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Integrated Precision Medicine: The Role of Electronic Health Records in Delivering Personalized Treatment

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Abstract

Precision Medicine involves the delivery of a targeted, personalized treatment for a given patient. By harnessing the power of electronic health records (EHR), we are increasingly able to practice precision medicine to improve patient outcomes. In this article, we introduce the scientific community at large to important building blocks for personalized treatment, such as terminology standards that are the foundation of the EHR and allow for exchange of health information across systems. We briefly review different types of clinical decision support (CDS) and present the current state of CDS, which is already improving the care patients receive with genetic profile-based tailored recommendations regarding diagnostic and treatment plans. We also report on

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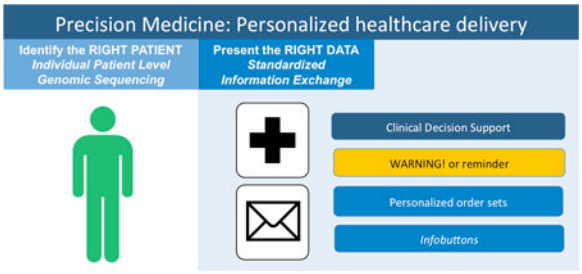
limitations of current systems, which are slowly beginning to integrate new genomic data into patient records but still present many challenges. Finally, we discuss future directions and how the EHR can evolve to increase the capacity of the healthcare system in delivering Precision Medicine at the point of care.

Graphical Abstract



Building blocks of personalized healthcare delivery

PRECISION MEDICINE, ELECTRONIC HEALTH RECORDS, AND CLINICAL DECISION SUPPORT

In an era where the complexity of medicine grows exponentially, we face an acute need to develop systems that will integrate disparate data sources, provide real-time decision support, and enhance our ability to positively impact patient outcomes. The full spectrum of Precision Medicine spans the discovery of a patient-specific pattern of disease progression, determination of the precise therapy for that pattern, and the corresponding personalized delivery of care. EHRs are instrumental across this spectrum, but in this article we will focus on personalized healthcare delivery based on the rapidly evolving knowledge base brought about by advances in genomic medicine. Integration of implementation science with basic and translational sciences is essential to fully realize the potential of therapeutic discoveries. The landscape of the electronic health record has substantially evolved over the course of the past decade from basic adoption to sophisticated decision support. The evolution of complex terminologies that serve to electronically communicate shared data is a critical component. We explain here key terms and contextual applications of EHRs (Appendix 1). The following two example cases highlight current opportunities and challenges in personalized treatment given the current state of EHR systems.

Personalized treatment: example use cases

Case 1: N.M. is a 72 years old man with a history of atrial fibrillation and prior stroke who had been taking anticoagulant medication (warfarin) for 1 year. He presented with 7 days of runny nose, fever, and a new onset of pain in the left ear. On exam, he was noted to have otitis media, and his doctor was planning to start him on penicillin. He was aware of an increased risk of minor bleeding due to this drug combination (warfarin and penicillin), but felt that the risks were small. Three days later, the patient presented with sudden onset headache, weakness of the right arm, and difficulty with speech and vision. He was transported via ambulance to the

hospital due to concern for stroke. On CT imaging of the brain, he was noted to have an acute stroke due to a subarachnoid hemorrhage, and underwent emergent neurosurgery. On further lab work, his INR was noted to be 8.4, significantly increased from a value of 2.1 three days before (the target INR range on warfarin is between 2 and 3). A potential explanation was that the interaction between warfarin and penicillin contributed to this increase in INR. As the patient was recovering in the ICU, his family brought in reports of a commercial genotyping assay that the patient had performed recently as part of a research study in another facility. That testing revealed the patient carried a specific CYP2C9 variant, which significantly increases the risk of life-threatening bleeding in patients taking warfarin and penicillin together.

