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

5 November 2014, 12:30-14:00 Eastern U.S. Time

Strength *through Collaboration*

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

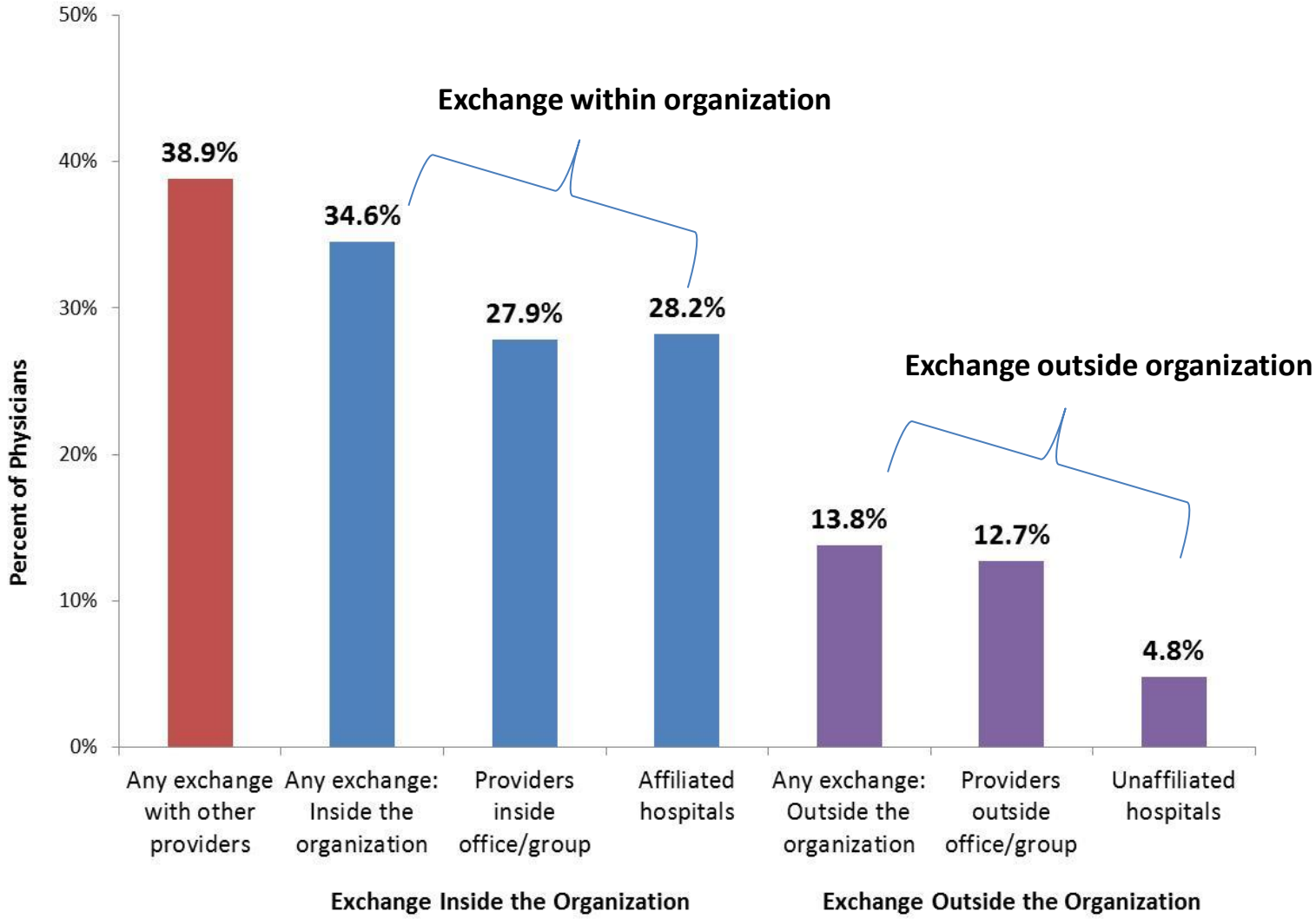
Currently Inefficient ~17-year cycle

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

Research findings to inform healthcare decisions

Data Exchange Among Physicians – NOT 'Interoperable'



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’

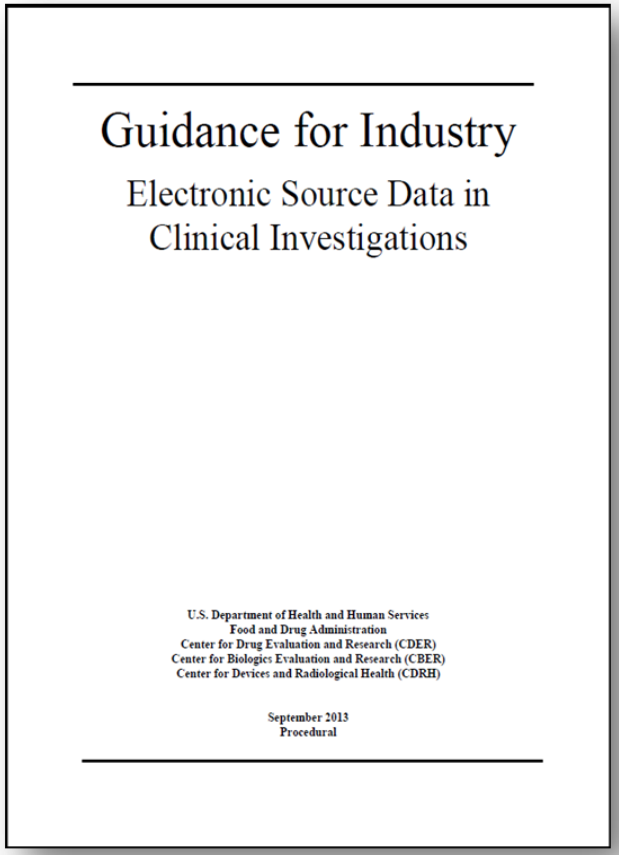
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

09 June 2010
EMA/INS/GCP/454280/2010
GCP Inspectors Working Group (GCP IWG)
Date for coming into effect 01 August 2010

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.
3. **CDISC e-source standard requirements-CDISC** (Clinical Data Interchange Standards Consortium) Version 1.0 20 November 2006.



Guidance for Industry

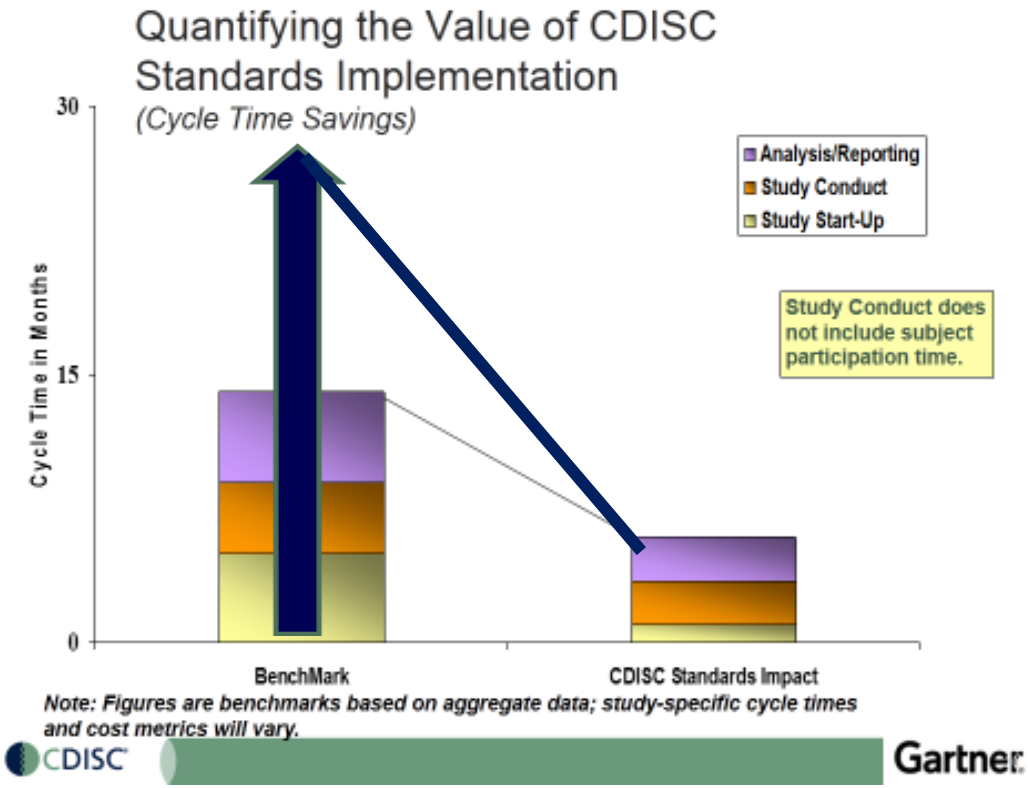
Electronic Source Data in Clinical Investigations

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

September 2013
Procedural

eSource = data entered electronically first, i.e.EHRs, eDiaries….

