# Shot in the Arm: COVID-19 Boost to RWD

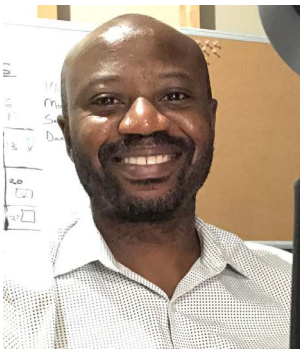
## Times Have Changed

It's early 2021 in the Northeast and a major snowstorm has just been announced. Schools will be closed for the next two days. Kids will be home and likely, quite happy to be off from school. Under normal circumstances, parents would be home too, trying to work and probably attempting to create some sort of scheduled structure for the kids. But this is post-2020 and COVID-19 has all but erased what we used to call snow days. Snowstorms and hail may come, but the children can now continue with school as though nothing happened at all. We have all heard it a thousand times, but these truly are unprecedented times — COVID-19 has upended the world as we knew it.

While the snow day-nostalgic kids may disagree, the pandemic has simultaneously created many opportunities for individuals, brands, companies, industries, and nations alike. The raging pandemic forced us to withdraw and physically isolate. Healthcare (battling the pandemic) and technology (combatting the physical isolation) were two of most affected and transformed industries. The race to find a cure for COVID-19 accelerated the adoption of several processes, methodologies, and technologies from which will all benefit for many years to come. Real-world data (RWD) and the resulting real-world evidence (RWE) saw a major boost during this time, in part because both straddle the intersection of healthcare and technology. As a data practitioner in a healthcare organization that helps clients drive behavior change, the impact of RWD and RWE hits close to home.

## The COVID-19 Boost

RWD refers to the various forms of data from sources like electronic health records (EHRs), insurance claims and billing, patient registries, labs, personal devices, health applications, surveys, etc. When harnessed together, RWD becomes a potent source of empirical RWE that sheds almost real-time insights on disease progression, at risk populations, effective interventions, and post-authorization effects. The potential advantages of RWD are a transformation from evidence-based medicine to the era of big data.



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The understanding, appreciation, and overall experience with RWD is being magnified by the pandemic. in a short time and at scale, RWD has demonstrated its erstwhile potential to speed up candidate discovery, drug development, patient management, and ultimately, better health outcomes.

In 2020, RWD played a prominent role in expanding our understanding of COVID-19 and its secondary effects. Collated datasets across nations, institutions, and technologies helped shed light on the magnitude, trends, symptoms, risk factors, and racial disparities of the pandemic. RWD also provided contextual insights like hospitalizations, testing, screening, procedures, patient, and healthcare professional behavior change, as well as non–COVID-19 mortalities attributable to the pandemic. As treatments were being administered, RWD provided close to real-time insights about which interventions, practices, or medications were working and which were not. This accelerated application of data was concurrently happening beyond the COVID-19 studies and vaccine development and delving into other therapeutic areas like oncology. Although we are still in the throngs of the pandemic, our learnings about how COVID-19 fast-tracked the adoption of RWD is already emerging. We are beginning to see outlines of patterns, accomplishments, and downsides. For example, we are seeing larger and richer datasets, a broader footprint of RWD's awareness and appreciation, wider ranges of RWD-related collaborations, implementation of creative study methodologies, higher regulatory interests, and more informed scrutiny of its shortcomings as we look to continued improvement in these areas.

## The High Points

On a positive note, the pandemic has improved collaborations, the scope of data capture, the profile of observational studies, and the attention and advocacy of regulators.

**Accelerated data collaborations and partnerships:** The global scale and urgency of the pandemic helped cut through bureaucracies, boarders, and organizational divides. The COVID-19 Evidence Accelerator, for example, brought together top health data aggregation and analytics experts from across th FDA, the Reagan-Udall Foundation, Friends of Cancer Research, National Institutes of Health (NIH), Veteran's Administration, Patient-Centered Outcomes Research Institute (PCORI), and other private organizations to exchange ideas and compare findings to combat the pandemic. This has since translated into other FDA data collaboration relationships and a few other evidence accelerators. Our knowledge of the increased risk of hospitalization, being on ventilation, and death of oncology patients was gathered from the RWD data cooperative effort between the FDA's Oncology Center of Excellence and Syapse. The National COVID Cohort Collaborative (N3C) is a massive NIH effort that has collated one of the largest datasets about clinical data related to COVID-19 symptoms and patient outcomes in the United States. The Aetion and Cegedim Health Data collaboration in Europe, Medidata, TriNetX, and Datavant are all examples of COVID-19-motivated alliances for clinical research and discovery. Apple and Google worked together to build the COVID-19 Exposure Notification app.

