

Aligning Shared Evidentiary Needs Among Payers and Regulators for a Real-World Data Ecosystem



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Executive Summary

In the face of rapid innovation, a strong need exists for improved evidence generation capabilities to answer critical questions faced by regulators and payers. Systematically collecting real-world data to generate real-world evidence may provide the means to supplement the evidence available for newly approved novel therapies. Under the auspices of the Duke-Margolis Real-World Evidence (RWE) Collaborative and the Center's Value for Medical Products Consortium, a multi-stakeholder working group considered how the health care community might align to ensure real-world data is capable of generating evidence that meets the needs of payers and regulators.

Primarily through the lens of three disease use cases (Alzheimer's disease, cardiovascular disease, and spinal muscular atrophy), this paper explores considerations and provides recommendations to stakeholders for building a robust real-world data ecosystem through seven key themes. Additionally, data governance and resource needs are considered.

To build a robust real-world data ecosystem, policymakers and other key stakeholders should take the following steps:

- Provide resources needed to support electronic health record (EHR) interoperability between clinical research networks and central claims data repositories, such as those funded by Patient-Centered Outcomes Research Institute (PCORI);
- Provide additional funding for the United States Food and Drug Administration's (FDA) Sentinel Initiative and other existing initiatives focused on safety and effectiveness (e.g., registries or observational studies that monitor the safety and effectiveness of therapies granted accelerated approval);
- Reconsider bans on unique patient identifier funding and encourage the Department of Health and Human Services (HHS) through the Office of the National Coordinator for Health IT to advance unique patient identifier development;
- Harmonize stakeholder goals and initiatives by cultivating and supporting pre-competitive, public-private partnerships.

If implemented, we believe the recommendations herein support robust post-market data collection that could enable efficient generation of evidence to supplement clinical trial results and further enable learning health care systems.

Introduction

As the pace of medical innovation increases and novel therapies are approved, regulators and payers face unprecedented pressure not only to surveil the safety and efficacy of such therapies, but also help ensure affordable access to those therapies. Indeed, regulators and payers have different roles in facilitating patient access to and clinically vetting and implementing new therapies. Yet, for new technologies and treatments intended to have long-term impacts, evidence of long-term health outcomes, safety and efficacy, and durability of treatment effects is often limited or insufficient to support decisions that ultimately impact patients and health plan beneficiaries.

Differences in evidence generation goals and data capabilities across regulators and payers ultimately affect broader patient access to new therapies.

Most notably, available evidence on the real-world efficacy of new treatments at the time of regulatory approval may not be sufficient to payers who cover the costs of such treatments. This is especially true for therapies that have received accelerated regulatory approval. In 2021, 74 percent of all approvals were under expedited regulatory pathways and many of these are high-cost therapies for rare conditions.ⁱ Differences in evidence generation goals and data capabilities across regulators and payers ultimately affect broader patient access to new therapies. For example, U.S. FDA's evidentiary goals are based on assessments of therapeutic safety and efficacy. On the other hand, payers make coverage and payment decisions based on medical necessity, cost, and the availability of comparator treatments. For this reason, the liminal state between regulatory approval and payors coverage often varies across therapeutics, potentially resulting in limited patient access to newly approved therapies and system- or practice-level variation in the clinical implementation of such therapies.ⁱⁱⁱ

Systematic real-world data (RWD) collection and curation may alleviate challenges associated with relying on limited real-world efficacy and safety evidence for certain therapeutics at the time of regulatory approval. Yet, many RWD collection efforts face limitations, including but not limited to misaligned priorities among regulators and payers as well as redundant and uncoordinated data collection, which ultimately lead to administrative burdens for providers and low value delivery to patients.

Further developing a shared RWD ecosystem, pieces of which exist already, can help alleviate these challenges. For example, the Office of the National Coordinator for Health Information Technology (ONC) created the United States Core Data for Interoperability (USCDI) to support interoperability. The FDA has leveraged its Sentinel System for years to conduct safety surveillance of medical products. Related efforts in the FDA's Biologics Effectiveness and Safety (BEST) Initiative and the National Evaluation System for health Technology (NEST) are also underway. In Europe, the Data Analysis and Real-World Interrogation Network (DARWIN-EU) is working to provide timely and reliable evidence on the use, safety, and effectiveness of medical products from real world health care databases across the European Union. Health Level 7 International (HL7) has been leading the effort to expand Fast Healthcare Interoperability Resources (FHIR)-based tools. Additional FDA post-market requirements as well as the Centers for Medicare and Medicaid Services' (CMS) Coverage with Evidence Developmentⁱⁱ (CED) program, which imposes evidentiary requirements on certain medical products with new FDA approval, also help inform this ecosystem.

