University of Utah
- University of Washington
- University of Wisconsin - Madison (*including Marshfield Clinic*)
- Virginia Commonwealth University
- Weill Cornell Medical College

Academic Health Centers (does not include AHCs that are part of a CTSA):

- Arizona State University
- City of Hope, Los Angeles
- Georgia Health Sciences University, Augusta
- Hartford Hospital, CN
- HealthShare Montana
- Massachusetts Veterans Epidemiology Research and Information Center (MAVERICK), Boston
- Nemours
- Phoenix Children's Hospital
- Regenstrief Institute
- Thomas Jefferson University
- University of Connecticut Health Center
- University of Missouri School of Medicine
- University of Tennessee Health Sciences Center
- Wake Forest University Baptist Medical Center

HMOs:

- Group Health Cooperative
- Kaiser Permanente

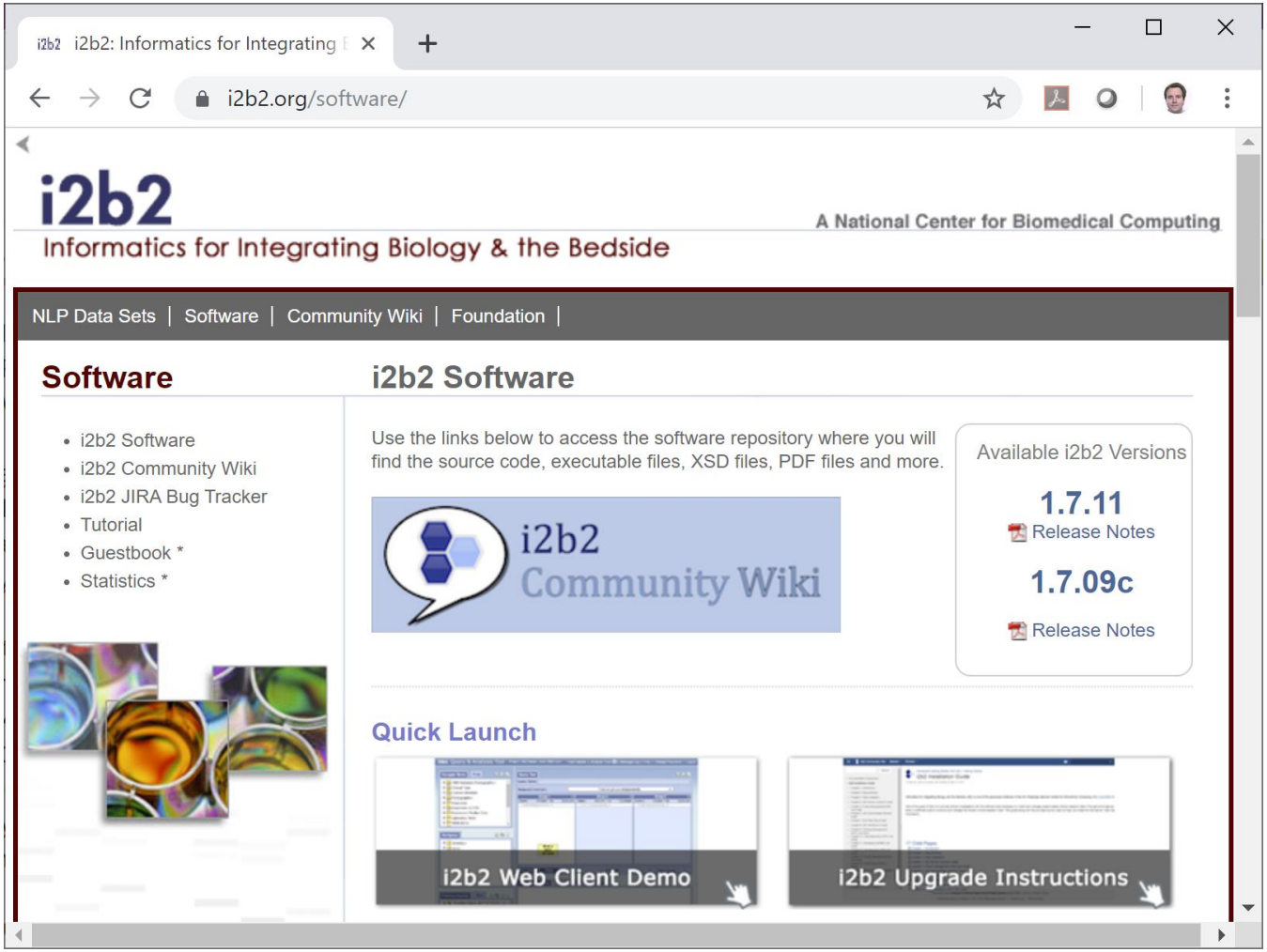
International:

- Georges Pompidou Hospital, Paris, France
- Hospital of the Free University of Brussels, Belgium
- Inserm U936, Rennes, France
- Institute for Data Technology and Informatics (IDI), NTNU, Norway
- Institute for Molecular Medicine Finland (FIMM)
- Karolinska Institute, Sweden
- Landspitali University Hospital, Reykjavik, Iceland
- Tokyo Medical and Dental University, Japan
- University of Bordeau Segalen, France
- University of Erlangen-Nuremberg, Germany
- University of Goettingen, Goettingen, Germany
- University of Leicester and Hospitals, England (Biomed. Res. Informatics Ctr. for Clin. Sci)
- University of Pavia, Pavia, Italy
- University of Seoul, Seoul, Korea

Companies:

- Johnson and Johnson (TransMART)
- GE Healthcare Clinical Data Services

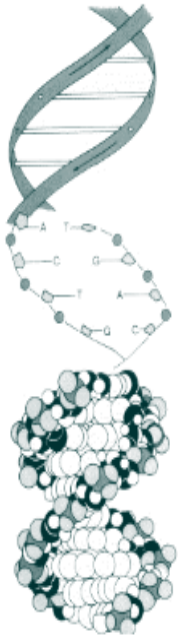
I2b2 Software components are distributed as open source



