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Breaking New Ground with RWE:

How Some Pharmacos are Poised to Realize a $1 Billion Opportunity

The pharma industry has invested substantial resources in Real World Evidence (RWE). Differential success rates have been observed, with little consensus on best practice or value potential; the most successful companies have realized substantial value across the product lifecycle through RWE platforms and these RWE leaders are poised to capture sustained value.

What's the conventional wisdom on RWE?

- RWE and patient outcomes are becoming a powerful currency for engagement and demonstrating product value
- Hundreds of examples of RWE–based payer decisions impacting product use seen[1]
- Most pharmacos are making major RWE investments

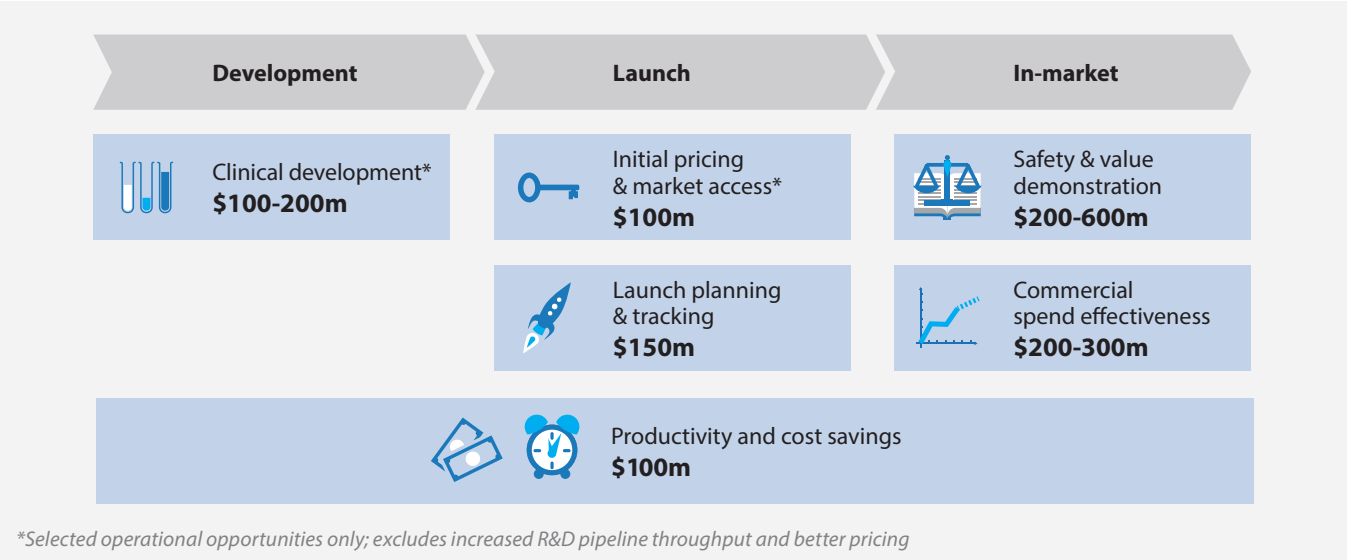
What new RWE opportunities are emerging?

- Demonstrating product value for PMA is only one of six major RWE impact areas
- Extending RWE use, such as to commercial spend effectiveness or launch planning, can realize $1bn in value (Figure 1)
- Platforms enabling on-demand RWE insights are driving value capture and PMR substitution

What are the implications for pharma execs?

- RWE needs commercial leadership and investment beyond immediate business challenges
- Making trade-offs on TAs and market focus accelerates overall impact
- Explicit performance goals, including faster timelines for scientific analyses, is key

FIGURE 1. VALUE CAPTURE FROM RWE ACROSS LIFECYCLE FOR A TOP-10 PHARMACO



[1]Hughes B, Kessler M. RWE market impact on medicines: A lens for pharma. IMS Health Access Point 2013; 3(6): 12-17

The Commercial organization must champion RWE to broaden its value beyond traditional applications and realize its full potential.

A few leading companies have broken new ground in driving a systematic – rather than opportunistic – approach to RWE. They're implementing RWE platforms that move beyond narrow study-based approaches to create sustained value across the product lifecycle and disease franchises. Applied systematically, RWE could realize $1 billion in value for a top-10 pharmaco.

Companies that have not experienced the breadth and depth of RWE applications firsthand may find this figure astounding, particularly if they view RWE as a tool primarily to support market access and demonstrate product value. Leaders, however, regard this figure as an achievable target based on the value realized from their own RWE platforms.

What have leading companies (some claiming to be capturing ~$500 million as they strive to reach $1 billion) done differently? Their experiences suggest Four Golden Principles of RWE transformation:

1. **RWE capabilities should converge in a platform.** Leaders consolidate budgets and make longer-term investments in information, technology and analytics tools to open up a range of uses not possible with registry-style or study-by-study RWE approaches.
2. **Narrow precedes broad.** Leaders focus on select therapeutic areas and markets to ensure that their investments lead to differential value.
3. **Commercial leads the charge.** While medical/HEOR departments may lead *implementation*, the Commercial organization must champion efforts to broaden RWE's application and value.
4. **Speed is a goal.** Leaders seek speed to insight, and can perform end-to-end scientific studies in weeks. In their vision of on-demand insights, quality and speed are harmonious, not trade-offs.

Other companies can benefit from these lessons if they move quickly to compete with leaders who are constantly uncovering new opportunities and improving their own approaches.

Shaking free of traditional thinking on RWE and making meaningful, wise investments can capture dramatic, sustained value – even $1 billion annually for each of the largest companies.

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Contents

Executive Summary **01**

Quantifiable RWE Capture: Exemplary Companies Aiming for $1 Billion Potential **04**

Case Study 1: Scaling Across Functions 04

Case Study 2: From Cost Saving to Commercial Applications 05

Four Golden Principles: Learning from RWE Leaders **07**

1. RWE Capabilities Should Converge in a Platform 08

2. Narrow Precedes Broad 10

3. Commercial Leads the Charge 10

4. Speed is a Goal 11

Where Companies Stumble **11**

Can RWE be a Permanent Competitive Advantage? **12**

Appendix

Estimating the Opportunity Potential of RWE 14

Optimizing Commercial Spend Effectiveness 16

Demonstrating Ongoing Safety and Value 17

Improving Launch Planning and Tracking 19

Better Initial Pricing and Market Access 19

Increasing Productivity and Cost Savings 20

Improving Clinical Development 21

Summary and Comments on Financial Estimate 22

About the Authors **23**

Real-World Evidence (RWE) has long been heralded as a "game changer" for the life sciences industry. As outlined in IMS Health's paper RWE market impact[1], its impact in pricing and market access decisions is proliferating.

RWE is drawn from robust anonymous patient-level data using sound scientific and commercial analytics. It is not about amassing "Big Data" so much as performing targeted analyses on ever expanding healthcare datasets.

While RWE is known to complement data from Randomized Clinical Trials (RCTs), its real potential is in moving decisions away from perceptions and broad extrapolations to the actual facts about patient journeys and outcomes. With innovations in data and technology, RWE is replacing other information sources such as non-behavioral primary market research (PMR), standard market reports, consumption/market data purchases, observational studies, and even selected spending on RCTs.

RWE is delivering deeper insights about patient care, treatment pathways, and drug effectiveness than previously thought possible. Companies are using RWE to support clinical development, improve launches, and drive better commercial results in physician targeting, detailing, and promotional activities. Indeed, commercial spend effectiveness is emerging as one of the biggest sources of RWE value.

Quantifiable RWE Capture: Exemplary Companies Aiming for $1 Billion Potential

Two examples of the journeys that leading companies have taken with RWE help demonstrate how this promise can be realized across an expansive set of opportunities and functions.

CASE STUDY 1: SCALING ACROSS FUNCTIONS

One company started its RWE journey in a typical way: a need to demonstrate the value and safety of one of its products, a $1 billion oncology therapy. A challenge from the Food & Drug Administration (FDA) and potential label changes put up to $500 million of revenue directly at risk. It developed an RWE platform to avoid that risk and then extended its use to improve commercial spend effectiveness and, most recently, clinical development.