The efforts noted above can improve post-market evidence development by supporting the generation of important new knowledge for care decisions and give stakeholders a clearer understanding of the risks and benefits of a new intervention. For example, BEST Initiative has explored rates of myocarditis and pericarditis from COVID-19 vaccines using claims databases.ⁱⁱⁱ

In addition, instances exist in which stakeholders' evidentiary goals were aligned through a national registry when CMS issued national Medicare coverage for technology with CED.^{iv} As these efforts advance, it will be important to identify opportunities to scale the ecosystem as well as best practices for the community.

To further explore these concepts and identify opportunities for harmonization between regulators and payers, members of the Duke-Margolis RWE Collaborative and Value for Medical Products Consortium explored the landscape of shared post-market evidence needs, including efforts that are underway to set meaningful data collection standards. This exploration was informed

by three disease-based use cases — monoclonal antibody treatments for Alzheimer's disease, gene therapy treatments for spinal muscular atrophy (SMA), and therapies and medical devices to treat cardiovascular disease (CVD).

This paper is informed by a November 16, 2021, private workshop, "Aligning to Address Shared Evidentiary Needs in Data Collection and Characterization," hosted by the Duke-Margolis Real-World Evidence Collaborative and the Value for Medical Products Consortium, by several regular working group and stakeholder calls with members of these groups, and by literature cited throughout this document. Please see the end of this document for a list of participants in the working group.

Use Case Background

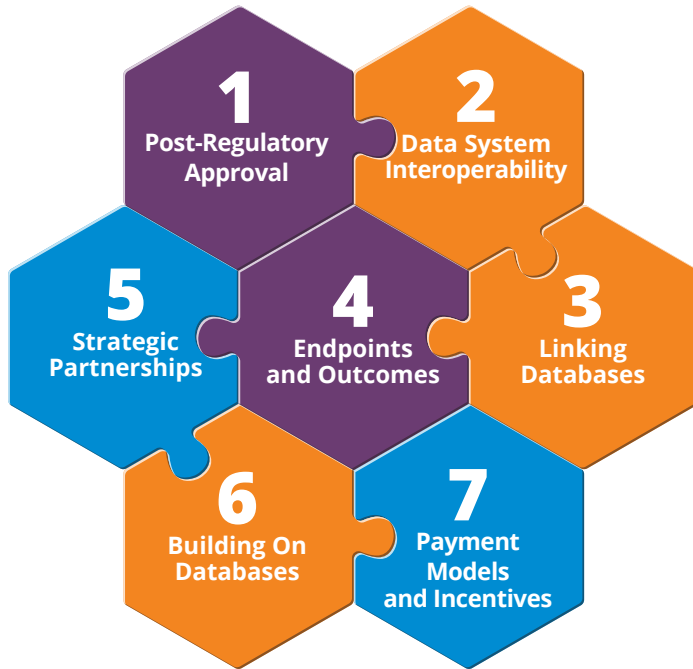
SMA is a rare genetic neuromuscular disease that results in muscular weakness and significant disability, leading to a drastically shortened lifespan. The FDA has approved three treatments for SMA, including Zolgensma, a gene replacement therapy, and Spinraza and Evrysdi, two therapies that enhance the SMN2 gene. In particular, the approval of Zolgensma represents the beginning of a new paradigm for treating SMA. As we highlight in this paper, a robust RWD ecosystem can help collect data on the safety and effectiveness of these therapies over time.

CVD are a group of disorders of the heart and blood vessels. It is the leading cause of death affecting approximately 82.6 million people in the United States. There are many types and combinations of drugs available to treat CVD as well as eight types of devices to treat the heart. Given the breadth of available therapies to treat CVD, there is an opportunity to gather data from patients in clinical and prospective studies as well as passive RWD from EHRs since the endpoints are definitive for CVD products (e.g., prevention of myocardial infarction). This data can show the value of new products versus older products and presents a starting point to compare clinical trial data and RWE from an outcomes standpoint. However, several open questions remain, including how to collect data on combinations of therapies and track patient adherence.