This bad outcome could have been averted if the genetic testing result had been available via health information exchange between the two organizations, and a point-of-care clinical decision support (CDS) system was in place to alert the prescribing physician of this potentially significant drug-drug interaction.[1]

Case 2: C.P. is a 68 years old female diagnosed with breast cancer that was discovered by screening mammography. As with many breast cancer patients, C.P. has been asked to make a variety of treatment decisions. After much deliberation, she settled on lumpectomy and radiation. Her surgery went smoothly, as did radiation. She was found to have a 1 cm low-grade tumor and a negative lymph node biopsy. Her tumor was positive for estrogen and progesterone receptors. The next step along her treatment pathway would be chemotherapy. Like many patients her age, C.P. was hesitant about undergoing chemotherapy.[2] Chemotherapy is one of the riskiest components of the breast cancer treatment, exposing patients to an increased risk of serious infections, cardiopulmonary complications and poorly tolerated side effects including nausea and hair loss.[3] It has been shown to decrease risk of metastasis in many trials.[4] Small tumors (<.5 cm) in patients with negative lymph nodes do not require chemotherapy but, given the size of C.P.'s tumor, there was no clear recommendation.[5] Without a precision medicine approach, clinicians would attempt to integrate information about C.P.'s health status, personal preferences and data from large studies to decide about chemotherapy. Instead, C.P.'s oncologist employed a 21-gene recurrence score (RS) assay to predict the likelihood of distant metastasis and assess the benefit she would get from chemotherapy.[6] C.P.'s score indicated high risk of recurrence and chemotherapy was recommended.

The RS has been shown to alter treatment recommendations for breast cancer patients, such as in this case.[7] Its incorporation into the EHR is a clear example of CDS.

BUILDING BLOCKS: STANDARDIZING AND EXCHANGING DATA TO DRIVE CLINICAL DECISION SUPPORT

Adoption of EHR and order entry systems has continued to increase, spurred by federal incentives and mandates.[8] These electronic systems facilitate increasingly effective CDS, defined by (healthit.gov) as systems or processes that "[provide] clinicians, staff, patients or other individuals with knowledge and person-specific information, intelligently filtered or presented at appropriate times, to enhance health and health care."[9]

A number of accurate data sources are required to drive appropriate opportunities for CDS. As illustrated in the two cases above, a substantial amount of data needs to be present at the time of care delivery in order to optimize opportunities for improved outcomes and treatment. The respective data sources include different types, such as diagnoses, ordered medications, completed procedures, and completed lab tests. Appendix 1 provides a glossary of key terms related to the use and sharing of clinical data as contextualized by the preceding cases.

Data Models and Terminology Standards

Each type of data has an associated terminology that enables the vocabulary to be operationalized within the context of the EHR. These terminology systems have unique data formatting, coding, domain coverages, and hierarchical relationships between a specific instantiation, such as *amoxicillin capsule 250 mg*, and a concept, such as *penicillin*. Terminology standards have the ability to influence design and utilization of the respective data. For example, a medication such as *warfarin* (Case 1) in the National Drug Code (NDC) file will include not only the medication itself, but also the type and strength of the product (e.g., 5 mg tablet) and the quantity included in the product (e.g., 100 tablets).[10, 11]

In order to facilitate common data formatting and structure that enables effective communication between healthcare organizations, the use of standardized medical terminologies is critical. Current opportunities and challenges with the use and exchange of health data are listed in Table 1. Often, new data types have complexity that is not adequately represented or matured in the standard vocabulary of its domain. In addition, non-automated processes such as specimen interpretation by a pathologist or image interpretation by a radiologist are dictated and archived as free text in an unstructured, non-standardized format. Relevant data need to be identified and parsed from the unstructured narrative texts using natural language processing (NLP) techniques so that they can be used by a CDS tool.

Causality and association are often inferred from context. Some EHR systems do not accurately code the time of many events. Additionally, many variables lack intensity qualifiers. For instance, most symptoms are coded as present or absent and are not scaled (*pain* is an exception).

