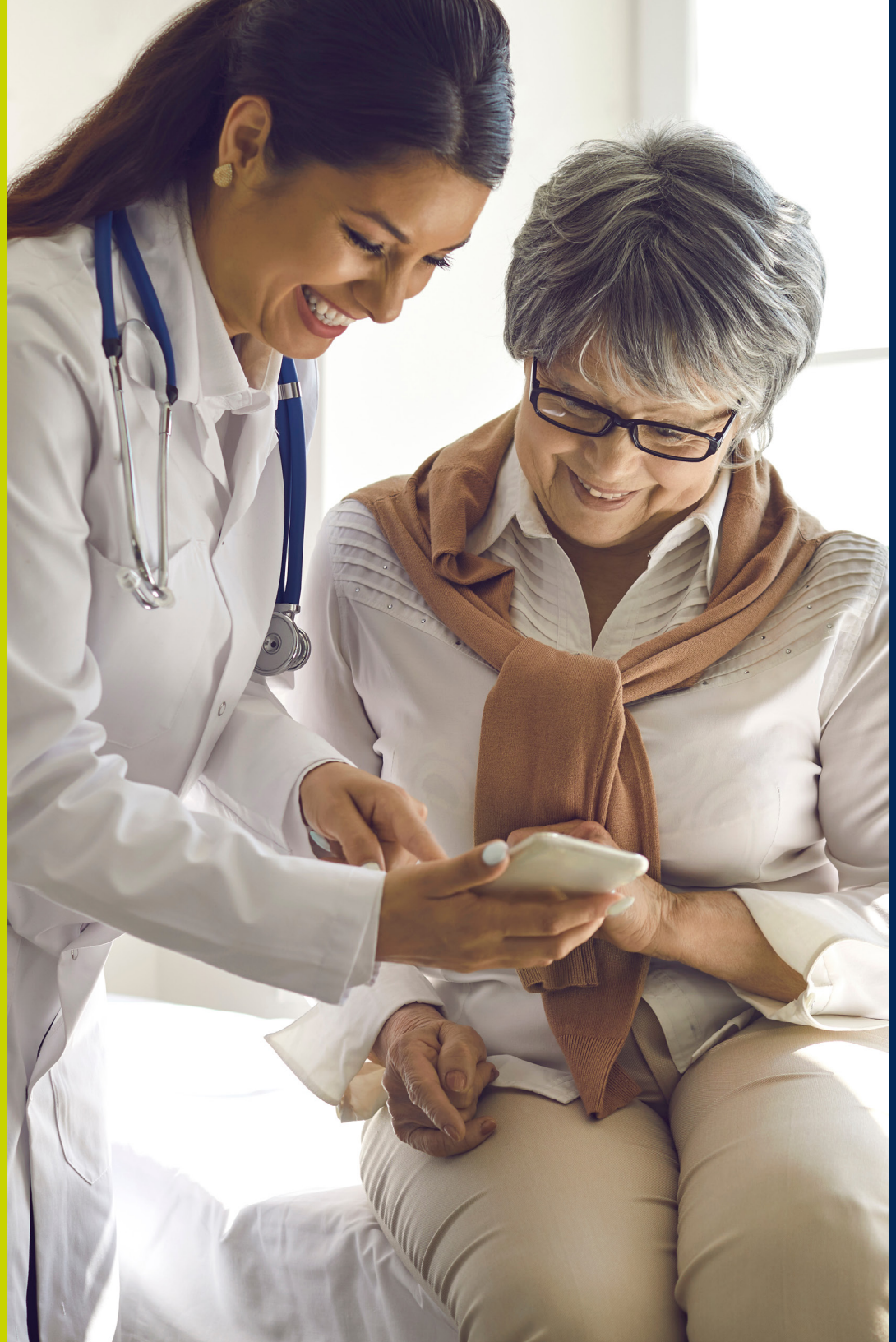


6 Data Linkage Use Cases to Future-Proof Your Clinical Trial

Connect clinical trial data and real world data to gain a fuller view of the patient journey and enhance your evidence generation with Medidata Link

Use Cases

Introduction

Clinical trials remain the gold standard for regulatory decision making in medicine. However, patients who participate in clinical trials continue generating a wealth of real-world data (RWD) in their interactions with the larger healthcare ecosystem before, during, and after a trial. Trial patients' RWD, such as medical claims, electronic medical records (EMR), registry data, and wearable device data, that are routinely collected in the background can supplement active collection of clinical trial data (CTD) and provide a substantially deeper insight on benefits, risks, and cost of treatments.