In Alzheimer's disease, aducanumab, a monoclonal antibody treatment, was recently granted approval through the FDA's accelerated approval program. Under this program, regulatory approvals may be based on a determination that the product has an effect on a surrogate endpoint or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, and that is reasonably likely to predict an effect on irreversible morbidity or mortality. In the case of aducanumab, the surrogate endpoint was reduction in beta-amyloid plaque, an indicator that has been frequently evaluated as a marker for disease severity in patients with Alzheimer's disease. However, evidence linking this surrogate endpoint to improved cognitive and functional outcomes for Alzheimer's disease patients is largely inconclusive.^v The need for additional evidence on accelerated approvals like this one represents an opportunity to develop new real-world endpoints and leverage RWD to contribute to the broader totality of evidence for novel therapies.

As a result of this process, **seven themes emerged as challenges and opportunities to building a robust data ecosystem meant to leverage RWD and RWE to support regulatory and payer decision-making:**

RWD Ecosystem to Meet Shared Evidentiary Needs



- 1 Post-regulatory approval** evidence generation to inform payer and regulator decision-making
- 2 Data system interoperability** to facilitate the use, sharing, and exchange of RWD across multiple systems
- 3 Linking databases** to maximize data analysis capabilities
- 4 Standardized endpoints and outcomes** measures to evaluate real-world effectiveness
- 5 Strategic partnerships** to facilitate data collaborations and sharing
- 6 Building on existing databases** as a starting point toward more robust data collection.
- 7 Payment models and incentives** to support long-term RWD collection and analysis.

This paper explores these themes, discussing important considerations and providing recommendations related to each for building a robust data ecosystem equipped to support both regulatory and payer decision-making through the use of RWD and RWE. Additionally, use-case agnostic considerations for data governance as well as needs for additional resources to support ecosystem development are explored.



1 Post-Regulatory Approval Evidence Generation to Inform Payer and Regulator Decision-Making

Many opportunities in the post-regulatory approval setting exist to build an ecosystem harmonized for payer and regulatory decision making. A single-administration therapy for SMA, like Zolgensma, warrants not only an understanding among regulators and payers about the immediate benefits of Zolgensma but also the long-term efficacy and safety of the therapy, which today remains unknown. Continuous and strategic RWD collection may be useful to regulators seeking to monitor the long-term safety of early-administered, one-time therapies like Zolgensma as well as for

payers who seek to understand if and how such treatments provide immediate impact and long-term value. Likewise, longitudinally following Alzheimer's therapies in the real-world setting will offer more evidence of the long-term value of these products.

For CVD, therapies and devices often need to be assessed or compared post-regulatory approval to determine the best patient care strategies. This need is especially true given the breadth of available therapies and devices to treat CVD. Indeed, opportunities exist to explore ways in which RWE can be leveraged to determine

if existing therapies are efficacious in CVD population profiles excluded from preceding clinical trials. For instance, CVD drug efficacy trials typically exclude certain populations (e.g., geriatric patients and or patients with co-morbid conditions) from pre-market randomized controlled trials or pivotal studies for scientific reasons. RWE-driven studies conducted in the

post-market setting, including studies that examine patient-level outcomes (e.g., patient-reported outcomes) can be useful to examine the comparative and/or combined effectiveness of CVD treatments.

2

Data System Interoperability to Facilitate the Use, Sharing, and Exchange of RWD across Multiple Systems

A major barrier to building the envisioned RWD ecosystem is the lack of interoperable systems in the health care setting. In the SMA space, while multiple therapies can be captured in one registry, several registries currently exist for SMA.^{vi, vii, viii} Patients who receive Zolgensma will likely be covered under either public or private insurance and thus, potentially listed in separate registries. It is important for these separate registries to be interoperable to enable larger scale data analysis. Similarly, for Alzheimer's disease, registries for new monoclonal antibody treatments should be interoperable with data collected in untreated patients at Alzheimer's Disease Research Centers and at other medical centers to enable valuable means of comparing outcome for treated and untreated patients. In CVD care, RWE gaps tend to emerge when a registry is anchored to a specific clinical care site and a patient either changes provider locations or dies away of the facility, (e.g., emergency department, home, etc.) . Thus, challenges like patient data portability and tracking and linking patient data from multiple sources are to be expected.