Value of Using Standards Even Greater Now!



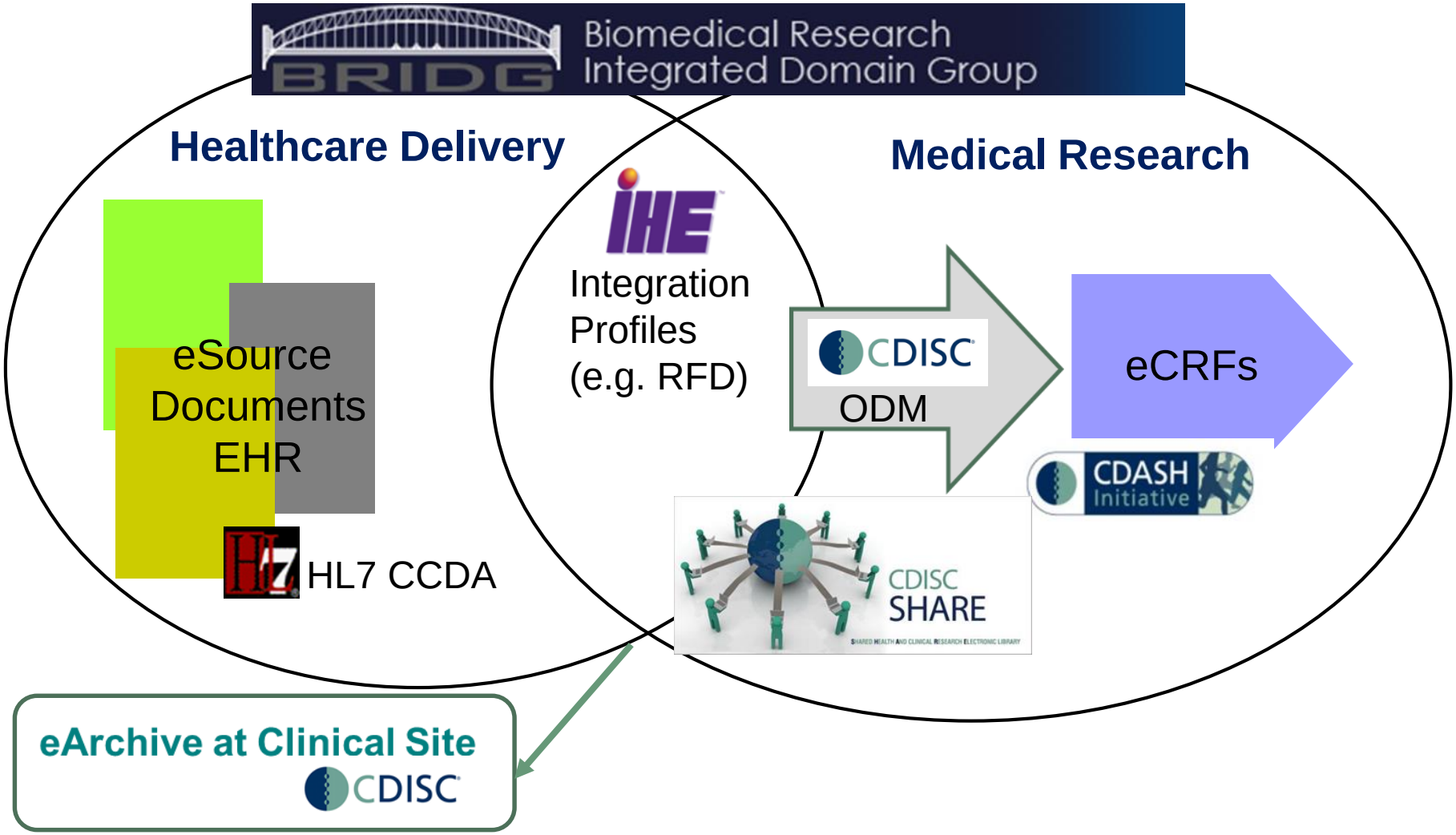
2007 CDISC Business Case

2014 Business Case

Current Landscape 2014

- Study Complexity
- # Datapoints
- Data Management
- Time/Resources
- Cost of Research

Synergistic Standards Currently Available for EHR-enabled Research



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***

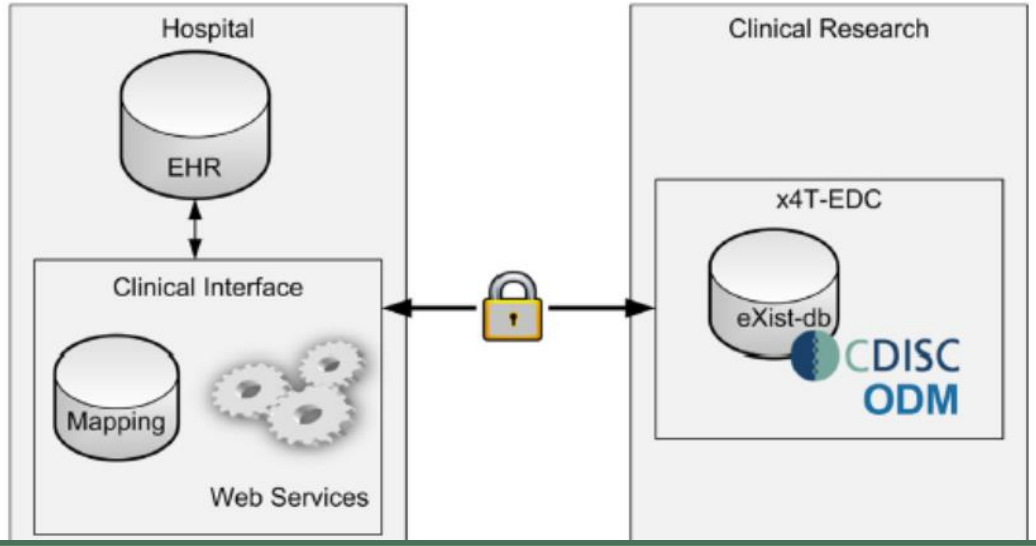
Source: Michael Ibara, Pfizer

Examples from Europe

Innovative Medicines Initiative

A joint undertaking between Academia & Industry

TRANSFoRm Query Formulation Workbench



University of Muenster: Bruland, Forster, Breil, Standaer, Dugas, Fritz

eSOURCE

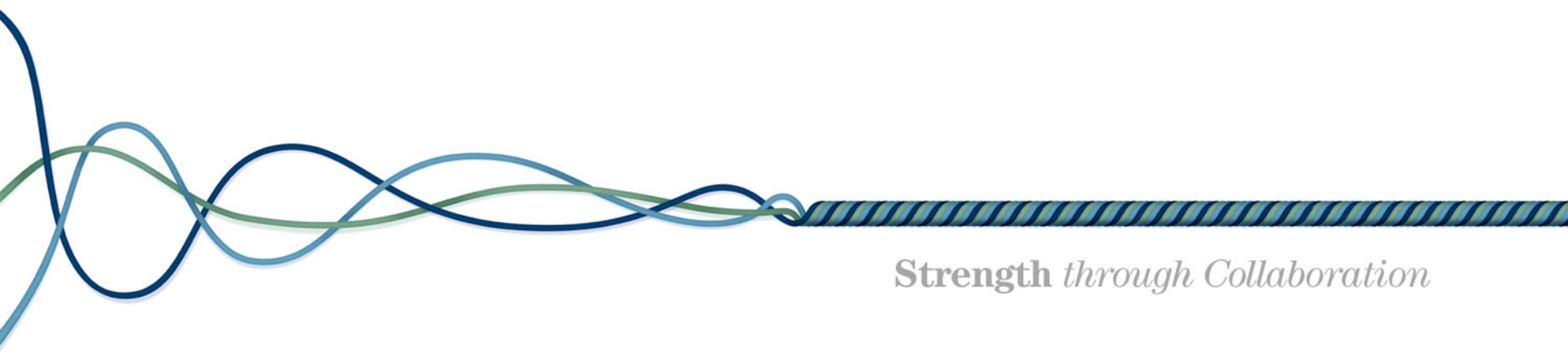
- Documentation time decreased by 70%
- Patient enrollment increased
- Completeness of mandatory elements increased 82% to 100%

What are the barriers and how can we break through them? One Example…

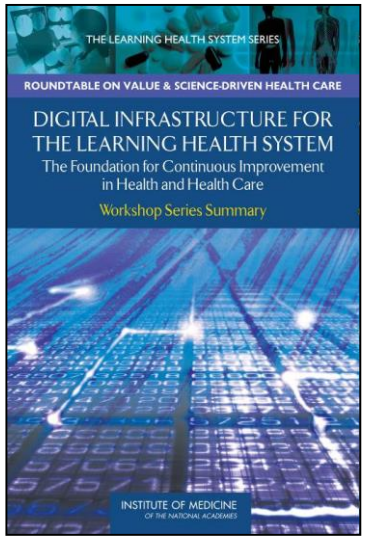
- **Common Misperception**: These standards only work for interventional/regulated studies!
- **Proposed "Solution":** Let's develop NEW standards for OUR use!

