Follow-up that outlasts the site relationship

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Summary

When long-term follow-up depends on participants returning to the original treatment site, the dataset increasingly reflects those still able and willing to return. The resulting risk of selection bias matters, even when its direction cannot be assumed. Long-term follow-up for certain cell and gene therapies can extend to 15 years. A study that relies on a 15-year relationship with one institution is built on a foundation that changes in residence, care, health, and willingness to travel will erode, and the people lost first are unlikely to be a random sample of the cohort. A durable follow-up model has to address both continuity of data collection and who remains represented in the data.

PicnicResearch brings together ongoing medical-record retrieval across identified treating providers, virtual visits under central investigator oversight, locally arranged examinations and laboratory collection (if necessary), and participant engagement through the PicnicHealth app. One PicnicResearch coordinating team connects these activities and manages protocol implementation, version control, training, and any required retrospective review across participants.

The central test is whether the study continues to obtain the required evidence as participants' lives and care change, including after they stop returning to the original site. This paper describes the model, its relationship to FDA guidance, and the measures sponsors can use to evaluate its performance.

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A long-term study needs a durable basis for follow-up

Why should a 15-year evidence obligation depend on a 15-year relationship with one treatment center? The hospital that administers a therapy may remain central to a participant's care, become one of several providers, or eventually cease to be involved. A study needs to work across those circumstances. Changes in where people live, receive care, and can reasonably attend visits are foreseeable conditions to design for from the outset.

When evidence collection depends heavily on return visits to the original site, those changes create a predictable risk of missing the very observations the study was established to obtain. A participant may receive a new diagnosis or treatment elsewhere while becoming less connected to the institution responsible for follow-up. The study's need for that information persists even when the original site relationship does not.

Participant-reported experience illustrates the challenge. A 2024 Emily Whitehead Foundation and Catalyst Healthcare Consulting survey included 96 CAR-T recipients and caregivers, predominantly caregivers and families of pediatric patients. Among respondents whose treatment was more than 12 months earlier, 20% reported having stopped attending follow-up appointments. Among those more than 12 months after treatment who still attended, 38% did not anticipate attending for the full 15 years. Distance to the site was reported as a challenge by 64% of respondents.[3] This self-selected, cross-sectional survey identifies barriers and concerns; it does not estimate a 15-year dropout rate or establish that stopping visits means losing all follow-up data.

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The scientific consequence is selective observation

If continued observation depends on who remains able and willing to return, the resulting evidence increasingly reflects that selected group. Distance, resources, caregiving demands, and health status all influence participation. Where these factors also relate to the outcomes under study, incomplete follow-up can introduce selection bias, affecting estimates of long-term safety or effectiveness as well as their precision.

The direction of that bias cannot be assumed. Participants in poorer health may have difficulty traveling, while those who feel well may see less reason to attend. An apparently reassuring dataset could reflect missed events; an apparently high event rate could reflect disproportionate retention of participants with continuing clinical needs. Either is possible. What matters is that the observed participants may differ systematically from those no longer observed, so fewer events recorded cannot automatically be interpreted as fewer events occurring.

This is a design vulnerability that warrants action before a study misses a decade of observations. A follow-up plan that treats predictable changes in participants' lives as exceptions is poorly suited to its time horizon. It should include ways to sustain observation when return visits become impractical, alongside methods to assess who is being lost and what information remains obtainable.

Start with the follow-up requirements

FDA's 2020 guidance on long-term follow-up after gene therapy takes a product- and risk-specific approach: 15 years for integrating vectors and up to 15 years for genome-editing products. It describes what to monitor, including new malignancies and new or worsening neurologic, autoimmune, and hematologic conditions, and it recommends annual physical examinations during the first five years, appropriate laboratory evaluation, and product-specific monitoring. It explicitly contemplates observations from healthcare providers outside the trial, while preserving investigator's responsibility for the data.[1]

FDA's 2024 guidance on decentralized trial elements addresses telehealth, local healthcare providers, and other study activities away from traditional sites.[2] Read together, the two documents support combining collection methods. The suitability of a particular approach remains specific to the product, protocol, and intended use of the data.

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For each protocol, the practical task is to specify the observation needed, its timing, its source, and who reviews and acts on it. The collection plan separates information available from routine care from assessments the study must arrange, defines how missing information will be pursued, and sets the point at which an unresolved gap is escalated.

The following framework translates study needs into collection methods and follow-up decisions. It is an operating-design framework; the regulatory requirements for a given product are set by the guidance and the protocol.

Study need	Collection approach	What requires additional follow-up
Events occurring across care settings	Longitudinal record retrieval	Unidentified providers, unavailable records, incomplete documentation
Protocol-specific symptoms and event histories	Scheduled virtual visits	Clinical assessment and source confirmation where needed
Examinations and laboratory assessments	Local providers and arranged collection	Protocol-specific timing, procedures, and sample handling
Safety review and escalation	Investigator oversight and defined reporting pathways	Uncertain relatedness, missing clinical details, further investigation

How the PicnicResearch model brings the components together

Medical records provide the longitudinal clinical context

Participants authorize PicnicResearch to retrieve their medical records through a process based on their right of access. Retrieval continues throughout follow-up across identified treating providers, including additional providers identified as participants' care changes: the original trial site and the other hospitals, clinics, and practices a participant uses. Those records document hospitalizations, diagnoses, subsequent treatments, and other protocol-relevant events without requiring a return

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visit to the original site. Repeated retrieval adds information that was unavailable at an earlier assessment.