Built platform in response to safety challenge for $1bn product

- Developed RWE platform with "off-the-shelf" claims data
- Partnered with providers to enrich platform with outcomes data
- Put brand challenges to rest rapidly including FDA response in <2 weeks

Extended platform to Commercial, improving physician segmentation

- Based highly targeted marketing campaigns on observed patient pathways, doubling sales growth
- Shared forecasting and disease progression models with providers for use in service planning

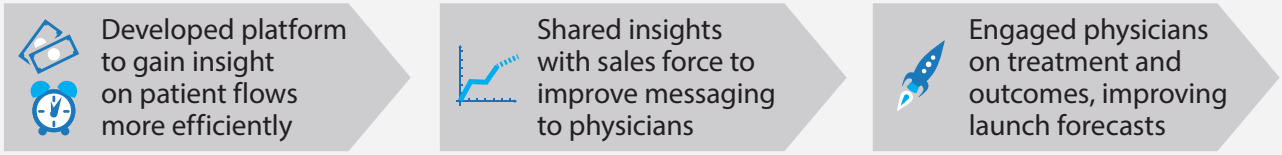
Increased data depth to enable clinical development

- Enhancement of the platform continues with the addition of linkage to tissue samples
- Enables more effective Ph II-III design translations

[1]*Hughes B, Kessler M. RWE market impact on medicines: A lens for pharma. IMS Health Access Point 2013; 3(6): 12-17*

CASE STUDY 2: FROM COST SAVING TO COMMERCIAL APPLICATIONS

Other leaders begin their RWE journey with a tactical focus on costs. One company got its start in RWE hoping to reduce primary market research spend; it created patient journeys based on RWE, leading to more systematic commercial use of RWE insights, ultimately improving launch tracking.



- RWE provided better insights on patient flows at 25-50% of the cost of PMR, with results received four months earlier
- Analyses were repeatable at minimal cost, allowing impact of marketing and patient engagement to be tracked

- Transferred information to the sales force on under-treatment of patient segments, to support better messaging to physicians
- Enabled more meaningful sales rep discussions, with physicians seeing reps as adding value

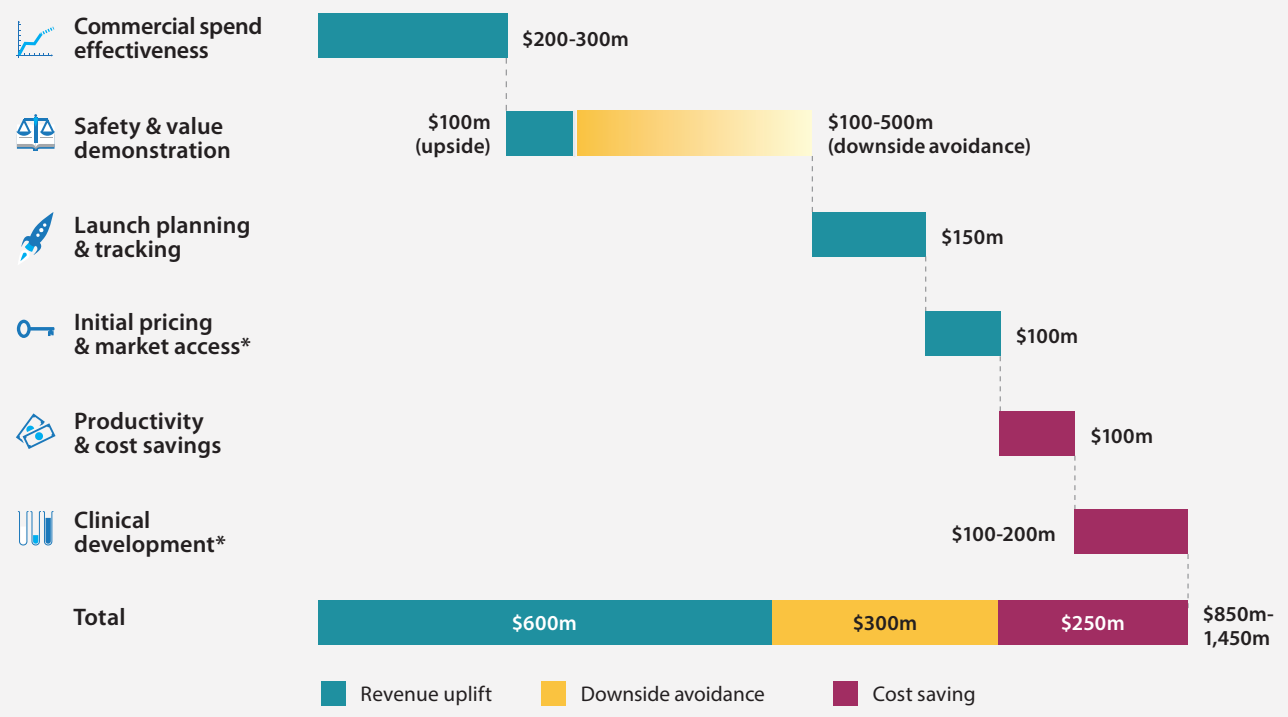
- Shared insights on treatment and outcomes directly with healthcare providers via models in mobile channels
- Improved launch commercial forecasts by 20%

These case studies have a strong focus on demonstrating product value and optimizing commercial spend effectiveness. However, there are six major areas of RWE application that collectively drive the $1 billion potential (see Figure 2). While certain uses of RWE are well accepted and commonly practiced – such as for pricing and market access – today, fewer pharmacos are using RWE to improve launch planning, clinical development, and save costs, missing out on significant RWE-generated value.

IMS Health clients piloting RWE in launch planning have seen significant impact. One client, launching into a crowded chronic disease market, adapted standard patient segments into detailed physician segments based on the actual number of patients meeting its target profile (which can vary 10-fold across similar sites of healthcare providers). By focusing on physicians with relevant patients, the company achieved significant product uptake in pilot markets, exceeding expectations by 10 to 20 percent.

Other companies have captured major productivity gains and cost savings. One company needed to understand diagnosis patterns to establish market sizing for a new compound ahead of launch. It was set to invest $3 to $5 million in a multi-centre, prospective observational study. Instead, given the therapy was suitable only after a specific diagnostic test, the company used its RWE platform to analyze lab tests via retrospective data. The answer was not only more accurate, but it was also delivered in just two weeks at two percent of the original budget.

