MEDIDATA | ai

WHITE PAPER

# Connecting Patient-level Clinical Trial Data to Real World Data

## Unlocking a new frontier of evidence generation with Medidata Link

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# Introduction

Clinical development teams are under continual pressure to create faster and safer interventions for increasingly complex diseases. Historically, regulators have relied solely on clinical trials to prove effectiveness and safety. Although clinical trials provide robust views of outcomes specified within study protocols, they are not always representative of the broader populations that exist in the real world.[1] This means that the results of a clinical trial may vary across patient populations seen in routine clinical practice.[2] Recent investigations into novel conditions such as Vaping Associated Pulmonary Injury or the intense speed of COVID-19 vaccine emergency use authorizations (EUA) have highlighted the need to bridge key evidence gaps in our existing clinical processes.[3]

Sponsors have started to bridge evidence gaps by connecting real world data (RWD) sources like electronic medical records (EMR), insurance claims, wearable devices, and genomics to clinical trials in order to understand real world outcomes. In response to this growing trend, regulators have passed key legislation and issued guidance to support RWD usage in regulatory decision making.[4] Now, sponsors have a clearer path forward in using linked RWD and clinical trial data (CTD) at the patient-level to aid in regulatory decision making. These once disparate data sources can be combined to more holistically describe a patient's healthcare journey. With innovative data linkage technologies like tokenization, researchers are beginning to gain a deeper understanding of patients' diseases, treatments, and outcomes to close critical evidence gaps. Data linkage unlocks a new frontier in evidence generation where sponsors can finally monitor long-term safety, track patients lost to follow up (LTFU), improve commercial forecasting, and better demonstrate treatment effectiveness.

### DATA LINKAGE IN THE INDUSTRY

- Sponsors are increasing the use of RWD in submissions: From 2019 to 2020, the number of FDA-approved new drug applications (NDAs)/ biologics license applications (BLAs) that utilized real world evidence (RWE) to evidence safety and/or effectiveness rose from 53% to 78%.[5]
- Linked data can mitigate the significant impacts of patients being LTFU. Phase III clinical trials often struggle with high rates of patient dropout (~30%).[6]
- Post-approval market access depends on RWD, but there is a latency in availability. It can take years post-trial for RWD to mature enough for sponsors to gain useful insights.

While some organizations have attempted to conduct data linkage in-house, they often struggle to ensure that their approaches meet the complicated security, regulatory, and privacy requirements necessary to create tokens and link patient data at scale. In-house data linkage also runs the risk of unblinding and re-identifying trial patients. Other organizations are developing custom solutions for specific trials, but face difficulties scaling across entire trial portfolios. This leads to inefficiencies, greater costs, and increased burden to patients and sites. Medidata Link addresses these challenges with flexibility and scalability in mind to enable patient-level data linkage.

