Genomics informatics interoperability standards supporting precision medicine across health IT systems

Ben McAlister

Sr Solution Strategist, Interoperability Strategy, Europe

SNOMED International
Leading healthcare terminology, worldwide

SNOMED International Genomics and Precision Medicine Clinical Reference Group

April 2019 Business Meeting Genomics Session, 11th April 2019

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"We believe that genomic data and the genomic aspects of precision medicine should be incorporated into the routine clinical workflow in as seamless and transparent a fashion as possible."

David McCallie Jr., Cerner Senior Vice President of Medical Informatics

genomeweb, Cerner Banking on Third-Party Apps for Genomic Integration, Starting with PGx, 28th Dec 2018

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Introduction

Roles

- Associate Vice Chair for Standards, British Computer Society (BCS) Health and Care Group
- BCS representative, British Standards Institute (BSI) IST/35 Health Informatics Committee
- Member at large, Health Level Seven (HL7) UK Management Board
- Member, IHE UK Steering Committee
- Vendor representative, INTEROPen Board

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Introduction

Agenda

- Health IT vendor perspective
- Standards landscape
- Challenges and possible ways forward

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Health IT vendor perspective

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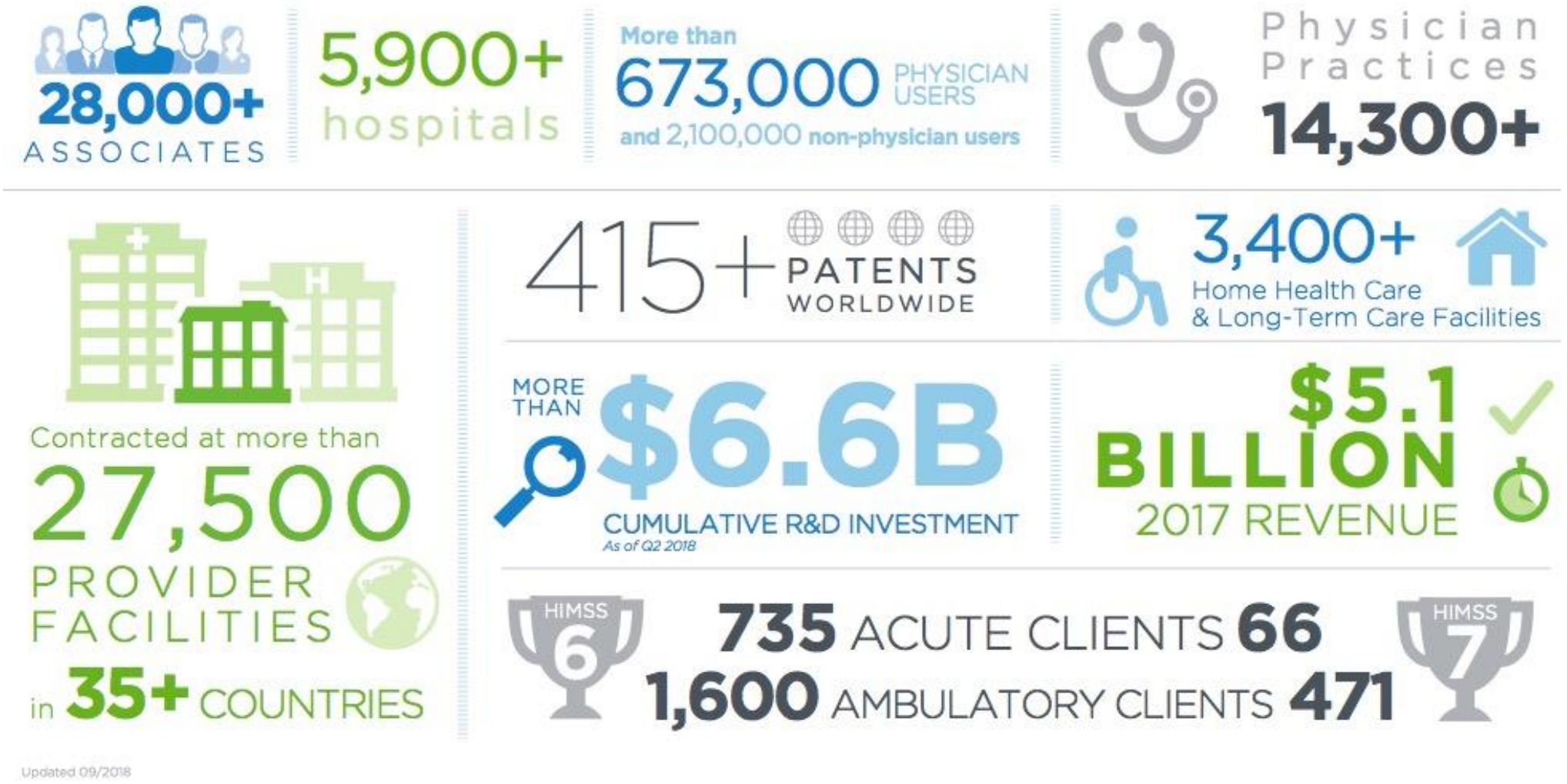
Health IT vendor perspective

Cerner overview



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Health IT vendor perspective

Solution portfolio

Services
- *ITWorks*[SM]
- *RevWorks*[SM]

Future state
- Cloud-enabled
- Continuous deployment
- Open
- Interoperable
- Collaborative

3 PLATFORMS • 1 ARCHITECTURE • 1 EXPERIENCE

Enable high performance organization • Lower total cost of ownership • Data liquidity

Provider | Employer | Consumer | Health plan | Government

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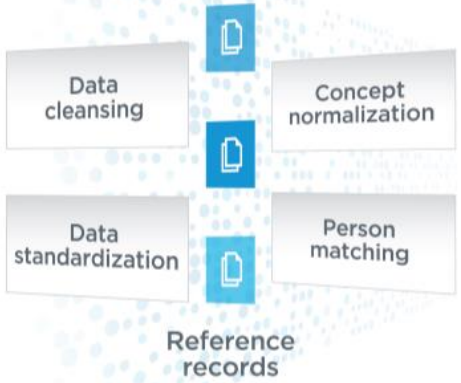
Health IT vendor perspective