FIGURE 2. VALUE CAPTURE FROM RWE FOR A TOP-10 PHARMACO

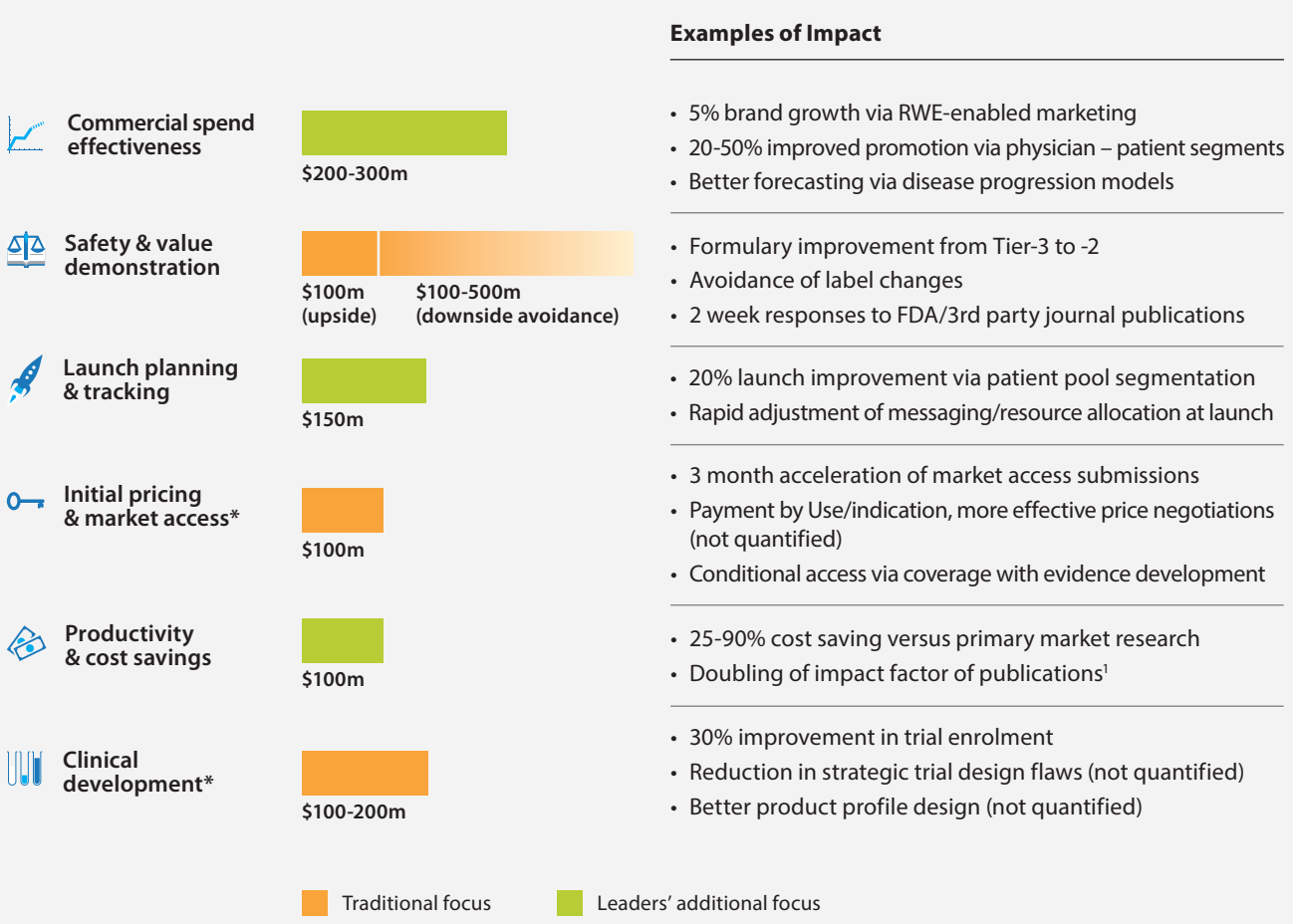


Selected operational opportunities only; excludes increased R&D pipeline throughput and better pricing

Finally, RWE's value in clinical development should be front and center of any strategy, given its longer-term promise to enable pipeline acceleration and adaptive licensing. Companies are already seeing early, albeit major, successes in enabling translational research or continuous evidence generation from phase II to IV. However, there are not enough examples currently to put a dollar value on this long-term benefit; therefore we focus on more immediate operational gains in clinical development possible today, such as tapping EMRs to double enrolment rates into trials.

Figure 3 highlights how these case studies align with the six opportunity areas as well as areas that leading companies in RWE are pushing further. An explanation of the quantification is detailed in the Appendix. Note this is still not the full picture of value – only that which can be quantified via case studies. In areas that may make or break a product's value, such as clinical development or pricing, the potential impact of RWE far exceeds this estimate.

FIGURE 3. CASE STUDIES OF RWE IMPACT ACROSS OPPORTUNITY AREAS



[1]Hruby GW et al. J Am Med Inform Assoc 2013;20:563-567.

*Selected operational opportunities only; excludes increased R&D pipeline throughput and better pricing

The value of RWE has moved from theory to reality: the interesting question is why only selected companies are close to harnessing it or even have meaningful RWE strategies in place?

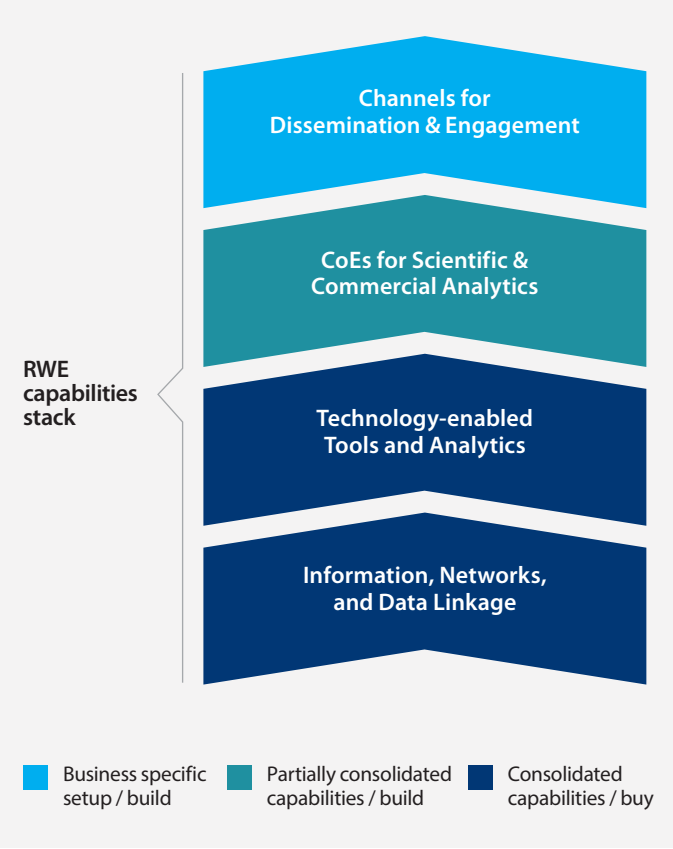
Four Golden Principles: Learning from RWE Leaders

IMS Health engages with all top-20 pharmacos on RWE strategy. In our regular interaction with these companies, we've observed dynamics that set leading companies apart in their approach to realizing RWE value systematically. Their experiences imply at least Four Golden Principles for distinctive RWE transformations. Leaders amongst the largest pharmacos are well on their way to realizing the $1 billion potential that RWE represents, and other companies that adopt these Principles will strengthen their own chances of success and may enhance their investment returns.

1. RWE CAPABILITIES SHOULD CONVERGE IN A PLATFORM

In most companies, RWE is not a consolidated function. In contrast, RWE leaders take a comprehensive and scaled approach to developing the required capabilities. They think carefully about what capabilities to buy versus build and how best to balance the benefits of centralization (economies of skill) with the benefits of embedding capabilities within the business unit (responsiveness to business needs). The necessary layers of capabilities are described in Figure 4 and include:

FIGURE 4. CAPABILITIES LAYERS IN AN RWE PLATFORM



- **Information, Networks, and Data Linkage.** Increasingly, technology is enabling managed access with consent to new information and, where information governance requires record-level data to remain external or in a specific geography, distributed queries. Additionally, leaders develop relationships with healthcare stakeholders to gain access to specific data sources relevant to their research needs. They are able to link datasets, complying with privacy laws, using technologies that anonymize data at source or integrate routine databases with traditional prospective data. The result is a rich end-to-end view of patient journeys.
- **Technology-enabled Tools and Analytics.** Leaders provide users with direct access to data insights through user-friendly interfaces. Pre-defined, validated queries facilitate simple requests without the need for a programmer, with the ability to re-use and catalogue a library of standard methods. This flexibility, coupled with high-performance architecture, reduces time to insight for users through an increasing range of RWE-specific tools offered by commercial vendors. This does not replace highly experienced scientific and statistical staff, but rather ensures they are focused on value-added tasks, instead of routine ones.
- **CoEs for Scientific and Commercial Analytics.** Leaders are standardizing analytics across markets and data sources, pooling analysts in a flexible and scalable service capacity. Scientific and Commercial Centers of Excellence (CoEs) still tend to be managed separately, allowing companies to gain economies of skill where possible, but also to develop deep analytical methods specific to a therapeutic area or function.
- **Channels for Dissemination and Engagement.** Leaders are formalizing the use of RWE across global and local channels to engage stakeholders. This ranges from global branding programs that promote the overall credibility of RWE platforms to locally deployed initiatives to improve Medical and Pricing & Market Access teams' RWE capabilities. Internally, on-demand RWE insights are being embedded into operational processes across functions.