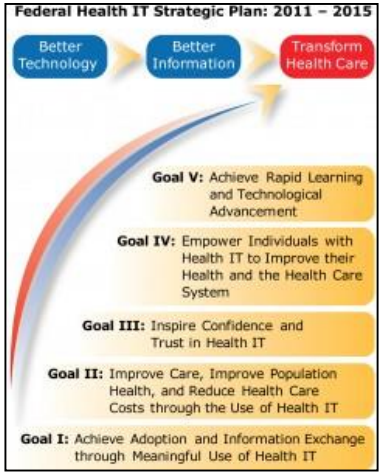
- **Fact**: *Consensus-based standards cited (IHE and CDISC) have proven to be useful and valuable for outcomes research, observational studies, registries, device studies, nutritional research, public health, safety reporting, outbreak surveillance AND regulated interventional research…**around the world.***

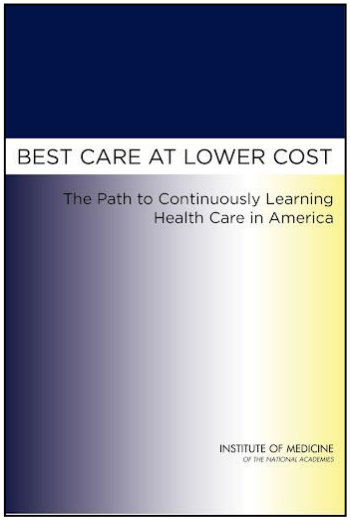
What does all of this have to do with the Learning Health System, Learning Health Community and Essential Standards to Enable Research (ESTEL)?



A National-Scale Learning Health System: Background from the U.S. Institute of Medicine of the National Academies

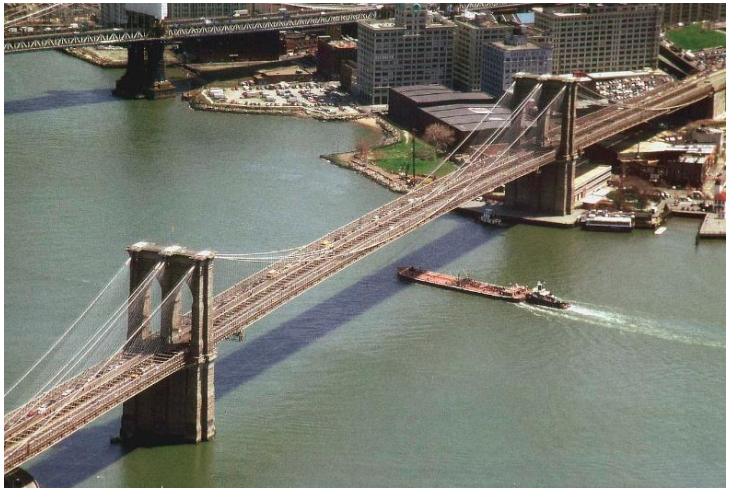






"A Learning Health System is one in which progress in science, informatics, and care culture align to generate new knowledge as an ongoing, natural by-product of the care experience, and seamlessly refine and deliver best practices for continuous improvement in health and health care."

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.

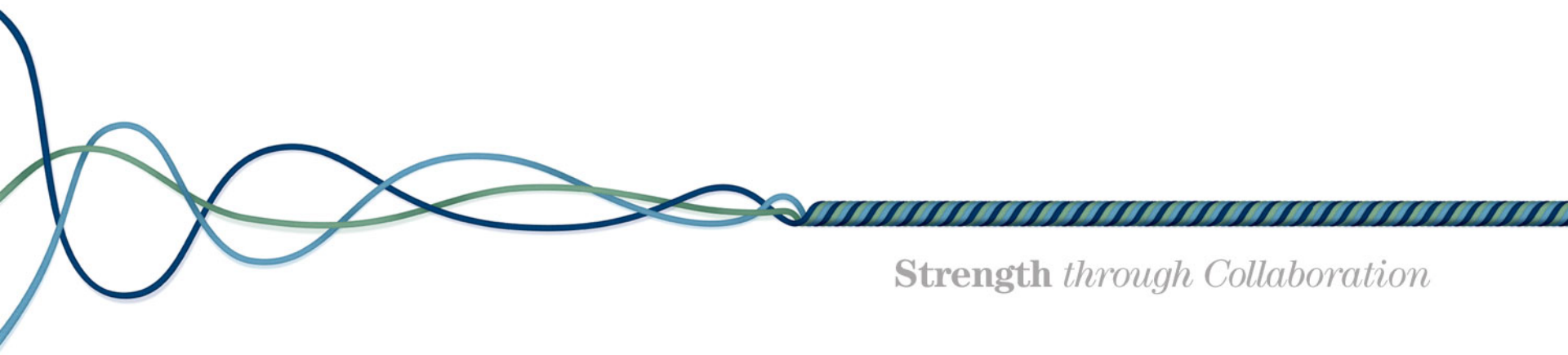
A Learning Health System Should…

Support Data Sharing across various entities; technology is here and the world is changing.

A Learning Health System Should…

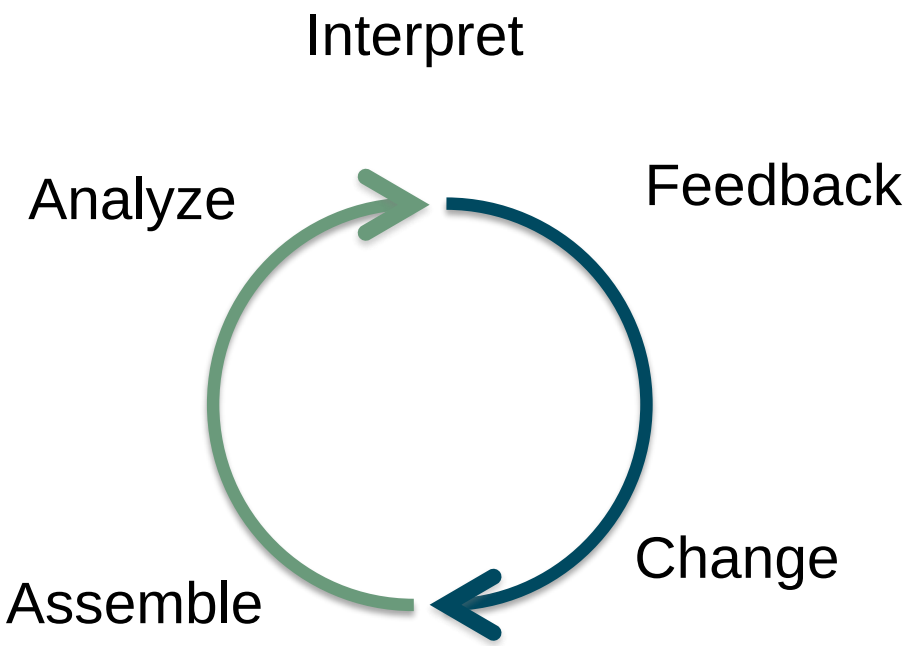
Engage Patients, including the assimilation of patient reported outcomes and personal health information.