HealtheIntent

Aggregate and normalize



Create and apply intelligence

Act and measure

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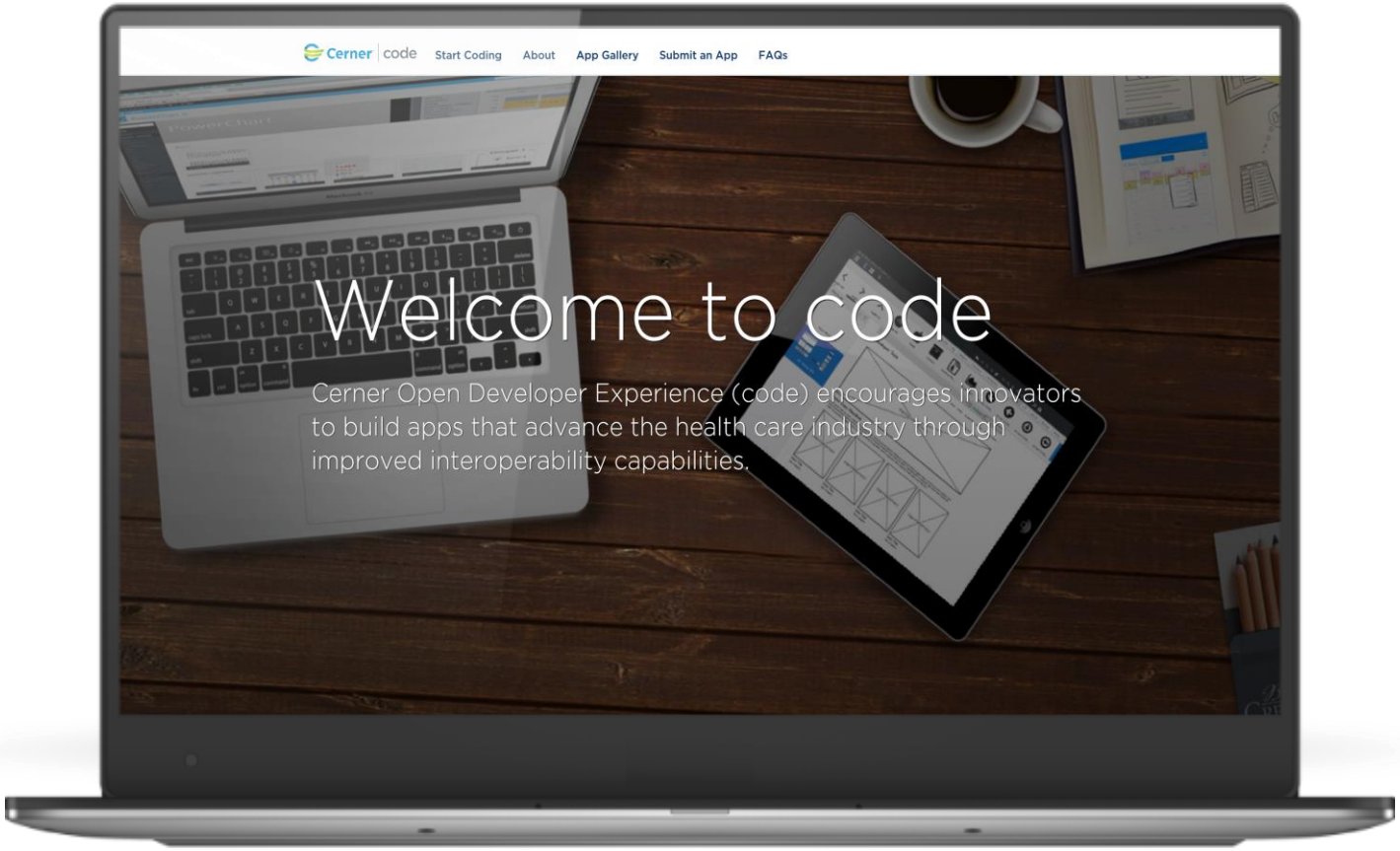
Health IT vendor perspective

Open Platforms

- Cerner Open Developer Experience (code)
  - https://code.cerner.com/
- Open APIs - Ignite
  - EHR
    - https://fhir.cerner.com/
  - Population Health
    - https://docs.healtheintent.com/



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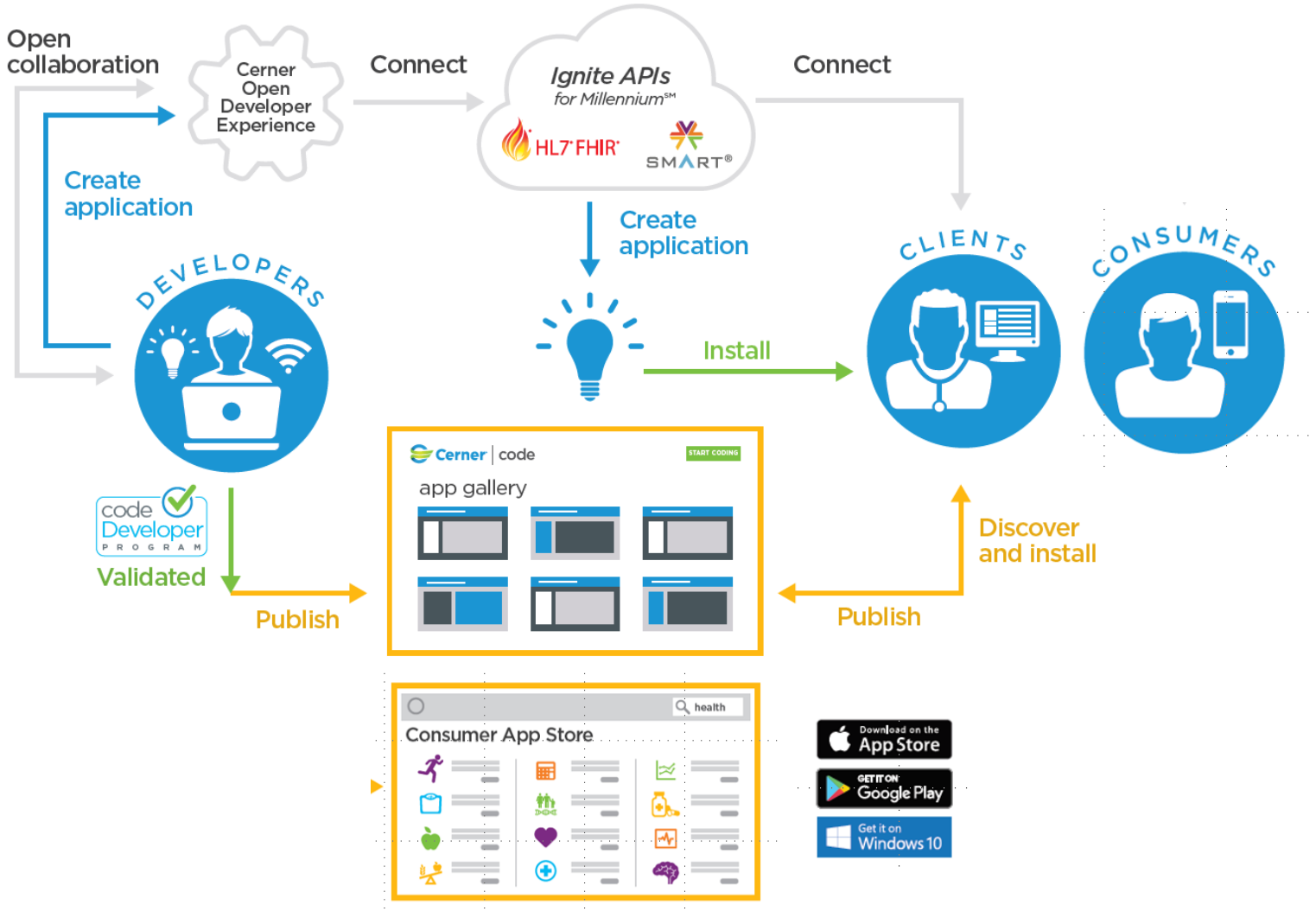
Health IT vendor perspective

Open Platforms



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Health IT vendor perspective

Discern Ontology

- Concept normalisation for population health and EHR FHIR API concept mapping
- Supports rules engine that drives registries
- https://docs.healtheintent.com/api/v1/ontology/