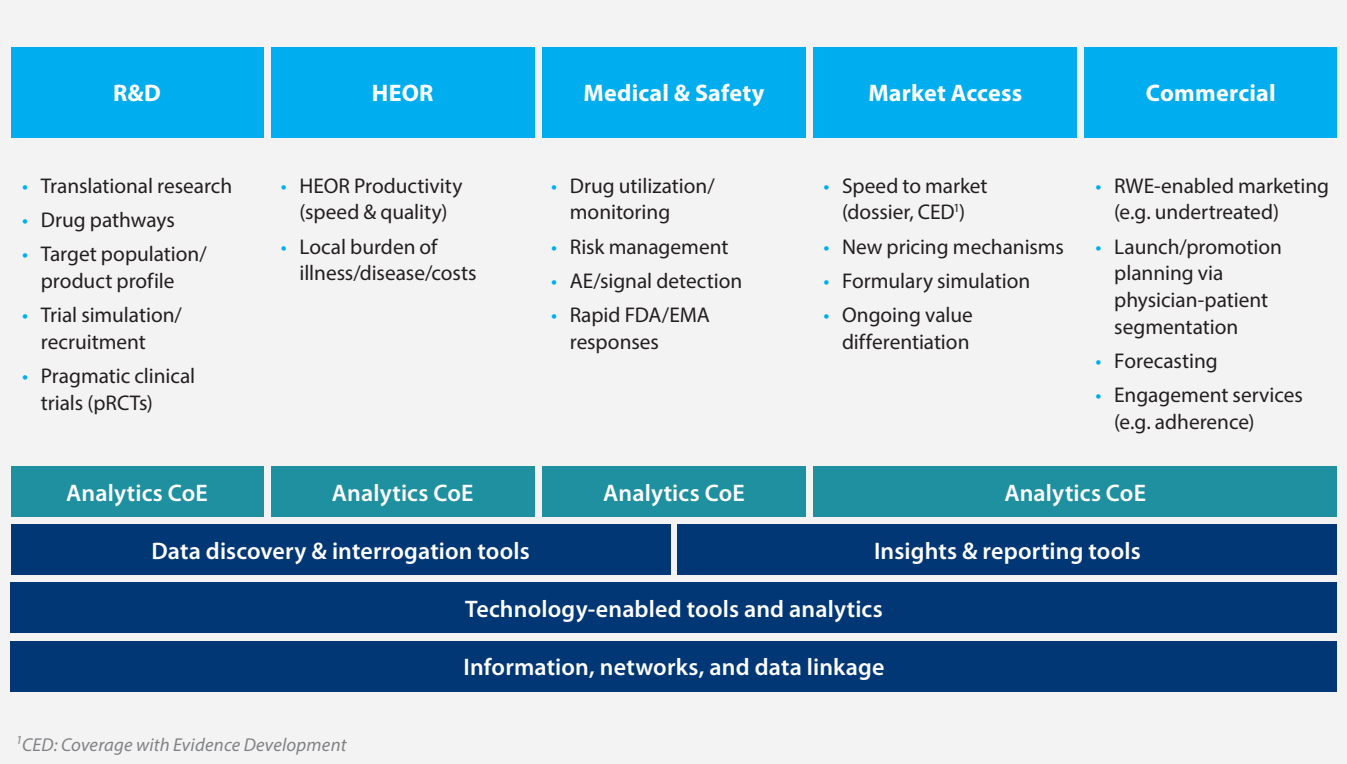
Leaders typically rely on a set of best-of-breed vendors for information and data acquisition, often going beyond off-the-shelf offerings. These vendors and partners offer sophisticated data analytics and linkage capabilities, for instance new techniques such as integrated EMR and primary data collection (e.g., eCRF). This changes the cost structure of research, coming in at up to 30% cheaper, and enables long-term follow-up for studies. Eventually this offers the potential for large scale pragmatic trials.

A single technology-enabled platform, increasingly offered by commercial vendors, can be tailored to the two distinct user groups: Scientific functions will use it as a data discovery and interrogation tool, querying patient-level data directly while Commercial functions will use it for insights and reporting based on standardized, pre-programmed analytics.

A number of analytical CoEs may support these user groups, and themselves be highly advanced users of tools, but even this represents a major change from the traditional, highly fragmented teams (Figure 5). Analytical and dissemination capabilities drawn from these tools are often seen as sources of competitive advantage, and are therefore largely built in-house.

Dissemination and engagement is usually localized to a particular franchise or market, with each traditional function within a pharma company serving as a channel. One exception to this, however, is the branding and external promotion of the RWE platform since establishing a platform that stakeholders value and trust is a potential source of competitive advantage. Publicly promoted RWE platform brands include Amgen's OSCER (Oncology Services Comprehensive Electronic Records), Novartis' VERO (Value of Evidence in the Real-wOrld), and Pfizer's RWDnA (Real World Data and Analytics).

FIGURE 5. PLATFORM DEPLOYMENT TO FUNCTIONS



[1]CED: Coverage with Evidence Development

2. NARROW PRECEDES BROAD

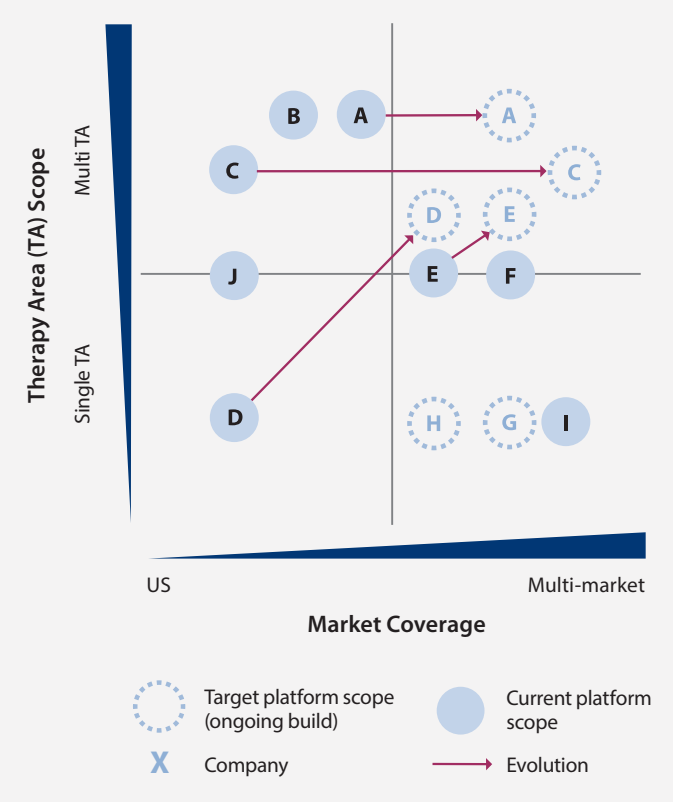
Companies must funnel their investment into a "must-win" therapeutic area. It is our belief that companies can only be distinctive in areas where they have internal expertise and products/treatments that give them credibility and real-world experience with stakeholders. Many emerging leaders have elected to use RWE in one or two therapeutic areas where there is a strong pipeline and in-market portfolio and within mission-critical markets (to include the U.S. and up to three to five additional markets worldwide).

Even today, no one has full RWE platform capabilities across multiple therapeutic areas and in multiple geographies. However, companies have had successes in single therapeutic areas or with single market approaches that they have expanded over time, as shown by the migration of individual platforms in Figure 6.

This concept of *narrow precedes broad* also applies to developing internal momentum for the platform. Given that the trigger for developing a platform is often a specific brand challenge, whereas the long-term value is in addressing other brand goals, the number and type of customers that the platform serves will expand over time. The platform itself can be built with an eye to supporting more TAs and geographies over time.

Many will debate this view given the desire to drive distinctive capabilities simultaneously in all key therapeutic areas, markets, and functions. The reality is that it takes several years to develop the necessary capabilities and deliver value, which is easier to do when those involved are aligned by common data and/or challenges, often defined by TA. Companies defining a transformation agenda must set the right expectations: there is no silver bullet solution, but rather success requires a multi-year effort of continuous improvement.

FIGURE 6. ADVANCED PLATFORM STRATEGIES BY THERAPEUTIC AREA AND GEOGRAPHICAL SCOPE



3. COMMERCIAL LEADS THE CHARGE

The need for Commercial to lead the initiative in a domain traditionally viewed as Scientific (e.g., HEOR, Epidemiology, Safety), is not immediately obvious. However, leaders realize that the Scientific function can be the data custodian and users of RWE for protocol-driven studies while the Commercial function can be given appropriate access to drive strategic decisions. Strong governance, with access to data insights for nominated individuals outside of the Scientific department enables scale in RWE investments.

