Decentralized Research Playbook

In this decentralized research playbook:

Introduction

The current public health crisis has accelerated collecting data in a decentralized manner. The biopharmacuetical industry had already begun to harness transformative approaches to collecting data in novel ways, including from remote sources across a wide range of settings and using diverse modalities. The pandemic has proven to be a catalyst for an even more comprehensive set of solutions to collect critical evidence beyond the walls of the traditional study setting. Regulatory agencies propelled this trend by releasing new guidances.[1]

Each study requires a unique approach and has a different degree of decentralization that may be available. The endpoints of interest, design (retrospective, prospective, hybrid), geography, clinical assessments, disease markers (genetic, biomarker), patient generated data, setting of care, and availability of external real world data each contribute to the decision of whether a particular design has attributes that can benefit from a more decentralized approach.

With so many factors that influence design, UBC's team of epidemiologists, clinical scientist, and health policy experts have established a practical assessment across a key set of these domains. With a new wave of decentralization feasibility upon us, this assessment is one of the most critical first steps our clients undertake.

The UBC Decentralized Research Playbook is intended to help inform and offer a practical assessment method to our partners who are looking to most effectively leverage decentralized techniques and technologies to deliver on their research programs. UBC is offering this playbook to help you plan, prioritize and educate internal partners and leaders as you help your company enter the world of decentralized approaches to late stage product development and postmarketing evaluations.

[1] Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency Guidance for Industry, Investigators, and Institutional Review Boards March 2020 Updated on January 27, 2021

Platforms for Consideration

Although a fundamental shift towards more remote management of research was already underway within the biopharmaceutical industry, the public health crisis has accelerated the collection of data in a decentralized manner.

The following technologies are being leveraged to provide a comprehensive set of solutions for collecting critical evidence beyond the walls of the traditional study setting.

Wearable Sensors

e.g., Wrist, Skin, Cuffs, Finger, Headbands

Consideration for the use of wearable devices in clinical trials should always begin with the scientific approach: starting with the scientific research question, the clinical endpoints to be collected, the quality of the device and a strong understanding of the therapeutic area and entire patient journey.

Sample applications include safety monitoring (vital signs, heart rate), mobility, movement, sleep endpoints (actigraphy, tremor activity), reminders, adherence support or remote intervention via the mobile device.

Remote In-Home Nursing

A careful review of the project specific initiatives and data collection objectives may reveal that select visits are suitable to occur in the patients home. Clinical nurses are project trained to perform lab sample collection, drug administration, and routine assessments, potentially reaching patients who may not be located near a brick and mortar site. These tactics can extend the reach and participation of study participants.

30%

of healthcare consumers cited that a *'nurse coming to my home for some visits'* would favorably influence their decision to participate in a clinical trial.

(BBK, Worldwide Study Voices, 2020)

Data Aggregation, Anonymization & Enrichment

The adoption of decentralized study designs is accompanied by a proliferation of data collection streams. Organizing these disparate sources of data into a unified environment that enables the generation of insights from linked and interoperable datasets for researchers is essential. Combining data collected through traditional studies with real world data significantly amplifies the ability to answer important questions about the safety and effectiveness of medicines.

Real world data architecture solutions provides comprehensive data ingestion, aggregation, and warehousing for your project. This allows you to trace the patient journey, consolidate registry and clinical site data, characterize payer and provider behaviors, and to enhance data with healthcare marketplace real-world datasets.

Digital Recruitment & Real World Evidence Databases

Capitalizing on electronic health records (EHR) and real world data for direct to patient recruitment enables sponsors to recruit patients in an effective and targeted manner, leveraging very specific International Classification of Diseases (ICD-10-CM/PCS) codes, and through partnerships with major healthcare networks and connected ecosystems.

By utilizing pharmacy and medical claims, laboratory and EHR data, sponsors and research organizations can directly identify and recruit patients for participation in research. By assessing specific pharmacy and medical claims data, laboratory or other disease or indication specific relevant diagnostic test results, we can pre-identify highly targeted pre-qualified patients to speed up enrollment, reduce time and effort spent on patients that are not an immediate fit, lower the cost of screen failures and ultimately streamline program start up.

Replicating intricate exclusion and inclusion criteria within real world data sources to target the eligible patient population for your study. Better characterizes the physician and patient population, forecasts patient recruitment and facilitates informed decision-making. Sponsors are also utilizing patient communities of consented study participants to share trial updates and communicate about future study opportunities.

