2010 Fall i2b2 Academic Users' Group Meeting: Field Report from the CARRA*net* Registry Informatics Development Team

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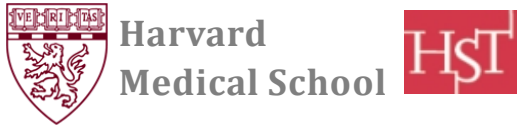
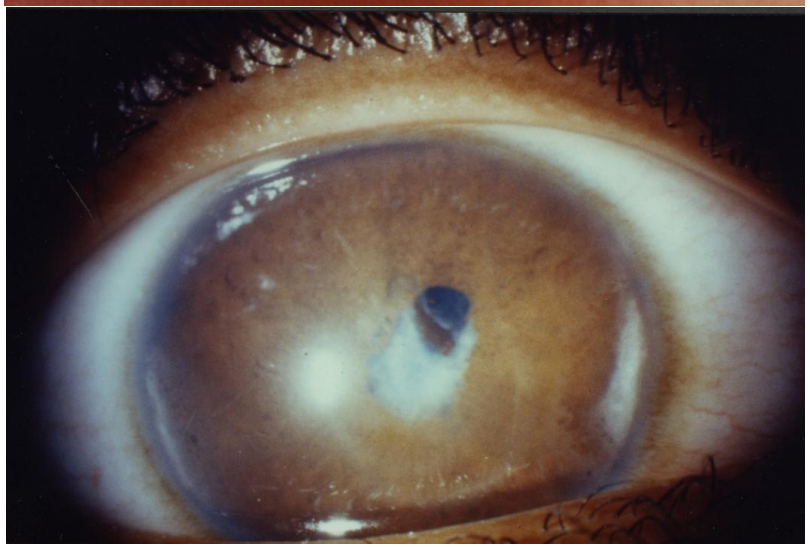
October 13, 2010

NIH Natcher Auditorium



Registries and Reasons:
Juvenile Idiopathic Arthritis & Risk for Eye Disease



Going ‘Retro’:
Translating Research into Improved Care through Registries

- Cystic Fibrosis Foundation
  - LeRoy Matthews, Warren Warwick, Don Berwick, and others

ANNALS OF MEDICINE

THE BELL CURVE

What happens when patients find out how good their doctors really are?

BY ATUL GAWANDE

Every illness is a story, and Annie Page's began with the kinds of small, unexceptional details that mean nothing until seen in hindsight. Like the fact that, when she was a baby, her father sometimes called her Little Potato Chip, because her skin tasted salty when he kissed her. Or that Annie's mother noticed that her breathing was sometimes a little wheezy, though the pediatrician

lection pad of dry filter paper is taped over it to absorb the sweat for half an hour. A technician then measures the concentration of chloride in the pad.

Over the phone, the doctor told Honor that her daughter's chloride level was far higher than normal. Honor is a hospital pharmacist, and she had come across children with abnormal results like this. "All I knew was that it meant

cystic fibrosis in the "Nelson Textbook of Pediatrics"—the bible of the specialty—was written by one of the hospital's pediatricians. The Pages called and were given an appointment for the next morning.

"We were there for hours, meeting with all the different members of the team," Honor recalled. "They took Annie's blood pressure,

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Tool in Cystic Fibrosis Fight: A Registry

Christopher Capozziello for The New York Times

SUPPLIES DATA Caroline Castonguay reports to a medical team that includes a physician, nurse, social worker, nutritionist and a clinical research coordinator.

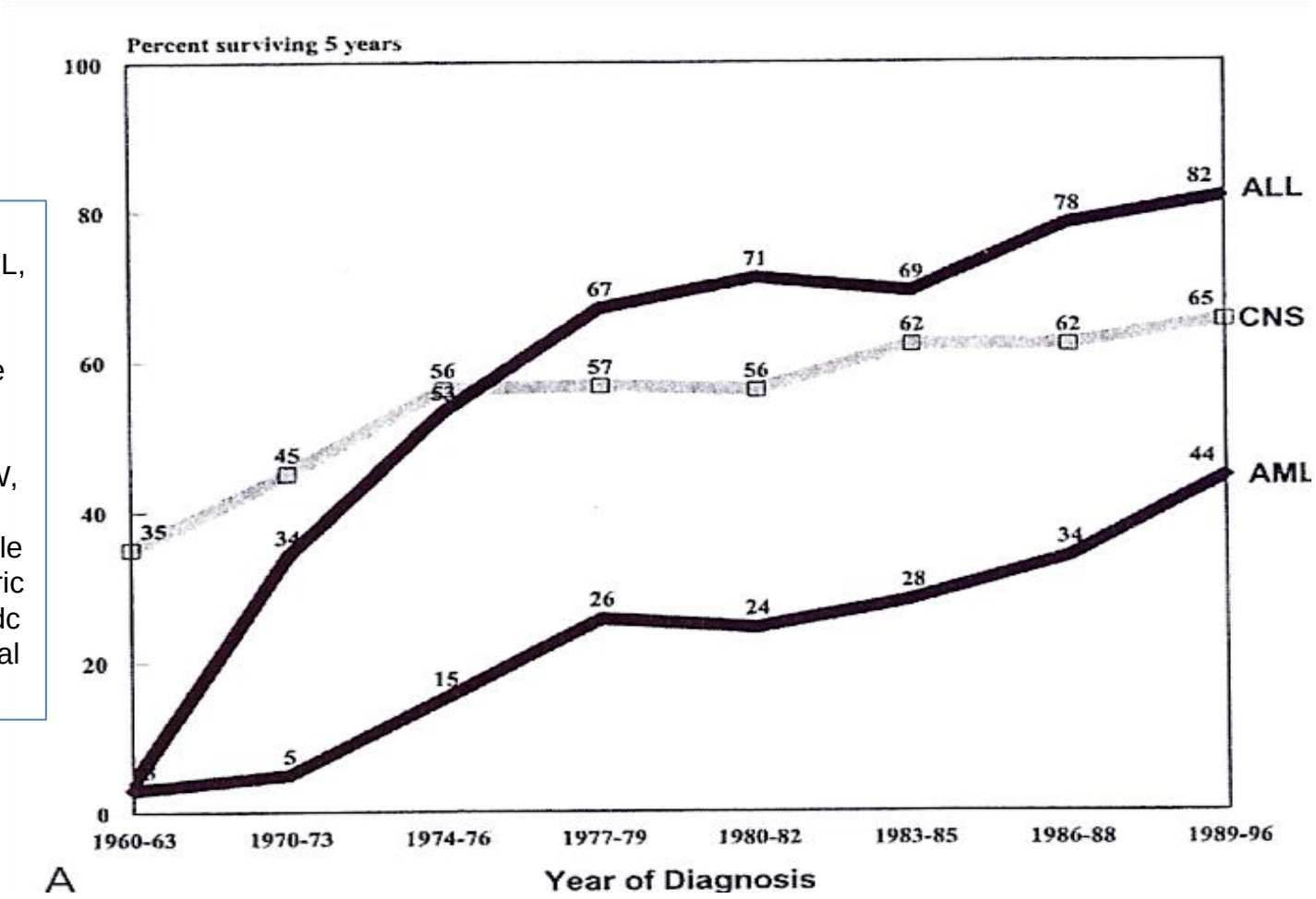
By MILT FREUDENHEIM
Published: December 21, 2009