The disconnect between clinical trials and RWD is historically caused by patient privacy concerns. This gap delays access to critical efficacy, effectiveness, safety, and utilization data – ultimately becoming a detriment to patients. In recent years, the fragmented nature of healthcare data has prevented a rapid and clear analysis into the impact of "long" COVID-19, or the actual healthcare journey and impact of Vaping-Associated Pulmonary Injury (VAPI). However, novel tokenization technologies that enable privacy preserved data linkage are shifting the existing paradigm of clinical trials. Sponsors have begun connecting traditional CTD to RWD data sources at the patient-level. These RWD-enhanced CTD more holistically describe the patient's trajectories, characteristics, and outcomes and help sponsors close critical gaps in evidence generation. With a deeper understanding of patient's diseases, treatments, and outcomes, the industry is unlocking a new frontier in evidence generation, opening up limitless applications for tracking patients lost to follow-up, contextualizing patient reported outcomes, demonstrating treatment effectiveness and cost, and long-term safety monitoring.

Medidata Link is the only centralized technology solution that works across multiple research sites to connect patient-level CTD and RWD, powered by and fully integrated with the Medidata Clinical Cloud unified platform. The Medidata team harmonizes and analyzes CTD and RWD with unrivaled data management and analytics expertise while also giving sponsors the flexibility to perform their own in-house analyses. Medidata Link helps sponsors generate the best evidence and insights from their connected data through:

SCALABLE PII INGESTION: Centrally process personally-identifying information (PII) using our site-facing form that embeds into existing trial workflows, or directly from patients via the myMedidata patient portal.

SECURE AND COMPLIANT DATA MANAGEMENT: Medidata Link is fully integrated with technologies from industry-leading tokenization vendors, providing a flexible approach to patient-level data linkage while protecting sensitive information within Medidata's secure environments. This provides end-to-end data management, with linkage to industry leading US-based RWD ecosystems that minimizes the risk of re-identifying patients.

CONTINUOUS EVIDENCE GENERATION: Explore a variety of use cases applicable across the entire clinical development continuum to provide critical insights into the patient journey. Linked data outputs are directly available to the sponsor or can be further augmented with bespoke analytics from Medidata AI.

In this eBook, we discuss Medidata Link use cases in varied indications across the clinical development lifecycle. These sample use cases can be applied to a wide range of therapeutic areas. Whether you are future-proofing your clinical programs or looking to ensure the success of a single trial, our scalable data linkage solution can help every trial achieve its full potential.

Linking Clinical Trials to Real World Data

Traditionally, CTD and RWD reside in separate silos. This limits our understanding of patient trajectories pre-trial, renders some healthcare encounters invisible during the trial, and disconnects long-term effectiveness and safety data for years post-trial. The ability to connect these data sources while still prioritizing patient privacy has long eluded the industry due to privacy, logistical, and technological barriers. Medidata Link now offers sponsors and regulators with a centralized, privacy-preserving approach that enables data linkage at the patient-level. Our approach is built on the backbones of Rave, Medidata's world class clinical data management platform. Our solution is seamless and ensures no interference with usual processes for patient recruitment, data collection, data blinding and study fidelity, and analytical aspects of your clinical trial.

CONSENT GATHERING: Medidata Link offers a flexible approach to collecting consent, supporting paper and/or electronic consent tools. This ensures portfolio-level scalability regardless of whether mechanisms vary across studies. Medidata Link also makes the consent withdrawal process easy, ensuring that the linked dataset is compliant and that the sponsor is not at risk of using patients who have withdrawn their consent.

PII COLLECTION: In order to link data at the patient level, PII must be captured, stored, and managed in a secure manner compliant with privacy laws. Medidata Link supports multiple methods of PII collection, ranging from patient entry (via the myMedidata patient portal) or clinician/staff entry (via the Medidata Site-Facing Portal) to eliminate the need for site-based tokenization solutions.