In cases where substantial value misalignment exists across these registries and other RWD systems, accompanying variation in the quality, interoperability, and robustness of those systems, is likely, commonly due to resource availability and/or constraints faced by the system owners and/or operators. In such cases, incentives should be structured to facilitate and sustain value alignment across disparate RWD systems.

To begin addressing some of these challenges, ONC and CMS released interoperability and access rules in 2020 that establish policies meant to increase patient access to data and promote interoperability between health data sources. CMS' rule requires payers to build Application Programming Interfaces (APIs) that would allow payer-to-payer information exchange. Yet, payers are concerned about the operational challenges of implementing this rule and any ensuing risks to data quality in the absence of specific standards.^{ix} CMS is currently exercising enforcement discretion on this provision of the rule while more conversations take place with key stakeholders. Though initially challenging to implement, the approaches outlined in these ONC and CMS interoperability and access rules are critical to creating a robust data infrastructure that balances access with privacy.

3

Linking Databases to Maximize Data Analysis Capabilities

Linking separate RWD sources represents an opportunity to build a more robust ecosystem. For example, in CVD, there are opportunities to leverage the current breadth of data sources, including clinical trial data sources and EHRs, as a strategy to examine the real-world comparative and/or combined effectiveness of therapeutics and devices. This strategy, however, likely will present ongoing challenges (e.g., technical, legal, etc.) associated with data access, linkage and management across multiple systems. To meet these challenges, an ideal RWD structure would include access to real-time data that can be collected over time to address longitudinal data needs. It also would include components to reduce the burden of manual data entry and enhance linkages across other databases to maximize data analysis capabilities further.

Importantly, the lack of unique patient identifiers (UPIs) in the United States is a hurdle to building an interconnected, multi-stakeholder data system. A legislative ban on research funding for UPIs has limited federal-level work on developing a

Collecting longitudinal data is often a challenge as patients change care settings or providers. The lack of longitudinal data impairs the ability to make decisions in a range of disease areas, including cardiovascular care, as well as long-term follow up on gene therapies. Well-implemented UPIs, or other technologies and policies supporting the connection of disparate data sources, have the potential to unlock substantial efficiencies in the ability to collect and use longitudinal data.

robust solution. Though efforts have been made to overturn this ban, none have been successful. Policymakers should consider the benefits of UPIs, support the mitigation of any risks associated with overturning this ban, and encourage HHS through ONC to advance UPI development in the United States. While not a perfect solution alone, UPIs are useful for linking or combining data sources, supporting the creation of clinical trial infrastructure, and ultimately, empowering decision makers striving to create learning health care systems.

4

Standardized Endpoints and Outcomes Measures to Evaluate Real-World Effectiveness

Using RWD to generate RWE is hampered in many settings by the lack of standardized endpoints and outcome measures. In Alzheimer's disease, for example, agreed upon endpoints and outcome measures are needed to investigate therapies in the real world. Using one standardized outcome, like admittance to a nursing home or use of 24-hour in-home care could be a useful outcome to evaluate longitudinal functional outcomes following Alzheimer's disease treatment. Dementia rating scales to collect and track changes in cognitive status over time, alongside patient-functional outcome measures, might help ascertain a therapy's real-world value. However, some of the assessment measures used in those treatments' pre-approval clinical trials, including aducanumab, are complex to administer and are generally not

used outside of clinical research settings. For the other monoclonal antibody treatments in the class that may be covered in prospective studies, a need exists to agree on other outcome measures that can be used more easily in real-world settings. Gathering diverse data with definitive endpoints from patients (e.g., prevention of myocardial infarction) is also one strategy to examine the real-world comparative and/or combined effectiveness of a broad array of CVD products.