SIGN IN TO

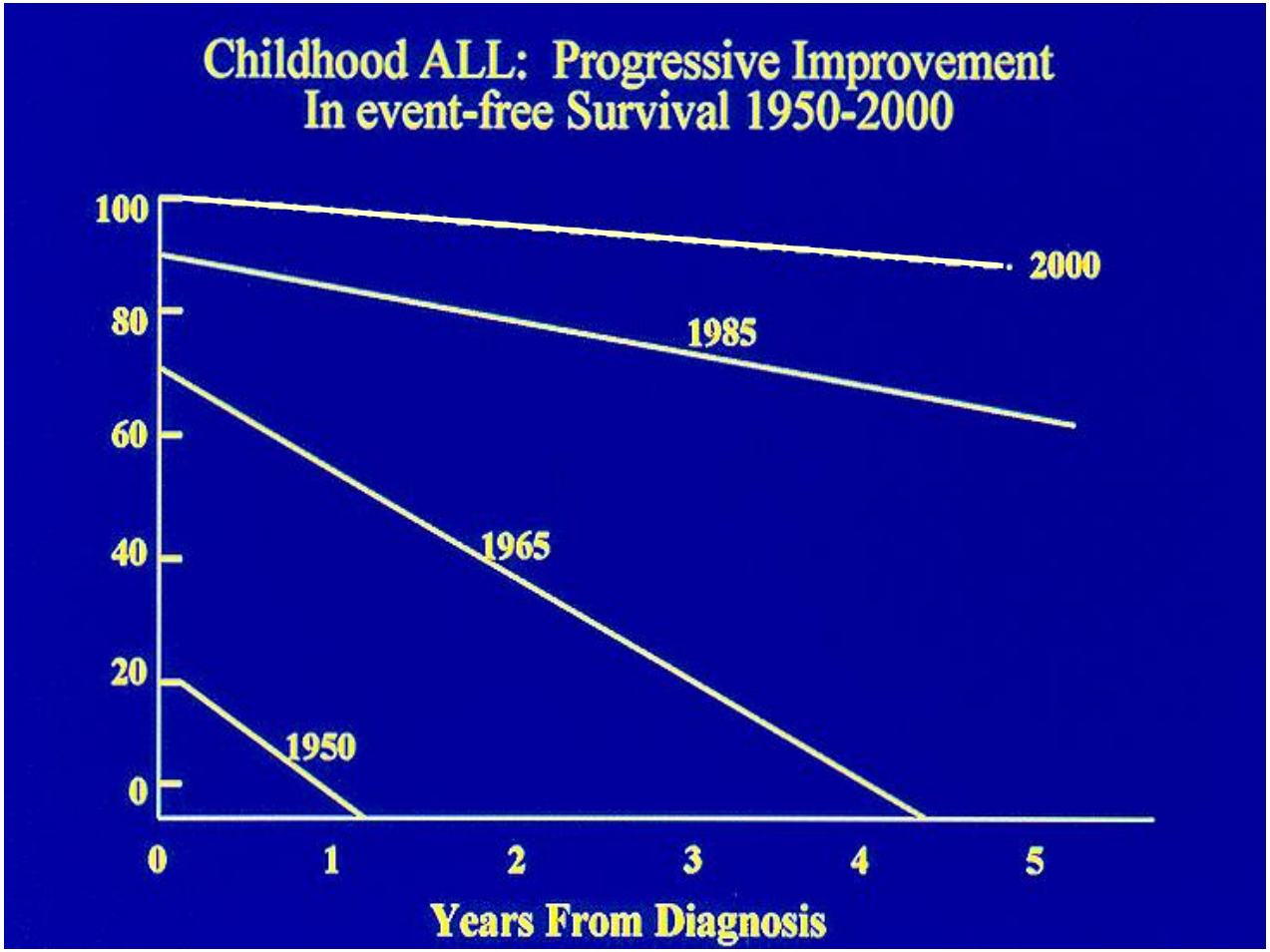
Left: Gawande A, The Bell Curve. New Yorker Magazine 12/2004
Right: http://www.nytimes.com/2009/12/22/health/22cyst.html

The Pediatric Oncology Story

Source:
Gurney JG & Bondy ML, "Epidemiology of Childhood Cancer", in Principles and Practice of Pediatric Oncology, 5th ed, Pizzo PA and Poplack DA, eds, LWW, 2005; and http://www.mcw.edu/FileLibrary/Groups/Pediatrics/Hemoc/03_childhoodcancer_incidencesurvival_and_mortality_v2.ppt



The Pediatric Oncology Story (cont'd)



Source:
Sharon Murphy, Pediatric Oncology Group, personal communication

The Pediatric Oncology Story: Protocol-Based Care, 1981-1991

- Patients enrolled on SPOG/POG Protocol: Survival = 76%, N=120
- Patients not enrolled in study: Survival = 52%, N = 42

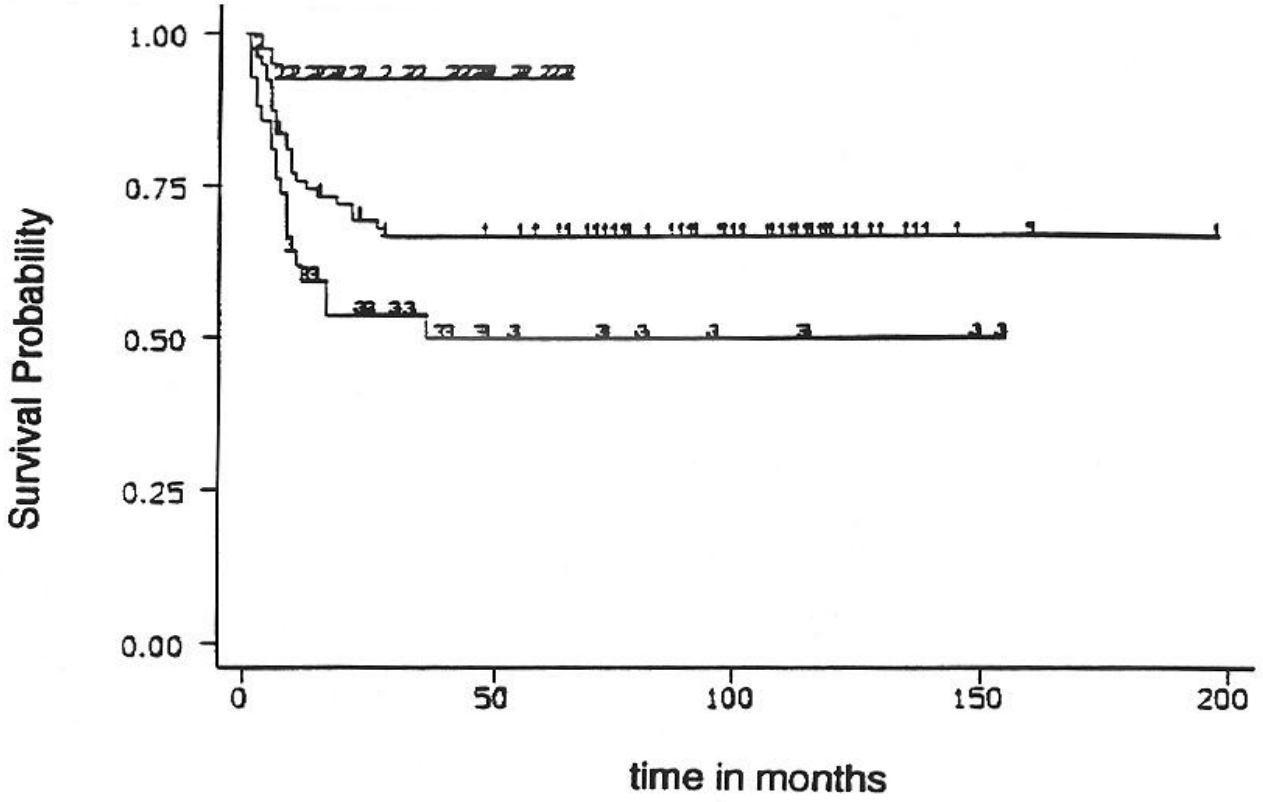
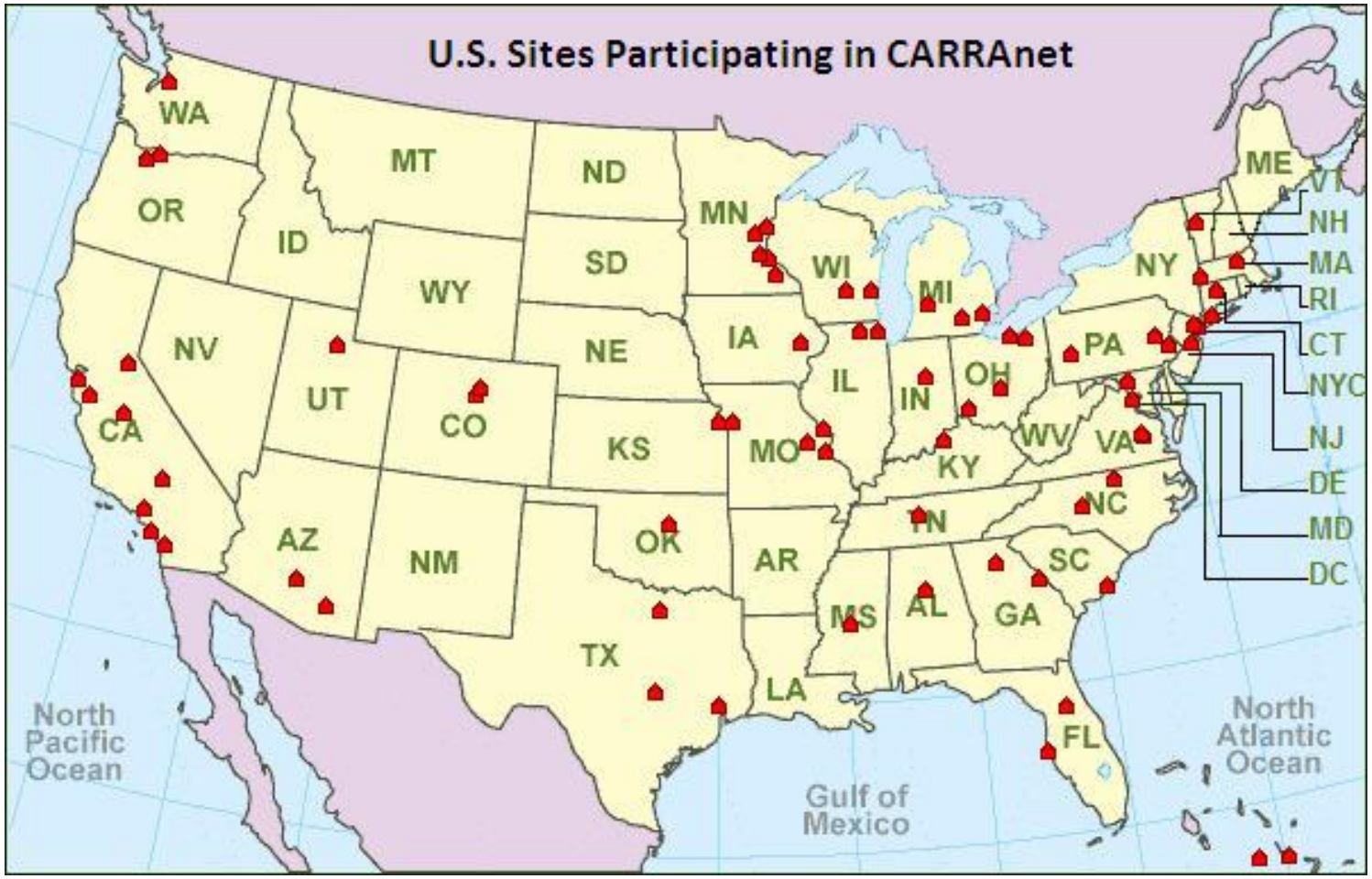


