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THE NORTH CAROLINA TRANSLATIONAL & CLINICAL SCIENCES INSTITUTE

UNC
COLLABORATIVE STUDIES COORDINATING CENTER
DEPARTMENT OF BIOSTATISTICS

DATA MANAGEMENT SOLUTIONS FOR CTSA SETTINGS: A CASE STUDY FROM UNC

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Outline

- Data management as a core service of NIH Coordinating Centers
- UNC's TraCS data management initiative
- TraCS DMS: Design and Development
  - System overview
  - Screen shots
- Progress/challenges to date
- Cost model for investigators

NIH Coordinating Center Model

- Key component of federally funded, multi-center studies
  - Clinical trials
  - Epidemiological/observational studies
  - Patient registries
- Services include
  - Project management and coordination
  - Data management (new data collection or existing data integration)
  - Statistical aspects of study design and analysis
  - Management of central labs/reading centers
  - Data dissemination and publications
  - QC/QA
- Scientific purpose is to ensure consistency across centers in study design and conduct
  - Critical for epidemiological studies in absence of randomization

Collaborative Studies Coordinating Center (CSCC)

- Resides in the Department of Biostatistics
- Founded in 1971 as the Lipids Research Clinics (LRC) Data Coordinating Center
- 2nd oldest and longest continuously-funded NIH coordinating center
- Currently includes 90 faculty, staff, and students
  - Matrix organizational structure
  - Functional areas: Data management; Statistics; Statistical Programming; Project management; Clinical monitoring
- Over 20 studies: clinical trials, epidemiology studies, patient registries, pharmaco-epid studies
- Disease areas: cardiovascular, pulmonary, mental health, kidney, injury prevention, periodontal, fetal health, etc.

CSCC Data Management

- Tradition of innovation in data management and statistical computing
  - First CC to implement remote data entry (1986; for ARIC)
  - One of the first CCs to implement web-based data entry (2001)
- Currently implementing data collection via ‘smart pens’ and ‘digital tablets’
  - In clinic settings (TraCS)
  - For household screening in the field (HCHS)

TraCS Data Management Service

- Key initiative of both the Biomedical Informatics and Biostatistics Cores
- Included in UNC's initial CTSA submission (Jan 2007) and resubmission (Oct 2007)
- An early milestone to show visible and meaningful progress
- Rationale:
  - In spite of a proliferation of systems and services across campus, many clinical and translational investigators have no access to systems beyond a spreadsheet for single-keyed data entry
  - Little or no coordination across campus systems exists
- Goal: Every TraCS investigator has access to a secure, high quality, data management system for data capture, processing, management, and reporting

TraCS Data Management Service

- Vision:
  - Scope: all data collected under TraCS approved protocols
  - Integration: use of data standards to promote data sharing
  - Scalability: small, single-center to complex, multi-site studies
- Planned implementation:
  - TraCS Data Management Service created and located within TraCS Institute for easy access
  - Build upon existing GIC Informatics resources in Med School
  - Hire IT manager to direct service
  - New systems development would leverage resources and experience within CSCC
  - Hire project manager/statistician in Bios Core to advise investigators on data collection modalities and serve as liaison to Data Management Service

TraCS Data Management Service

- Initial steps – conducted in parallel
  - Prototype design components based on use cases
  - Buy vs Build determination
- Commercial package evaluation
  - Analysts' reports (IDC 2004 vendor comparison)
  - Informatics consortium (CTSA Wiki; UW EDC Evaluation Project)
  - Informal CTSA networking
  - On-campus vendor meetings
- Results
  - Velos most common among centers contacted
  - OpenClinica appeared to be most viable solution

TraCS Data Management Service

- OpenClinica
  - Open source—important for state-wide reach of TraCS
  - Widespread use among clinical research centers
  - Paid service support model
  - Technology platform aligned well with internal development
  - Appears flexible for external system integration
- Short-term solution:
  - REDCap offered an immediate solution for small, less complex studies
- Long-term solution:
  - Build system around OpenClinica for use with more complex (e.g., multi-site or regulatory) studies
- Early on, realized too much customization was required to make open source solution via OpenClinica feasible

TraCS Clinical Research Data Management System (TCR-DMS)

- Development timeline: Oct 2009 – June 2010
- 5th generation CSCC DMS
  - Co-direction of Hope Bryan, CSCC IT Manager, and Brent Lamm, TraCS IT Manager
- Development goals:
  - Standards-based to facilitate data sharing: file structures, variable definitions
  - State-of-art (next generation) systems design
  - Library of re-usable modules in object-oriented environment
  - Optimization of system performance

TraCS Data Management System (TCR-DMS)