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

CDISC®

CLINICAL DATA INTERCHANGE STANDARDS CONSORTIUM

Presentation by Landen Bain

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

Strength *through Collaboration*

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
  - Landen Bain, research/healthcare perspective
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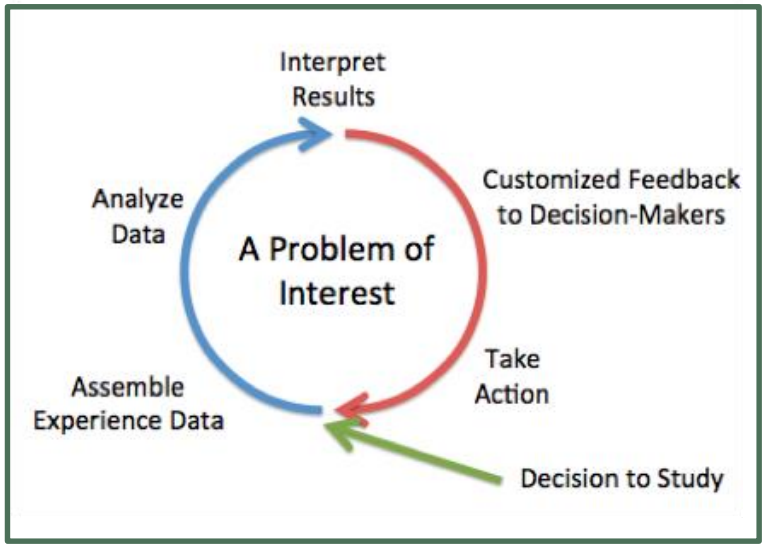
Learning Health *System*
vs
Learning Health *Cycle*

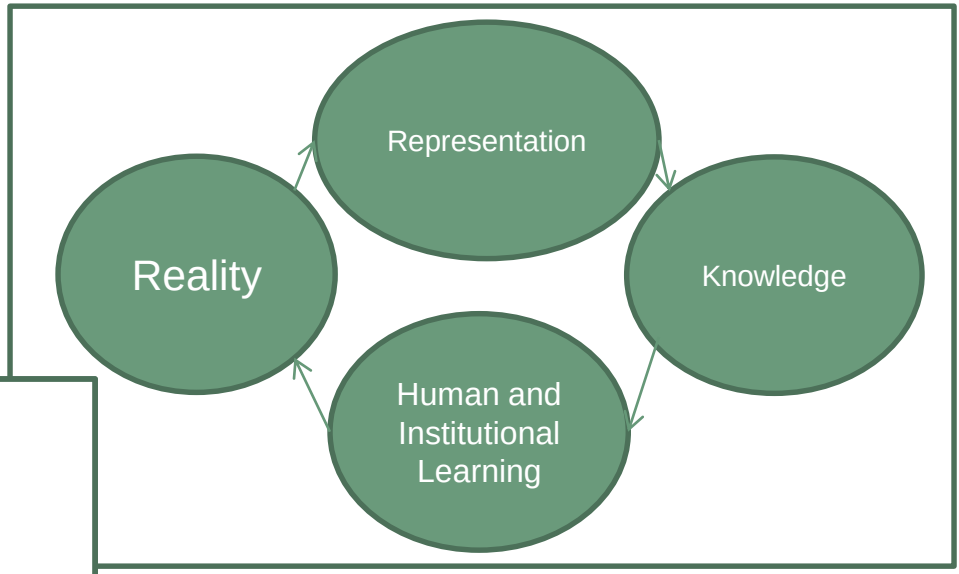
- Learning Health System: an emergent Ultra Large Scale System, not so much built as evolved
- Learning Health Cycle, a.k.a. Learning Loop – a manageable components of the LHS