Fig. 1. Survival curves. Group 1: study patients on SPOG protocols (n = 79) = middle curve; Group 2: study patients on POG protocols (n = 41) = upper curve; Group 3: non-study patients (n = 42) = lower curve.

Sources:
1. Wagner HP, et al. Childhood NHL in Switzerland: incidence and survival of 120 study and 42 non-study patients. Med Pediatr Oncol. 1995 May; 24(5):279-80.
2. Sharon Murphy, Pediatric Oncology Group, personal communication

CARRA*net* Grand Opportunities Grant National Registry

NIAMS RC2AR058934, Sites=60, Target Enrollment=20,000



So, what's wrong with most existing clinical registries?

- Cannot readily access one's own data
- Difficult to modify databases after-the-fact
  - Changing and adding fields can be problematic
  - Often unclear how to accommodate changes in data elements over time
- Challenge to collect and analyze similar data across different databases
  - Geographic boundaries (e.g. U.S. vs. foreign)
  - Subspecialty divide (e.g. rheum – nephro – IBD)

Not to mention…

- Long-term follow-up: Crossing the pediatric to adult care transition – a ‘Data Canyon’
- High cost of reinventing the wheel with a custom solution for each new registry

CARRA*net* Design Principles

- Build a valuable base of shared clinical research data
  - All investigators agree to collect a parsimonious ‘common data set’ to be shared
  - Able to layer additional, individual or group-based data sets on top of base data
- Enable ready, equitable access to data
  - Ensure *full, near real-time* access to self-contributed data
  - Incorporate flexible model for different sets of data to be shared among different groups of investigators
- Enable users to directly visualize and analyze data
- Maintain data security and network reliability

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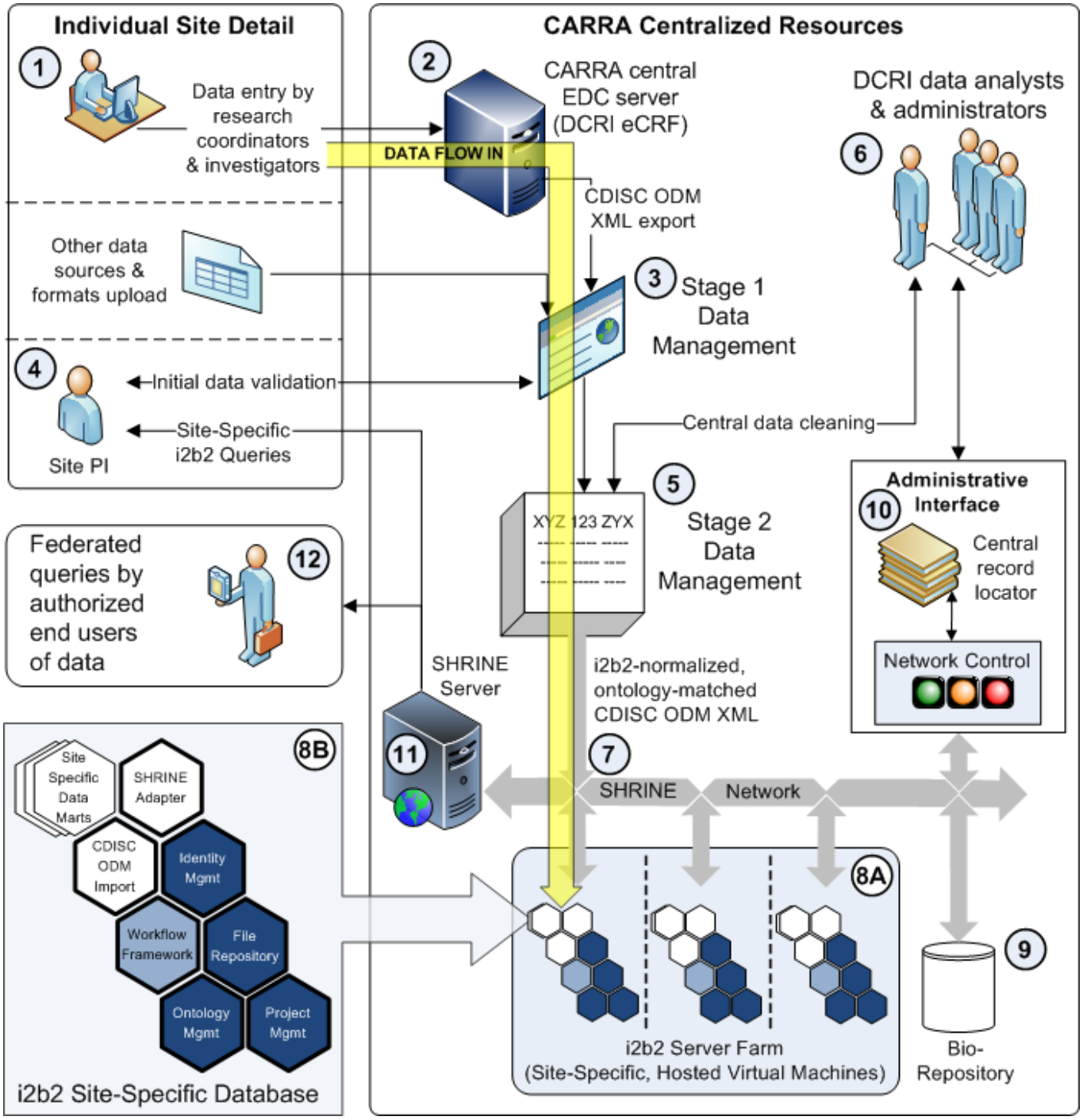
Childhood Arthritis & Rheumatology Research Alliance (CARRA)

