EXECUTIVE VISION

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The Role of Medical Affairs in Improving Patient Outcomes with Real-World Evidence

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INTRODUCTION

In the biopharmaceutical and MedTech industries, it has traditionally been the role of Research & Development (R&D) to manage clinical trials leading to approval of a new drug, device or diagnostic, at which point Medical Affairs would manage a program of post-approval studies to continue evolving the company's understanding of uses, benefits and risks. The growth of Real-World Evidence (RWE) from sources including patient registries, claims data, electronic medical records, digital health technologies and many others has driven a sea change in this model. Today, Medical Affairs uses RWE alongside, or even in some cases instead of, clinical studies, across the product lifecycle to inform clinical trial design, provide context for reimbursement decisions, generate real world effectiveness data, and expand access to emerging health innovations. Even more so, the use of RWE provides an opportunity for Medical Affairs to realize the goal at the center of its mission: To improve the lives of patients, caregivers and others affected by health conditions. Following are ways Medical Affairs departments, teams and individuals can use RWE to benefit patients.

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REAL-WORLD POPULATIONS

Clinical trials in controlled populations generally lead to regulatory approval. In part, this is due to the scientific complexity of clinical trials: Proof of efficacy is required to earn approval and testing a drug in a defined population most likely to benefit provides the highest likelihood of generating this proof and thus making new treatment options available to patients beyond the context of clinical trials. Finding that same proof of efficacy in a less selected population would take many more trial participants, delay access, risk diluting the signal of response, and require far more resources. Medical Affairs' use of RWE studies post-approval can give assurance to patients and regulators that the outcome of a clinical study is applicable to a broader patient population, such as those with comorbidities or co-medications. In this way, RWE can help Medical Affairs teams extend clinical trial results from the individual patients on trial to the heterogenous patient population that seeks treatment.

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PERSONALIZED MEDICINE

Medical Affairs collaborates in the use of RWE outside safety and efficacy trials to prospectively identify potential biomarkers that may predict response to drugs in development, helping Clinical Development colleagues and eventually healthcare professionals (HCPs) personalize their use of health innovations for the patients predicted to benefit. After market, Medical Affairs leads the use of RWE to retrospectively identify biomarkers that may predict response, and also leads evidence generation and scientific communication efforts to ensure adherence to biomarker assessments that may impact outcomes (aka, ensuring HCPs are using drugs/devices/diagnostics in accordance with biomarker assessments). This approach to RWE is a major driver of the ability to apply personalized medicine approaches, matching patient biomarkers to treatments most likely to provide clinical benefit.

REIMBURSEMENT

Patients benefit from a new drug, device or diagnostic only if they have access to it, and one essential enabler of access is reimbursement. Medical Affairs collaborates with departments including Health Economics & Outcomes Research (HEOR) and Market Access to provide evidence to payers describing the value of emerging treatments. In the context of reimbursement decisions, value is generally considered a calculation comparing a drug's cost to its benefits. Medical Affairs is not involved in the determination of cost. However, it informs the "denominator" of the value calculation that Medical Affairs has significant impact, often using RWE to describe the burden and natural history of disease and patient-centric aspects of value that go beyond safety/efficacy demonstrated in clinical trials (or suggesting the addition of these patient-centric endpoints to clinical trials.) Reimbursement agencies are increasingly making use of risk-based contracts in which medicines are approved for reimbursement based on objective demonstration of benefit; in these cases, RWE is often used to support industry claims for patient benefit.

RISK/BENEFIT

Randomized-controlled trials establish the benefit/risk profile of emerging health technologies. Post-marketing, RWE is used to monitor and/or confirm our understanding of the product's profile. Generally, risk is identified through the activities of the Pharmacovigilance department, with our understanding of benefit being continually updated through phase 4 clinical studies and, increasingly, through generating RWE. Also generally speaking, regulators most closely monitor risk and over time as drugs/devices/diagnostics are used with more patients, additional risks may be identified. It must be the role of Medical Affairs teams leveraging RWE to ensure our appreciation of benefit evolves along with our understanding of risk such that healthcare systems both have continued access to these treatments and learn to optimize benefit while minimizing risk.