Retrieval does not guarantee a complete record. Providers must be identified, records obtained, and the observation documented in the first place. A missing record, an assessment that was never performed, and a retrieved note that omits a required detail are different problems. The operating plan distinguishes them and specifies how each is pursued or recorded as unresolved.

Virtual visits add purposeful prospective assessment

Scheduled virtual visits ask protocol-specific questions, identify changes in care, and follow up on potential events. They capture symptoms and experiences not yet documented in routine care, and they identify additional providers from whom records should be requested. Investigator oversight connects these observations to clinical review. A participant's account clarifies an event's timing and circumstances; relatedness to a prior therapy requires clinical judgment informed by the available evidence. The protocol and operating plan define the scope of virtual assessments and the pathway for investigator review. Event-capture rules are specified separately from relatedness assessment, so that required events are not excluded merely because a routine-care note does not attribute them to the therapy.

Local assessments and laboratories complete the collection plan

When an examination, sample, or test is required, the collection plan specifies how it will be obtained: a local healthcare provider, mobile phlebotomy, a local laboratory, or sample shipment to a designated laboratory. A virtual encounter does not automatically replace a required physical examination. The protocol and operating plan define acceptable procedures, timing, and documentation, including any specialized testing or assessment that requires the original site.

Central coordination connects collection to action

One coordinating team manages the collection schedule, record requests, data queries, and application of the sponsor's definitions and completion guidelines. Common conventions, training, and quality review support consistent abstraction across participants. When the protocol or guidelines change, one team manages implementation, version control, training, and any required retrospective review, with effective dates and decisions documented. This provides a common process for updating collection rules and reviewing existing records. New examinations, specimens,

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or other prospective assessments still need to be obtained according to the applicable protocol requirements.

Because record retrieval takes time, the operating plan also gives participants and providers direct routes to report potential safety events promptly, with defined responsibilities for clinical review and escalation. Centralization simplifies oversight but does not guarantee accuracy: an error in a common process can affect many participants, which makes quality controls on that process essential.

Participant engagement supports continuity

Remote participation and locally arranged assessments reduce the need to travel to the original site. Through the PicnicHealth app, participants access their own retrieved records alongside study communications and tasks. That is a practical benefit during follow-up; its contribution to retention should be measured over time. Clear explanations of why follow-up continues, what participation involves, and how data will be used accompany those services.

The engagement plan also addresses contact updates, follow-up after missed activities, and alternatives for participants who cannot reliably use digital tools. Decentralization introduces its own dependencies, including continued contact, access to records, and access to suitable local services. Those dependencies require active management; reducing travel alone does not establish better retention or eliminate selection bias.

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Assessing data quality beyond agreement with site data

Where data are entered does not, by itself, establish their quality. For information documented in a clinical record and later entered into an EDC system, quality depends on the source documentation, the abstraction process, and the definitions applied. Other study data arise from protocol-directed examinations, tests, or investigator assessments, and their quality depends on those activities actually taking place.

This distinction matters when a coordinating center is compared with trial sites. Agreement on shared records can help assess consistency of abstraction. It cannot establish whether the shared record contains every event the study needs: two datasets can agree and still omit the same undocumented event. Conversely, an additional, verified event can improve completeness while reducing agreement with the site dataset. Each discrepancy requires review against the source material, protocol definitions, and observation period before it counts as evidence in either direction.

The case for the integrated model is therefore broader than concordance. It combines records across providers, direct participant contact, and arranged assessments because each addresses a different source of missing information. Whether that produces more complete or timely evidence should be assessed against the protocol, using documented sources and clinical review of discrepancies. Regulatory suitability likewise depends on intended use, collection methods, oversight, and data integrity.

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Measuring whether the model delivers

Evaluation should test the functions the model is intended to perform. A protocol-specific evaluation plan should address:

- Completion of required assessments within protocol windows, with reasons recorded for missing data.
- Retention and continuity of contact, including among participants who have stopped attending the original site, with visit attendance distinguished from continued outcome ascertainment.
- Differences in follow-up completeness across participant groups, including by distance, age, health status, and other relevant characteristics, to assess whether some groups become less represented over time.
- Completeness and timeliness of event capture, including mortality, against prespecified reference sources and with clinical review where appropriate.
- Incremental clinically relevant information contributed by outside records, virtual visits, and arranged assessments, with comparable observation periods and verified event definitions.
- Time from awareness of a potential safety event to clinical review and required escalation.
- Participant burden, and the resources needed to sustain follow-up for the full period.

Comparisons with site datasets can contribute to this evaluation, provided observation periods, definitions, and source availability are understood. Each discrepancy should be investigated before it is attributed to either dataset. Agreement remains useful for shared data elements; it is one input to a broader assessment of whether the study is getting the evidence it needs. Analyses should also examine the pattern and reasons for missing follow-up and assess how plausible outcomes among participants with incomplete data would affect the conclusions. A high overall retention rate can conceal important gaps within particular groups.

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Conclusion

A long-term evidence obligation needs a follow-up model designed to remain viable when participants' relationship with the original treatment site changes. Reliance on continued return visits creates a foreseeable vulnerability: the study can lose observations and progressively lose representation of people who are less able or willing to attend. That vulnerability should be addressed in the study design from the beginning.

PicnicResearch combines longitudinal records, prospective contact under investigator oversight, locally arranged assessments, and central coordination to reduce that dependence. Its performance should be judged by the evidence it obtains across the full follow-up period, including for participants who no longer return to the original site.

The goal is to preserve the study's ability to answer its scientific questions as participants return to their lives. That requires attention to both how much evidence is collected and whose experience it continues to represent.

If you are planning long-term follow-up for a cell or gene therapy program, our scientific team can walk through how this model would apply to your protocol.

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