Recent Community Project Releases

- Incorporation of FHIR into i2b2
  - FHIR Cell to allow single patient's data to be returned in FHIR
  - FHIR Ontology and ETL to allow direct import of FHIR into i2b2
  - FHIR Cell to allow i2b2 to extend to FHIR query endpoints
- I2b2-based system for Accruing Patients for Clinical Trials
  - Extensions to SHRINE for management of clinical trials
  - Web Client Plug-ins to extend SHRINE queries to local i2b2-based patient recruitment
- i2b2-based system to query and return data from Observation-Fact tables contained in multiple different i2b2 Hives

PARTNERS HEALTHCARE



Improve Quality of i2b2 Queries through Machine Learning

Psychological Medicine (2012), **42**, 41–50. © Cambridge University Press 2011
doi:10.1017/S0033291711000997

ORIGINAL ARTICLE

Using electronic medical records to enable large-scale studies in psychiatry: treatment resistant depression as a model

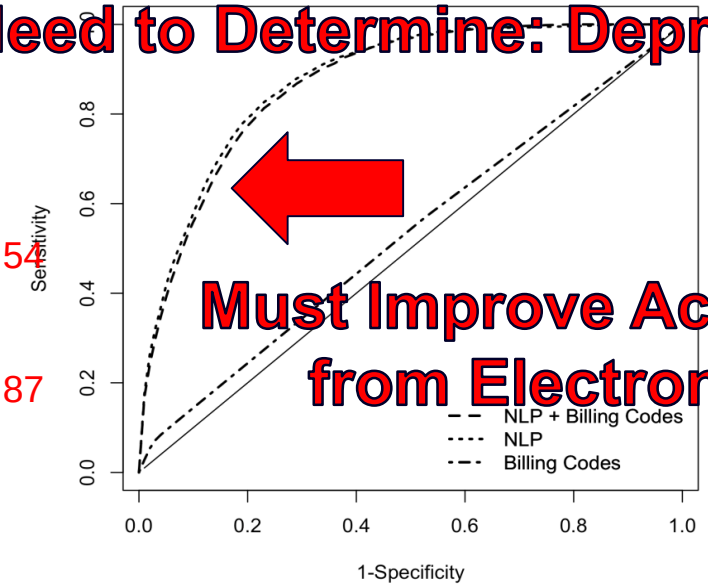
R. H. Perlis[1,2*], D. V. Iosifescu[1,3], V. M. Castro[4], S. N. Murphy[5], V. S. Gainer[4], J. Minnier[6], T. Cai[6], S. Goryachev[4], Q. Zeng[7], P. J. Gallagher[2], M. Fava[1], J. B. Weilburg[1], S. E. Churchill[8], I. S. Kohane[9] and J. W. Smoller[2]

Use Phenotyping Algorithms to define cohorts of treatment-resistant and treatment-responsive depression

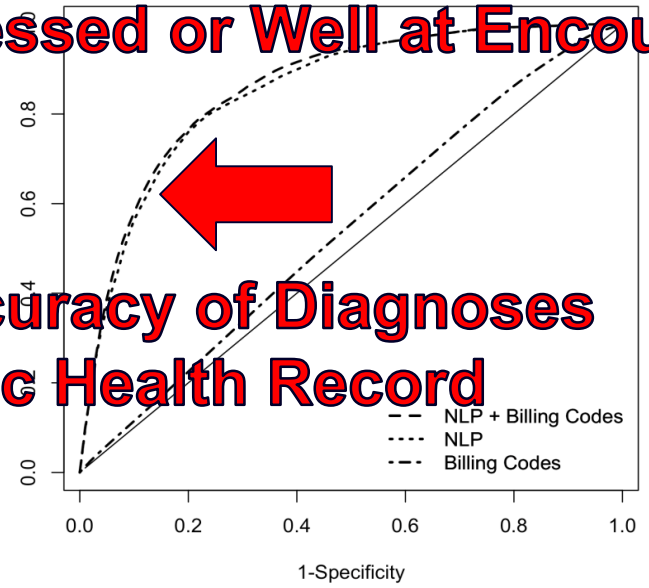
Need to Determine: Depressed or Well at Encounter