Precision Medicine is developing a new vocabulary related to genetic conditions, which has yet to be standardized in the EHR. Genetic test results should follow relevant data standards, such as LOINC, HL7 Genomics, HGVS, etc., that contain information about test findings and potential risk; yet, this a challenge since these standards are not adopted by all laboratories. The rapid evolution of tests makes this challenging for the field of genetics, posing challenges for discrete data retrieval of this information in the EHR. Precision medicine also relies on other types of data that were not traditionally recorded in EHRs. Patient reported outcomes (PROs) are still early in standardization and the reporting is highly variant according to race, ethnicity, and literacy. PROs are vital to enhance our understanding of the value of healthcare to its primary “customers”. Patient preferences, for example, are not universally standardized today but this is necessary because they are intimately connected with the definition of “value”.

The process of translating clinical information across terminologies is called “data harmonization”. Mapping between terminology systems makes this possible, but increases complexity and the risk of introducing errors. Yet, this mapping across standard terminologies is essential for clinical decision support, quality measurement, research, and information exchange across healthcare systems.

Health Information exchange

The Health Information Technology for Economics and Clinical Health (HITECH) Act of 2009 was proposed to promote interoperable health information.[12, 13] *Meaningful Use* of EHR is an incentive program put forth by the Medicare and Medicaid programs in response to HITECH to promote effective use of EHR systems.[14, 15] The receipt of the incentive payment requires hospitals and providers to prove their “meaningful use” of EHR by satisfying a set of requirements such as recording patient information in a structured format, ordering medications using a computerized order entry system, and sharing test results with patients using personal health records tethered to the EHR system. Health information exchange (HIE) initiatives aim at realizing timely and appropriate level of access to the patient level of health information stored in the EHR by healthcare providers through a secure means to exchanging health data among healthcare organizations.[16] Having complete information about disease progression and treatment data at the point of care helps healthcare providers make better treatment decisions and achieve better patient outcomes. Utilizing information collected from different healthcare systems is an important step towards this goal. The Nationwide Health Information Network (NwHIN) specifies data and messaging standards, services, and policies required realizing secure exchange of health information on Internet.[17]

HIE covers three types of data exchange: (1) *Directed exchange* that occurs between healthcare providers to complete the planned healthcare services such as sending and receiving laboratory test orders and results, exchanging patient referral documents, etc. (2) *Query-based exchange* that occurs when a healthcare provider delivers unplanned services and requires accessing necessary health information about the patient. For example, when an emergency room physician needs to access patient’s disease history, current medications, allergies, etc. (3) *Consumer-mediated exchange* that lets patients control their health information. In this model, patients grant access to their health information to healthcare providers.[18]

However, establishing a sustainable HIE is not a trivial task; there are a number of technical and non-technical barriers that need to be addressed first. For example, lack of business incentives, specifically concerns on losing patients to other hospitals by making their health data available anywhere, has long been recognized as a factor that makes some healthcare systems hesitant to embrace HIEs.[8, 19] Patients and providers sometimes opt out from HIEs due to privacy concerns.[20] Other recognized challenges are poor data standardization,[19] inefficient processes of sorting through overloaded unselective information of a patient,[21] and difficulties in understanding the shared data in the absence of context when detailed clinical notes are withheld due to privacy concerns.[22]

DELIVERING PERSONALIZED CARE WITH CDS SYSTEMS

CDS systems help providers and patients answer certain types of questions in the course of care, such as what the most likely diagnosis is, what tests are most appropriate to arrive at the diagnosis, and what treatment would be best. In addition, CDS can help optimize the effectiveness and efficiency of care delivery, and can highlight when patients' conditions do not follow expected trajectories. (Appendix 2)

