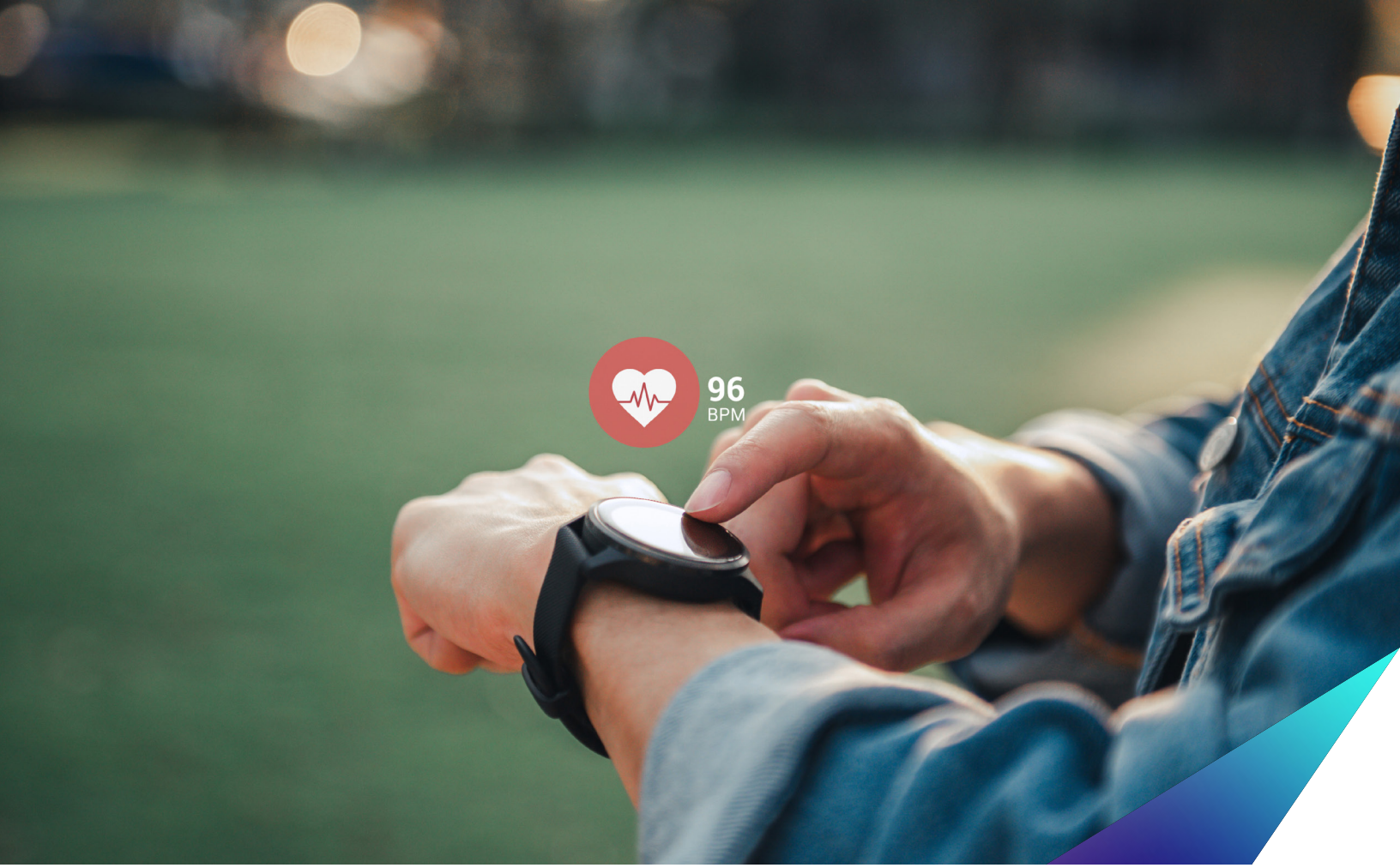

Managing real-world evidence from mobile devices

Real-world evidence (RWE) extracted from mobile devices as real-world data (RWD) sources promises to accelerate clinical trials. Management of RWE through a digital health enterprise platform (DHEP) that acts as a central repository in digital clinical trials forms the basis for successful adoption of RWD using mobile devices in clinical organizations.