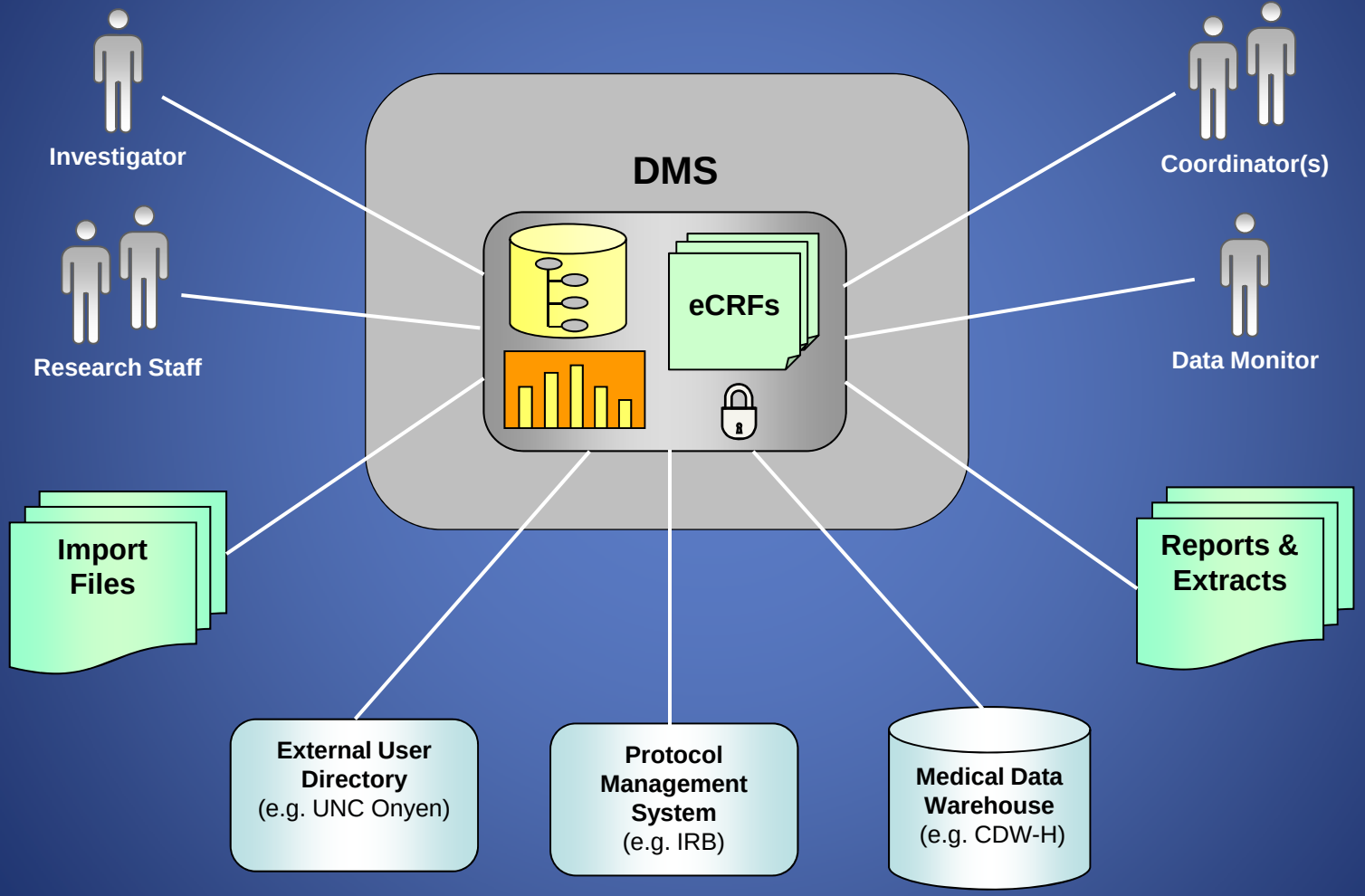
- TCR-DMS Development goals, cont.
  - Allow easy access at *low cost* for TraCS investigators
    - Minimize customization required for each protocol via use of standard CRFs
  - Features
    - Options for randomization and other algorithms
    - Real-time reporting/tracking
    - Real-time edit, queries, and resolution
  - Data security: FDA 21 CFR Part 11 compliance
- Need a new name! *Naming contest in progress…*

System Overview

TCR- DMS

- A clinical data management system, to support:
  - Clinical Trials
  - Patient Registries
  - Longitudinal & Observational Studies
- Key functionality included:
  - Study configuration - Protocol details, visit schedules, site specific definitions, eligibility determination & treatment assignment
  - *Case Report Form (eCRF) management* - online form design, custom and standard eCRFs from central library
  - *Electronic data capture* - custom field validation, complex conditional logic, automated data queries
  - *Integration of external data feeds* - laboratory and reading center imports
  - *Data extract and reporting* - CDISC ODM data interchange, standard and ad hoc reports

System Overview

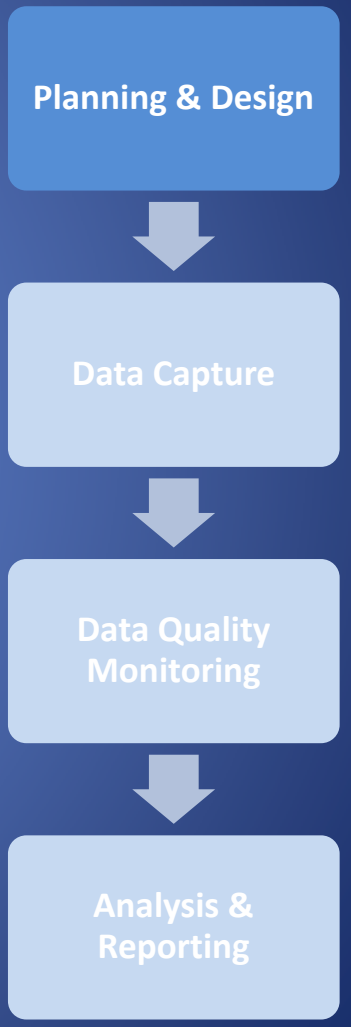


Study Phase: *Planning & Design*

- Specification of study and key protocol parameters
- Definition of sites, including primary contacts and users
- Creation and customization of case report forms
- Implementation of visit schedules with associated case report forms and data imports
- Define coding dictionaries (e.g. medications)

