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Flipping the Script: A Buyers' Perspective on the Value of Data

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Flipping the Script: A Buyers' Perspective on the Value of Data

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Abstract:

By 2030, the market for commercialized Health IT data will be larger than the market for the technologies used to create and manage them ($45.1B vs $38.5B). Increasingly, healthcare organizations list data as an asset and create business models around commercialization of that data. There are no standard methods, however, for determining the actual value of that data to patients, clinicians and administrators, though it may be generally defined as

$$data\ value = \frac{patient\ or\ business\ outcomes - drug\ or\ other\ toxicity}{cost}.$$

In contrast, consumers who license these data base its value on the potential future business or research impacts of the insights and evidence that they can derive, less the costs to acquire, process, analyze and visualize it. In this analysis, we will apply this healthcare data value model from the perspective of the patient, provider, and pharma to deliver a first-of-its-kind valuation framework. We use it to estimate the impact of data standards on value to drive awareness on the importance of such standards for so-called “real world data” from healthcare and wellness in life science research.

Introduction

Academic literature and trade journals have discussed how to determine the value of data from the data generator's, or supplier's, point of view. Some of these articles[1] describe ways to monetize healthcare data for licensing to external organizations; other articles[2] focus on the internal value that can be produced at scale for the data generating healthcare system. None to our knowledge has focused on the data users' perspective on the value of data.

Healthcare data rarely use the same data definitions for the same concepts as do life science organizations and often lack common shared meaning, or semantics, which is referred to as the "chasm of semantic despair[i]". A second major challenge for use of raw healthcare data or even that translated to conform to a common data model[ii] for research purposes is data quality. Key data elements can be unstructured or unavailable, thousands of measures that come from an inpatient stay may have unclear applicability[iii] and other data elements collected at different times for the same patient may directly conflict with one another[iv] – just as a few examples. These challenges reduce the number and kinds of hypotheses or questions that can be addressed, as well as the confidence one can have in the answers. Six-sigma led to differentiation of physical products in the manufacturing industry by quality[v], evidence and insights generated using high quality and complete data have a competitive advantage and a higher value.

The value of data can be defined as $data\ value = \frac{patient\ or\ business\ outcomes - drug\ or\ other\ toxicity}{cost}$

where patient or business outcome is defined in this case as how well the data are able to readily and accurately address the question or hypothesis at hand and toxicity the unintended consequences. Data toxicity is a trait often overlooked, wherein they may not only be of low quality, but also produce negative value or harm[vi]. Data toxicity can be driven by frequent null values, lack of standard definitions causing, poor data models or documentation, poor user experience, and/or insufficient deidentification,

other patient privacy issues, and data breaches. Cost includes licenses of the electronic health records systems used to generate the data, storage, retrieval, quality control and assurance, and analysis or visualizations. In addition, there are sporadic one-time costs including the cost to mitigate regulatory changes[vii] (e.g., General Data Protection Regulation (GPDR), Personal Information Protection Law (PIPL), etc).

Meaningful Use (MU) mandated a common set of data elements that must be included within all U.S. Office of the National Coordinator (ONC)-certified EHRs, and thereafter standards and interoperability gained increasing focus. MU has evolved over time into a national standard for interoperability of all actionable health information. Interoperability is an essential part of health care activities ranging from day-to-day health care delivery to health equity to public health emergency response as it covers syntactic, or common data structures, and semantic, or shared definitions, standards required to meaningfully exchange data. When first introduced, there was general agreement that data quality deserved more focus in terms of valuation[viii]. Although there is ongoing work in the testing and use of FHIR-based Quality Measures for use in Quality Measurement programs, including Centers for Medicare & Medicaid Services (CMS), Merit-based Incentive Payment System (MIPS), Gaps in Care (GIC) and Clinical Decision Support (CDS) use cases[ix], no common agreement exists for defining healthcare data value.

In the early 20th century, the invention of the medical record number, the establishment of international classification of disease (ICD) codes, and a push by professional organizations for hospitals to keep consistent records led to increasing quality and completeness of health data. In 1972, the first electronic medical record (EMR) was created,[x] with uptake limited to academic institutions for decades. Regulatory incentives including Meaningful Use (MU), the Meri-Based Incentive Payment System (MIPS) and Medicare Access and CHIP Reauthorization Act (MACRA) in the US were created to encourage hospitals and providers to adopt electronic health records (EHRs). From 2009 to 2021, EHR adoption in the US

increased from 48% to 88%[xi]. Electronic health records for general practitioners (GPs) were introduced at scale in the UK in the 1990s at no cost, with EHR vendors generating revenue by licensing data to pharmaceutical companies. By 1996, 96% of GPs used an EHR[xii].

By the early 1980s healthcare claims research began to emerge,[xiii] initially with statistical models built using medical, pharmacy and administrative claims' diagnosis codes to predict future healthcare costs [xiv],[xv]. Financial services companies enabled healthcare organizations' use of their own financial metrics, such as list price, charges, and reimbursement amounts, between those organizations' claims and payers. Starting in the 1990s, IMS Health (now IQVIA) licensed data on physician prescribing behaviors to pharmaceutical companies to help tailor their sales force strategy. Some physicians felt this was an invasion of privacy and persuaded several states to pass laws prohibiting the sale or license of information about prescribing behavior. IMS pursued the issue to the Supreme Court, which ruled in 2011 that in favor of licensing the prescribing data on free speech grounds[xvi].

Healthcare Data Landscape:

As the amount of data has grown, so too has the scope and structure of the healthcare data landscape. The US Federal Trade Commission (FTC)[xvii] defines four main categories: 1) The Patient, 2) Data Collectors, 3) Data Brokers, and 4) Data Users. This forms a natural hierarchy where the patient directly interacts with the data collectors, who interact with the data brokers, who make data available to the data users. For healthcare, data collectors interact with the patient (e.g., healthcare providers, hospitals, and pharmacies). With the increase of direct-to-consumer interaction, there are also newer data collectors, including wearable device manufacturers, direct-to-consumer laboratories, and even genetic testing companies. Data brokers are largely technology companies, including those who mediate claims or develop EHRs or claims software, that aggregate data from multiple sources to build a larger cohort of individual patients over time. Data users license data from the brokers for research,

commercial, or other uses (e.g., academia, life science companies). Data users refer to licensed data as "secondary use" meaning that research is secondary to the data's primary use – documentation of the patient's healthcare journey[xviii].

Data users spend approximately $30 billion per year licensing healthcare data[xix]. Technology companies, regulators, and even patients and physicians' groups have all made statements on the benefit of using electronic healthcare data for patients, physicians, health systems, and society. Here, we measure that value from the perspective of the key stakeholders involved in creating, licensing, and using healthcare data.

Healthcare value:

In healthcare, value is commonly defined by the conceptual equation:

$$value = \frac{patient\ or\ business\ outcomes - drug\ or\ other\ toxicity}{cost}$$

where efficacy measures how well something works for its intended purpose, toxicity reflects the unintended consequences of that action or object, and cost represents the time, money, and opportunity costs of a specific action or object.

