Using i2b2 data to determine clinical trial feasibility in the TriNetX network

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HEALTH IS ALL WE DO

Disclaimer

In addition to my faculty position at the Sidney Kimmel Cancer Center, Thomas Jefferson University in Philadelphia, I am a consultant for the TriNetX Corporation.

To be discussed …

- Brief overview of cancer clinical trial accrual problem.
- Jefferson's participation in the TriNetX network.

Problem confronting clinical trials research: studies that fail to accrue

An Institute of Medicine report[1] on cancer cooperative group trials found that 40% were never completed because of failure to achieve minimum accrual goals:

"The ultimate inefficiency is a clinical trial that is never completed because of insufficient patient accrual, and this happens far too often."

1. Nass SJ, Moses HL, Mendelsohn J, editors. Committee on Cancer Clinical Trials and the NCI Cooperative Group Program Board on Health Care Services; A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program. Washington DC: National Academies Press, 2010.

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Failed trials delay research and waste funds and patient effort

Institutional and pharma trials, as well as cooperative group trials, often fail to complete because of insufficient patient recruitment.

These non-accruing trials are often kept open for many months before closure, consuming personnel resources in their setup and operation at a significant cost to institutions, without providing any return in definitive research findings.

Furthermore, while many of these trials register zero patients, others accrue some patients, resulting in thousands of patients nationwide who are recruited to unproductive research studies.[2]

2. Cheng, S., M. Dietrich, S. Finnigan, A. Sandler, J. Crites, L. Ferranti, A. Wu, and D. Dilts. A sense of urgency: Evaluating the link between clinical trial development time and the accrual performance of CTEP-sponsored studies. 2009 ASCO Annual Meeting Proceedings. J of Clinical Oncology, 2009.

A study we conducted showed that cohort definition via i2b2 can be used to predict accrual for proposed clinical trials

Design-phase prediction of potential cancer clinical trial accrual success using a research data mart

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ABSTRACT

Background Many cancer interventional clinical trials are not completed because the required number of eligible patients are not enrolled.

Objective To assess the value of using a research data mart (RDM) during the design of cancer clinical trials as a predictor of potential patient accrual, so that less trials fail to meet enrollment requirements.

Materials and methods The eligibility criteria for 90 interventional cancer trials were translated into i2b2 RDM queries and cohort sizes obtained for the 2 years prior to the trial initiation. These RDM cohort numbers were compared to the trial accrual requirements, generating predictions of accrual success. These predictions were then compared to the actual accrual performance to evaluate the ability of this methodology to predict the trials' likelihood of enrolling sufficient patients.

Results Our methodology predicted successful accrual (specificity) with 0.969 (=31/32 trials) accuracy (95% CI 0.908 to 1) and predicted failed accrual (sensitivity) with 0.397 (=23/58 trials) accuracy (95% CI 0.271 to 0.522). The positive predictive value, or precision rate, is 0.958 (=23/24) (95% CI 0.878 to 1).

Discussion A prediction of 'failed accrual' by this methodology is very reliable, whereas a prediction of accrual success is less so, as causes of accrual failure other than an insufficient eligible patient pool are not considered.

Conclusions The application of this methodology to cancer clinical design would significantly improve cancer clinical research by reducing the costly efforts expended initiating trials that predictably will fail to meet accrual

As important as interventional clinical trials are in translational research, these studies may never accrue the statistically required number of participants to complete the study's research plan. An Institute of Medicine (IOM) report on cancer cooperative group trials found that 40% were never completed because of failure to achieve minimum accrual goals.[1] The IOM report states, 'The ultimate inefficiency is a clinical trial that is never completed because of insufficient patient accrual, and this happens far too often.' These non-accruing trials are often kept open for many months before closure, consuming personnel resources in their setup and operation at a significant cost to institutions, without providing any return in definitive research findings. Furthermore, while many of these trials register zero patients, others accrue some patients, resulting in thousands of patients nationwide who are recruited to unproductive research studies.[2] A number of studies have investigated barriers to clinical trial accrual, and reported various physician-related and patient-related obstacles.[3–9] Physician barriers cited include inadequate reimbursement, lack of support resources, the irrelevance of available studies to the practice population, and treatment preferences. Patient barriers cited include concerns and uncertainty about treatments, treatment preferences, unavailability of an appropriate trial, lack of awareness of trials, and transportation and other logistical constraints. These cited studies all have focused on accrual issues occurring *after* trial activation. Recently, however, Schroen *et al*[10] have

Overall result of our study

If the methodology predicts "failed accrual" – the patient population required by the trial's design does not exist at this institution – we should trust this prediction and should not proceed to open the trial with its current eligibility criteria.