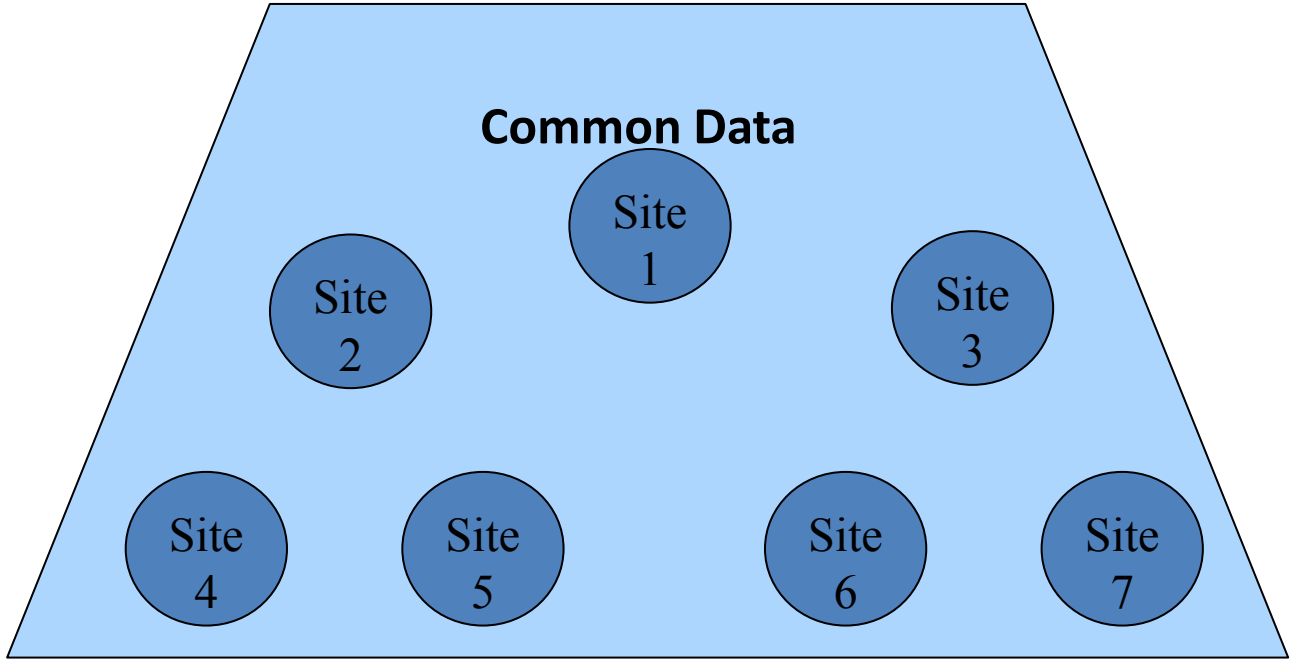
- Investigator-sponsored research network representing essentially all North American pediatric rheumatologists (N~300) & ~64 sites in United States
- Received Grand Opportunities and Challenge Grant to improve care through clinical and comparative effectiveness research
- CARRA*net* GO Grant Targets
  - 60 sites, 20,000 subjects
  - Long-term longitudinal follow-up (every 6 months)
- CARRA*net* GO Status
  - First site activated and enrolling subjects on May 27, 2010
  - 20 sites activated as of 10/08/2010
  - 13 sites entering data
  - Nearly 700 subjects enrolled to date ☺

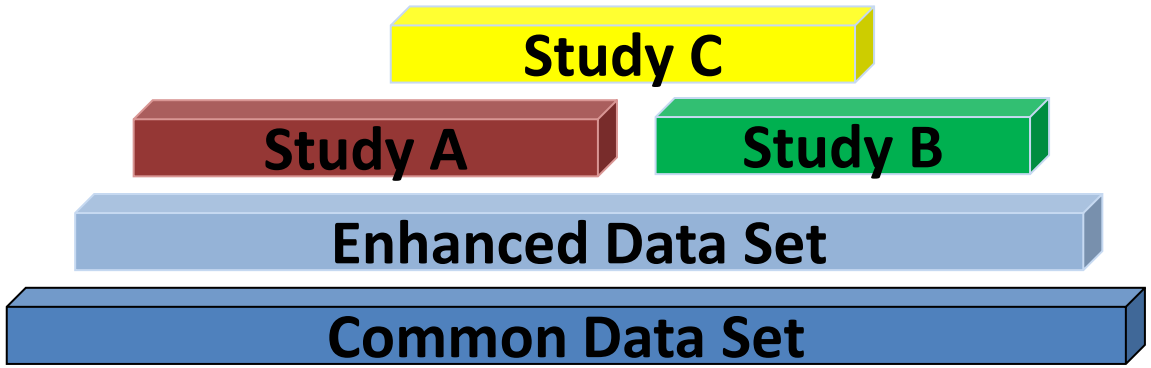
CARRA*net* Development Partners

- Duke Clinical Research Institute
  - Prime, acts as CRO, coordinates clinical and development components
  - Electronic Data Capture, data export
- Cincinnati Children's Hospital
  - Front end user interface, reporting and business intelligence-like features
- Children's Hospital Boston
  - i2b2/SHRINE development & integration
- Harvard Medical School
  - Data export (CDISC ODM) to i2b2 import
  - SHRINE/SPIN coordinated development

