Precision Health

26

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Learning Objectives

- Define precision health and other related concepts.
- Describe the components that enable precision health to flourish.
- Present clinical examples of the application of precision health.
- Identify the healthcare informatics and technology considerations that support precision health.
- Discuss the barriers and future opportunities of precision health.

Practice Domains: Tasks, Knowledge, and Skills

- Domain 4: Data Governance and Data Analytics
    - 4.05. Access and incorporate information from emerging data sources (e.g., imaging, bioinformatics, internet of things (IoT), patient-generated, social determinants) to augment the practice of precision medicine
    - K108. Precision medicine (customized treatment plans based on patient-specific data)

Case Vignette

Sid is a 16y/o boy who is currently being treated with atomoxetine in the adolescent clinic for Attention-Deficit Hyperactivity Disorder (ADHD) at your healthcare institution. His parents report that he has been on this medication for over a year, and they have not observed any significant changes in his behavior in school and at home. His parents also noted that he has recently lost weight, constantly complaining of vague abdominal pains, headaches, and feeling fatigue, especially after his atomoxetine dose was increased a few weeks ago. The physician suspects side effects from the medication. Learning about the recent pharmacogenomics pilot in the health system, the physician wondered if Sid is a candidate for pharmacogenomic testing. Upon discussion with Sid's parents, a blood sample was taken and sent for genetic analysis. The laboratory test result returned, documenting that Sid has the genetic mutation that causes decreased CYP2D6 enzyme activity ("poor metabolizer"), leading to increased levels of atomoxetine and increased risk of side effects compared with the increased risk of side effects CYP2D6 normal metabolizers. Learning about this test result, the physician contacted his parents and decided to discontinue atomoxetine and move the patient to an alternative medication.

Your health system's clinical and research leaders plan to invest in a precision health pharmacogenomics program to pave the way for "personalized medicine." As their CMIO, you were asked to present the informatics infrastructure needed to support such a program. The leaders want to use the patient's genetic data to determine the best treatment options for improving outcomes and minimizing adverse drug reactions. They want to pilot their pharmacogenomics program on patients with behavioral problems. ***How would you explore this opportunity and present an informed discussion regarding the required informatics infrastructure to support the effort?***

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J. T. Finnell, B. E. Dixon (eds.), *Clinical Informatics Study Guide*, https://doi.org/10.1007/978-3-030-93765-2_26

Introduction

Precision Health (PH) offers a very broad and all-encompassing view of health, and it has very important considerations for clinical informatics. It aims to support individualized care to address wellness opportunities and provide targeted therapies to prevent, predict, and treat diseases. At the same time, it provides "dynamic linkages between research and practice as well as medicine, population health, and public health" [1]. This integrated view of health also incorporates a wide swathe of efforts, ranging from promoting health, preventing, diagnosing, and treating illnesses using actionable data derived from genomics, environmental, behavioral, and social antecedents of health and diseases.

PH is often interchanged with terms like "Personalized Medicine" or "Precision Medicine". While they may be similar in some respects, Personalized Medicine is concerned with a medical practice that leverages the patient's "genetic profile to guide decisions made regarding the prevention, diagnosis, and treatment of disease" [2]. Similarly, providing an updated view of personalized medicine, Precision Medicine is concerned with treating and preventing diseases by factoring in the patient's variations in genetic, environmental, and lifestyle considerations [3].

It is also noteworthy to distinguish between "genetics" and "genomics", as they are often coined interchangeably. The World Health Organization (WHO) describes that the "main difference between genomics and genetics is that genetics scrutinizes the functioning and composition of the single gene whereas genomics addresses all genes and their interrelationships to identify their combined influence on the growth and development of the organism" [4]. Genetics is concerned with the hereditary aspects of the genes and their health effects. In contrast, genomics, a more recent term, is concerned with the patient's whole genome, including the genetic interaction between the individual's genes and the environment [5]. Genes undergo mutation in somatic or germinal tissues. Somatic mutations are not hereditary, whereas germline mutations can be transmitted from parent to offspring [6]. For example, some mutations are acquired after birth (somatic), causing cancer in specific cells in the body. Cancer cannot be inherited by offspring.

On the other hand, mutations in the germ cells (via parent's eggs and sperms) are represented in all offspring cells. Its presence predisposes the offspring to certain diseases, depending on its gene expression or whether the mutation is an inherited dominant or recessive trait. Distinguishing between the two types of mutation is important in counseling the family regarding the risk of transmitting the mutation and taking proactive measures to reduce the risk for those with hereditary or germline mutations.

Precision Health

One of the main goals of PH is the ability to tailor the care plans based on the individual's specific risks and predisposition, including the person's genes, environment, and lifestyle. PH is often contrasted with "Population-based" healthcare, where care is often ascribed to a "one-size-fits-all" approach, in contrast with the "tailored" approach in PH. For example, in population-based healthcare, typical recommendations of a healthy diet, exercise, smoking, and alcohol consumption is standard fare, including following clinical pathways and care guidelines for specific disease processes. With the advent of more precise health markers such as genetic mutations, blood types, and other biologic indicators, it is possible to "tailor" the treatment based on the specific individual risk profiles. More importantly, in PH, it is also possible to identify the individual's specific gaps in their behavioral, social, and environmental determinants of health and further design the interventions based on the person's needs, hence the term "one-size-does-NOT-fit-all". PH seeks to leverage molecular, digital, and epidemiological information to manage and personalize the care to the individual.

The goal of PH includes the prediction, prevention, and treatment of disease so that the individual patient can maximize health and wellbeing. It considers the variables beyond healthcare and genetics medicine and includes social, environmental, and behavioral determinants of health, thereby expanding the lens of health from a broader perspective. PH is concerned with (1) predicting disease risk or preventing disease onset before the disease symptoms become apparent, (2) detecting disease onset as soon as it is clinically present and being able to provide a set of differential diagnoses, and (3) treat the disease with utmost precision and efficacy, while avoiding adverse events.

"Imprecision" Healthcare

Today's "one-size-fits-all" approach to medicine is considered "imprecise healthcare", where treatment interventions are aimed at a specific disease population under very common and generalized scenarios. This means that, on average, the treatment will be efficacious in generalizable clinical settings. The Number-Needed-to-Treat (NNT) is often used to measure the efficacy and safety of the medical intervention [7]. It is the average number of patients who need to be treated to avoid one additional adverse outcome. An NNT of 1 is the perfect treatment where all patients who received the intervention improved, whereas an NNT of 100 means that you have to treat 100 people to prevent one additional adverse outcome. The rest of the patients would not have benefited from the treatment or could even suffer an adverse effect. For example, the NNT to prevent one atherosclerotic cardiovascular disease for the cholesterol-lowering class of statins over ten years ranges from 3 to 61, depending on other patient risks and associated cholesterol levels [8].

Precision health is an alternative "one-size-does-NOT-fit all", where the treatment is tailored to the individual's specific risk profiles. Hence, patients with a specific mutation on the gene SLCO1B1 are more likely to incur statin-induced myopathy. Learning about this unique aspect of the individual offers an opportunity to present a specific set of recommendations. Therefore, learning about the patient's genetic predispositions can maximize drug efficacy and improve safety [8].

It is often believed that the patient's zip code is a major determinant of health. For example, the "Delmar Divide" in St. Louis, MO depicts a stark contrast between economic, literacy, and health outcomes of people living in the neighborhoods north of the Delmar Boulevard, where it is predominantly poor and African American, less educated, and individuals have a higher prevalence of heart disease and cancer, compared to the people living south of the Delmar Divide, where they are more white and more affluent, with better educational status, and health outcomes [9]. PH envisions a future wherein healthcare is focused on the treatment of the disease and considers the patient's genetic code and lifestyle as inputs into the calculus for improving health.

The ability to access the patient's genome, phenome, biome, and home (i.e., social determinants of health, environment, lifestyle) data and information can provide a more holistic view of the individual's health and healthcare opportunities.

PH Is an Informatics Opportunity

Clinical informatics is the application of computer science and information technology in healthcare [10]. Furthermore, clinical informaticians are concerned with the analysis, design, implementation, and evaluation of clinical information systems to improve the quality and safety of care, enhance the patient-provider experience and improve individual and population health outcomes [11]. As PH becomes more ingrained into clinical practice, informaticians will be intimately involved in the planning, design, implementation, optimization, and evaluation of the PH tools. Being an interprofessional field of practice, informaticians coordinate and integrate knowledge about the different variety of domains involved in PH; they are also vital in the optimal delivery of clinical decision support aimed at predicting, preventing, and treating diseases [12].

It is estimated that medical knowledge will double every two months [13]. To support the full breadth of PH, clinicians must be able to integrate a broad range of information pertinent to the individual's care delivery, including not only medically relevant information but also considering the biomedical, social, environmental, and behavioral determinants of health [14]. This is a great opportunity for informatics and how clinical decision-making can be best supported by an information resource that complements the limitations of human cognition [15].