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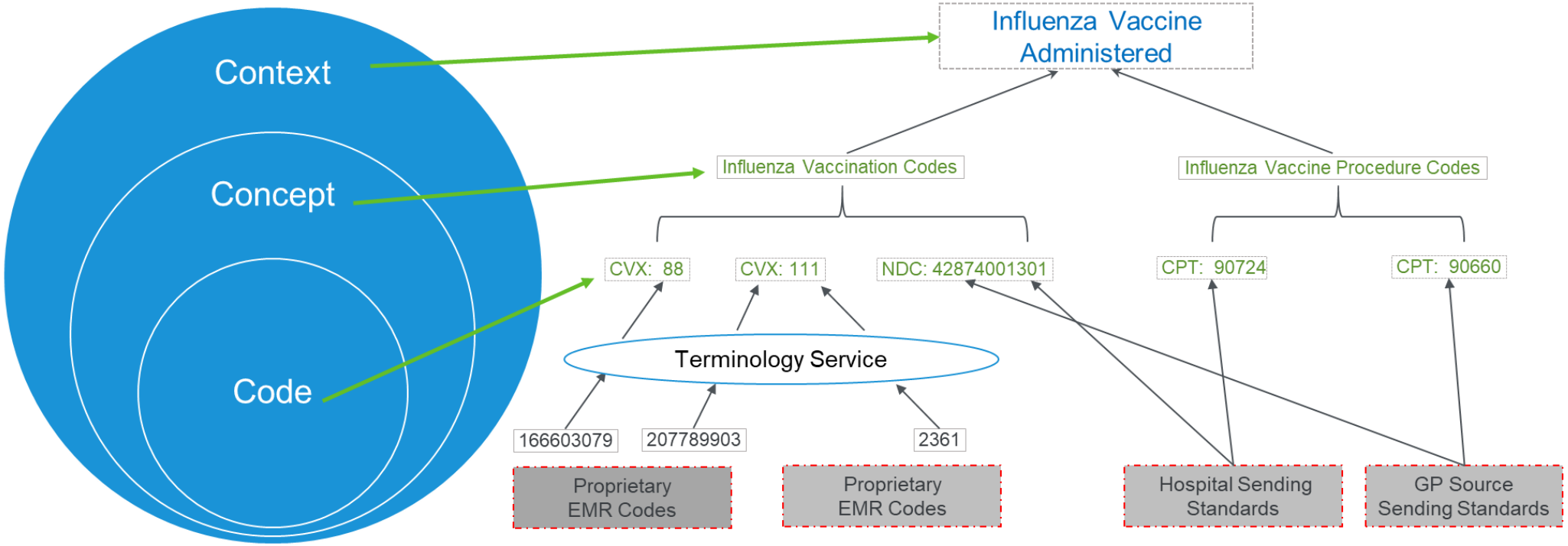
Health IT vendor perspective

Discern Ontology



Standardisation and Normalisation Example: Influenza Vaccine

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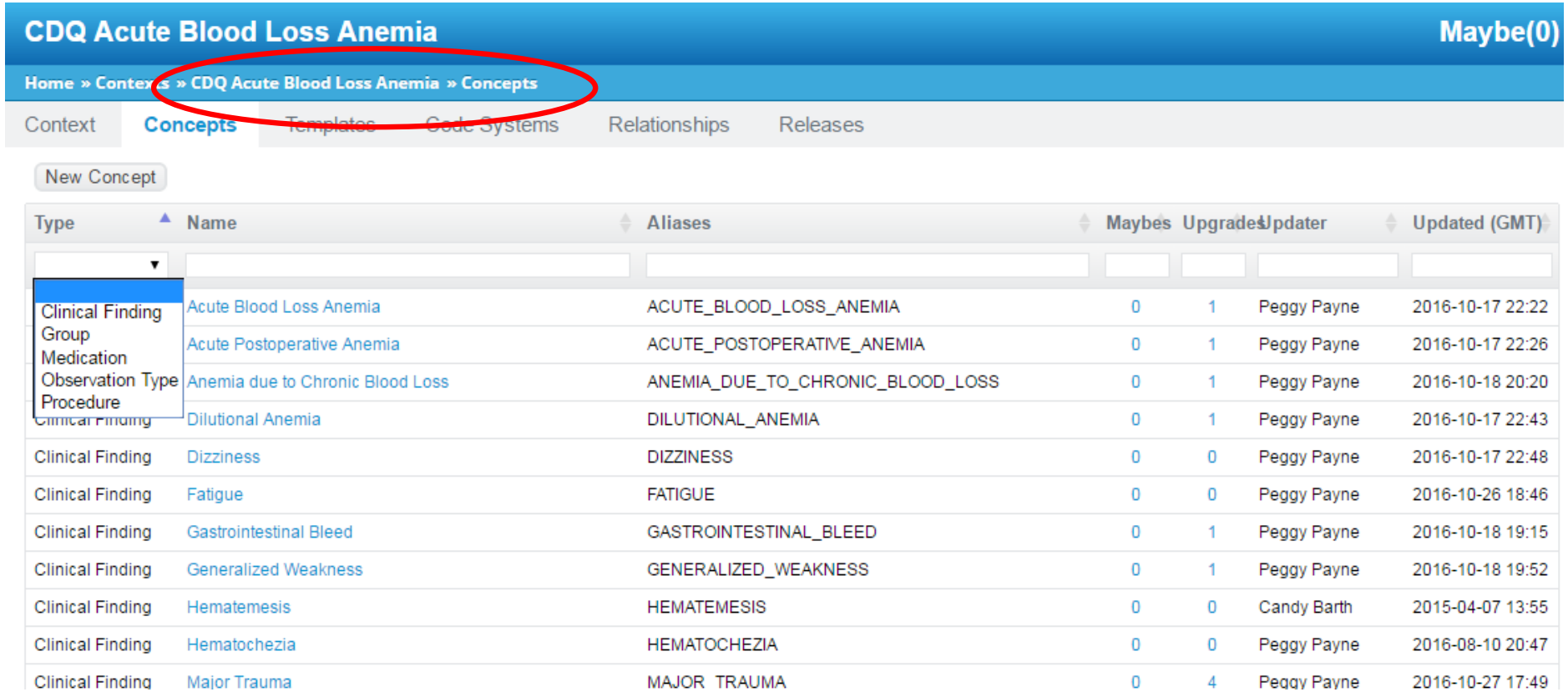
Health IT vendor perspective

Discern Ontology



Type	Name	Aliases	Maybes	Upgrades	Updater	Updated (GMT)
	Acute Blood Loss Anemia	ACUTE_BLOOD_LOSS_ANEMIA	0	1	Peggy Payne	2016-10-17 22:22
	Acute Postoperative Anemia	ACUTE_POSTOPERATIVE_ANEMIA	0	1	Peggy Payne	2016-10-17 22:26
	Anemia due to Chronic Blood Loss	ANEMIA_DUE_TO_CHRONIC_BLOOD_LOSS	0	1	Peggy Payne	2016-10-18 20:20
	Dilutional Anemia	DILUTIONAL_ANEMIA	0	1	Peggy Payne	2016-10-17 22:43
Clinical Finding	Dizziness	DIZZINESS	0	0	Peggy Payne	2016-10-17 22:48
Clinical Finding	Fatigue	FATIGUE	0	0	Peggy Payne	2016-10-26 18:46
Clinical Finding	Gastrointestinal Bleed	GASTROINTESTINAL_BLEED	0	1	Peggy Payne	2016-10-18 19:15
Clinical Finding	Generalized Weakness	GENERALIZED_WEAKNESS	0	1	Peggy Payne	2016-10-18 19:52
Clinical Finding	Hematemesis	HEMATEMESIS	0	0	Candy Barth	2015-04-07 13:55
Clinical Finding	Hematochezia	HEMATOCHEZIA	0	0	Peggy Payne	2016-08-10 20:47
Clinical Finding	Major Trauma	MAJOR_TRAUMA	0	4	Peggy Payne	2016-10-27 17:49