DE-IDENTIFICATION & TOKEN GENERATION: Medidata Link is pre-integrated with tokenization technology from our industry-leading partners, HealthVerity and Datavant, to transform captured PII into de-identified tokens. Tokens are encrypted, irreversible series of letters and numbers that effectively "de-identify" the patient and are used to enable longitudinal data linkage. The Medidata Link platform has been designed to be fully flexible, and can support alternative tokenization technologies.

CONNECTION TO RWD ECOSYSTEMS: Medidata Link provides streamlined outputs that detail Rave subject IDs with their associated tokens. This enables sponsors to find the data that includes their trial cohorts from broad RWD ecosystems, including claims, EMR, and labs datasets that generally provide up to a 80-90% coverage rate of a trial population. Because Medidata Link can generate tokens from multiple vendors at any point, sponsors can selectively pick their RWD. This maximizes the coverage of their clinical cohort in the real world and ultimately increases the robustness of the linked dataset.

Use Case

01

Tracking Patients Lost to Follow-Up

01

Tracking Patients Lost to Follow-Up

CHALLENGE

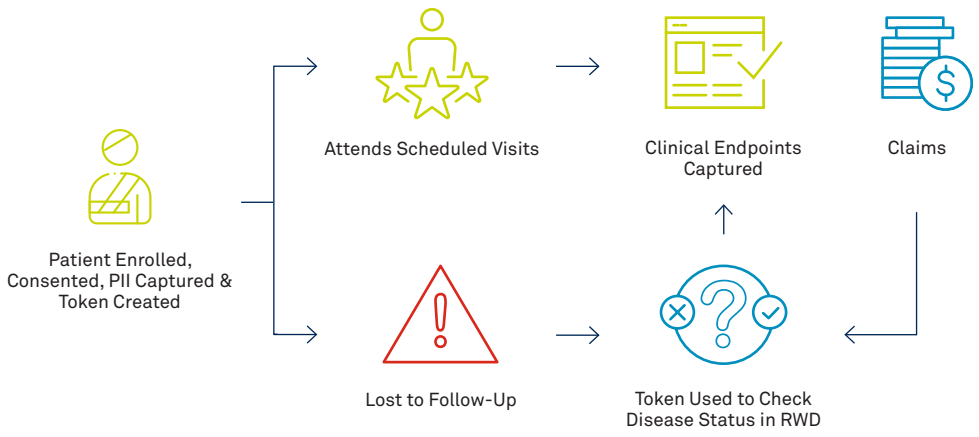
When a patient is lost to follow-up (LTFU) in a clinical trial, it has significant downstream impacts on study costs and evidence generation, as sponsors might miss key clinical endpoints. To mitigate this risk, sponsors often extend recruitment efforts or plan larger studies than initially required. In some cases, too many lost patients can be a significant detriment to generating statistically valid effect estimates. Using linked RWD makes it possible to supplement trial data for patients LTFU. This enables sponsors to continue to generate meaningful endpoints despite potential patient dropout.

SOLUTION

- By linking CTD to RWD, sponsors can derive key clinical endpoints in all linked patients, even if they are LTFU, by monitoring their RWD. This can provide richer insights into overall survival (OS), progression-free survival (PFS), or changes to treatment pathways for an entire cohort, mitigating the negative effects of patient dropout.
- Linkage to RWD can help understand why patients drop out from trials (e.g. they may have been unable to participate due to an unrelated health event). Sponsors and regulators require more information on the circumstances of why a patient is LTFU – whether it is caused by suboptimal trial design, or because of undetected safety issues.

THE BOTTOM LINE

Medidata Link can help supplement capture of clinical endpoints for patients through their RWD, even in cases where they are LTFU. This can mitigate the need to recruit larger cohorts to compensate for lost patients, help sponsors meet regulatory standards, and reduce study cost and burden.



SAMPLE USE CASE

ONCOLOGY

An oncology diagnostic company running a Phase III trial is studying the accuracy of their test for early prediction of cancer. However, the sponsor is concerned that a high patient dropout rate (on average 19%) may undermine validity of their findings or require them to conduct a larger trial. [1]

SAMPLE APPROACH

- Medidata Link's site-facing form can collect PII and consent during a patient visit without adding to patient or site burden.
- Collected PII can be used to link patients' CTD to their RWD to understand the underlying reasons for patients LTFU and longitudinally confirm clinical endpoints over time.
- Insights gained from those patients LTFU can help ensure the study maintains statistical power, while patterns in LTFU circumstances can potentially be used to inform future study design.