Big data and PH are linked together. The recent increase in the adoption of electronic health records presents an opportunity to cultivate large data sets for healthcare analytics, natural language processing, machine learning, and artificial intelligence [16]. Clinical informaticians supporting PH will be increasingly skilled in using data science tools to support the growth of computable health care data and information resources [17]. In addition, the disparate nature of the healthcare data supporting PH will need robust interoperability and integration profiles. Combining data sets from different sources, such as the genome, phenome, social, environmental, or electronic health records, will need modern informatics and data science tools to transform these vast heterogeneous datasets into meaningful and actionable knowledge [18]. The rapid advancement of healthcare-related data science technologies presents a great opportunity to apply predictive analytics to support integrated precision medicine and population health initiatives [19]. Healthcare data science will be among the important core competencies of informaticians in the era of PH [20].

Precision Health Examples

Oncology

The promise of identifying the specific genetic sequence mutation that predisposes a cell to turn cancerous and target treatments to address the molecular aberration is a goal of precision oncology [21]. A mutation in the Bcr-Abl tyrosine kinase gene was identified as the trigger for chronic myelogenous leukemia, previously thought to be untreatable. The drug imatinib is cytotoxic to cells containing the Bcr-Abl, thereby selectively inhibiting tyrosine kinase activity in leukemic cells [22]. The BRCA genes (short for "BReast CAncer") are known to suppress cancer growth in cells via DNA repair functions. A mutation in the BRCA genes has been associate with a person's risk for breast cancer [23]. Learning about this mutation early allows for early detection and treatment, reducing the potential health risk to patients and their families.

Immunology

Advancements in understanding how the immune system mediates the expression of cancer and other immune system diseases led to several novel and targeted precision immunotherapies [24]. For example, our immune system is regulated by stimulating or inhibiting the function of the cell's immune receptors. Monoclonal antibody drugs such as pembrolizumab and nivolumab bind to specific receptors on lymphocytes and blocking the effects of immune-suppressing ligands, thereby restoring T-cell response [25]. Compared to traditional chemotherapy and radiotherapy, immunotherapy harnesses the patient's natural immune cells to selectively target cancerous and avoiding normal cells, making the treatment safer and more effective.

Infectious Diseases

Precision medicine advancements in infectious disease therapy are brought about by integrating molecular and genomic technologies and applied to individual patient care and population health. More precise diagnostic tests that detect pathogenic DNA or RNA via microbial nucleic acids, broader and more rapid testing offers rapid pathogen identification, exact antibiotic selection, developing better vaccines, leading to early diagnosis, more effective use of medications, and reduce disease burden. For example, the traditional way of detecting bacterial pathogens is through plating and culture methods, where the "detection" is made by humans inspecting the organism growth in the culture medium. This has built-in delay and uncertainty due to observer and process variability. Detecting the specific nucleic-acid signature of the bacterial pathogen's DNA offers a more rapid, accurate, and precise detection [26].

Pharmacogenomics

Pharmacogenomics is a promising field in medicine that utilizes the knowledge of the individual's genetic makeup to help predict the likelihood of adverse drug events or subtherapeutic response to treatment [27]. As described in the clinical vignette early in the chapter, pharmacogenomics contributes to precision health vision by targeting therapies based on the patient's specific genetic predispositions and associated response to the medication. For example, patients with sickle cell disease are often plagued with recurring pain crises, and it is typical to manage the pain with the opioid drug codeine. Codeine is metabolized to morphine primarily by the cytochrome P450 2D6 (CYP2D6) enzyme. A mutation in the CYP2D6 gene can affect enzyme activity. Depending on the variant, it can lead to either a decrease or increase in drug metabolism, causing ineffective treatment or increased side effects, respectively [28].

Antecedents to Precision Health

The current advances in biomedical and health information technologies, increasingly available computable biomedical data, changing regulatory programs, advances in high-performance computing resources, and data science set the foundation for innovations in precision healthcare.

Biomedical Knowledge and Scientific Discovery

The healthcare industry has seen rapid development in all areas of biomedicine due to advances in technology. One of the more recent examples of informatics-led precision immunology is mRNA technology in developing the COVID-19 vaccine [29]. Immediately upon discovering the SARS-CoV-2 gene sequence, the scientific, healthcare, governmental, and drug companies worked together and developed the COVID-19 vaccines with great speed and immunogenic efficacy [30]. We now have the technology to accelerate vaccine development in a faster, more effective manner.

Following ongoing trends in genomic medicine, genome data has become more affordable. As of August 2020, the National Human Genome Research Institute (NHGRI) reported a continued downward trend in genome sequencing cost, with a rate of declining cost better than Moore's Law (Fig. 26.1). It has also made genome data are more available now more than ever [31] (Table 26.1).

There are more publicly available clinical data sets available to scientists and researchers. For example, the National Institute of Child Health and Human Development (NICHD) established the Data and Specimen Hub (DASH) to provide online access to data from its research and provides several resources and tools (tissue banks and repositories, datasets, and databases, model organisms, genome and DNA sequences, and resource libraries) for researchers [32]. It includes, among others, every data produced by the Adolescent Brain Cognitive Development (ABCD) Study, which is a landmark, longitudinal study of brain development and child health [33]. Another publicly available clinical dataset is MIT's Medical Information Mart for Intensive Care (MIMIC) database [34]. MIMIC is a robust collection of de-identified clinical information derived from a large academic medical center's intensive care units. Data from the dataset is used by teaching institutions, researchers, and by quality and safety stakeholders [35].

Digital and Information Technology

The continued rise in digital technologies continues to drive innovation in all sectors of our society. During the COVID-19 pandemic, the digital platforms were ready to support the societal and public health endeavors needed to adjust to the crisis. Work/learn from home, social distancing, and lockdown protocols necessitated digital technologies such as video conferencing, eCommerce, online entertainment, cloud computing, among others, to flourish [36]. Telehealth

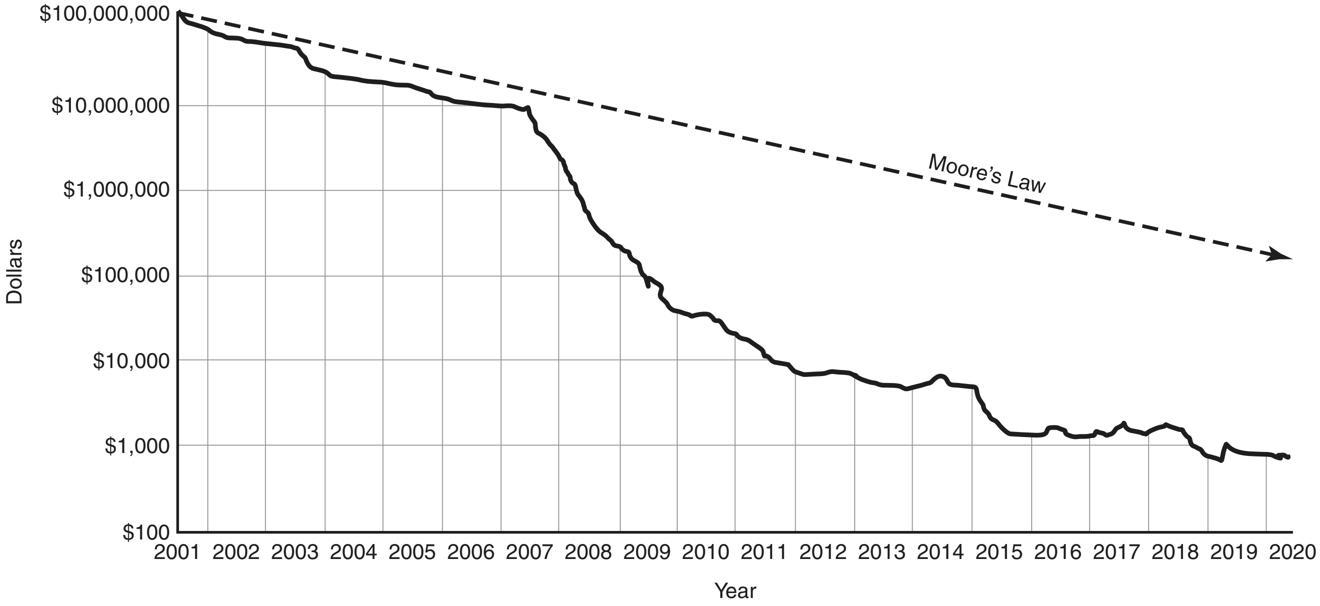

Fig. 26.1 Cost of Genome Sequencing. The decreasing costs associated with genomic tests allowed providers and patients to assess individual risks to medications (pharmacogenomics), learn about familial relationships (genealogy), as well as confirm presence or absence of genetic marker associated with diseases and other individual risks to health. Source: The National Human Genome Research Institute (NHGRI)

