Learning Health Community: ESTEL Initiative Update

Speakers:
- Rebecca Kush, PhD, President, CDISC
- Kevin Sullivan, PhD, Associate Professor and Endowed Faculty Fellow of Computer Science, University of Virginia
- Landen Bain, Healthcare Liaison, CDISC
- Ken Pool, MD, Chief Operating Officer, Oz Systems

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Information from healthcare (private, aggregated) to enable research

Healthcare

• Quality healthcare
• Informed decisions
• Personalized medicine
• Patient safety and privacy
• Public health
• Improved therapies
• Efficiencies/reduced costs

Research

• Discovery of new therapies
• Understanding diseases
• Testing/comparing therapies (CER)
• Assessing efficacy
• Monitoring safety
• Understanding responses (genomics, biomarkers)
• Public health/quality evaluations
• Post-marketing surveillance

Currently Inefficient
~17-year cycle

Research findings to inform healthcare decisions
Data Exchange Among Physicians – NOT ‘Interoperable’

Exchange within organization
- Any exchange with other providers: 38.9%
- Any exchange: Inside the organization: 34.6%
- Providers inside office/group: 27.9%
- Affiliated hospitals: 28.2%

Exchange outside organization
- Any exchange: Outside the organization: 13.8%
- Providers outside office/group: 12.7%
- Unaffiliated hospitals: 4.8%

Furukawa M. et al Health Affairs, Aug, 2014
Current Environment for Clinical Research – Biopharmaceutical Development

- Time and cost of developing a drug increased dramatically
- Biopharmaceutical companies focused on profits in developing products
- Research studies more complex for numerous reasons
- Many clinicians do one study and no more
- Only a small percentage of eligible patients participate in research
- Data re-entered from the EHR or Medical Record into Research (e)Case Report Forms
- EHR use increasing, but NOT used prospectively for research
- Research and Healthcare still seem ‘separate worlds’
Reflection paper on expectations for electronic source data and data transcribed to electronic data collection tools in clinical trials

References
2. CDISC (Clinical Data Interchange Standards Consortium) Clinical Research Glossary Version 8.0, DECEMBER 2009
http://www.cdisc.org/stuff/contentmgr/files/0/be650811feb46f381f0af41ca40ade2e/misc/cdisc_2009_glossary.pdf.

eSource = data entered electronically first, i.e. EHRs, eDiaries....
Value of Using Standards Even Greater Now!

2007 CDISC Business Case

2014 Business Case

Current Landscape 2014

Study Complexity
# Datapoints
Data Management
Time/Resources
Cost of Research
Synergistic Standards Currently Available for EHR-enabled Research

Healthcare Delivery
- eSource
- Documents EHR
- HL7 CCDA

Medical Research
- Integration Profiles (e.g. RFD)
- ODM

eCRFs

eArchive at Clinical Site
ASTER (AE Reporting from EHRs)
30 Ambulatory care physicians at Harvard and Brigham and Women’s with Pfizer, CDISC, CRIX
Nov 08 – Jun 09, > 200 Reports Sent to FDA

Physician Reporting:
* 91% of participating physicians had submitted no ADE reports in the prior year
* During the study, participants reported an average of approximately 5 reports in a 3 month time period
* All participants reported at least 1 AD
* Process: Time to report decreased from ~35 min to < 1 min

Source: Michael Ibara, Pfizer
Examples from Europe

TRANSFoRm Query Formulation Workbench

- Documentation time decreased by 70%
- Patient enrollment increased
- Completeness of mandatory elements increased 82% to 100%

University of Muenster: Bruland, Forster, Breil, Standaer, Dugas, Fritz
What are the barriers and how can we break through them?
One Example…

- **Common Misperception**: These standards only work for interventional/regulated studies!
- **Proposed “Solution”**: Let’s develop NEW standards for OUR use!

