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Real-world data as real-world evidence: Establishing the meaning of data as a prerequisite to determining secondary-use value

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ABSTRACT

The U.S. Food and Drug Administration (FDA) defines real world data (RWD) as data about patient health status that are routinely generated and collected through a variety of sources, such as through provision of clinical care. Real world evidence (RWE) is defined as the clinical evidence gathered through analysis of RWD (U.S FDA 2018).

Data cannot become evidence until their meaning and value have been established. This is especially true when making secondary-use of data gathered for other primary purposes, as is often the case for use of RWD. 'Meaning' and 'value' are distinct constructs and should be evaluated as such. 'Meaning' is objective, factual and agnostic to data's use. 'Value' is subjective and situational, pegged to data's intended use.

This paper introduces a framework that can be applied to discover and evaluate the meaning of data, by focusing on attributes and questions within five distinct data-related categories: provenance, governance, measurement, quality and validity. This paper provides examples of the application of this framework to both traditional and emerging RWD sources that have been used in a secondary-use manner as evidence or are being explored for their secondary-use potential.

INTRODUCTION

The volume of available and computable RWD has increased exponentially in recent years, and the sources through which those data are created and generated have diversified. The adoption of electronic health record (EHR) platforms by providers has fueled the creation of these data, as has the increased availability and use of devices, sensors and apps (Daniel 2018; Hsueh 2017; Meystre 2017). Additionally, the format and structure of RWD have also shifted. For example, health insurance claims data sources contain largely structured data elements, while data stored in an EHR are more likely to be semi- or unstructured; and data collected and created by patient and consumer wearables have the ability to generate transactional data (e.g., sequential monitoring of heart rate, respiratory rate, blood pressure, blood glucose, etc) without the active participation of its user (other than simply wearing the device). This digital transformation of healthcare data has shifted the healthcare data landscape and ecosystem, both quantitatively and qualitatively.

At the same time, secondary-use—re-use of data outside of the primary purpose(s) for which they were originally collected/created—of health data is widespread and with growing demand (Safran 2007). The need to leverage non-experimental data to support evidence generation has been acknowledged by the FDA (Sherman 2016; U.S. FDA 2018) and mandated by Congress (Rep. Rangel 2010; Rep. Bonamici 2015).

Secondary-uses are varied and include topics such as evaluation of value-based care models to reduce healthcare costs and reward clinical quality, fraud detection, clinical effectiveness research, population health management, biosurveillance, and medical product safety surveillance (Daniel 2018; Hsueh 2017; Meystre 2017; Safran 2017).

This increase in data volume and expanded diversification has led to a reckoning of understanding exactly who is creating and controlling the data, who is using the data and for what purpose(s), and whether the data are fit-for-use for these secondary-use purposes.

THE MEANING AND VALUE OF DATA

'Meaning' and 'value' are distinct constructs and should be evaluated as such. 'Meaning' is objective, factual and agnostic to data's use. 'Value' is subjective and situational, pegged to data's intended use. An understanding of data's 'meaning' should precede any assessment of 'value'. In order to assess data's fit-for-purpose and value-for-use within specific use-case contexts, one must first understand what the data mean and what they represent.

DATA MEANING

In order to establish meaning, there are several core foundational elements the need to be assessed and evaluated. These core foundational elements appear in Table 1. Knowing the primary purpose(s) for why data were created, and who controls and/or owns their usage, helps to understand specific data elements that are likely to be high-quality, well-populated and accurate. This information is significant to the evaluation of value and fit-for-purpose within specific contexts and use-cases.

Foundational Element	Questions to Address
Provenance	Where do the data come from? Who created them and how? What are the data's primary use(s)?
Governance	Who owns the data? Who controls the data? Where do the data reside?
Measurement	What are the data measuring? How? When? Where? Why?
Quality	What is the extent of data missingness, characterized at both the item- and observation-levels? Is the missingness at random or not at random? What is the level of conformity with data standards and expected value-sets?
Validity	How accurate are the data in measuring what they are intended to measure (primary use)?

