

STRIDE – An Integrated, Standards-Based Translational Research Informatics Platform

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Abstract

STRIDE (Stanford Translational Research Integrated Database Environment) is a research and development project at Stanford University to create a standards-based informatics platform supporting clinical and translational research. STRIDE consists of three integrated components: a clinical data warehouse, based on the HL7 Reference Information Model (RIM), containing clinical information on over 1.3 million pediatric and adult patients cared for at Stanford University Medical Center since 1995; an application development framework for building research data management applications on the STRIDE platform and a biospecimen data management system. STRIDE's semantic model uses standardized terminologies, such as SNOMED, RxNorm, ICD and CPT, to represent important biomedical concepts and their relationships. The system is in daily use at Stanford and is an important component of Stanford University's CTSA (Clinical and Translational Science Award) Informatics Program.

Introduction

Informatics has emerged as an important contributor to effective clinical and translational research (CTR), particularly within NIH's Clinical and Translational Science Awards (CTSA) program¹. In 2003 the Institute of Medicine's (IOM) Clinical Research Roundtable published a report on challenges facing the national research enterprise². They recommended the development of information systems "designed to meet the needs of clinical research". In 2005, as a follow up to this report, Payne et al conducted a qualitative study of how informatics was being used to support translational research at several leading academic medical centers³. They found that fragmentation of resources frequently hindered the effective use of informatics in CTR and that Electronic Health Record (EHR) systems were of limited value in supporting translational research. In 2008 DiLaura et al looked at the use of informatics in the clinical research enterprise at 52 U.S. sites⁴ and found little progress, other than in planning, strategy and governance, since a similar study conducted by them in 2005. In 2008, many of the same challenges listed in the IOM report were again identified by

Williams et al in their report on lessons learned from the Clinical Research Networks Initiative⁵. A 2009 review on reuse of clinical data for CTR emphasized the need for integrating clinical research projects with data repositories built up during documentation of routine clinical care⁶. Over the past few years a number of integrated sharable CTR informatics models have emerged, including caBIG⁷ and i2b2⁸.

In 2002, Stanford University School of Medicine launched a new strategic plan called "Translating Discoveries"⁹, that included the goal to "promote the development of those interdisciplinary research collaborations most likely to lead to improved health through the exploitation of new knowledge of biosciences and disease mechanisms". To support its broad goals related to CTR, the School created the Stanford Center for Clinical Informatics (SCCI), tasked with developing an enterprise-level informatics architecture supporting the needs of CTR, leveraging on the Stanford electronic health record. In 2003, SCCI began a multiyear research and development project to create an integrated, standards-based informatics platform addressing three major barriers to effective CTR: (1) efficient access to clinical data for research purposes; (2) availability of robust research data management solutions and (3) availability of an enterprise-level system for managing and discovering biospecimen data. This new system is called STRIDE (Stanford Translational Research Integrated Database Environment). This paper outlines the architecture and functionality of STRIDE, a system that is now in daily use at Stanford University Medical Center (SUMC) and is a core component of Stanford's CTSA informatics model.

Methods

STRIDE is built on the Oracle 11g relational database platform and uses an n-tiered architecture. Data is stored using an Entity-Attribute-Value (EAV) model¹⁰ and is represented by object-oriented data structures (entities, roles and acts) derived from the HL7 Reference Information Model (RIM)^{11,12}. The system includes a Master Person Index (MPI) that is dynamically populated from clinical, research and biospecimen data. The STRIDE MPI is the only fully integrated enterprise MPI operating at SUMC.

The STRIDE physical database layer is organized into three logical database partitions: (1) a Clinical Data Warehouse (CDW); (2) Research Database Management supporting multiple logically separate research databases and (3) the Biospecimen Data Repository, which supports multiple separate biospecimen databases. All three components rely on the same underlying architecture and services. Data can be linked across all three partitions. For example, with IRB approval, research and/or biospecimen data can be merged with clinical data from the Clinical Data Warehouse.

STRIDE's semantic layer consists of a framework supporting multiple terminologies, including ICD9-CM, ICDO, CPT, RxNorm and SNOMED. This mixed terminology model supports standards-based data entry, data integration, hierarchical concept-based retrieval and data interoperability. As an example, using RxNorm to represent pharmacy data in STRIDE allows the system to merge drug information from the two different vendor drug models used at SUMC, with dynamic integration of pediatric and adult medication orders within the CDW. Additionally, the semantic model allows linkage from RxNorm to SNOMED drug classes.