Key Features:

- ❖ Configurable subject id assignment schemes – automated sequencing and pre-defined list support
- ❖ Customizable required fields for enrollment
- ❖ Granular authorization model – site and event level permissions assignment
- ❖ Online creation and customization of case report forms ***(* v2)***
- ❖ Support for elaborate graphically designed forms

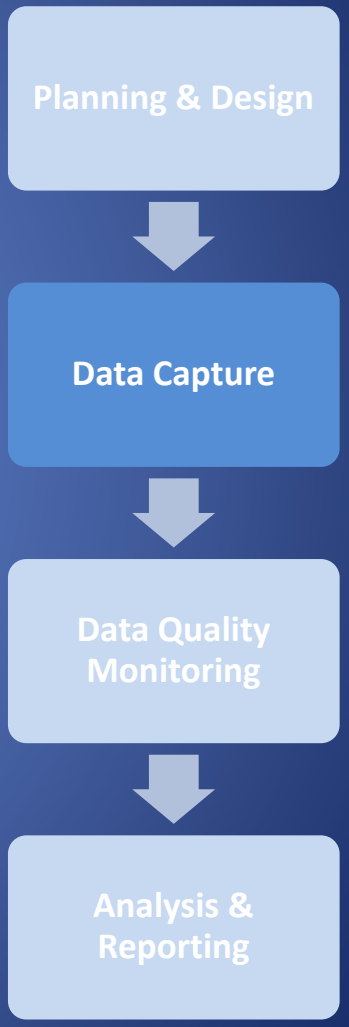


Study Phase: *Data Capture*

- Capture of research subject data via electronic case report forms
- Real-time validation against pre-defined:
  - Conditional field logic
  - Acceptable values
- Central upload of exam data from laboratory or reading center – merged with form captured data
- Central and/or geographically distributed data capture into single study

Key Features:

- ❖ Full auditing of all user interface interactions
- ❖ Auto-save of form data during data collection to prevent data loss
- ❖ Ability to override specified valid values appropriate justification

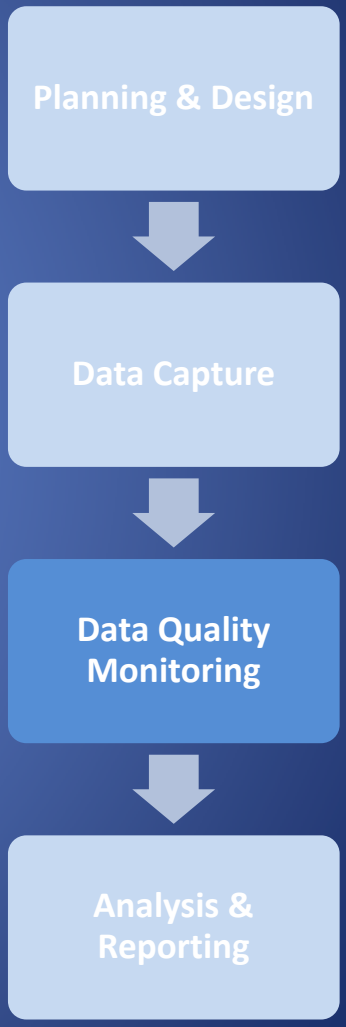


Study Phase: *Data Quality Monitoring*

- Define and execute standard reports for study specific data quality checks
- Review and resolve automatically generated data queries
- Lock completed and validated case report form data
- Ad hoc reporting to investigate data discrepancies
- Revise case report forms to accommodate study modifications

Key Features:

- Enforced separation, through authorization model, of duties between users performing data capture and data monitoring
- System restriction of modifications to locked data
- Revision tracking of updated case report forms

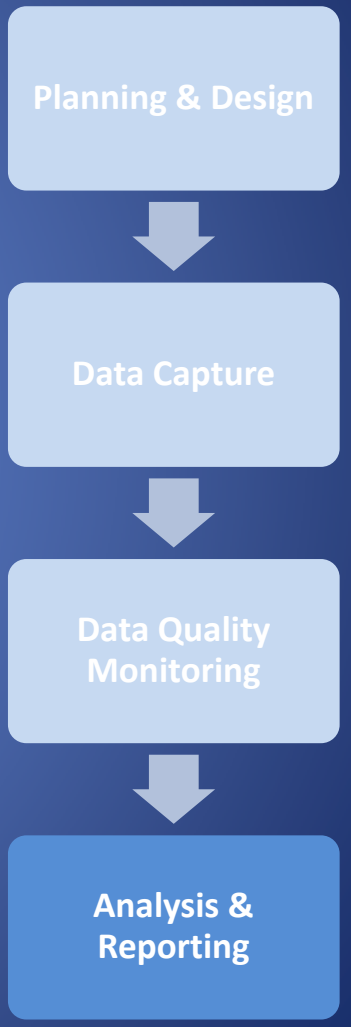


Study Phase: *Analysis & Reporting*

- Pre-defined and ad hoc reporting for study oversight (e.g. recruitment tracking)
- CDISC Operational Data Model (ODM) data extraction for input to analysis software
- Association of all data items to analysis variable names (i.e. SAS variable names)
- File download into common file types (e.g. CSV, SAS, Stata, SPSS)