With SMA and other single-use gene therapies, short-, intermediate-, and long-term outcomes measures to evaluate durability should be considered. In the short- and intermediate-term, emphasis should focus on safety measures to understand how the therapy is attenuating the

disease while also allowing the nervous system to recover and respond to facilitate long-term survival. In the long-term, emphasis should focus on quality-of-life measures, how the disease impacts diagnosed children and their families, and the overall cost to society. Ultimately, outcome measures should be simple yet valuable for care providers and families. Past work by Duke-Margolis and its Real-World Evidence Collaborative includes a [roadmap](#) that explores key considerations for developing endpoints for use in the real-world.^{xii}

Related to the development of these standardized endpoints and outcomes measures is the importance of patient and provider education

from drug developers to help them understand the validated measures and endpoints used to evaluate the therapy. Differences in capabilities among and across health systems, medical centers, and smaller clinics to collect RWD is likely. Educational efforts around validated measures and endpoints can help mitigate administrative difficulties associated with RWD capture among large and small patient-provider settings. For example, existing efforts to evaluate RWD sources through public-private partnerships, including the ROADMAP project in Alzheimer's disease, have supported increased disease understanding and may help streamline decision-making processes.^{xiii}



5 Strategic Partnerships to Facilitate Data Collaborations and Sharing

Stakeholders identified the power of broad partnerships to facilitate the collaborations necessary to address the challenges and take advantage of the opportunities highlighted herein. In Alzheimer's disease, opportunity exists for

A note on analytic methods:

Traditional RWD analyses employ biostatisticians, clinicians, epidemiologists, economists, and other experts to employ classical descriptive and statistical analytic methods. While this paper does not explore analytic methods issues in depth, it is important to note that it will be necessary for stakeholders to partner to develop and refine advanced analytic methods that aggregate data and to build algorithms for each use case. Advanced analytics have the potential to generate evidence for stakeholders by combining data sources and processing large amounts of data (e.g., genetic and genomic information). Therefore, improving analytical methods knowledge can enable broad consensus/ understanding of when RWE is appropriate, what questions RWE can answer that traditional clinical evidence cannot, and how to ensure objective evaluation of the RWE quality stakeholders should build data infrastructure capabilities with these analytic needs in mind. As part of the partnerships discussed here, stakeholders in a given disease space should work together to ensure the appropriate analytic methods are identified.

stakeholders to collaborate in a pre-competitive environment to build a registry that includes a broad and representative patient population to evaluate new therapies against conventional therapies. However, capturing health outcomes using large amounts of data from a single data source comes with certain challenges. In an example with SMA, a longitudinal cohort study of more than 3 million commercial insurance members reported that one in five members dis-enrolled each year, making it difficult to track long-term patient outcomes following coverage decisions for FDA-approved therapeutics. Therefore, registries that would have the broadest possible population also should harness RWD from a wide variety of sources. To accomplish this, partnerships among registry owners or managers, industry, and other key stakeholders are critical to establish shared short-, intermediate-, and long-term evidentiary standards and goals for one-time therapies like Zolgensma, as well as subsequent and/or concomitant therapies that might be required depending on patient needs.

Data partnerships typically require buy-in and support among and between policymakers, public agencies, and private enterprises. Pilot programs for such partnerships are key to develop

best practices and frameworks, inform policy, set grantmaking priorities, and other important initiatives. Such pilot programs would be conducted best in partnership with health systems and other stakeholders that own and manage relevant or well-suited RWD systems. Some early efforts like

the CardioHealth Alliance,^{xv} The National Treatment and Diagnostic Alzheimer's Registry^{xvi} and ROADMAP in Alzheimer's disease,^{xvii} and the Canadian Neuromuscular Disease Registry^{xviii} may provide instructive models for further partnerships in other areas.



6 Building on Existing Databases as a Starting Point Toward More Robust Data Collection

One foundation for partnerships to build on is existing databases and registries. Existing registries, such as The Alzheimer's Disease Neuroimaging Initiative (ADNI), the IDEAS study on amyloid PET, and the National Alzheimer's Coordinating Center (NACC), which coordinate data collection and foster collaborative research among Alzheimer's Disease Research Centers across the country, could serve as a starting point to build more robust data collection mechanisms for both larger and smaller clinics. In the CVD space, Yale has made promising steps to accomplish many of the goals explored here with the Yale New Haven Health System Heart

Failure Registry.^{xix} Similarly, existing registries in the SMA and CVD space likewise could be leveraged.^{xx, xxi, xxii} The FDA's recently disseminated draft guidance on using registries to inform regulatory decisions covers considerations regarding a registry's fit-for-use in regulatory decision-making, considerations to link registries to other RWD sources, and considerations to support FDA review of submissions that include registry data.^{xxiii} Once final, the FDA's guidance may be helpful to inform the development of registry initiatives suited to meeting shared evidentiary goals to monitor monoclonal antibody treatment outcomes in Alzheimer's disease patients.