Getz et al. [44] noted that Across **3400 clinical trials,** more than **40%** had amended protocols prior to the first subject visit, delaying trials by **4 months**.

(Getz, K.A., Zuckerman, R., Cropp, A.B., Measuring the Incidence, Causes, and Repercussions of Protocol Amendments 2011)

Telehealth

Telehealth has been around for years and has proven to be an integral component for delivery of healthcare and for clinical studies. Telehealth extends the healthcare provider's ability to reach patients during the current health crisis by reducing barriers for site personnel and patient communication and providing a fully compliant virtual environment for multiple types of interactions. Virtual visits ensure sites securely capture data from remote participants during, in between, and in lieu of in-clinic site visits. Telehealth visits can help ensure that critical data are recorded in real time and assessments are complete.

Corporate funding for digital health including venture capital, debt and public market financing reached $21.6 billion in 2020, up 103% compared to $10.6 billion in 2019, according to a year-end report by research firm Mercom Capital Group.

(COVID-19 supercharged digital health funding in 2020 to reach record levels: report, Fierce Pharma, 2020)

Direct to Patient Data Collection

Clinical Outcomes Assessments, Patient Reported Outcomes

Through valid and reliable data obtained directly from the patient using electronic methods such as diaries, questionnaires, and validated assessment tools, stakeholders are provided immediate access to the data. Through reminders, study staff can ensure compliance with ePRO/eCOA completion alongside real-time tracking of responses.

Virtual Assistants

With the growing adoption of digital health tools, particularly influenced by the pandemic, patients are becoming much more involved in their care and are showing increased interest in participating in research and communicating through digital healthcare channels. Virtual assistants are a powerful communication tool for patients participating in a clinical study by facilitating the enrollment of appropriate patients, supporting the consent process, sending reminder messages ahead of visits, providing patients a preview of what to expect for upcoming study milestones, and addressing any questions patients may have in real-time. This ensures engaged and dedicated participants in the study.

A virtual assistant can also check in throughout the study to see if patients have any questions and provide contact information for study personnel. The potential use cases and applications for virtual assistants in research is still untapped.

Why Virtual Assistants? Consider this:

60% of consumers prefer to message businesses over any other channel

80% of US adults use text messaging regularly

97% of text messages are opened in < 3 minutes

(Study Shows U.S. Customers Prefer Texting With Businesses. Avochato 2019)

External Registries & Foundations

Foundations and external registries are particularly important to furthering the understanding of product that might have a rare or orphan designation and populations where less may be known about the disease process and epidemiology. Important clinical, safety, effectiveness, and commercial discussions between biopharmaceutical manufacturers and foundations can create mutual alignment of the foundation's medical, scientific and advocacy agendas and manufacturer's product-specific clinical development goals. Data sharing agreements between these parties can be established to ensure access to critical patient data in a secure, HIPAA-compliant manner, captured through innovative real world technologies and infrastructure. These data points may include information collected by healthcare settings or direct-to-patient virtual engagement.

Evidence Generation Strategies Framework

As the market, regulators, biopharma, patients, and healthcare providers all converge on new operating models, it's important to understand whether or not a particular design has elements that can benefit from a decentralized model.

There is not a one size fits all hybrid or fully decentralized study design, and the below graphic frames what you must consider when determining whether you can incorporate decentralized study elements. This is not intended to be exhaustive, but to provide a strong framework to help you plan, prioritize, and educate internal partners as you enter into the design of a decentralized trial.

