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Beyond Efficacy: Using Real-World Data to Identify and Address Implementation Barriers Across the Pharmaceutical Product Lifecycle

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ABSTRACT

Implementation barriers are key instruments to seeing the holistic picture to ensure patients receive new medicines. In the setting of the pharmaceutical industry, "implementation barriers" can be defined as obstacles that prevent a medicine from achieving its intended impact before and after approval. Common categories include clinical, operational, regulatory and health technology assessment (HTA), access, and behavioral and system barriers. Addressing these implementation barriers in an efficient and timely way would greatly assist to inform healthcare decision making and thereby accelerate adoption by clinicians and patients of new medical innovations. Real-World Data (RWD) has been used extensively over the years to describe many pieces of the pharma puzzle and has become an essential observational tool. Descriptive studies using RWD abound on the burden of illness, (comparative) effectiveness, (comparative) safety, patient journey, treatment use and switching, just to name a few. RWD hasn't been used in a structured way to address implementation barriers but has tremendous potential for doing so. RWD is most powerful and strategically useful not when it merely measures, but when it explains why, for example, the uptake of a product is low. It is the search for "why" that renders RWD so important for the identification of implementation barriers. Unfortunately, most RWD studies stop at the measurement level. A structured approach to what RWD is required and what steps should be taken to discover implementation barriers using RWD. The approach is outlined for rare diseases and a detailed example for ATTR-CM is shown and explained. Qualitative methods and AI play an important role in enhancing the power of RWD to investigate implementation barriers and the role they play in ensuring that a new innovation actually reaches the patient, increasing the value proposition for patients, healthcare systems, and industry

Keywords: implementation barriers, implementation science, integrated evidence, patient journey, clinical adoption, electronic health records, natural language processing, artificial intelligence

Implementation Barriers offer a holistic picture of evidence needs

Pharmaceutical research has been constructed to excel at providing evidence on the efficacy and safety of medicines because, without regulatory approval, there is no product. Expertise has grown in the areas of market access and health economics and outcomes research (HEOR) to also provide evidence to secure product reimbursement. The idea is that once regulatory approval and reimbursement are in place, the healthcare system will take over, physicians will prescribe the new product, the patient will take the new product, and everyone will benefit.

Unfortunately, this simplistic approach doesn't provide the holistic picture of the realities inherent in satisfying the "purpose" of pharmaceutical research, i.e., that patients actually receive the new innovations that they need. Many other barriers stand in the way that often go overlooked such that a more holistic way of looking at issues critical to the "purpose" is needed[1]. (See Figure 1.)

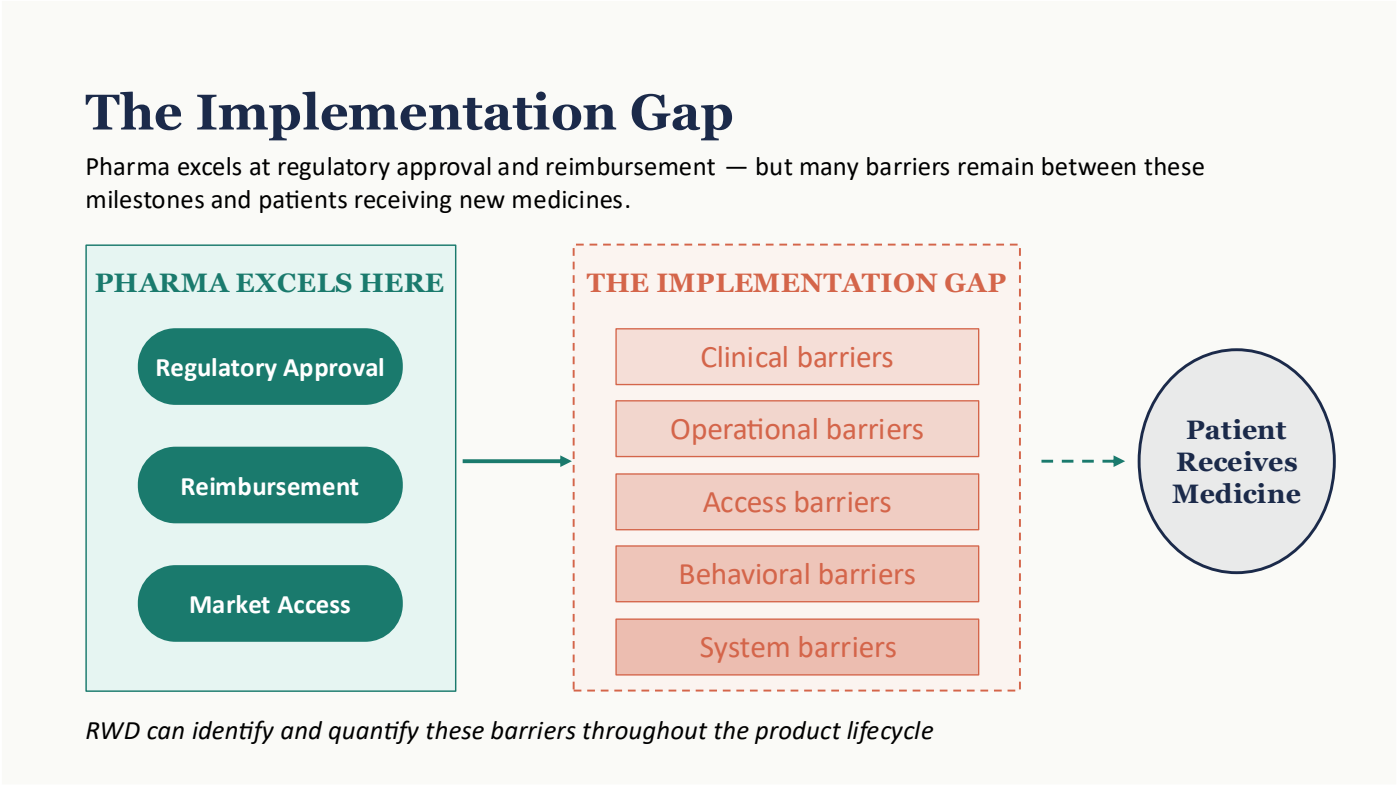

Figure 1. The Implementation Gap — barriers between regulatory milestones and patient access.

It is difficult to coordinate evidence generation activities among such a diverse collection of functional areas including research, clinical development, medical affairs, market access, and HEOR[2]. In addition, pharma companies have concerns about the level of investment required to adequately support the generation of integrated evidence activities and its inherent value proposition[3,4].

Investing in a holistic set of goals and barriers can address practical questions for all involved stakeholders and lead to improvement in health policy, health management, and service delivery[5]. Early clinical adoption and reaching the optimal set of patients are drivers of value of a new medicine from the point of view of patients, healthcare systems, and industry. These value drivers can be used to model the impact of integrated evidence activities and return on investment and/or expected net present value can be calculated and serve to quantify the value of the proposed evidence activities[6]. The consequence of not investing in evidence activities that ensure that patients actually receive the new innovation they need can be dramatic, leading to unrealized sales for pharma, poor patient outcomes, and inefficient healthcare systems[7].