Table 1. Five foundational elements of data *meaning*

DATA VALUE

The approach and framework to assessing 'value' is similar regardless of context and use-case, and can be summarized in the steps below:

1. Establish and document *meaning* across foundational elements (see Table 1)
2. Define a plan/use-case/test-case for intended re-use/secondary-use of data, including specific study population and questions to be addressed
3. Assess how accurately 'meaning' across the foundational elements coalesces with intended secondary-use use-case

Secondary-use of RWD for regulatory purposes has been discussed in the literature (Daniel 2018; Girman 2018). Data considerations for detailing the concept of contextually fit-for-purpose RWD for regulatory purposes included a focus on data relevance and data quality. The methods and attributes outlined by these studies for assessing and determining data relevance and quality from a *value*

perspective are strongly related to the five foundational elements of data meaning outlined and defined in Table 1 (Daniel 2018; Girman 2018).

EXAMPLES OF REAL-WORLD DATA SOURCES AND THEIR MEANING

Daniel, et al (2018), made a distinction between two types of RWD: *established* versus *emerging* sources of RWD (Daniel 2018). In this paper, established sources are defined as the more commonly used RWD sources, that have been used and subjected to more rigorous assessments and methods, and *are already in-use for regulatory, policy or financial decision-making*. These sources include, but may not be limited to, health insurance claims data and data from EHRs.

Emerging sources of RWD include those data sources that have not yet been used to the extent of the established sources, have not yet been subjected to the same rigorous levels of scientific exploration and scrutiny, and *are not yet in-use to support regulatory, policy or financial decision-making*. These include, but may not be limited to, patient and consumer wearables and sensors (Evenson 2015), apps (Furberg 2016), social media (Freifeld 2014), EHR event log (Dymek 2018), and environmental sensor and sentinel data (Peake 2018; Hsueh 2017).

This section of the paper applies the criteria defined in Table 1 to one *established* RWD source and one *emerging* RWD source. Table 2 presents a summary assessment of health insurance claims data, as an example of an established RWD source (Aviles-Santa 2017; Wilson 2012). Insurance claims data include the data elements collected and/or derived following a billable, medically-attended healthcare encounter (Tyree 2006). Table 3 presents a summary assessment of consumer wearables data, as an example of an emerging RWD source (Evenson 2015; Peake 2018). Consumer wearables data include a wide-range of data generated by consumer-grade (as opposed to clinical- or regulatory-grade) wearable devices, sensors or apps.

ESTABLISHED DATA SOURCE EXAMPLE: CLAIMS DATA

As discussed above, insurance claims data include data elements collected and/or derived to support processing payments to clinical providers following provision of medically-attended care. Table 2 below contains a summary of the attributes of claims data along the five foundational elements identified in this paper as being foundational to understanding data meaning.

Foundational element	Summary assessment
Provenance	The primary purpose of health insurance claims is for payers to reimburse health care providers for services rendered; that is, to pay the bills. Claims data capture the breadth of an individual's billable, medically attended care over a defined period of observation represented by health insurance enrollment in a commercial or public insurance plan. The observed medically attended care is without respect to a specific provider or facility; that is, all of the providers or facilities who provide patient care are present, as long as the care provided was a billable event to trigger a claim.
Governance	Payers—insurance companies—own and control the data that are generated from their reimbursement of medical bills. A recent panel, however, indicated wide re-use of these data for a range of purposes—proprietary, research, monitoring—that places these data into the hands of organizational other than the one(s) that initially created them (e.g., data aggregators), often without the knowledge of providers or patients (Safran 2007).