This conceptual understanding will be used to estimate the value of data collected for secondary use as part of the healthcare ecosystem. The value to patients and healthcare providers (data collectors) will first be attempted to be quantified, following the hierarchy established above. Lastly, the efficacy, toxicity, and cost of data from the perspective of a pharmaceutical company (data users) will be examined.

Business and Patient Outcomes of Healthcare Data

To assess the efficacy of healthcare data collection for each of the stakeholders, healthcare data will be considered to be effective when the generation and collection of those data accomplishes the intended purpose.

Patient Outcomes

For patients, data generation and storage are associated with good patient outcomes when those data lead to an action aimed at improving the patient's health or when those data provide them new information about their health.

First, consider the case when healthcare data from laboratory tests, imaging analyses, and other procedures or observations leads to diagnosis and actionable treatment. For CMS patients in the US, laboratory tests are the largest category of procedures, by volume, while only making up 3% of the total cost of care[xx]. These tests inform 70% of clinical decisions[xxi]. Further, they can be repeated over time to capture additional clinical information, such as physicians relying not only on the raw PSA values for monitoring prostate cancer patients, but also on the time it takes for PSA to double[xxii].

Collecting data about prescribed medications, allergies and ongoing care plans can help healthcare providers to remind patients to refill their medications, or schedule important preventive care exams like a colonoscopy or a mammogram. Recent studies from the Susan G. Komen Breast Cancer Foundation show that a mammogram can accurately detect cancer 87% of the time[xxiii]. The use of reminders in a physician's EHR has been associated with an increase in compliance with recommended guidance around mammograms[xxiv]. Electronic prescription systems have also been effective in identifying and preventing potential drug-drug interactions and adverse events, with one study estimating that compared to paper charts, the use of a computerized prescription system with built in clinical decision support resulted in half as many preventable adverse events and half as many medication errors[xxv]. Computer-based decision support tools have a wide range of other applications for

streamlining and improving healthcare[xxvi]. They can improve antimicrobial stewardship[xxvii] thereby reducing the likelihood of multidrug resistance or other sequelae of antibiotic overuse, and also improve vaccine uptake[xxviii], a critical need in the era of a pandemic.

These data are not only used by providers for decision support. When patients have access to their own healthcare data via patient portals, recent data suggest that about 30% of patients log into these applications at least once, and of these, 2/3 accessed their patient portals six or more times during the year[xxix]. This underscores the utility of healthcare data across the spectrum of care.

The healthcare data discussed so far are derived from tests ordered and interpreted by a physician or other healthcare provider. However, there is also an increasing trend of patients initiating their own data collection outside of what is collected by their providers. Companies like Ulta Lab Services[xxx] and PersonaLabs[xxxi] offer direct to consumer laboratory testing. Invitae[xxxii], Genesight[xxxiii], and GRAIL[xxxiv] alongside companies like 23andMe[xxxv] and AncestryDNA[xxxvi] offer direct to consumer genetic testing. The direct-to-consumer lab market in the US is expected to grow from $3.7B in 2022 to $21.6B in 2032[xxxvii].

On top of this, millions of patients have invested their money in wearables aimed at improving their health. The wearable device market was estimated to be $138 Billion in 2022 and expected to grow to close to $500 billion over the next 10 years[xxxviii]. A recent analysis highlighted that nearly 35% of iPhone users in the US also wear an Apple Watch, and in 2021 Apple eclipsed the 100 million wrist mark[xxxix]. Adding on the number of patients using other wearable devices from Garmin, Fitbit/Google, Amazon, and other manufacturers underscore the massive amount of health data being collected daily. Patients are now able to monitor their own heart rate, cardiovascular fitness, oxygen saturation, sleep, nutrition, hydration, and exercise.

Finally, data are also collected for informational purposes, largely via wearable devices, are beginning to lead to new diagnoses and treatments. One example of this is the algorithm, now a standard part of the

Apple Watch, for detecting irregular heart rate that may be atrial fibrillation. In a 2019 study by Perez, the team found that approximately 0.52% of Apple Watch wearers received an irregular pulse alert[xl]. Of the people who receive an irregular pulse, 57% visit their HCP for further assessment.

Provider Outcomes

Healthcare data have good outcomes for providers when they lead to higher quality or more efficient patient care, when it increases provider satisfaction and when the use of data generation and storage leads to additional revenue.

Emerging diagnostics and other tests that leverage precision medicine can allow physicians to identify specific disease types and subtypes for patients with cancer, immunological disorders, rare diseases, and others. This precision medicine paradigm requires data generation and interpretation on an unprecedented scale.

Physician satisfaction is directly impacted by whether they believe they and their practice are providing high quality care. Physicians also perceive EHRs and data collection as facilitating high quality care[xli].

Based on common narratives in health care there are at least four ways in which data may improve physician revenue: 1) by increasing the number of patients that can be seen in a day, 2) by increasing the revenue per visit using revenue cycle management systems and services, 3) by enabling physicians to participate in risk-based agreements, and 4) by direct data monetization. Of the four, the only one of these benefits that can be substantiated with evidence is the strong positive benefit on revenue cycle billing and enhanced coding, with an impact on the unpaid or underpaid claims and point-of-service collection opportunities[xlii, xliii, xliv]. While much of the benefit here appears to be anecdotal, some studies quantify this increased revenue at approximately 3,000/provider/quarter[xlv]. In reviewing participation in risk-based programs, studies show that most HCPs participating in these programs showed either mixed positive/negative results or no impact whatsoever for the HCP[xlvi].

Finally, the most direct financial benefit to providers anticipated is in the potential for higher revenue due to direct monetization of their deidentified data, but there is no evidence of widespread direct HCP impact[xlvii]. The revenue from data licenses seems to accrue to health systems, government entities, and data brokers[xlviii].

Pharma Outcomes

Healthcare data are useful for pharmaceutical companies when they help them to bring new medications to the market. This means that the data must help to discover new assets, to develop those assets via a clinical development program leading to regulatory approval, and to ensure that those approved medicines are reimbursed by private and public payers, a body of work generally known as access. These data are used in research by pharmaceutical companies and others as secondary data and referred to as real-world data (RWD) and any evidence generated using those data are real world evidence (RWE)[xlix].

In recent years, there has been an increase in the use of healthcare data to inform the drug discovery process. Insights generated from RWD are used to guide pipeline and portfolio strategy, for example by informing the development of target product profiles with RWD-informed estimates of incidence and prevalence. Molecular and clinicogenomic RWD can be used to understand viral genomics, antigenic targets, and to generate hypotheses about resistance to common cancer drugs[l].