Initially:
AUC = 0.54

Finally:
AUC = 0.87



Must Improve Accuracy of Diagnoses from Electronic Health Record

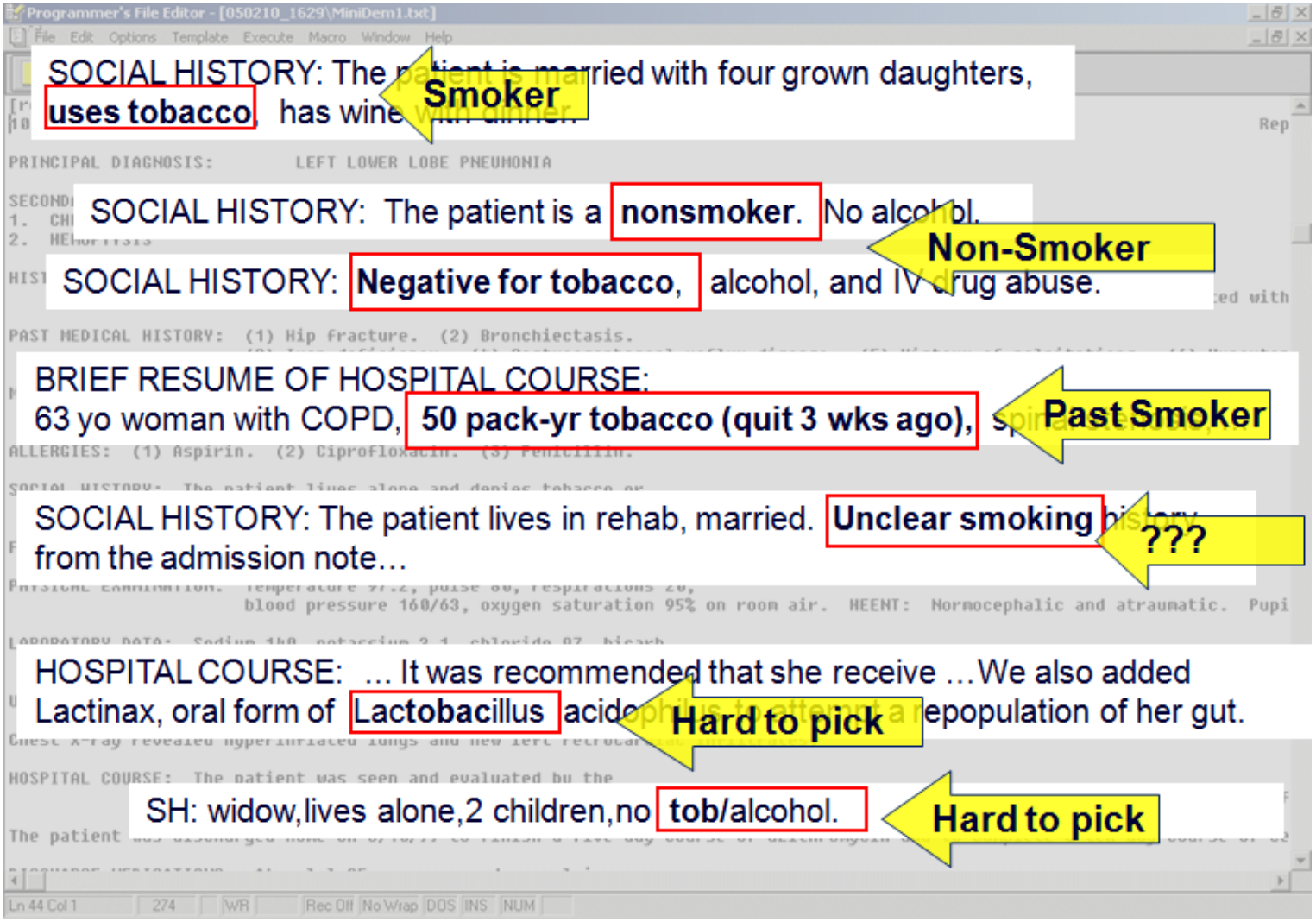


Initially:
AUC = 0.55

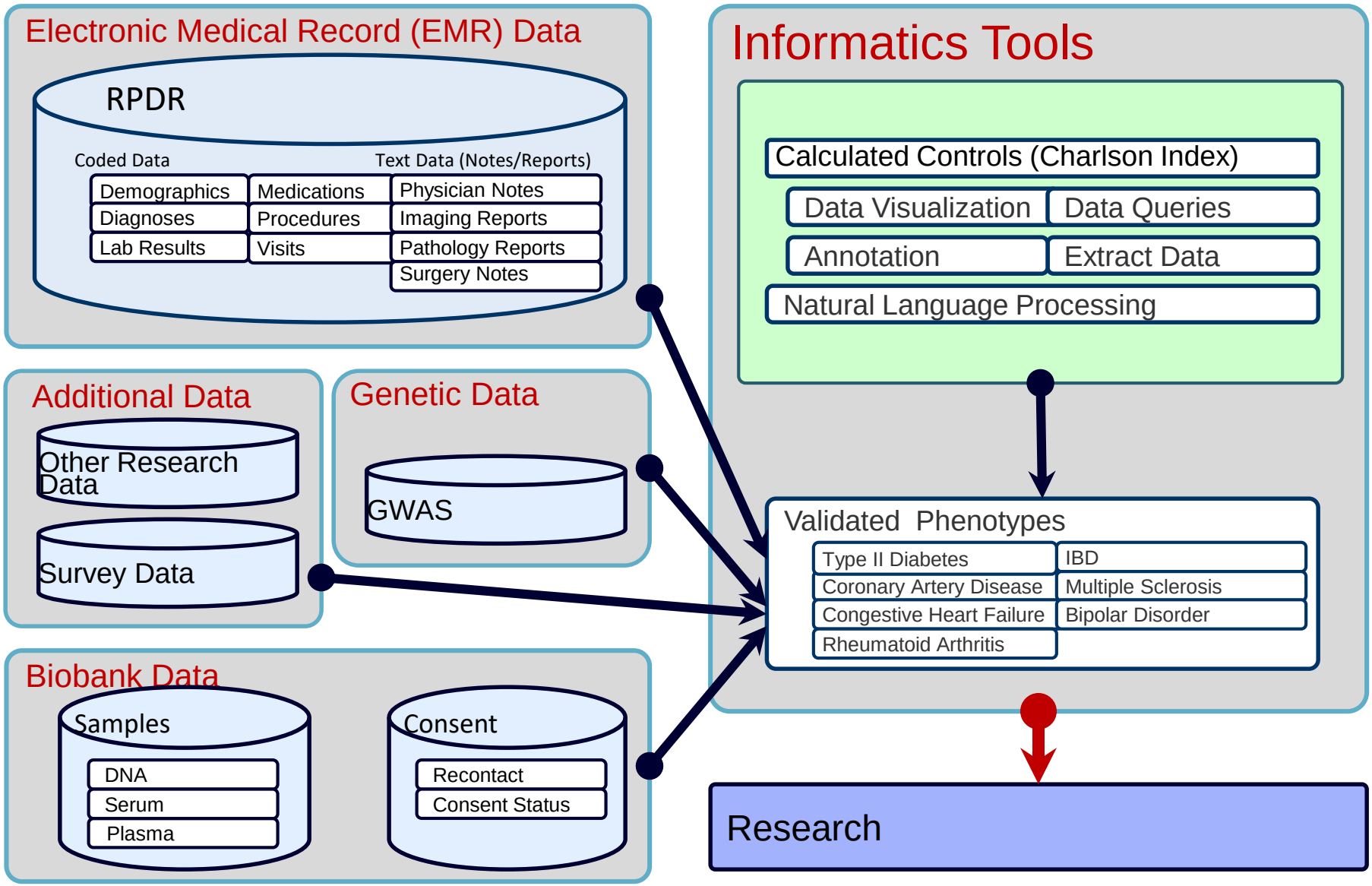
Finally:
AUC = 0.86

Clinical Status	Model	Specificity	Sensitivity	Precision	AUC
Depressed	Billing Codes	0.95	0.09 (0.03)	0.57 (0.14)	0.54 (0.02)
Depressed	NLP	0.95	0.42 (0.05)	0.78 (0.02)	0.88 (0.02)
Depressed	NLP + Billing Codes	0.95	0.39 (0.06)	0.78 (0.02)	0.87 (0.02)
Well	Billing Codes	0.95	0.06 (0.02)	0.26 (0.27)	0.55 (0.03)
Well	NLP	0.95	0.37 (0.06)	0.86 (0.02)	0.85 (0.02)
Well	NLP + Billing Codes	0.95	0.39 (0.07)	0.85 (0.02)	0.86 (0.02)

Use NLP to extract the relevant features from the set of patient notes.