Table 26.1 Examples of online genomic research resources

Resource	URL	Notes
The National Human Genome Research Institute (NHGRI) Genome Sequencing Program (GSP)	https://www.genome.gov/Funded-Programs-Projects/NHGRI-Genome-Sequencing-Program	Genome sequencing projects currently in production and funded by NHGRI.
National Center for Biotechnology Information (NCBI) Human Genome Guide	https://www.ncbi.nlm.nih.gov/genome/guide/human/	One-stop shop for browsing online information about the human genes
University of California Santa Cruz (UCSC) Human Genome Browser Gateway	http://genome.cse.ucsc.edu/cgi-bin/hgGateway	Human genome browser, as well as other species
Ensembl Human Genome Server	http://useast.ensembl.org/Homo_sapiens/Info/Index	Human genome browser, as well as other species
GeneMap99	https://www.ncbi.nlm.nih.gov/projects/genome/genemap99/	A New Gene Map of the Human Genome
Marshfield Comprehensive Human Genetic Maps	https://www.biostat.wisc.edu/~kbroman/publications/mfdmaps/	Contains links to comprehensive human genetic linkage maps

The links above are examples of genomic online resources compiled by the National Human Genome Research Institute (NHGRI). The NHGRI NHGRI is also at the forefront of exploring the ethics, legal, social aspects of genomics, as well as leading the efforts in genomic research and education. The NHGRI website is a good resource for informaticians wanting to learn about the role of genomics in precision health.
Source: The National Human Genome Research Institute (NHGRI). https://www.genome.gov/10000375/online-research-resources#nhgri. Accessed 25 Jun 2021

technologies became a key modality to provide continuity of care during the pandemic [37]. This digital front is also driving fast-paced growth with consumer technologies. Consumer spending on technologies in the US posted over $420 billion in record sales in 2020 and is projected to increase to $460 billion by the end of 2021 [38].

Big tech companies are adopting healthcare once again. Fueled by the pandemic and healthcare consumers' and providers' heavy reliance on a digital platform to support business continuity, 2021 saw the shift of efforts by big tech to adopt healthcare solutions. Amazon, for instance, is moving into the urgent and primary care services with Amazon Care for patients and leveraging their cloud computing platform in offering data science and analytics services with Amazon Healthlake [39, 40]. Apple is leveraging its consumer-facing products to link patient data to healthcare providers, researchers, and payers [41]. As early as iOS version 11.3 in 2018, Apple has opened its Health app to interoperate with EHRs, interfacing via HL7 CDA (Clinical Document Architecture) and FHIR (Fast Healthcare Interoperability Resources) standard [42]. Google Health leverages Alphabet's artificial intelligence tools to improve consumer and healthcare providers to support search and research activities to improve health [43]. Finally, Microsoft leveraged its cloud computing technologies to provide healthcare institutions the ability to manage their healthcare data [44]. For their natural language processing and healthcare artificial intelligence products, they also recently acquired Nuance to increase their presence in the healthcare market and beyond [45]. Meanwhile, IBM's Watson Health continues to innovate on its artificial intelligence capabilities, despite growing concerns about its ability to provide accurate clinical treatment advice [46, 47, 48].

Social and Environmental Determinants of Health Data

According to the U.S. Centers for Disease Control and Prevention (CDC), social determinants of health (SDOH) are the "conditions in the places where people live, learn, work, and play that affect a wide range of health and quality-of life-risks and outcomes" [49]. Scientists and researchers can have access to SDOH data sets available from CDC and AHRQ [50, 51]. (Table 26.2) Integrating disparate data sources at the patient level requires robust patient identification protocols and interoperability standards, as well as data sharing, privacy/confidentiality preserving policies. To address the technical and implementation aspects of SDOH data sharing, the U.S. Office of the National Coordinator for Health Information Technology (ONC) has established a set of programs that can serve as a foundation and a catalyst for the capture, sharing, and use of SDOH with health IT [52].

Changing Regulatory Efforts

Governmental and regulatory efforts that promote the use of health IT are very important in creating PH conditions. Adopting healthcare standards for interoperability, health information exchange, privacy and security policies, patient identification standards are crucial to integrating disparate data about the individual and population health.

The integration of disparate data sources that will enable the coordinated care that supports PH must be supported by robust interoperability standards. The information exchange must support syntactic and semantic data transfer, allowing for the clinical, genomic, social, and environmental data to be used to coordinate care from the individual patient to the public health level. An itemized list of the clinical systems interoperability standards useful for PH can be found in Table 26.3.

The Health Information Technology for Economic and Clinical Health (HITECH) Act was implemented as part of the American Recovery and Reinvestment Act of 2009 to incentivize providers and hospitals participating in Medicaid and Medicare programs to adopt and meaningfully use of certified health information technology and electronic health records [53]. The HITECH Act also included disincentives or penalties for non-compliance in the latter phases while promoting the documentation and submission of electronic clinical quality measures [54]. By 2017, towards the end of the program, 96% of the community hospitals in the US and 86% of office-based providers have adopted EHR under the incentive program, paving the way for the increased EHR functionality and adoption of interoperable systems that allow for electronic submission of population-based health measures, patient electronic access to their health information, bidirectional EHR communication with immunization registries and health information exchanges, as well as increased e-prescribing capabilities, among others [55]. In 2018, the program was renamed as Promoting Interoperability Program to align more with ongoing federal programs and set the sights beyond the HITECH act focusing on furthering the EHR-based measurement program, adopting robust interoperability functionalities, and improving patient access to their own personal health information [56]. In concert with other public and private health IT adoption efforts, the incentive programs allowed for the rapid increase in EHR uptake by healthcare providers and institutions. Coupled with the adoption of interoperability standards, this led to the increase in the availability of computable clinical data that can be used to advance quality and safety initiatives, care coordination activities, data mining, and analytics and foster the clinical data foundations for precision health.

The 2015 Precision Medicine Initiative, spearheaded by the Obama administration, was launched to include a broad set of initiatives that can serve as a substrate for the adoption of precision health. The initiatives include programs that will advance clinical science, informatics, advocacy, and policies supporting individualized care [57]. The Precision Medicine Initiative envisions a future where clinicians can customize the prevention, treatment, and coordination of patient care based on the "unique characteristics, including their genome sequence, microbiome composition, health history, lifestyle, and diet" of the individual patient [58]. The program rightfully identified the informatics infrastructure needed to support the integration of a variety of data types, including clinical data, microbiome, metabolome, among others, and the interoperability standards that support the secure exchange of data for clinical and research purposes.

The twenty-first Century Cures Act was established into law on December 16, 2016, to hasten the development of medical innovations (drugs, devices) and deliver healthcare products to patients more efficiently. The law also included health IT provisions for the ONC to establish programs to increase the adoption of technology standards that ensure patients' access to their healthcare information [59]. Adopted broadly by the healthcare industry in the latter part of 2020, the "information blocking" provisions of the Cures Act was

Table 26.2 Examples of Social Determinants of Health (SDOH) data sources

Data resource	URL	Level of data available	Notes
Chronic Disease Indicators	https://www.cdc.gov/cdi/index.html	state, territory, select large metropolitan areas	Publicly available state and selected metropolitan-level data for chronic diseases and risk factors, including overarching conditions such as SDOH.
Chronic Kidney Disease (CKD) Surveillance System	https://nccd.cdc.gov/CKD/default.aspx	national	National database that offers interactive, trending, surveillance information on CKD, it's risk factors and complications. It also includes SDOH information such as household food insecurity score.
Compendium of Federal Datasets Addressing Health Disparities	https://www.minorityhealth.hhs.gov/omh/browse.aspx?lvl=1&lvlid=4	multiple	Established by the Interdepartmental Health Equity Collaborative (IHEC) and the HHS Office of Minority Health to foster inter-agency efforts and provides data about the socioeconomic factors, social determinants of health, and health equity, including > 250 available databases containing population-based opioid use/research, and other biorepositories
Disability and Health Data System (DHDS)	https://www.cdc.gov/ncbddd/disabilityandhealth/dhds/overview.html	state	State-level database containing information about adults with disabilities (six functional disability types: cognitive, hearing, mobility, vision, self-care, and independent living) as well as other adult health topics including smoking, obesity, heart disease, and diabetes. DHDS allows customizable data maps, charts, and tables, as well as categorize by disability, age, gender, race and ethnicity.
500 Cities: Local Data for Better Health	https://www.cdc.gov/places/	city, census tract	Database containing city- and census-tract-level small area estimates for chronic disease risk factors, health outcomes, and clinical preventive service use for the largest 500 cities in the US. It also includes health insurance status.
Interactive Atlas of Heart Disease and Stroke	https://nccd.cdc.gov/dhdspatlas/	national, state, territory, county, census tract	Contains county-level mapping of heart disease and stroke by race/ethnicity, gender, and age group, including social and economic factors by census tract and county along with the locations of health services.
National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP) AtlasPlus	https://www.cdc.gov/nchhstp/atlas/index.htm	national, state, select territories	Provides information to CDC's surveillance data on HIV, viral hepatitis, sexually transmitted diseases (STDs), and tuberculosis (TB), including social and economic data. Users can view interactive maps, graphs, tables, and figures showing geographic patterns and time trends.
National Environmental Public Health Tracking Network	https://ephtracking.cdc.gov/	national, state, county	Integrated online data on population-based health, exposure, and hazard information and data from a variety of national, state, and city sources, including maps, tables, and charts with data about environmental indicators (e.g., particulate matter in the air).
The Social Vulnerability Index	https://www.atsdr.cdc.gov/placeandhealth/svi/index.html	census tract	Contains US census data about specific community's predisposition to require help during external stresses as natural or human-caused disasters, or disease outbreaks. Users can use this information to estimate human suffering and economic loss during disasters.
Vulnerable Populations Footprint Tool	https://www.communitycommons.org/collections/Maps-and-Data	state, county, city, census tract	Interactive tool that identifies poverty rates and low education levels in specific areas.
Social Determinants of Health Database (Beta Version)	https://www.ahrq.gov/sdoh/data-analytics/sdoh-data.html	county, zip code	Comprehensive online resource established by the Patient Centered Outcomes Research (PCOR) Trust Fund at the Agency for Healthcare Quality and Research (AHRQ). It contains SDOH domains such as social context (e.g., age, race/ethnicity, veteran status), economic context (e.g., income, unemployment rate), ncing the visioneducation, physical infrastructure (e.g., housing, crime, transportation), and healthcare context (e.g., health insurance).