Quantifying the impact of such barriers has been undertaken and, for example, it is estimated that clinician behavior interventions tend to produce small-to-moderate improvements (often single-digit absolute changes[8]). When applied to large eligible populations, the single-digit changes can translate into double-digit revenue effects early. Furthermore, persistence/adherence gains from pharmacist-led and reminder-based programs can be material, albeit variable. Access friction can be a huge choke point, where the association between PA/cost-sharing and abandonment/delays adds to the magnitude of inefficiencies. Addressing the above-mentioned barriers through a fit-for-purpose integrated evidence plan should justify a peak sales that is achieved one year earlier and 5% higher or even two years earlier and 10% higher. This translates to higher 10-year cumulative sales of 24% and 50%, respectively. For a blockbuster drug earning peak sales of $1 billion per year, this amounts to roughly $1.3 billion and $2.8 billion, respectively. These are certainly worthwhile gains for industry to work toward while at the same time improving clinical practice and, ultimately, the wellbeing of the patient.

Implementation barriers are key instruments to seeing the holistic picture to ensure patients receive new medicines. In the setting of the pharmaceutical industry,

"implementation barriers" can be defined as obstacles that prevent a medicine from achieving its intended impact before and after approval. Common categories include clinical, operational, regulatory and health technology assessment (HTA), access, and behavioral and system barriers (see Figure 2). Addressing these implementation barriers in an efficient and timely way would greatly assist to inform healthcare decision making and thereby accelerate adoption by clinicians and patients of new medical innovations.

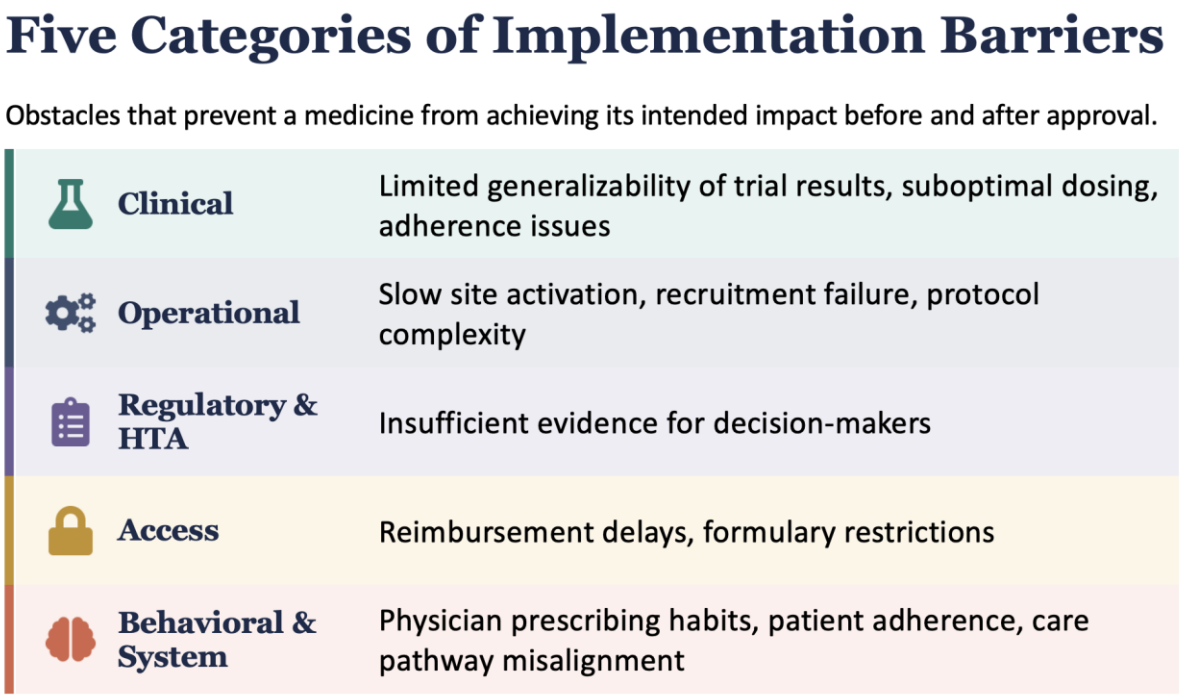

Figure 2. Five Categories of Implementation Barriers.

Real world data (RWD) can help expose these barriers because it reflects how medicines are developed, prescribed, paid for, and used. Furthermore, the implementation barriers are distributed across the product lifecycle allowing for the early detection of a potential issue so that action can be taken before the issue becomes a "barrier."

Two important types of Implementation Barriers

There are many forms of implementation barriers reflecting the complexity of pharmaceutical research and healthcare systems. In addition to the barrier topics as listed in the table above, it is useful to classify them into one of two types: procedural and behavioral. Procedural barriers are caused by system rules, incentives, or infrastructure, not clinician beliefs. Behavioral barriers arise from beliefs, norms, habits, or risk perceptions among clinicians or patients.

The distinction between procedural and behavioral barriers is important from a RWD methods approach, taking ownership of which pharma function will tackle it, how the barrier should be appropriately addressed, and which stakeholders in the healthcare system need to be involved. Of particular note, behavioral barriers are difficult to identify, suffer from a lack of ownership, and are often addressed, if at all, using an ineffective evidence generation method. Examples of both procedural and behavioral barriers are shown in Table 1 (list is illustrative only and not exhaustive).

Table 1: Procedural vs. Behavioral Barriers.

Procedural Barriers	Behavioral Barriers
Diagnostic test not, or poorly, reimbursed	Therapeutic inertia ("Current therapy is good enough")
Test or treatment only available in certain settings	Risk aversion to new medicines
Prior authorization or step therapy requirements	Guideline lag
Referral bottlenecks	Referral hesitancy
Site-of-care restrictions	Preference for familiar workflows
	Patient reluctance

Real World Data can answer more than "does the drug work"

RWD has been used extensively over the years to describe many pieces of the pharma puzzle and has become an essential observational tool. Descriptive studies using RWD abound on the burden of illness, (comparative) effectiveness, (comparative) safety, patient journey, treatment use and switching, just to name a few.

Among healthcare and research communities, there has been an increasing need to translate scientific findings

into normal clinical practice[9]. This is supported by a growing body of literature that demonstrates an inefficient translation between clinical research and clinical care[10,11]. The translational gap is the subject of the field of implementation science that uses RWD and qualitative methods to identify and overcome barriers[12]. RWD stands to play an important role in bringing new innovations to clinical practice. The annual growth rate in the real-world evidence (RWE) market is forecast to increase 14.8% between 2025 and 2030[13]. Tapping into RWD to identify and address implementation barriers as part of the increased use of RWE would assist with decision making at many different levels across several stakeholders.

RWD hasn't been used in a structured way to address implementation barriers but has tremendous potential for doing so. Consider the issue of the uptake of a new medicine. RWD is most powerful and strategically useful not when it merely measures, but when it explains *why* the uptake is low. It is the search for "why" that renders RWD so important for the identification of implementation barriers. Unfortunately, most RWD studies stop at the measurement level. Examples of how to structure queries into RWD to answer why barriers exist are provided below in Figure 3.