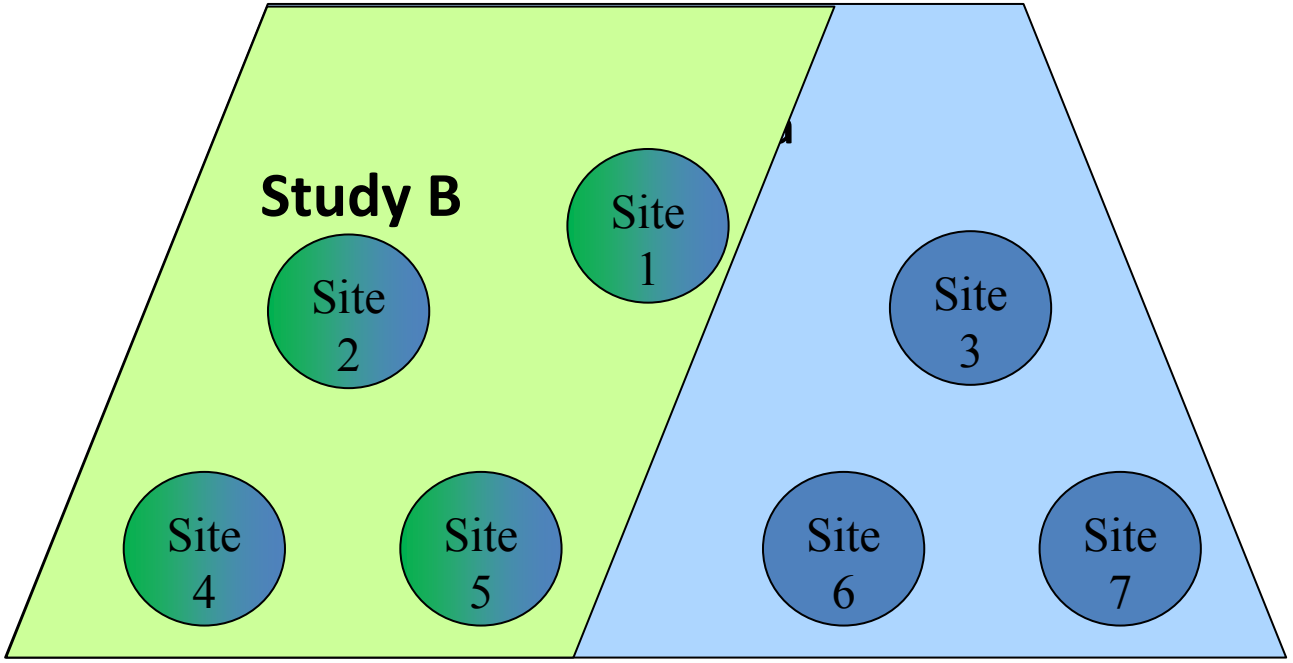

Individual Site Detail
1
Data entry by research coordinators & investigators
Other data sources & formats upload
4
Initial data validation
Site-Specific i2b2 Queries
Site PI
Federated queries by authorized end users of data
12
CARRA Centralized Resources
2
CARRA central EDC server (DCRI eCRF)
DATA FLOW IN
CDISC ODM XML export
DCRI data analysts & administrators
6
3
Stage 1 Data Management
Central data cleaning
5
XYZ 123 ZYX
Stage 2 Data Management
Administrative Interface
10
Central record locator
Network Control
SHRINE Server
11
i2b2-normalized, ontology-matched CDISC ODM XML
7
SHRINE
Network
8B
Site Specific Data Marts
SHRINE Adapter
CDISC ODM Import
Identity Mgmt
Workflow Framework
File Repository
Ontology Mgmt
Project Mgmt
i2b2 Site-Specific Database
8A
i2b2 Server Farm
(Site-Specific, Hosted Virtual Machines)
9
Bio-Repository

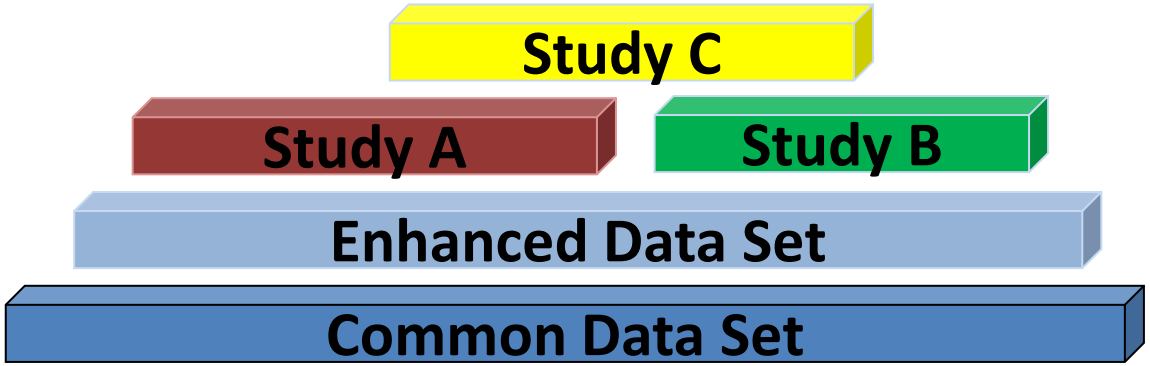
SHRINE/i2b2 for Layered, Multi-Site, Multi-Study Registries



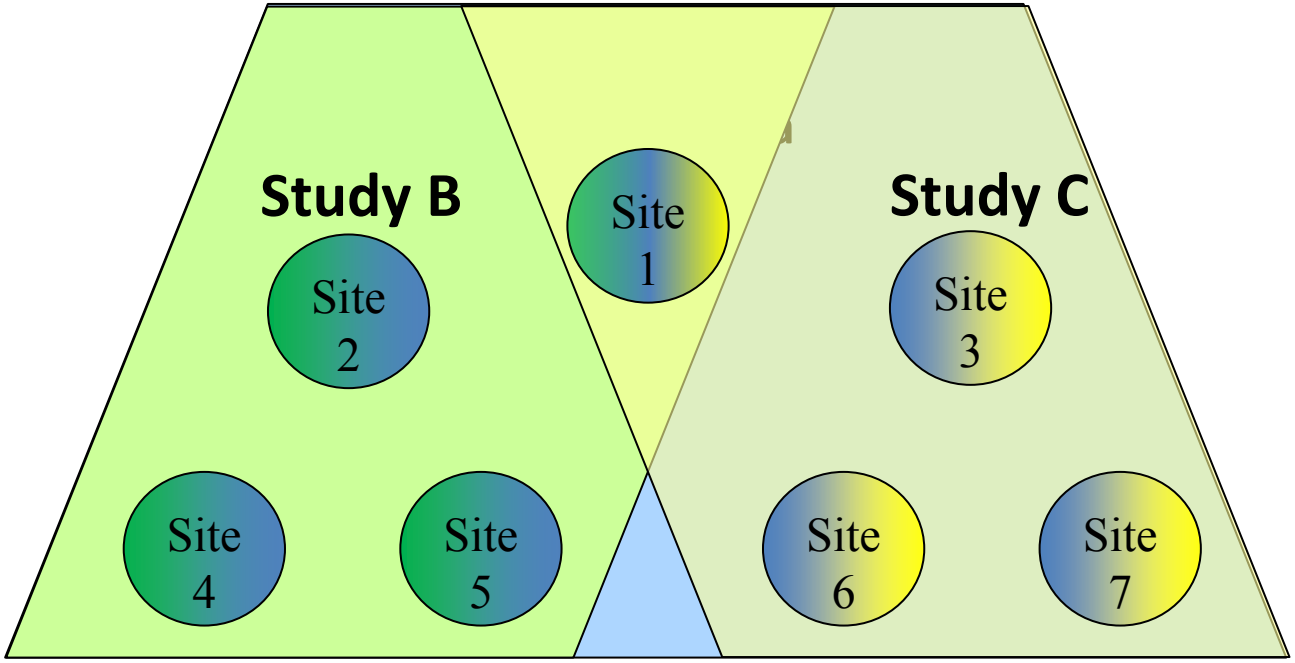


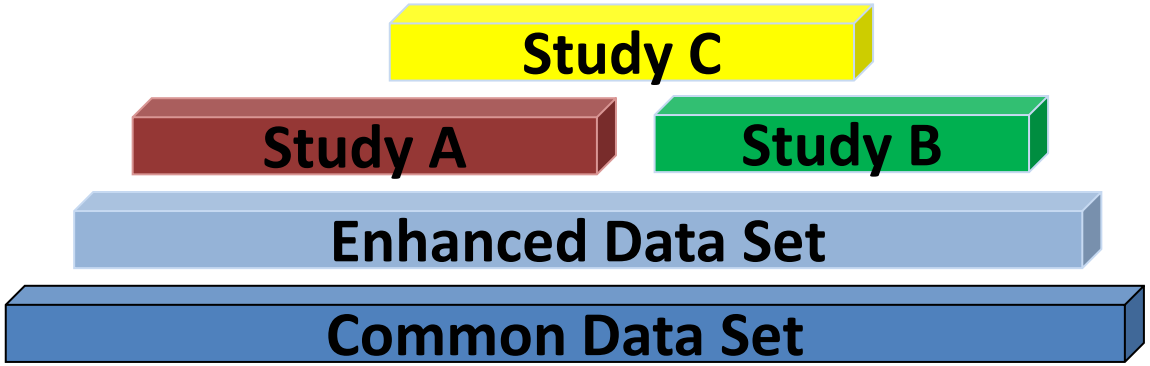
SHRINE/i2b2 for Layered, Multi-Site, Multi-Study Registries