7 Payment Models and Incentives to Support Long-Term RWD Collection and Analysis

Collecting high-quality, complete, fit-for-purpose data is critical to support a robust RWD ecosystem. However, collecting and storing such data comes with costs in time and resources that should not be underestimated, especially in terms of determining who would bear the costs. Misalignment among stakeholders around who benefits most from the data and who pays the costs ultimately affects the overall value proposition, especially in instances where long-term data collection is needed or would be best. To address this dilemma as it would occur in real-world practice, effective incentives are needed to fully engage stakeholders, including providers and patients, who can contribute to generation and collection of such data.

Participants in the CVD breakout session considered ways to structure payment models and incentives for long-term RWD collection and analysis, focusing on value-alignment needed among health systems and other key stakeholders, including patient data registries, to accomplish this goal. For instance, there are several existing patient data registries for CVD that may or may not be interoperable with EHR systems.^{xxiv} As mentioned above, sustainable incentives should be used to facilitate value alignment across disparate RWD systems.

Health care providers who struggle to find time and resources needed to deliver effective care often struggle with the demands of tedious and

time-consuming data entry procedures. Much of the data collection burden, especially for EHR and registry data, falls on clinicians or registry owners. Health system workflows should ensure that such burdens are minimized through sufficient staffing and resources. Automating some data collection activities, such as prior authorization determinations, is one option to streamline data collection. In CVD, SMA, and other disease areas, consideration should be given to structuring payment models and incentives for long-term RWD collection and analysis, focusing on value-alignment needed among health systems and other key stakeholders, including patient data registries, to accomplish this goal. For instance, several patient data registries for CVD exist that may or may not be interoperable with EHR systems.

Using high-quality and validated wearables, survey measures, or other instruments to collect patient-reported data is also another area ripe for incentives. Patient-level or -reported data collected in real-world settings would disperse the data collection burden, rendering value especially in cases where data might feed into data registries and contribute to the body or totality of evidence on the safety and effectiveness of new therapies granted accelerated approval by the FDA. Therefore, payers and regulators should collaborate to revisit their guidelines, guidance documents, and policies to align on what is needed to cover and monitor patient populations appropriately using RWD.^{xxvi}

Without proper reimbursement or payment to support the significant amount of clinician time and effort, the goal of collecting and synthesizing high quality, complete, fit-for-purpose data becomes lost

Payers also could explore strategies to reimburse clinicians for the time required to input data of value to the payers. Without proper reimbursement or payment to support the significant amount of clinician time and effort, the goal of collecting and synthesizing high quality, complete, fit-for-purpose data becomes lost.^{xxv} CMS also might consider additional incentives, like requiring participation in a data registry or CED program, to obtain reimbursement for prescribing or dispensing certain treatments or for using intuitive, structured data systems to help reduce burden or burnout from tedious data entry processes.

ADDITIONAL CONSIDERATION #1: Data Governance and Management

When building a shared evidence infrastructure that considers the teams above, data and system governance must be forethought. Data and system governance are challenging yet rewarding endeavors when the right questions are addressed early in the data system development process. For example, questions might include:

- Who makes decisions about how the data are accessed and used?
- Who is responsible for ensuring the data are fit for use?
- Who owns the data and where do the data live?
- Who analyzes the data and how?
- How are necessary privacy and transparency considerations implemented?

As stakeholders contemplate these questions, they should consider and determine which elements of governance should be centralized either within government agencies or disease-specific organizations and those that should remain decentralized. A distributed data network, like the FDA's Sentinel Initiative, is one privacy-preserving model to consider--as the data does not leave the environments of individual data partners. Instead, the Sentinel Operations Center queries data partners and then receives de-identified query results. The Sentinel System also uses a common data model to ensure all data is formatted consistently across the distributed data network.

It is vital that patients are central in any RWD ecosystem. While most RWD generated today comes from clinician inputs (e.g., registry, claims, and EHR data), an increasing amount of RWD is likely to come directly from patients through their wearable devices, phones, and other digital health tools. As the RWD ecosystem is built, scalable approaches to collecting data from

patients and linking it to other sources of RWD or clinical data are important for building more robust datasets. Furthermore, stakeholders must ensure that data collection from patients does not exacerbate health inequities, so such approaches must consider vulnerable populations including those with limited access to digital health technology. Accomplishing this approach to data collection in a patient-centered way will require new informed consent mechanisms and direct patient engagement in research. It is important that patients know what their data are being used for and see the results and benefits of contributing their data.