Key Features:

- ❖ Field-level storage of captured data by standard types (e.g. integer, float, date) for enhanced data integrity
- ❖ Ability to perform cross-CRF and cross-study reporting due to form-independent data model



Scalability

- Designed to support full range of research studies

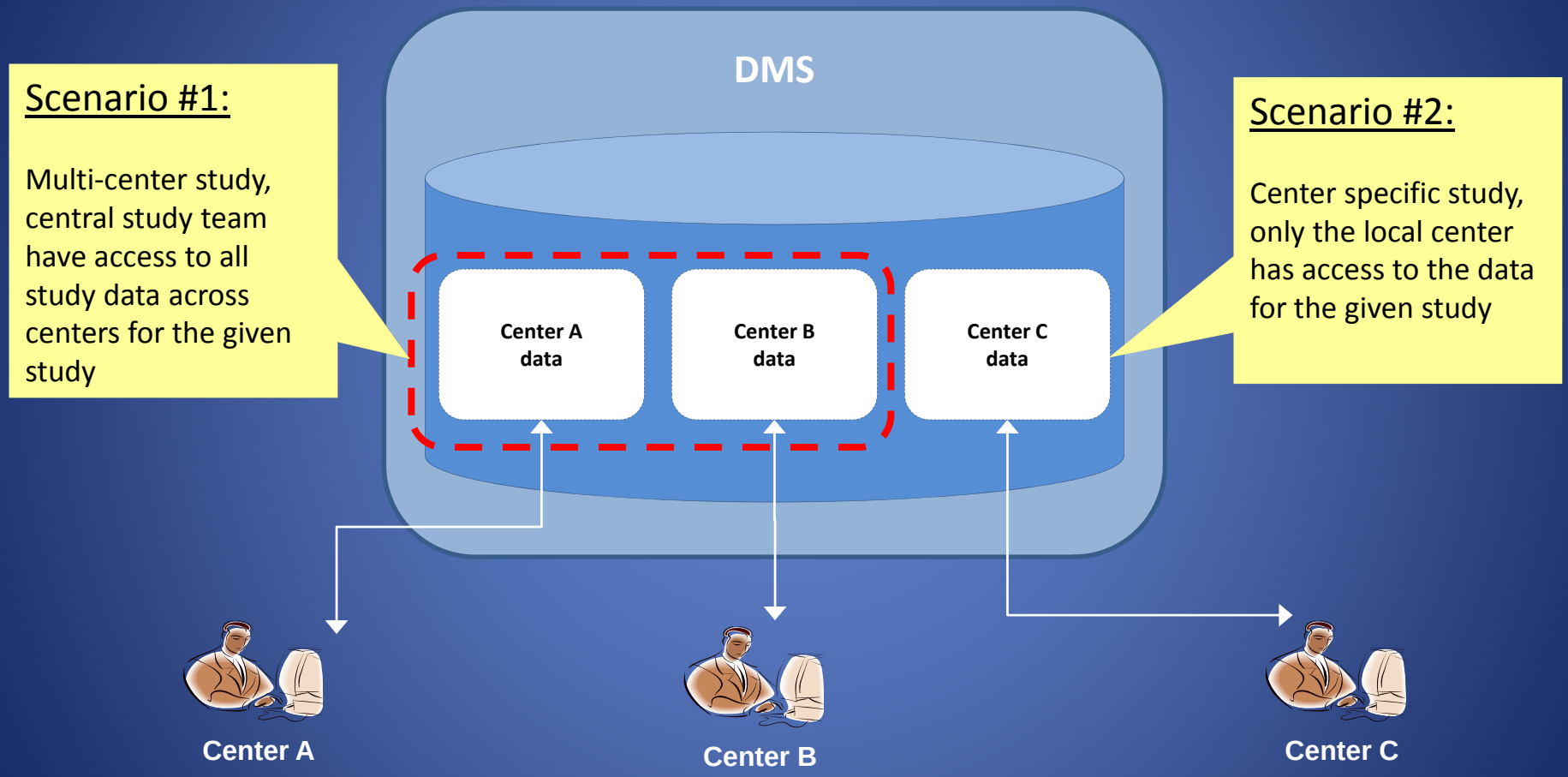
- Small / simple installation footprint to support laptop installations where network connectivity is unavailable
  - 100% web-based Java for full platform compatibility
  - Support for MySQL as database management system
  - CDISC ODM functionality to upload/merge data into larger study instance

- Scalable to support large, long-term, multi-site studies
  - Support for high-end database management systems (e.g. Oracle, DB2)
  - Capability to implement as single study instance, or multi-study instance with secure logical separation of data