RWD Signals That Reveal Implementation Barriers

RWD is most powerful when it explains why uptake is low — not just measures it.

Category	Barrier Type	Key RWD Signals	Example Interpretation
Procedural	Diagnostic & Reimbursement	Low testing rates; regional/payer variation; delays between Dx and Tx	If testing varies sharply by payer → reimbursement, access, or logistics issue
Procedural	Access & Authorization	Rx abandonment; long time to dispensing; discontinuation at first fill	Drop-off aligns with payer type → coverage rules, cost-sharing, or admin burden
Behavioral	Clinician Inertia	Slow uptake despite reimbursement; variation by clinician/site	Two identical sites, different uptake → clinician preference, risk perception, or habit
Behavioral	Current Tx Sufficient	Continued suboptimal therapy despite poor outcomes; delayed switching	Patients meet escalation criteria but remain on existing therapy for months/years

KEY INSIGHT: When two sites with identical payer mix show radically different uptake → behavioral. When drop-off aligns with payer type → procedural.

Figure 3. RWD Signals That Reveal Implementation Barriers.

Rare disease process

To show how RWD might be used in practice to identify, or at least suggest, implementation barriers, a process is presented here from a typical rare disease in a funnel (Figure 4).

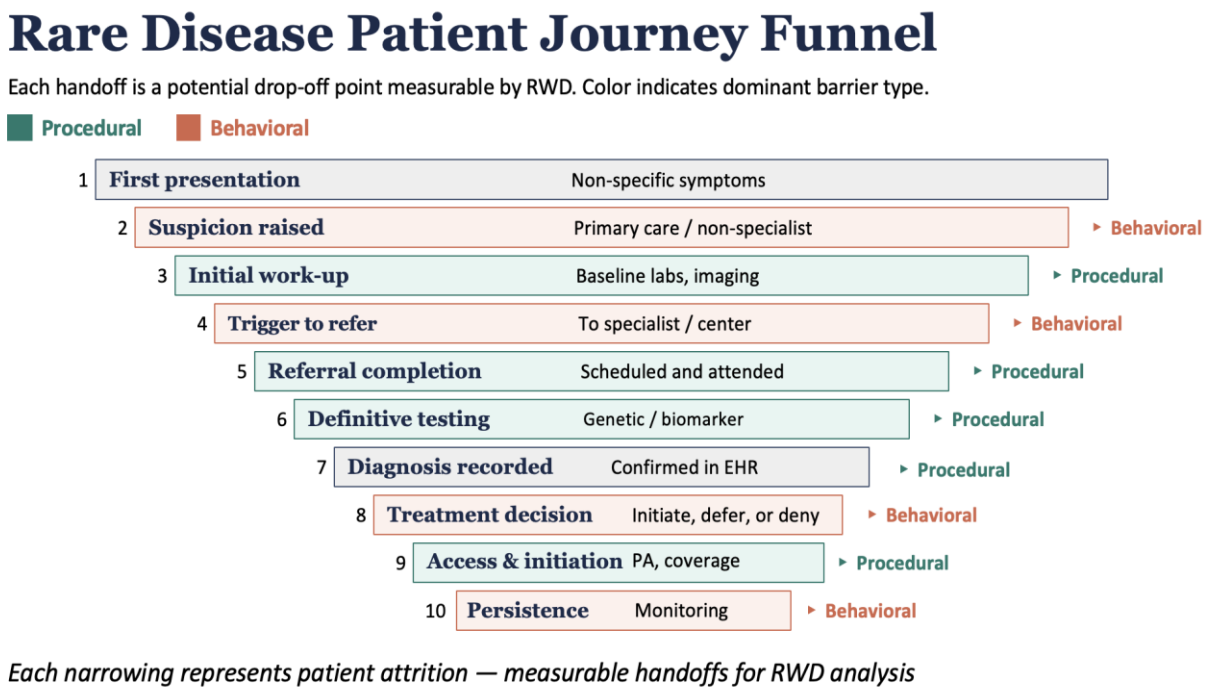

Figure 4. Rare Disease Patient Journey Funnel — each handoff is a potential drop-off point measurable by RWD. The pathway for rare disease designed with measurable handoffs facilitates the definition of endpoints that can be studied using RWD. The research would follow the logic as laid out in the decision tree in Figure 5. The decision tree begins by asking "where is the first major drop-off".

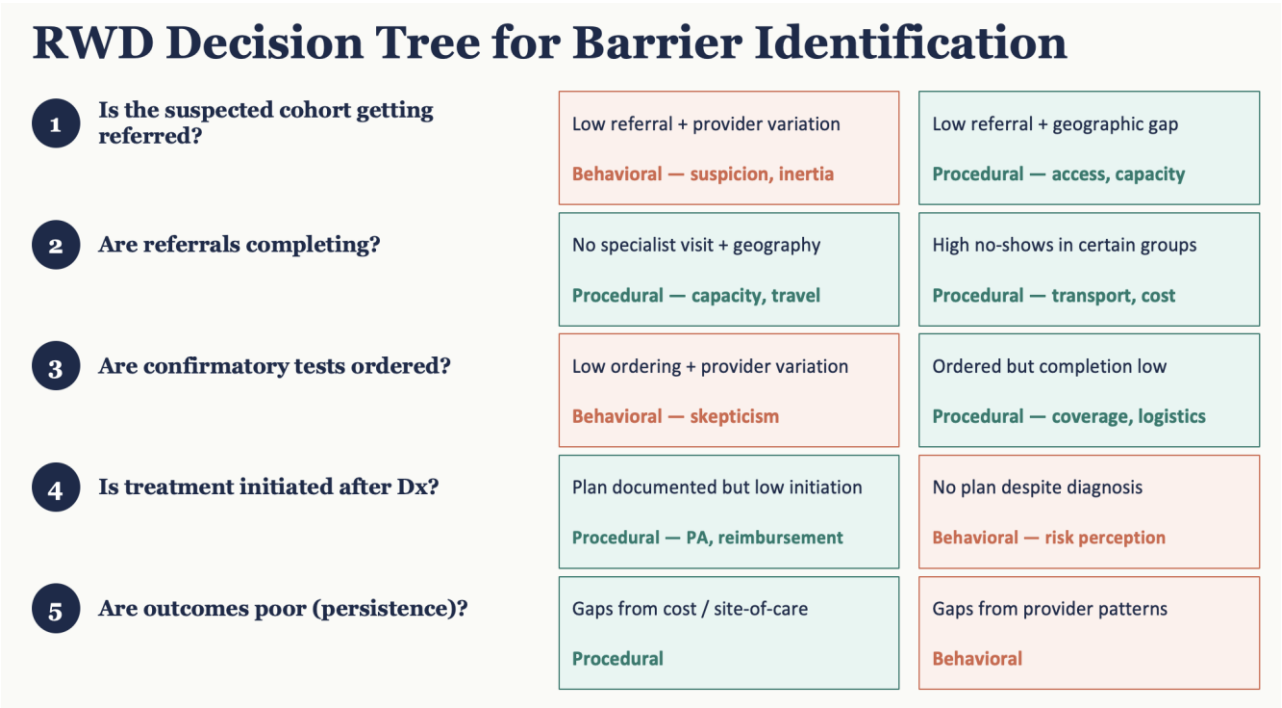

Figure 5. RWD Decision Tree for Barrier Identification.