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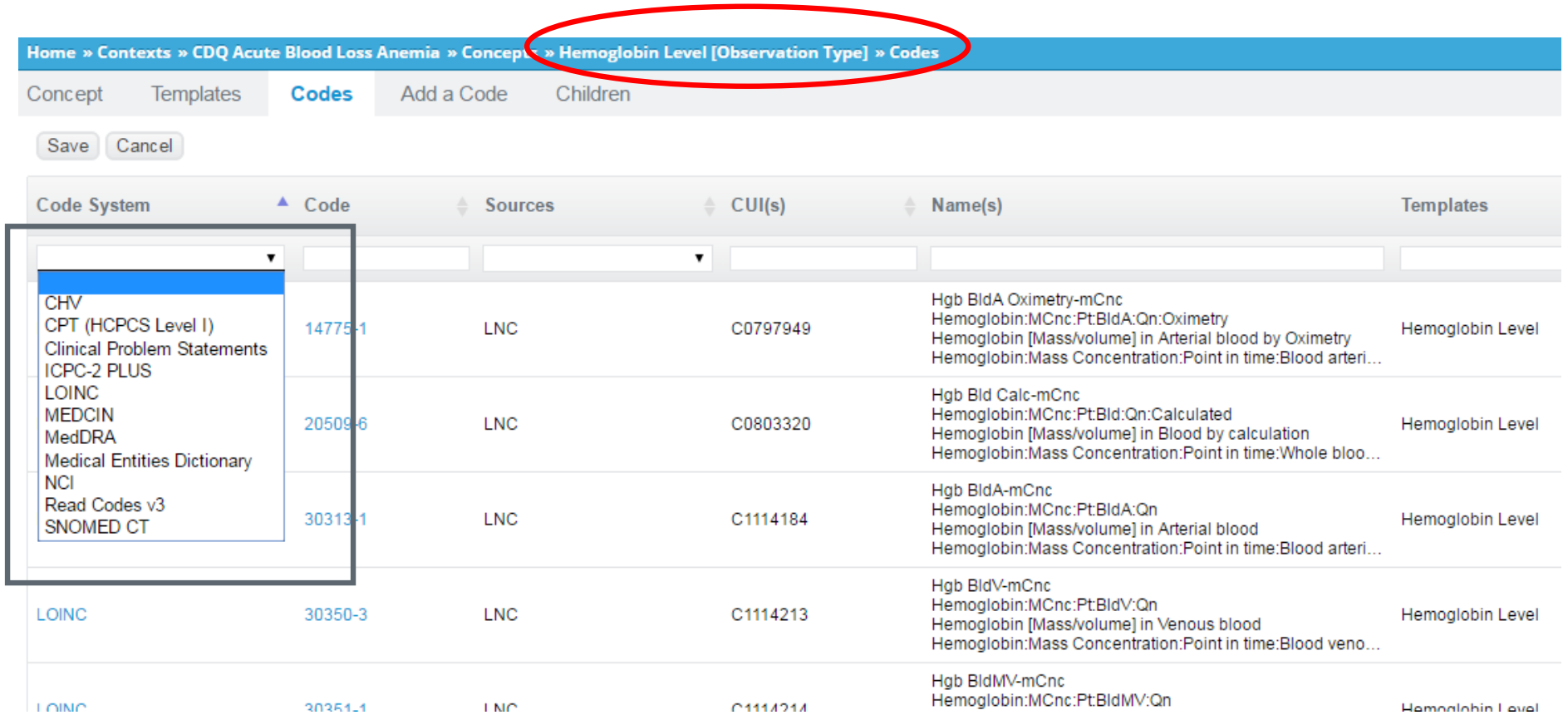
Health IT vendor perspective

Discern Ontology



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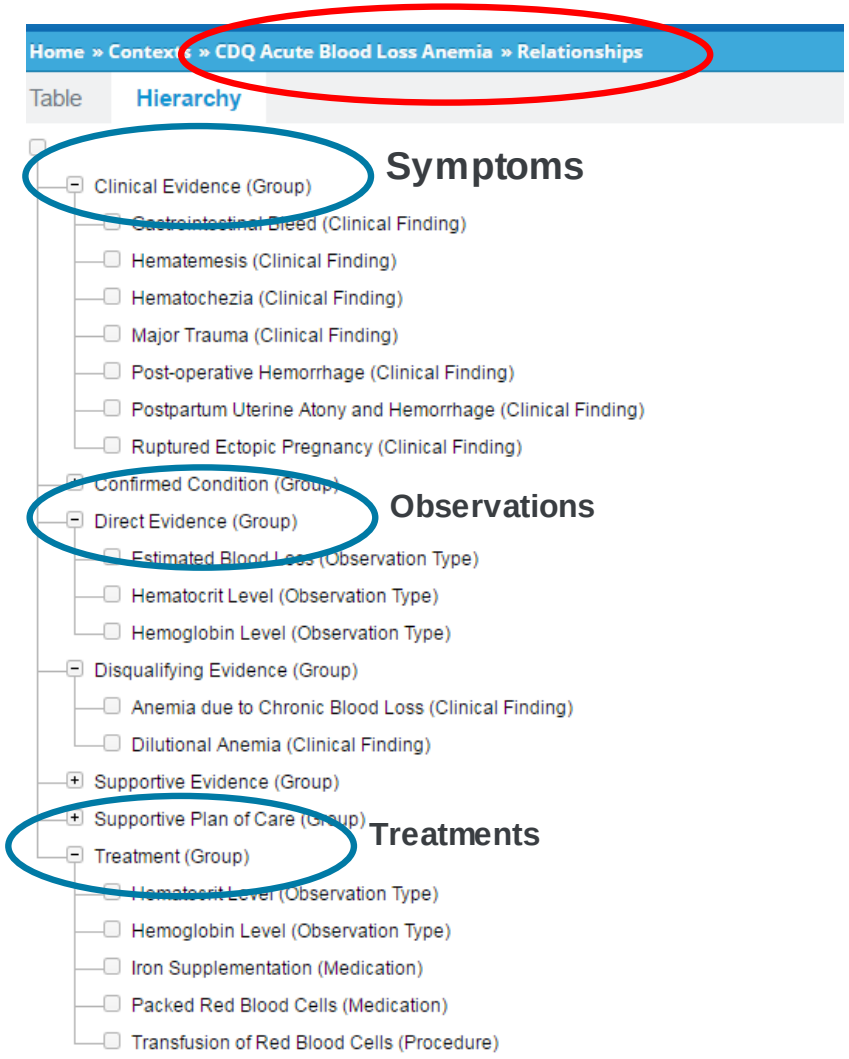
Health IT vendor perspective

Discern Ontology



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Health IT vendor perspective

Cerner Associates driving Genomics

- Kevin Power, Director of Genomics Solutions and Co-Chair on the HL7 Clinical Genomics Work Group
- Terah Collins, Senior Strategist for Precision Medicine and Genomics
- Marc Overhage, Chief Medical Informatics Officer & VP Intelligence Strategy

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Health IT vendor perspective

Genomic Precision Medicine related health IT system contexts

- Electronic Health Record (EHR)
- Consumer
- Laboratory Information Management Systems (LIMS)
- Population Health
- Research

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Health IT vendor perspective

Genomic Precision Medicine client priorities

- Pharmacogenomics
  - Oncology
  - Cardiovascular
  - Mental Health
  - Pain Management
- Oncology
  - Somatic sequencing
- Newborn screening
- Rare and undiagnosed disease

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Health IT vendor perspective

EHR

- Millennium
  - Model Experience -> Precision Medicine -> Pharmacogenomics
    - Decision Support Rules
      - High Risk Genotype
      - Drug-metabolizing enzymes
      - Transporters
  - Ignite API for Millennium
    - YouScript
      - https://code.cerner.com/en/apps/youscript
    - MyLegacy by Family Care Path
      - https://code.cerner.com/apps/mylegacy

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Health IT vendor perspective

Consumer

- Millennium
  - Ignite API for Millennium
    - Apple Health
      - https://code.cerner.com/apps/apple-health
    - MyLegacy by Family Care Path
      - https://code.cerner.com/apps/mylegacy
  - HealtheLife, Patient Portal
- CommonWell Members Enable Patient Access to Their Health Data
- All of Us Research Program to Test Options for Returning Results

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Health IT vendor perspective

LIMS

- LabSequence
  - Workflow engine – Polymerase Chain Reaction (PCR), Microarray, Multiplex Ligation-dependent Probe Amplification (MLPA), Next Generation Sequencing (NGS) etc
  - API available for customising and integrating with devices and software

