tranSMART: Use cases from deployments highlighting emerging models for precompetitive collaboration and open source sustainability

Asif Dhar, CMIO and Principal
Deloitte Consulting LLP
What is tranSMART?

tranSMART was started in 2008 by Johnson & Johnson and Recombinant by Deloitte to integrate, explore, and share genomic and clinical data.

Its goals were to develop for Open Source, the cloud, and precompetitive sharing. Based on i2b2 and was first deployed on Amazon.

Solution Won “2010 Bio-IT World Best Practices Award” in Knowledge Management and “CIO 100” award for the platform's innovation and potential to advance translational research.

tranSMART provides an open source solution for knowledge management in translational medicine.
tranSMART helps answer questions…

- How should a disease be stratified into different groups of subpopulations based on clinical and ‘omic data?
- What is the best biomarker or diagnostic strategy for a given compound or disease to achieve ‘effectiveness and safety’?
- How do we store and share data within our organization and in consortia relating to combined biological and genetic observations and study results?
- How should a new study be designed based on the experience from internal data, observational data (EMR), and public data sets?
- What is the correlation between animal data, cell line models, and human data?
Representative view
Create subsets and generate statistics

Subsets are specified based on clinical attributes

There is a statistically significant difference based on the treatment the patient received.
Representative view (cont.)

Correlate multiple types of data sources

Variables are specified

Expression of BRCA1 is significantly suppressed by the compound between the 2 hour and 24 hour measurement
Representative view (cont.)

Search, visualize, and explore known correlations
The tranSMART Platform is Being Adopted:

over 35 organizations have implemented tranSMART

<table>
<thead>
<tr>
<th>Start Organization</th>
<th>Type</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008 Johnson &amp; Johnson</td>
<td>Pharma</td>
<td>Production</td>
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<tr>
<td>2008 Recombinant by Deloitte</td>
<td>Services</td>
<td>Multiple</td>
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<tr>
<td>2010 Sage Bionetworks</td>
<td>Non Profit</td>
<td>Production</td>
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<tr>
<td>2010 Thomson Reuters</td>
<td>Services</td>
<td>Support</td>
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<td>2010 U-BIOPRED</td>
<td>Consortium</td>
<td>Production</td>
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<td>2011 SAFE-T</td>
<td>Consortium</td>
<td>Pilot</td>
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<tr>
<td>2011 University of Michigan, Comprehensive Cancer Center</td>
<td>Academic</td>
<td>Production</td>
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<tr>
<td>2012 APHP-HEGP Paris France</td>
<td>Academic</td>
<td>Production</td>
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<tr>
<td>2012 BT Cure</td>
<td>Consortium</td>
<td>Pilot</td>
</tr>
<tr>
<td>2012 CTMM/TraIT</td>
<td>Consortium</td>
<td>Dev</td>
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<tr>
<td>2012 FDA</td>
<td>Government</td>
<td>Dev</td>
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<tr>
<td>2012 IMI/eTRIKS</td>
<td>Consortium</td>
<td>Dev</td>
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<tr>
<td>2012 Merck</td>
<td>Pharma</td>
<td>Pilot</td>
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<tr>
<td>2012 Millennium Pharmaceuticals</td>
<td>Pharma</td>
<td>Production</td>
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<tr>
<td>2012 One Mind for Research (1M4R)</td>
<td>Non Profit</td>
<td>Production</td>
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<tr>
<td>2012 Pfizer</td>
<td>Pharma</td>
<td>Production</td>
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<tr>
<td>2012 Roche</td>
<td>Pharma</td>
<td>Evaluation</td>
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<tr>
<td>2012 Sanofi-Aventis</td>
<td>Pharma</td>
<td>Dev</td>
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<tr>
<td>2012 St. Jude</td>
<td>Non Profit</td>
<td>Dev</td>
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<tr>
<td>University of Michigan, Computational Medicine &amp; Bioinformatics</td>
<td>Academic</td>
<td>Multiple</td>
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<tr>
<td>2013 Agios</td>
<td>Biotech</td>
<td>Evaluation</td>
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<tr>
<td>2013 CARPEM – Cancer personalized medicine</td>
<td>Academic</td>
<td>Dev</td>
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<tr>
<td>2013 Harvard University / Boston Children's Hospital</td>
<td>Academic</td>
<td>Autism Pilot</td>
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<td>2013 Boehringer Ingelheim</td>
<td>Pharma</td>
<td>Pilot</td>
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<tr>
<td>2013 Bristol Myers Squibb</td>
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<td>Evaluation</td>
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<tr>
<td>2013 BT Global Services</td>
<td>Services</td>
<td>Pilot</td>
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<tr>
<td>2013 Accelerated Cure Project for MS</td>
<td>Non Profit</td>
<td>Dev</td>
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<tr>
<td>2014 Personalized medicine and colorectal cancers (France)</td>
<td>Academic</td>
<td>Dev</td>
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<tr>
<td>2014 PCORI PRRN Phelan-McDermid Syndrome Data Network</td>
<td>Academic</td>
<td>Dev</td>
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</tbody>
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International Research Initiatives
IMI – eTRIKS, EMIF
CTMM – TraIT