Effective CDS can be constructed in various ways. Some tools, such as *Infobuttons*, provide individuals ready access to relevant clinical guidelines when actively sought out or "pulled."[23] Other systems, including alerts, reminders, and event detectors, will proactively "push" information to individuals with varying levels of interruption and urgency. Certain CDS tools can straddle the "push" or "pull" approaches depending on how well they can be integrated into the EHR. For example, risk calculators or differential diagnosis generators can be automatically engaged if all the required data elements are available; otherwise, they can be made available for individuals to enter the data manually. Another class of CDS systems is designed to provide clinicians guidance on the appropriate evidence-based care for certain disease states, and to reduce variation in delivery of that care. These systems include order sets, care pathways, and documentation templates. Finally, data summarization and visualization tools address the growing issue of "information overload" facing patients and clinicians and provide CDS by displaying a filtered version of clinical data in a manner better aligned with human cognition and decision-making.

Early leaders in CDS have provided valuable lessons and best practices to maximize the impact of these systems.[24, 25] One framework developed by Osheroff and colleagues is known as the "five rights"—that effective CDS requires that the right information be provided to the right person in the right format and communication channel at the right time in the workflow.[24] This framework highlights many of the challenges faced when designing CDS systems for use in clinical settings. Often, such systems have failed to demonstrate tangible improvements when the five rights are not appropriately addressed; even if they are, the rigidity of the support tools or the phenomenon of alert fatigue may limit the effectiveness of CDS.[26] Another significant challenge is the ongoing maintenance of the knowledge base underlying CDS systems, as new clinical research informing these tools is being constantly generated.

There are some published examples of CDS solutions which overcome these challenges. Two of the most successful and widely used applications of computerized clinical decision support have been evidence-based order sets and alerts (for minimizing medication alerts, especially of drug-drug interactions and drug dose adjustment). For example, Ballard and colleagues observed that implementation of a standardized heart failure order set resulted in reduced inpatient mortality (odds ratio [OR], 0.49; 95% confidence intervals [CI], 0.28–0.88), and improved compliance with core measures (OR, 1.51; 95% CI, 1.08–2.12).[27] Similarly, with the use of a smart order set on evidence-based, risk-appropriate venous thromboembolism prophylaxis, Zeidan and colleagues observed a significant decline in 90-d risk of venous thromboembolism after hospital discharge (pre- vs. post: 2.5% vs. 0.7%, $p=0.002$) and complete elimination of preventable harm (1.1% vs. 0%, $p<0.001$), paralleling

an increase in prescription of risk-appropriate venous thromboembolism prophylaxis (65.6% vs. 90.1%, p<0.001).[28] To evaluate the impact of clinical decision support on medication prescription patterns in patients with kidney disease (who often require dose adjustment or drug discontinuation of certain medications based on dynamic renal function), Awdishu and colleagues designed a cluster-randomized trial comparing clinical decision support through real-time alerts generated based on dynamic and integrated monitoring of renal function vs. usual workflow in patients with kidney disease. Over a course of 1 year, 4068 alerts were generated recommending either dose adjustment (n=827) or drug discontinuation (n=3241). The investigators observed that physicians randomized to CDS were significantly more likely to make drug adjustments, as compared to physicians in usual workflow (17.0% vs. 5.7%, p<0.001).[29]

In our examples, Case 1 showed that the CYP2C9 variant could explain why the co-administration of both penicillin and warfarin resulted in the higher than intended level of anticoagulation and the subsequent development of a hemorrhagic stroke. It illustrates several requirements for effective CDS. First, the CYP2C9 test occurred at an outside hospital – mechanisms for health information exchange between the hospitals would have been needed to bring the test information to the clinician at the point of care. Second, the provider had to agree that this variant implied an increased risk for a dangerous interaction between these two medications. An alert would have needed to be in place to notify the clinician at the time penicillin was ordered, and to outline the risks of giving penicillin and warfarin together for this patient. Such a CDS tool could have guided the clinician toward better treatment by suggesting an alternative medication.