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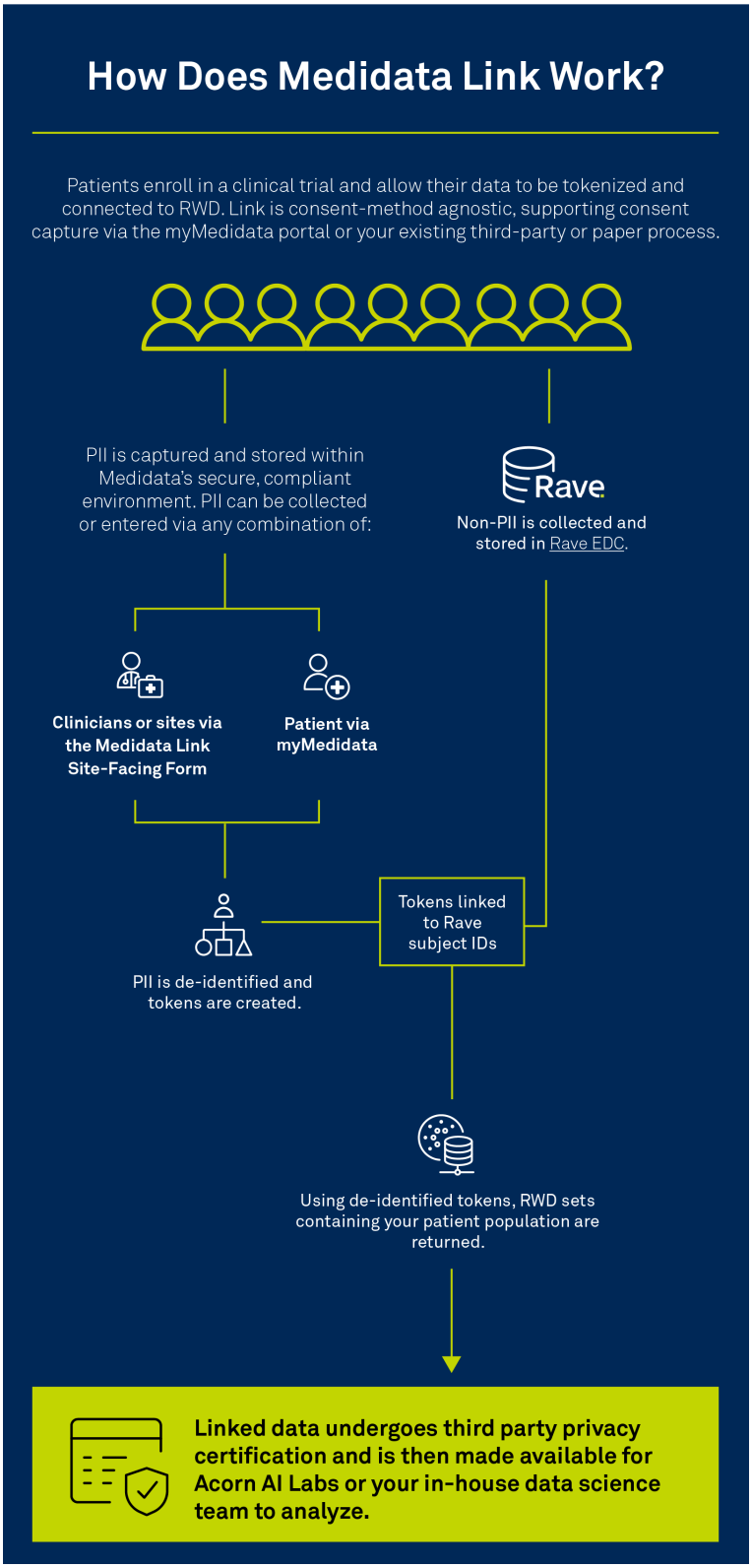
# Overview of Medidata Link

Medidata Link is the first centralized data linkage solution that works flexibly across research sites and integrates with multiple token vendors to connect patient-level CTD to the broadest ecosystem of RWD — powered by the Medidata Clinical Cloud unified life sciences platform. The solution seamlessly integrates into existing clinical workflows, safely manages data linkage consent status, and collects personally-identifiable information (PII) with minimal burden to sponsors, sites, or patients. The Medidata AI Labs team harmonizes and analyzes CTD and RWD with unrivaled data management and analytics expertise, while also giving sponsors the option to perform their own in-house analyses. Medidata Link enables sponsors to generate long-term safety and effectiveness evidence, continue to collect meaningful endpoints even if a patient is LTFU, and quantify healthcare resource utilization (HCRU) — providing continuous evidence generation capabilities throughout and beyond the clinical development cycle.

## LINKING CLINICAL TRIAL AND REAL WORLD DATA VIA TOKENIZATION

Medidata Link leverages our tokenization technology partnerships and pre-built engineering pipelines to collect a consenting patient's PII and creates an encrypted, de-identified "token." This token is then used to assess and find the patient's RWD within our partners' RWD ecosystems. Our secure environment is fully HIPAA compliant and privacy-certified, allowing sponsors to centralize data collection while minimizing the risk of unblinding or re-identifying trial patients. With access to the richest RWD ecosystems, sponsors unlock an array of diagnoses and treatments over time - across multiple physicians, hospitals, pharmacies, labs, and even insurers.

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# Key Features of a Scalable Data Linkage Solution

## CONSENT METHOD AGNOSTIC WITH FLEXIBLE PII CAPTURE

To create de-identified tokens, patients must consent to having their CTD linked with RWD sources. Medidata Link supports integrations with paper consent, myMedidata eConsent, and third party eConsent. Sponsors can collect PII through flexible options like one-time site-based entry, patient entry, or file transfer — ensuring scalability across the entire clinical development pipeline.