Social determinants of health (SDOH) data are not routinely gathered in computable forms in the electronic health record. The data sets that are available in the links above are examples of data resources that can help the clinical informatician learn about the types of SDOH information that can impact precision healthcare delivery.

Source: Centers for Disease Control and Prevention. https://www.cdc.gov/socialdeterminants/data/index.htm. Accessed 25 May 2021
Agency for Healthcare Quality and Research. https://www.ahrq.gov/sdoh/data-analytics/sdoh-data.html. Accessed 25 May 2021

put in play by ONC to allow for immediate and timely electronic access to patient data, as well as establishing HIT certification criteria for software applications to integrate with EHRs via application programming interfaces, or APIs. This has broad implications not only for the ability of patients to gain access to their own healthcare data but also allows the patients to use interoperable software to access disparate sources of data via standard APIs.

Table 26.3 Examples of interoperability standards relevant to precision health

Standards	Notes
Vocabulary/Terminology Standards	
Current Procedural Terminology (CPT®)	Billing codes for healthcare procedures maintained by the American Medical Association (AMA)
Healthcare Common Procedure Coding System (HCSPCS)	Healthcare procedure codes for Medicare services, maintained by the Centers for Medicare & Medicaid Services (CMS)
The International Statistical Classification of Diseases and Related Health Problems (ICD)	Code sets for classifying diseases, signs and symptoms, abnormal findings, complaints, social circumstances, and external causes of injury or diseases. Maintained by the World Health Organization (WHO), its current version is ICD-10; ICD-11 is targeted to be available in January 2022.
Logical Observation Identifiers Names and Codes (LOINC®)	Code sets for health measurements, observations, and documents, maintained by the Regenstrief Institute.
National Drug Code (NDC)	Codes for medications that are manufactured, prepared, propagated, compounded, or processed for commercial distribution, maintained by the US Federal Drug Administration (FDA)
RadLex	Radiology code sets for indexing and retrieval of radiology information resources, maintained by the Radiological Society of North America. It complements other standard code sets such as SNOMED-Clinical Terms and DICOM.
RxNorm	Terminology for clinical drugs, maintained by the US National Library of Medicine. It specifies standard codes and identifiers for the combinations of ingredients, strengths, and dose forms of medications in the US market.
Systematized Nomenclature of Medicine-Clinical Terms (SNOMED-CT)	Code sets for clinical concepts, maintained by The International Health Terminology Standards Development Organization (IHTSDO). Often used by EHRs to represent computable clinical concepts. SNOMED codes are often considered as the “answers” to the “questions” posed by the lab tests posed by LOINC terms.
CVX and MVX vaccine codes	Codes for vaccines [Vaccines Administered (CVX)] and manufacturers [Manufacturers of Vaccines (MVX)], maintained by the Centers for Disease Control and Prevention (CDC), useful in bidirectional immunization registry interoperability efforts.
The Unified Code for Units of Measure (UCUM)	Code sets for units of measures used in international science, engineering, and business, typically adopted by other standards such as DICOM, HL7 to support semantic interoperability. Maintained by the Regenstrief Institute and the UCUM Organization.
Content Standards	
HL7 Version 3 Clinical Document Architecture (CDA®)	An XML-based document markup HL7 standard that provides specifications for the structure of clinical data, or “CDA documents”, while maintain semantic interoperability during health information exchange between clinical information systems.
Consolidated CDA (C-CDA)	A package containing a library of standardized HL7 CDA formatted documents (care plan, consult note, continuity of care, diagnostic imaging report, discharge summary, procedure note, history and physical, operative note, progress note, transfer summary), used by certified EHRs in compliance with Meaningful Use. The CCDA incorporates references to terminologies and value sets required by federal HIT program.
HL7 Version 2.x (V2)	A widely adopted health industry messaging standard that provides specifications for the exchange of administrative and clinical data between clinical information systems.
HL7 Fast Healthcare Interoperability Resources (FHIR)	A recent and upcoming standard in HL7 that codes for resources (file format and data elements) and application programming interface (API) specifications EHR interoperability. The HL7 FHIR Release 4 version includes standards for collecting, coding and retrieving genomics data (FHIR Genomics)
The Global Alliance for Genomics and Health (GA4GH) Browser Extensible Data (BED) Format	The GA4GH is a policy-framing and technical standards-setting institution that promotes responsible sharing or genomic data. It has established an API and data model (GA4GH BED, currently on version 1.0) for the exchange of full sequence genomic information across multiple research organizations and platforms.
Transport Standards	
Digital Imaging and Communications in Medicine (DICOM)	The standard for communicating and managing medical imaging information and related data. DICOM is used for storing and transferring of medical images across systems and devices (scanners, workstations, network, picture archiving and communication systems, or PACS). DICOM is maintained by the American College of Radiology (ACR) and National Electrical Manufacturers Association (NEMA).
Direct Secure Messaging standard	Direct is a health information exchange (HIE) HIPAA compliant standard messaging protocol that allows providers to securely move healthcare information to other providers over the internet using encryption services, usually as part of complying with federal health IT mandates such as Meaningful Use. Just like a regular email services, the Direct messaging is managed by a Health Information Service Provider, or HISP, which an accredited network service operator that enables nationwide clinical data exchange using Direct Secure Messaging (aka Direct, Direct Messaging and the Direct Project).

Table 26.3 (continued)

Standards	Notes
HL7 Fast Healthcare Interoperability Resources (FHIR®)	See above.
Privacy and Security Standards	
HIPAA Privacy Rule	Defines the national standards to safeguard patient's medical records and other personal health information. It applies to health plans, healthcare clearinghouses, and healthcare providers that conduct certain healthcare transactions electronically. It defines how institutions use and disclose health information without patient authorization. It also provides patient's the rights to manage how their personal health information (PHI) is used by healthcare institutions. In 2013, the Privacy Rule was modified to include genetic information as PHI.
HIPAA Security Rule	Defines the national standards for safeguarding the confidentiality, integrity, and availability of electronically protected health information. It requires institutions, or "covered entities", to have the technical and non-technical mechanisms to secure patient's protected health information.
General Data Protection Regulation (GDPR)	The GDPR is a regulatory effort that defines the privacy and security regulations for managing data about individuals in the European Union (EU). This data includes healthcare information.
Genetic Information Nondiscrimination Act of 2008 (GINA)	In Title II of GINA, it is illegal to discriminate against employees or applicants because of genetic information. Law took effect in the US on November 21, 2009.
The Freedom of Information Act (FOIA)	The Cures Act provided provisions to amend the Section 301 of the Public Health Service Act to include genomic information as exemptions from FOIA requests.

Integrating information across disparate data sources will require syntactic and semantic interoperability. More importantly, as more computable information is exchanged between healthcare information systems, it is vital to ensure that the patient's privacy and confidentiality preferences are protected during health information exchange

Adapted from The Healthcare Information and Management Systems Society (HIMSS): Interoperability in Healthcare. https://www.himss.org/resources/interoperability-healthcare. 7 Jun 2021

The HIPAA rules that were defined in 1996 were also updated in 2013 to support the patient data sharing provisions of the HITECH Act. During the COVID pandemic, some of the HIPAA provisions were relaxed to support the telehealth programs needed to address the social distancing and lockdown of public health protocols [60]. The Office of Civil Rights proposed in December 2020 to amend the current HIPAA rules to address the interoperability standards that limit the coordination and communication across patients and healthcare stakeholders. In such a way, it continues to support the privacy and security of protected health information [61].