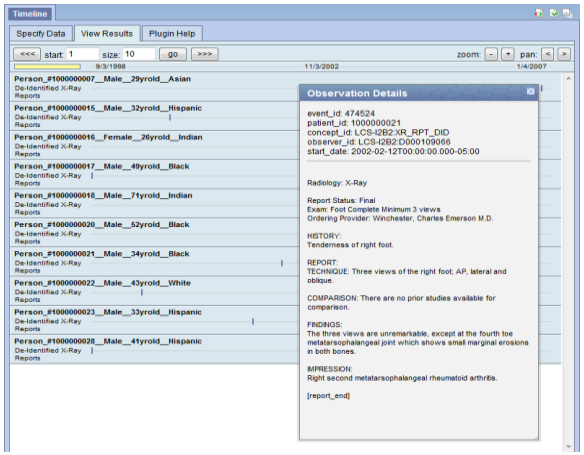


Data Integration in Biobank Portal

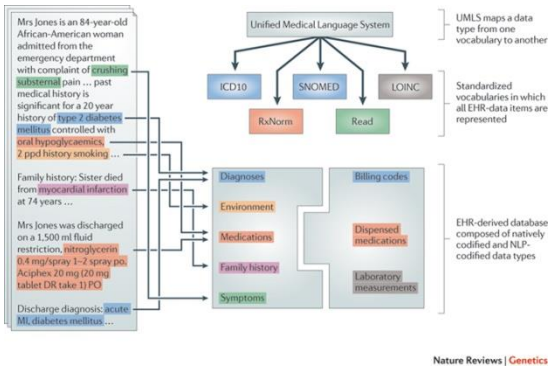


Curating a Disease Algorithm with a Gold Standard

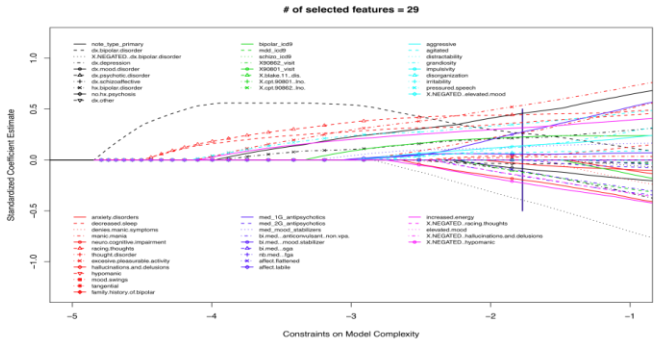
1. Create a gold standard training set.



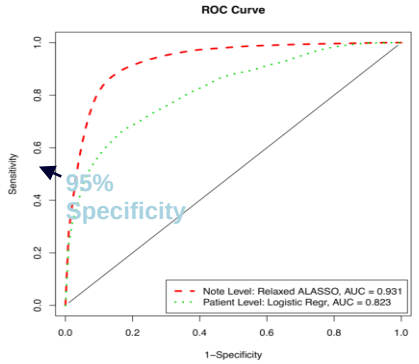
2. Create a comprehensive list of features from patient's electronic data that describe the disease of interest



3. Develop the classification algorithm. Using the data analysis file and the training set from step 1, assess the frequency of each variable. Remove variables with low prevalence. Apply adaptive LASSO penalized logistic regression to identify highly predictive variables for the algorithm

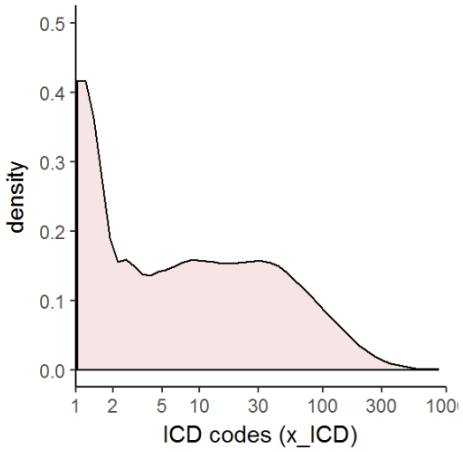


4. Apply the algorithm to all subjects in the superset and assign each subject a probability of having the phenotype

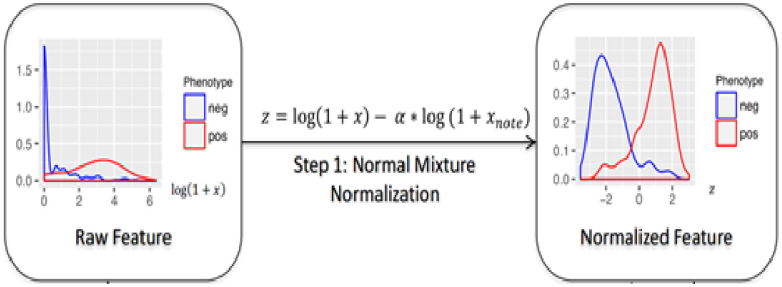


Curating a Disease Algorithm with a Silver Standard

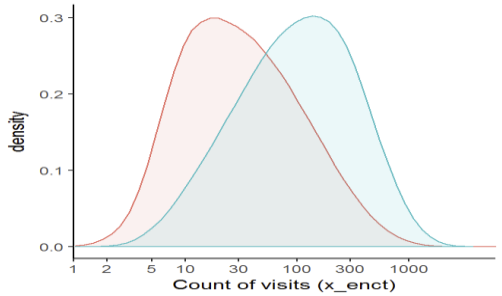
1. **Query for total number of mentions of disease**