1 Ramsey, Leslie. "Recruitment Rates Rising, but Retention Rates Fall, According to New Study." CenterWatch, February 21, 2020. https://www.centerwatch.com/articles/24543-recruitment-rates-rising-but-retention-rates-fall-according-to-new-study#:~:text=CNS%20trial%20dropout%20rates%20grew,percent%20dropout%20rate%20in%202019.

Use Case

02

Reducing Patient Burden and Augmenting Decentralized Clinical Trials

02

Reducing Patient Burden and Augmenting Decentralized Clinical Trials

CHALLENGE

Long-term follow-up of patients in clinical trials involves substantial logistical, clinical, and economic burden, leading to dropout rates of up to 30%.[2] In the aftermath of the COVID-19 pandemic, decentralized clinical trials (DCTs) have become increasingly viable. Sponsors and CROs are beginning to adopt DCT technologies that reduce the frequency of patient/investigator contact points to lower burden and administrative costs. Linking RWD to these studies provides additional patient insights during the DCT.

SOLUTION

- CTD and RWD linkage can fill data gaps during periods with limited follow up contact or investigator access, allowing sponsors to utilize RWD to track key outcomes over time for trials with extended monitoring periods.
- With a robust CTD and RWD linkage strategy, investigators can design trials that leverage decentralized elements to relieve contact burden without reducing insights into the comprehensive patient journey (e.g. using linked RWD to monitor the outcomes of patients within the standard-of-care (SoC) arm despite a lower frequency of in-person contact).
- When CTD and RWD are linked, some endpoints that are traditionally collected in-person can be accessed remotely. This can lead to reduced patient attrition and decreased study operational costs without sacrificing visibility into key clinical endpoints.

THE BOTTOM LINE

Medidata Link enables sponsors and CROs to reduce patient contact points with DCT technologies without impacting data collected. The augmentation of CTD with RWD lessens the need for frequent follow-up visits, decreases study operational costs, and reduces patient burden while limiting costly investigator-led follow-ups.

2 The pandemic is pushing for quick adoption of virtualization technology; trials are becoming more complex and requiring longer enrollment periods - **during the pandemic there was a 9% reduction in clinical trial enrollment each week;** Unger JM, Xiao H, LeBlanc M, Hershman DL, Blanke CD. Cancer Clinical Trial Participation at the 1-Year Anniversary of the Outbreak of the COVID-19 Pandemic. JAMA Netw Open. 2021;4(7):e2118433. doi:10.1001/jamanetworkopen.2021.18433.

SAMPLE USE CASE

CARDIOVASCULAR

A biopharmaceutical company running a Phase III coronary artery disease trial includes a well-established SoC for their control arm patients. The outcomes of this SoC treatment are well-documented, but trial patients in the control arm must still endure frequent follow-ups and a high degree of contact burden while participating. The sponsor is looking to leverage decentralized technologies to reduce control arm patient burden, but is concerned about missing key insights due to longer periods between in person contact.

SAMPLE APPROACH

- The sponsor's clinical trial can be designed to leverage a claims dataset to augment trial data and significantly reduce the number of in-person patient visits required in the latter stages of the trial — particularly for patients on a treatment arm with a well-documented SoC.
- Linked CTD and RWD can create a fully longitudinal view of each patient within both treatment arms, giving the sponsor insight into events that otherwise may not have been visible through traditional contact points.
- Medidata Link can help the sponsor gain confidence in their DCT solutions, increasing patient centricity and trial accessibility without sacrificing data robustness.

Traditional Trial Design
1x Surgery
5x Rx Administration
20x Quarterly Follow Up
High Patient Burden

RWD Enhanced Hybrid DCT
1x Surgery
5x Rx Administration
5x Annual Follow up
60x PRO Submissions
60x Monthly Claims Analytics
Minimal Patient Burden

Use Case

03

Monitoring and Contextualizing Patient Reported Outcomes

03

Monitoring and Contextualizing Patient Reported Outcomes

CHALLENGE

Patient reported outcomes (PROs) have become a key part of premarket submissions, and are widely seen as a way to improve communication between patients and providers. PROs can provide an objective evaluation of the patient experience, but their application and interpretation can vary based on construct (e.g. pain score vs. physical function).[3] Additionally, certain commonly used outcome metrics, such as fatigue measures, are difficult to assess without larger sample sizes.