RWE holds potential for saving both time and money in development activities by making clinical trials more efficient (clinical trial setup, label expansions, post market surveillance). The US Federal Drug Administration (FDA), European Medicines Agency (EMA) and several other regulating bodies have issued guidance on the use of RWE as part of regulatory submissions[li]. The EMA has taken this a bit further via its Data Analysis and Real World Interrogation Network (DARWIN EU) initiative. DARWIN EU is an industry first initiative where a regulator will sponsor the generation of its own RWE[lii].

The most established use of real-world healthcare data by pharmaceutical companies is in access. Eighty six percent of health technology agencies in the European Network for Health Technology Assessment (EUnetHTA) reported accepting RWD, specifically in the form of patient registries[liii]. The FDA has accepted RWE for post approval commitments since 1998 and the EMA since 2007[liv]. In many cases, these health technology assessments (HTAs) and postmarketing commitments would be impossible or prohibitively expensive to carry out via a randomized control trial (RCT).

Drug or Other Toxicity

Toxicity is defined as the unintended negative consequences from the generation, collection and use of healthcare data.

Patient Toxicity

Toxicity resulting from the generation and capture of healthcare data about specific patients includes risk of data breaches or other loss of privacy, potential for inaccurate data, and denial of benefits due to certain high-risk or pre-existing conditions identified in the data.

With regard to data breaches, a 2022 analysis recognized that there were more than 1,800 cases of compromised data reported in the US alone[lv]. A separate 2022 news article by Onclave Networks states that stolen healthcare records account for the overwhelming majority of identity theft sources[lvi]. The probability of a data breach at a hospital is roughly 3% per year[lvii] and over 380 million healthcare records have been disclosed by breach in the last 15 years.[lviii].

In October 2023, 23andMe reported that they had experienced a data breach in an attack specifically targeting Ashkenazi Jews[lix]. However, not all privacy risk is related to a breach. In early 2023, Vanderbilt University provided the state of Tennessee access to the healthcare records for their transgender patients in response to newly passed laws criminalizing some gender affirming care[lx]. In both cases,

patients who were seeking healthcare or information about their health provided sensitive information with a certain expectation of privacy that the holders of their health care data were not able to meet.

Some patients choose to opt out of sharing their data. Those in certain geographies including NHS patients in the UK and patients in the states of Oregon and California can opt out of sharing their data with researchers. When patients are given the option to opt out of this data sharing, 3%-21% of patients choose to do so[lxi].

In the case of inaccurate conclusions based on analyzed data, as an example for wearable devices, false positive alerts are common. In the atrial fibrillation example for Apple Watch, only 36% of patients who sought medical care after seeing an abnormal heart rate alert were referred for follow up. Because of this, it can be deduced that HCP did not recommend further testing or review for the remaining 64%[lxii]. Other diagnostic tests have limitations in diagnostic accuracy – and development of new tests is difficult as computation of accuracy necessitates a gold standard. Sometimes that gold standard can be worse than the new test. Further clinical decision making may also be error prone as repeated experiments using autopsy, case report, and self-report from patients and providers indicate that 10%-15% of diagnoses are incorrect[lxiii],[lxiv]

The final unintended consequence of healthcare data collection is related to denial of benefits or services based on that information. Current laws including the Genetic Information Nondiscrimination Act (GINA), the Affordable Care Act, and the Healthcare Information Portability and Accountability Act (HIPAA) prohibit health insurance companies from denying coverage due to genetic factors and other pre-existing conditions, the same protections do not apply to life or disability insurance, and patients with certain genetic conditions may find themselves unable to obtain these policies[lxv].

Provider Toxicity

The primary unintended consequences of healthcare data collection to healthcare providers are burnout and the potential impact of a data breach.

The level of data collection, technology use, and the use of EHRs are correlated to provider burnout[lxvi],[lxvii]. A study in the *Annals of Internal Medicine* identified that the annual rate of turnover of physicians increased by 43% (from 5.3% annual to 7.6% annual) from 2010 to 2018 with referenced studies suggesting an association with enhanced EHR use and burnout[lxviii]. A study of 155,000 physicians and approximately 100 million encounters found that physicians spend an average of 16 minutes and 14 seconds per encounter working the EHR[lxix]. Repeatedly, data collection and entry burden of EHRs is identified as a top contributor to physician burnout[lxx] . The burden of data collection is high enough that some physicians now work with scribes, a member of the care team dedicated to entering all relevant data and information into the EHR[lxxi].

A study published in *Healthcare* (Basel) covers the risk of a data breach for HCPs. From 2005 to 2019, healthcare service providers made up over 61% of all data breaches reported in the Privacy Rights Clearinghouse (PRC) database. In the last 5 years of this period (2015-2019), healthcare service providers make up nearly 77% of all data breaches in the PRC Database[lxxii]. If a healthcare provider in the US suffers a significant breach of their data, media attention will follow, and they may be required to offer remediation to patients and pay fines that can be as high as $10,000 per element of PHI. In some cases, they may even face criminal prosecution[lxxiii].

Between 2016 and 2021, the number of annual ransomware attacks targeting healthcare facilities in the US doubled, from 43 to 91. Data for 42 million patients were exposed and 44% of attacks resulted in a disruption to healthcare[lxxiv].

Pharma Toxicity

The key toxicity related to healthcare data use for RWE is the bias that is inherent in RWE generation using secondary healthcare data. The primary use of RWD is day to day delivery of healthcare, not research. When RWE generation protocols are constructed, an attempt is made to identify all potential biases and to use appropriate methodologies to mitigate or correct for those biases. However, it is not always possible to fully eliminate or address all bias in a real-world dataset[lxxv].[lxxvi] The largest bias is likely the most difficult to remedy – that patients must seek care to have any data collected. Given there are major socioeconomic and other factors that drive healthcare access and availability, selection bias in who's data are available is paramount.

Next, we will consider the impact of inaccurate data or inaccurate conclusions based on analyzed data. Data quality is one of the most important considerations when evaluating a data source for generation of RWE. If inaccurate, missing, or other biased data are used for any analysis, the results of that analysis may be biased or wrong. Without data quality assurance (obtaining correct data at the source) and data quality control (fixing any inaccuracies found after collection) plans in place, the quality of any evidence generated could be compromised.

RCT-DUPLICATE, an FDA funded study to test whether using RWE would have led to the same regulatory decisions as RCTs, showed that there are some populations where real world evidence is consistently unable to duplicate the results from RCTs[lxxvii]. It is common for the FDA to decline to consider RWE because they do not believe they can interpret the results[lxxviii].

Cost

For this analysis, the cost of generating and storing healthcare data, including the costs of building and maintaining systems for protecting and working with the data, are considered.

Patient Cost

In 2019, Medicare Part B, which covers about 25% of Americans, spent $7.7B on lab tests[lxxix]. Additionally, patients are expected to spend an additional $3.6B[lxxx] in 2023 on direct to patient laboratory testing, and 39% of Americans own a wearable device[lxxxi] with the latest Apple Watch costing $399 or more[lxxxii]. In addition to money, patients often must invest significant time to receive a diagnosis. The average time from disease onset to diagnosis 6.3 years for type 2 diabetes[lxxxiii] and 2.1 years for multiple sclerosis[lxxxiv].