- **Fact**: Consensus-based standards cited (IHE and CDISC) have proven to be useful and valuable for outcomes research, observational studies, registries, device studies, nutritional research, public health, safety reporting, outbreak surveillance AND regulated interventional research… *around the world.*
What does all of this have to do with the Learning Health System, Learning Health Community and Essential Standards to Enable Research (ESTEL)?
“A Learning Health System is one in which progress in science, informatics, and care culture align to generate new knowledge as an ongoing, natural by-product of the care experience, and seamlessly refine and deliver best practices for continuous improvement in health and health care.”
A Learning Health System Should…

Support all types of learning---Research, Quality, Public Health and related activities
A Learning Health System Should…

Support BIG data for data mining, signal detection and analytics.
A Learning Health System Should…

Support the collection of high quality research data for Data Science.
A Learning Health System Should…

Streamline regulated research to accelerate development of new therapies and reduce costs.
A Learning Health System Should...

Support Data Sharing across various entities; technology is here and the world is changing.
A Learning Health System Should…

Engage Patients, including the assimilation of patient reported outcomes and personal health information.
What are we doing to Enable a Learning Health System (using Essential Standards)?
Learning Health Community (launched 2012)

- Infrastructure can enable necessary virtuous cycle of study, learning and improvement
- This requires assembly of data, analysis, and feedback

CORE VALUES ENDORSED

- Person-focused
- Privacy
- Inclusiveness
- Transparency
- Accessibility
- Governance
- Cooperative and Participatory Leadership
- Scientific Integrity
- Value
The Learning Health Community

- Grew out of the 2012 “Learning Health Summit”
- A self-organizing, multi-stakeholder coalition of the willing
- 60 “endorsers” plus > 600 others expressing interest
- “Summit” Planning Committee became the Community’s Coordinating Committee
- Catalyzing, leading, and participating in initiatives to realize a Learning Health System:
  - Standards (ESTEL) (initiated February 2013)
  - Governance (initiated 27 October 2014)
  - Technology
Essential Standards to Enable Learning (ESTEL) Charter

Purpose and Scope:

**To define a parsimonious/essential/minimum core set of standards** that could enable a standards-based yet flexible and scalable LHS in accordance with the following goals:

- a) Ease the burden for any clinician to participate in a research study or other learning activity;
- b) Increase the capacity for learning from data;
- c) Obtain knowledge and results in an actionable form to contribute to building the LHS;
- d) Ensure that the data obtained can be readily aggregated and/or compared; and
- e) Ensure that the data uphold scientific integrity.

~ December 2012
Activities to Date Relative to ESTEL

- May 2012 – Learning Health Community Summit
- Q4 2013 – ESTEL Name and Charter
- February 2013 – ESTEL Launch @ CDISC Office
- March 2013 – ESTEL Webinar
- July 2013 – ESTEL “Exec” Group @ IOM
- September 2013 – Second ESTEL F2F @ Duke
- Fall 2013 – CDISC requested to ‘host’ LHC
- Oct 2013 – March 2014 - Teleconferences
- April 2014 – Third ESTEL F2F @ AHRQ
- September 2014 – Small group of ‘big thinkers’ met at CDISC offices in Austin (TX Medical Association)
Charge for September 11 ESTEL Meeting

• Draft a straw man of an ideal architecture that ‘leapfrogs conventional thinking but lands on dry land’. Take the long view, then back off towards conventional thinking as required by our realities.

• Participants (small meeting of big thinkers)
  - Landen Bain, research/healthcare perspective
  - Ken Pool, public health software developer’s perspective
  - Wes Rishel, the best of historical and current thinking
  - George Cole, EHR pragmatist
  - Kevin Sullivan, computer scientist unshackled by healthcare background
  - Frederik Malfait, Semantic web developer with pharma and Euro perspectives
  - John Loonsk, public health architecture advocate
Increasing Focus as a Practical Way Forward: Essential Standards to Essential Structures, & The Learning System to Learning Cycles

Kevin Sullivan
University of Virginia
Department of Computer Science
ESTEL Webinar, Nov. 5, 2014
Overview

- Focus on learning cycles as path to learning system
- Focus on essential structures, standards in context
- The Learning Health Cycle as an essential structure
- The role of standards in learning health cycles
Emphasis on Learning Cycles