SOLUTION

- Linked CTD and RWD can help contextualize PROs against quantifiable RWD measures over time. This enables sponsors to track how PROs correlate with other outcomes, such as prescribing patterns or hospitalizations, to create robust quantitative insights.
- Contextualization of PROs against quantitative changes in RWD makes it possible to use more patient-centric technologies during the trial, resulting in a more comprehensive understanding of the patient experience.
- Combining RWD with PROs can enhance their robustness and provide more actionable insights than would otherwise be available within the normal constructs of a clinical trial. This is particularly useful in payor conversations, but also contributes to a greater understanding of an experimental therapy's impact at the patient level and helps researchers design more patient-centric studies.

THE BOTTOM LINE

Medidata Link augments PROs by aligning them against quantitative changes in RWD for robust insights into the patient experience.

3 Hamilton, D. F., Giesinger, J. M., & Giesinger, K. (2017). It is merely subjective opinion that patient-reported outcome measures are not objective tools. Bone & joint research, 6(12), 665–666. https://doi.org/10.1302/2046-3758.612.BJR-2017-0347

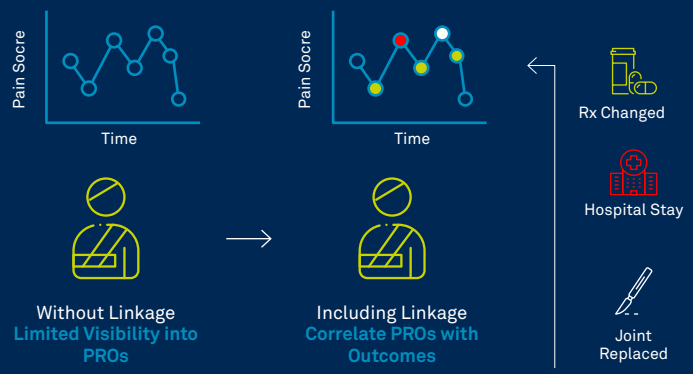
SAMPLE USE CASE

IMMUNOLOGY (RHEUMATOID ARTHRITIS)

A biopharmaceutical company running a Phase III rheumatoid arthritis trial wants to more accurately understand the factors impacting pain scoring assessments over time without increasing trial size to boost statistical significance. Immunology trials rely on assessments focused on pain, functionality, and activity levels. PROs are often combined with structural endpoints, but the sponsor contextualizing these outcomes as they relate to healthcare resource utilization.

SAMPLE APPROACH

- The sponsor can link medical and pharmacy claims data with clinically-captured PROs for an enhanced view into the pain-management journey (e.g. prescription fills, supportive care).
- Through data linkage, PROs can be contextualized against RWD-based analyses (e.g. time to surgery compared to SoC, time-to-joint replacement, assessment of long term activity levels).



Use Case

04

Quantifying Healthcare Resource Utilization

04

Quantifying Healthcare Resource Utilization

CHALLENGE

Healthcare resource utilization (HCRU) variables are crucial endpoints needed to support payer and provider discussions. However, because of significant additional burden in data collection, they are not usually captured in clinical trials. To support market access activities, sponsors often have to rely on extrapolating limited data or waiting years for RWD to accumulate post-commercialization. This lag can lead to a loss of competitive advantage at launch, and reduced market penetration.

SOLUTION

- Sponsors can use linked CTD and RWD to immediately investigate the utilization and cost data appearing in RWD from patients on the trial, rapidly supporting payor and provider discussions rather than waiting years for RWD alone to accumulate.
- Data linkage can bring greater insight into the true costs and burdens associated with inpatient and outpatient activities, as well as prescribing patterns that occur before, during, and after the trial.
- Linked CTD and RWD can help illustrate the comprehensive patient pathway to delineate between different sources of cost burden. By measuring HCRU and through linked data, sponsors can quantify a therapy's impact on the healthcare system — particularly in comparison to the standard of care.
- Access to cost data will enable trial cost-effectiveness analyses that are invaluable for early positioning and coverage of novel products.