Provider Cost

For healthcare providers, the costs to perform enhanced data gathering and utilization are significant. They include the cost to invest or upgrade core systems to allow for this data gathering and required related training. Physicians also bear the burden and accountability for data collection as well as the accuracy of the data.

Initial costs for implementation (per physician) of an EHR considering licensing, training, and lost time range from $15,000 – $75,000 for small practices[lxxxv],[lxxxvi],[lxxxvii]. After the first year, ongoing maintenance (upgrades, hardware, software) may run between $4,000 – $17,100 per physician[lxxxviii].

Physicians are accountable for the data in a medical record. In the US and many other geographies, the medical record is considered a legal document[lxxxix]. Per US malpractice law, physicians are also accountable for appropriately reacting to any data in the record in a timely manner[xc]. As the amount and complexity of data grow, physicians have begun to adopt clinical decision support systems to help them with knowledge management[xci]. However, there is some indication that these systems may add to physician burnout due to the sheer number of alerts generated[xcii]. In fact, the complexities in some decision support tools have led to separate applications to help fine tune any alerts so they do not overwhelm providers and the most important alerts remain actionable[xciii].

Pharma Costs

The costs for pharmaceutical companies can be spread over multiple categories including the cost to license data, to standardize and harmonize data, and the cost to execute RWE and insight generation using the data.

With respect to the costs to license data, a paper published in the *Clinical Pharmacology & Therapeutics* journal stated that the costs vary. Specifically, "annual licenses for large, closed network, third-party, private payer claims data in the United States generally costing $100k–300k per therapeutic area (TA), or $400k–$800k for all TAs, structured EHR data costing $1–3 million per TA, and specialty unstructured EHR data requiring extensive curation costing $3–5 million per TA. (Dagenais, et al 2021)"

The FDA and EMA have both issued guidance to help guide the process of using healthcare data to generate evidence about the efficacy and safety of medicines[xciv]. This includes steps to validate all exposures, endpoints, and covariates, the creation of an audit trail so that all data can be traced back to the medical record where it was captured, and full pre-specification of protocols and statistical analysis plans[xcv]. There is enough complexity in the use of RWD and generation of subsequent RWE that most large pharmaceutical companies have teams dedicated to working with real world healthcare data.

Value

In the final section of the analysis, insights about the effectiveness, toxicity and cost of healthcare data generation, collection, and storage will be combined to help understand the value of the data to the patient, provider, and pharmaceutical company stakeholders.

Patient Value

When healthcare data are generated and results in a correct and effective diagnosis and treatment plan, those data are beneficial for patients. Approximately 30% of patients will regularly access their healthcare data via patient portals, hundreds of millions of people have purchased and use wearable

devices that collect healthcare data, and a small but growing set of patients are willing to invest their own money in direct-to-consumer testing[xcvi]. As discussed previously, the benefits associated with these data collection activities are not without risk. Given that healthcare records are breached, data are exposed and sold on the open market, and these breaches lead to identity theft, it is reasonable to be concerned as a patient. Patients are further concerned with privacy even when posed with the option to share data through established and trusted channels, where 1 in 10 patients opt to exclude their data from sharing. There are likely several competing priorities leading to these privacy concerns among patients. From misunderstanding, to lack of trust, history of being targeted by data breeches, or a past benefit from data sharing, it appears that data collection/sharing has more value for some patients than for others.

Provider Value

In light of our prior discussion, the authors conclude that of all stakeholders in this analysis, providers see the least value from healthcare data generation. This may be due to the large burden of data collection that is borne by physicians and the rest of the care team. While there is certainly value to providers in the large data collection systems that have been established in healthcare, there is also a significant burden for physicians and other members of the care team. This burden entails ensuring that the correct data are captured accurately at the point of care, especially when attempting to make diagnoses or treatment decisions.

When companies that manufacture EHRs are working with their clients to design new features and improve their systems, they frequently work to minimize the number of clicks required for a specific action. Continuing to lean into this mentality and to automate as much data collection as possible could help to reduce burden over time. Those designing data collection systems can also ensure that there is a clear need and use for all data they are asking providers to enter in their systems.

The explosion of data collection and subsequent evidence generation is leading to information overload for physicians[xcvii]. There is a call for the development of new tools to help physicians extract important new evidence from the literature and use that evidence to help their patients. Applications like Up To Date[xcviii] bring current relevant evidence for specific patients directly to physicians, often within their EHR so physicians never have to click away from their core workflow application. In oncology, key guidelines from National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) and others are frequently digitized and made available in the EHR[xcix]. Other applications require the physician to navigate away from their EHR and interact with a second application. This can be effective but adds a significant burden for providers[c].

Novel data generation introduces special challenges for physicians. When physicians order genetic sequencing tests, some are unsure how to interpret the resulting report[ci]. In a new extension of this problem, the Association of Community Cancer Centers (ACCC) in early 2023 launched an initiative to help providers develop a workflow for managing the case when patients arrived at an oncology practice having taken a multi cancer early detection test, such as GRAIL's, which indicated they had cancer[cii]. This was unprecedented as these sorts of tests were only recently approved for use and are generally still only available to patients willing to pay out of pocket[ciii].

Pharma Value

While it would be impossible for patients and providers to avoid interacting with real world health care data, pharmaceutical companies only use healthcare data to the extent that they see value in doing so. For pharmaceutical companies, the value of data are in what insights can be generated from them.

Pharmaceutical companies use RWD to generate RWE, which inform internal scientific and business decisions as well as generate new knowledge for scientific discovery.

Insights from data analyses are generally used for risk reduction. Assumptions about key variables like incidence and prevalence of a disease or common current treatment patterns can be double checked using RWD to ensure that they are correct. RWD makes a good complement to data generated via an RCT because the population of patients enrolled in an RCT are rarely an exact match for the population of patients who are prescribed the medication in the real world.

Evidence is generated to further the scientific understanding of a disease or it's treatment. Because it is relatively less expensive to develop evidence using RWD as compared with research that requires primary data collection such as an RCT, a more comprehensive evidence package can be generated with RWD so long as the research questions are appropriate for real world study[civ].

Discussion

In the sections above, ways in which healthcare data has value for patients, providers, and pharmaceutical companies as well as the ways in which healthcare data can be costly or even dangerous are outlined. Four main domains hold the keys to increase the value of healthcare data. First, data security should be improved, and only data that are useful for the patient and provider should be collected. Second, Health IT systems should embrace good user experience design along with true interoperability to reduce the burden on healthcare providers collecting the data. Third, all healthcare data should be collected with sufficient metadata, provenance, and data quality standards to allow it to be used for regulatory purposes. Finally, there should be mechanisms throughout the data lifecycle that allow all stakeholders to identify and (in the case of patient and provider) to correct any errors.