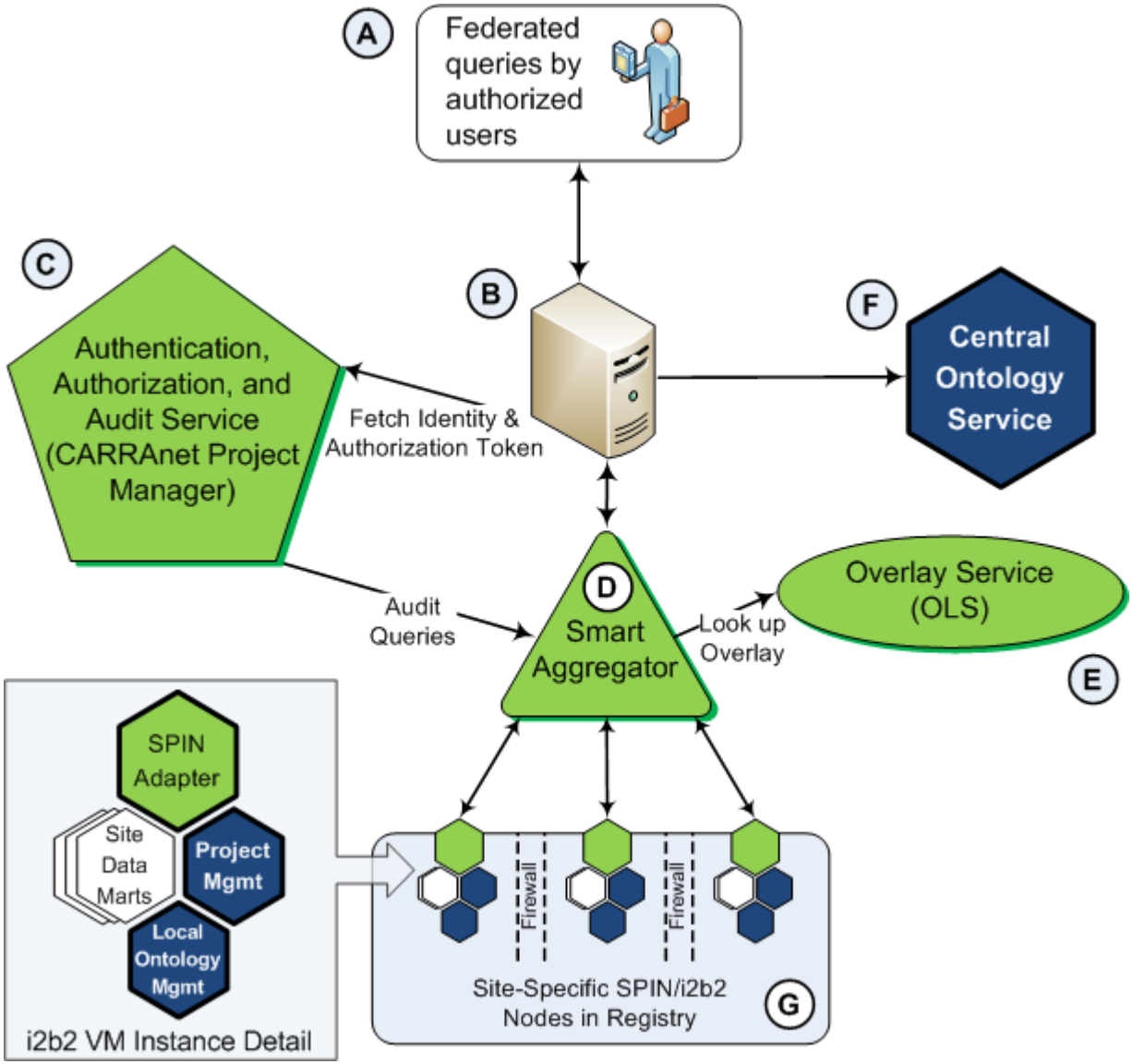


SHRINE/i2b2 for Layered, Multi-Site, Multi-Study Registries



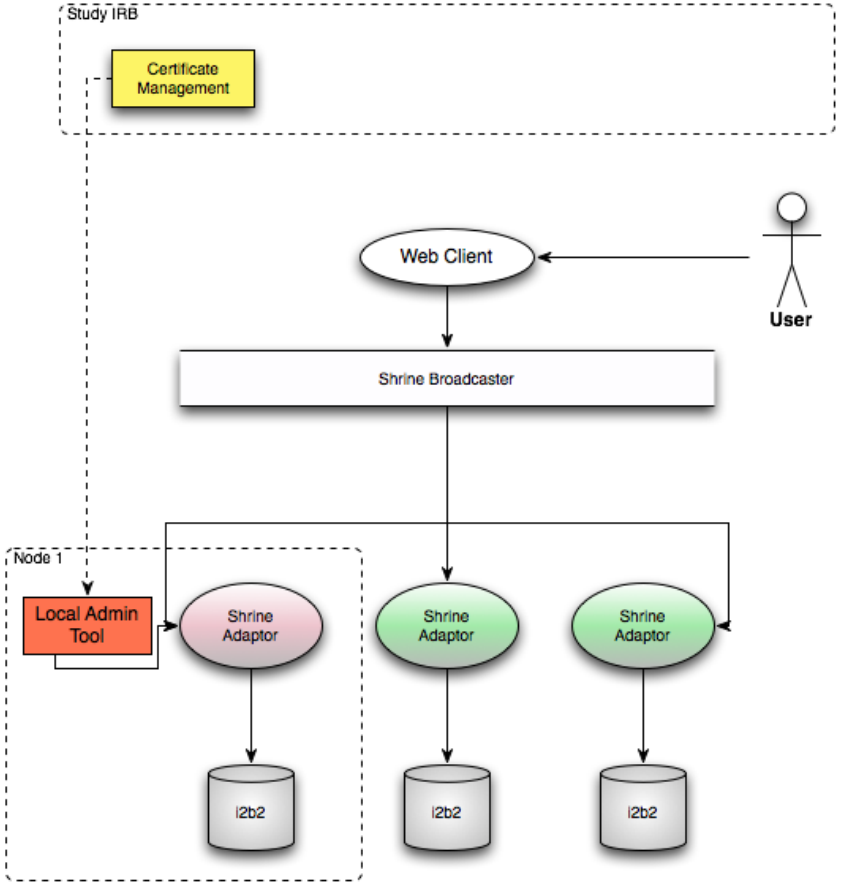


CARRA*net* SHRINE/SPIN Framework Enhancements



Certificate & Admin Enhancements

Local Admin Certificate Management



Capistrano for bulk admin of 60 VMs

- Automatically deploy software to X number of virtual machines leveraging ssh and shared keys
- Software updates/rollbacks can be deployed simultaneously across entire network
- Allows us to run commands on the remote machines, stop tomcat across all 60 sites, restart tomcat, install software, setup databases, etc. for deployment and maintenance
- Extensible, ruby based software
- Envision all 60 sites administered by a single admin

CARRAnet Subscription Model: Early Functionality

CARRA*net* Admin

Manage Users | Manage Studies | Status | Logout

Manage Users

Username	Studies	Delete User	Edit User
admin	[Demo]	x	Edit User
StudyUser1	[LimitedGroup1]	x	Edit User
StudyUser2	[LimitedGroup2, LimitedGroup3]	x	Edit User
StudyUser3	[LimitedGroup3]	x	Edit User

Add User

CARRA*net* Admin

Manage Users | Manage Studies | Status | Logout

Cluster Status

Machine ID	Machine Hostname	Status
carranet node 1	https://shrine-node-1:8081/shrine-cell/QueryToolService/aggregate?wsdl	
carranet node 2	https://shrine-node-2:8081/shrine-cell/QueryToolService/aggregate?wsdl	
carranet node 3	https://shrine-node-3:8081/shrine-cell/QueryToolService/aggregate?wsdl	
carranet node 4	https://shrine-node-4:8081/shrine-cell/QueryToolService/aggregate?wsdl	
carranet node 5	https://shrine-node-5:8081/shrine-cell/QueryToolService/aggregate?wsdl	