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Executive summary

The increasing use of real-world data (RWD) offer huge potential for the life sciences industry in terms of how outcomes in clinical trials could be managed. Patients, investigators, and sponsors profit from RWD by fewer site visits, having reliable data, design clinical studies based on real-time, continuous data and the ability to make informed decisions earlier, which promises to advance drug development. Mobile devices such as smartphones and wearables act as RWD sources and allow the extraction of real-world evidence (RWE) that could be submitted to health authorities. RWD could change how clinical trial phases are designed and thus augment expensive clinical trials.

A digital health enterprise platform (DHEP) is the critical infrastructure required to manage data assets from mobile devices centrally within clinical organizations. It can address key challenges in storing and exchanging data between partner organizations and thus allow interoperability and collaboration between organizations. Critical success factors for RWE management from management, technical, regulatory, data standard and stakeholder perspectives need to be considered to leverage full value out of RWD.

Real-world data and evidence

Increasing use of real-world data (RWD) in clinical trials promises to advance the development of life-saving drugs and therapies. RWD increases the accuracy of the data collection and the ability for pharma/ biotech companies to make informed decisions earlier and effectively. Prior to the COVID-19 pandemic, the use of RWD and RWE was on the rise; however, the pandemic accelerated the need for pharma/ biotech companies to adopt RWD approach in order to minimize disruptions to their clinical programs and ensure that patients with unmet medical needs are treated.

RWD are data relating to the health status of patients as well as to health care delivery coming from various sources[1]. These sources include Electronic Health Records (EHR), patient-generated data, product and disease registries, data from mobile devices, and claims and billing data. RWD offer huge benefits for the life sciences industry in terms of how data in clinical trials are managed. Patients receive near real-time feedback and here will be fewer potential site visits. Investigators/sponsors review data in near real-time, identify any safety concerns that could have been missed and any patient incompliance through regular review of the data, thus enabling sponsors to make informed decisions earlier.

RWE is derived from the analysis of RWD and provides "the clinical evidence about the usage and potential benefits or risks of a medical product".[2] It could come from various study designs and analyses, and includes randomized clinical trials, observational studies etc., and has become an important pillar in health care decision making.

There is consensus among leading health authorities such as the FDA and the EMA that RWE augment expensive clinical trials. The EMA is piloting the DARWIN EU real-world database that would allow health authorities to analyze the evaluation of medicinal products[3]. There has been a shift in use of RWD in non-randomized interventional studies and non-randomized non-interventional studies, including secondary end point data and to a lesser extend so in randomized interventional studies. In the future, as RWD/ RWE adoption becomes more common and accepted by the regulatory authorities, it could change how clinical trials are designed, where RWE could support the approval of digital therapeutics. Mobile devices such as apps, smart auto-injectors and internet of things (IoT) devices

1 FDA (2022), Real-World Evidence. https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence

2 FDA (2018), Framework for FDA's Real-World Evidence Program. https://www.fda.gov/media/120060/download

3 Raps (2022), EMA, HMA outline evolution of DARWIN EU real-world database, https://www.raps.org/news-and-articles/news-articles/2022/8/ema-hma-outline-evolution-of-darwin-eu-real-world

Figure 1: Mobile devices as RWD sources

play key roles in making digital therapeutics a reality and thus help increase patient compliance.

Mobile devices such as smartphones and wearables have become ubiquitous and could act as key sources of RWE in the coming decades. An example of an application that can be prescribed by doctors to help patients improve their sleep without the need for sleeping pills is the Sleepio app from NHS Apps Library in the UK[4]. Many cloud-based digital health apps are available on mobile devices that could act as data sources in clinical studies. Data from mobile devices are increasingly being used to support regulatory decisions and this paper focuses on how data from mobile devices could be better leveraged as RWE.