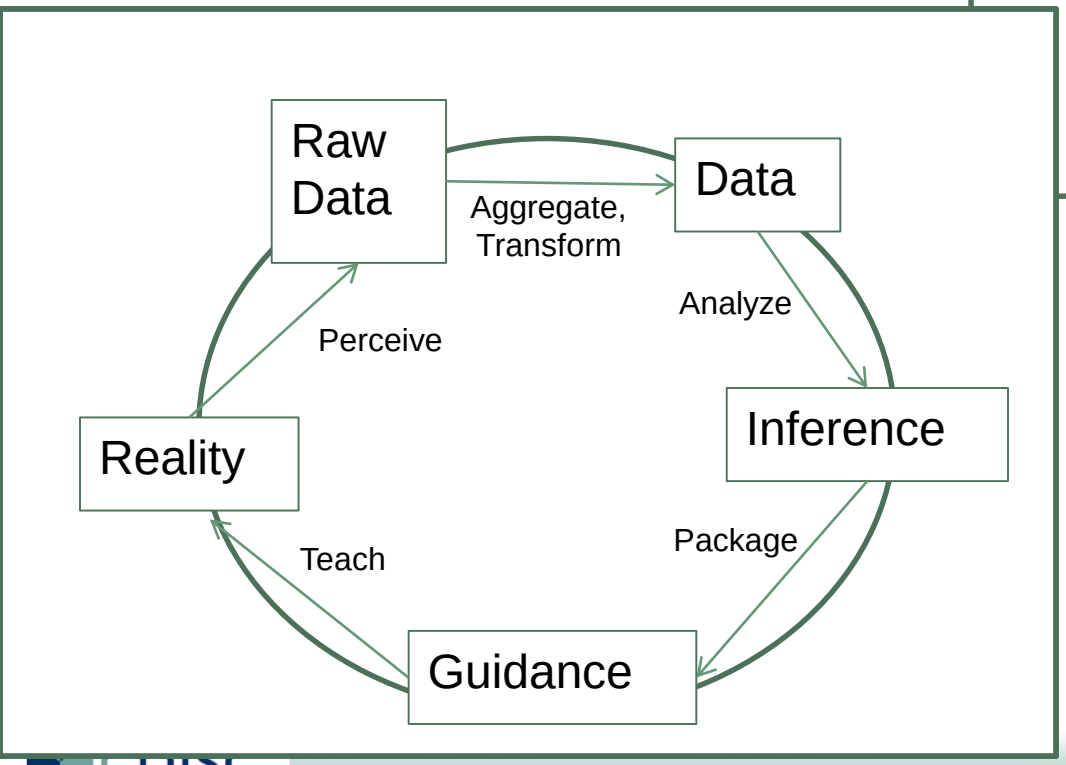
LHS defined

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

Learning Cycle – From Concept to Framework to Entities and Activities



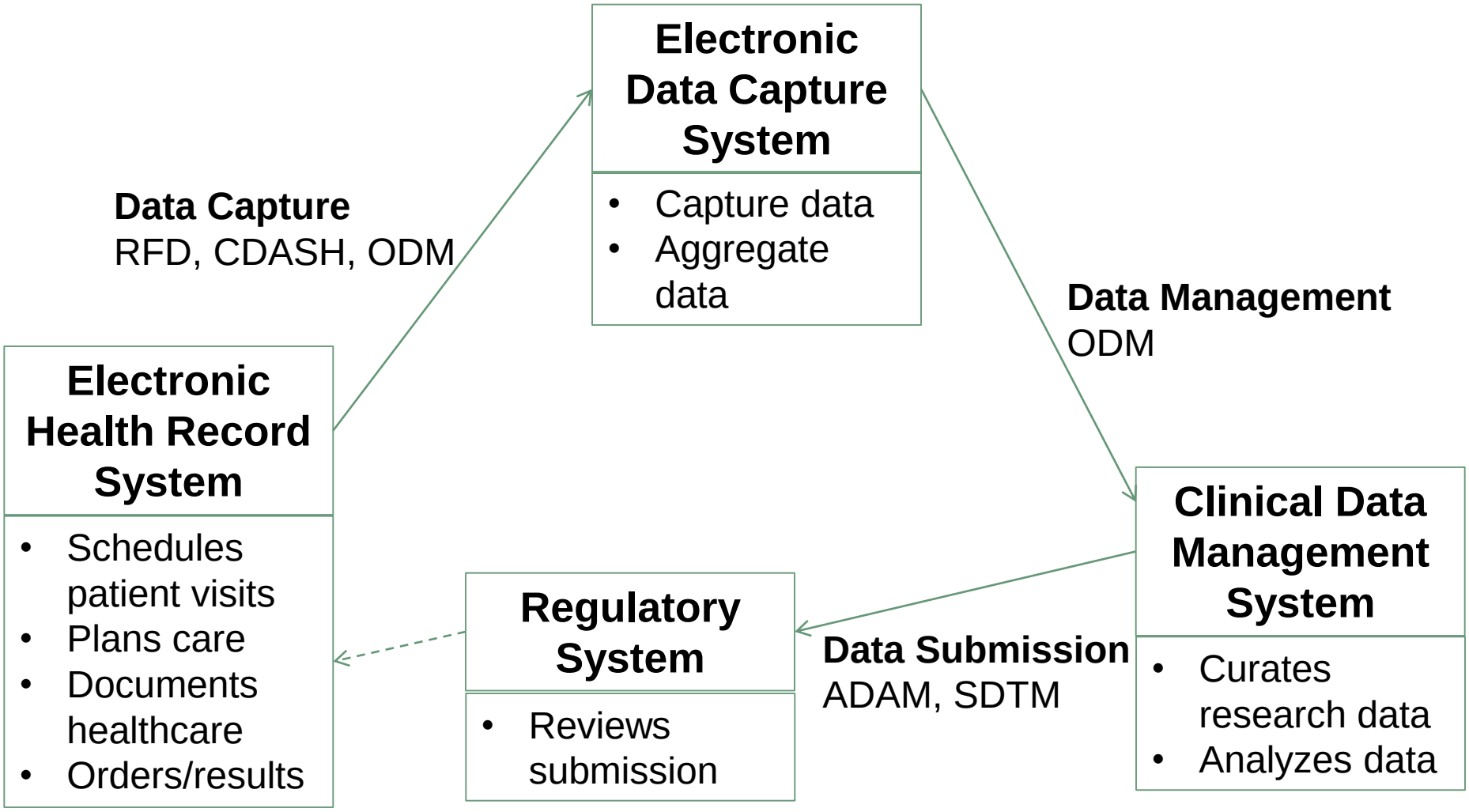




Research Learning Loop

- 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

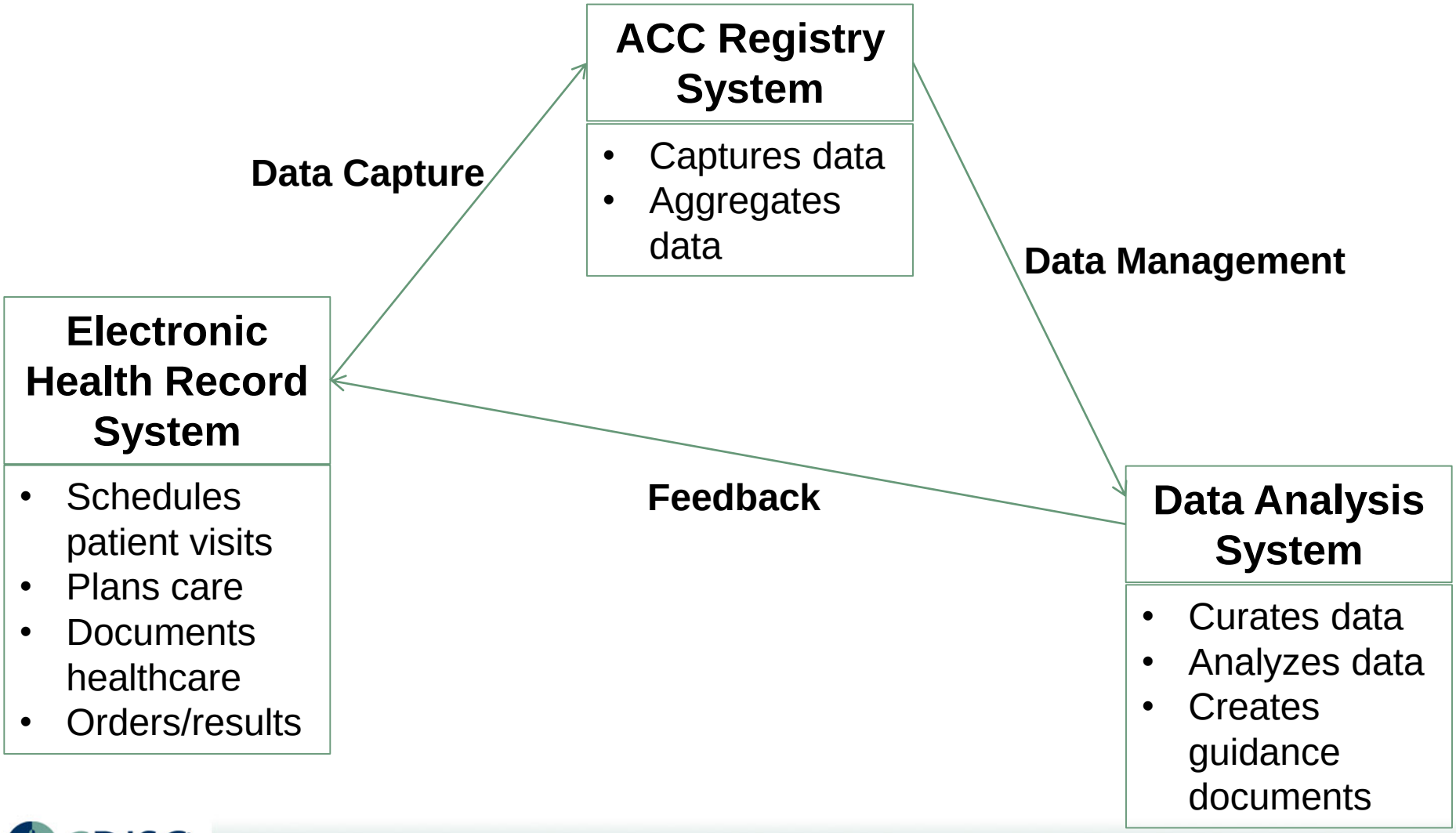
Research Learning Loop: Systems and Standards



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



oz systems

Pillars of the LHS

K D Pool MD

COO for OZ Systems

Tom the Builder

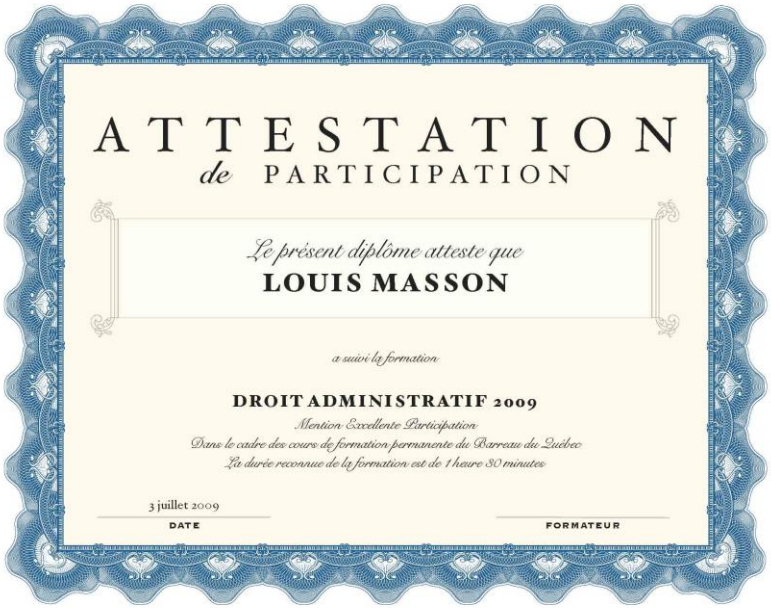
- My job is to build stuff
  - Kevin has laid out the supply list
  - Landen has described what he wants in his cathedral
  - I build what Landen wants using the supplies Kevin has laid out

Getting TO PLAY:
Rules of Engagement

- Will be established by the governance committee.
- Likely will include:

LHS IS GREAT!

Agree to Abide



ATTESTATION
de PARTICIPATION

Le présent diplôme atteste que
LOUIS MASSON

a suivi la formation

DROIT ADMINISTRATIF 2009
Mention Excellente Participation
Dans le cadre des cours de formation permanente du Barreau du Québec
La durée reconnue de la formation est de 1 heure 30 minutes

3 juillet 2009
DATE

FORMATEUR

Use framework

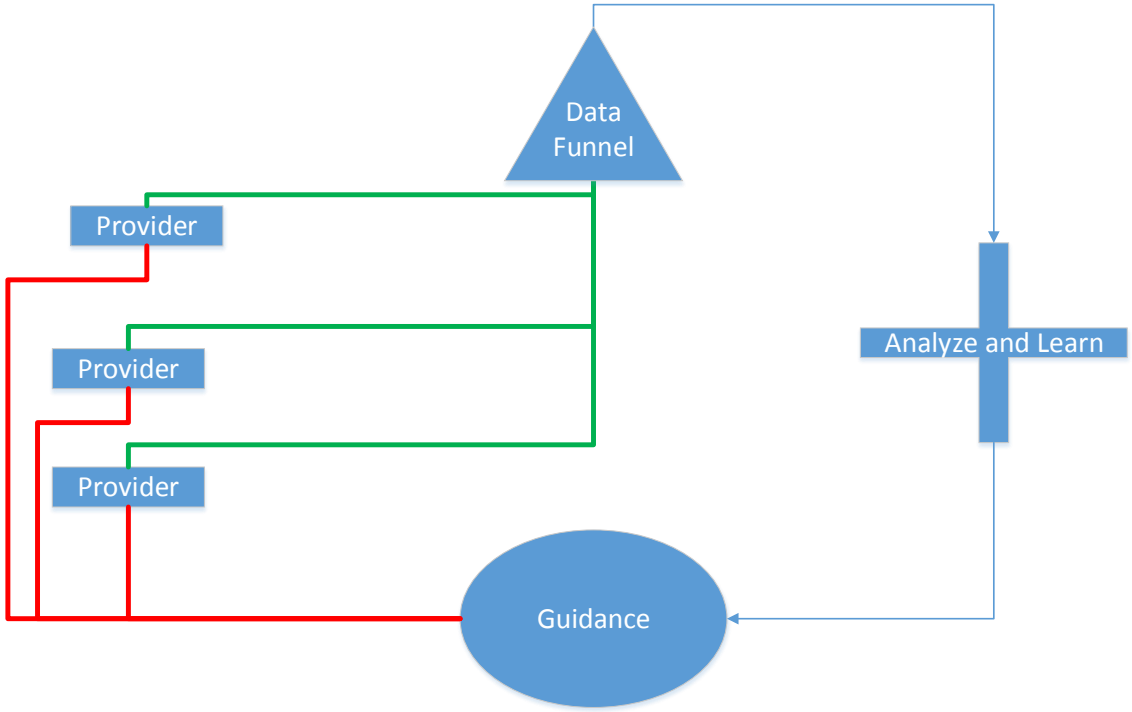
HERE IS MY ID

What does Landen's cathedral do?