The argument for Commercial leadership of RWE capability planning and investment is two-fold. Firstly, the largest immediate financial value of RWE is in supporting about-to-launch and launched products, areas for which Commercial drives decision making. Many decisions related to labeling and identifying target patients, contracting and pricing strategies, and launch planning are transformed by RWE, requiring that Commercial be close to RWE strategy. Ultimately, only franchise leaders can really champion the longer-term investment in their patients and key markets.

Secondly, scientific disciplines favor a narrower range of RWE strategy options (such as primary observational research and registry building), than the directional insight that reflects some of RWE's commercial value for rapid decision making. While the internal scientific community must be a core part of the process to ensure that the RWE analyses are robust and fit-for-purpose, Commercial must drive application of insights to rapid decision making.

How can Commercial initiate its leadership role in a pragmatic way? More product teams are now sharing their commercial priorities across functions and then mapping their current and pending evidence plans against them. One such company reoriented several expensive prospective studies to build a platform capability to link key information sets for needed insights. Therefore, longer-term evidence planning, and Commercial's ability to remove barriers across an organization, is an emerging vehicle for RWE leadership.

4. SPEED IS A GOAL

Platform-based RWE capabilities challenge the paradigm that significant time is required to develop robust, scientific-led insights. If existing data agreements are in place and pre-defined analytics have been established, analyses can start almost immediately. In companies where RWE delivery teams have customer service mindset, of which we are aware of at least three, full scientific studies using platform-enabled analytics have been done in less than one month, rather than up to a year.

The speed of developing quality insights from RWE can provide Commercial teams with feedback on changes in the market and the impact of their actions within weeks. Leading organizations realize that such speed only matters if they are willing to act on that new information promptly. Such actions could mean changing sales call plans, reprioritizing physician targets, changing or dropping promotional plans, and even engaging with payers more frequently or differently. RWE leaders make this more real-time information available, adopt more dynamic marketing plans, and empower key account managers and others to leverage new information.

Where Companies Stumble

Most of the top-20 pharma companies are attuned to the benefits of RWE. They have RWE communications, reference an RWE strategy in their annual reports, and/or have an RWE senior executive. However, leaders are differentiated from the rest of the pack in that they take a very strategic approach to RWE.

While trial and error is to be expected in a new domain, the companies that have seen limited value from RWE have either had limited real ambition, or fallen into three common traps:

- **Heavy process orientation.** One company spent months developing SOPs to unite slower-paced RWE activities run by Scientific teams with commercial planning cycles. It was only in rolling this out to an affiliate which had already addressed core RWE performance (defining a Service Level Agreement for a two-week RWE study feasibility), that they realized the SOP-writing process was distracting them from true transformation.

- **Rush for deals and access.** When RWE initially gained prominence, a few high-profile deals in the U.S. and the fear of being locked out from data ignited a race among companies to develop RWE partnerships. Market dynamics have since changed, but some companies are still measuring their success by the quantity of partnerships they've signed. Meanwhile, they admit privately that they've not established the detailed approaches required to extract full value from them. In contrast, leaders have more focused partnerships and rely on novel, technology-enabled sourcing models.
- **A lack of innovation and trade-offs.** Performing large-scale analyses of EMRs or claims databases has been integral to unlocking the value of RWE. Yet some companies have focused their RWE investments on traditional methods such as registries, given their familiarity with this type of source and perceived higher quality. However, greater value capture is only possible with databases or approaches that are extendible, which can feed mid- to long-term objectives, gradually leaving companies leveraging inflexible, non-scalable sources behind in the RWE arms race.

There are many other traps and challenges, for example companies headquartered in EU or Asia have shown signs of particular difficulty of ensuring global and U.S. alignment in RWE strategies.

Can RWE be a Permanent Competitive Advantage?

Not surprisingly, RWE leaders are ushering in the next wave of value by piloting ways to engage health systems and by developing value-added services that leverage their platforms. Indeed, stakeholders could welcome the use of RWE, given a growing appetite for engagement across health systems, ongoing health system reform, and the evolving burden of risk in countries such as the U.S.

Initial pilots have focused on supporting branded products directly by managing reimbursement, using highly accurate adherence algorithms to improve ROI, and studying dosing algorithms to improve treatment effectiveness. This is now expanding beyond the single product to whole therapeutic areas, which is of more value for payers and providers. RWE now features in forecasting, process-of-care metrics, and operational decisions (supporting diagnosis algorithms or risk stratification at the individual patient level).

Finally, differential strategies have emerged for the use of RWE. What remains to be seen is the pace at which this value is unlocked in the industry and which companies are able to establish distinctive capabilities in specific therapeutic areas. Given the breadth of possibilities for taking advantage of RWE – many of which are still unfolding – and the time required to develop capabilities, current leaders will have a competitive advantage for some time. For other companies, several key questions arise, and the onus is on Commercial leaders to ensure they are addressed as soon as possible:

- What are our longer term business challenges that require insights about actual practice (e.g., indication-based pricing models in oncology)?
- Which investments and trade-offs (e.g., markets, brands) can be made to enable focused advances in supporting them?
- Have we clearly defined measurable performance improvements (e.g., delivery speed, analysis types) for investments?
- How can organizational conditions and incentives help drive a multi-year journey, which will surely involve setbacks, and require cross-functional collaboration?

Our focus has been on quantifying the financial impact of RWE for pharma, excluding its promise to accelerate development of new medicines. Pharma-generated RWE only succeeds in changing healthcare provisions when the advantages accrue to payers and patients[2]. Hence, RWE presents not only a major opportunity for the life sciences industry, but also for the healthcare system overall. A company that captures $1 billion in RWE value for itself ultimately creates improvements in the healthcare system valued in the tens of billions of dollars. Now that RWE is having such impact, it has come of age.

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[2]*Hughes B, Kessler M. RWE market impact on medicines: A lens for pharma. IMS Health Access Point 2013; 3(6): 12-17*

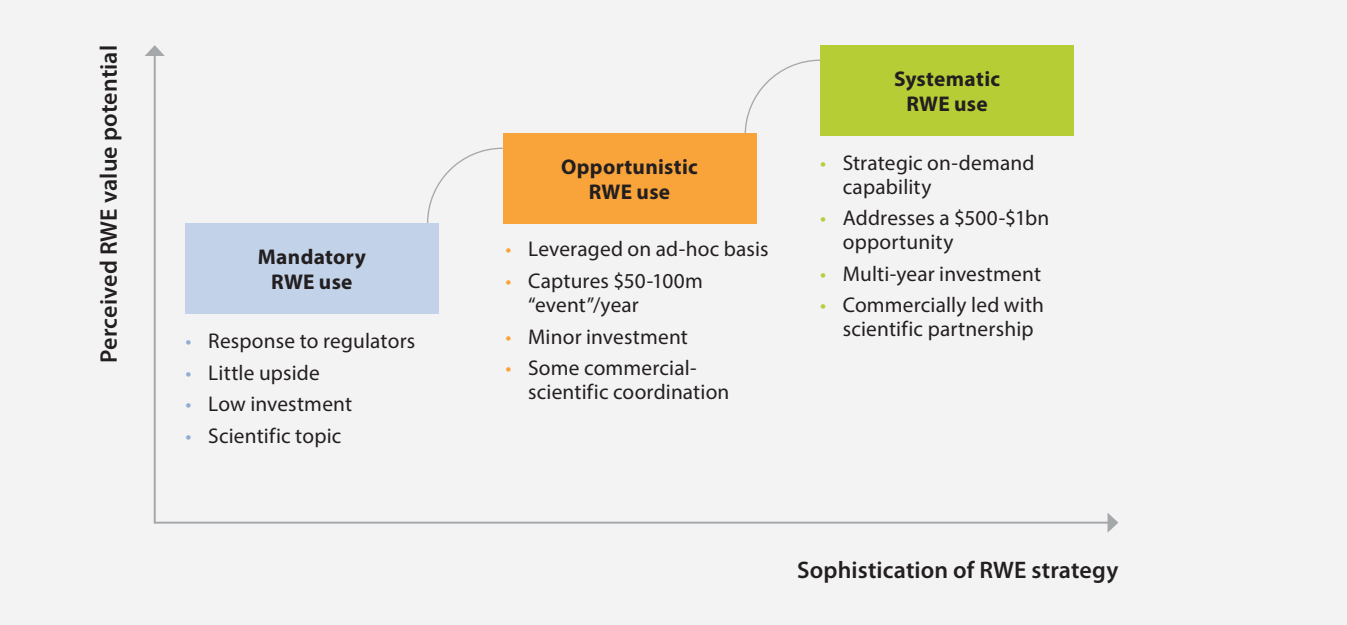
Appendix

ESTIMATING THE OPPORTUNITY POTENTIAL OF RWE

Many industry reports and consultancy companies have trumpeted the potential of RWE, which is sometimes framed as large-scale, data-driven patient analytics, "Big Data" in healthcare, or simply open data. The general consensus is that it offers $300 to 450 billion[3] in top-down opportunity for U.S. healthcare alone[4]. At the same time, many life science companies are seeing *ad hoc* value from selected RWE case studies, often demonstrating as much as $100 million of bottom-up impact[5]. Between these two estimates, how much value should a major actor such as a top pharma company expect to unlock from RWE?