The decision tree is designed to give meaning to results that can be derived from RWD that include *why* actions are being observed. With the detailed information on why things are happening, it is then possible to create a fit-for-purpose evidence strategy for addressing them allowing for better decision making.

An example of using RWD to identify implementation barriers from the literature includes a retrospective study using electronic health records to investigate the administrative delay to starting high-cost therapy after prescription in cystic fibrosis[14]. The time from prescription written to medication initiation was compared between an integrated health system specialty pharmacy vs external specialty pharmacy. This procedural barrier treats the delay between Rx and start as a modifiable implementation problem and tests an organizational implementation lever (embedded pharmacy team).

Rare diseases present distinct challenges in identifying suitable real-world data (RWD) sources. A foundational problem is the absence of well-defined ICD-10 codes for many conditions 15 — a gap driven by limited clinician recognition, the absence of established reimbursement or treatment pathways, and disease heterogeneity rooted in genetic or biomarker variability. As a result, structured

claims and encounter data alone are often insufficient to confirm diagnosis or characterize the undiagnosed and untreated population. Two broad strategies have emerged to address this.

DEEP, AGGREGATED ELECTRONIC HEALTH RECORD DATA

The first strategy relies on large-scale, aggregated EHR data with rich unstructured content — clinical notes, radiology and pathology reports, genetic test results, and laboratory data. Advances in large language models (LLMs) now make it feasible to extract diagnostically relevant features from these datasets at scale, enabling identification of rare diagnoses, treatment rationales, and outcome patterns that would be invisible in structured fields alone[16,17].

Even so, aggregate EHR data from integrated delivery networks (IDNs) has limitations. Patient volumes may be too low to support meaningful analysis, and IDN data often underrepresents the specialty settings — dermatology, urology, metabolic disease clinics — where rare disease patients are actually managed. Specialty EHR networks operating at national scale can fill this gap[18]. Linking these specialty records to national claims databases further expands the picture, capturing the full sequence of interventions, referrals, and diagnostic workups across care settings.

TARGETED, PROTOCOL-DRIVEN DATA COLLECTION

The second strategy takes a more direct approach: IRB-approved protocols developed in collaboration with Academic Medical Centers (AMCs) whose investigators specialize in the relevant condition. Multi-site rare disease studies at AMCs are increasingly well-supported — including through ARPA-H's RAPID initiative[19], which is advancing AI-based rare disease detection across health systems. These collaborations typically proceed under a waiver of informed consent, though the health system partnership itself requires careful attention to local implementation and data governance.

For conditions where patients are geographically dispersed and not concentrated in any single health system, patient-initiated data sharing offers a practical complement. Patients can now authorize access to their own EHR records through portal credentials at the point of research consent, with automated systems pulling updated records into a central repository on a rolling basis. Engaging rare disease advocacy organizations and condition-specific patient communities — including social media and peer support groups — is an effective way to reach this distributed population. These patients and families are often highly motivated to contribute their data to research that may directly improve their care.

APPLYING THE FRAMEWORK: TRANSTHYRETIN AMYLOID CARDIOMYOPATHY AS A WORKED EXAMPLE

Transthyretin amyloid cardiomyopathy (ATTR-CM) offers a compelling illustration of how the rare disease framework — the patient journey with measurable handoffs (Figure 4) and the decision tree for barrier classification (Figure 5) — can be operationalized using real-world data. ATTR-CM is caused by misfolded transthyretin protein depositing as amyloid in the heart, producing progressive heart failure in two forms: a hereditary variant (ATTRv, driven by TTR gene mutations including the V122I variant prevalent in individuals of African descent) and a wild-type form (ATTRwt) associated with aging. Once considered exceedingly rare, autopsy studies now find cardiac amyloidosis in roughly 5% of unselected adults, with over 90% of cases neither diagnosed nor suspected ante mortem[20]. Geographic disparity analyses show lower reported amyloidosis mortality in regions with fewer specialist centers — a pattern more consistent with underdetection than true prevalence variation[21]. The approval of tafamidis in 2019, the first disease-modifying therapy, transformed the stakes: an effective treatment exists, but implementation barriers remain the primary obstacle to patient benefit. (See Figure 6.)