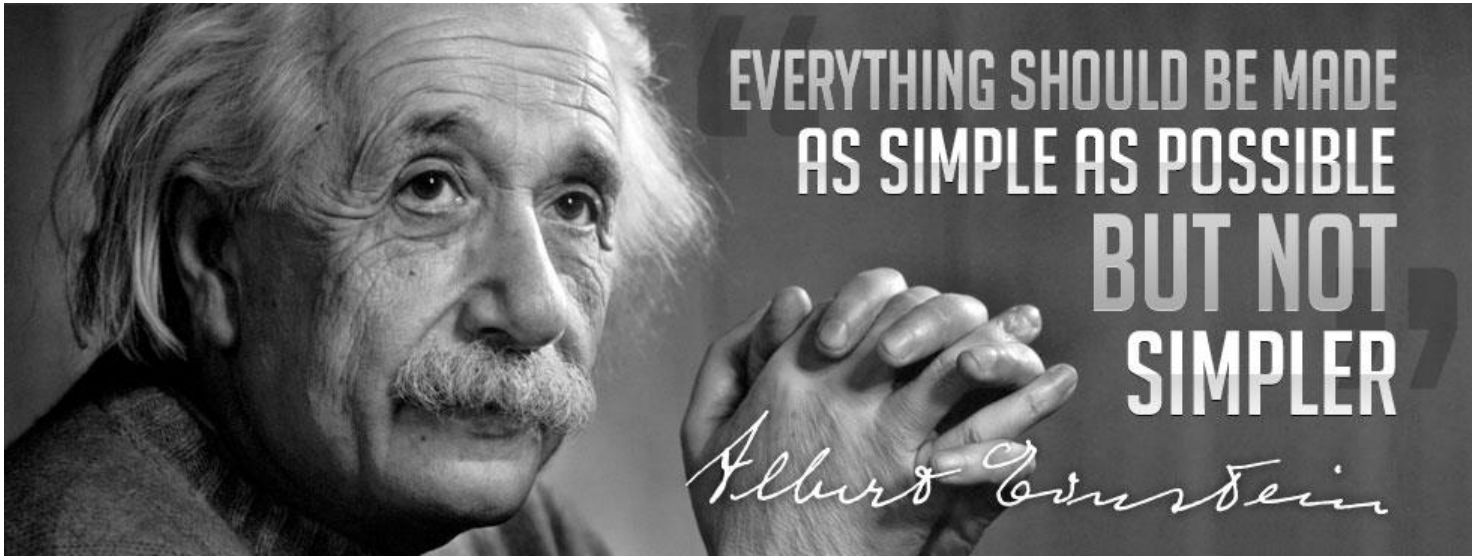
- Providers from around the country see patients with defibrillators.
- As they see them they complete forms reporting on the patient outcomes/experience.
- These data are brought together and subjected to rigorous analysis.
- The analytic results are reviewed by an august body who use them as the basis 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



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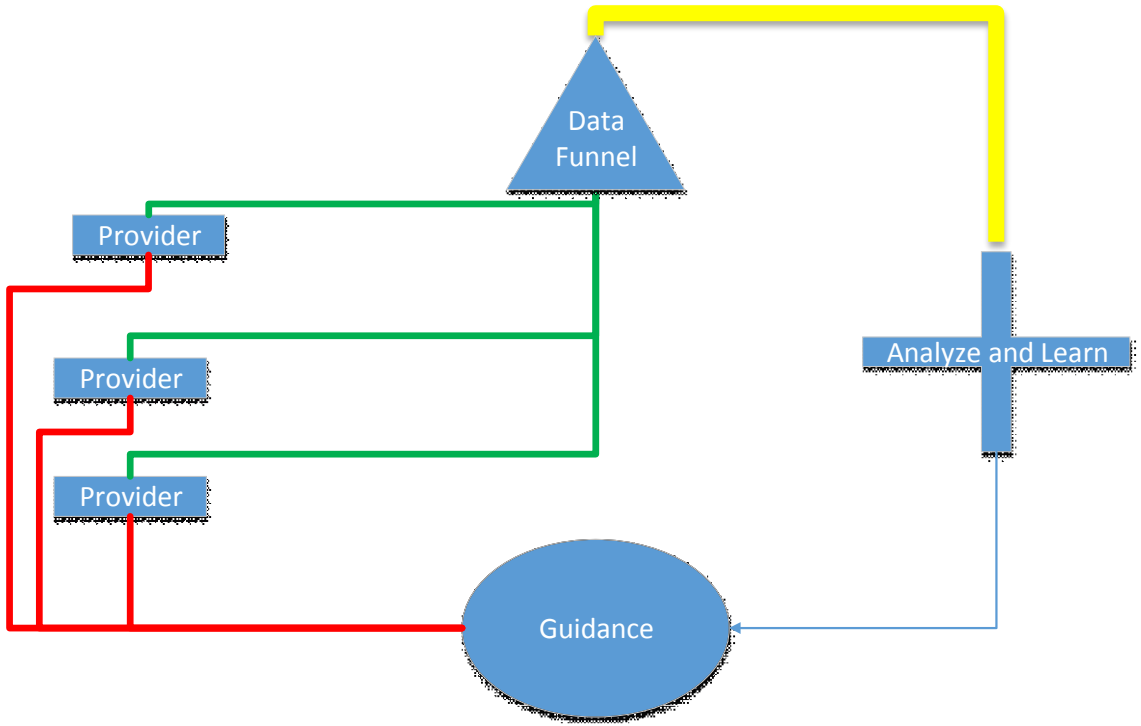

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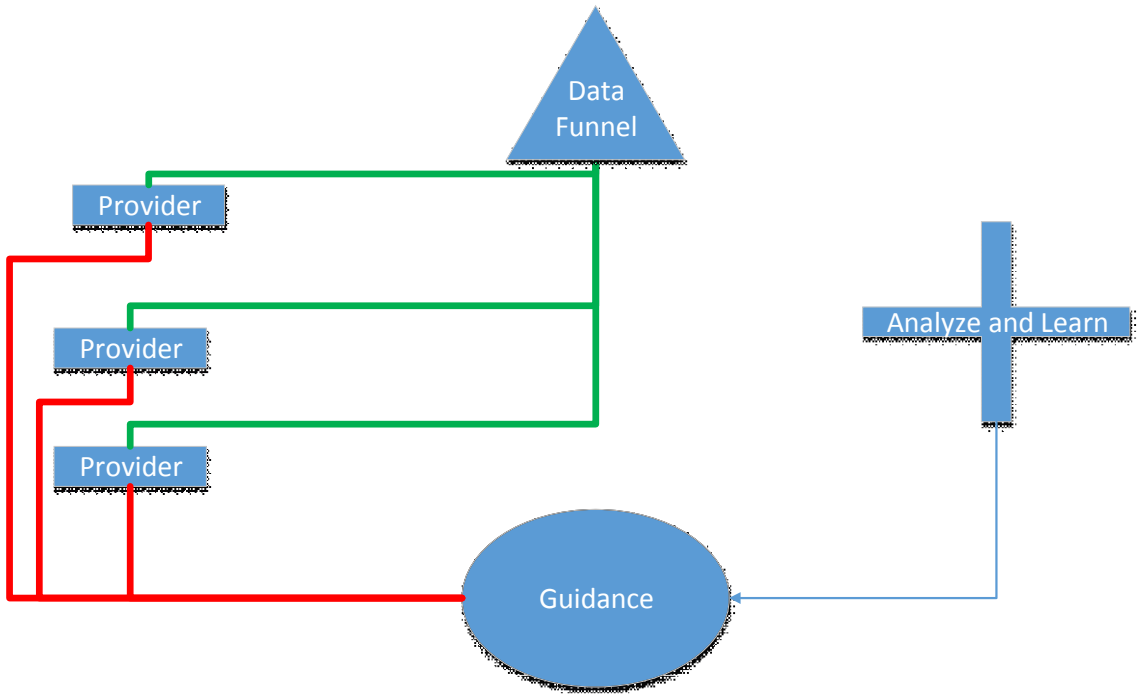