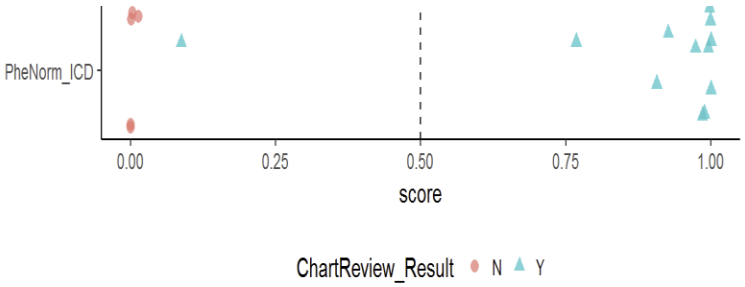
2. **Fit the mentions of disease to two curves normalizing for # of visits**

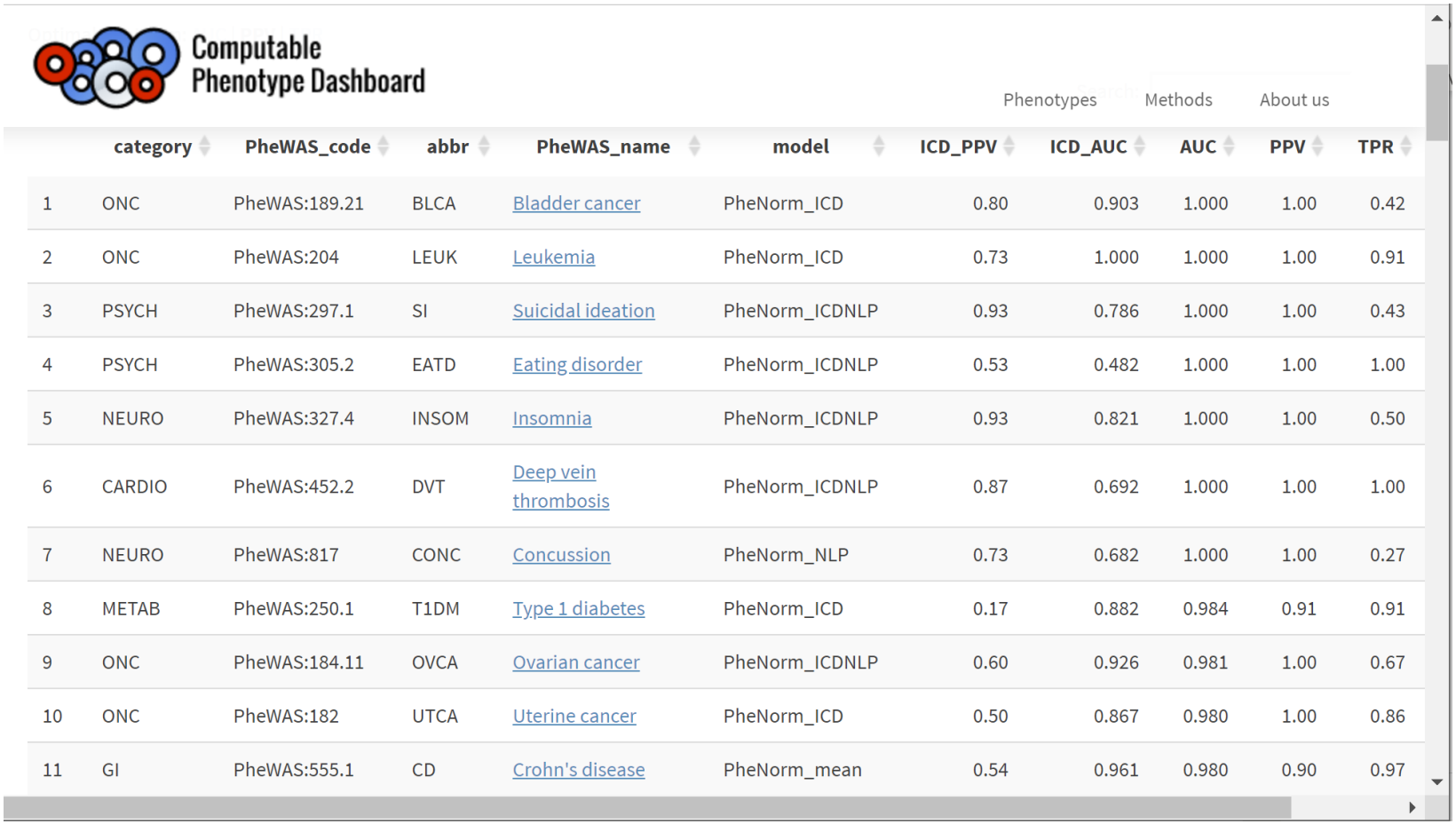


3. **Resolve the curves and separate into two groups, these are actually equal to patients with and without the disease**



4. **Apply the algorithm to all subjects** and assign each subject a probability of having the phenotype