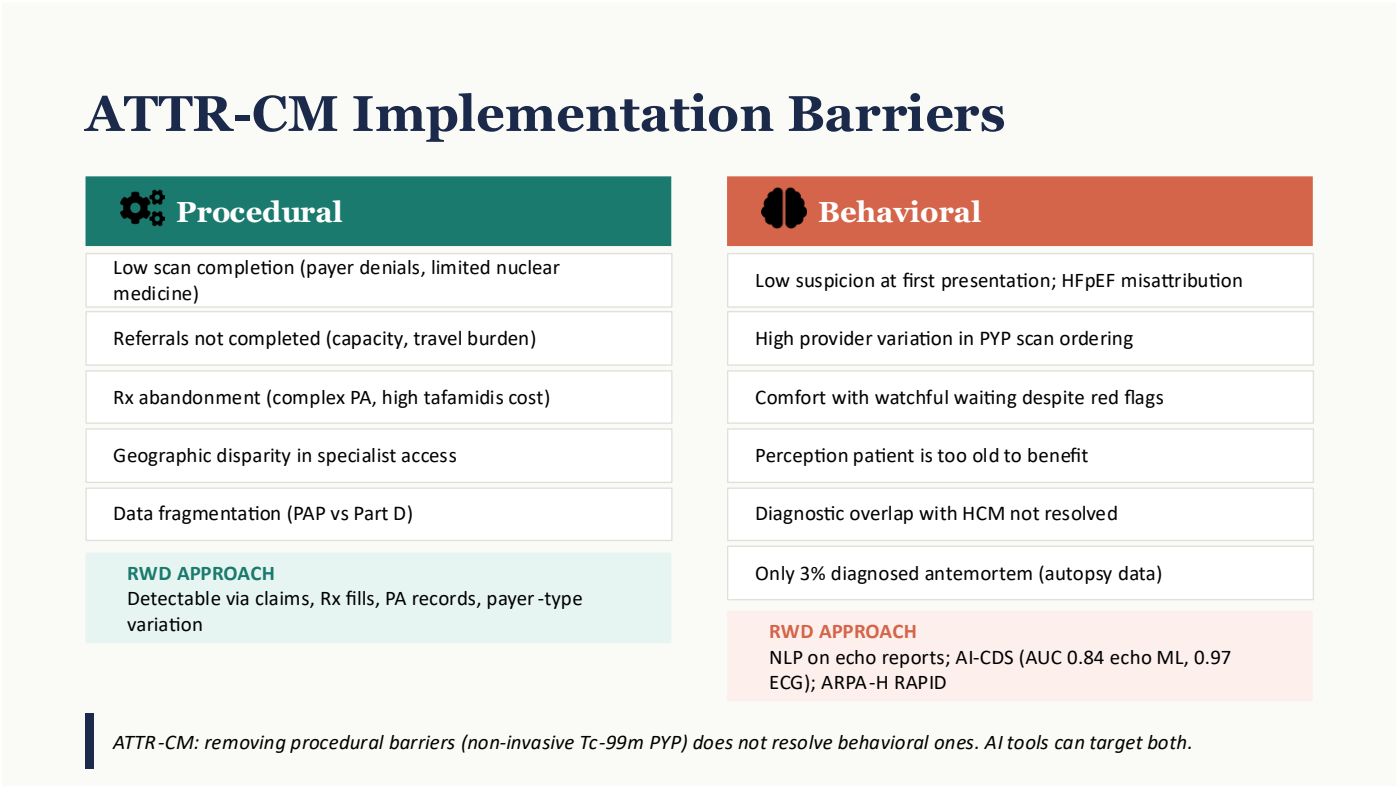

Figure 6. ATTR-CM Implementation Barriers — procedural vs. behavioral classification.

THE TRANSTHYRETIN AMYLOID CARDIOMYOPATHY PATIENT JOURNEY AND ITS MEASURABLE HANDOFFS

Mapping ATTR-CM onto the rare disease journey (Figure 4) reveals where barriers concentrate. The typical pathway begins with a patient presenting to primary care or a general cardiologist with heart failure symptoms — dyspnea, fatigue, volume overload — often accompanied by "red flag" features such as bilateral carpal tunnel syndrome, lumbar spinal stenosis, unexplained left ventricular hypertrophy, or low-voltage ECG despite thick walls. Expert consensus recommendations have codified these red flags[22]. At first presentation, the diagnosis of ATTR-CM is rarely considered; instead the patient is classified as having HFpEF or hypertensive heart disease. A UK cohort study found diagnosis was delayed more than four years in 42% of cases, with patients using hospital services a median of 17 times before diagnosis[23]. When suspicion is raised, confirmatory testing via technetium-99m pyrophosphate (Tc-99m PYP) bone scintigraphy enables non-invasive diagnosis[24], followed by genetic testing to distinguish ATTRv from ATTRwt, treatment access navigation, and long-term persistence. A Japanese claims study documented a median 15.5-month delay from heart failure onset to ATTR-CM diagnosis, with carpal tunnel syndrome appearing a median of 18 months before cardiac diagnosis[25].

OPERATIONALIZING THE JOURNEY IN REAL-WORLD DATA

Structured data — claims and coded EHR fields. Each journey handoff can be translated into specific data concepts extractable from claims and EHR sources. The suspected ATTR-CM cohort can be identified through phenotypic algorithms built from diagnosis codes (ICD-10-CM I50.x for heart failure, E85.x for amyloidosis), procedure codes (CPT 78472 for Tc-99m PYP scintigraphy, CPT 64721 for carpal tunnel release), medication fills (NDC codes for tafamidis), and co-occurring "red flag" conditions — bilateral carpal tunnel (G56.0x), lumbar spinal stenosis (M48.06), aortic stenosis (I35.0). Combined with echocardiographic findings coded in structured fields (LV wall thickness, diastolic dysfunction grade), these elements allow construction of a computable phenotype: patients with HFpEF plus LVH plus one or more extracardiac red flags who have never received an amyloid workup. For each patient matching this profile, RWD can then trace each downstream handoff: Was a PYP scan ordered? Completed? Was amyloidosis diagnosed? Was tafamidis prescribed? Filled? Persisted on? Each transition is a measurable endpoint; each gap is a candidate barrier.

Unstructured data — NLP/LLMs on clinical narratives. Structured codes miss diagnostically relevant information embedded in imaging reports and clinical notes. For ATTR-CM, echocardiography reports frequently describe findings suggestive of infiltrative disease — "granular sparkling," "ground-glass myocardial appearance," "severe diastolic dysfunction with restrictive filling" — that are not captured in discrete fields. Natural language processing or increasingly LLM pipelines can extract these concepts at scale, flagging patients whose imaging narratives contain infiltrative features but lack an amyloidosis diagnosis code. AI pipelines applied to cardiology consult notes can identify documented suspicion ("consider amyloid workup") that never progressed to a completed test — making visible the gap between suspicion raised (Journey Step 2) and confirmatory testing completed (Step 6). As the framework notes, advances in large language models now make such extraction feasible at scale.

APPLYING THE DECISION TREE TO CLASSIFY BARRIERS

Steps 1–2: Referral and suspicion. The largest patient drop-off in ATTR-CM occurs at the earliest stages. RWD

can quantify the rate at which patients matching the phenotypic profile ever receive a Tc-99m PYP scan or amyloid workup. An autopsy study of sudden cardiac death victims found that only 3% with histologically confirmed cardiac amyloidosis had a known diagnosis before death, despite 39% having had antemortem cardiac symptoms[26]. Per the decision tree logic: if workup rates are low with large provider-level variation — some clinicians routinely order PYP scans while others in similar settings do not — the pattern indicates a behavioral barrier (low suspicion, therapeutic inertia). If uniformly low in regions lacking specialist or nuclear medicine capacity, the barrier is procedural. Geographic disparity data showing that southern US states report the lowest amyloidosis mortality despite having the highest proportions of Black individuals at elevated ATTRv risk further supports underdetection where specialist access is lowest.

Step 3: Confirmatory testing. For patients reaching a specialist, RWD tracks whether PYP scans are ordered and completed. High provider-level variation in ordering suggests behavioral barriers rooted in differing diagnostic thresholds. Low completion rates correlated with payer denials or limited nuclear medicine facility availability indicate procedural barriers. Genetic testing to distinguish ATTRv from ATTRwt may similarly be underutilized, identifiable through claims analysis of molecular diagnostic procedure codes following ATTR-CM diagnosis.

Step 4: Treatment initiation. Tafamidis requires prior authorization and carries a high list price. The RWD signals from Figure 3 apply directly: high prescription abandonment rates, long time-to-first-fill, and disparities by payer type indicate procedural barriers. A US Medicare study found that 35% of tafamidis-treated patients received the drug through a patient assistance program rather than their Medicare Part D plan, and that adherence was significantly underestimated when PAP data were excluded — illustrating how access barriers and data fragmentation interact[27]. If treatment is not initiated despite favorable access conditions — two sites with identical payer mix showing markedly different prescribing rates — the barrier is behavioral: clinician comfort with watchful waiting or perception that the patient is too old to benefit.

Step 5: Persistence and adherence.
Real-world studies from Japan and Germany report high adherence once patients initiate tafamidis (mMPR ≥80% in 93–95% of patients; 12-month persistence approximately 78%), suggesting that post-initiation barriers are relatively modest[28,29]. Early discontinuation or refill gaps correlated with payer type or out-of-pocket burden signal procedural barriers; those correlated with low provider follow-up intensity or site-of-care patterns signal behavioral ones.