To answer this, we took an in-depth look at IMS Health clients who are RWE leaders, examining the financial impact of RWE within their case studies. We observed major differences in perceived value from RWE across companies. A few companies regarded RWE as a cost of doing business, and most could cite one or two case studies that demonstrated up to $100m in value. A small, select set of companies already claimed to have captured $500 million of impact, while acknowledging that significant additional value can be secured via advancement of their ongoing RWE strategies. Their systematic approach to RWE has unlocked a new wave of value (Figure 7).

FIGURE 7. THE RWE VALUE CONTINUUM



If, however, the individual best practices from these selected leading companies were all to be applied systematically to the major franchises of a top-10 pharma company, the potential impact could easily reach $850 to $1,450 million. Achieving this requires that capabilities be built systematically in six areas where RWE creates major value – going beyond traditional focus areas for RWE.

[3] *All monetary values are expressed in U.S. Dollars.*

[4] *Chui M, Manyika J, van kuiken S. What executives should know about open data. McKinsey Quarterly. January 2014.*

[5] *Hughes B, Kessler M. RWE market impact on medicines: A lens for pharma. IMS Health Access Point 2013; 3(6): 12-17*

These six areas, which generate revenue growth and cost or productivity improvements throughout the product lifecycle, are:

Optimizing commercial spend effectiveness. Brand growth via RWE-enabled marketing, improved promotion via physician-patient segments, and better forecasting via disease progression models.

Demonstrating ongoing safety and value. Supports continued access and reimbursement through responding to FDA/3rd party queries and publications, as well as avoiding label changes and protecting brand from generic entry (traditional domain for RWE[6]).

Improving launch planning and tracking. Accurate patient pool segmentation and rapid adjustment of messaging/resource allocation at launch.

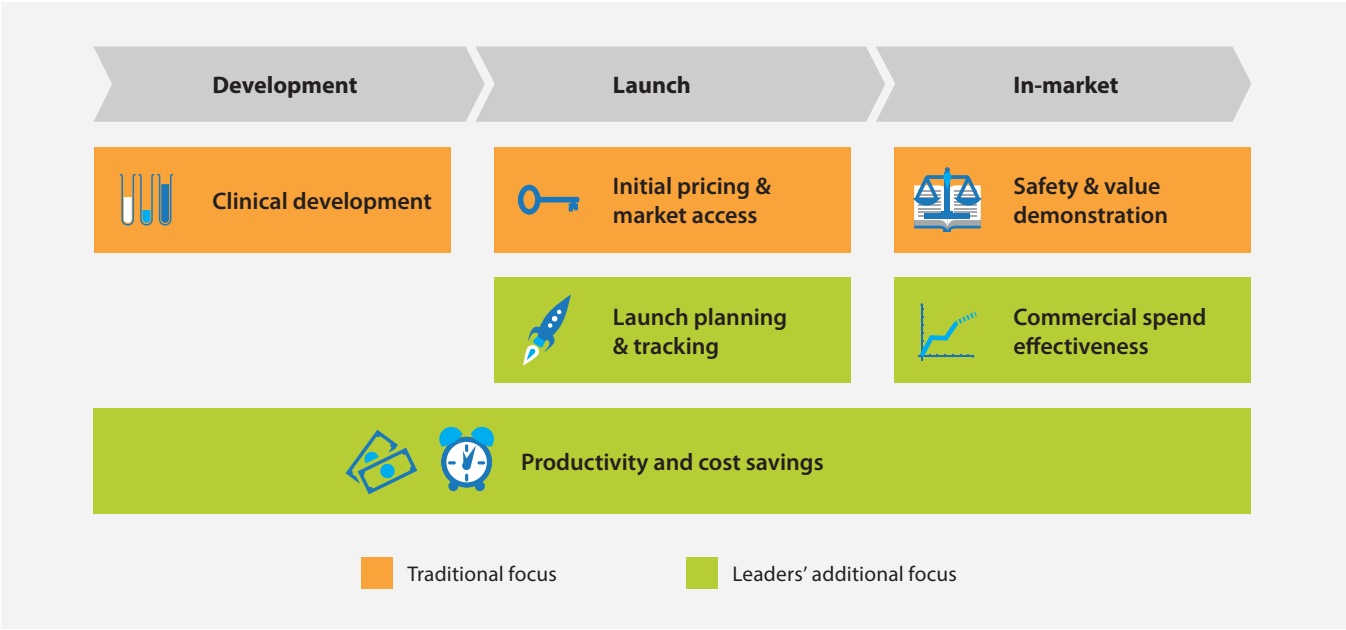
Better initial pricing and market access. Accelerates market access submissions, payment by use/indication for more effective price negotiations, and conditional access via coverage with evidence development.

Increasing productivity and cost savings. Reduces duplicate primary research spending and doubles impact factor of publications.

Improving clinical development. Improves trial enrolment, reduction in strategic design flaws, and better product profile design.

As seen in Figure 8, typically companies have focused RWE on demonstrating value, market access, and clinical development. With industrialized RWE capabilities and an on-demand platform, the approach is shifting from opportunistic applications to a systematic strategy across all six areas. This is bringing about a step change in RWE value.

FIGURE 8. EXPANDING FOCUS OF RWE



[6]*Hughes B, Kessler M. RWE market impact on medicines: A lens for pharma. IMS Health Access Point 2013; 3(6): 12-17*

OPTIMIZING COMMERCIAL SPEND EFFECTIVENESS

By systematically connecting different datasets, companies can deepen their understanding of patient journeys and market dynamics. Marketing and sales efforts can be transformed by focusing on very specific points along the patient journey or in the physician decision-making process, or by gaining a deeper understanding of latent (rather than relative-to-competitor) sales potential.

By performing patient-centered analytics with RWE to improve physician-patient segmentation and targeting, detailing strategies, and promotional spending, companies have increased their detailing effectiveness by 15 percent (by not calling on physicians in the lowest deciles for new-to-brand prescribing) and their promotional effectiveness by up to 50 percent. RWE-driven alerts to the sales force have also been very successful. For instance, analyses of granular patient data and EMRs enable reps to see (via lab test results) what proportion of patients passing through a physician's office eligible for a treatment actually receive the product.

Example 1: Boosting Sales Performance with RWE-Enabled Field Alerts
A top-10 international pharmaceutical company sought to improve the market performance of its diabetes product. The business analytics team went beyond looking at national trends within Anonymous Patient-Level Data (APLD) to monitoring new-to-brand prescription volumes in physician-specific APLD.

Reps received alerts on physicians' new patient starts and add-on therapies so that they were able to spend less time asking doctors *what* they do and instead more time discussing *why* they do it. In fact, 80 percent of reps reported that the alerts significantly improved their pre-call planning. The company now has a much better view of what is driving prescribing behaviour and can quickly disseminate this information to the field – where it matters most.

Example 2: Improving Field Force Productivity by Focusing on the Dynamic Market
Faced with increasing competition from a new molecule as well as from generics, a leading pharmaceutical company with a product treating the central nervous system needed to rationalize its sampling strategy. Previously, the company had given its sales reps the authority to dispense samples to the more than 100,000 called-on physicians as they saw fit.

The company benefited from a proprietary methodology for analysing promotion responsiveness at the physician level. It learned that it had been over sampling from a profitability standpoint in nearly all physician segments. Ultimately, it reduced samples by 20 percent, reallocating them against the "right" prescribers. This move generated an additional $2 million in sales and $5 million in profit.