More recently, 2021 saw a dramatic change in how healthcare providers are reimbursed based on their documentation. To reduce the administrative burden associated with billing and the well documented "note bloat" attributed to the advent of EHRs, the CMS "Patients over paperwork" program, led by the Office of Burden Reduction & Health Informatics, established the framework for provider reimbursement based on medical decision -making and time spent with the clinical interaction [62, 63]. This initiative can potentially improve the quality of clinical documentation and accounting of the time allocated to patient care in ambulatory care settings.

Finally, one of the key foundations for properly identifying unique patients across disparate data sources is having a robust set of patient identifiers [64]. It took a while for the US government to open to the possibility of a national unique health identifier [65]. Although HIPAA of 1996 calls for a unique patient ID, strong federal law language prevents the adoption of such a standard. In September 2017, the Senate recommended that CMS work with ONC on accurately identifying patients' health information [66]. However, in May 2017, President Trump signed the "National Patient ID" law to allow federal funds to develop a national patient-matching process that can safely and accurately identify the patient [67].

Components of Precision Health

The overall health of an individual is determined by five major contributing factors, namely the person's genetics (30%), social situation (15%), environmental exposure (5%), behavior (40%), and medical care (10%) [68]. Therefore, addressing the overall health of an individual goes beyond medical care, which accounts for a smaller contribution compared to the person's genome or behavioral patterns, as an example. An informatician needs to pay attention to the different components that impact the person's overall health because they become fodder to the development of predictive models, analytics, and other methodologies that evaluate health risks, diagnostic accuracy, and health outcomes. In addition, precision health requires a solid data science infrastructure. The necessary integration of heterogeneous and disparate data sources while maintaining data validity and semantic interoperability will be an ever-increasing informatics opportunity.

Clinical Care

Today, clinical information systems collect a lot of primary clinical data. EHRs collect and store patient-level healthcare information such as health problems, procedures, vital signs, diagnostic test results, images, notes, other patient identifiers, administrative, communication, clinical decision support, and reports surrounding the patient's healthcare. It also contains data about the care team and clinical processes and workflows derived from the EHR logs [69]. Personal Health Records (PHR) are also good sources of clinical information. While EHRs are primarily geared towards providers' information needs, the PHRs collect health information capture from patients and allow patients to view their healthcare information. PHRs are often tethered to EHRs (aka patient portals) or can also be a standalone system. When integrated with the EHR, PHRs allow providers and patients to collaborate and develop a shared understanding of the healthcare goals [70]. The increasing adoption of wearable sensors, both commercial and consumer-grade, provides a new way of collecting patient-level clinical data that can be used for care delivery and science. In contrast to EHRs and PHRs, clinical data can be collected with our human intervention, representing relevant physiologic measurements and lifestyle and behavior-related data about the person [71] (Table 26.4).

Genetics and Biology

Genetics and biology have a big influence on a person's health [72]. Informatics plays a major role in collecting, processing, storing, and distributing biospecimen information for healthcare and research purposes. The growth of microarray technologies allowed healthcare institutions to perform genomic sequences and other analyses with relative ease and efficiency [73]. The use Next-Generation Sequencing (NGS) technologies (i.e., whole-genome sequencing (WGS), whole-exome sequencing (WES)) are increasingly common in the clinical to help clinicians detect genetic variants that could influence diagnosis and treatment decisions. When merged with information from the EHR, lifestyle, social or environmental exposure information, the resulting wide-ranging dataset can serve as the foundation for data science and advanced analytics to help uncover insights for delivering individualized diagnostics and treatment [74, 75].

Behavioral Factors

Behavioral health data is often challenging to find in EHR data [76]. Knowledge about the patient's health behaviors such as alcohol or drug use, mental health, nutrition, and physical activity can provide insight into the barriers and gaps in the individual's healthcare. Systems interoperability is vital to connecting healthcare institutions across the continuum of care, from the primary care and specialty care services to the inpatient and behavioral care settings. Traditionally, these care settings are siloed, and in the precision healthcare setting, bridging behavioral health with clinical care will improve the effective delivery of care to the individual and support population health.

Environmental and Social factors

The person's physical and social environment affects individual and population health. Exposure to harmful substances (e.g., air pollution, toxic gases), access to health optimizing services and resources (e.g., healthy foods, recreational spaces, clinics), and local community development, or lack thereof (e.g., good transportation system, road access), among others, can impact people's health [77, 78, 79, 80]. Many of these factors are influenced by the person's

Table 26.4 Example of wearable sensors

Device type	Clinical data	Example commercial devices
Wrist worn sensors	Actigraphy, Heart rate, Blood Pressure, Electrodermal activity	Actiwatch Spectrum by Phillips, ActiGraph Link by ActiGraph, E4 by Empatica, ViSi Mobile by Sotera Wireless
Skin patch sensors	Electrocardiography, actigraphy, skin temperature	BioStampRC by MC10, HealthPatch by Vital Connect, BodyGuardian by Preventice
Cuff sensors	Heart rate, Blood Pressure	Intellisense Digital BP Monitor by Omron Healthcare
Finger worn sensors	Heart rate, Oxygen Saturation	iSpO2 Pulse Oximeter by Massimo
Clothing embedded sensors	Heart rate, Heart Rate Variability, electrocardiography, respiratory rate, actigraphy	Smart shirts by Hexoskin
Headband sensors	Electroencephalogram, Electromyography	EEG (Electroencephalogram), EMG (Electromyography)

Wearable healthcare devices and technologies allow for real-time monitoring of the person's activities, lifestyle, behavior, and can also detect biochemical and physiologic data. Some of these technologies connect wirelessly to smartphones and other connected devices. Wearable devices collect large amounts of data that can be mined and used as a component of delivering precision healthcare

Source: Izmailova ES, Wagner JA, Perakslis ED. Wearable Devices in Clinical Trials: Hype and Hypothesis. Clin Pharmacol Ther. 2018;104(1):42–52 socioeconomic situation, as exemplified by the "Delmar Divide" mentioned earlier in the chapter. Data about the person's environment and social situation are usually collected outside of the clinical care settings and are not routinely captured in the EHR [81]. However, with the increasing adoption of health IT and integration across disparate systems, EHRs are poised to support the longitudinal collection and capture of vital data that can help address disparities in health, environmental and social wellbeing [82]. The CDC has established the National Environmental Public Health Tracking Network (Tracking Network), coordinating health-related and environmental data from local, regional and national resources. It has also exposed these tools via their "Data Explorer" tool, allowing users to interact with the data related to environmental and environmental hazards, health effects, and population health [83].

Informatics Infrastructure and Considerations for Precision Health

A strong informatics foundation is needed to support Precision Health initiatives. The ability to synthesize heterogeneous, complex, and disparate datasets and derive useful and actionable information at the point of decision making is an important informatics objective. More importantly, informatics tools and processes must allow for the democratization of the data, providing the average non-technical decision maker unfettered access to actionable information promptly and without delay.

Supporting Discovery Activities

Informatics infrastructure that supports precision health should allow end-users to perform discovery activities with relative ease. They have access to tools that enable them to connect to multiple relevant data sources that are of good quality, can share their data across the organization, and be able to perform analytics to gain more insights into the healthcare opportunities, as well as exploring ideas for care improvement or research. Academic institutional tools such as the Informatics for Integrating Biology and the Bedside (i2b2) [84] and TriNetX [85] offer a well-curated set of deidentified clinical data via standardized, normalized data models to consumers and researchers of healthcare information, where users can choose from a variety of clinical variables, biomarkers, procedures, genetic information, among others, without learning how to code or programming. Increasingly, EHR systems offer end-user tools to query clinical information directly from its databases. For example, the Epic EHR system has a built-in analytics tool (SlicerDicer) that allows clinicians to perform robust data searches and database queries, customizing searches to particular groups of patients, diagnoses, or interventions [86].

Supporting Hypothesis Generating Activities

A hypothesis is a theory about the mechanisms that led to the observed phenomenon. Scientific methods and statistical tools are used to prove or disprove the hypothesis. Hypothesis generation is concerned with "how knowledge is activated about plausible hypotheses which should be considered during hypothesis evaluation—the calling to mind of possible hypotheses." [87] The investigator can explore a set of information resources or databases to look for specific patterns and associations or scenarios worth looking into and then identify which hypotheses can be tested later on. The discovery tools described above can also be used for hypothesis-generating activities within healthcare organizations. Informatics tools such as DiseaseConnect are an example of a public-facing online resource that can integrate complex omics, research literature, genome, and gene expression to visualize disease-disease, drug-disease relationship, and molecular mechanisms [88].

Support for Hypothesis Testing Activities

In seeking new knowledge, investigators develop hypotheses about the relationships, collect data and perform statistical tests, and then draw inferences on the test results. Hypothesis testing is concerned with evaluating the evidence from the data source or sample and then determining the generalizability of the results to a different or a broader population [89]. Hypothesis testing is usually performed using statistical software. A commercially available product such as SAS, SPSS, and Stata, among others, are used to manipulate, visualize, test, and report the results in a meaningful way. Meanwhile, R (r-project.org), CDC's Epic Info (www.cdc.gov/epiinfo/), and pandas (pandas.pydata.org), among others, are readily accessible as open-source packages. Consumer-grade tools like Microsoft Excel® can perform robust statistical tests and reporting capabilities.