Table 2: Procedural vs. Behavioral Barriers in ATTR-CM.

Barrier Type	Root Cause	ATTR-CM Examples	Solutions
Procedural	System access, logistics, capacity, or cost — objective, workflow-based problems	Low scan completion due to payer denials or limited nuclear medicine access (Step 3) Referrals not completed due to capacity or travel burden (Step 2) Prescription abandonment from complex prior authorization or high cost (Step 4)	Access programs Coverage advocacy Logistical solutions AI-driven workflow automation
Behavioral	Clinician knowledge, attitude, or practice variation — subjective, decision-making barriers	Low clinical suspicion at first presentation; misattribution to HFpEF (Step 1) High provider variation in PYP scan ordering (Step 3) Comfort with "watchful waiting" or perception patient is too old for treatment (Step 4)	Education & guidelines Clinical decision support AI tools for pattern recognition Implementation science

FROM MEASUREMENT TO ACTION: ARTIFICIAL INTELLIGENCE-DRIVEN TOOLS

Identifying barriers through RWD is a necessary first step, but the ultimate goal is to resolve them. For ATTR-CM, AI-driven tools can be deployed not only to measure barriers but to directly address them within the clinical workflow — a shift from AI as analytical instrument to AI as implementation intervention.

The most consequential behavioral barrier — low clinical suspicion at first presentation — is precisely the type that AI-based clinical decision support can target. Machine learning models trained on routine echocardiographic measurements have achieved AUCs of 0.84 for detecting cardiac amyloidosis[30]. An ECG-based algorithm improved cardiologist detection from AUC 0.69 to 0.97[31]. Deep learning on echocardiographic video offers vendor-agnostic automated strain measurement[32], and deep learning applied to bone scintigraphy can detect incidental cardiac uptake suggestive of amyloidosis on routine scans — retrospectively identifying patients who were imaged but never referred for amyloid workup[33]. A comprehensive review catalogs these and other approaches, noting their value for overcoming the

diagnostic overlap with hypertrophic cardiomyopathy[34]. When embedded in the EHR as clinical decision support, these tools can flag patients fitting the ATTR-CM phenotypic profile and alert the treating clinician at the point of care. Initiatives such as ARPA-H's RAPID program are specifically designed to advance AI-based rare disease detection across health systems.

AI can also address bottlenecks further along the journey. At the treatment access stage, AI tools can streamline prior authorization by auto-populating clinical documentation and matching patient records to payer coverage criteria — addressing the procedural barrier that manifests as prescription abandonment. Predictive models can identify patients at risk of discontinuation based on refill patterns and social determinants, enabling proactive outreach before gaps occur. For rare diseases where barriers are rooted in the scarcity of specialized knowledge across many care settings, AI effectively redistributes expertise — bringing specialist-level pattern recognition into generalist workflows. The RWD infrastructure that identified the barrier provides the means to measure the intervention's impact.

WHY TRANSTHYRETIN AMYLOID CARDIOMYOPATHY IS INSTRUCTIVE

ATTR-CM illustrates several features that make the implementation barrier framework particularly valuable. The disease sits at the intersection of common and rare: the presenting symptoms are ubiquitous, but the underlying cause is rare enough to be routinely overlooked, making the dominant barriers behavioral rather than procedural. A non-invasive diagnostic pathway now exists (Tc-99m PYP scintigraphy), removing what was once a major procedural barrier, yet underdiagnosis persists — demonstrating that removing procedural barriers does not automatically resolve behavioral ones. The high cost of tafamidis introduces layered access barriers that vary by health system and payer, creating natural variation that RWD is well-suited to characterize. And a growing body of published AI tools now offers the means to act on identified barriers directly within the care delivery environment. An RWD-led investigation would follow the decision tree to identify where the largest drop-off occurs, use the pattern of variation to classify barriers as procedural or behavioral, and directly inform the response — with the same RWD infrastructure providing the natural experiment to evaluate whether interventions are working.

The Opportunity with Artificial Intelligence and Available Real-World Data for Implementation Research

Historically, Real World Evidence teams have been constrained to mission-critical deliverables — comparative effectiveness, safety, and health economic analyses — with little capacity left over for implementation research. What has changed is that AI has reduced the marginal cost of conducting a RWD analysis to a fraction of what it was even two years ago[35]. Generative AI and purpose-built analytics platforms now automate much of the workflow that previously required specialized programming: cohort construction, variable definition, data quality checks, statistical analysis, and the drafting of study protocols and results reports. Several dedicated RWE platforms and major cloud providers now embed these capabilities, enabling non-technical users to move from a research question to analytic-ready output through natural language interaction rather than code. Some of these tools report reducing project cycle times by more than 80% compared to traditional programming approaches. At the same time, regulatory agencies including the FDA/ICH are beginning to adopt these same platforms for their own real-world data analyses, lending further credibility to the approach[36,37]. (See Figure 7.)

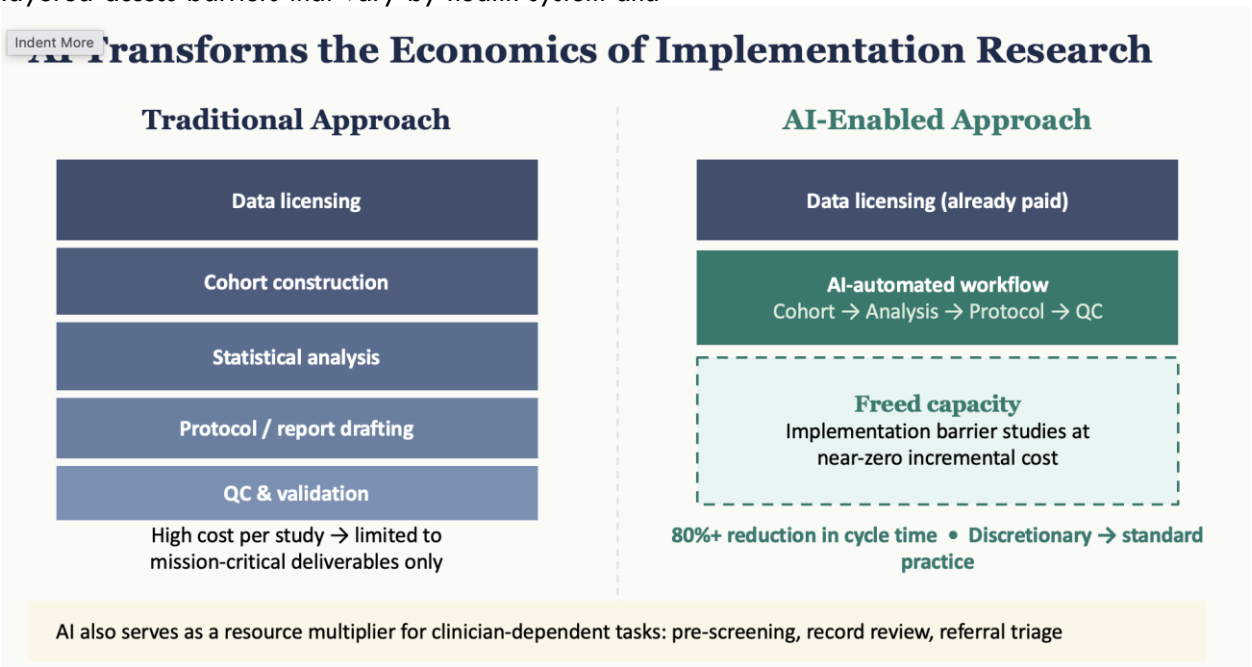

Figure 7. AI Transforms the Economics of Implementation Research.