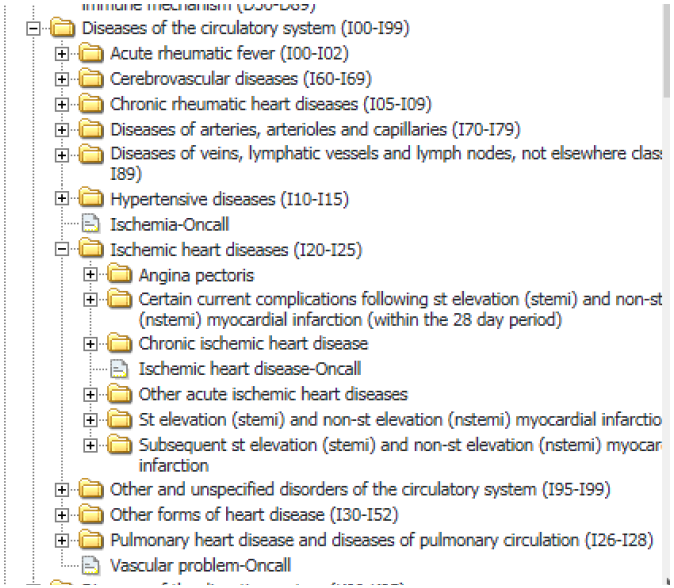


	category	PheWAS_code	abbr	PheWAS_name	model	ICD_PPV	ICD_AUC	AUC	PPV	TPR
1	ONC	PheWAS:189.21	BLCA	Bladder cancer	PheNorm_ICD	0.80	0.903	1.000	1.00	0.42
2	ONC	PheWAS:204	LEUK	Leukemia	PheNorm_ICD	0.73	1.000	1.000	1.00	0.91
3	PSYCH	PheWAS:297.1	SI	Suicidal ideation	PheNorm_ICDNLP	0.93	0.786	1.000	1.00	0.43
4	PSYCH	PheWAS:305.2	EATD	Eating disorder	PheNorm_ICDNLP	0.53	0.482	1.000	1.00	1.00
5	NEURO	PheWAS:327.4	INSOM	Insomnia	PheNorm_ICDNLP	0.93	0.821	1.000	1.00	0.50
6	CARDIO	PheWAS:452.2	DVT	Deep vein thrombosis	PheNorm_ICDNLP	0.87	0.692	1.000	1.00	1.00
7	NEURO	PheWAS:817	CONC	Concussion	PheNorm_NLP	0.73	0.682	1.000	1.00	0.27
8	METAB	PheWAS:250.1	T1DM	Type 1 diabetes	PheNorm_ICD	0.17	0.882	0.984	0.91	0.91
9	ONC	PheWAS:184.11	OVCA	Ovarian cancer	PheNorm_ICDNLP	0.60	0.926	0.981	1.00	0.67
10	ONC	PheWAS:182	UTCA	Uterine cancer	PheNorm_ICD	0.50	0.867	0.980	1.00	0.86
11	GI	PheWAS:555.1	CD	Crohn's disease	PheNorm_mean	0.54	0.961	0.980	0.90	0.97

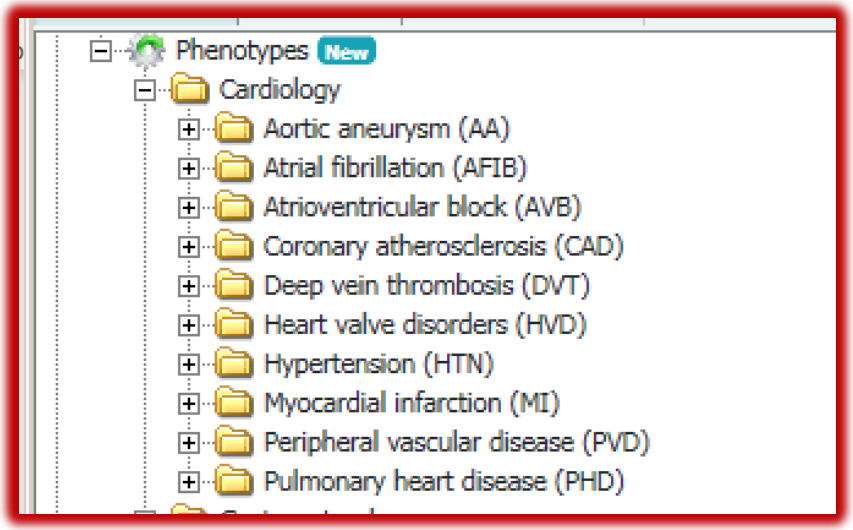
RESULT

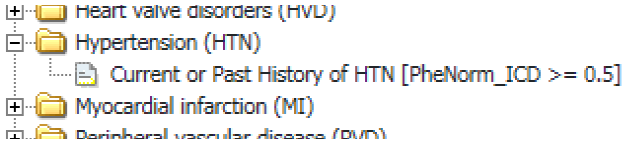
Accurate and Simple Disease Labels for Queries

Complicated



Simple





In Digitally Driven Healthcare, Disease Labels determine Algorithms for Managing Patient

Mary

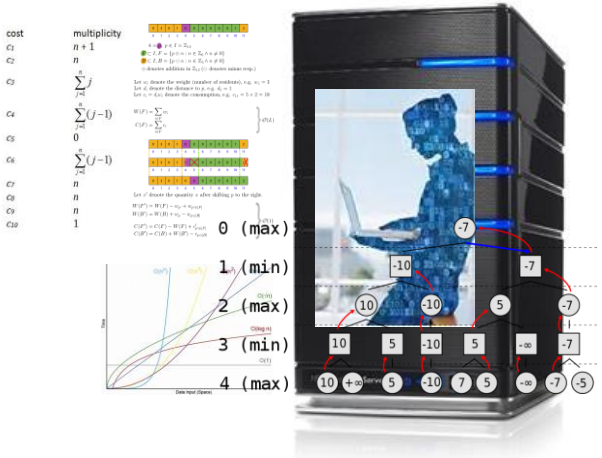
Followed for:

- Prevention
- Diabetes Type II
- Hypertension
- Heart Failure

Innovations Enabling Digital Care

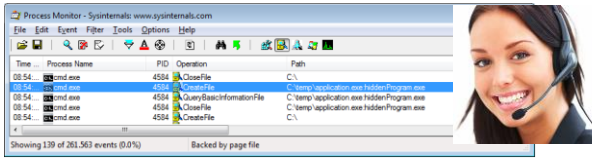
Digital and IoT devices continuously output Patient Data

```
1. for ( i = 1; i ≤ a1.length; i++ )
   1.1. j = i
   1.2. while ( a1[i] != a2[j] )
                if ( j ≥ a1.length)
                2.  return false
                1.  j++
   1.3. tmp = a2[j]
   1.4. a2[j] = a2[i]
   1.5. a2[i] = tmp
2. return true
```