THE BOTTOM LINE

Medidata Link accelerates market penetration, giving sponsors enhanced insight into health system burden and experimental therapy performance. By illustrating the comprehensive patient healthcare use and cost, there is an increase in trackable endpoints not normally available in a clinical trial. This ensures that sponsors do not miss key outcomes and provides payors with a longitudinal view of the economic burden of illness.

SAMPLE USE CASE

POOR PROGNOSIS ONCOLOGY (PANCREATIC CANCER)

A biopharmaceutical company running a Phase III study in pancreatic cancer wants to illustrate the total cost of care for their therapy compared to the SoC to prepare for payor conversations at launch. Late stage oncology patients often have poor prognoses and highly variable treatment pathways, particularly towards the end-of-life. Understanding the nuances of HCRU at this stage is extremely important to payors.

SAMPLE APPROACH

- CTD can be linked to medical claims, pharmacy claims, and EMR to provide a more comprehensive view of cost-of-care and resource utilization variables, such as treatment patterns and duration, outpatient costs, and hospitalizations.
- Linked data can help the sponsor compare their experimental therapy to the SoC, enabling them to quantify cost-savings or cost-effectiveness of treatment (e.g. reduction in hospital admissions, pharmacy costs).
- Linked CTD and RWD can provide a longitudinal view of the patient journey to enhance long-term outcome monitoring, informing a sponsor's understanding of HCRU.

Use Case

05

Evidence for Label Expansions

CHALLENGE

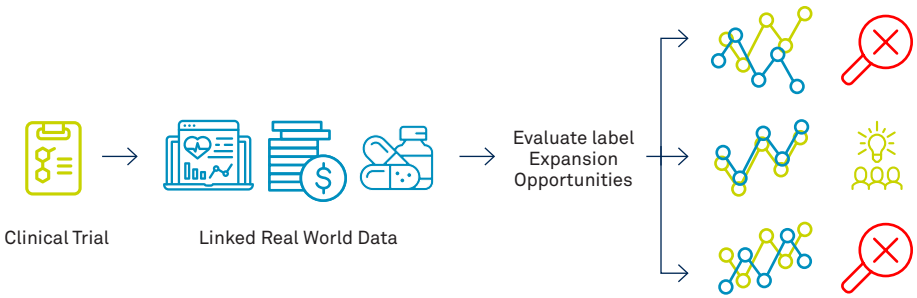
Traditionally, clinical trials are designed and powered to evaluate pre-specified outcomes in select patient populations. Therefore, investigators' and sponsors' insight remain limited to data collected within the boundaries of the trial protocol. It can take years after launch for RWD to mature enough to support a meaningful investigation into potential unintended treatment benefits and label expansions. Even then, the inherent shortcomings of RWD, such as unmeasured confounding and measurement error, limit investigators' ability to draw conclusions that meet regulatory grade evidence standards for label expansion.

SOLUTION

- CTD linkage to RWD expands researchers' insight into patient outcomes beyond the trial protocol, and without increasing burden for active data collection. This helps them discover treatment outcomes and benefits that were not included in the trial and otherwise will remain undetected.
- Linked CTD and RWD helps sponsors generate additional data for trial participants at low burden and cost. This can support exploratory analyses to identify and characterize patient subgroups with potential for label expansion and inform future trial design.
- Sufficiently large Phase III CTD that are linked to RWD can potentially provide sufficient regulatory grade evidence for label expansion.
- Linked CTD and RWD validates and calibrates RWD-based outcomes against adjudicated trial outcomes. This will alleviate outcome measurement errors in future RWD studies and increase confidence in their findings for label expansion.

THE BOTTOM LINE

Medidata Link can extend trial data beyond a study protocol to unveil patient subgroups experiencing larger net benefit – all while improving data quality and quantity to initiate regulatory conversations for label expansion. With data linkage, sponsors can leverage data from existing trials or calibrate RWD studies that can support evidence generation for label expansion studies.



SAMPLE USE CASE

CARDIOVASCULAR (ATRIAL FIBRILLATION)

While running a Phase III trial in atrial fibrillation, a pharmaceutical company noticed that patients using their therapy were seeing a reduction in stroke frequency. Since this was an unexpected outcome, study protocol has not included data elements that enable further exploration of patients subgroups. Label expansion studies are arduous, as the comorbidity and prescribing profiles of patients evolve over time and identifying novel subgroups requires data that are not usually planned and collected in the trial.