Example 3: Targeting Undertreated Patients to Enhance Sales Growth
Another company used RWE to identify clusters of patients that were undertreated for a specific condition, by querying EMR data for positive lab results without a subsequent follow-up treatment. This informed a targeted marketing campaign through which a decision aid (supported with RWE) was distributed to practitioners. Through this effective targeting, monthly sales growth rose from two to five percent.

Examples abound of the commercial impact that companies have enjoyed from applying RWE to specific commercial challenges. The key question is: *to what extent are these opportunities replicated across countries and therapy areas?*

Under-treatment of disease, as an example, applies to most therapy areas. In oncology, late or misdiagnosis occurs in 10 percent of cases. In other specialties, such as Rheumatoid Arthritis, it is more severe, with an average delay of nine months between symptom onset and treatment. And even in chronic disease such as diabetes, it is problematic: a third of early-onset patients remain undiagnosed. Understanding patient pathways can therefore have a massive impact across disease areas, although only a few markets have sufficiently rich data to support these analyses today.

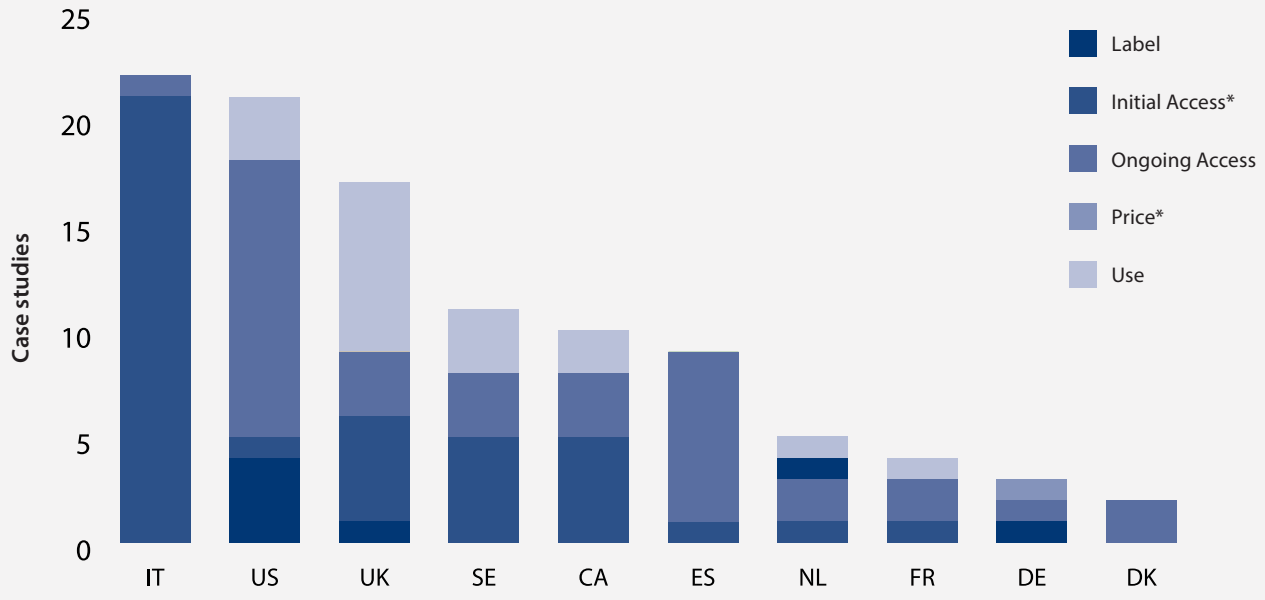
Overall, for a top-ten pharmaco with $5 billion in sales and marketing revenue and a margin of 4 percent to 6 percent that can be influenced by RWE, $200 million to $300 million is at stake.

Total revenue	% improvement via RWE	Total increased revenue
$5 billion	4-6%	$200-300 million

DEMONSTRATING ONGOING SAFETY AND VALUE

Safety and value demonstration studies are the historical domain of RWE, and they drive numerous decisions. This is not just about downside avoidance; as highlighted in IMS Health's white paper[7], these studies also drive increased product use up to the late stages of a brand's lifecycle (Figure 9).

FIGURE 9. DECISIONS LEVERING RWE IMPACTING PRODUCT USE (EXCLUDING SAFETY)[8]



Covers elements from "Better Initial Pricing and Market Access" section

[7]Hughes B, Kessler M. RWE market impact on medicines: A lens for pharma. IMS Health Access Point 2013; 3(6): 12-17

[8]Includes initial access & pricing examples relevant to launch; excludes pure safety examples

Example 1: Countering Challenges to Value and Cost-Effectiveness
Let's consider downside avoidance first. One U.S. company used RWE to address two challenges to its billion-dollar blockbuster: deep FDA scrutiny on potential dosage issues, and a spontaneous third-party publication in the NEJM. Both situations independently challenged the product's value and cost-effectiveness. Using its RWE platform, the company addressed both issues in a few weeks, including reproducing the exact analyses in the NEJM article. By rapidly using a large real-world dataset, it corrected the misleading results of analyses from smaller datasets. The value at stake in each case was ~$500 million and ~$100 million, respectively.

Example 2: Precluding a Change in the Treatment Paradigm
Another client with a blockbuster drug in a dominant market position faced the entry of a branded competitor that offered a similar clinical profile, but with the advantages of more convenient administration and reduced annual cost. To prevent a significant change in the treatment paradigm, the client undertook a comprehensive and proactive plan to generate RWE that could dispute the value claims of the newly launched entrant and create differentiation between the products. In one market, this has already precluded hospitals from implementing wholesale changes to their formularies, which has saved the company tens of millions of dollars in sales in a single geography alone. Further initiatives to generate RWE are in progress, with an even greater expected impact on the market and the company's bottom line.

Example 3: Reversing a Formulary Decision
To realize upside revenue potential, one client protected a mature product from generic competition by demonstrating higher survival rates and lower overall healthcare costs through a $250,000 RWE study. This reversed a formulary decision to secure $100+ million revenue.

How do these examples translate into regular downside avoidance or the realization of upside opportunities for a top-10 pharmaco?

Downside challenges for major $1+ billion products, which most top-10 pharma companies have, now occur almost annually. IMS Health's analysis of insulin analogue products shows that multiple pieces of third-party evidence that challenge leading brands' value are developed every year[9]. This said, typically market erosion affecting 10% of product value ($100 million), not catastrophic market positioning jeopardizing 50% of product value ($500 million), is the issue.

Upside opportunities are harder to assess, and to do so we have to rely on our clients' own analyses. One RWE leader reports that it has consistently achieved $100+ million in added revenue (10% of product value) in the last three years across its rich portfolio and markets.

Total revenue at stake	% influenced by RWE[2]	Total revenue impact
$1 billion[1]	10-50% (downside avoidance) 10% (upside)	$100-500 million (maintained) $100 million (increased)

[1]Assumes a top pharmaco has major products worth ~ $1 bn, which are focus of 1-2 value challenges a year
[2]Assumes 10-50% downside possible, but upside limited to 10% on potential revenue increase (based on case studies)

[9]IMS analysis retrospective RWE publications on Insulin (available on request)

IMPROVING LAUNCH PLANNING AND TRACKING

Launch planning requires understanding the current treatment pathway and stakeholder dynamics and then deciding how best to influence those dynamics to support a new product. As target populations become more specific, granular insight on exactly who treats a specific population becomes more critical to achieving step changes in launch segmentation and messaging. Misunderstanding the current situation wastes time and money.

IMS Health clients piloting these techniques have already seen significant impact. One client, planning to launch into a crowded chronic disease market, adapted standard patient ABCD segments into far more detailed and powerful segments based on the actual numbers of patients meeting its target profile (which can vary 10-fold across similar sites of healthcare providers). By focusing on physicians with relevant patients, the company achieved significant product uptake in pilot markets, exceeding expectations by 10 to 20 percent.

Other clients leverage the power of RWE more operationally, through tracking programs that enable rapid understanding of physician response and launch effectiveness, or through RWE-based engagement tools that model treatment patterns for prescribers. IMS Health clients using these novel techniques testify to seeing major impact, though few quantified case studies exist at this stage.