## SEAMLESSLY WORKS ACROSS ANY TRIAL OR SITE

The traditional method for data linkage relies on one-off, custom-built solutions that force sponsors to start from scratch for each trial run by different CROs. Medidata Link offers centralized workflows for linkage across any trial run by any CRO across R&D programs, giving sponsors additional flexibility in trial design and planning

## CENTRALIZED ENVIRONMENT AND FLEXIBLE TOKEN GENERATION

Medidata Link can generate tokens from multiple vendors at any point in a trial, enabling sponsors to selectively pick the most appropriate RWD on their own timeline. Using a centralized environment to generate multiple tokens from different tokenization vendors gives sponsors access to the largest ecosystem of RWD to link to clinical trial patients, increasing the likelihood of finding matches and robustness of the linked dataset. Medidata integrates with leading tokenization vendors to apply their de-identification software, produce patient tokens, and link trial patients to datasets in their RWD ecosystems so sponsors and CROs can bypass the risky, costly process of installing specific tokenization software at every site.

# Benefits to Patients, Sites, and Sponsors

## FOR PATIENTS

Data linkage enhances safety and effectiveness monitoring, decreasing the need for burdensome patient follow-ups and procedures. Medidata Link can lessen patient burden by helping sponsors design smarter trials supplemented with patients' RWD, resulting in less frequent in-person visits.

### BUILDING PATIENT TRUST FOR DATA LINKAGE

De-identified patient data is already widely used to understand care in the real world. For example, aggregated claims data is often used post-trial to understand HCRU (e.g. social determinants of health data can be leveraged to contextualize care management and health risk). Extending data linkage to clinical trials can ensure that clinical trial patients' invaluable contributions to research can continue after the trial itself has concluded. Ensuring patients are educated on the positive impacts of linking their trial data to the real world is critical to getting their buy-in.

Through Medidata's work with patient advocates in our Patient Design Studios, we validated that informed consent with clear and concise messaging is a crucial step in demonstrating the benefits of data linkage back to the patient. For instance, patients should be informed that by consenting to data linkage, they are helping researchers learn more about factors affecting disease states, as well as helping researchers monitor the safety and effectiveness of therapies beyond the patient's clinical trial or registry participation.

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## FOR SPONSORS

With Medidata Link, sponsors can immediately gain access to their trial participants' RWD. This can help overcome the historical delays associated with RWD not being available at scale for years post-approval. Sponsors can future-proof their trials by generating evidence not previously possible, understand their patient journeys and long-term outcomes sooner, and develop meaningful evidence that can be used for more successful commercialization programs.

Medidata Link has a number of use cases in varied indications across the clinical development lifecycle. Sponsors can use the solution to collect meaningful endpoints even if a patient is LTFU, contextualize patient reported outcomes (PROs) with quantitative data, and investigate the total HCRU for patients during and after a trial. Medidata Link can also be used to generate long-term safety and effectiveness evidence and augment data collection in decentralized clinical trials to reduce patient burden.

Data linkage also unlocks additional patient data to power further AI and machine learning technologies and accelerate evidence generation for label expansion studies.