STRIDE applications use a suite of Java Swing clients communicating with a set of services for managing demographic, clinical, research and reference data (including controlled vocabularies). These software services are organized in a Service Oriented Architecture (SOA) with the baseline services serving not only client applications but also the clinical and research data services within the core system stack (Figure 1).

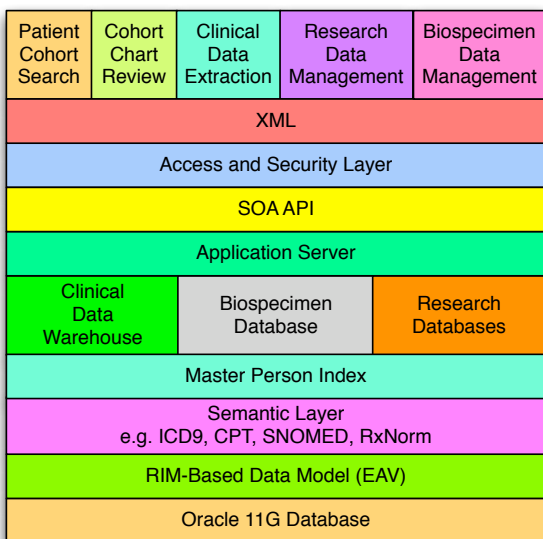


Figure 1. STRIDE Architecture Stack

STRIDE client applications, written in Java, are created using reusable components to facilitate rapid application development. A rich application programming interface (API) permits client applications to dynamically specify the content of data retrieval queries which are then translated on the server side into SQL scoped by the data visibility rules in the STRIDE access and security layer, resulting in dynamically reconfigurable data sets called Virtual Private Databases¹³ (VPD) which support highly detailed access control rules.

As of February 2009 the STRIDE CDW contained fully-identified merged demographic and clinical information on over 1.3 million pediatric and adult patients cared for at Stanford University Medical Center (SUMC) since 1995. Table 1 shows the major classes of data stored in the CDW, along with counts and starting year. Stanford pharmacy data is currently being added. All clinical documents and reports are full-text indexed and searchable using Oracle Text¹⁴. The CDW was initially populated with legacy clinical data extracts from the two SUMC EHR systems (Lucile Packard Children's Hospital at Stanford uses Cerner and Stanford Hospital and Clinics uses Epic). The CDW is now populated, in real-time, using HL7 message feeds from a variety of SUMC clinical systems. These version 2.x HL7 messages are parsed by STRIDE to create HL7 RIM-based data structures and linked to patient identifiers in the STRIDE MPI.

Clinical Encounters	8.8 Million (Since 1994)
Diagnoses (ICD9)	14 Million (Since 1994)
Procedures (CPT, ICD9)	9.5 Million (Since 1994)
Radiology Reports (Full-Text)	1.7 Million (Since 2005)
Pathology Reports (Full-Text)	1 Million (Since 1995)
Clinical Documents (Full-Text)	4.4 Million (Since 2005)
Laboratory Test Results	87 Million (Since 2000)

Table 1. STRIDE CDW Data (February 2009)

Stanford researchers can search the CDW to identify potential research patient cohorts using a self-service visual query tool called the Anonymous Patient Cohort Discovery Tool (Figure 2). This Java