Assuming a combination of these techniques, a 25 percent improvement potential for a top-10 pharma, with revenue expectations for new therapies of $1.2 billion (of which $600 million is addressable by RWE) can yield $150 million in revenue acceleration.

New launch revenue	RWE-addressable revenue	Revenue uplift via RWE	Total increased revenue
$1.2 billion[1]	$600 million[2]	25%	$150 million

[1]Assumes pharmaco generates $30bn in revenue, with average patent life of 15 years; need to replace ~$1.2bn in revenue per year to cover loss of revenue following patent expiry
[2]Assumes 50% addressable, based on markets where RWE capabilities currently exist (U.S. and 4-6 other major markets)

BETTER INITIAL PRICING AND MARKET ACCESS

While the application of RWE to pricing and market access is widely accepted, with examples of its impact (Figure 9), there are challenges in using RWE this early in the product lifecycle. National reimbursement decisions rely on efficacy data from clinical trials and value for money (cost-effectiveness) calculations, with seemingly rigid submission requirements that may not be accommodating to RWE. However, there are opportunities to support RCT results with RWE, speeding the initial submission and reducing the number of iterations between submission and final decision. The result is that products get to market faster.

Having country-specific data at one's disposal cuts the time spent in searching for relevant data sources and conducting analyses in the months leading up to a submission. Instead, key inputs can be prepared in weeks. These include justification of the standard of care from real-world practice, precise number of treatment-eligible patients for the budget impact model, and real-world use of the comparator in the cost-effectiveness model.

Such uses of RWE support and contextualize the results of RCTs and also correct misconceptions where data were previously lacking. While it is rare to see the impact of RWE be dramatic for a single submission in a single geography, it can be when multiplied across geographies or for multiple submissions within the company's key therapy area.

Opportunities are, therefore, both strategic (articulating the value of a new drug to payers) and operational (assembling arguments and standard requirements for dossier submission). Strategically, various case studies show RWE's differential impact in price negotiation[10], but as opportunities are more sporadic across therapy areas, we've focused on the operational aspects for this estimate of opportunity.

One company leading in RWE capabilities identified this as a major opportunity. Via consistent RWE capabilities across six markets, the company reduced timelines for developing dossier evidence from months to weeks, targeting an earlier submission date by two months.

For a top-10 pharma company with revenue expectations for new therapies of $1.2 billion (with $600 million addressable by RWE), improving operational aspects of market access can accelerate revenue by 15%, equivalent to $100 million.

Total revenue at stake	RWE-addressable revenue	Assumed acceleration	Total increased revenue
$1.2 billion[1]	$600 million[2]	15%[3]	$100 million

[1]Assumes pharmaco generates $30bn in revenue; need to replace ~$1.2bn in revenue per year following loss of patents
[2]Assumes 50% addressable, based on markets where RWE capabilities currently exist (U.S. and 4-6 other major markets)
[3]Assumes a 2-3 month access acceleration, and consequent accelerated uplift through initial product lifecycle

Operational benefits only. Excludes improved pricing or new pricing mechanisms

INCREASING PRODUCTIVITY AND COST SAVINGS

RWE platforms drive not only major upside opportunities as outlined above, but also significant advances in productivity and cost savings by focusing resources where they can have the most impact. RWE also reduces reliance on activities – such as primary market research – that are often less scalable, more time consuming, and less cost effective.

To understand the potential impact, let's look at a major U.S. academic medical center that implemented its own version of a RWE platform and measured the change in research productivity. It doubled its publication output, and the quality (journal impact factor) also nearly doubled for a four-fold increase in productivity. Various factors drove this improvement, with platforms and associated tools offering a real opportunity to industrialize research processes through speed and the elimination of repetitive, low-value tasks.

This translates to the pharma industry even more easily. Recently, one client planning to launch a new asset wanted to assess the market potential and to understand the disease epidemiology. It was preparing to invest $3 to $5 million in a multi-centre, prospective, observational study. Instead, given that the therapy was suitable only after a specific diagnostic test, the company was able to use an RWE platform to analyze lab tests via retrospective data. With this, the client had an accurate estimate of its market size based on a large patient sample in just two weeks.

[10]Hughes B, Kessler M. RWE market impact on medicines: A lens for pharma. IMS Health Access Point 2013; 3(6): 12-17

How extendable are these techniques? One IMS Health client examined its entire portfolio of observational research and market insight, including 200+ concurrent studies worldwide. It discovered that only five percent of the work was conducted retrospectively or using RWE platforms, but that up to 33 percent of the projects could have been conducted this way, avoiding costly primary research. Thus, while primary market research – and particularly behavioral research – will always have a major role, today it is potentially over-utilized compared to RWE.

For a top-10 pharma company with a global budget of $800 million across Scientific and Commercial domains (excluding RCTs), $400 million of which is in markets where RWE capabilities can be built, a savings rate of 25% from RWE represents $100+ million in potential cost savings.

Total spend	RWE-addressable spend	Assumed RWE saving rate	Total cost savings
$800 million[1]	$400 million[2]	25%[3]	$100 million

[1]Excludes Clinical/RCT spend, but includes non-international primary market research studies (scientific & commercial)
[2]Assumes 50% addressable, based on markets where RWE capabilities currently exist (U.S. + 4-6 other major markets)
[3]Blending savings rate based on 33% of studies addressed by RWE platforms, with up to 90% cost savings rate

IMPROVING CLINICAL DEVELOPMENT

RWE is regarded as having the ability to improve clinical development via enabling translational research, better understanding of drug pathways, higher value population and product profiles, and trial simulation/recruitment. Examples include linking tissue banks to EMRs to expand Phase II sample sets to meaningfully sized populations to improve interpretation and later-phase design, and trial simulation using RWE to ensure that trials likely to fail are not initiated (over 30 percent of trials fail for strategic rather than operational reasons[11]). However, quantifiable estimates of the financial impact of these applications to improve medicine development are relatively rare and therefore the examples here are based on operational savings rather than the full long-term value potential.

Even for well-designed Phase III trials there are major operational challenges. The majority run significantly behind schedule and patient recruitment remains a major challenge. Today RWE can enable real-time protocol simulation as well as immediate sharing of protocols with providers to initiate recruitment. Tapping EMRs can double enrolment rates, which typically drive 30 percent of costs. Aforementioned integrated EMR-eCRF data collection also drives down costs by up to 30 percent. A top-10 pharma company spending $2 billion on clinical development annually, of which $500 million is addressable by RWE, can expect to apply these techniques to gain 20 to 40 percent efficiency in spending, or $100 to $200 million.

Total spend	Addressable spend	Assumed saving rate	Total Cost Savings
$2 billion	$500 million[1]	20-40%	$100-200 million

[1]Assumes half of spend addressable in 50% of markets based on where RWE capabilities currently exist (U.S. and 4-6 other major markets)
Operational benefits only. Excludes strategic improvements in discovery and development such as increased success rates for NMEs

[11]Arrowsmith, J. Nature Reviews Drug Discovery 2011; 10: 328-329

SUMMARY AND COMMENTS ON FINANCIAL ESTIMATE

Beyond these valuations for life science companies, two points should be noted: 1) much more value is being created in the health system than estimated here from a single life science company's view and 2) the investments required can be trivial in comparison to the value realized.

Life sciences companies can create opportunities to engage health systems successfully via robust evidence and by supporting win-win decisions that demonstrate value across stakeholders. The value captured is therefore multiplied across health systems, and our analysis offers credence to others' assertions that it is approximately $300 billion[12].

In terms of investment, even RWE leaders are only spending a few tens of millions of dollars a year to recoup $500 million. Our analysis has not captured the full value at stake (focusing more on operational value and not fully capturing strategic value in clinical development or pricing), nor shown indisputably that this exists for every company. Yet, executives need only be convinced that part of this value is at stake to take action. And, the lessons from leaders highlight the fact that how a company executes its RWE investment is perhaps more important than how much it invests.

If investments are made wisely and pitfalls in traditional thinking on RWE are avoided, for leading life science companies and their partners across healthcare, RWE is one of the most attractive investments that can be made today.

[12]*Chui M, Manyika J, van kuiken S. What executives should know about open data. McKinsey Quarterly. January 2014.*

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