Pharma & Biotech
Sanofi, Millennium, Pfizer, JNJ, Roche

Government Aligned Institutions
FDA

Non-Profits
1Mind4Research, Orion Bionetworks, Critical Path Institute

Hospitals / Academics
U Michigan, Harvard / Boston Children's Hospital, HEGP, Johns Hopkins, St. Jude

Service Providers
Recombinant by Deloitte, theHyve, Rancho Biosciences, BTGS, Thomson Reuters, Saama Tech, Cognizant
What’s cool: Collaborations around data

Collaborative sharing of consortium data — U-BIOPRED respiratory repository

- Demonstration in 2010–2011
- Model for use of tranSMART tools for precompetitive data sharing
- Used an academic cloud host (Imperial College)
- Expanded into eTRIKS (EU 24M Euro) IMI initiative
- Additional collaboration examples include sharing of curated ADNI (Alzheimers) data from One Mind to Pfizer in tranSMART format
Indication selection and directed trial process using tranSMART

Steps

1. Identify signature
2. Confirm predictive model
3. Predict high impact populations
4. Run directed trial/protocol

Analytic Method

- Data Trust & tranSMART
- Correlate signature from in vitro data
- Stratify historical trials/studies
- Screen known data sets for signature
- Genomics panel as protocol criteria

Steps Analytic Method

Identify signature Correlate signature from in vitro data
Confirm predictive model Stratify historical trials/studies
Predict high impact populations Screen known data sets for signature
Run directed trial/protocol Genomics panel as protocol criteria
## Empowering users via tranSMART

<table>
<thead>
<tr>
<th>User profile</th>
<th>tranSMART</th>
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</thead>
<tbody>
<tr>
<td><strong>Leadership</strong> (CHIO/CTO/CIO/Product owners)</td>
<td>• Provides easy access to product submission data for all studies and across all centers through a single portal</td>
</tr>
</tbody>
</table>
| **Medical reviewers** | • Facilitates a systematic review of the data through rapid examination of pertinent qualitative and quantitative data elements within each study or across studies  
• Ability to examine cohorts, subgroups, or outliers within each study or across studies  
• Perform cursory statistical analysis to determine if more advanced analyses are needed  
• Provides access to other data sources, such as post-marketing adverse events or registry data |
| **Biostatisticians** | • Export relevant subsets of data for further analysis using other statistical packages and tools, such as R, SAS, Stata, or JMP |
| **Bioresearch Monitoring Program (BIMO) reviewer** | • Perform site-based statistical analysis such as Forest Plots, Logistic Regression to determine if more advanced analyses are needed |
| **Data stewards** | • Ability to load and verify data only once and make it accessible to all reviewers |
What’s cool: Active and growing tranSMART community