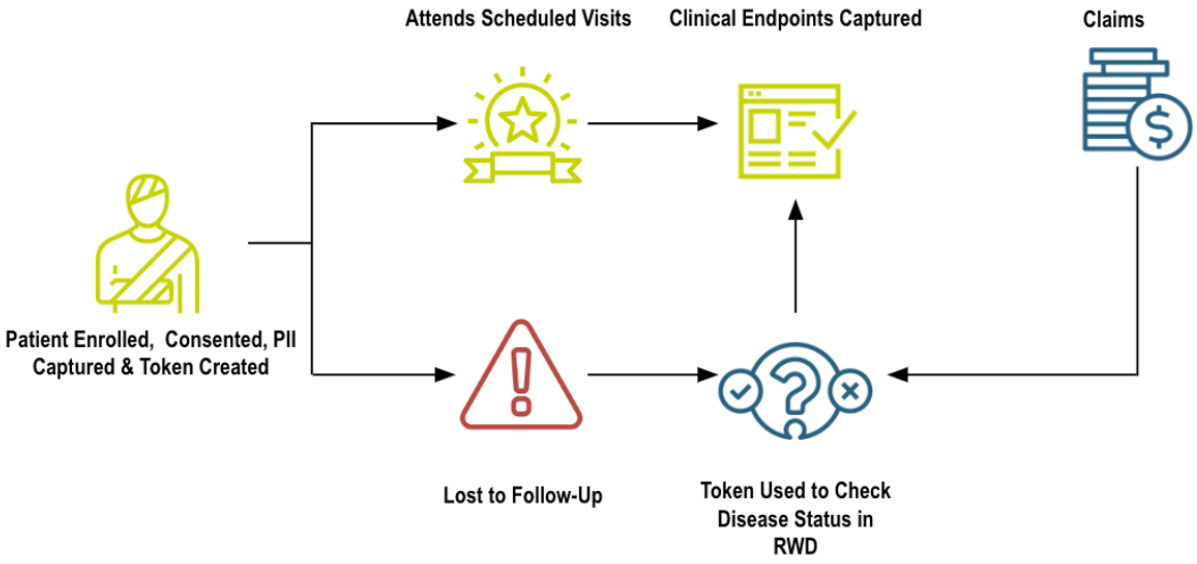
## FOR SITES

Medidata Link's centralized approach to data linkage reduces administrative burden on sites while seamlessly fitting into existing clinical processes. To facilitate the adoption of data linkage at sites, Medidata Link manages consent status, supports flexible site-based PII ingestion, and integrates into existing Rave workflows. This means sites do not have to install new software or undergo extensive training if sponsors want to create multiple tokens.

# Data Linkage Use Cases

## PATIENTS LOST TO FOLLOW-UP

When a patient is LTFU in a clinical trial, it has significant downstream impacts on study costs and evidence generation. To compensate, sponsors often extend recruitment efforts or plan larger studies to mitigate the risks of losing patients. In some cases, too many lost patients can be a significant detriment to generating statistically valid outputs. By linking CTD with RWD, sponsors can assess key clinical endpoints, such as overall survival (OS), hospitalizations, or changes to treatment pathways, for those LTFU. Sponsors can also continuously capture clinical endpoints, even in cases of a patient being LTFU, by monitoring patient activity in the real world. The insights from linking to RWD of LTFU patients can help ensure that the study maintains statistical power, while patterns in LTFU patients endpoints can inform future study design.

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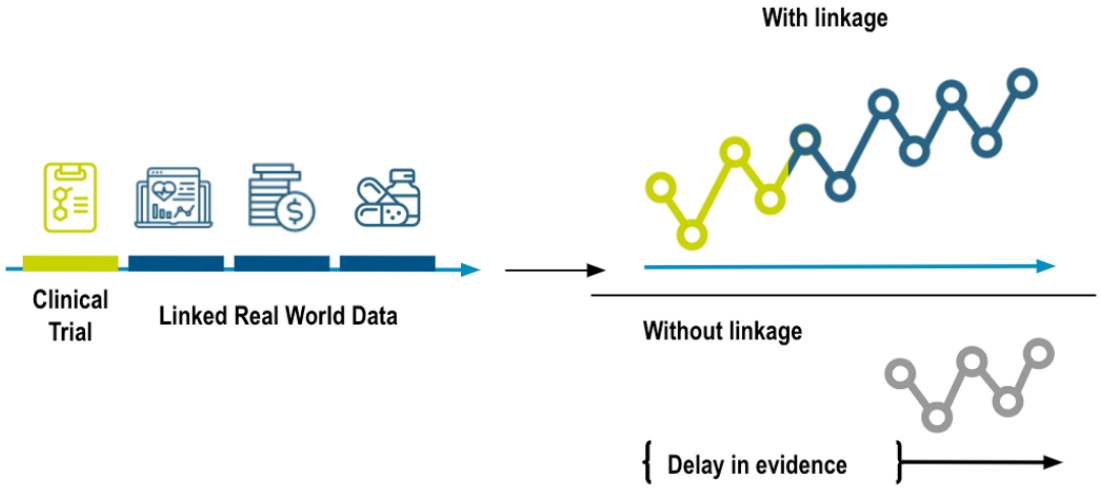
## POST-MARKET LONG-TERM SAFETY AND EFFECTIVENESS TRACKING

Tracking long-term outcomes after a trial is burdensome, often requiring sites to manually reach out to patients. Meeting the requirements for robust safety information is a key concern. Data linkage can provide faster and deeper insights into trial patient safety and effectiveness outcomes, reducing patient and sponsor burden during long-term follow-up. Sponsors can overcome the latency in RWD accumulation by gaining immediate access to a cohort's activity in the real world (e.g. long-term durability of response and effectiveness of experimental therapy against other standards of care). Linked CTD and RWD can mitigate patient risk by identifying safety signals across patient subgroups faster.