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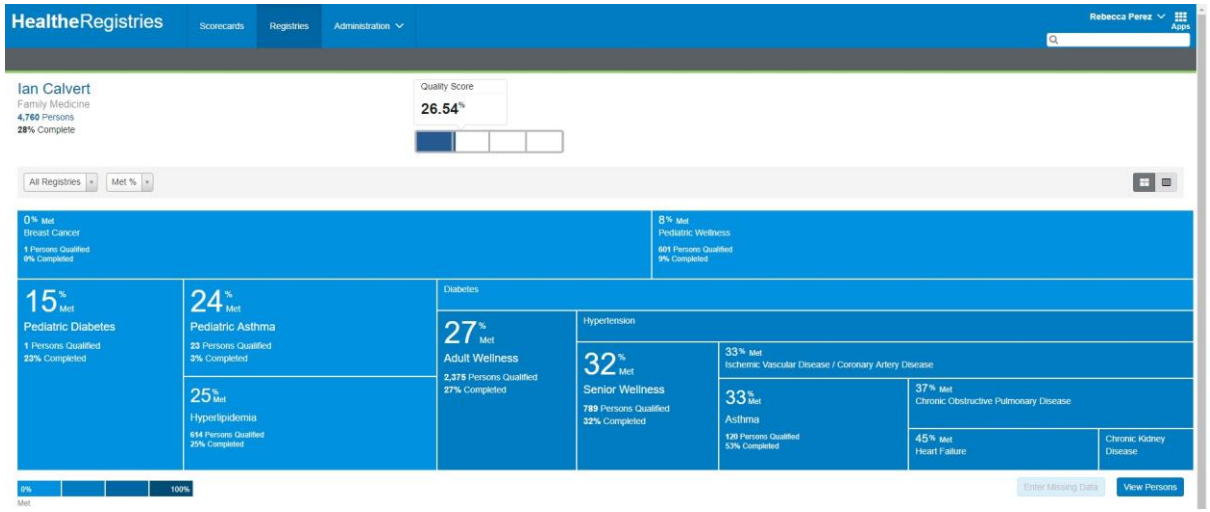
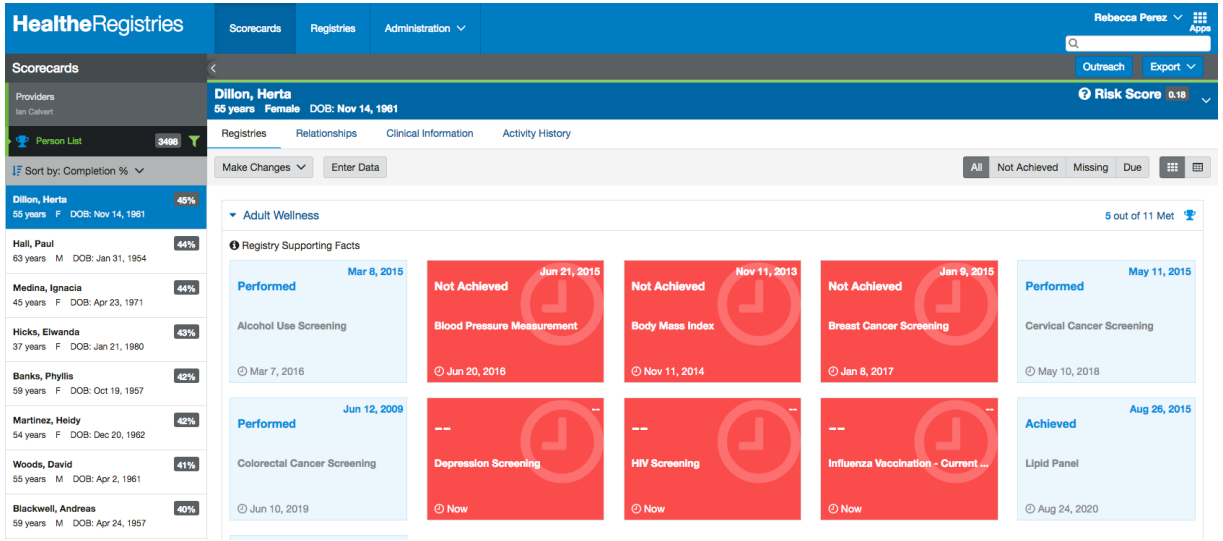
Health IT vendor perspective

Population Health

- HealtheIntent
  - HealtheRegistries
    - Using Cerner ‘Synapse’ Domain Specific Language and Rules Engine (using Drools and Clojure)





Inclusion

Inclusion Criteria Description	

	• Person's age is ≥ CRA as of the last day of the current measurement period.
	• **AND** at least one of the following:
	  • A problem of Diabetes Mellitus Type 1 (not in a resolved or inactive status) at any time prior to the end of the current measurement period.
	  • **OR** A problem of Diabetes Mellitus Type 2 (not in a resolved or inactive status) at any time prior to the end of the current measurement period.
	  • **OR** A problem of Diabetes Mellitus Other (not in a resolved or inactive status) at any time prior to the end of the current measurement period.
	  • **OR** Any 2 or more HbA1c level ≥ 6.5%, on different dates of service, during the current measurement period or prior measurement period.
	  • **OR** Any 2 or more Estimated Average Glucose level ≥ 140 mg/dl, on different dates of service, during the current measurement period or prior measurement period.
	  • **OR** Any 2 or more Estimated Average Glucose level ≥ 7.8 mmol/l, on different dates of service, during the current measurement period or prior measurement period.
	  • **OR** Any HbA1c level ≥ 9% during the current measurement period or prior measurement period.
	  • **OR** Any Estimated Average Glucose level ≥ 212 mg/dl, during the current measurement period or prior measurement period.
	  • **OR** Any Estimated Average Glucose level ≥ 11.8 mmol/l during the current measurement period or prior measurement period.
	  • **OR** An Insulin Medication with a start date during the current measurement period or prior two measurement periods,
	  • **AND** Insulin Medication start date is not during an ED Visit or Inpatient Visit or Ambulatory Surgery.
	  • **AND** Person has a diagnosis of Diabetes Type 1, 2, Other during the current or prior measurement period.
	  • **OR** Person has a problem of Diabetes Type 1, 2, Other (not in a resolved or inactive status) at anytime prior to the end of the current measurement period.
	  • **OR** A start date for any Diabetic Medication (EXCLUDING Insulin, Stand-alone Metformin and Stand-alone Incretin Mimetic Medications) within the 18 months prior to the end of the current measurement period.
	  • **AND** Person does NOT have a condition of Gestational Diabetes on the same date as the dispensing event of the Diabetic Medication.
	• **OR** Any of the following:
	  • A diagnosis of Diabetes Mellitus Type 1 during the current measurement period or prior measurement period.
	  • **AND** Fasting Plasma Glucose > 126 mg/dL during the current measurement period or the prior measurement period.
	  • **OR** A diagnosis of Diabetes Mellitus Type 2 during the current measurement period or prior measurement period.
	  • **AND** at least one of the following:

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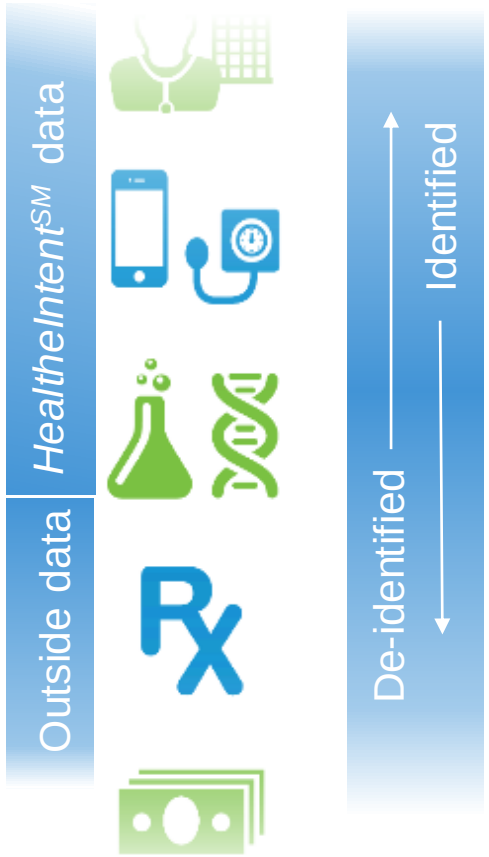
Health IT vendor perspective