PATIENT

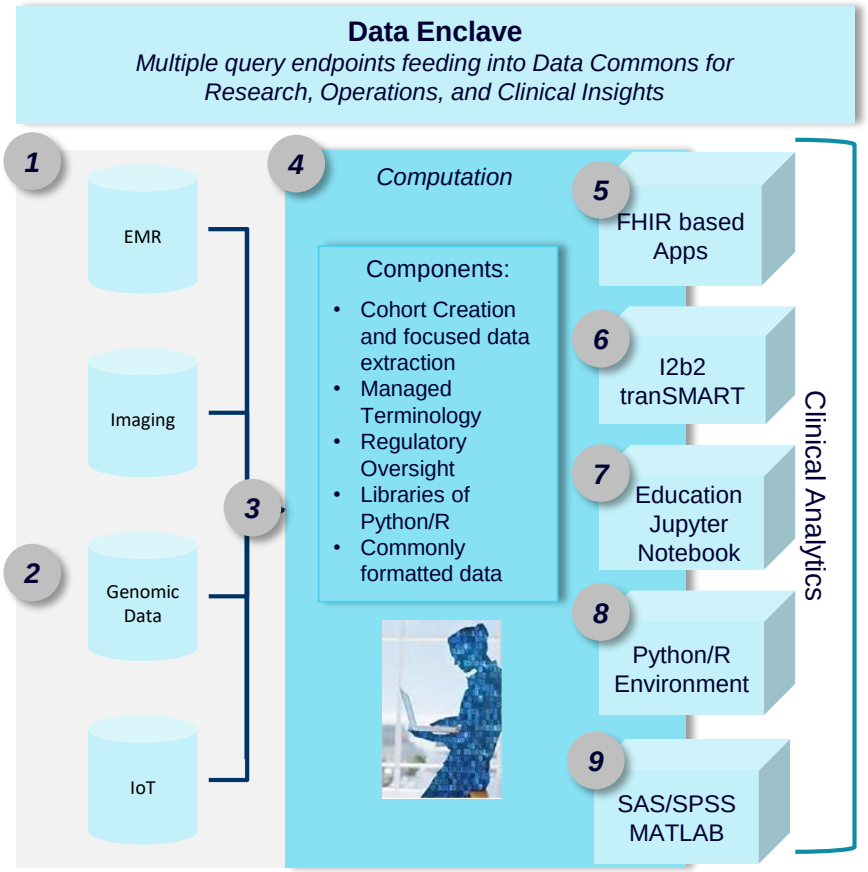
Digital Twin of patient enables continuous assessment of patient with Real Time Algorithms



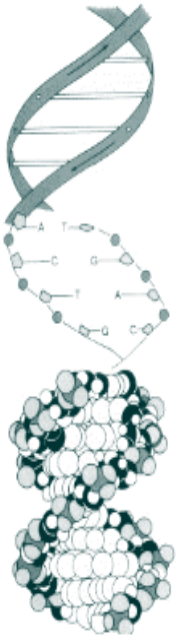
Navigator Model dramatically increases Frequency and Convenience for Patient Communication

System drives Pragmatic Clinical Trials Leading to Continuous Process Improvement

Digital Twin for Continuously Assessing Patient



Data Enclave	
1	Enable Data Extracts, perhaps some are Federated
2	Combine and Link data, put in common OMOP/i2b2 format
3	Conduit to Data Enclave
Technical Solution Development	
4	Healthcare Ready Bundle
Research and Clinical Application Projects	
5	FHIR based SMART Apps
6	I2b2 tranSMART with Fractalis plugin (next version of SmartR plugin)
7	Jupyter Notebook with AI Visualizations – code can advance to production
8	Python/R Environment full interactive development in Data Lake



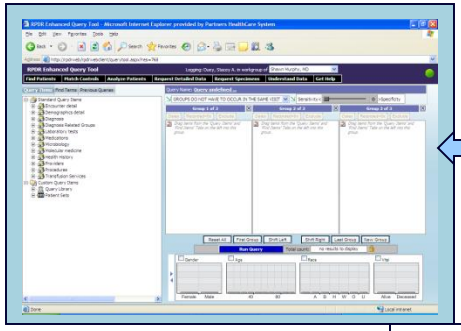
Combining i2b2 with tranSMART

i2b2 used for Big Clinical Data

1) Queries for aggregate patient numbers

- Warehouse of in & outpatient clinical data
- 6.7 million Partners Healthcare patients
- 3.1 billion diagnoses, medications, genomics, procedures, laboratories, & physical findings coupled to demographic & visit data
- Authorized use by faculty status
- Clinicians can construct complex queries
- Queries cannot identify individuals, internally can produce identifiers for (2)

Query construction in web tool



De-identified Data Warehouse

Z731984X
Z74902XX
...
...

Encrypted identifiers

2) Returns detailed patient data

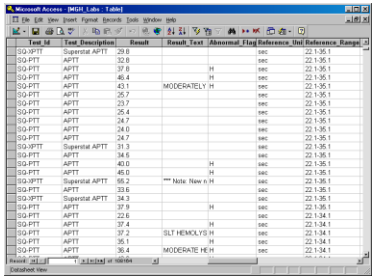
- Start with list of specific patients, usually from (1)
- Authorized use by IRB Protocol
- Returns contact and PCP information, demographics, providers, visits, diagnoses, medications, procedures, laboratories, microbiology, reports (discharge, LMR, operative, radiology, pathology, cardiology, pulmonary, endoscopy), and images into a Microsoft Access database and text files.

0000004
2185793
...
...