SAMPLE APPROACH

- Clinical data from the Phase III trial can be linked to EMR, medical claims, and pharmacy claims for visibility into the comprehensive patient journey, allowing for greater access to safety and effectiveness data.
- Routine monitoring and analysis of cohorts over time can help researchers identify patients with differential responses, even as comorbidity profiles evolve.
- Linked CTD and RWD can accelerate insights on potentially-eligible patient groups by years, leveraging existing Phase III clinical data to reduce reliance on costly label expansion studies.

Use Case

06

Long-Term Safety and Effectiveness Tracking

06

Long-Term Safety and Effectiveness Tracking

CHALLENGE

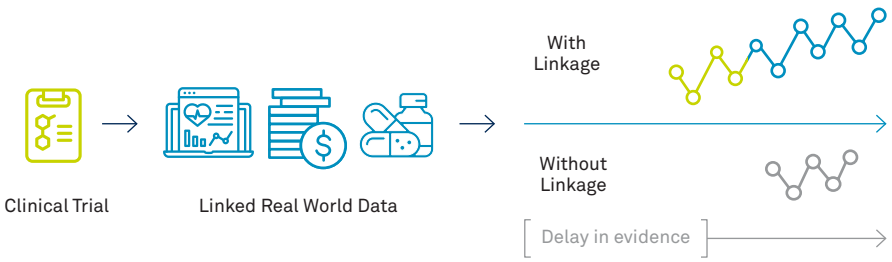
Post-authorization surveillance is critical to fully understand the long-term effectiveness and safety profiles of therapies. However, sponsors have limited insight into their clinical cohort once the trial concludes, because tracking patients is burdensome and expensive. Meeting the regulatory requirements for monitoring safety information is a chief concern.

SOLUTION

- Linking trial patients to their RWD allows sponsors to track their effectiveness and safety outcomes even after trial completion. By tapping into routinely collected RWD, sponsors gain deeper insights into long-term outcomes while reducing patient and sponsor follow-up burden.
- Linked CTD and RWD can mitigate patient risk by associating safety signals with efficacy data during extended follow-up to characterize risk-benefit balance across patient subgroups.

THE BOTTOM LINE

Medidata Link enables the capture of enhanced safety and effectiveness data without adding significant burden. This can augment submissions, improve internal decision-making, and bolster launch-planning activities. Faster and more robust evidence generation is also a key factor for several regulatory scenarios such as Emergency Use Authorizations, Accelerated Approvals, or Breakthrough Therapy Designations.



SAMPLE USE CASE

INFECTIOUS DISEASE (COVID-19)

A large biopharmaceutical company is running an investigational study in COVID-19. The sponsor is struggling to track long-term safety and efficacy endpoints. Due to the unprecedented nature of the COVID-19 pandemic, there is little information about safety and long-term benefit of these novel products. To satisfy regulatory requirements for Emergency Use Approval (EUA), the sponsor needs longitudinal data-tracking to meet safety regulations at a massive scale without adding significant follow-up burden.

SAMPLE APPROACH

- Linked CTD and RWD can help the sponsor monitor patients after the trial concludes to capture their long-term safety and effectiveness endpoints that otherwise would not be feasible to obtain.
- Medidata Link can help the sponsor assess the statistical significance of safety events by estimating event rates while protecting trial fidelity and blinding.
- Leveraging linked CTD and RWD, the sponsor can compare the long-term durability of response and effectiveness of their experimental therapy against other SoC.

About Medidata

Medidata is leading the digital transformation of life sciences, creating hope for millions of patients. Medidata helps generate the evidence and insights to help pharmaceutical, biotech, medical device and diagnostics companies, and academic researchers accelerate value, minimize risk, and optimize outcomes. More than one million registered users across 1,800 customers and partners access the world's most-used platform for clinical development, commercial, and real-world data. Medidata, a Dassault Systèmes company (Euronext Paris: #13065, DSY.PA), is headquartered in New York City and has offices around the world to meet the needs of its customers. Discover more at **www.medidata.com** and follow us **@medidata**, The Operating System for Life Sciences™.

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