Many pharma organizations have started to use data from mobile devices as RWE. A key challenge is to obtain high-quality RWD in order to extract RWE. The data granularity needs to support questions from authorities. In the absence of data standards and guidelines from health authorities to collaborate between organizations, pharma organizations need to address several challenges to fully leverage the valuable data. Investment in personnel, technologies and external partnerships will be required to build the technical infrastructure to support the ingestion, consolidation and analysis of RWD. Some of the key challenges include lack of technical infrastructure to analyze RWD, data security, data governance and data quality concerns[5]. Further deficiencies include a missing central analytics platform and capability, lack of standardized approach to ingest data and self-service analytic tools. Furthermore, adherence to data privacy regulations from the respective health authorities need to be ensured while managing RWD.

This paper addresses how RWE, especially from mobile devices, could be realized in a manner to allow interoperability and collaboration between organizations, and thus fully leverage the value from data. It discusses the technical capabilities that form the basis to manage RWD. Further, the best practices in managing critical aspects are discussed to overcome the common challenges for using data from mobile devices as RWE.

4 Sleepio (2022), https://onboarding.sleepio.com/sleepio/nhs/120#1/1?utm_campaign=null&utm_medium=null&utm_source=NHSAppsLibrary

5 Deloitte (2020), RWE focus is shifting to R&D, early investments begin to pay off, https://www2.deloitte.com/content/dam/insights/us/articles/6578_CHS-RWE-benchmarking-survey/DI_RWE%20benchmarking%20survey%20(SECURED).pdf