Research

- HealtheIntent
  - HealtheDataLab



Anonymization or De-identification

Physical storage & processing

Role-based access control

User tools

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Health IT vendor perspective

Client initiatives

- The Alliance for Genomics (TAG)
  - Pete Celano, Director of Consumer Health Initiatives, MedStar Health, MedStar Institute of Innovation
    - https://www.cerner.com/blog/ep-100-future-of-precision-medicine

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Health IT vendor perspective

Client initiatives

- The Alliance for Genomics (TAG)
  - Presentations to date
    - Illumina
    - YouScript
    - Dignity Health and Catholic Health Initiatives, Precision Medicine Alliance LLC
    - Million Veteran Program
    - HudsonAlpha Institute for Biotechnology
    - American Heart Association, Institute for Precision Cardiovascular Medicine
    - Helix
    - Myriad
    - AWS
    - Cerner
      - Pharmacogenomics
      - HealtheDataLab

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Standards landscape

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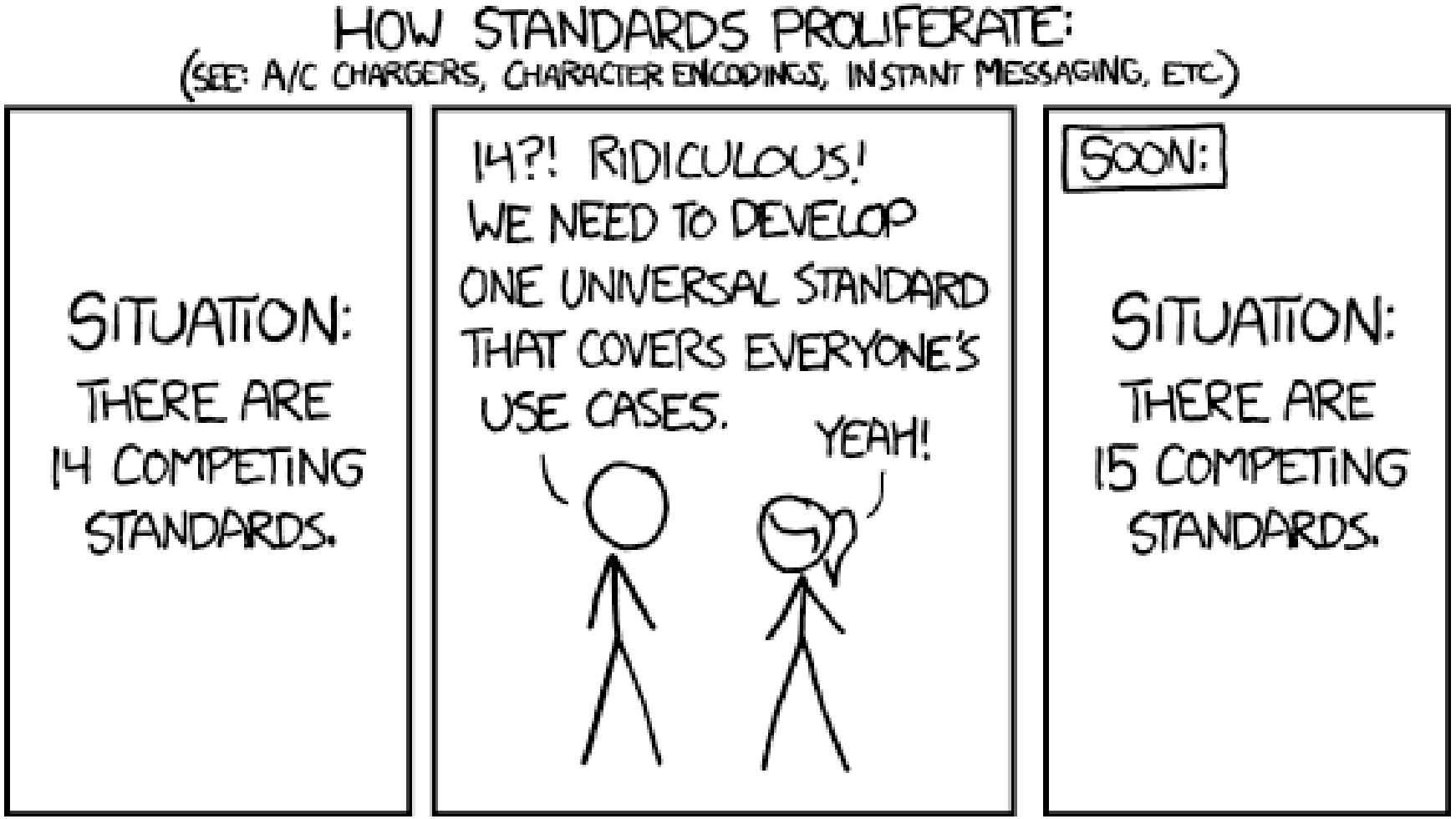
Standards landscape



xkcd

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Standards landscape

ISO/TC 215 Health Informatics Committee Proposal

- ISO/TC 215 N 2776 - Proposal for Subcommittee on "Genomics informatics“
  - Proposed liaison organisations and survey of similar work
    - Other ISO Committees
      - ISO/TC 276 Biotechnology
      - ISO/IEC JTC 1/SC29 Coding of audio, picture, multimedia and hypermedia information
    - Global Alliance for Genomics and Health (GA4GH) and driver projects
    - HL7 International Clinical Genomics Working Group
    - Clinical Data Interchange Standards Consortium (CDISC)
    - SNOMED International
    - Regenstrief Logical Observation Identifiers Names and Codes (LOINC)
    - National Cancer Institute Enterprise Vocabulary Services NCI Thesaurus (NCIt)
    - Massive Analysis and Quality Control (MAQC) Society

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Standards landscape

ISO/TC 215 Health Informatics Committee Proposal

- ISO/TC215 SC1 Genomic Informatics proposed initial active programme of work
  - ISO/IS 25720:2009 Health Informatics - Genomic sequence variation markup language (GSVML)
  - ISO/TS 20428:2017 Health Informatics - Data elements and their metadata for describing structured clinical genomic sequence information in electronic health records
  - ISO/CD 21393 Health Informatics - Omics Markup Language (OML) (in development)
  - ISO/NP TS 23357 Clinical genomics data sharing specification for next generation sequencing (in development)
  - ISO/AWI TR 21394 Health Informatics - Whole genome sequence markup language (WGML) (in development)
  - ISO/AWI TR 22693 Health Informatics - Structured clinical gene fusion report in electronic health records (in development)
  - ISO/PWI 22690 Health Informatics - Reliability assessment criteria for high-throughput gene-expression data (in development)
  - ISO/DTS 22692 Health Informatics - Quality control metrics for DNA sequencing (in development)

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Standards landscape

GA4GH Work Streams

- Key Technical Work Streams
  - Genomics Knowledge Standards
  - Clinical and Phenotypic Data Capture
- Other Work Streams
  - Foundational
    - Data Security
    - Regulatory & Ethics
  - Technical
    - Cloud
    - Data Use & Researcher Idenities (DURI)
    - Discovery
    - Large Scale Genomics

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Standards landscape

GA4GH Driver Projects

- Key projects
  - Monarch Initiative
    - Human Phenotype Ontology (HPO)
  - Clinical Genome Resource (ClinGen)
  - Variant Interpretation for Cancer Consortium (VICC)