- Learning Health System is ultra-large scale, fractal, emergent
- Will comprise learning cycles at many scales, many domains
- Learning cycles will be iterated as a process to radically improve performance in given domains by *learning from reality*
- What's new in computer science is our ability to *perceive and compute on the output of reality in detail and at scale*
- Yet a full cycle is not just cyber but also physical and social
- Develop learning cycle framework (LCF) as a feasible, useful step on a path to a pervasively learning health system
Increase Short-Term Focus on Essential Structures

- Learning cycle an essential structure for learning health system
- Learning cycles are bounded, determinate, automatable
- There is a tremendous diversity of individual instances
  - Health conditions and domains of practice
  - Underlying implementation technologies
  - Need for and participants in data sharing
  - Important protocol and data standards
  - Details of observation, inference, teaching ...
- Yet there are also common structures, dynamics, and issues
- Capture these in concept of flexible Learning Cycle Framework
Learning Cycle Framework

- Captures shared structure, behavior, issues, growth potential
  - Compositionality of learning cycles
  - Hierarchy of specializations (e.g., standards)
- Specific learning cycles (such as ACC, I-SPY) will constitute individual framework instances
- Basis for recognizing, describing, designing, composing, and improving learning cycles; catalytic concept for the ecosystem
- An important manageable step on path toward broader LHS
- Need to develop applications, engineering foundations, science of learning cyber-physical-social software-intensive ecosystems
Role of Standards

- Framework should survive over decades and across diverse practice domains
- Standards specifications are essential
  - will vary over time and across diverse areas
  - are supporting elements in larger structure
  - will emerge, evolve, settle as we learn by doing
- Premature commitments limit applicability of architecture
- Don't prematurely bind specific standards
- Maintain flexibility to learn from reality!
Thanks and Extra Slides
Simple Formal Model of One Cycle

- Given computational and propositional types and functions involving objects of these types, and a learn function that composes the given functions into a learning cycle

- What this model says is that learning involves
  - Perceiving (sensing, measuring, recording) reality, yielding data
  - Transforming data (e.g., aggregating across sites) into a useful form
  - Analyzing this data to produce observations (e.g., by machine learning)
  - Drawing inferences (propositions) from data (e.g., the learned function is good)
  - Elevating propositions to the status of hypotheses to be tested
  - Testing these hypotheses by running experiments yielding evidence
  - Elevating hypotheses supported by data to the status of theories
  - Packaging theories and supporting evidence as guidance for practice
  - Teaching learners (e.g., physicians) this guidance

- This structure allows for variations in how almost all of this is done

- It shows how informal diagrams can be formalized as mathematical specifications, indeed as specifications from which implementation elements can be synthesized
Formal Model as Coq Typeclass

Class LS := {
  reality: Type
; data: Set
; observation: Set
; inference: Prop
; hypothesis: Prop
; experiment: Set
; evidence: Type
; theory: Prop
; guidance: Type
; learner: Type

; perceive: reality -> data
; transform: data -> data
; analyze: data -> observation
; infer: observation -> inference
; hypothesize: inference -> hypothesis
; test: hypothesis -> experiment -> evidence
; theorize: hypothesis -> evidence -> theory
; package: theory -> evidence -> guidance
; teach: learner -> guidance -> learner

; learn (l: learner) (r: reality) (exp: experiment): learner :=
  let hyp := (hypothesize (infer (analyze (transform (perceive r))))) in
  (let evid := (test hyp exp) in
    teach l (package (theorize hyp evid) evid))
}.  
Some challenges

- Mathematical-logic framework specification and mechanical synthesis of frameworks implementations
- Express and realizing critical non-functional properties
- Theory of cyber-physical-human learning systems
- End-to-end cyber-physical-social architectures
- Tradeoffs involving cost, latency, accuracy, safety, etc
- Learning to improve learning performance
- Roles of key ecosystem players
- Compositionality of learning cycles
- Perceiving and learning across domain boundaries
Presentation by Landen Bain

The CDISC Vision is to Inform Patient Care & Safety Through Higher Quality Medical Research
Outline

• Becky Kush – background and history
• Kevin Sullivan – description of ESTEL framework
• Landen Bain – learning loop opportunities
• Ken Pool – immediate instantiations.
From Essential *Standards* to Essential *Structures* That Enable Learning

- The original task of “ESTEL” was to name standards that enable learning.
- Along the way, the group realized that before we could name standards, we had to envision the structure.
- The 9-11 group met to discuss the structures that must be articulated before the standards can be specified.
The charge for September 11

• Draft a straw man of an ideal architecture that ‘leapfrogs conventional thinking but lands on dry land.” Take the long view, then back off towards conventional thinking as required by our realities.