The value of data are in what can be done with them. A patient can get a diagnosis. A physician can make the right treatment choice. And a pharmaceutical company can discover a new medicine and safely bring it to market to improve the health of the patient. This is not linear, however. Each aspect has interplays with the others and the cycle is continuous. Once the medication is on the market and the

patient is taking it, data are used to monitor its effectiveness and ensure it remains the most effective and safe choice.

REFERENCES

[i] Chute, C.G. Crossing the chasm of semantic despair: integrating knowledge and data from science and clinical practice. Clinical Research Forum – IT Roundtable, Washington DC < https://cdn.ymaws.com/sites/crforum.site-ym.com/resource/resmgr/docs/IT_Roundtable/CRF_IT_Roundtable_3Nov2017re.pdf> (November 2, 2017). Accessed October 13, 2023.

[ii] Overhage JM, Ryan PB, Reich CG, Hartzema AG, Stang PE. Validation of a common data model for active safety surveillance research. J Am Med Inform Assoc. 2012;19(1):54-60. doi:10.1136/amiajnl-2011-000376

[iii] Kirby C, Ambros PF, Billiter D, et al. Development of an open-source, flexible framework for complex inter-institutional disparate data sharing and collaboration. AMIA Jt Summits Transl Sci Proc. 2013;2013:103. Published 2013 Mar 18.

[iv] Koppel R. Patient Safety and Health Information Technology: Learning from Our Mistakes. PSNet Accessed October 8, 2023. https://psnet.ahrq.gov/perspective/patient-safety-and-health-information-technology-learning-our-mistakes

[v] Klefsjö, B., Wiklund, H. and Edgeman, R.L. (2001), "Six sigma seen as a methodology for total quality management", Measuring Business Excellence, Vol. 5 No. 1, pp. 31-35. https://doi.org/10.1108/13683040110385809

[vi] Kent J. Poor Data Quality, Weak Algorithms Lead to Patient Matching Issues. Health IT Analytics. February 13, 2020. Accessed October 13, 2023.

[vii] Chander A, Abraham M, Chandy S, Fang Y, Park D, Yu I. Achieving Privacy: Costs of Compliance and Enforcement of Data Protection Regulation. Georgetown Law Faculty Publications and Other Works. 2374. March 03, 2021. Accessed October 13, 2023. https://scholarship.law.georgetown.edu/facpub/2374

[viii] Powell K, Alexander G. Mitigating Barriers to Interoperability in Health Care: OJNI. On - Line Journal of Nursing Informatics 2019;23(2)-6.

[ix] Seeman J. JULY 2022 HL7® FHIR® CONNECTATHON 3. U.S. Centers for Medicare & Medicaid Services. May 10, 2022. Accessed October 13, 2023. https://www.youtube.com/watch?v=ReiQFzodp_A

[x] Honavar SG. Electronic medical records - The good, the bad and the ugly. Indian J Ophthalmol. 2020;68(3):417-418. doi:10.4103/ijo.IJO_278_20

[xi]'Office-based Physician Electronic Health Record Adoption,' Health IT Quick-Stat #50. Office of the National Coordinator for Health Information Technology. Accessed September 29, 2023. https://www.healthit.gov/data/quickstats/office-based-physician-electronic-health-record-adoption.

[xii] McMillan B, Eastham R, Brown B, Fitton R, Dickinson D. Primary Care Patient Records in the United Kingdom: Past, Present, and Future Research Priorities. J Med Internet Res. 2018;20(12):e11293. Published 2018 Dec 19. doi:10.2196/11293

[xiiixiii] Roos, L. L., Nicol, J. P., Johnson, C. F., & Roos, N. P. (1979). Using Administrative Data Banks for Research and Evaluation: A Case Study. Evaluation Quarterly, 3(2), 236-255. https://doi.org/10.1177/0193841X7900300204

[xiv] Ash A, Porell F, Gruenberg L, Sawitz E, Beiser A. Adjusting Medicare capitation payments using prior hospitalization data. Health Care Financ Rev. 1989;10(4) 17-29.

[xv] Keeler EB, Manning WG, Newhouse JP, Sloss EM, Wasserman J. The external costs of a sedentary life-style. Am J Public Health. 1989 Aug;79(8):975-81. doi: 10.2105/ajph.79.8.975.

[xvi] Tanner A. How Data Brokers Make Money Off Your Medical Records. February 1, 2016. Accessed September 29, 2023. https://www.scientificamerican.com/article/how-data-brokers-make-money-off-your-medical-records/

[xvii] Protecting Consumer Privacy in an Era of Rapid Change: Recommendations For Businesses and Policymakers. Federal Trade Commission. March, 2012. Accessed September 29, 2023. https://www.ftc.gov/reports/protecting-consumer-privacy-era-rapid-change-recommendations-businesses-policymakers

[xviii] Safran C, Bloomrosen M, Hammond WE, et al. Toward a national framework for the secondary use of health data: an American Medical Informatics Association White Paper. J Am Med Inform Assoc. 2007;14(1):1-9. doi:10.1197/jamia.M2273

[xix] Bryant K, Knowles M, Krasniansky A, Day S, Evans B, Somaiya M, Suresh U. 2022 year-end digital health funding: Lessons at the end of a funding cycle. Rock Health. January 9, 2023. Accessed September 29, 2023. https://rockhealth.com/insights/2022-year-end-digital-health-funding-lessons-at-the-end-of-a-funding-cycle/

[xx] Samuel C, Kim E, Hosein A, Moritz C, Novello M, Swisher S, Brooks M, Lowe K, Tantameng C, Collins B, Amoroso A, Henry M. Medicare Part B Spending on Lab Tests Increased in 2021, Driven By Higher Volume of COVID-19 Tests, Genetic Tests, and Chemistry Tests. U.S. Department of Health and Human Services Office of Inspector General. December 19, 2022. OEI-09-22-00400. Accessed September 29, 2023. https://oig.hhs.gov/oei/reports/OEI-09-22-00400.asp

[xxi] Rohr UP, Binder C, Dieterle T, Giusti F, Messina CG, Toerien E, et al. The Value of In Vitro Diagnostic Testing in Medical Practice: A Status Report. PLoS One. 2016;11:e0149856.

[xxii] Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Guideline Name V.4.2023. © National Comprehensive Cancer Network, Inc. 202X. All rights reserved. Accessed October 10, 2023. To view the most recent and complete version of the guideline, go online to NCCN.org.