As the amount and types of real-world health data grow, additional consideration must be given to ensuring that sensitive personal health data is properly protected. However, many novel sources of insightful health data are not covered or protected by the Health Insurance Portability and Accountability Act (HIPAA). Any effort to build RWD ecosystems must take privacy into account, while allowing patients access to their data and a voice in determining how their data are used. In the absence of clear federal legislation on privacy protections for health-related data, stakeholders should take it upon themselves to ensure that any use of sensitive data has privacy protections in place.

ADDITIONAL CONSIDERATION #2: Need for Additional Resources and Funding

Federal support for the various data infrastructure considerations discussed above could reduce the burden of data collection costs as a simple solution in the near term, thus enabling easier and broader data collection. For long-term sustainability of such initiatives, more options, possibilities, and opportunities should be explored. Existing federal efforts also could be enhanced with additional funding. Additional resources at PCORI could support EHR interoperability between its clinical research network participants and create a central claims data repository. Within FDA, additional funding for its Sentinel Initiative could accelerate existing efforts to increase the system's ability to answer effectiveness questions in addition to its more established safety surveillance role. These efforts could be combined with additional resources at CMS to fund registries or observational studies that assess the safety and effectiveness of new therapies approved by FDA accelerated approval. Additionally, increasing access to Medicare data, even at a cost to researchers, could provide valuable support for furthering an RWD ecosystem. Collaboration

among these federal efforts will help ensure resources are used efficiently to answer a broader range of questions.

Finally, value-based payment (VBP) models can be leveraged to encourage post-market evidence development among key stakeholders. Ideally, VBP models built for this purpose should be supported on a long-term basis to cultivate a sophisticated data infrastructure that aligns with regulator and payer post-market evidence needs. Key stakeholders involved in the curation of value-based payment models should collaborate to ensure that payment models are feasible both financially and practically and without a significant cost and time burden to a single party or group. Furthermore, payers need to be able to adapt to evolving evidence as clinical care contexts change over time. Having clear expectations for payer evidence needs in post-market settings will enable medical product developers to make plans for RWE generation well in advance.

Conclusion

The challenges and opportunities summarized herein and in prior work^{xxvii} indicate a lack of a robust data ecosystem as one of the major barriers to broader adoption and use of high quality RWD. While federal agencies and policymakers have a vital role in supporting the development of this ecosystem, those that generate or use RWD also must offer important contributions to inform meaningful next steps in this process. The seven key themes and additional considerations around data governance and resource provision detailed here indicate that much work remains to build infrastructure for data linkage and interoperability, establish governance structures and new data partnerships, and develop relevant real-world endpoints and incentives for providers and patients, all while protecting and educating patients. While health care systems, drug sponsors, governments, and payers determine how to move forward from the COVID-19 pandemic, now is the time to build the equitable data ecosystem we need for evaluating modern therapies in the real-world. However, no one stakeholder can do it alone. Building this needed ecosystem will take buy-in and alignment between stakeholders across the life cycle of medical products.

Shared Evidentiary Opportunities Working Group Members

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This paper was also informed by the expert collaborators in the Duke-Margolis Real-World Evidence Collaborative Advisory Group. We thank the members of the Advisory Group, especially those from the 2021 cohort, for informing the development of this paper. The following list reflects the 2021 Advisory Group roster, which advised on the initial development of this work stream.

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Listed 2021 member affiliations may not reflect current affiliations. For a current roster of the Duke-Margolis Real-World Evidence Collaborative's Advisory Group, please visit the RWE Collaborative page on the Duke-Margolis Center for Health Policy [website](#).

Value for Medical Products Consortium

This paper was additionally informed by the expert collaborators in the Duke-Margolis Value for Medical Products Consortium. In previous publications, this group was referred to as the Value-Based Payment Consortium. We thank the members of the Advisory Group for informing the development of this paper. The following list reflects the current membership as of June 2022.

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This paper was additionally informed by the expert collaborators in the Duke-Margolis Value for Medical Products Consortium. In previous publications, this group was referred to as the Value-Based Payment Consortium. We thank the members of the Advisory Group for informing the development of this paper. The following list reflects the current membership as of June 2022.

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