Foundational element	Summary assessment
Measurement	Diagnoses and treatments are recorded using well-structured and established coding systems utilized for billing (e.g., ICD-9-CM, CPT, NDCs, and so forth). Since the details of the provided medically-attended care are dependent on the specificity and granularity of these coding systems, certain details about the care may be lacking, particularly with respect to clinical and temporal granularity (e.g., specific lab test values, vital signs, chief complaints and problem lists, medications administered during an inpatient stay, temporal precision as to the course of care provided). Only medically attended care for which a bill was submitted and paid are captured (e.g., care paid for out-of-pocket and over-the-counter drugs are not captured).
Quality	The quality and completeness of individual data elements can vary greatly. In general, the data elements that are mandatory for the primary purposes for which the data were collected--paying bills--are of the highest quality. For example, service dates and billing codes for services rendered are critical for payment and therefore considered to be of better quality and completeness than data on race and ethnicity, which are not mission-critical to the goal of paying bills.
Validity	Coding for clinical services provided can differ by facilities and physicians (both within and across facilities). Clinical services or products (in the case of pharmacy claims) that end up on a claim are heavily influenced by services or products covered by payers (e.g., if a particular clinical service/procedure is not contained within an insurer's schedule of benefits or if drug is not contained in an insurance plan's drug formulary, those events will not be captured in claims).

Table 2. Claims data summary assessment along the five foundational elements of *meaning*

EMERGING DATA SOURCE EXAMPLE: CONSUMER WEARABLES DATA

As discussed above, consumer wearables include data elements collected, generated and/or derived during the act of using a consumer-grade wearable device, such as an activity tracker. Table 3 below contains a summary of the attributes of consumer wearables data along the five elements identified in this paper as being foundational to understanding data meaning.

Foundational element	Summary assessment
Provenance	Consumer wearables include a range of different devices that measure and track a variety of healthcare-related activity metrics, including but not limited to, steps, distance, physical activity, hydration status, energy expenditure, and sleep.

Foundational element	Summary assessment
Governance	Data generated from wearable devices vary as to where the data get stored and, by extension, which entity(ies) have access to the data. For devices that require apps to collect and display data and metrics, those app data can be widely shared outside of the individual consumer who is generating the data.
Measurement	The measurement method used by wearable devices depends in large part on the type of device and what is being measured. In general, though, two categories of measurement exist to measure physical activity and movement: [1] Direct, or [2] Indirect. An example of direct recordation of objective, physiological data is electrocardiogram data. An example of indirect measurement includes energy supply metrics, such as calories expended.
Quality	Missingness of data is highly dependent on user-behavior; that is, consumer wearables that passively collect data can only do so when worn (and worn properly) and those that actively collect data can only do so when explicitly indicated to do so by the user. The quality and accuracy of consumer wearable devices varies widely depending on the type of activity being tracked. For example, accuracy of devices that track number of steps taken have been found to be higher than that of devices tracking energy expenditure and sleep. More research is needed as the market of devices expands, though, as are standards for consistent assessment of the same.
Validity	The literature reports that only about 5% of wearable technologies have been formally validated (Peake 2018). There is currently no globally agreed-upon, evidence-based definition of the properties needed to determine the properties necessary to consider a tracker valid and reliable. The validity of data and metrics generated by individual trackers can vary widely depending on a number of factors, including type of tracker, manufacturer, and user-behavior such as exactly how and where a tracker was worn (e.g., wrist, waist, pocket) and if/how it was initialized before use. In general, the meaning and validity of indirectly measured metrics carry a higher degree of uncertainty (Peake 2018).

Table 3. Consumer wearables data summary assessment along the five foundational elements of *meaning*

CONCLUSION

The volume of available and computable RWD has increased exponentially in recent years, and the demand for making secondary-use of these data has similarly increased.

The expanding volume of data increases the importance of understand the meaning of these data before they can be assessed for value in specific use-cases. Data meaning and value are different; meaning is objective, whereas value is subjective and contextual.

This paper introduced a framework of five foundational elements, and questions, to address to objectively assess the data meaning as a prerequisite to determining their value within specific contextual use-case settings.

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