DHEP capabilities

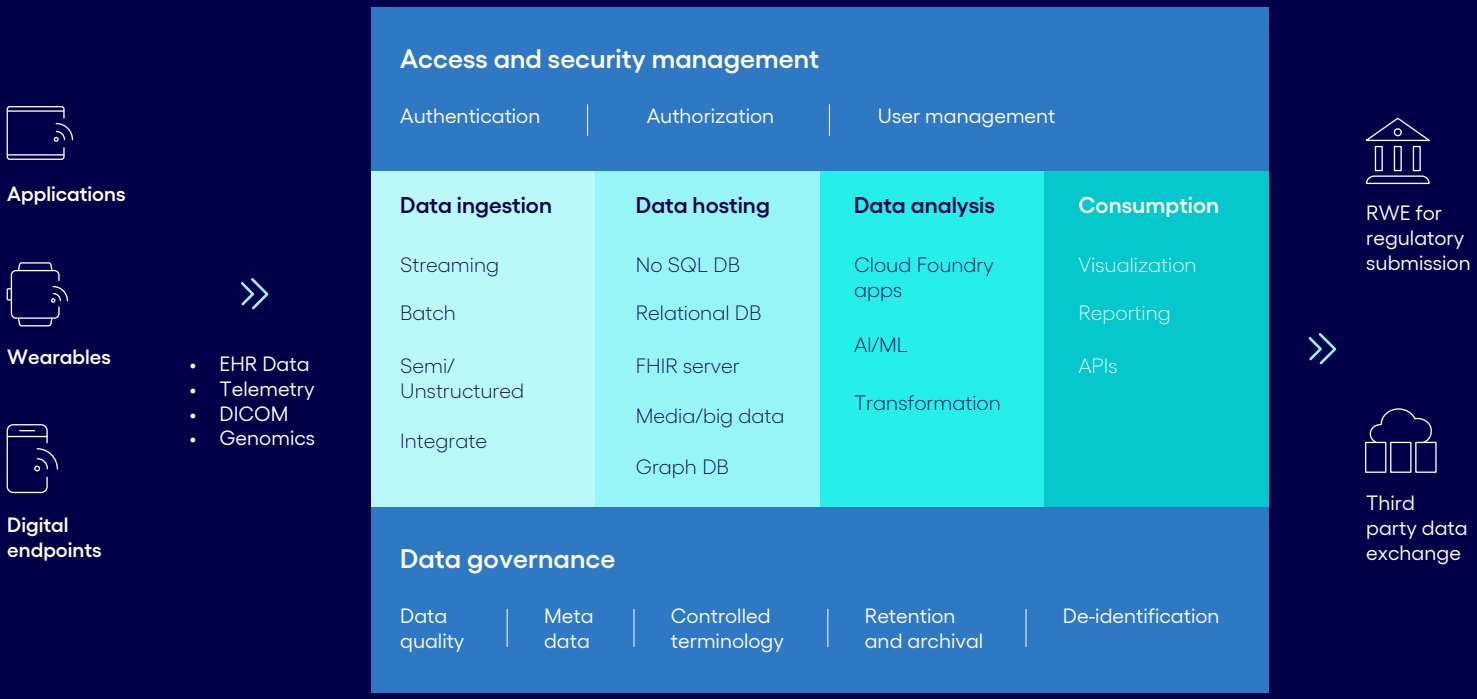

Figure 2: Digital health enterprise platform

Digital health enterprise platform

The critical infrastructure for ensuring seamless management of RWD is the digital health enterprise platform (DHEP) that can manage data assets centrally. This cloud-based platform would become the single source of data for mobile or digital devices in clinical trials, and includes data ingestion, hosting, analytics and visualization capabilities. The benefits of cloud infrastructure include scalability of resources, centralized security and speed required for managing RWD.

The platform would manage users and devices through its access and security management controls. These controls would enable secure data sharing and hosting. This platform would ingest data from multiple RWD and clinical trial data sources. Data sources such as digital health apps, smart injectors, wearables, IoT, third-party applications, laboratory applications etc. will connect and store data centrally in a DHEP. This would entail dealing with a wide variety of structured, semi-structured and unstructured data. The integration of the DHEP with all these sources ensures that the extraction of RWE would become more efficient and comprehensive.

A DHEP would enable hosting a variety of data sets which include electronic health records, telemetry for IoT device data, and digital imaging and communications in medicine (DICOM) for images, and object storage for videos and documents. These different formats would be supported by multiple databases or database services on the platform.

To facilitate RWE generation, a DHEP would provide levers for transforming data based on specific reporting and analytics needs, and creating sandboxes for data scientists to explore and train artificial intelligence and machine learning (AI/ML) models. A DHEP could host custom-built and standard applications (Cloud Foundry apps) to manage services and ensure that business processes and data required to create RWE will be in place.

A DHEP would generate reports and dashboards that support visualizing and consuming the evidence and insights. Analytic insights could further be shared with clinical trial systems.

A DHEP would also allow external systems to interface and transfer data through an application programming interface (API) that further results in the generation of RWE required for submission to health authorities. The DHEP platform would also be supported with rich data management capabilities such as metadata, data quality, retention and archival and de-identification to govern the data and aid in generation of RWE efficiently.

Quick take

How a digital health enterprise platform can become the enabler of digital clinical trials

A leader in life sciences had the challenge to integrate the legacy clinical trial platform with digital devices like IoT devices, health apps, wearables etc. Extensive investments were required to connect the existing trial platform to mobile devices, and the client decided to buy a cloud-based DHEP from a leading vendor. The primary aim was to conduct all digital clinical trials involving mobile devices, images or custom-built applications using the platform. Our digital health expert team advised and implemented this platform configuration initiative. The external cloud-based platform was GxP certified over a period of six months. Configuration and GxP validation of the system was a requirement to be performed by the project team before the platform could be used. Once the platform was qualified, each resource or space allocated for digital trial use cases needed to be configured and qualified to maintain the GxP status of the platform. In the case of custom-built applications, the business processes had to tested and qualified separately.

One of the main use cases has been to develop digital therapeutics for existing blockbuster drugs in the market. Digitizing therapies using health apps and smart-auto injectors connected to the DHEP allowed patients and caregivers to monitor the medication intake and thus improve therapy adherence. The compliance with data privacy (e.g., GDPR) and security regulations was a requirement since patients' personal data from all over the world would be stored on the platform. A data privacy expert checked the data regulations of specific countries, in which the platform was hosted. Analytic applications provided overview of the therapy-related informationtion and allowed monitoring of the cloud security and access. The platform was further connected to the clinical trial platform, which allowed the consolidation and analysis of RWE.