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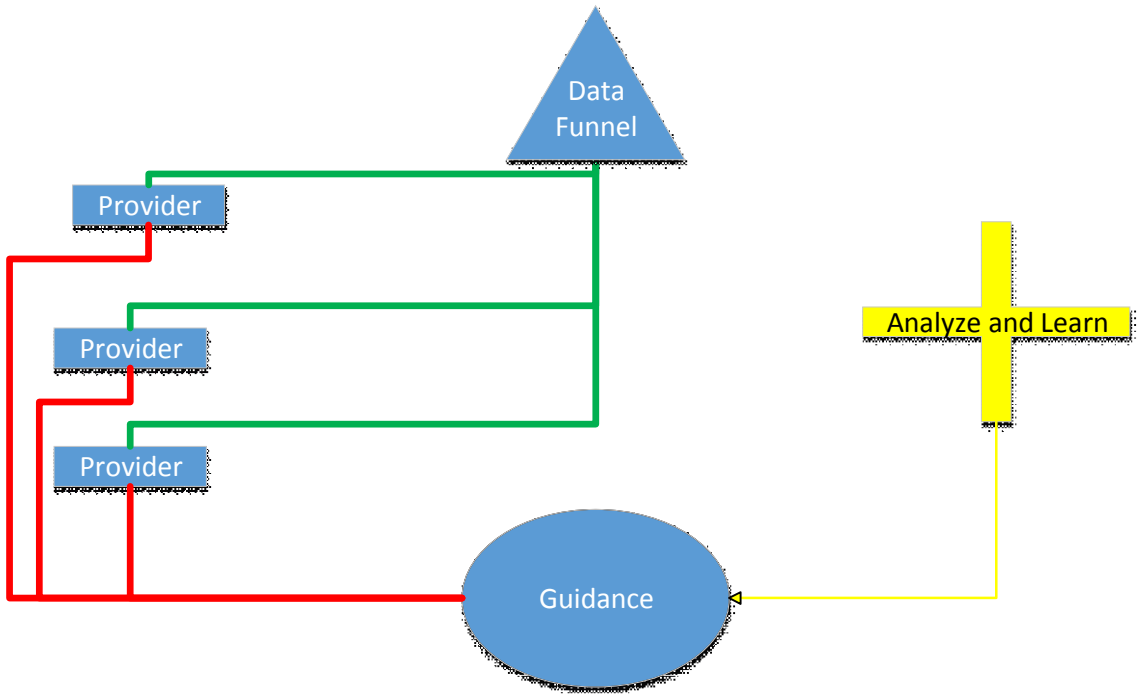

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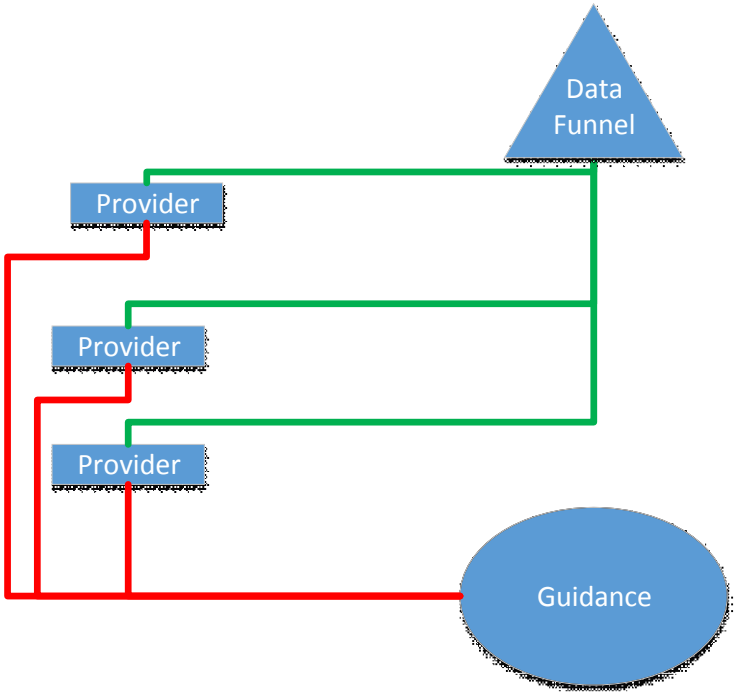

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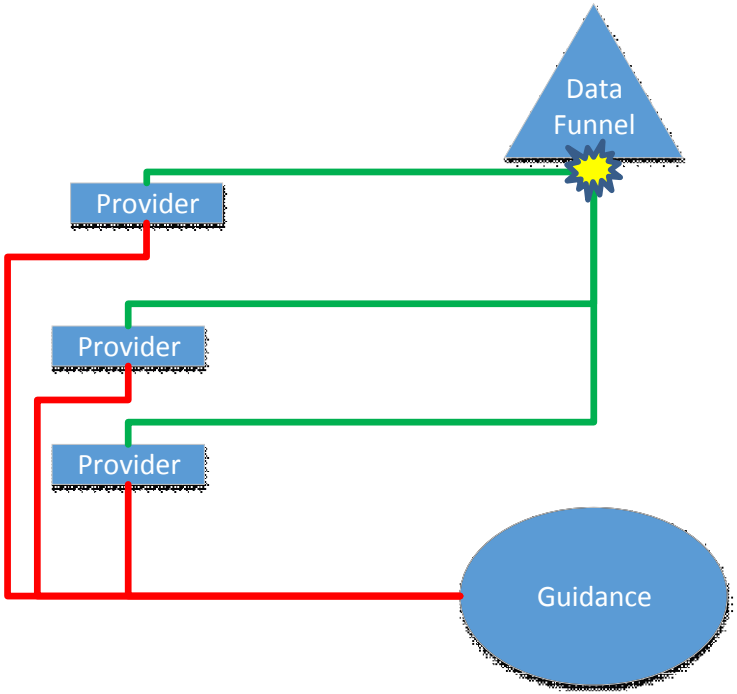

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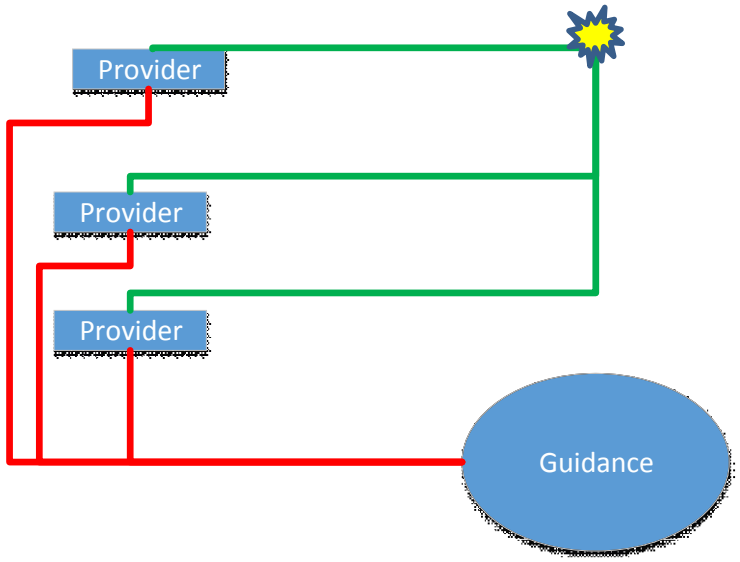

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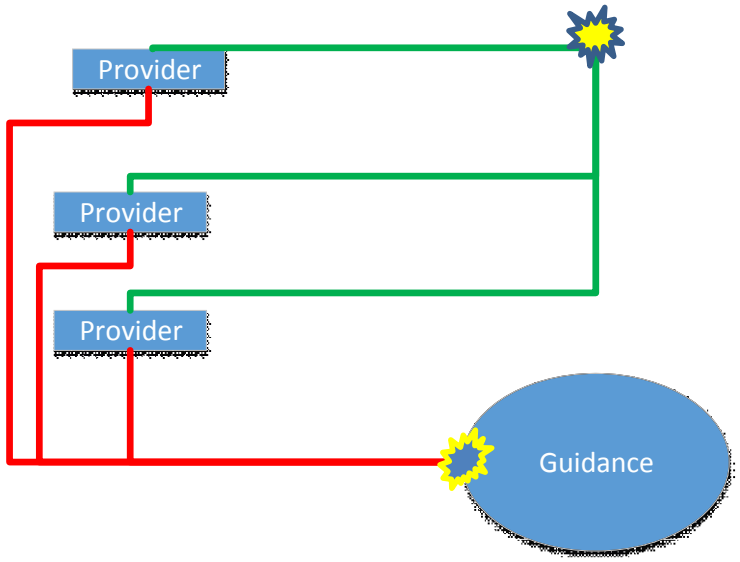