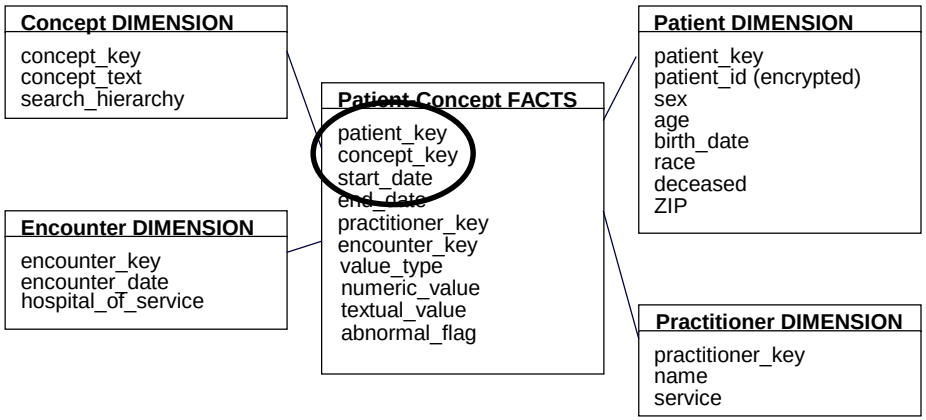
OR

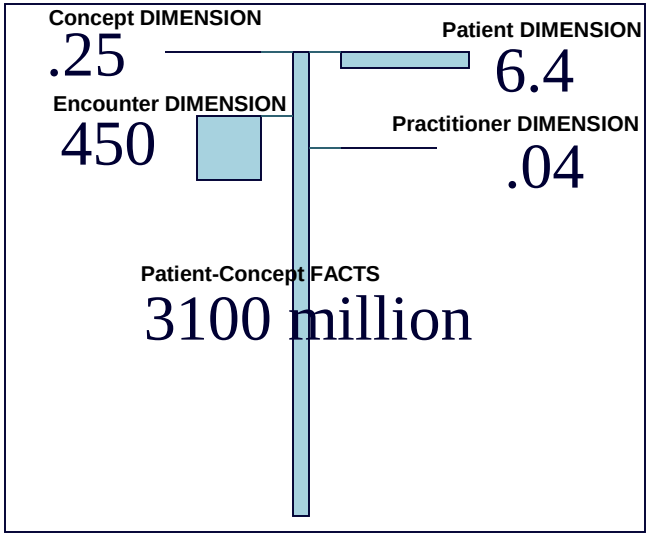
0000004
2185793
...
...

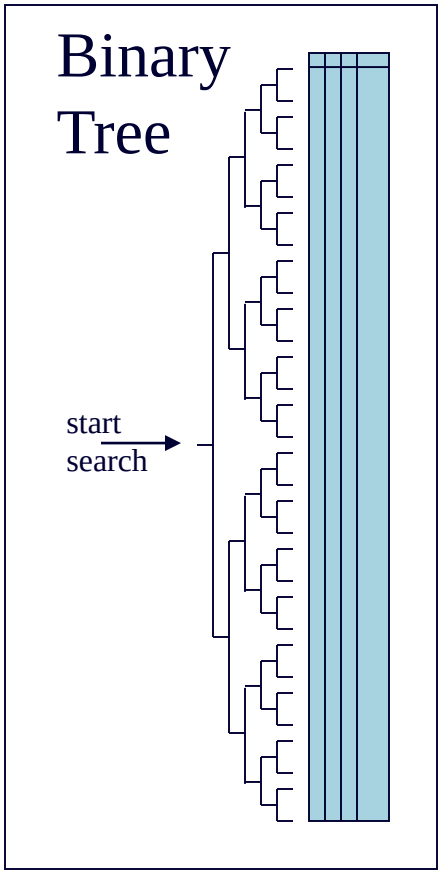
Real identifiers



Enabled by Star Schema







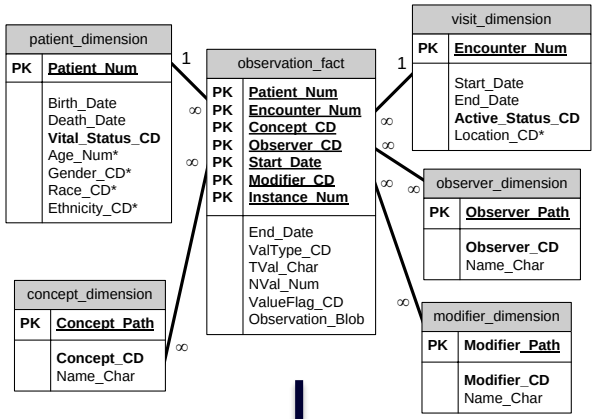
Start Schema enables both i2b2 and tranSMART

i2b2

tranSMART

CLINICAL HOSPITAL DATA

CLINICAL TRIAL DATA



REDCap

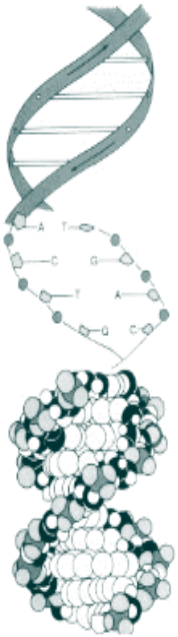
Fractalis

Risks with i2b2 - tranSMART common Database Instance

- Privacy Models different
- Database collisions from simultaneous actions
  - Principle risk is updating
- Index optimization different for different use cases
- Inherent assumptions about data are different
  - "One fact" per study visit regardless of time

Tribute to…

- Jeff Klann
- Michael Mendis
- Kavi Wagholikar
- Lori Phillips
- Isaac Kohane
- Kenneth Mandl
- Joshua Mandel
- Griffin Weber
- Paul Avillach
- Christopher Herrick
- Vivian Gainer
- Victor Castro
- Nich Wattanasin
- Wayne Chan
- David Wang
- Andrew Cagan
- Bhaswati Ghosh
- Retta Metta
- Adam Landman
- Willian Gordon



I2b2, SHRINE, and SMART Information and Software on the Web

i2b2 Homepage (https://www.i2b2.org)

i2b2 Software (https://www.i2b2.org/software)

i2b2 Community Site (https://community.i2b2.org)

SMART Platforms Homepage (http://smarthealthit.org)

Partners Healthcare, NIH/NCBC/BD2K; /NIMH; /NCATS; /NIBIB; /NHGRI

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NIH U54 LM008748
NIH U01 HG008685
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NIH U54 HG007963
NIH R01 AT006364
NIH R01 AT005280
NIH P01 AT006663

THANK YOU