[xxiii] Siu AL; U.S. Preventive Services Task Force. Screening for Breast Cancer: U.S. Preventive Services Task Force Recommendation Statement [published correction appears in Ann Intern Med. 2016 Mar 15;164(6):448]. Ann Intern Med. 2016;164(4):279-296. doi:10.7326/M15-2886

[xxiv] Siembida EJ, Radhakrishnan A, Nowak SA, Parker AM, Pollack CE. Linking Reminders and Physician Breast Cancer Screening Recommendations: Results From a National Survey. JCO Clin Cancer Inform. 2017;1:1-10. doi:10.1200/CCI.17.00090

[xxv] Nuckols TK, Smith-Spangler C, Morton SC, et al. The effectiveness of computerized order entry at reducing preventable adverse drug events and medication errors in hospital settings: a systematic review and meta-analysis. Syst Rev. 2014;3:56. Published 2014 Jun 4. doi:10.1186/2046-4053-3-56

[xxvi] Sutton, RT, Pincock, D, Baumgart, DC et al. An overview of clinical decision support systems: benefits, risks, and strategies for success. npj Digit. Med. 2020;3:17. doi:10.1038/s41746-020-0221-y

[xxvii] Patrick E. Beeler, Stefan P. Kuster, Emmanuel Eschmann, Rainer Weber, Jürg Blaser, Earlier switching from intravenous to oral antibiotics owing to electronic reminders, International Journal of Antimicrobial Agents. 2015;46:4. doi: 10.1016/j.ijantimicag.2015.06.013.

[xxviii] Shrader L, Myerburg S, Larson E. Clinical Decision Support for Immunization Uptake and Use in Immunization Health Information Systems. *Online J Public Health Inform*. 2020;12(1):e10. Published 2020 Jul 24. doi:10.5210/ojphi.v12i1.10602

[xxix] Johnson C, Richwine C, & Patel V. Individuals' Access and Use of Patient Portals and Smartphone Health Apps, 2020. ONC Data Brief, no.57. Office of the National Coordinator for Health Information Technology: Washington DC. September, 2021. Accessed September 29, 2023. https://www.healthit.gov/data/data-briefs/individuals-access-and-use-patient-portals-and-smartphone-health-apps-2020

[xxx] Ulta Lab Tests. Accessed October 07, 2023. https://www.ultalabtests.com/

[xxxi] PERSONALABS. Accessed October 07, 2023. https://www.personalabs.com/

[xxxii] Invitae. Accessed October 07, 2023. https://www.invitae.com/

[xxxiii] GENESight. Accessed October 07, 2023. https://genesight.com/

[xxxiv] Grail. Accessed October 07, 2023. https://grail.com/

[xxxv] 23andMe. Accessed October 07, 2023. https://www.23andme.com/

[xxxvi] AncestryDNA. Accessed October 07, 2023. https://www.ancestry.com/dna/

[xxxvii] Direct to Consumer Laboratory Testing Market. Precedence Research. October, 2023. Accessed October 08, 2023. https://www.precedenceresearch.com/direct-to-consumer-laboratory-testing-market

[xxxviii] Wearable Technology Market. Precedence Research. September, 2023. Accessed October 08, 2023. https://www.precedenceresearch.com/wearable-technology-market

[xxxix] Cybart N. Apple Watch Is Now Worn on 100 Million Wrists. Above Avalon. February 11, 2021. Accessed October 08, 2023. https://www.aboveavalon.com/notes/2021/2/11/apple-watch-is-now-worn-on-100-million-wrists

[xl] Perez MV, Mahaffey KW, Hedlin H, et al. Large-Scale Assessment of a Smartwatch to Identify Atrial Fibrillation. N Engl J Med. 2019;381(20):1909-1917. doi:10.1056/NEJMoa1901183

[xli] Friedberg MW, Chen PG, Van Busum KR, et al. Factors Affecting Physician Professional Satisfaction and Their Implications for Patient Care, Health Systems, and Health Policy. Rand Health Q. 2014;3(4):1. Published 2014 Dec 1.

[xlii] LaPointe, J. Hospitals Looking Beyond EHR to Improve Revenue Cycle Performance. Revcycle Intelligence. September 25, 2019. Accessed September 15, 2023. https://revcycleintelligence.com/news/hospitals-looking-beyond-ehr-to-improve-revenue-cycle-performance

[xliii] Are you ready to stop the bleeding of lost revenues? James Moore. Accessed September 15, 2023. https://www.jmco.com/business-advisory/revenue-cycle-enhancement/

[xliv] Tierney, G. MD, Smith, C. FHFMA, MS, CIA, CISA, CFE, Wilberg, E. MBA, CHFP. Case Study: Physician Revenue Cycle Improvements in an Integrated Health System. History of the Healthcare Financial Management Association. March 03, 2017. Accessed September 15, 2023. https://www.hfma.org/revenue-cycle/physician-group-revenue-cycle/53128/

[xlv] Howley MJ, Chou EY, Hansen N, Dalrymple PW. The long-term financial impact of electronic health record implementation. J Am Med Inform Assoc. 2015;22(2):443-452. doi:10.1136/amiajnl-2014-002686

[xlvi] Leao DLL, Cremers HP, van Veghel D, Pavlova M, Groot W. The Impact of Value-Based Payment Models for Networks of Care and Transmural Care: A Systematic Literature Review. Appl Health Econ Health Policy. 2023;21(3):441-466. doi:10.1007/s40258-023-00790-z

[xlvii] Healthcare Data Monetization Market by Type (Direct, Indirect), Deployment (On-premise, Cloud), End User (Pharmaceutical & Biotechnology Companies, Healthcare Payers, Healthcare Providers, Medical Technology Companies), Region - Global Forecast to 2028. Markets and Markets. June 2023. Accessed September 15, 2023. https://www.marketsandmarkets.com/Market-Reports/healthcare-data-monetization-market-56622234.html

[xlviii] Tanner A. How Data Brokers Make Money Off Your Medical Records. February 1, 2016. Accessed September 29, 2023. https://www.scientificamerican.com/article/how-data-brokers-make-money-off-your-medical-records/

[xlix] Dagenais S, Russo L, Madsen A, Webster J, Becnel L. Use of Real-World Evidence to Drive Drug Development Strategy and Inform Clinical Trial Design. Clin Pharmacol Ther. 2022;111(1):77-89. doi:10.1002/cpt.2480

[l] Dagenais S, Russo L, Madsen A, Webster J, Becnel L. Use of Real-World Evidence to Drive Drug Development Strategy and Inform Clinical Trial Design. Clin Pharmacol Ther. 2022;111(1):77-89. doi:10.1002/cpt.2480

[li] National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Health Sciences Policy; Shore C, Gee AW, Kahn B, et al., eds. Examining the Impact of Real-World Evidence on Medical Product Development: Proceedings of a Workshop Series. Washington (DC): National Academies Press (US); February 6, 2019.