Standards Supported

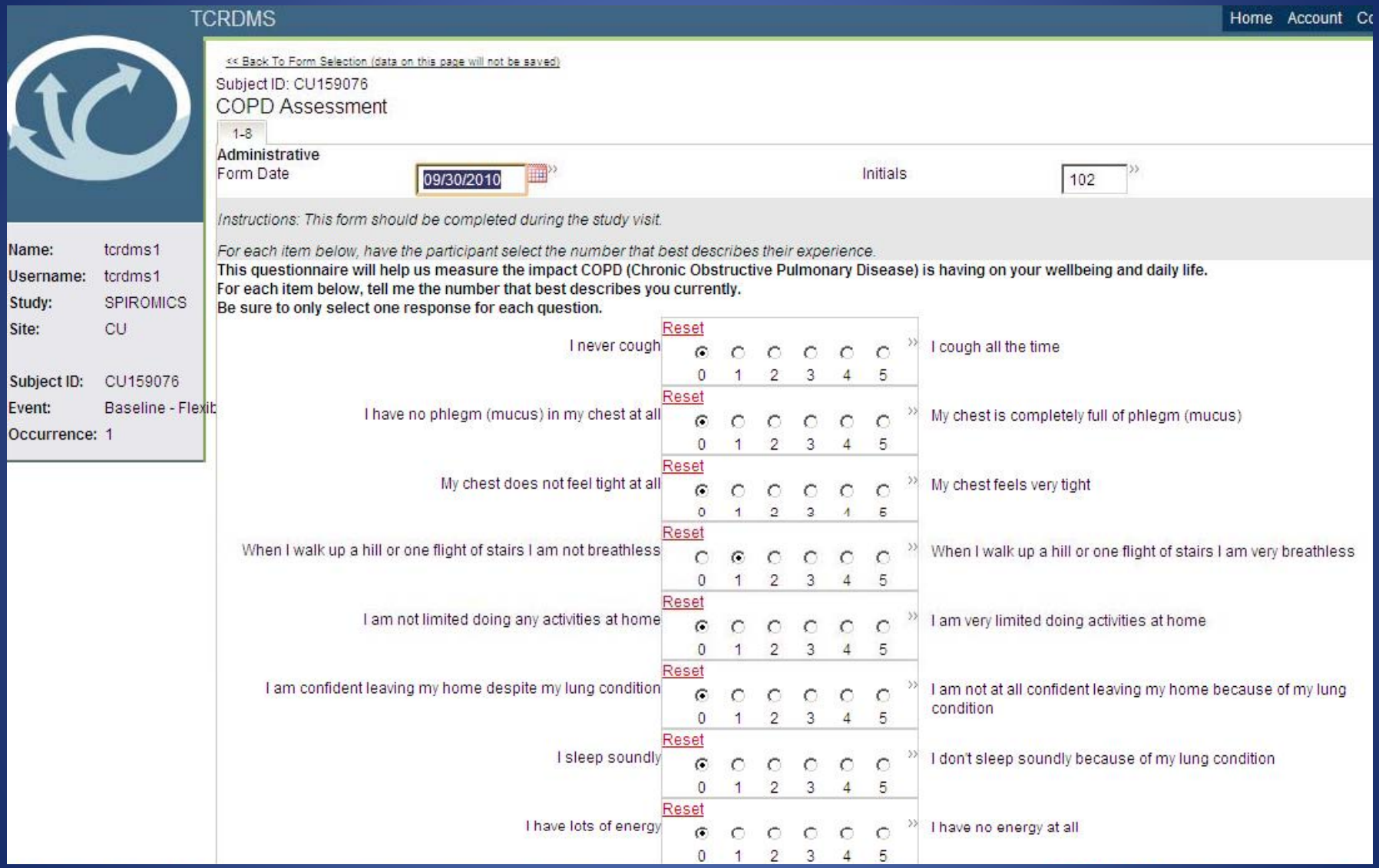
- CDISC Operational Data Model (ODM)
  - Data format for interchange and archival of data
  - Standard XML file includes study data, meta-data, audit information
  - Compatible with many software systems
  - Adopted by FDA and potentially by NIH
- CDISC Clinical Data Acquisition Standards Harmonization (CDASH)
  - Basic standards for data collection including best practices for CRF design
  - Recommended set of data collection elements for 16 domains
- FDA 21 CFR Part 11 - information security *(Version 2)*
  - System validation
  - Audit trail
  - System access controls
  - Electronic signatures