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Standards landscape

GA4GH Driver Projects

- Other
  - All of Us Research Program
  - Australian Genomics
  - Autism Sharing Initiative
  - BRCA Challenge
  - Canadian Distributed Infrastructure for Genomics (CanDIG)
  - ELIXIR Beacon
  - European Genome-phenome Archive (EGA), European Variation Archive (EVA), and European Nucleotide Archive (ENA)
  - National Institute of Environmental Health Science (NIEH) EpiShare
  - European-Canadian Cancer Network (EUCANCan)
  - European Joint Programme on Rare Disease (EJP RD)
  - GEnome Medical alliance Japan (GEM Japan)

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Standards landscape

HL7 International Clinical Genomics Working Group

- Confluence Work Group Home
- Wiki
- Existing Products, v2, v3, CDA Implementation Guides Domain Analysis Models
- FHIR Implementation Guides
  - Genomics Implementation Guidance
  - Genetic Reporting Implementation Guide (Jan 2019 v0.3.0: STU 1 Ballot 2)
    - New MolecularSequence resource plus DiagnosticReport and Observation resource profiles
    - General Genomic Reporting, Variant Reporting, Cytogenic Reporting, Pharacogenomic Reporting, Histocompatability Reporting

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Standards landscape

CDISC

- Study Data Tabulation Model Implementation Guide (SDTMIG)-Pharmacogenomics/Genetics (PGx) v1.0

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Standards landscape

SNOMED International

- Genomics and Precision Medicine Clinical Reference Group
- Seminars
  - Genomics Symposium (Ontologies for Clinical Value) - London, 12th, April 2018
  - "Making it real" - Genomics session, Vancouver, 17th, October 2018
- Observable and Investigation Model Project Home
- SNOMED on FHIR

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Standards landscape

LOINC

- Standardised terms for genetic test ordering and reporting, and genetic findings (observations about the specimen's genetic characteristics)
- Links between LOINC and other genetic terminologies and coding systems
- https://loinc.org/genetics/ coming soon
- Deckard J, et al. J Am Med Inform Assoc 2015;22:621–627. Supporting interoperability of genetic data with LOINC

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Standards landscape

NCI

- National Cancer Institute Enterprise Vocabulary Services NCI Thesaurus (NCIt)
  - Provides reference terminology for many NCI and other systems. Covers vocabulary for clinical care, translational and basic research, and public information and administrative activities.
    - Features:
      - Stable, unique codes for biomedical concepts;
      - Preferred terms, synonyms, research codes, external source codes, and other information;
      - Over 100,000 textual definitions;
      - Links to NCI Metathesaurus and other information sources;
      - Over 400,000 cross-links between concepts, providing formal logic-based definition of many concepts;
      - Extensive content integrated from NCI and other partners, much available as separate NCIt subsets
      - Updated frequently by a team of subject matter experts.

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Standards landscape

Other related organisations and initiatives

- Online Mendelian Inheritance in Man (OMIM)
- Institut National de la Santé et de la Recherche Médicale (INSERM) Orphanet
- European Bioinformatics Initiative (EBI)
  - Other related EBI initiatives not referenced by ISO proposal, ChEMBL etc
- University of Maryland School of Medicine Institute for Genome Science Disease Ontology (DO)
- Alliance of Genome Resources Gene Ontology (GO)
- Basic Formal Ontology (BFO)
  - From which GO, HPO, DO, Information Artefact Ontology (IAO) among others are derived
- Open Biological and Biomedical Ontology (OBO) Foundry

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Standards landscape

Indirectly related organisations and initiatives

- HL7
  - FHIR
    - Other pertinent resources
      - Phenotype
        - Patient, Condition (Diagnosis, Problem), Observation, Allergy etc
      - FamilyHistory
      - Interventions
        - MedicationRequest and related, Procedure, CarePlan, ServiceRequest etc
    - Security
      - Authenticatiion and Authorisation, Consent, Provenance, AuditEvent

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Standards landscape

Indirectly related organisations and initiatives

- HL7 continued
  - Clinical Quality Language (CQL)
  - FHIRPath
  - Terminology Service
  - Bulk data
  - Regional Implementation Guides, Argonaut Data Query, CareConnect Core API, other
- GraphQL (Using GraphQL with FHIR)
- Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group
- MAGIC
- Observational Health Sciences Data Science and Informatics (OHDSI) OMOP Data Model

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Standards landscape

Indirectly related organisations and initiatives

- SMART Health IT
  - SMART on FHIR (in collaboration with HL7)
  - CDS Hooks (in collaboration with HL7)
  - Sync for Science (S4S)

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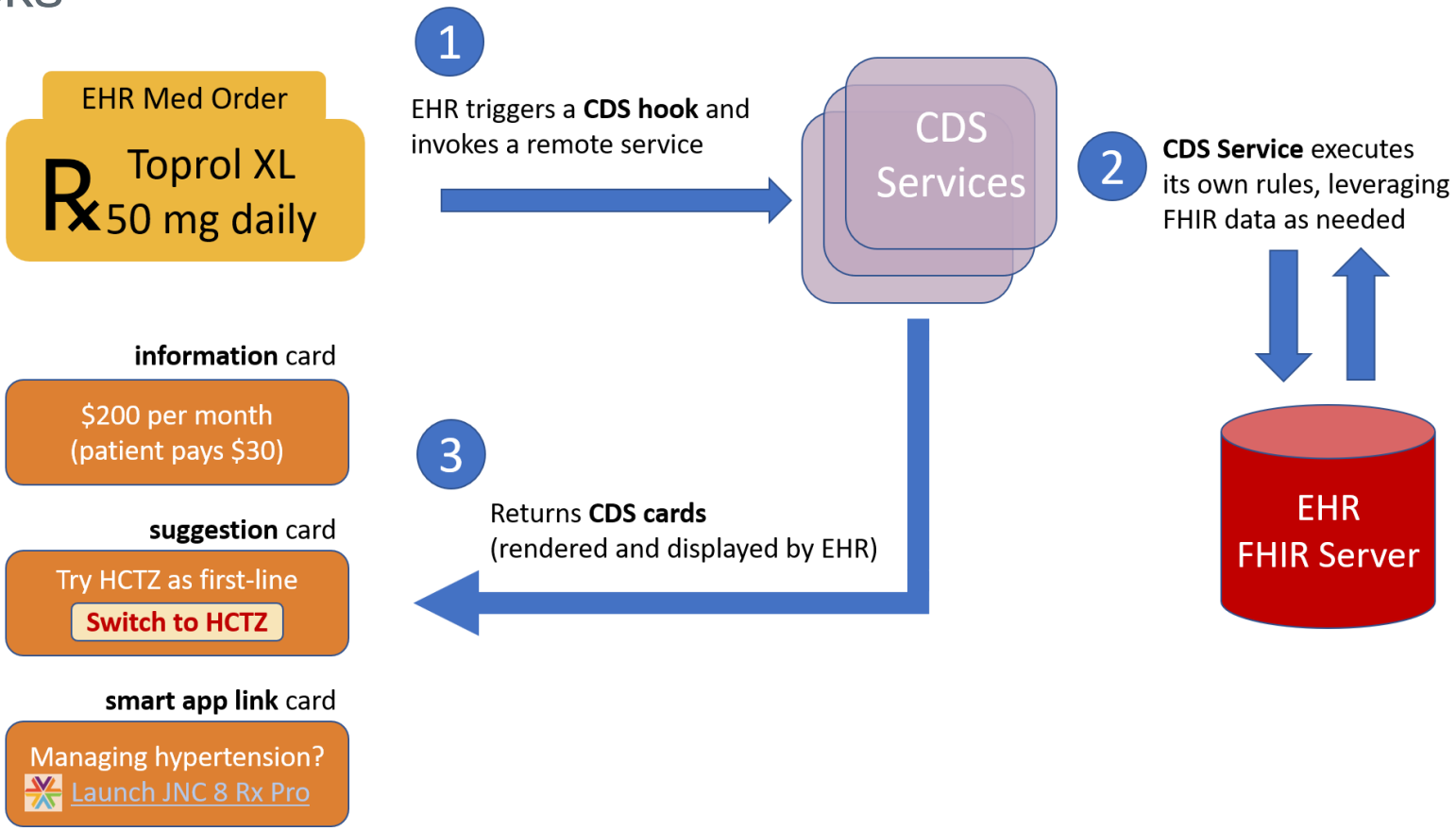
Standards landscape