The strategic implication is straightforward. Most biopharma organizations have already licensed the real-world data assets they need for their core evidence programs[38]. That same data — claims, EHR, specialty registries — is available for implementation research at essentially zero incremental data cost. When AI also

removes the analytical labor bottleneck, the economic case for running implementation barrier studies within existing data licenses becomes compelling. RWD-based implementation research shifts from a discretionary investment to a low-cost extension of evidence activities the organization is already conducting.

Artificial Intelligence as a Resource Multiplier for Clinician-Dependent Tasks

Beyond analytical efficiency, AI can also address a distinct class of implementation bottleneck: tasks that depend on scarce clinician time. Where the barrier is the availability of qualified personnel to review medical records, screen patients, or triage referrals, AI tools developed with appropriate clinical oversight can serve as a resource multiplier. For example, an AI system operating under physician supervision could pre-screen patient records against guideline criteria, flagging potential candidates for specialist referral or diagnostic testing, and summarizing records for clinician review. The sponsor team can support this by funding the development, validation, and deployment of such digital tools — or by conducting research into the safety, efficacy, and cost-effectiveness of AI-augmented clinical workflows as a mechanism to overcome healthcare provider labor constraints. This is a qualitatively different contribution from data analysis: it positions the sponsor as a partner in solving healthcare delivery problems, not merely in generating evidence.

Real-World Data on Its Own May Not Be Enough

Pure EHR/claims data can strongly suggest behavioral barriers but confirmation needs at least one light qualitative element. A practical approach is to use RWD to formulate ideas on behavioral barriers that then direct qualitative efforts such as short clinical surveys, advisory boards, or chart notes using NLP/AI. The RWD results are used to target who to ask and what to ask. The advantage of this approach is that it keeps RWD central and avoids undirected, qualitative research.

For the rare disease process, the research would still be RWD-led, but certain components would be strengthened. The additional component might consist of NLP/LLMs on clinician notes for phrases like “no need to refer,” “symptoms mild,” or “watching waiting.” Another approach might be to issue a brief clinician survey targeted to high- vs low-referring sites where the sampling is guided by RWD. These are merely examples of what could be done but would have to be customized according to the findings in the RWD study.

An illustrative example of combining RWD with qualitative methods describes a needs assessment and implementation-planning approach that explicitly includes population-level claims analysis alongside surveys, semi-structured interviews, focus groups, then maps findings into behavioral determinants and implementation frameworks[39]. The RWD tells you where the drop-off is (e.g., prescribing vs initiation vs persistence), and the qualitative work tells you which modifiable determinant (knowledge, beliefs, social influence, perceived sufficiency of current care, etc.) is driving it, i.e., what would need to change.

Behavioral Implementation Barriers

All barriers are important because they impede the implementation goal of a new medicine actually reaching a patient. Pharma is not structured to uncover implementation barriers in a systematic way so some may be identified but others are simply overlooked. Implementation barriers of a behavioral nature are often ignored, or addressed in a suboptimal fashion.

RWD is used by Pharma early in the product lifecycle and would lend itself well to the early identification of implementation barriers, both procedural and behavioral, that will likely challenge the use of the intended medicine. Once identified, implementation science can be used to give a structured, systematic, and scientific approach to address all implementation barriers, including behavioral ones. In many disease areas, behavioral implementation barriers block the patient journey and become the key to the successful uptake of a new medicine and its use by patients.

Conclusion

The systematic consideration of implementation barriers offers a holistic way of viewing evidence needs that will lead to a quicker and fuller way of achieving the “purpose” of pharmaceutical research, i.e., that patients receive the medicines that they need. To achieve this goal, RWD provides a way of identifying implementation barriers that can guide evidence generation activities that not only have a purpose, but that will have an impact throughout the product lifecycle and into real clinical practice. Classification into procedural and behavioral barriers is introduced here as a way to establish the evidence strategy and to extract the appropriate toolkit for executing the strategy. Implementation Science is a strong approach to address implementation barriers, especially those of a behavioral nature, and deserves a special place in the toolkit.

RWD is typically licensed by Pharma and could easily provide a cost-effective way to provide a holistic view of barriers, starting very early in the research pipeline. According to the disease area or the nature of the research questions, deep RWD may be required or RWD enhanced by qualitative research. In addition, AI should be considered as a tool to extend the impact of RWD in the search for implementation barriers and their solutions. The ATTR-CM worked example demonstrates how the framework’s components — the patient journey, the decision tree, and the procedural/behavioral classification — can be applied to a real disease area to generate actionable insights from existing data.

In short, implementation barriers exist, can be found using RWD, and can lead to improved decision-making for patients, healthcare systems, and industry.