Data Isolation & Sharing

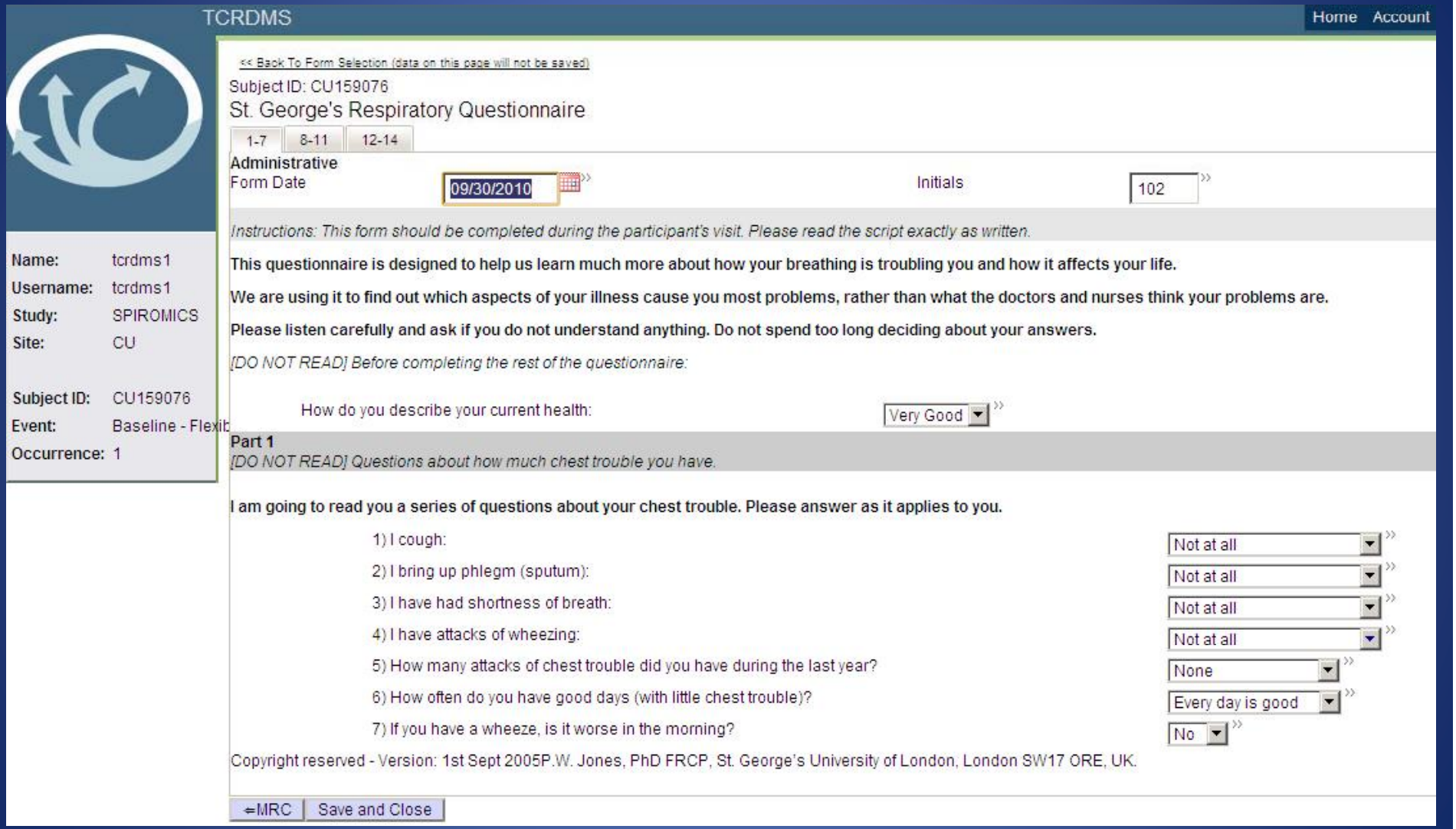


Screen Shots

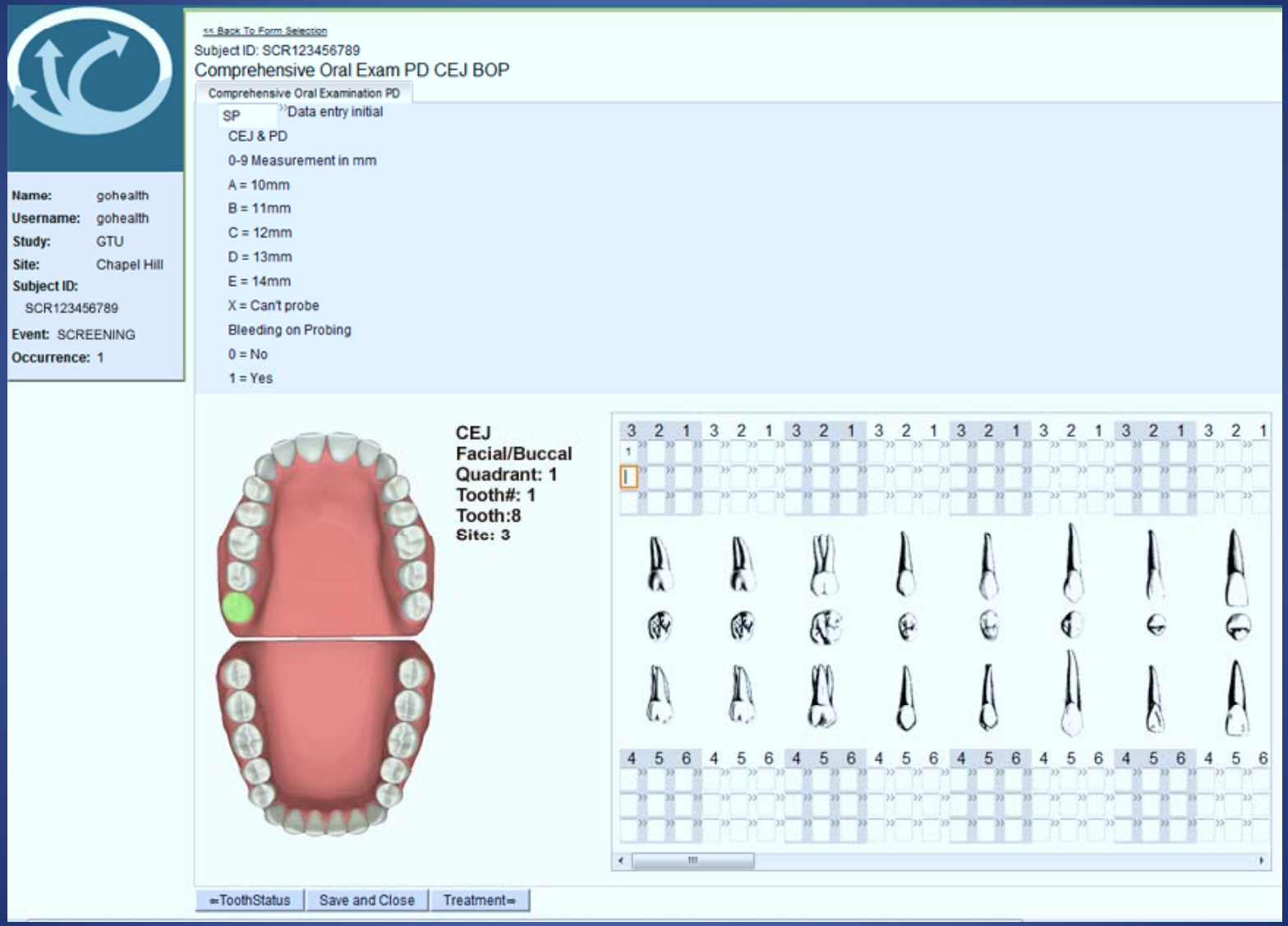
COPD Assessment Form



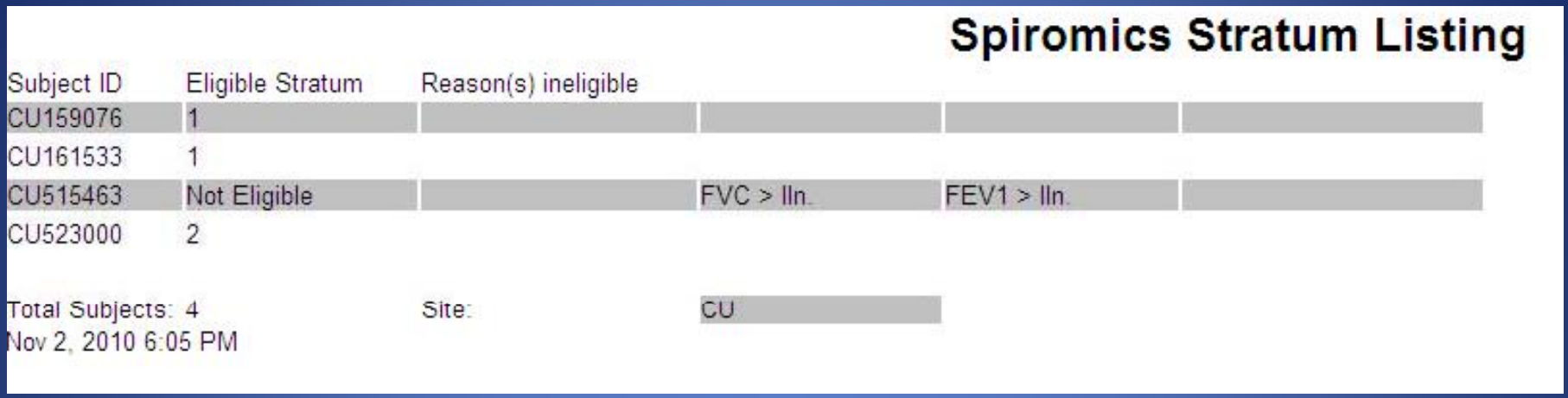
Respiratory Questionnaire



Oral Exam Form



Stratum Report



Spiromics Stratum Listing

Subject ID	Eligible Stratum	Reason(s) ineligible			
CU159076	1				
CU161533	1				
CU515463	Not Eligible		FVC > lln.	FEV1 > lln.	
CU523000	2				