Informatics Tools for Treatment and Maintaining Precision Health

Not all EHRs are created equal in terms of their ability to support all the healthcare enterprise's business, clinical, and administrative activities [90, 91]. In particular, precision health's far-reaching aim to deliver individualized care to the patient will need more robust tools and capabilities to support personalized clinical decision-making at the point of care [92].

Clinical Decision Support Systems

Maintaining PH information is complex and always evolving. Human cognition will no longer be sufficient to manage these vast and constantly updated sources of information that will be relevant to provide individualized care. Integrating clinical decision support systems (CDSS) into clinician workflow will be necessary to support the practice of PH [93]. Indeed, Friedman's Theorem of Biomedical Informatics holds true for PH, in that "a person working in partnership with an information resource is 'better' than that same person unassisted" [94]. For example, for a clinician to keep up with the information from the genetic predispositions, social and environmental, medications, and other clinical information will require augmentation by an "information resource". In the clinical vignette above, where the patient is being prescribed the drug atomoxetine for ADHD, a CDSS mechanism that will alert the prescribing clinician about the presence of the CYP2D6*10 variant, which is known to be common in individuals who lack CYP2D6 activity, posing a significant risk for adverse events and poor drug efficacy [95]. Several CDSS modalities can support precision medicine activities. Order sets, flowsheets, dashboards, note templates are a form of passive CDSS, while the commonly known alerts, reminders, and prompts are considered active CDSS [96]. They are often integrated into the EHR or PHR and interact with the end-user managing the information resource. EHR systems must be able to incorporate complex decision rules, integrate data from disparate resources, and present the most timely information at the time of decision making. Informaticians will be heavily involved in implementing and managing precision health's five (5) "rights" of clinical decision support [97].

Health Information Exchanges

Healthcare Information Exchange (HIEs) is the electronic transmission of health care data across disparate organizations and systems, enabling clinicians and healthcare decision-makers to securely access and share vital medical information. The HITECH Act was instrumental in promoting the adoption of state-based HIEs in the US [98]. A recent ONC report to Congress noted that less than 50% of ambulatory physicians' offices could exchange electronic healthcare data across HIEs. Less than a third of them can integrate this information into their EHRs [99]. In precision health, new HIE standards and protocols will need to seamlessly and securely integrate genetic, social and environmental, wearables and clinical data across disparate systems.

Care Coordination Toolsets

Getting the right information is important, but taking action with the information is among the most important aspects of delivering precision health. Since the patient's care goes beyond the physician's office, the hospital, or the emergency room, what happens to the delivery of care outside traditional medical brick-and-mortar facilities impacts the patient's overall health. Systems of care must be able to support care coordination services so that the patient's personal, behavioral, or financial concerns are addressed promptly and help alleviate gaps in food insecurity, inadequate shelter, lack of transportation, access to medication, and home assistance, among others. EHR systems in conjunction with a robust HIE will enable the care team to review the patient's most current health visits, medications, diagnoses, and problem lists, procedures, functional, behavioral, and developmental evaluations, and screenings, scheduled visits, treatment guidelines, and other social-medical services, and have the opportunity to coordinate the services along the care continuum [100].

Telehealth

Telehealth adoption surged with the COVID pandemic as healthcare institutions provided continuity of care to overcome the public health protocols for lockdowns and social distancing [101]. The US federal government also relaxed several regulations (i.e., HIPAA, CMS and Children's Health Insurance Program, medical licensure), billing and reimbursement, insurance coverage, and telehealth sites to ensure that the public can safely, securely, and with minimal delay, deploy telehealth services using the most available and practical information and communication technology platforms that are at hand [102]. Telehealth is poised to support the demands for precision health. The care team can provide safe and cost-effective ways to integrate care in the patient's homes and provide chronic care management and coordination among specialists, primary care providers, nurses, and ancillary team members. Informatics consideration for telehealth will include modalities that support synchronous (real-time), asynchronous (store-forward, secure messaging), and remote monitoring capabilities [103].

Integrating telehealth technology into the EHR workflow will streamline the care team's workflow, increasing its usability. Personal health monitoring devices such as wearable heart monitors, Bluetooth-enabled weighing scales, blood pressure monitors, glucometers, among others, can provide patient-level data to the care team, augment remote monitoring telemedicine technologies. Integrating personal healthcare devices will play a significant role in care coordination and virtual care monitoring [104]. Integrating the telehealth platform to the healthcare institution's EHR and patient portal or PHR greatly improves acceptance and usability by providers and patients. This workflow integration reduces multiple logins, duplicate documentation, the need for technical support, and the overall technology burden. Informaticians need to keep this in mind when implementing telehealth solutions to support a broad set of use cases for precision healthcare (Table 26.5).

Bench to Bedside Research Informatics Tools

PH will require an informatics infrastructure that can translate massive amounts of disparate information acquired from bench research, new discoveries in diagnostics and therapeutics, and patient-level to population-level databases [105]. For example, emerging programs such as the NIH's All of Us Research Program, https://www.researchallofus.org/, previously known as Precision Medicine Initiative (PMI) Cohort, collects health information from a large sampling of the population, allowing individuals to contribute personal information (lifestyle, medical history, utilization, physiologic measurements, etc.) for research. The program allows researchers to access this de-identified data securely for research. The data includes participant-provided information such as surveys and physical measurements and EHR-based data (diagnoses, procedures, lab tests, etc.) contributed by healthcare providers [106]. Sync for Science (S4S, http://syncfor.science/) is another government-industry collaboration project that utilizes HL7's SMART on FHIR (Substitutable Medical Apps, Reusable Technology on Fast Healthcare Interoperability Resources) standard to enable patients to share their health data securely via an API for purposes of care coordination and research. These tools set the foundation for a more robust informatics platform for precision health science.

Health Services Research

Health services research is the "multidisciplinary field of inquiry, both basic and applied, that examines access to, and the use, costs, quality, delivery, organization, financing, and outcomes of health care services to produce new knowledge about the structure, processes, and effects of health services for individuals and populations" [107]. Similar to PH, HSR aims to determine the best way to deliver safe, high-quality healthcare cost-effectively while reducing adverse events and medical errors. New sources of data, such as EHR and PHR data, increasingly available data from insurance companies, person-level social media data, patient-generated data (see Chap. 24), and provider-originating data from sites like http://sermo.com offers new opportunities to perform research and informing policies on caring for individuals and population health in the context of precision health [108].

Learning Health System Informatics Infrastructure

Friedman laid out the infrastructure that would support the LHS from an informatics perspective. He describes that (1) Learning is the ability to support "continuous improvement through the collection and analysis of data, creating new knowledge, and the application of the new knowledge to influence practice; (2) overall Health is the ultimate outcome of interest, similar to PH; and finally, (3) System refers to the subcomponents of the structure that act in alignment to achieve its goals. The informatics infrastructure supporting LHS is also important in PH, where each person's information is a vital data point for learning, where

Table 26.5 Telehealth Use Cases for Precision Health

Use case	Description	Timing	Video	Information transferred
Provider to Provider Communication Services				
e-Consultations	Clinician consults another clinician (i.e., primary care provider consulting a specialist) about a patient	Asynchronous	No	Medical records, images
Video consultation	Clinician video conferencing another clinician in real-time (i.e., telestroke consultation)	Synchronous	Yes	Medical records, images
e-ICU monitoring	Clinicians monitor patients remotely using video, telemetry data in real-time	Synchronous	Yes	Medical records, images, telemetry
Direct to Consumer Communication Services				
Second Opinion	Patient communicates electronically to clinician requesting for a second opinion on a health concern	Asynchronous	No	Medical records, images
e-Visit	Clinician communicates with patient using secure messaging to provide formal medical recommendations and services	Asynchronous	No	Patient reported information, medical records, images
Remote Patient Monitoring	Clinicians monitoring patients directly from their connected electronic medical devices, or wearables	Synchronous	No	Telemetry, patient reported information
Video visit	Clinician interacts with patient in real-time using video conferencing technology (i.e., virtual office visit)	Synchronous	Yes	Patient reported information

The COVID-19 pandemic proved the importance of telehealth in providing continuity of care remotely. The use cases itemized above are examples of how telehealth can serve a role in the overall precision healthcare delivery framework

Adapted from the American Hospital Association: Telehealth, A Path to Virtual Integrated Care Report. https://www.aha.org/system/files/media/file/2019/02/MarketInsights_TeleHealthReport.pdf. Accessed 25 Jun 2021 knowledge about processes, workflows and healthcare practices and resulting outcomes are incorporated back into the decision-making and learning process, and where learning and improvement are continuous and on-going and are supported by a socio-technical framework within organizations, large or small [109].