Evidence Generation Strategies Framework

Design	**Real World Evidence (RWE) Guidance**	Is there any existing country-specific regulatory statement on acceptance of RWE as accompanying or supporting evidence generation?
	Precedent Design	Has any prior program involving this product or treatment leveraged RWE or real world data (RWD) as part of regulatory submission and/or for data collection/acquisition?
Operational	**Geography - Design Acceptability**	Are decentralized data collection approaches understood and acceptable within the countries / regions; considerations for HCPs, caregivers, patients within the therapeutic area?
	Geography - Regulatory Acceptability	Are decentralized data collection approaches permissible by country regulations, health authorities, local IRBs/ECs? Is your platform standardized enough to bring in external data to pass regulatory audits?
	In-Home Clinical Services	Following a final review of the endpoints of interest and the schedule of assessments, which components of the program could be administered in the home to support remote data collection?
	Burden Displacement	Will decentralized approaches streamline or compliment data collection for those involved or shift/increase the burden? Specific considerations should include number of stakeholders involved, technology interface and need for training.
	Quality Management + Oversight	Are SOPs established, reviewed, and implemented to ensure to regulatory authorities and ethtics bodies that the rights and wellbeing of the patient, Good Clinical Practices (GCP) and maintain the quality of data in this remote setting? Do you have an established strategy to ensure audit-readiness?
Epidemiology	**Disease Prevalence + Incidence**	What is the size of the population you are studying? This can be indicative of complexity to find the patient or availability of data surrounding the population of interest.
	Targeted Indication	The indication of your product will influence what is collected, and where / how it is documented. This will help you assess whether or not that information can be captured in a remote manner.
	Site of Care - Treatment Administration	Where the physician and patient interacts, and how the product is administered/ dispensed will impact design, communication, and collection strategies.
	Site of Care - Treatment Follow-Up	Where are patients located for follow-up and post-treatment for assessments and data collection? This impacts the complexity of design, communication, and collection strategies.
RWD Technology & Infrastructure	**Connectivitity + Interoperability**	Do your patients have access to the internet for computers or mobile devices?
	Identifiability + Tokenization	Do you have access to enough of the patient information to create a unique token that will allow you to link the unqiue patient to EMR's and RWD?
	Agreements with Data Provider	Do you have sharing agreements in place to integrate with RWD systems for consent with the patient and the patient's site?
	Country Specific Compliance	What are the local guidances and policies of each country of interest with regards to patient aggregated data?
	Patient Level vs Aggregated	Do you have a defined aggregate standard for third parties to provide data into system, and integrate with potential patient level data?
	Structured vs Unstructured	Do you have a process in place to import and allow for structured as well as unstructured data before importing it into the study database?
	Types of Data Collected	What types of data are you collecting and studying? These include death registry, EMR, lab, medical and pharmacy claims, wearables, ePRO, eCOA, biobanking, biosamples.

Example Protocol Visit Schedule

	-4	0	1	2	4	8	12	16	20	24	28	32	36	40	44	48	52	Follow-Up
Demographics	✓																	
Screening Blood Test	✓																	
Baseline Blood Test		✓																
Consent	✓																	
Routine Safety Bloods		✓			✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Efficacy Bloods		✓			✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Radiography	✓	✓					✓			✓			✓			✓	✓	
Patient Assessment of Illness		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Physician Assessment of Illness		✓				✓				✓			✓			✓	✓	
General Efficacy Clinical		✓			✓	✓	✓		✓	✓		✓	✓		✓	✓	✓	✓
General Safety Clinical		✓			✓	✓	✓		✓	✓		✓	✓		✓	✓	✓	✓
Specialist Test - Bloods					✓		✓			✓							✓	
Specialist Tests - Other					✓		✓			✓							✓	
End of Treatment Score																	✓	
Drug Administration		✓			✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Drug / IP Supply			✓	✓				✓	✓		✓	✓		✓	✓			
ePRO / eCOA Completion		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	

Site Visit · Digital Visit · Nurse Visit · Remote Visit

Radiography · Physician Assessment · Patient / Caregiver Assessment · Special Tests

UBC

NEXUS

INTEGRATED EVIDENCE DEVELOPMENT

Bringing It All Together

UBC, a full-service clinical development, late stage, and patient support organization, answers the markets demands for decentralized research.

With over one hundred fifty years of combined industry experience, UBC's Senior Consulting Group comprised of epidemiologists, clinician, regulatory scientists, and health policy experts, offers unparalleled advisory and consulting services.

Our deeply committed consultants engage with our clients to provide and build protocol-specific, virtual evidence generation strategies help ensure their study successfully recruits patients, meets target enrollment, and keep subjects engaged in a decentralized model.

Nexus brings together UBC's scientific and epidemiology expertise in real-world evidence development consulting, robust real world data partnerships, virtual and digital patient engagement technologies, in-home nursing and clinical support, and comprehensive infrastructure to anonymize, link, and enrich real world data in a singular environment to our life science partners.

As the industry converges on new operating models, UBC can help you understand whether your particular design has elements that can benefit from a decentralized model. To learn more about how UBC will assess your current portfolio of upcoming programs through a lens of decentralized approaches, contact us here www.ubc.com/decentralized.