Case 2 highlights the potential ways by which CDS systems can improve the quality, safety and efficiency of the care delivered by our health care system. A risk assessment tool, such as OncotypeDx,[30] indicated the risk of cancer recurrence and clarified the risk-benefit tradeoff of undergoing chemotherapy. To get to that point, her clinician needed to be aware of the appropriateness of this test for her particular scenario as well as be able to accurately interpret the test results. Different CDS systems (Table 2) might make this process more reliable, including: 1) order sets or care pathways that guide clinicians caring for similar patients down a step-wise decision-making process that includes this specific tumor genome panel; 2) alerts or reminders for the clinician to order the tumor genome panel, if appropriate; and 3) *Infobuttons* that provide the patient and clinician access to current guidelines and test interpretation.

Simple CDS as described in the example cases is currently available. However, as the use of genetic tests based on whole genome sequences becomes more common, the evidence base will have to evolve to support their use in guiding clinical decisions. Since practicing clinicians will likely find it difficult to keep their knowledge up to date in this area, it is critical that interpretation and recommendations be done by more sophisticated CDS that operates “behind the scenes”. CDS systems will play a large role in Precision Medicine by incorporating the evidence base into clinical practice. However, maintaining the underlying knowledge base driving such systems will require significant effort.

THE ROAD AHEAD

Realizing the goals envisioned that electronic health records will enable us to provide better, safer, and more effective care is an active pursuit for our healthcare systems. Through data integration and real-time decision support, we have the capacity to alter patient outcomes and drive value-driven care. Precision Medicine impresses the need to rapidly adopt an evolving knowledge base brought about by advances in genomic medicine and making it actionable by putting it at the hands of clinicians who can intervene. To get there, we need vision, a culture of sharing, commitment to standardized terminologies, and iterative learning. Our knowledge on the associations among gene, disease, and the effectiveness of various therapeutic approaches is still quite limited.[44–48] Making new discoveries at the molecular or cell level is still much needed thus often the emphasis of articles describing Precision Medicine but it is actually one component in a vast spectrum of activities that are necessary to make it happen in practice. At the end of this spectrum lies implementation through guidance of actions by patients, caregivers, and healthcare providers. We focused this article at this less prominently but equally important component of Precision Medicine to help the scientific community at large understand why it is critical to "close the loop" (Figure 1).

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Appendix 1

Glossary of Key Terms including Reference and Case Context

Abbreviation	Full name	Reference	Case Context
CDM[49–52]	Common Data Model	http://mini-sentinel.org/data_activities/distributed_db_and_data/default.aspx	Standardized data storage Many Common Data Models exist for various use cases
OMOP[53]	Observational Medical Outcomes Partnership	http://www.ohdsi.org/data-standardization/the-common-data-model/	Standardized formatting of data
LOINC	Logical Observation Identifiers Names and Codes	http://loinc.org	Lab formatting and code for the INR test
NDC	National Drug Code	http://www.fda.gov/Drugs/InformationOnDrugs/ucm142438.htm	Code to support identification of Warfarin or chemotherapy medication

Abbreviation	Full name	Reference	Case Context
RxNorm	Normalized names for clinical drug (Rx)	https://www.nlm.nih.gov/research/umls/rxnorm/	Normalized names to support warfarin in system
ICD	International Classification of Diseases	http://www.who.int/classifications/icd/en/	Classification of specific disease such as intermittent atrial fibrillation
SNOMED-CT	Systematized Nomenclature of Medicine – Clinical Terms	http://www.ihtsdo.org/snomed-ct	Groupings of clinical terms that enable aggregation of concepts such as breast cancer
RadLex	Radiology Lexicon	http://www.radlex.org	Terms for identification of CT imaging or mammography
DICOM	Digital Imaging and Communication in Medicine	http://dicom.nema.org	Standard format for digital imaging transmittal
HGVS	Human Genome Variation Society code	http://www.hgvs.org	Standardized name and syntax for describing genetic variations
NACCR	The North American Association of Central Cancer Registries	http://www.naaccr.org	Centralized repository of cancer registries
CPT	Current Procedural Terminology	http://www.ama-assn.org/ama/pub/physician-resources/solutions-managing-your-practice/coding-billing-insurance/cpt/about-cpt.page?	Standardized terms that describe procedure such as lumpectomy, R breast with axillary dissection
IMO	Intelligent Medical Objects	https://www.e-imo.com	Intelligent Medical Objects is a privately held company specializing in developing, managing and licensing medical vocabularies and terminology maps