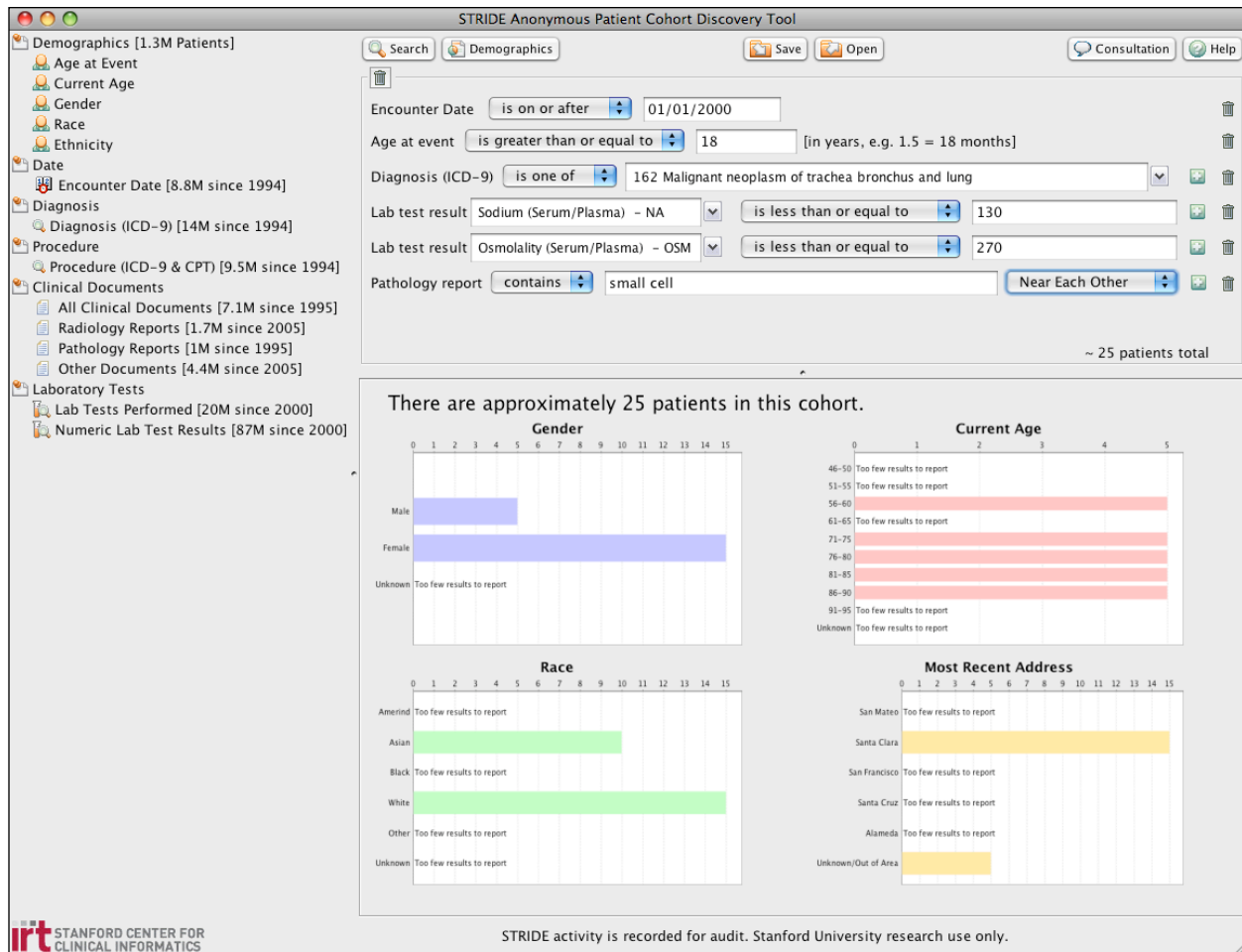


Figure 2. STRIDE Anonymous Patient Cohort Discovery Tool

application, inspired by the earlier work of Murphy et al¹⁵, uses an intuitive drag and drop interface to create and execute queries in real time, answering the question “does the STRIDE CDW contain a cohort of patients with these attributes?” No individual patient data is exposed by this tool and binning¹⁶ is used to prevent identification of individual patients within small cohort sets. All research patient cohort searches are logged for audit purposes. Patient cohorts of interest can be saved within the central STRIDE system for later use in IRB-approved chart review or research data set extraction.

STRIDE also provides a research cohort chart review tool designed to allow efficient examination of clinical data to assist in determining if patients are suitable for inclusion in research studies. Each user can maintain a personal library of research patient cohorts within STRIDE, with access to protected health information (PHI) controlled by IRB approval.

STRIDE is operated as a Stanford IRB-approved research protocol, with a waiver of informed consent

and HIPAA authorization, that permits all clinical data captured as part of routine patient care at SUMC to be transferred to the STRIDE CDW. The transfer of clinical data to the CDW is further governed by a detailed agreement between Stanford’s two hospitals and the Stanford University School of Medicine, where the STRIDE project is based. The STRIDE project works closely with the Stanford University IRB and School of Medicine Privacy Officer to ensure data is only used in an authorized manner. Identified clinical data in the CDW is only released to IRB-approved research studies that have received the appropriate IRB approval. Fully de-identified data is made available for Stanford research projects that has been determined to qualify as a non-human subject research study. Patient contact information is only released to studies that have a detailed IRB approved recruitment strategy. All STRIDE applications have a robust logging framework and audit capabilities.