Healthcare Information Technology (HIT) Considerations for Precision Health

The HIT innovations that will ultimately support PH will need to focus on human factors, clinical workflows, and clinical decision support. Human-centered design should promote usability and end-user functional requirements and allows the technology to support real-world activities such as care coordination, patient engagement, continuous improvement, and timely, safer care [110]. Figure 26.2 depicts the ecosystem of information resources, actors and stakeholders, and the interplay of data science and decision support opportunities that foster the implementation science of precision health [111]. The key technologies that clinical informaticians likely play a big role in rolling out precision medicine initiatives are described below.

Electronic Health Records

Electronic health records play an important role in Precision Health [112]. The ability of the EHR to collect, store, retrieve, share, and organize clinically relevant data from a variety of data sources is vital for PH. In addition, by following interoperability standards, EHRs can interact with external systems to gain access to patient-level information outside of medical care. Moreover, social determinants of health and genomic data will also increasingly become more important data that need to be captured in the EHR. Accurate, discrete, and computable data offers a great opportunity for deploying CDSS. The ever-increasing role of EHRs in the care settings will continue to evolve in delivering personalized care. This also involves EHR vendors becoming more engaged with their end-users, improving its usability and human factors design to become an efficient tool for delivering efficient, individualized care.

Patient Portals

Like EHRs, patient portals and personal health records are important components in the precision health technology stack. They become very important communication, patient engagement, care coordination, scheduling platform, and a source for patient-oriented outcome data. Patients who have access to their own healthcare information have a great opportunity to become more engaged with their care. Patient portals also allow patients to get involved in research, similar to NIH’s All of Us Research described above.

Internet of Things

Internet of Things (IoT) are interconnected technology devices that constantly bidirectionally communicate across the internet without any human intervention. This includes appliances, wearables, biometric scanners, and other “smart” devices like Amazon’s Alexa, Google’s Home, or Apple Watch. Healthcare-related IoT such as health monitors, mobile apps, medical devices, and other electronic wearables integrate seamlessly over the cloud and connect with EHRs, PHRs, telehealth, and other healthcare applications. The healthcare, well-being, and other big data collected across IoT networks can be used by healthcare providers to develop customized preventative, proactive treatment, therapies, and services for the patient [113].

Laboratory Systems

Laboratory Systems have long been leaders in healthcare digitization, moving data about individual patient’s laboratory results across healthcare information systems. To support Precision Health, laboratory systems will need to develop more robust in vitro diagnostic testing, including genomic, epigenomic, proteomic, metabolomic, theragnostic testing capabilities, in addition to supporting streamlined workflows for ordering clinicians as well as efficient reporting capabilities between laboratory testing instruments, laboratory information systems (LIS), EHRs and other facilities or external systems. Data derived from the LIS and connected instruments can be used to support day-to-day lab operations, quality and safety efforts, and research. For precision health, a fully integrated laboratory system can provide high-quality clinical, genomic, and other diagnostic data that can be used to develop personalized care and treatment strategies [114].

Genetic Analysis Instruments

Genomics plays a very important role in advancing precision health. Genetic testing instruments identify the variations in genes, chromosomes or proteins, and confirm the presence or absence of a genetic disorder. Clinically, genetic testing is often performed in newborn screening, carrier testing, prenatal testing, forensic and other diagnostic testing, using blood, hair, skin, amniotic fluid, or other tissues. As of 2018, it was

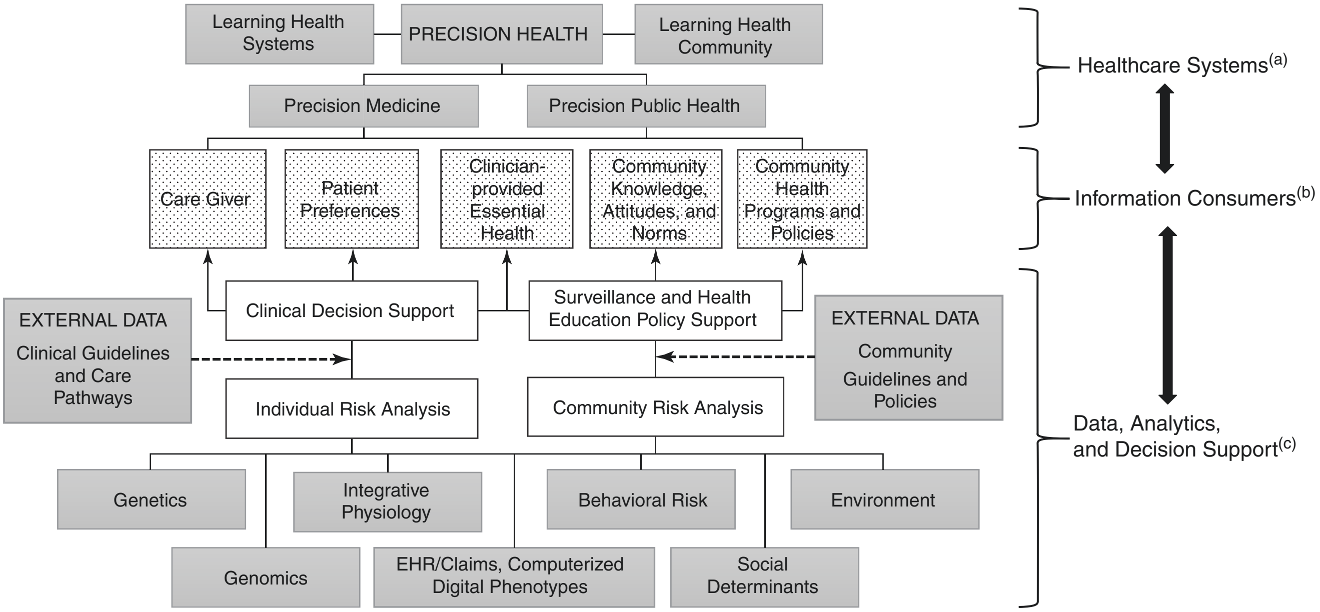

Fig. 26.2 Informatics Opportunities Supporting Precision Health. Precision Health requires the integration of information resources, analytics and clinical decision support systems, regulatory and policy frameworks, as the healthcare provider workflows in order to maximize its health value for patients. Informaticians will need to consider the specific areas where they can make a significant contribution. (**a**) Healthcare Systems are integral to the implementation of Precision Health. Institutions must have the infrastructure (people, process, technology, policy) in place to leverage the care coordination, continuous learning and the healthcare team culture to incorporate the individual's specific healthcare opportunities and preferences across the care continuum. (**b**) Information Consumers are the actors in the healthcare ecosystem, which includes the patient and their families or care givers, the healthcare providers and the care team, as well as the community decision makers that develop programs that influences the care that is being provided to the patient. (**c**) Informaticians play major role in this category. Data, Analytics and Clinical Decision Support serves as the foundation for the information flow the decision makers and consumers of health. Adapted from Pearson TA, et al. J Am Coll Cardiol. 2020; 76(3):306–320. (Used with permission from Pearson TA and Elsevier)

estimated that there are over 75,000 genetic tests available for patients in the marketplace, and more are coming out daily! [115] Moreover, the rise of lower-cost consumer-based genetic testing engages the patient directly, offering diagnostic tests looking at the individual's ancestry, phenotype, lifestyle, biometric markers for informational and preventative purposes [116]. Genetic testing often requires collecting the patient's personal information through questionnaires or interviews, including other medical and family histories. The ability of the genetic testing instruments to become integrated with LIS, EHR, PHR, and other clinical applications will enable the care team to confirm, rule out, or predict genetic risks and individualize the therapy and healthcare services to the patient's individual's genetic markers.

Devices and Interfaces

The future of precision health will be transformed by various sources, forms, and amounts of healthcare data collected via medical devices and applications. These sources of information provide the care team, patients, and other decision-makers about personal and population-based health status, care gaps, and the processes and outcomes of care delivery. The data that are being generated will require a robust set of interoperability standards that maintain the syntactic and semantic qualities of the healthcare data [117]. In 2020, the US Food and Drug Administration launched the Digital Health Center of Excellence program to advance digital health innovations such as mobile health devices, software as a medical device (SaMD), healthcare wearable devices, and technologies that will further the benefit to individual patients. The program will establish efforts that promote innovation in digital health products, foster digital health science and research, as well as stimulate strategic partnerships with product developers, regulatory bodies, consumers to remove regulatory barriers to innovation and fast track the delivery of safe and quality digital health products for the patient and the consumer [118].

Data Standards

Finally, adhering to common data standards, including data elements, interchange formats, terminologies, and other knowledge representation artifacts, allow bidirectional communication across disparate systems [119]. ONC has been a strong proponent for advancing the standards that supports precision health. In January 2021, ONC launched the "Advancing Standards for Precision Medicine" program to identify key data needs and establish testing standards that advance precision health, including data from mobile health, sensors, and wearable devices, and social determinants of health data, complementing its earlier efforts to support the data standards need to move clinical (Sync for Science) and genome (Sync for Genes) data [120, 121]. These programs enable individual patients to contribute research data using health app and standard APIs (i.e., HL7 SMART on FHIR, OAuth 2.0 Authorization Framework).