Abbreviation	Full name	Reference	Case Context
PROMIS	Patient – Reported Outcomes Measurement Information System	http://www.healthmeasures.net/explore-measurement-systems/promis	Validated sets of measures designed assess physical, emotional, social aspects of health
Exchange of Health Information			
HIE[54]	Health Information Exchange	https://www.healthit.gov/providers-professionals/health-information-exchange/what-hie	Shared EMR based results between health systems related to hospitalization from hemorrhage
Communication Standards			
HL7	Health Level 7	http://www.hl7.org	Formatting that enables import of a file about genetic test into the EHR
C-CDA[55]	Consolidated Clinical Document Architecture	http://www.hl7.org/implement/standards/product_brief.cfm?product_id=258	File formatting for data exchange
FHIR	Fast Healthcare Interoperability Resource	http://www.hl7.org/fhir/?ref=learnmore	Specifications that support complex record exchange between organizations

Appendix 2

Purposes and methodologies of clinical decision support. Adapted from Greenes[1]

Purpose	Potential methodologies
Answering questions	Links to references InfoButtons
Making decisions	
• Diagnosis	Differential Diagnosis generators Probability calculators Alerts and reminders Documentation templates
• Test selection	Evidence-based ordersets Alerts and reminders Documentation templates
• Choice of treatment	Evidence-based ordersets Documentation templates
• Prognosis	Predictive modeling Risk scoring systems
Optimizing workflow	Care pathways and protocols Evidence-based ordersets Alerts and reminders

Purpose	Potential methodologies
	Documentation templates
Monitoring actions	Alerts and reminders Rule-based event detection
Focusing attention and enhancing visualization	Data visualization and summarization techniques