Total Subjects: 4 Site: CU

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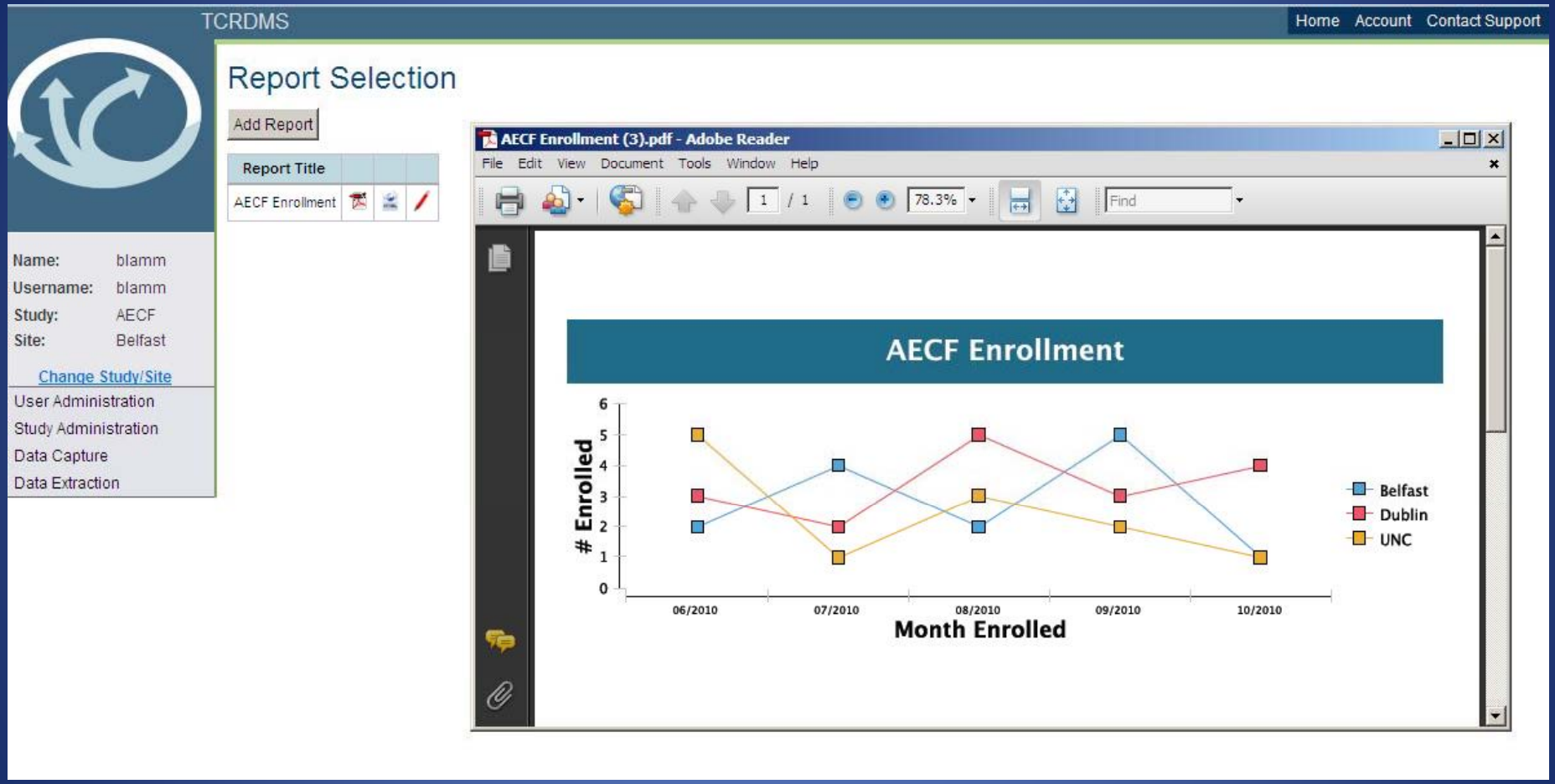
Enrollment Report



Progress

- Functionality
  - Screen painter in testing
  - Automatic updates for query resolution in development
- Staffing
  - Delays in hiring project/data manager position in Biostatistics Core
- Usage
  - REDCap used, in use, or planned use in ~40 studies
  - TCR-DMS in use for 4 large, multi-site studies (3 CSCC studies and 1 TraCS study)

Challenges

- Cost recovery
  - Ongoing challenge to convince investigators with GCRC experience (informatics services at no charge) to include data management costs in grant applications
  - Secure funding for system maintenance and enhancements
    - Recharge center
    - Include budget for specific enhancements in grant applications
  - Cost model –*see budget document*
- Data security issues – move towards model where patient level data are stored on TraCS servers with secure remote access from desktops/laptops

Future

- Interoperability
  - Electronic transfer of UNC patient chart data from EMR warehouse to automatically populate data entry screens
    - Pilot tested in breast cancer clinics; in development for statewide cancer registry
    - Also in development for UNC patients as part of Bronchiectasis patient registry
  - Eventual expansion to download patient level data from EMR warehouses at other institutions(?)
  - Could facilitate data sharing among CTSA institutions
- TCR-DMS as proprietary software -
  - Share with other CTSA sites (e.g., REDCap model)?
  - Commercialize?

Background Material

Technical Details

- Web-based user interface, support all major browsers
  - JEE platform: JSF (MVC), Hibernate (ORM), JQuery (+JavaScript), Spring, AspectJ
- Database-independent, support all major relational database mgmt systems
  - No vendor-specific code, Java Persistence Architecture (JPA) implementation of data model
- JEE-compliant, support all major web containers
  - Developed and tested with Apache Tomcat, other commercial-grade containers could be utilized
- Support for LDAP integration for single sign-on (SSO), including multiple LDAP integrations per installation
  - Spring security model - external and/or local authentication support available

Key Technical Challenges

- Addressing the diversity of study specific data requirements without the need for custom software development
  - Commonly used techniques sacrifice strong data typing / validation
  - Decompose forms into atomic typed data elements; recomposed dynamically for UI rendering
- Supporting complex conditional logic (e.g., skipped fields, cross-form dependencies and outcomes)
  - Typically only available in ultra high-end (i.e., expensive) commercial packages or through costly custom development
  - Chaining of logical expressions to implement infinitely complex dependencies without custom programming
- Ensuring robust data integrity, while providing real-time validation with support for situational overrides
  - Traditionally implemented via post-submission validation with no ability to override
  - Client-side validation / override (real-time); full validation redundancy server-side