CARRA*net* Admin

Manage Users | Manage Studies | Status | Logout

Manage Study Groups

Study	Machines	Edit	Delete
Demo	[carranet node 1, carranet node 2, carranet node 3, carranet node 4, carranet node 5]	edit	delete
LimitedGroup1	[carranet node 1, carranet node 2]	edit	delete
LimitedGroup2	[carranet node 4, carranet node 5]	edit	delete
LimitedGroup3	[carranet node 2, carranet node 3, carranet node 4]	edit	delete

New study group

Study Group

LimitedGroup4

Machines

carranet node 1
carranet node 2
carranet node 3
carranet node 4
carranet node 5

Submit

Cancel

CARRA*net* Admin

Manage Users | Manage Studies | Status | Logout

Manage Cluster Machines

MachineId	Hostname	Edit	Delete
carranet node 1	https://shrine-node-1:8081/shrine-cell/QueryToolService/aggregate?wsdl	edit	delete
carranet node 2	https://shrine-node-2:8081/shrine-cell/QueryToolService/aggregate?wsdl	edit	delete
carranet node 3	https://shrine-node-3:8081/shrine-cell/QueryToolService/aggregate?wsdl	edit	delete
carranet node 4	https://shrine-node-4:8081/shrine-cell/QueryToolService/aggregate?wsdl	edit	delete
carranet node 5	https://shrine-node-5:8081/shrine-cell/QueryToolService/aggregate?wsdl	edit	delete

New Machine

MachineId

New Machine

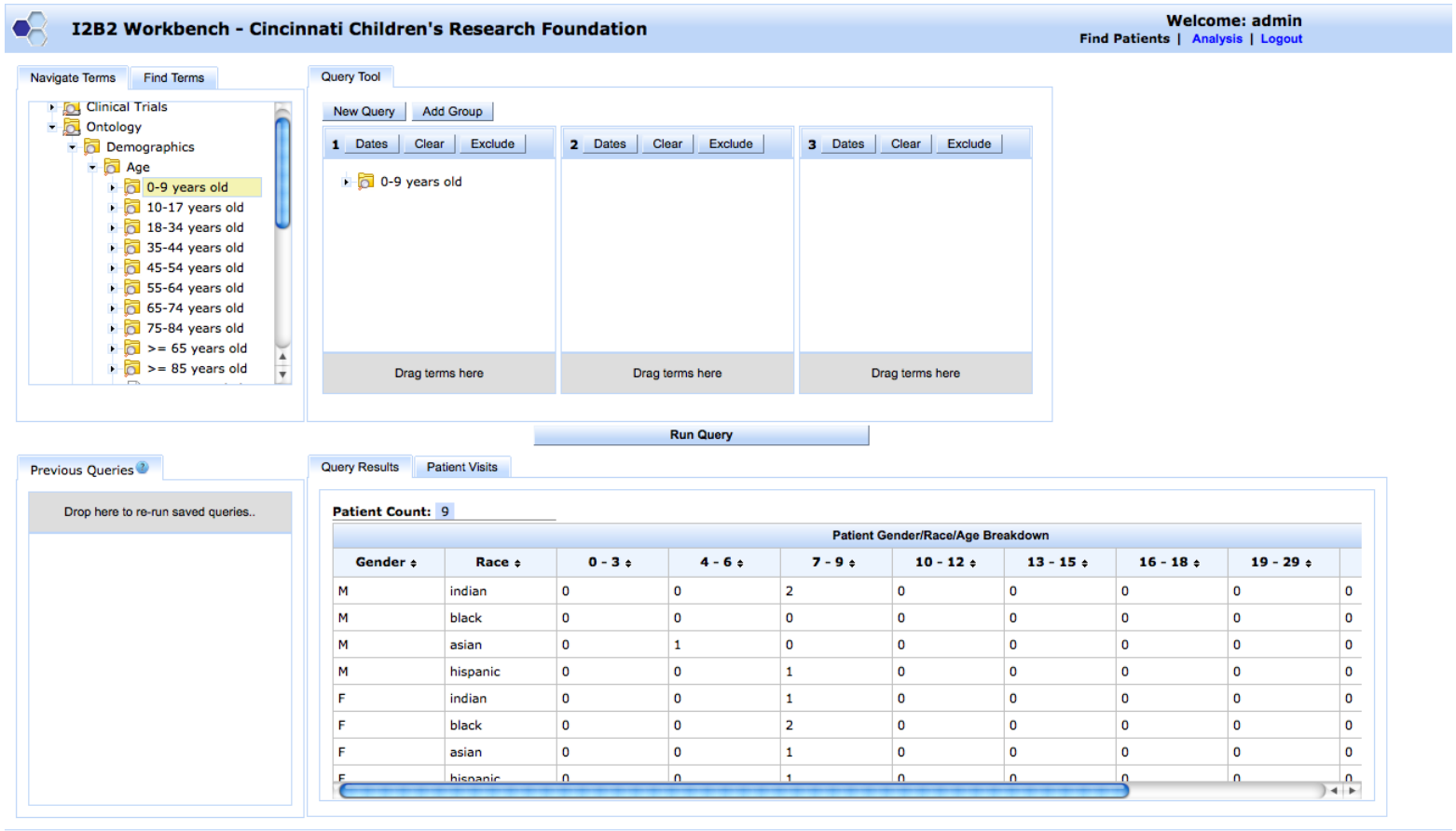
endpoint URI

https://node-uri:8081/shrine-cell/QueryToolService/aggregate?wsdl

Submit

Cancel

Moving Towards 'Self-Service' Model for Federated Data Sharing of Registry Data



Amazon EC2 Deployable Demo Environment

CARRA *net* Live Demo

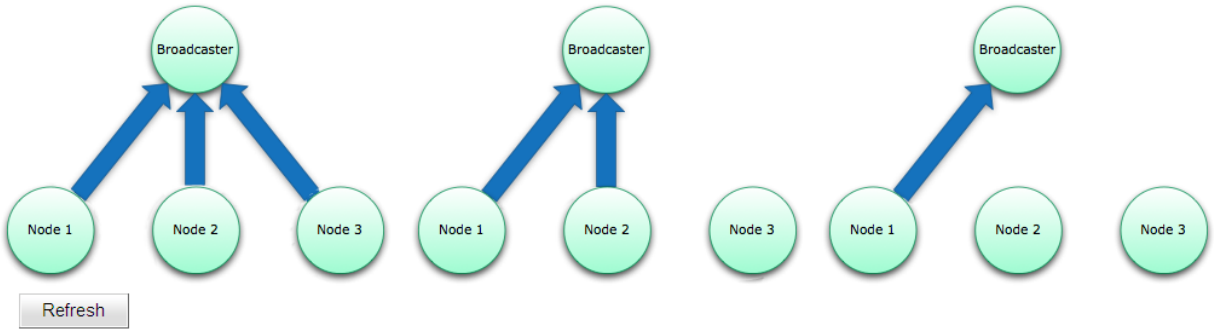
Welcome to this live demonstration of the CARRANet project. The CARRANet project aims to connect multiple i2b2 data repositories together in order to form a collaborative study network. Our vision is to create the next generation platform for building and sharing large patient registries.