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LABEL EXPANSION

Label expansion is another mechanism to ensure access for patients who are likely to receive benefit. For one example of many, oncology treatments are often approved for applications in one type of cancer defined by where it occurs in the body, with additional indications added to the label based on post-approval studies. Increasingly RWE is augmenting or taking the place of post-approval clinical studies to demonstrate effectiveness in new or related conditions. Likewise, RWE is being used to expand access for patients excluded from the initial indicated population due to comorbidities or other risk factors. For example, patients might be excluded from a clinical trial based on a risk factor such as high liver enzymes; but RWE could show that patients whose doctors prescribe a medication despite this biomarker of risk do not, in fact, have a higher incidence of adverse events. In this case, benefitting patients is not always about adding to a drug's list of positives, but also includes identifying and removing barriers.

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EFFICIENCY

A company is only likely to invest in label-expansion studies during the window between approval and loss of exclusivity (LOE). During this time, studies seek to demonstrate benefit to as many patients as possible before LOE. The use of RWE can speed results and decrease the required investment such that studies that might not have been prioritized as part of the clinical development program are now able to move forward. For instance, imagine an oncology product approved to treat breast cancer. Few companies would invest in studies to extend the approval to patients with biliary tract cancer – the return would simply not be worth the investment. But a Medical Affairs team could use RWE to identify and analyze situations in which the medication was prescribed for biliary tract cancer patients off-label, with the possibility of extending the label to these patients based on positive outcomes. For these patients, access to the drug could be lifesaving. Likewise, clinical trials have historically compared a drug's effect to placebo, requiring enrollment of patients into both arms. Today, trials are increasingly requiring new drugs be measured against an active comparator (often against standard of care). If RWE can be used to define outcomes of patients treated with an active comparator, in some scenarios companies may be able to forgo the placebo arm of clinical trials, making it possible to complete more trials, overall, and thus benefit more patients. This is especially useful in situations comparing outcomes in disease spaces with many therapeutic options: RWE may allow Medical Affairs teams to, perhaps, run a traditional phase 4 clinical study of the company's drug, but then compare study results to RWE analyses of patient outcomes from many existing treatments.

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UPTAKE

Just because a beneficial drug/device/diagnostic is accessible from a regulatory and reimbursement standpoint does not necessarily mean that it will be used. HCP product adoption is also required. Insights may help Medical Affairs teams identify knowledge/practice gaps that lead to under-utilization of beneficial medications, and RWE studies can help address these gaps. For example, many regional/country healthcare systems prefer to approve the use of products based on study results conducted with local populations. Companies are not likely to complete clinical studies in each geography but may use RWE to localize results to geographically distinct populations.

TRIAL DESIGN

One compelling argument for the involvement of Medical Affairs early in the drug development process is the function's ability to identify patient-centric clinical trial endpoints. These endpoints, often focused on quality-of-life issues, are becoming increasingly essential as healthcare moves to a more holistic understanding of "benefit" that goes beyond safety and efficacy. RWE used to crystallize understanding of, for example, natural progression of disease, can help to pinpoint the issues associated with diseases or conditions that truly affect patients' lives (e.g., issues of sleep, energy, nutrition and sexual function). By including these patient-centric factors as formalized endpoints in clinical trials, Medical Affairs can help to ensure the products developed by industry go beyond extending patients' lives to speak to the real issues that affect overall patient wellbeing.

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CONCLUSION

The sources of generating RWE and the sophistication of tools to analyze data have now evolved to the point that RWE studies are recognized as a legitimate form of data generation – even by regulatory and reimbursement agencies. Meanwhile, Medical Affairs teams are using RWE to survey the patient landscape to identify patients beyond the narrow clinical trial populations who are likely to benefit. It used to be that Medical Affairs involvement was defined by the development lifecycle, with Medical Affairs picking up where R&D left off (i.e., at approval). RWE has led to redefining this distinction, with Medical Affairs more appropriately involved across the lifecycle in all studies not involving regulatory approval (and collaborating on studies that do). No matter where data is generated within the company, Medical Affairs is best positioned to integrate this data into understanding and actions that ensure the drugs, diagnostics and devices developed by industry make a true impact on patients' lives.