Medidata Link enables the capture of enhanced safety and effectiveness data without adding significant burden. This additional data can enable further AI and machine learning technologies to uncover patient subgroups, 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.

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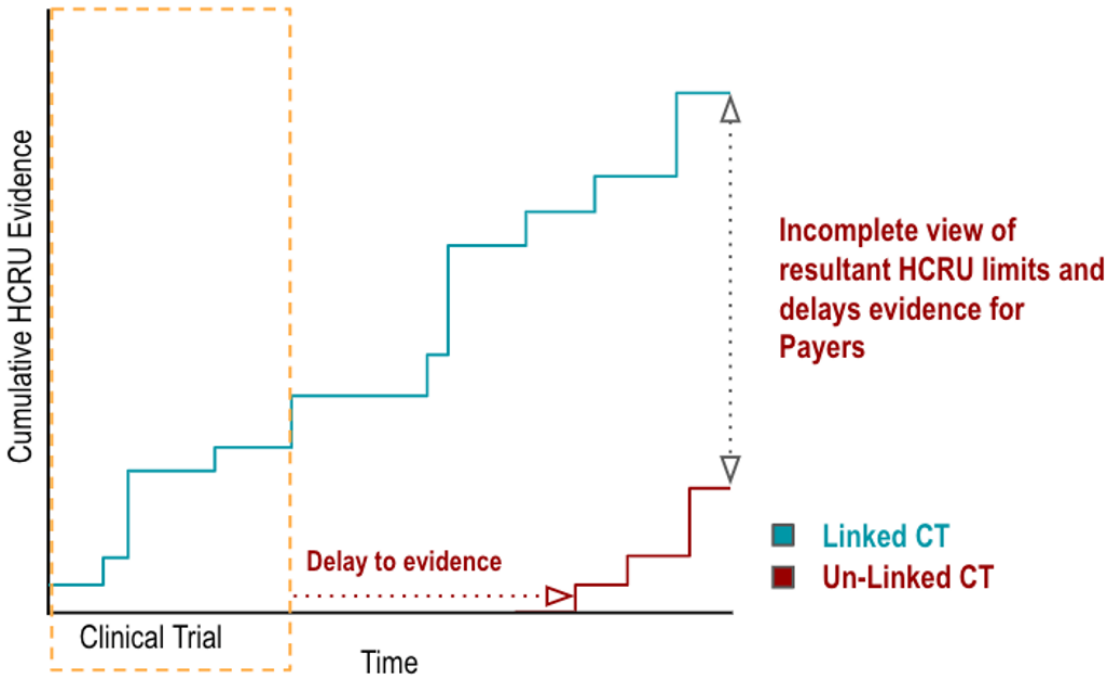
## QUANTIFYING HEALTHCARE RESOURCE UTILIZATION

Although HCRU is crucial to supporting payor and provider discussions, it is difficult to measure within the protocolized and finite period of a clinical trial. To support market access activities, sponsors often have to rely on extrapolating limited data or waiting years for RWD to accumulate after commercialization. Instead, sponsors can use RWD to immediately bolster their understanding of trial patient data to support payor and provider discussions rather than waiting years for RWD to accumulate. Linked CTD and RWD can help illustrate the comprehensive patient pathway to delineate between different sources of cost burden. By measuring HCRU through linked data, sponsors can qualify and quantify a therapy's impact on cost of care over time and more broadly on the healthcare system – particularly in comparison to the standard of care.




# Summary

Medidata Link offers a centralized approach to connecting CTD to RWD at the patient-level, accelerating clinical development, commercialization, and evidence generation activities. It seamlessly integrates into existing clinical workflows, safely manages data linkage consent status, and collects PII with minimal burden to sponsors, sites, or patients. By connecting patients participating in a trial to RWD, sponsors can overcome the latency in generating RWE to inform medical and future pipeline decisions. Medidata Link unlocks the full potential of linked data to bring sponsors into the next generation of clinical development.



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# Footnotes

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