[lii] Darwin-Eu. Accessed Oct 08, 2023. https://www.darwin-eu.org/

[liii] Hogervorst MA, Pontén J, Vreman RA, Mantel-Teeuwisse AK, Goettsch WG. Real World Data in Health Technology Assessment of Complex Health Technologies. Front Pharmacol. 2022;13:837302. Published 2022 Feb 10. doi:10.3389/fphar.2022.837302

[liv] Mofid S, Bolislis WR, Kühler TC. Real-World Data in the Postapproval Setting as Applied by the EMA and the US FDA. Clin Ther. 2022;44(2):306-322. doi:10.1016/j.clinthera.2021.12.010

[lv] Petrosyan A. Cyber crime: number of compromises and impacted individuals in U.S. 2005-2022. Statista. August 29, 2023. Accessed October 08, 2023.

[lvi] Largest Healthcare Data Breaches Reported in February 2022 Confirms Need for Network Security Based on Zero Trust Microsegmentation. Globe Newswire. March 31, 2022. Accessed September 30, 2023. https://www.globenewswire.com/en/news-release/2022/03/31/2413675/0/en/Largest-Healthcare-Data-Breaches-Reported-in-February-2022-Confirms-Need-for-Network-Security-Based-on-Zero-Trust-Microsegmentation.html.

[lvii] Muoio, D. Hospitals' risk of data breach doubles just before, after a merger deal, research shows. Fierce Healthcare. Fierce Healthcare. August 07, 2023. Accessed September 15, 2023. https://www.fiercehealthcare.com/providers/hospitals-risk-data-breach-doubles-just-after-merger-deal-research-shows

[lviii] Pascual A. 2013 Identity Fraud Report: Data Breaches Becoming a Treasure Trove for Fraudsters. Javelin Strategy. February 20, 2013. Accessed September 30, 2023. https://javelinstrategy.com/research/2013-identity-fraud-report-data-breaches-becoming-treasure-trove-fraudsters

[lix] Newman L. 23andMe User Data Stolen in Targeted Attack on Ashkenazi Jews. Wired. October 06, 2023. Accessed October 08, 2023. https://www.wired.com/story/23andme-credential-stuffing-data-stolen/

[lx] Hospital turns over transgender patient records to Tennessee attorney general in investigation. Associated Press. June 20, 2023. Accessed October 08, 2023. https://apnews.com/article/transgender-youth-records-vanderbilt-tennessee-4a4e7d846cfb05ed6feefc7deef24ef1

[lxi] de Man Y, Wieland-Jorna Y, Torensma B, et al. Opt-In and Opt-Out Consent Procedures for the Reuse of Routinely Recorded Health Data in Scientific Research and Their Consequences for Consent Rate and Consent Bias: Systematic Review. J Med Internet Res. 2023;25:e42131. Published 2023 Feb 28. doi:10.2196/42131

[lxii] Feldman K, Duncan RG, Nguyen A, et al. Will Apple devices' passive atrial fibrillation detection prevent strokes? Estimating the proportion of high-risk actionable patients with real-world user data. J Am Med Inform Assoc. 2022;29(6):1040-1049. doi:10.1093/jamia/ocac009

[lxiii] Graber ML. The incidence of diagnostic error in medicine. BMJ Qual Saf. 2013;22 Suppl 2(Suppl 2):ii21-ii27. doi:10.1136/bmjqs-2012-001615

[lxiv] Leape LL, Berwick DM, Bates DW. Counting Deaths Due to Medical Errors—Reply. *JAMA.* 2002;288(19):2405. doi:10.1001/jama.288.19.2405-JLT1120-2-3

[lxv] Seaver LH, Khushf G, King NMP, et al. Points to consider to avoid unfair discrimination and the misuse of genetic information: A statement of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2022;24(3):512-520. doi:10.1016/j.gim.2021.11.002

[lxvi] Jankovic I, Chen JH. Clinical Decision Support and Implications for the Clinician Burnout Crisis. Yearb Med Inform. 2020;29(1):145-154. doi:10.1055/s-0040-1701986

[lxvii] National Academies of Sciences, Engineering, and Medicine. Chapter 6: Factors Contributing to Clinician Burnout and Professional Well-Being. In: National Academies of Sciences, Engineering, and Medicine. Taking Action Against Clinician Burnout: A Systems Approach to Professional Well-Being. Washington, DC: The National Academies Press; 2019:170-171.

[lxviii]Bond AM, Casalino LP, Tai-Seale M, et al. Physician Turnover in the United States. Ann Intern Med. 2023;176(7):896-903. doi:10.7326/M22-2504.

[lxix] Overhage JM, McCallie D Jr. Physician Time Spent Using the Electronic Health Record During Outpatient Encounters: A Descriptive Study [published correction appears in Ann Intern Med. 2020 Oct 6;173(7):596]. Ann Intern Med. 2020;172(3):169-174. doi:10.7326/M18-3684

[lxx]Robertson SL, Robinson MD, Reid A. Electronic Health Record Effects on Work-Life Balance and Burnout Within the I3 Population Collaborative. J Grad Med Educ. 2017;9(4):479-484. doi:10.4300/JGME-D-16-00123.1.

[lxxi] Corby S, Ash JS, Mohan V, et al. A qualitative study of provider burnout: do medical scribes hinder or help?. JAMIA Open. 2021;4(3):ooab047. Published 2021 Aug 12. doi:10.1093/jamiaopen/ooab047

[lxxii] Seh AH, Zarour M, Alenezi M, et al. Healthcare Data Breaches: Insights and Implications. Healthcare (Basel). 2020;8(2):133. Published 2020 May 13. doi:10.3390/healthcare8020133

[lxxiii] Breach Notification Rule. U.S. Department of Health and Human Services. Accessed October 08, 2023. https://www.hhs.gov/hipaa/for-professionals/breach-notification/index.html

[lxxiv] Neprash HT, McGlave CC, Cross DA, et al. Trends in Ransomware Attacks on US Hospitals, Clinics, and Other Health Care Delivery Organizations, 2016-2021. *JAMA Health Forum.* 2022;3(12):e224873. doi:10.1001/jamahealthforum.2022.4873

[lxxv] Jarada TN, O'Sullivan DE, Brenner DR, Cheung WY, Boyne DJ. Selection Bias in Real-World Data Studies Used to Support Health Technology Assessments: A Case Study in Metastatic Cancer. Curr Oncol. 2023;30(2):1945-1953. Published 2023 Feb 6. doi:10.3390/curroncol30020151

[lxxvi] Agarwal P, Moshier E, Ru M, et al. Immortal Time Bias in Observational Studies of Time-to-Event Outcomes: Assessing Effects of Postmastectomy Radiation Therapy Using the National Cancer Database. Cancer Control. 2018;25(1):1073274818789355. doi:10.1177/1073274818789355