- tranSMART developer and user meeting in Amsterdam, June 17–19, 2013
- Over 80 global attendees
- Deloitte led sessions on future tranSMART architecture recommendations

- tranSMART Developer Meeting in Paris, November 5–7, 2013
- Over 120 global attendees

- tranSMART hackathon Boston, February 4–7, 2014
- 4 developers from the Netherlands, 4 developers from London, and 10 US developers attended the three-day hackathon hosted by Deloitte
- Focused on active development of 1.2 release across member sites

Archived presentations: http://lanyrd.com/2013/transmart-community-meeting/
### Version 1.2 feature list (Prioritized in Paris)

<table>
<thead>
<tr>
<th>Functionality</th>
<th>Developed By</th>
<th>Priority</th>
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<tbody>
<tr>
<td>R Interface</td>
<td>Takeda</td>
<td>1</td>
</tr>
<tr>
<td>Genome-wide association study (GWAS) search AND visualization</td>
<td>Pfizer</td>
<td>1</td>
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<tr>
<td>Browse and search enhancements</td>
<td>Sanofi</td>
<td>1</td>
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<tr>
<td>High-dimension data model (RNAseq, proteomics, metabolomics, RBM)</td>
<td>Sanofi</td>
<td>1</td>
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<tr>
<td>Time series data</td>
<td>Sanofi</td>
<td>1</td>
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<tr>
<td>Sample ID incorporation</td>
<td>Sanofi</td>
<td>1</td>
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<tr>
<td>VCF data type support</td>
<td>OncoTrack</td>
<td>1</td>
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<tr>
<td>Incremental data loading</td>
<td>Sanofi</td>
<td>2</td>
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<tr>
<td>Dalliance Genome Browser</td>
<td>TraIT</td>
<td>2</td>
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<tr>
<td>Faceted search</td>
<td>J&amp;J</td>
<td>2</td>
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<tr>
<td>Cross-study analysis</td>
<td>Recombinant</td>
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<tr>
<td>TR Metacore integration/Cytoscape Integration</td>
<td>TR</td>
<td>3</td>
</tr>
<tr>
<td>Array CGH</td>
<td>TraIT</td>
<td>3</td>
</tr>
<tr>
<td>Galaxy integration</td>
<td>TraIT</td>
<td>3</td>
</tr>
</tbody>
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### Unaddressed market needs

- Large-scale genomics support (NGS tools)
- Fit into broad informatics approach to scientific information management
- Increase visualization systems and tools
- Packaged access to data and scientific pipelines
- Realization of data collaboration opportunity
Deloitte commercial approach

- Omics analysis
- Extend open source
- Analysis archive
- Data delivery pipelines

- Visually explore large populations
- View temporal relationships
- Select cohorts to analyze
- Identify basic correlations

- Data consortia and licensed data sets
- Data integration, cleansing, enrichment tools
- Data models and analytics frameworks
- Cloud and on-premise deployment tools
- Commercial open source support
- Informatics and statistical models

- Propensity-matched subsets
- Identify advanced correlations
- Compare treatment effectiveness
- Access curated data sets
- Subscription access to reports
Development of a learning loop that leverages RWE and the experience of health care providers

1. Collaborate to develop new insights
2. Focused studies to generate new evidence
3. Implement learning
4. Evaluating evidence from studies
5. Validating evidence in real world
Vision: Leveraging tranSMART + workbench to identify insights from existing study

- Using Deloitte’s translational research tools suite of tools for evaluating current studies
- Studying phenotypic and genotypic profile of patients participating in a recent Asthma study
- Variants of PDE4 gene and CYP 450 gene indicate variation in outcomes (however not statistically significant)

**Step 1**
Viewing at insights into a single research study, specifically, a box plot of a gene signature list against all participants in an asthma study who have genomic data loaded. This shows us large variants in two distinct subgroups (Type I and Type IV).