References

1. Olson M, Freitas R. Are you implementation ready? An alternative patient and healthcare system-centered model for pharma. J Comp Eff Res. 2025;14(9). doi:10.57264/cer-2025-0094
2. Olson M. Developing an integrated strategy for evidence generation. J Comp Eff Res. 2017;7(1):5-9.
3. Malamis P, Howle J. The limited future of real world data? Applied Clinical Trials. 2022. https://www.appliedclinicaltrialsonline.com/view/the-limited-future-of-real-world-data. Accessed February 26, 2026.
4. Malamis P, Howley J. Current and future use of real-world data. Applied Clinical Trials. Updated January 14, 2025. https://www.appliedclinicaltrialsonline.com/view/current-and-future-use-of-real-world-data. Accessed February 26, 2026.
5. Theobald S, Brandes N, Gyapong M, et al. Implementation research: new imperatives and opportunities in global health. Lancet. 2018;392(10160):2214-2228.
6. DiMasi J, Getz K, Kaitin K, et al. Assessing the value of integrated evidence approaches in drug development. Ther Innov Regul Sci. 2025;59(4):808-816. doi:10.1007/s43441-025-00778-y
7. Olson M, Zullig LL, De Geest S. How pharma can amplify product value with implementation science. J Comp Eff Res. 2024;13(10). doi:10.57264/cer-2024-0076
8. Ivers N, Grimshaw J, Jamtvedt G, et al. Audit and feedback: effects on professional service. Cochrane Database Syst Rev. 2025. doi:10.1002/14651858.CD000259.pub4
9. Booth C, Tannock I. Randomized controlled trials and population-based observational research: partners in the evolution of medical evidence. Br J Cancer. 2014;110:551-555.
10. Lenfant C. Clinical research to clinical practice—lost in translation? N Engl J Med. 2003;349:868-874.
11. Abu-Odah H, Said N, Nair S, et al. Identifying barriers and facilitators of translating research evidence into clinical practice: a systematic review of reviews. Health Soc Care Community. 2022;30(6):3265-3276.
12. Olson M, Rootkin L. The triple win—implementation science benefits patients, healthcare systems and industry alike. J Comp Eff Res. 2022;11(9):639-642. doi:10.2217/cer-2022-0058
13. MarketsandMarkets. Real world evidence/RWE solutions market by component—global forecast to 2030. 2025. https://www.marketsandmarkets.com/Market-Reports/real-world-evidence-solution-market-76173991.html. Accessed February 26, 2026.
14. Roder L, McCann G, Kish T, et al. Impact of pharmacy services on time to elexacaftor-tezacaftor-ivacaftor initiation. J Manag Care Spec Pharm. 2022;28(9):989-996. doi:10.18553/jmcp.2022.28.9.989
15. Hess LM, Espinosa O, Engel-Nitz NM, et al. Challenges of using ICD-9-CM and ICD-10-CM codes for soft-tissue sarcoma in databases for health services research. Perspect Health Inf Manag. 2019;16(Spring):1a.
16. Cai J, Wang S, Luo Y, et al. Bridging clinical narratives and structured phenotypes with LLMs and sentence transformers. J Genet Genomics. 2026. doi:10.1016/j.jgg.2026.02.009
17. Kaster L, Liu Y, Geller V, et al. Comparison of rule- and LLM-based phenotype extraction for neurofibromatosis type[1]. J Am Med Inform Assoc. 2025;32(11):1663-1673. doi:10.1093/jamia/ocaf155
18. Verana Health. What claims data is missing for real-world evidence generation and how EHR data fills the gap. 2024. https://veranahealth.com/what-claims-data-is-missing-for-real-world-evidence-generation-and-how-ehr-data-fills-the-gap/.
19. ARPA-H. ARPA-H launches program to accelerate rare disease diagnosis (RAPID). 2025. https://arpa-h.gov/news-and-events/arpa-h-launches-program-accelerate-rare-disease-diagnosis.
20. Baschong A, Metzger F, Grize L, et al. Cardiac amyloidosis in a Swiss autopsy cohort. Swiss Med Wkly. 2025;155:4541. doi:10.57187/s.4541
21. Alexander KM, Orav J, Singh A, et al. Geographic disparities in reported US amyloidosis mortality from 1979 to 2015. JAMA Cardiol. 2018;3(9):865-870. doi:10.1001/jamacardio.2018.2093
22. Maurer MS, Elliott P, Comenzo R, et al. Expert consensus recommendations for the suspicion and diagnosis of transthyretin cardiac amyloidosis. Circ Heart Fail. 2019;12(9):e006075. doi:10.1161/CIRCHEARTFAILURE.119.006075
23. Lane T, Fontana M, Martinez-Naharro A, et al. Natural history, quality of life, and outcome in cardiac transthyretin amyloidosis. Circulation. 2019;140(1):16-26. doi:10.1161/CIRCULATIONAHA.118.038169
24. Gillmore JD, Maurer MS, Falk RH, et al. Nonbiopsy diagnosis of cardiac transthyretin amyloidosis. Circulation. 2016;133(24):2404-2412. doi:10.1161/CIRCULATIONAHA.116.021612
25. Minamisawa M, Motoki H, Izawa A, et al. Patient journey to transthyretin cardiac amyloidosis diagnosis—a Japanese claims database study. Circ J. 2025;89(4):432-441. doi:10.1253/circj.CJ-24-0666
26. Ciliberti G, Schirinzi S, Pieroni M, et al. Antemortem underdiagnosis of cardiac amyloidosis in sudden cardiac death victims. JACC Clin Electrophysiol. 2025;12(2):343-349. doi:10.1016/j.jacep.2025.10.003
27. Chung H, Janiga J, Kim J, et al. Adherence and persistence to tafamidis treatment among Medicare beneficiaries in the presence of a patient assistance program. Sci Rep. 2024;14(1):16261. doi:10.1038/s41598-024-62660-5
28. Kato T, Izawa H, Ando Y, et al. Tafamidis medication adherence and persistence in patients with transthyretin amyloid cardiomyopathy in Japan. ESC Heart Fail. 2024;11(5):2881-2888. doi:10.1002/ehf2.14736
29. Attal S, Finkenstein I, Brandt P, et al. Tafamidis 61 mg patient characteristics and persistency: German

statutory health insurance data. Cardiol Ther. 2024;13(2):369-378. doi:10.1007/s40119-024-00365-6
30. Chang RS, Ryabets-Lienhard A, Rikhi A, et al. Detection of cardiac amyloidosis using machine learning on routine echocardiographic measurements. Open Heart. 2024;11(2):e002884. doi:10.1136/openhrt-2024-002884
31. Schrutka L, Duca F, Binder C, et al. Machine learning-derived electrocardiographic algorithm for the detection of cardiac amyloidosis. Heart. 2022;108(14):1137-1147. doi:10.1136/heartjnl-2021-319846
32. Ouyang D, He B, Ghorbani A, et al. Deep learning-derived myocardial strain. JACC Cardiovasc Imaging. 2024. doi:10.1016/j.jcmg.2024.01.011
33. Slomka PJ, Miller RJH. Can deep learning detect incidental abnormal cardiac uptake related to amyloidosis on routine bone scintigraphy? JACC Cardiovasc Imaging. 2023;16(8):1096-1098. doi:10.1016/j.jcmg.2023.01.018
34. Allegra A, Caserta S, Genovese S, et al. Machine learning approaches in diagnosis, prognosis and treatment selection of cardiac amyloidosis. Int J Mol Sci. 2023;24(6):5680. doi:10.3390/ijms24065680
35. Podichetty JT, Manigault KR, Engel-Nitz NM, et al. How AI transforms every step of regulatory submission: from real-world evidence to clinical study reports. Clin Transl Sci. 2025;18(12):e70434. doi:10.1111/cts.70434
36. US Food and Drug Administration. FDA announces completion of first AI-assisted scientific review pilot. Published May 2025. https://www.fda.gov/news-events/press-announcements/fda-announces-completion-first-ai-assisted-scientific-review-pilot-and-aggressive-agency-wide-ai.
37. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. ICH M14 guideline: general principles for planning and design of pharmacoepidemiological safety studies using real-world data. Published September 2025.
38. Deloitte Center for Health Solutions. Real-world evidence benchmarking study. 2025. https://www.deloitte.com/us/en/what-we-do/capabilities/converge/articles/real-world-evidence-ai-in-pharmaceuticals.html.
39. Hankins JS, Shih SM, Nwosu EC, et al. Evaluating the implementation of a multi-level eHealth study to improve hydroxyurea utilization in sickle cell disease. Front Health Serv. 2023;2:1024541. doi:10.3389/frhs.2022.1024541