Indirectly related organisations and initiatives

- CDS Hooks



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Standards landscape

Indirectly related organisations and initiatives

- ISO
  - ISO/IEC JTC 1/SC 32 Data management and interchange
    - ISO/IEC 11179-1:2015 Information technology -- Metadata registries (MDR)
      - ISO/IEC 11179-1:2015 Part 1: Framework
      - ISO/IEC 11179-2:2005 Part 2: Classification
      - ISO/IEC TR 11179-2 Inform Part 2: Classification (Under development)
      - ISO/IEC 11179-3:2013 Part 3: Registry metamodel and basic attributes
      - ISO/IEC 11179-3:2013/DAmd 1 (Under development)
      - ISO/IEC 11179-4:2004 Part 4: Formulation of data definitions
      - ISO/IEC 11179-5:2015 Part 5: Naming principles
      - ISO/IEC 11179-6:2015 Part 6: Registration
      - ISO/IEC DIS 11179-7 Part 7: Metamodel for data set registration (Under development)

      - Metadataworks
        - Genomics England
        - 'Model Driven Data Management in Healthcare' David Milward, Best Paper award at MODELSWARD 2019 International Conference on Model-Driven Engineering and Software Development
          - Metadata Management Language (MDML)

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Standards landscape

Indirectly related organisations and initiatives

- ISO
  - Identification of Medicinal Products (IDMP)
    - FHIR MedicationKnowledge resource
  - ISO 13606 Health informatics -- Electronic health record communication
    - openEHR

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Challenges and possible ways forward

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Challenges and possible ways forward

Challenges

- Knowledge representation and reasoning conundrum
- Authentication and authorisation
- Ethics

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Challenges and possible ways forward

Knowledge representation and reasoning conundrum

- Knowledge? Classifications/terminologies, ontologies, Domain Specific Languages (DSLs), information models…
- Relationship between classifications/terminologies and ontologies
- Relationship between different ontologies
- Relationship between information model representations of EHR, classifications/terminologies and ontologies
- Reasoning

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Challenges and possible ways forward

Relationship between classifications/terminologies and ontologies

- Examples
  - ICD10 -> ICD11 <-> SNOMED CT alignment
  - LOINC <-> SNOMED CT

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Challenges and possible ways forward

Relationship between different ontologies

- BFO as key component in alignment efforts
  - Alignment of SNOMED with BFO
    - Stakeholder Engagement for Consultant Terminologist Project IHTSDO-836, entitled “Concept Model: Presence” David Sperzel, MD, MS, August-September 2016
      - SNOMED CT and formal ontological principles p.17
    - SNOMED CT standard ontology based on the ontology for general medical science El-Sappagh et al. BMC Medical Informatics and Decision Making (2018) 18:76

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Challenges and possible ways forward

Relationship between information model representations of EHR, classifications/terminologies and ontologies

- ZOUD
- Standards based EHR information models
  - FHIR
  - ISO 13606 / openEHR
  - INTEROPen Digital Health Rewired Panel Paper: FHIR and openEHR
- Articulating relationships
  - BFO and IAO as possible component in alignment efforts
    - FHIR and Ontology - Barry Smith, Fourth Clinical and Translational Science Ontology Workshop 2015
    - https://wolandscat.net/tag/ontologies/ https://wolandscat.net/tag/ontology/
  - http://yosemiteproject.org/

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Challenges and possible ways forward

Reasoning

- Rector AL, Rogers J, Taweel A. Models and inference methods for clinical systems: a principled approach. Stud Health Technol Inform. 2004;107(Pt 1):79–83
- Workflow, CDS Hooks
- DSLs, CQL
  - Beyond the Curly Braces: Exploring CQL on FHIR based CBK, Mobilizing Computable Biomedical Knowledge (MCBK) Marc Overhage with Motive Medical Intelligence, July 2018
- Rules engines/reasoners

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Challenges and possible ways forward

Authentication and authorisation

- SMART on FHIR
- FHIR Security

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Challenges and possible ways forward

Ethics

- NIH National Human Genome Resource Institute
  - Ethical, Legal and Social Issues in Genomic Medicine
    - Genetic Discrimination
    - Intellectual Property and Genomics
    - Regulation of Genetic Tests
    - Privacy in Genomics
- Knowledge sharing and resource distribution

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Challenges and possible ways forward

Pragmatism

The pragmatic maxim

> *Consider the practical effects of the objects of your conception. Then, your conception of those effects is the whole of your conception of the object.*
>
> Charles Sanders Peirce

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Challenges and possible ways forward

Continued collaboration…

- aligning classifications/terminologies with ontologies
- aligning different ontologies, with SNOMED, BFO and derivatives being a key components of alignment efforts
- aligning EHR information model representations of, classifications/terminologies and ontologies, with FHIR, SNOMED, BFO and derivatives being key components in alignment efforts
- progressing approaches to reasoning and clinical decision support with CDS Hooks and CQL being key components
- progressing approaches to Authentication and Authorisation with SMART on FHIR and FHIR Security being key components
- progressing ethics
- engaging industry and being pragmatic!

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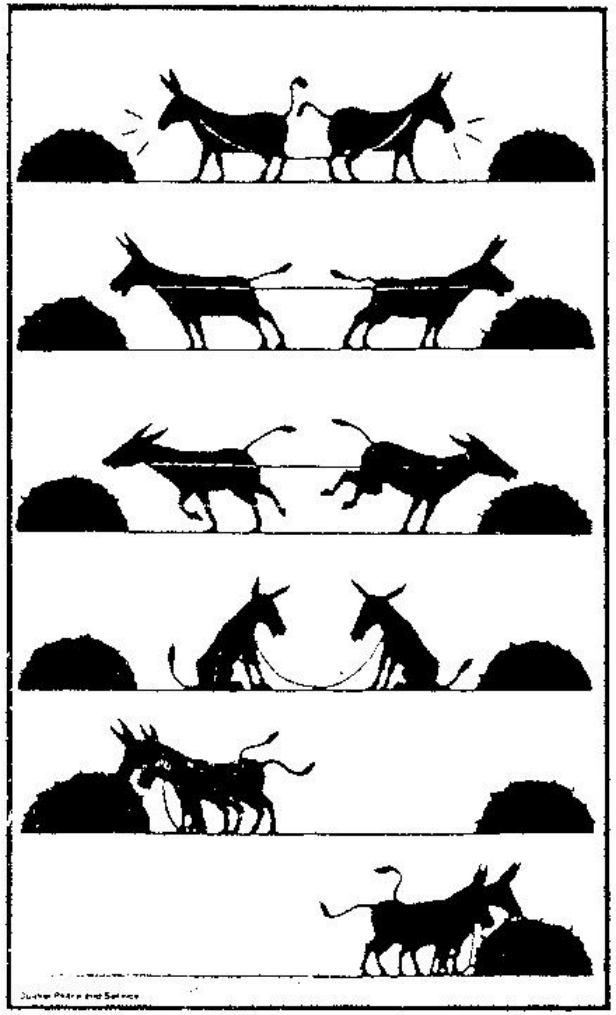
Challenges and possible ways forward

Cooperation is better than conflict!



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Thank you.

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