Barriers to Precision Health Adoption

Delivering precision healthcare is a paradigm shift. It is a culture change for care providers, healthcare administrators, health informatics stakeholders, policy and regulatory bodies, and patients. Below are some of the commonly known sets of constraints in realizing the practice of precision health as part of routine care.

Provider Awareness

Healthcare providers are important to promoting and adopting precision healthcare practices. One of the pivotal practices in PH is the shift of genomic testing and interpretation from the specialists (i.e., geneticists, genetic counselors) to primary care providers. Therefore, it will be necessary for healthcare providers to brush up on their knowledge of genomics, molecular biology, and biochemistry to convey vital information about the genetic test, results in interpretation, and the treatment strategies for the individual patient. Many front-line providers have concerns about their ability to provide accurate guidance and recommendations based on patient's genomic testing results [122]. They also are concerned with their preparedness, confidence, and knowledge about ordering genetic tests [123]. Informaticians and proponents of precision health will need to implement strategies for educating the care team on how to best incorporate precision health workflows into their practice.

Cost and Financing

One of the uncertainties in adopting practices that support precision health is the financing of precision care services [124]. Laboratory departments will need to install new instruments to support the "omics" studies, develop new mechanisms for testing and results in interpretation and counseling, training lab personnel with the new "omics" tests, integrate the test ordering and results in review with the EHR and other ancillary systems in support of personalized care [125].

Reimbursement

Testing for genetic predispositions is newer, and with associate costs, reimbursement from payors and insurance companies could be an issue. The technologies needed to support precision health may not readily fit into existing healthcare billing and reimbursement processes [126]. New approaches will need to be in place to manage costs and payment for more advanced personalized genetic tests [127]. Providers are unfamiliar with the patient's cost burden of the genetic testing, while institutions are not familiar with whether insurance will cover the genetic testing related to precision care [128].

Patient

One of the great opportunities for PH is to empower the patient to have greater control over the prevention, maintenance, and treatment options that impact their health. PH is concerned with massive amounts of personal data, coordinated to develop customized care recommendations. Clinical data can be de-identified, but genetic data cannot [129]. While the healthcare industry (providers, payors, regulators) becomes more permissive with data sharing, linking disparate data sources, collocating genomic data with clinical data to advance precision healthcare and research, the patient's privacy and confidentiality must be maintained to reconcile the patient's rights with the value being offered by the increasing transparency and disclosure of personal healthcare information in big data medicine [130].

EHR Integration Barriers

Finally, there are still technological barriers to fully adopting the promise of precision healthcare. While the US is enjoying fewer barriers to adopting EHRs and increasing the ability for healthcare applications to integrate via standard communication protocols, a few notable opportunities need to be described.

- *Data and Interoperability standards*—EHRs have been the beneficiary of intense focus on interoperability; however, patient-level digital health tools have limited success with being integrated into the EHR workflows. For example, the plug-and-play pairing of Bluetooth digital scales, blood pressure monitors, and glucometers continue to be a challenge [131]. To address this, ONC launched the Advancing Standards for Precision Medicine (ASPM) project in 2018 to advance the implementation of interoperability and data standards needed to support the vision for precision health [132].

- *Genetic data*—Since much of healthcare now requires the care team to interact with the EHR, the EHR needs to capture and store the genetic data required to support PH. In 2007, the eMERGE project was launched to explore the issues vital to integrating genomic data into the EHR [133]. Discrete, actionable genomic data is vital to implementing the CDSS supporting personalized care. More recent standards like the HL7 FHIR offer great promise for incorporating relevant genetic data into the clinical workflows of the EHR [134].
- *SDOH data*—SDOH data must first be captured in discrete and computable forms in the EHR before it can be used to drive decision support mechanisms. This, however, requires clinical process changes (i.e., screening protocols) and configuration of the EHR so clinicians can leverage this information during the clinical interaction. The majority of the SDOH data are not captured within the EHR, and if available, they are found in unstructured data [135]. The emergence of tools like Aunt Bertha (https://company.auntbertha.com) and NowPow (https://www.nowpow.com) interface with EHR systems and offer services that allow healthcare institutions, patients and families to access local community resources that can help address social and environmental care gaps. The ONC advanced standards for collecting SDOH data across healthcare applications through its health IT certification program. Key to this effort is the adoption of standardized mobile healthcare and application programming interfaces (APIs) [136].

Emerging Informatics Trends for Precision Health

Informaticians play an important role in advancing precision health initiatives [137]. Innovation in health IT allows organizations and healthcare stakeholders to store, combine, access massive amounts of data from disparate sources, including clinical, omics, social, environmental, behavioral, wearables, among others. Informaticians will have to grapple with predictive models, algorithms, and high-performance computing activities as healthcare decision-makers increase their demand for transforming data into actionable information and knowledge that ultimately improves health outcomes. Informaticians will need to up their game, not only on knowledge management, human factors design, project management, research, leadership, and systems management but also on their data analytics abilities [138, 139]. In June 2021, the US federal government launched an ONC-led DHHS Public Health Informatics and Technology Workforce program that committed funds to train thousands of healthcare informatics and data science experts. It also aims "to root out pervasive health and socioeconomic inequities that have been exacerbated by the pandemic and ensure our health care system is better equipped for the next public health emergency", including strengthening the local and state public health reporting and data analyses capabilities around race and ethnicity-related issues [140].

Platform for Artificial Intelligence

One of the main challenges of precision health is that it requires the integration and analysis of multidimensional data from various sources to arrive at personalized care recommendations for the patient. This is an opportunity for healthcare data science to flourish. Artificial intelligence models and algorithms can leverage robust computing resources to provide insight from different biological and clinical datasets [141]. Combining patient and population-level data allow healthcare decision-makers to better correlate the clinical and biologic indicators, stratify and categorize specific intervention/outcome scenarios, classify cost-effectiveness profiles, and ultimately allowing the patient and the provider to arrive at the optimal plan of care that provides timely, safe, better care given the opportunity costs [142].

Synthetic Healthcare Data

One of the dilemmas for advancing healthcare big data efforts is the risk of violating patient privacy and confidentiality because of exposing identifiable personal health information. One of the emerging trends in data science is synthetic data, where the data are computer-generated and not derived primarily from real-world events. Synthetic data are often used to train machine learning models because they are readily available, eliminating the labor needed to collect, label, normalize real-world data, and generating big data in a very short period. Most importantly, it minimizes privacy concerns because the data was generated virtually [143]. Healthcare synthetic data can fabricate clinically, administrative, claims data about patients. Since they are not based on real individuals and events, there are no risks of exposing sensitive health information. The generated data can be further developed and validated to make it perform like real-world data. Then when the dataset is of sufficient quality, it can be used for simulation, integration with EHR, and other datasets, as well as used for research [144]. Testing scenarios, machine learning models, and algorithms with synthetic data offer a low-cost, low-risk strategy that can then be validated using real-world data [145]. For example, open-source vendors like Synthea (https://synthea.mitre.org) offer "large-scale fictional data" about patients in the state of Massachusetts. The synthetic data follows the HL7 FHIR data model (i.e., faux demographics, immunizations, clinical, and SDOH data), and users can download the dataset in HL7 FHIR, CCDA, or CSV formats [146].

Learning Health System

The Learning Health System Model provides a great foundation for precision healthcare. Learning health systems leverage process and outcomes data to support the care teams' and institutions' continuous improvement efforts and recycle the knowledge learned from the results back to the decision-makers promptly to further improve patient care [147, 148].

Summary

Precision health is an informatics opportunity. With the advent of newer technologies and innovations and declining costs for "omics" testing, the increasing amount of clinical, environmental, social, behavioral, and lifestyle data that is being generated for patients in the healthcare setting, and the emergence of capable and integrated health informatics and technology infrastructures (EHRs, HIEs, interoperability standards, etc.), the opportunity to harness the massive amounts of data into meaningful and actionable nuggets of information for improving the overall health of the individual patient is so exciting. Informaticians are poised to support secure data curation, sharing, and access to vital patient information in quality improvement and research. The clinical decision support systems that are needed to support personalized preventative and therapeutic strategies specific to the patient's overall health profile requires a solid understanding of the physiologic mechanisms of the disease (omics, SDOH, clinical), the specific workflows of the care team, and its health system (providers, policies, care pathways, reimbursement), the health IT infrastructure (EHR, HIE, PHR, databases), and, more importantly, the patient's need for privacy, confidentiality and healthcare education.

Questions for Discussion

1. What is precision health?
2. List and describe at least two components of precision health.
3. What advantage(s) does precision health offer clinicians over traditional "one-size-fits-all" approaches to medicine?
4. How well do existing electronic health record systems support precision health?
5. What would you do to enhance EHR systems to better support precision health?
6. What role do patients play in precision health?

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