• Participants
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Learning Health System vs Learning Health Cycle

• Learning Health System: an emergent Ultra Large Scale System, not so much built as evolved
• Learning Health Cycle, a.k.a. Learning Loop – a manageable components of the LHS
LHS defined

A learning health system consists of a set of information systems interoperating within a structure for the purpose of automating learning loops.
Research Learning Loop

- Clinical research is a learning loop that consists of a number of information systems interoperating around existing standards and technologies.
- The research loop exists, but is only partially automated, and takes a really long time (17 years?).
- The data capture side is farther along than the feedback side.
Research Learning Loop: Systems and Standards

Electronic Data Capture System
- Capture data
- Aggregate data

Data Capture
RFD, CDASH, ODM

Electronic Health Record System
- Schedules patient visits
- Plans care
- Documents healthcare
- Orders/results

Data Management
ODM

Regulatory System
- Reviews submission

Data Submission
ADAM, SDTM

Clinical Data Management System
- Curates research data
- Analyzes data
Registry Learning Loop

• Registries are often managed by professional associations

• Example: Academy of Clinical Chronologists (ACC) manages the Index of Chrono Dyslexics (ICD), a disease registry for those who suffer from chrono-dyslexia

• Like the research learning loop, the data capture side is farther along than the feedback side

• A number of systems interoperate to automate the learning loop
Registry Learning Loop: Systems and Standards

Electronic Health Record System
- Schedules patient visits
- Plans care
- Documents healthcare
- Orders/results

Data Capture

ACC Registry System
- Captures data
- Aggregates data

Data Management

Data Analysis System
- Curates data
- Analyzes data
- Creates guidance documents

Feedback
Pillars of the LHS
K D Pool MD
COO for OZ Systems
Tom the Builder

- My job is to build stuff
  - Kevin has laid out the supply list
  - Landen has described what he wants in his cathedral
  - I build what Landen wants using the supplies Kevin has laid out
Getting TO PLAY: Rules of Engagement

- Will be established by the governance committee.
- Likely will include:
LHS IS GREAT!

ENDORSED
Agree to Abide
Use framework
HERE IS MY ID
What does Landen’s cathedral do?

- Providers from around the country see patients with defibrillators.
- As they see them they complete forms reporting on the patient outcomes/experience.
- These data are brought together and subjected to rigorous analysis.
- The analytic results are reviewed by an august body who use them as the basis for guidelines.
- The guidelines are published as electronic guidance.
- When providers see patients then guidance targeted on that patient’s condition is instantly available at the point and time of care.
- Care improves.
- Repeat ad infinitum.
What Landen wants
Plans for Landen’s ACC LHS
Finding the building blocks

Everything should be made as simple as possible, but not simpler.
Plans for Landen’s ACC LHS
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Plans for Landen’s ACC LHS
BUILDING BLOCKS WE NEED

FUNNEL CONNECTION

GUIDANCE CONNECTION
FUNNEL CONNECTION

• IHE RFD FORM PROCESSOR

  – Information for providers:
    • IP address
    • Form ID
    • SSL encryption required
    • Pre-population documents accepted:
      – CCD
    • Supports provider designated Form Archiver
GUIDANCE CONNECTION

- HL7 CDS Knowledge Artifact with S&I Health eDecisions IG
  - Information for providers:
    - IP address
    - Artifact ID
Supplies: RFD Form Processor

Medieval Stone Bricks

21 Kismet Textures
Supplies: CDS Artifact
Select site for hosting
Use highly skilled labor
And soon we have a LHS
Don’t tell Landen how easy this was: He thinks I am a wizard
But I am just a simple builder of cathedrals