[lxxvii] Franklin JM, Patorno E, Desai RJ, et al. Emulating Randomized Clinical Trials With Nonrandomized Real-World Evidence Studies: First Results From the RCT DUPLICATE Initiative. Circulation. 2021;143(10):1002-1013. doi:10.1161/CIRCULATIONAHA.120.051718
[lxxviii] Purpura CA, Garry EM, Honig N, Case A, Rassen JA. The Role of Real-World Evidence in FDA-Approved New Drug and Biologics License Applications. Clin Pharmacol Ther. 2022;111(1):135-144. doi:10.1002/cpt.2474
[lxxix] Office of Inspector General. Despite Savings on Many Lab Tests in 2019, Total Medicare Spending Increased Slightly Because of Increased Utilization for Certain High-Priced Tests. Accessed October 10, 2023. https://oig.hhs.gov/oei/reports/OEI-09-20-00450.pdf
[lxxx] Direct to Consumer Laboratory Testing Market. Precedence Research. October, 2023. Accessed October 08, 2023. https://www.precedenceresearch.com/direct-to-consumer-laboratory-testing-market
[lxxxi] Tracking Wearable Tech Trends in the USA. M&C SAATCH PERFORMANCE. November 02, 2021. Accessed October 08, 2023. https://www.mcsaatchiperformance.com/news/tracking-wearable-tech-trends-in-the-usa/
[lxxxii] Watch - Apple. Accessed October 08, 2023. https://www.apple.com/watch
[lxxxiii] Porta M, Curletto G, Cipullo D, et al. Estimating the delay between onset and diagnosis of type 2 diabetes from the time course of retinopathy prevalence. Diabetes Care. 2014;37(6):1668-1674. doi:10.2337/dc13-2101
[lxxxiv] Fernández O, Fernández V, Arbizu T, et al. Characteristics of multiple sclerosis at onset and delay of diagnosis and treatment in Spain (the Novo Study). J Neurol. 2010;257(9):1500-1507. doi:10.1007/s00415-010-5560-1
[lxxxv] Fleming NS, Culler SD, McCorkle R, Becker ER, Ballard DJ. The financial and nonfinancial costs of implementing electronic health records in primary care practices. Health Aff (Millwood). 2011;30(3):481-489. doi:10.1377/hlthaff.2010.0768
[lxxxvi] Miller RH, West C, Brown TM, Sim I, Ganchoff C. The value of electronic health records in solo or small group practices. Health Aff (Millwood). 2005;24(5):1127-1137. doi:10.1377/hlthaff.24.5.1127
[lxxxvii] How much is this going to cost me? The Office of the National Coordinator for Health Information Technology (ONC). Accessed September 18, 2023. https://www.healthit.gov/faq/how-much-going-cost-me
[lxxxviii] Menachemi N, Collum TH. Benefits and drawbacks of electronic health record systems. Risk Manag Healthc Policy. 2011;4:47-55. doi:10.2147/RMHP.S12985

[lxxxix] Floyd PT, Oates JC, Acker JW, Warren RW. DEFINING THE MEDICAL RECORD: RELATIONSHIPS OF THE LEGAL MEDICAL RECORD, THE DESIGNATED RECORD SET, AND THE ELECTRONIC HEALTH RECORD. Perspect Health Inf Manag. 2021;18(4):1h. Published 2021 Oct 1.
[xc] Paterick ZR, Patel NJ, Ngo E, Chandrasekaran K, Jamil Tajik A, Paterick TE. Medical liability in the electronic medical records era. Proc (Bayl Univ Med Cent). 2018;31(4):558-561. Published 2018 Sep 11. doi:10.1080/08998280.2018.1471899
[xci] Jankovic I, Chen JH. Clinical Decision Support and Implications for the Clinician Burnout Crisis. Yearb Med Inform. 2020;29(1):145-154. doi:10.1055/s-0040-1701986
[xcii] Gregory ME , Russo E, Singh H. Electronic health record alert-related workload as a predictor of burnout in primary care providers. Appl Clin Inform2017; 8 (3): 686–97.
[xciii] Van Dort BA, Zheng WY, Sundar V, Baysari MT. Optimizing clinical decision support alerts in electronic medical records: a systematic review of reported strategies adopted by hospitals. J Am Med Inform Assoc. 2021;28(1):177-183. doi:10.1093/jamia/ocaa279
[xciv]Al-Faruque F. FDA's Califf: Expect to see more RWE-based regulatory decisions. Regulatory Focus. September 22, 2023. Accessed October 08, 2023. https://www.raps.org/News-and-Articles/News-Articles/2023/9/FDA%E2%80%99s-Califf-Expect-to-see-more-RWE-based-regulato.
[xcv] US Food & Drug Administration. Considerations for the Use of Real-World Data and Real-World Evidence To Support Regulatory Decision-Making for Drug and Biological Products. Accessed October 10, 2023. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-use-real-world-data-and-real-world-evidence-support-regulatory-decision-making-drug
[xcvi] Majumder MA, Guerrini CJ, McGuire AL. Direct-to-Consumer Genetic Testing: Value and Risk. *Annu Rev Med*. 2021;72:151-166. doi:10.1146/annurev-med-070119-114727

[xcvii] Leonard B, Reader R, Paun C, Schumaker E. Buried in data: A doctor's lament. Politico. February 08, 2023. Accessed October 08, 2023. https://www.politico.com/newsletters/future-pulse/2023/02/08/buried-in-data-a-doctors-lament-00081673

[xcviii] Evidence-Based Clinical Decision Support System. Wolters Kluwer. Accessed October 08, 2023. https://www.wolterskluwer.com/en/solutions/uptodate

[xcix] Atasoy H, Greenwood BN, McCullough JS. The Digitization of Patient Care: A Review of the Effects of Electronic Health Records on Health Care Quality and Utilization. Annu Rev Public Health. 2019;40:487-500. doi:10.1146/annurev-publhealth-040218-044206

[c] Conn J. 'Swivel chair' interoperability: FDA seeks solutions to mesh EHRs and drug research record systems. Modern Healthcare. August 01, 2015. Accessed October 08, 2023. https://www.modernhealthcare.com/article/20150801/MAGAZINE/308019979/swivel-chair-interoperability-fda-seeks-solutions-to-mesh-ehrs-and-drug-research-record-systems

[ci] Pasquier L, Minguet G, Moisdon-Chataigner S, et al. How do non-geneticist physicians deal with genetic tests? A qualitative analysis. Eur J Hum Genet. 2022;30(3):320-331. doi:10.1038/s41431-021-00884-z

[cii] Multi-Cancer Early Detection. Association of Community Cancer Centers. Accessed October 08, 2023. https://www.accc-cancer.org/home/learn/precision-medicine/cancer-diagnostics/multi-cancer-early-detection-changes-on-the-horizon

[ciii] Pet DB, Holm IA, Williams JL, et al. Physicians' perspectives on receiving unsolicited genomic results. Genet Med. 2019;21(2):311-318. doi:10.1038/s41436-018-0047-z

[civ] Franklin JM, Patorno E, Desai RJ, et al. Emulating Randomized Clinical Trials With Nonrandomized Real-World Evidence Studies: First Results From the RCT DUPLICATE Initiative. Circulation. 2021;143(10):1002-1013. doi:10.1161/CIRCULATIONAHA.120.051718