**Step 2**
Heatmap view limiting our selections to those subgroups showing the variance in genetic markers. It shows variations, but they are not as significant to generalize insights.
Vision: Pooled analysis of asthma studies to identify impact of genomics on treatment outcomes

- Performing a pooled analysis of “multiple studies” across various asthma studies
- Larger sample size enables studying phenotypic and genotypic profile of patients with greater confidence
- Analysis indicates variants of PDE4 gene and CYP 450 gene showing significant variation in outcomes for certain treatments

Step 3
Now we perform a comparison of multiple different study groups to observe first the phenotypic differences (Age, Sex, etc.) and then compare the specific variances of two gene variants between the study groups

Step 4
Heatmap view now indicates significant difference in terms of how the genetic variations are impacting the outcomes of treatments
Vision: Overview of Asthma patients in real-world to enable better characterization of disease

- Overview of all the asthma patients treated in the real world setting in the past decade
- Evaluation of current treatment paradigms in the real world and correlation with outcomes
- Identification of two key treatments medications that are the cornerstone of treatment for further evaluation

Step 5
Evaluating all the patients having ‘Asthma’ at Intermountain Healthcare to identify age, gender, disease frequency distribution. Identification of treatment, lifestyle, ethnicity and comorbidity patterns for the patients

Step 6
Ability to identify two most common medications used in patients with severe asthma condition for further evaluation using Outcomes Miner
Vision: Evaluation of outcomes for two asthma medications in real-world setting

- Comparison of patients on ‘Drug A’ versus ‘Drug B’ to identify difference in outcomes
- Evaluating ‘Emergency Room Visits for Asthma’ as an outcomes and then filtering them by ‘Emergency Visits specific to Asthma’
- Patients with CHF as comorbidity and treatment with Beta-blocker treatment indicate higher Emergency Visits.

Step 7
Evaluating ‘Emergency Room Visits’ as the outcome on the dashboard, overall more Emergency Room Visits for Asthma patients with CHF disease as comorbidity.

Step 8
Evaluating ‘Emergency Room Visits for Asthma’ as the outcome, high Emergency Room Visits for patients with beta blocker treatment for CHF.
Vision: Evaluation of outcomes for two asthma medications in real-world setting (cont.)

- Comparison indicates patients on ‘Drug A’ depression, neurological conditions and psychosis have high degree of correlation with Emergency Visits
- CHF and Beta Blockers believed to have an association with CYP 450 gene variants
- Indicates the need to further study impact of CYP 450 genes in drug outcomes

**Step 9**
Evaluating ‘Emergency Room Visits for Asthma’ as the outcome for patients on Drug A shows **same degree of correlation** with depression, neurological conditions and psychosis

**Step 10**
Evaluating ‘Emergency Room Visits for Asthma’ as the outcome for patients on Drug B shows **limited correlation** with depression, neurological conditions and psychosis
Questions/Conclusions
Asif Dhar, MD, MBA
Chief Medical Informatics Officer, Deloitte Consulting LLP Senior Fellow, Deloitte Center for Health Solutions, Washington, DC

Dr. Dhar is Deloitte’s Chief Medical Informatics Officer. He helps clients develop innovative strategies to improve clinical outcomes and therapeutic discovery. He has a keen acumen at understanding health care trends and developing growth and innovation strategies for clients across the health care value chain. His insights on health reform, information management and new care models are sought after by health care organizations across the Globe.

Dr. Dhar’s translational informatics and health care collaboration work is helping clients discover new approaches to optimize R&D. He has been retained by numerous provider systems, Cancer Centers, Life Science companies and Governmental Agencies to define translational research programs. Dr. Dhar is also a Senior Fellow with the Deloitte Center for Health Solutions. He developed the Center’s perspective on the ROI for Personalized Medicine with the Personalized Medicine Coalition which was presented at the American Association for the Advancement of Science.