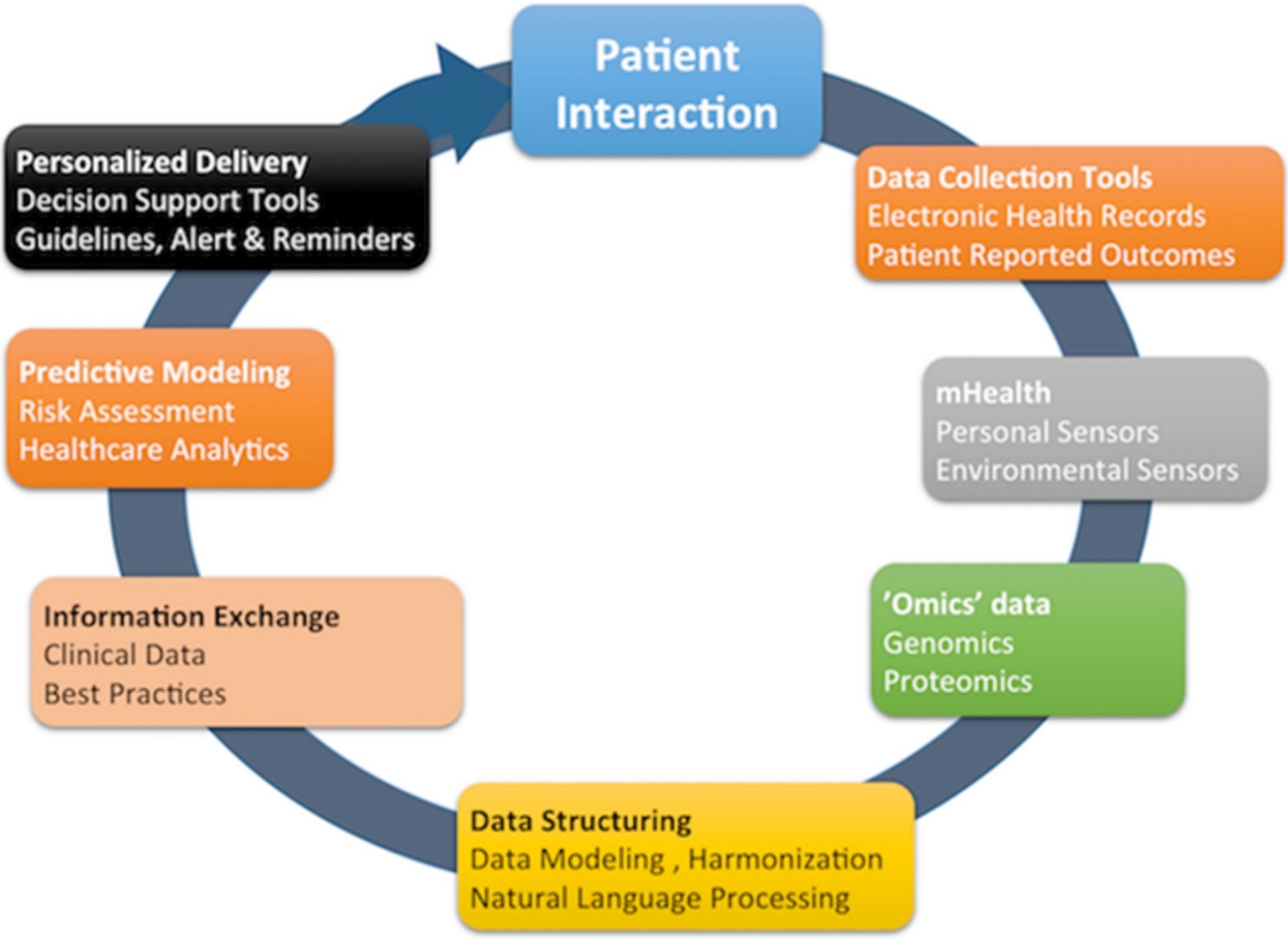

Figure 1.
Key components of Precision Medicine

Table 1

Data Sources for EHR relevant to drive Clinical Decision Support

Type of Information	Standardization	Opportunities	Challenges
Laboratory	LOINC, HGVS, HL7 FHIR value sets	Clinical laboratory tests have a mature standardization capabilities via LOINC LOINC and HL7 genomics groups have started developing standards for genetic tests - that enable standardized discrete coding of some genetic test information	• Not all clinical lab tests are encoded with LOINC (still in process in many institutions) • Discussions on including genetic text in EHR in a structured way have only recently commenced • Significant volumes of tests are performed at external laboratories with processes and results that lack standardization. • Laboratory orders are frequently matched in the computer to component results. • Genetic test results are not systematically incorporated into EMR in a searchable way. For example they are non-discretely stored in the EMR as a scanned PDF document or image at the UCSD Medical Center
Medication	RxNorm, NDC	Clinical drug names have been standardized using these codes Dictionaries provide the opportunity to include manufacturer, dosing, and route information	• Categorization is not clean as medications may have multiple indications both on and off label that skew groupings • Combination drugs may not neatly fit into clinical groupings • Deriving relevance related to effect over time, dosing intensity, or adherence are problematic
Diagnosis	ICD 9, ICD 10, SNOMED-CT	Most institutions adopt ICD system to support both active problem lists and encounter diagnoses Diagnosis names are interrelated; meaning that terms encoded with other one terminology such as SNOMED-CT, can be converted to ICD through cross-mapping established between the two systems	• Coding is frequently completed by a clinician with time constraints that may not search through the extensive terms for the true best fit (undercoding, miscoding) • ICD9 and 10 contain level of detail that may deviate from clinical relevance • ICD9 is historic and ICD10 current (codes expire and newly develop) • Not all codes are billable (irrelevant) • Some diagnoses are not encoded (missing) • SNOMED concepts are frequently not parsed into terms that support clinically specific workflows • IMO updates can impact term groupings and insert clinically mismatched concepts
Radiology	RadLex, SNOMED-CT DICOM	Standards to capture the key findings and metadata about the radiologic studies exist	• Radiology test related metadata may not be formatted in a structured way using a standard like DICOM • Radiology reports are in an unstructured narrative text format. Processing the text to tease out the key findings and mapping them to the standardized codes requires additional efforts/ resources that involves Natural Language Processing (NLP)
Pathology	SNOMED-CT HL7 (anatomic pathology)	Standards to capture the key findings and metadata about the pathology test exist NAACCR is interested in adopting standard for cancer pathology reporting	• Pathology reports are in a unstructured narrative text format or PDF. Processing the text to tease out the key findings and mapping them to the standardized codes requires additional efforts/resources (NLP) • Pathology frequently utilizes standardized nomenclature but does not record data in structured format
Clinical Evidence & Outcomes	OMOP CDM and all terminology systems listed above	EHR data stored in a clinical data warehouse serves a powerful knowledge resource	• There are types of data that are not sufficiently represented by the OMOP CDM such as patient reported outcomes