Federated Query Demonstration

Federated Query Page

Network Communication Demonstration

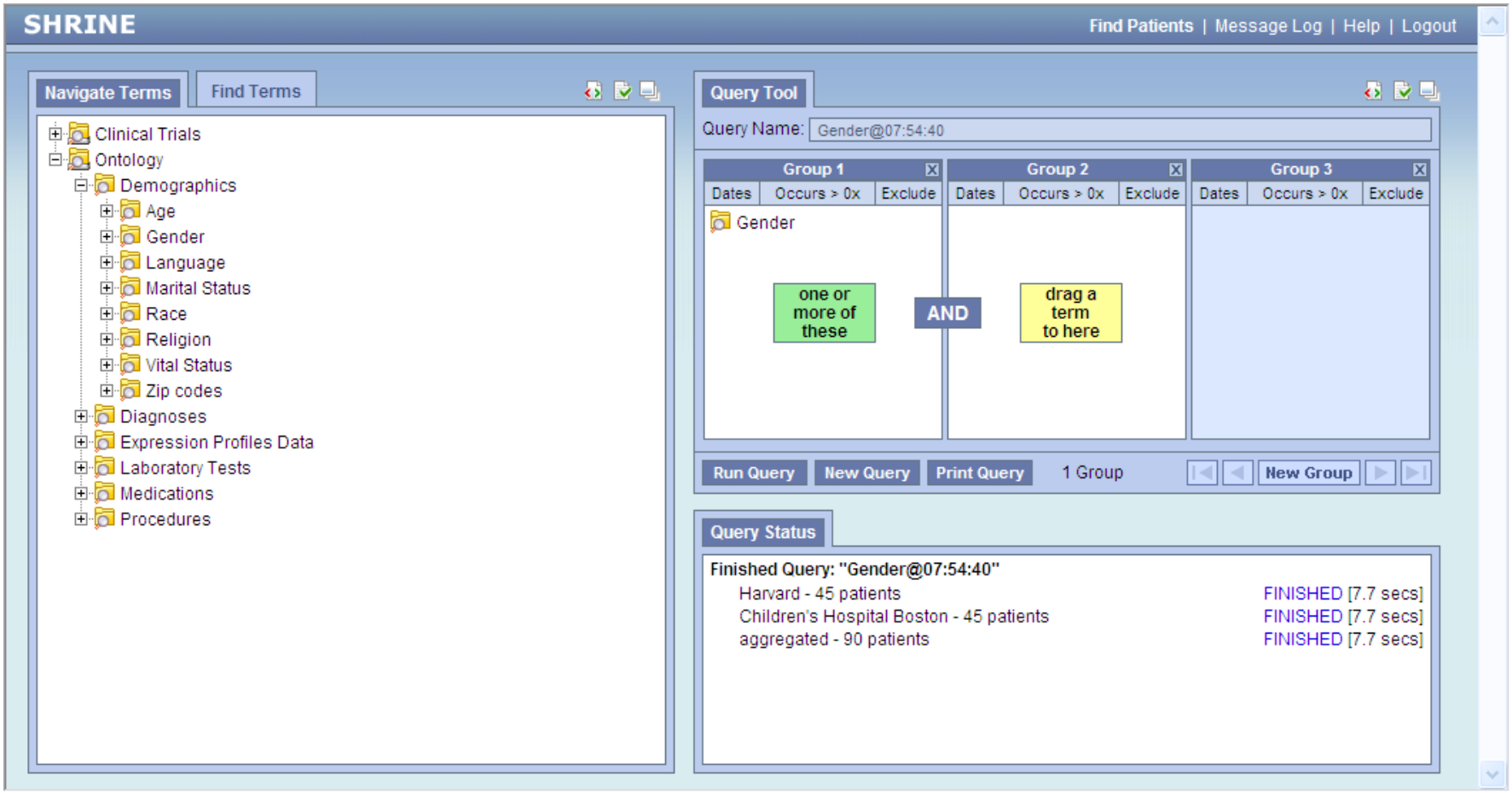
Below is a diagram that shows three different studies each with a different node membership. The memberships are described by the arrows. The node at the top is the CARRANet node that will federate queries across all the i2b2 nodes. The 3 nodes at the bottom are each an i2b2 instance that belong to different institutions. The current state of a node's connectivity to the network is represented by it's color (green is connected, red is not). These 3 studies happen to be on the same 3 node network.



The following links will take you to a view of how a local administrator would add their institution's node to the CARRANet network.

See Configuration Page for Node1
See Configuration Page for Node2
See Configuration Page for Node3

Amazon EC2 Deployable Demo Environment (Two Nodes Participating)



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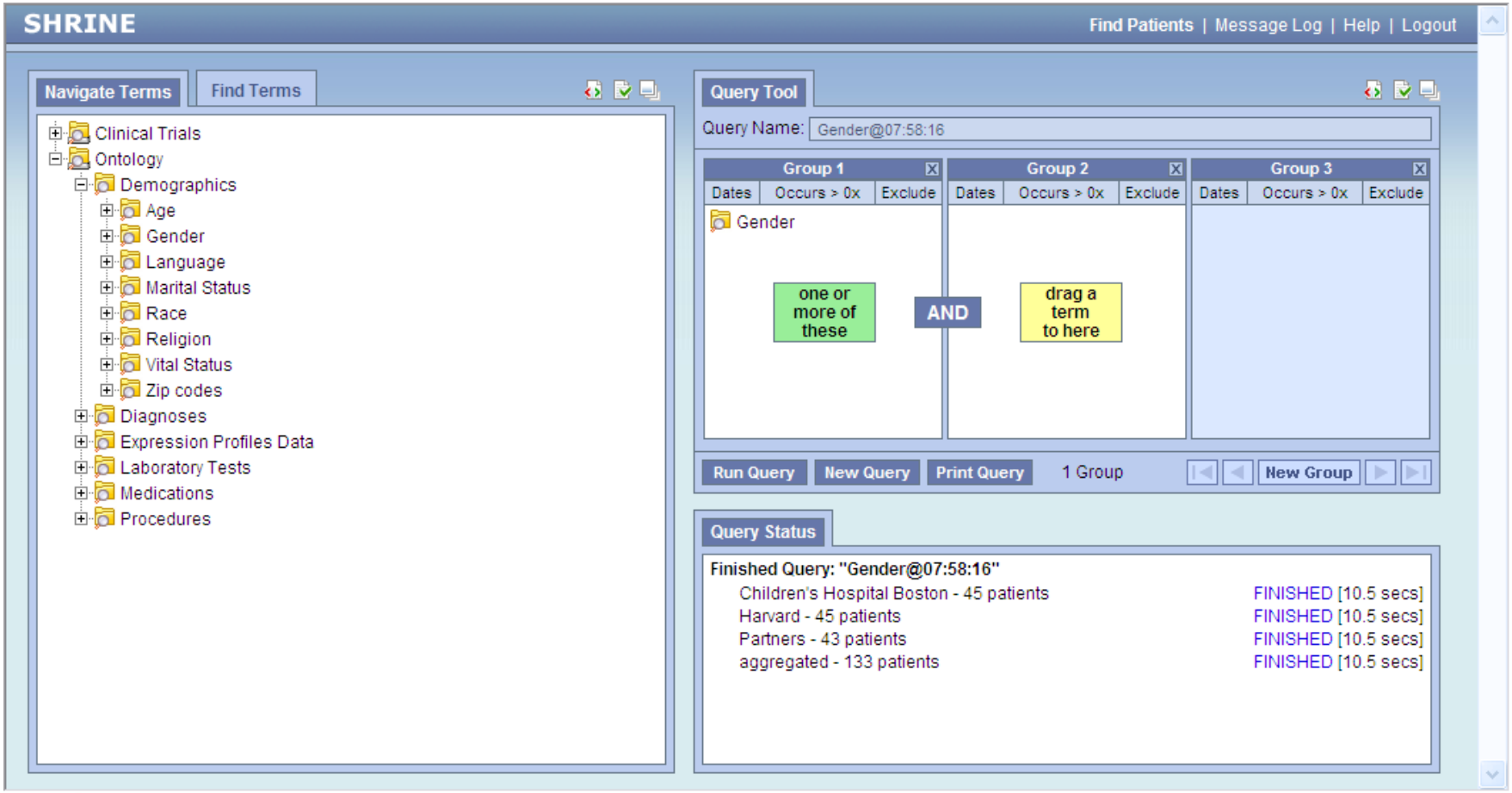
Amazon EC2 Deployable Demo Environment (Three Nodes Participating)



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Future Directions

- Multiple projects and networks
- Integrate with hospital-based i2b2 systems
- International collaborations

Many Thanks to the Organizations Supporting CARRA*net* Efforts

- NIAMS via RC2AR058934, RC1AR058605
- Friends of CARRA
- Arthritis Foundation
- American College of Rheumatology

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