Rich research data management applications, incorporating imaging data, if required, can be developed on the STRIDE platform. The STRIDE

application development workbench offers a wide variety of both stock and custom interface components, ranging from simple lists of values, numeric or text input fields and search-as-you-type data discovery widgets that permit users performing research data entry to rapidly search reference data for an appropriate value. The reference data underlying the data discovery widgets can be patient or physician identifiers or any of the controlled vocabularies used to codify data where appropriate. The orchestration of the underlying services, namely the MPI (Master Person index), tissue and image search, data extraction, data profile discovery, PACS image integration, data retrieval and data persistence services, is achieved by creating XML descriptor files specifying which services a given application requires. For applications using the data retrieval and persistence service, which includes all research data management applications, additional XML descriptors enumerate the labeling, ordering and placement of each reusable data capture component, permitting rapid development of custom data capture applications.

The STRIDE Biospecimen Data Repository provides registration, tracking and management functions for multiple separate biospecimen banks. Individual banks can store and manage biospecimen data privately within STRIDE, while aggregate biospecimen data can be searched across all banks. This allows the creation of a virtual enterprise biospecimen data repository to which data from additional banks can be added incrementally. As of February 2009, STRIDE contained data on approximately 42,000 biospecimens at Stanford (including tissue, DNA, bone marrow and a variety of blood components), managed in multiple banks. As all stored biospecimen data shares the same STRIDE MPI and the same core data elements (with clinical and pathologic data represented using SNOMED), aggregate anonymous searching across all biospecimen banks is supported, allowing Stanford researchers to discover and request biospecimen samples with specific characteristics. With appropriate IRB approval, biospecimen data can be linked to specific clinical data elements in the STRIDE CDW.

Results

The STRIDE project is a multiyear process of incremental development, testing and deployment of functional components to meet Stanford's specific CTR needs. Since 2004, the system has been used to meet the needs of a growing number of researchers. To most effectively connect researchers to STRIDE services we have, with funding from the School of Medicine, developed a free Informatics Consultation service. Researchers use a Web-based consultation request form to define their specific needs and schedule a meeting with SCCI staff. In many cases consultations result in the delivery of specific

STRIDE-related services, such as development of a research data management solution or provision of clinical data for research purposes. These consultations also provide us with valuable input as to what additional services are needed and how existing services might be enhanced. For example, user feedback suggested that in addition to current age (i.e. calculated age at time of query), the age of the patient at the time of a clinical encounter was an additional criterion that would be valuable when defining research cohort queries. This issue, which has been described in other CDWs supporting research¹⁷, was addressed and is now supported by the STRIDE Anonymous Patient Cohort Discovery Tool.

Building a data warehouse is often an iterative process¹⁸ in which the developer attempts to optimize resource allocation, data availability, technical complexity, scalability and end user needs to deliver incremental functionality, while maintaining the institutional support needed for an expensive multi-year initiative. The STRIDE CDW has been managed as a phased project in which, each academic year, we add new clinical data and deploy new system functionality. For example in the current academic year (September 2008-August 2009) we are adding SUMC pharmacy data to the CDW; deploying a new version of the Patient Cohort Discovery Tool that supports pharmacy-related search criteria (e.g. drug ingredients, drug classes and administration routes) and deploying a Research Cohort Chart Review Tool. We are currently weighing the question of how much of the available SUMC clinical data to aggregate within the physical data warehouse model versus accessing some data elements, as needed, in situ (i.e. from within the EHR itself). If the sole use of the CDW is providing access to clinical data extracts for research purposes, then a hybrid model may be adequate. However, if use of the CDW extends to tasks such as expanded research cohort identification or clinical data mining (an area of interest at Stanford) a high degree of integration is required.

STRIDE has been providing research data management services since 2004. To date multiple research data management applications and databases have been built on the STRIDE platform, ranging from one large multimedia-capable system supporting an entire academic department; various longitudinal patient registries (some incorporating radiology imaging data) and several less complex systems supporting small to medium sized research projects. In this latter category, we feel that the cost-benefit analysis may not warrant continued use of STRIDE as a solution and we are currently evaluating REDCap¹⁹ as an alternative institutional solution for managing data in small to medium sized research projects.

The STRIDE Biospecimen Data Management system is as much a cultural strategy as it is a technology solution. Our hope is to encourage the owners of individual tissue banks at Stanford to use STRIDE, in return they agree to make their biospecimen data discoverable. We provide a self-service tool that Stanford researchers use to determine if any of the participating banks contain specimens of interest. They can then contact the individual bank operators to request specimens.

Discussion

STRIDE is fundamentally an effort to incrementally deploy a standards-based enterprise Informatics model supporting CTR that targets three well described barriers: access to clinical data for research purposes, flexible research data management solutions and robust biospecimen data management and discovery. Implementing all three components within the same database model and system architecture potentially offers a high level of data integration and sharing across components. The system is now a core part of Stanford's CTSA Informatics model.

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