However, a prediction of accrual success using this method is no guarantee that target goals will be met, since other factors (e.g., competing trials) are present in addition to patient population considerations.

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TriNetX clinical research network was born out of the pharma industry's to address the same issue of assessing clinical trial feasibility

The objective of this network is to make the clinical trial design and recruitment process more efficient by establishing a collaborative clinical trial research infrastructure between pharma and academic medical centers.

This infrastructure is centered on a federated network of academic i2b2 deployments, whose patient population characteristics are accessible by its member academic, pharma, and CRO organizations, thereby indicating *whether* and *where* the required trial patient populations exist.

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Current TriNetX academic members

Georgetown University Medical Center
Jefferson University and Hospitals
Temple University
Children's Hospital Colorado
Fondazione Salvatore Maugeri Clinica del Lavoro e della Riabilitazione I.R.C.C.S.
Penn University of Pennsylvania
University of Cincinnati
USF University of South Florida
University of Massachusetts Medical School
Cincinnati Children's Hospital Medical Center
UAB The University of Alabama at Birmingham
The University of Arizona
children's health
We make lives better UT Health Science Center San Antonio
UT Southwestern Medical Center
Children's National
University of Kentucky
MUSC Health Medical University of South Carolina
Washington University in St. Louis
Medical College of Wisconsin
Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico

New Providers since January 2016:

VCU Virginia Commonwealth University
Wisconsin University of Wisconsin-Madison
The University of Utah
Ochsner Health System
Mount Sinai
Nationwide Children's
West Virginia University
UAMS University of Arkansas for Medical Sciences

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Current TriNetX pharma members

NOVARTIS

Celgene

SANOFI

ICON

A Symbol of Excellence

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Jefferson TriNetX academic membership

Why Jefferson joined the TriNetX network

Jefferson TriNetX academic membership

Initial interest was prompted by a need for data visualization application for i2b2 data. The TriNetX tool offered several advantages:

- TriNetX application “sits” on top of i2b2 database, and requires no data reformatting or transfer.
- Data displays satisfied visualization requirements.
- No charge for the software, and reasonable deployment effort required of the Jefferson staff.

Jefferson TriNetX academic membership

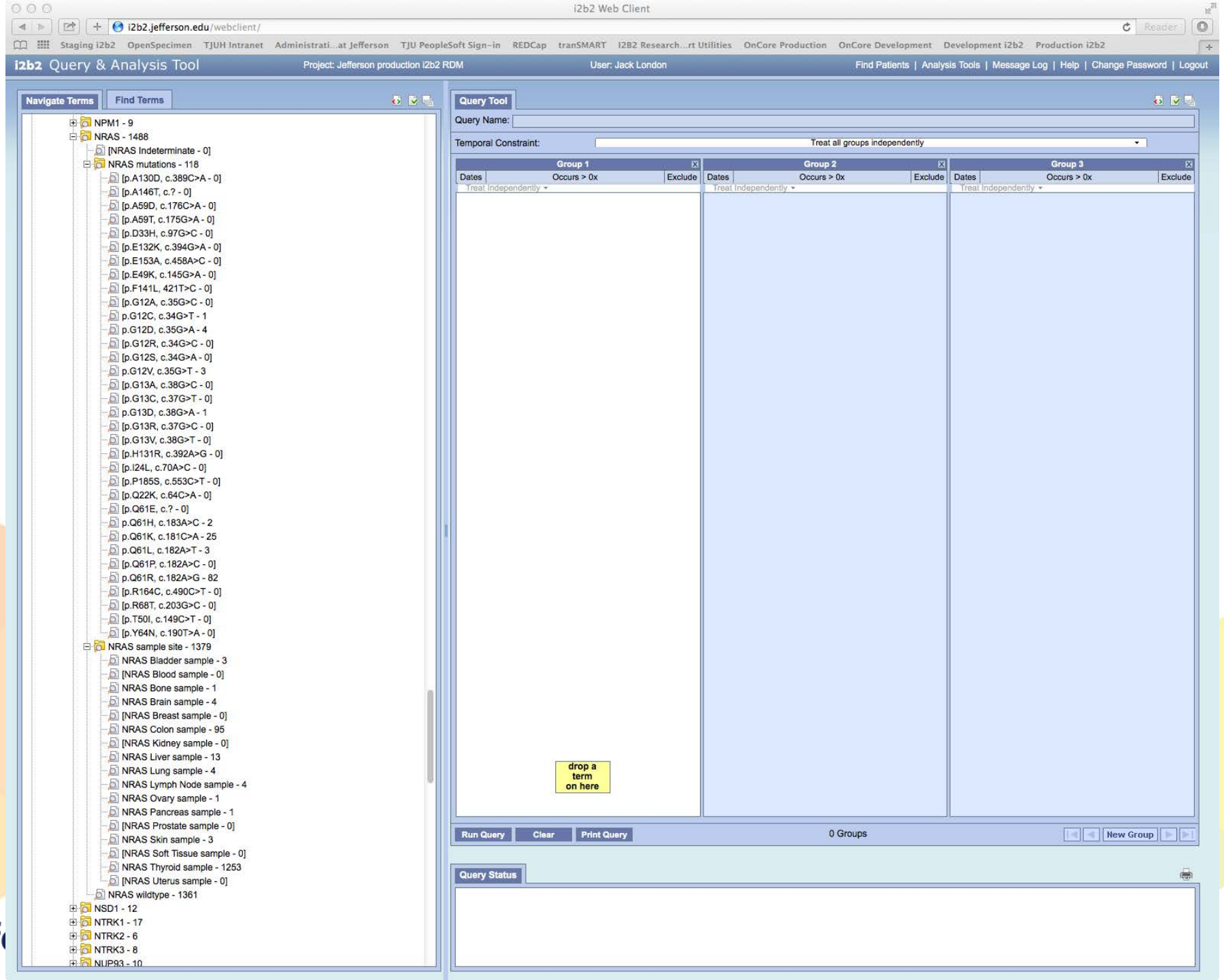
Joining the TriNetX network also offered several advantages:

- Facilitated clinical trial collaboration with pharma.
- Facilitated data sharing with other academic provider members.
- Network deployment presented minimal legal / I.T. security hurdles
  - Only aggregate counts and control over site identification
  - No firewall holes.

Jefferson's i2b2 deployment

In addition to EMR patient data (demographics, diagnoses, medications, labs, and procedures):

- Comprehensive data set for cancer patients
  - Tumor histology, stage, recurrence, treatment, disease-specific factors
- "Omic" molecular diagnostic patient data
  - Currently > 350 genes with > 4,100 mutations (both in-house and Foundation Medicine results)
- Biospecimen annotation
  - Specimen anatomic origin, class, type, pathology, slide images


i2b2 Web Client
i2b2.jefferson.edu/webclient/
Staging i2b2
OpenSpecimen
TJUH Intranet
Administrati...at Jefferson
TJU PeopleSoft Sign-in
REDCap
tranSMART
I2B2 Research...rt Utilities
OnCore Production
OnCore Development
Development i2b2
Production i2b2
i2b2 Query & Analysis Tool
Project: Jefferson production i2b2 RDM
User: Jack London
Find Patients | Analysis Tools | Message Log | Help | Change Password | Logout
Navigate Terms
Find Terms
NPM1 - 9
NRAS - 1488
[NRAS Indeterminate - 0]
NRAS mutations - 118
[p.A130D, c.389C>A - 0]
[p.A146T, c.? - 0]
[p.A59D, c.176C>A - 0]
[p.A59T, c.175G>A - 0]
[p.D33H, c.97G>C - 0]
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NRAS Bone sample - 1
NRAS Brain sample - 4
[NRAS Breast sample - 0]
NRAS Colon sample - 95
[NRAS Kidney sample - 0]
NRAS Liver sample - 13
NRAS Lung sample - 4
NRAS Lymph Node sample - 4
NRAS Ovary sample - 1
NRAS Pancreas sample - 1
[NRAS Prostate sample - 0]
NRAS Skin sample - 3
[NRAS Soft Tissue sample - 0]
NRAS Thyroid sample - 1253
[NRAS Uterus sample - 0]
NRAS wildtype - 1361
NSD1 - 12
NTRK1 - 17
NTRK2 - 6
NTRK3 - 8
NUP93 - 10
Query Tool
Query Name:
Temporal Constraint:
Treat all groups independently
Group 1
Group 2
Group 3
Dates
Occurs > 0x
Exclude
Treat Independently
drop a term on here
Run Query
Clear
Print Query
0 Groups
New Group
Query Status