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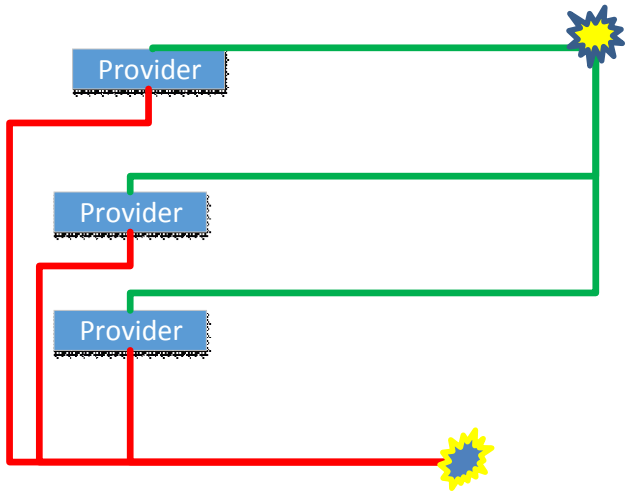
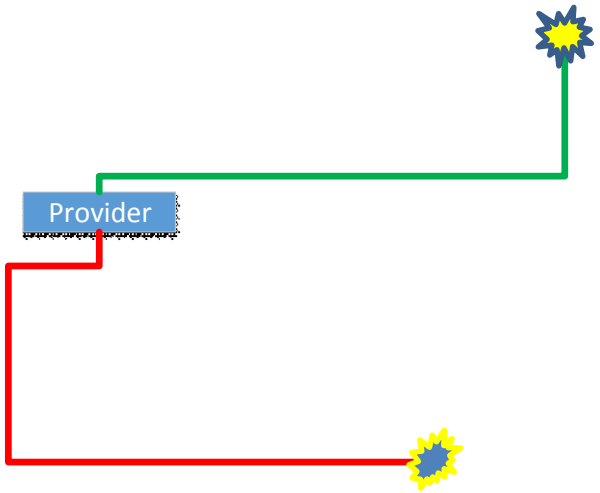
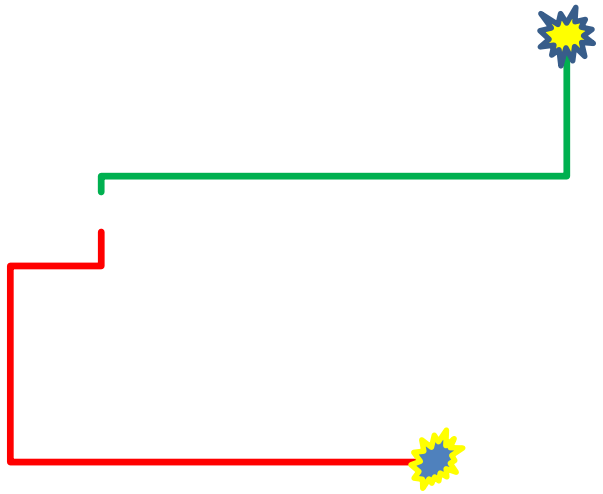


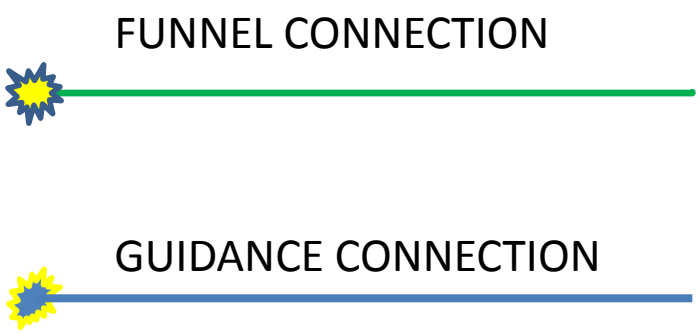
Plans for Landen's ACC LHS



Plans for Landen's ACC LHS



BUILDING BLOCKS WE NEED



Kevin's Supply List

福祿壽婴药閣

湯類

(1)	西湖牛肉羹 (每位)	$4.95
(2)	三絲鴨絲羹 (每位)	$4.95
(3)	雞茸粟米豆腐羹 (每位)	$4.95
(4)	魯肉魚肚羹 (每位)	$5.95
(5)	八寶冬瓜盅湯 (每位)	$6.50

頭盤

(8)	蒸茸鳳尾蝦 (每件)	$4.95
(9)	蒸茸帶子盒 (每件)	$4.95
(10)	百花炸釀蟹拑 (每件)	$5.50
(11)	脆皮香芒卷 (2條)	$5.50
(12)	菊汁掏釀蟹蝦 (每隻)	$7.95
(13)	流沙軟殼蟹 (每隻)	$10.95

鴨類

(14)	古法脆皮鴨 (半隻)	$16.95
(15)	北菰扒大鴨 (半隻)	$19.95
(16)	魚香鴨羹 (半隻)	$19.95
(17)	北京片皮鴨 (兩吃)	$44.95

雞類

(18)	啫啫雞窩羹	$12.95
(19)	檸香茄汁雞片	$14.95
(20)	鎮江滑雞件	$14.95
(21)	荷香金針雲耳蒸雞	$15.95
(22)	珍珠蛋香燒雞	$16.95
(23)	大漠風沙雞 (半隻)	$17.95
(24)	古法豉油雞 (一隻) 預定	$36.95

牛類

(25)	沙爹星遮牛肉	$14.95
(26)	x.o. 牛肉羹	$14.95
(27)	沙爹粉絲牛肉羹	$14.95
(28)	咖菜流瓜炒牛肉	$14.95
(29)	黑椒銀珀AAA牛柳粒	$24.95
(30)	黑椒美國AAA頂級牛扒件	$24.95

豬類

(31)	琵琶吊燒骨	$13.95
(32)	紀子菠蘿酥肉	$14.95
(33)	鎮江肉排	$15.95
(34)	菊汁掏肉排	$15.95

海鮮類

(35)	雀巢鵪鶉球	$21.95
(36)	日本煎大蝦	$22.95
(37)	百汁煎大蝦	$22.95
(38)	美極煎大蝦	$22.95
(39)	富貴黃金蝦	$22.95
(40)	椒鹽三鮮	$22.95
(41)	香檳桂花蚌雞片	$22.95
(42)	劍椒蒸帶子	$23.95
(43)	清蒸智利鱸魚柳 (一磅)	$34.95
(44)	毛家魚	$39.95
(45)	劍椒蒸鱸魚	$18/lb
(46)	百歲菊花魚	$18/lb
(47)	龍蝦	(時價)

豆腐類

(48)	麻皮玉子豆腐	$13.95
(49)	椒鹽豆腐粒	$13.95
(50)	墨汁紅肉碎豆腐粒	$14.95
(51)	鹹魚雞粒豆腐煲	$14.95
(52)	八珍豆腐煲	$15.95
(53)	蒜汁帶子蒸豆腐	$17.95

蔬菜類

(54)	豐燜茄子	$13.95
(55)	肉碎干燒四季豆	$13.95
(56)	京式麥螞薯	$14.95
(57)	蒜汁芥蘭遮	$14.95
(58)	上湯菇子澆白菜苗	$16.95
(59)	鮮腐皮扒豆腐	$17.95
(60)	瑤柱扒豆苗	$18.95
(61)	皇子菰扒白菜苗	$19.95

粉麵飯

(62)	揚州炒飯	$13.95
(63)	生菜雞牛肉炒飯	$13.95
(64)	鹹魚雞粒炒飯	$14.95
(65)	夏茸香白菜粒炒飯	$14.95
(66)	鴨腸湯飯	$14.95
(67)	菊汁掏雞飯	$14.95
(68)	干炒牛肉河	$14.95
(69)	廣東炒麵	$15.95
(70)	福建炆雪菜米	$16.95
(71)	福建炒飯	$16.95
(72)	蒜香海鬼炒飯	$16.95
(73)	揚州富伊麵	$18.95
(74)	海鮮炒麵	$20.95

Cynthia's Chinese Restaurant

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

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