The global platform was hosted in multiple countries in on all continents that allowed the management of mobile device data as required for each use case. It has established itself as the enabler of digital clinical trials and RWE from mobile devices within the organization.

Critical success factors for RWE management

In order to ensure that the RWE can be managed effectively, several best practices from the life sciences industry are recommended. These guidelines from management, technical, regulatory, data standard and stakeholder perspectives form critical success factors to manage RWE from mobile devices effectively.

- Establish a DHEP as the central data repository for mobile devices
- Provide capabilities to analyze RWD and extract evidence
- Adhere to country-specific data regulations
- Understand country-specific patients' acceptance of mobile technologies
- Establish data standards for collaboration and submission from the outset

Critical success factors for RWE management from mobile devices

Central data repository for mobile devices

A key aspect of RWE management in organizations is the centralization of data from mobile devices. More than the technical setup of study infrastructure, the management needs to support the use of a DHEP as the standard platform for conducting trials using mobile devices. Change management efforts within the enterprise to ensure that more teams would start to use the DHEP as the data repository instead of using different services from internal teams and external vendors. This change would result in the required economies of scale for a DHEP to succeed.

Analytics capabilities to provide data insights

Organizations need to develop data warehouses and lakes to analyze RWD stored in the DHEP and make sense of it. Data visualization applications and data scientists who could visualize trial data need to be in place to leverage the available data. Data scientists could write bespoke applications with required business and data processing information to create data insights. Some visualization tools allow study managers to produce RWE through self-service analytics; however, it requires the robust data modelling underneath the application to become successful.

Country-specific data regulations

Apart from ensuring that a DHEP is validated throughout its operation, patient data need to be secured and stored based on country-specific data regulations (e.g., GDPR, CSL). Mobile devices need to be developed in a way that the data could be deleted from DHEP and analytical systems once the patient revokes their consent to use it. Any breach of data regulations and security could lead to fines to clinical organizations and lack of trust by patients.

Patients' acceptance of mobile technologies

Mobile internet is a prerequisite for smooth integration of devices to the digital platform. It can be a challenge in countries or places with poor internet networks to transmit data live, which needs to be considered in the study design. Patients who are not accustomed to clinical studies with mobile devices need more targeted communications to establish trust in digital trials. Age groups and target groups need to be carefully weighed for digital studies as the use of digital technologies in the clinical studies is not fully established yet. Further, health apps and IoT devices need to be developed in a patient-centric way to encourage adoption.

Data standards for collaboration and submission

Data needs to be transferred between collaborating organizations such as analytics or data registry vendors using data standards that allow exchange between systems without the loss of semantics. HL7 FHIR has become the default mobile data standard for storage and exchange between partnering organizations. Another widely used data standard for RWD collection is Clinical Data Acquisition Standards Harmonization (CDASH) from the Clinical Data Interchange Standards Consortium (CDISC). Likewise, the Study Data Tabulation Model (SDTM) from CDISC has become an accepted standard for submission to the FDA. For submission of RWE to health authorities, the collected data formats HL7 FHIR/ CDASH or others require conversion to CDISC – SDTM.

Looking forward

Advances in digital technologies have resulted in increasing consideration of mobile devices as RWD sources in clinical trials, especially since the COVID-19 pandemic. However, there are several areas that require focus in the coming years for the wider adoption of RWD from mobile devices. RWD needs to be stored centrally in a DHEP to establish mobile devices as a key data source in digital clinical trials and thus integrate data within clinical organizations. The RWE from a DHEP could then be further linked to clinical trials and molecular data platforms to extract even more valuable insights. For RWD to gain wider acceptance from patients, the trust in RWD needs to be strengthened by resolving data governance related issues. Sponsors need to consider RWD in their product development strategy and understand the return on investment that RWD could bring in the long term. Further, regulatory authorities need to provide more directions in the use of RWD in trials and for collaboration between clinical organizations.

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