Type of Information	Standardization	Opportunities	Challenges
		OMOP CDM is recognized as a de facto standard and adopted by many institutions	• OMOP has not been universally adopted across organizations
Procedures	Terms to represent clinical procedures	Standardized terms that define common clinical procedures and their associated charges	• Process for approving new procedural codes is onerous as a result the library may incompletely represent activity detail • Many procedural codes are fairly generic and do not incorporate the level of details that impact outcomes

Table 2

Types of clinical decision support. Adapted from Greenes[1].

CDS type	Prerequisites	Strengths	Weaknesses	Example(s)
Links to references InfoButtons	Ability to link patient context with specific information sources	Facilitates access to current best evidence	Only engaged proactively by provider or patient (pull-mode)	KnowledgeLink[31]
Diagnosis (Dx) generators	Accurate identification of clinical features of patient's condition	Facilitates Bayesian reasoning May improve effectiveness and efficiency of diagnostic testing strategy	Dx algorithms may rely on unstructured data (needs manual entry or NLP) Have been difficult to integrate into clinical workflow	DxPlain[32], Isabel[33], VisualDx[34]
Probability calculators/Risk scoring systems	Access to components of model in computable format	Provides individualized predictions for prognosis or risk of events	Often difficult to obtain confidence intervals of predictions for individuals.	Yale New Haven Readmission Risk Score[35]
Alerts, reminders and rule-based event detection	Development of reliably computable definition of event or condition	Can bring important or urgent scenarios to attention of decision-makers	Patients and providers can become desensitized to alerts (alert fatigue).	Alerts for medications in kidney disease[36] and temporary catheter use.[37]
Evidence-based ordersets, care pathways and protocols	Careful review and understanding of ideal process	Facilitates evidence-based care May reduce variation of care	Labor-intensive to create May increase steps to placing orders	Ordersets for heart failure[38] and venous thromboembolism prophylaxis.[39]
Documentation templates	General agreement of ideal documentation	Can improve efficiency and completeness of documentation Can prompt consideration of diagnoses, treatments or care coordination	In some circumstances, may increase time of documentation May be difficult to document nuances of clinical scenario	Templates for documentation for breast cancer tumor board[40] and palliative care encounters.[41]
Data visualization and summarization techniques	Reliable methods to categorize and condense underlying data elements	Highlights key information for decision-making Reduces cognitive load Improves ability to make causal inferences from disparate data	Labor-intensive to create	Lifelines[42] and problem-oriented display of health records.[43]