**Expanded remote data and applications:** Safe access to healthcare for non-COVID-19 patients was one of the factors that forced the acceleration of reimbursements for telemedicine and remote patient monitoring. The Centers for Medicare & Medicaid Services estimated there were more than 12 million telehealth visits in 2020 and the Medical Economics 2020 Telehealth-EHR survey, reported that more than 77% of responding doctors used telehealth the first time because of

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the pandemic. With continuous remote monitoring, massive and wide ranges of datasets are being generated and captured. On the clinical trial front, many studies were slowed or halted altogether because data collection on premise became problematic. Some studies went remote and had to rely on connected devices and technologies for monitoring. Telehealth, telemonitoring, executing trials remotely and capturing data is a healthcare model that will likely continue in a post-COVID-19 world. These expanded and different datasets generated during the pandemic have become a rich source of information for addressing new, pandemic-related questions and inquiries that arise in other therapeutic areas.

**Raised awareness and acceptance of RWE:** Pre-COVID-19, there was a general awareness of the value of RWE or observational studies to complement randomized clinical trials (RCTs) for understanding the safety and effectiveness of medical products. However, the frequency and scale of deployment during COVID-19 has amplified awareness, discussions, appropriateness, as well as scrutiny of RWE. Part of the appeal is that RWE can be carried out relatively quickly, at scale, and at lower cost compared to RCTs, thereby reducing the burden on clinical trial sites. This was crucial during COVID-19. According to IQVIA, eight COVID-19-related observations were conducted in record time during early days of the pandemic. These studies helped evaluate many claims or hypotheses around the treatment, risks, and effectiveness of medications such as hydroxychloroquine and azithromycin. The cardiovascular warning was one of the resulting outcomes of this effort. Large observational data now allow for the understanding of subpopulation impact, which highlighted the higher risk to the African-American population. Health agencies, payers, and healthcare institutions are increasingly open to the use of RWE applications and the general public has greater access to, and is more aware of, its findings.

**Increased regulatory attention and advocacy:** The FDA has been active in the application of RWD, advocating efforts supporting the generation of evidence, monitoring the safety of COVID-19 diagnostics, as well as post-authorization and post-market surveillance of safety and efficacy of COVID-19 therapeutics. There were RWE study obstacles faced in the haste to understand the pandemic. While the 21st Century Cures act of 2016 already outlined parameters that impact RWD and RWE, the COVID-19 experience has prompted additional FDA review and need for further guidance. The FDA is championing several efforts to refine the role and approach of RWD in healthcare. The agency is looking into RWE's potential to contribute to regulatory decision-making about drug effectiveness. The FDA has issued guidelines that include encouragement of alternative data collection approaches as remote patient monitoring and data capture ramps up. It is also working on establishing standards and protocols in the approach to observational studies. These regulatory engagements are beneficial as they help provide an adoption pathway of execution for RWD-based studies.

## Work Still to Be Done

The speed, scale, and diversity of RWD and the resulting observational studies during the pandemic revealed various shortcomings. The unfortunate hydroxychloroquine situation is one notable example. Drs. AHJ Kim and SA Eisen captured this well in their contribution to The Lancet Rheumatology in November 2020: "Despite the low quality of this study due to poor handling of confounders and participants lost to follow-up who had poor outcomes, a surge of prescriptions for the therapeutic and prophylactic use of hydroxychloroquine created shortages for patients with systemic lupus erythematosus and other rheumatic diseases who rely on this medication to treat their disease."

**Data quality gaps:** A lot of work remains to be done in order to generate reliable and high-quality data across the highly-diversified healthcare data sources. The New England Journal of Medicine retracted the study that showed ACE inhibitors were not associated with increased mortality in patients with COVID-19, and The Lancet withdrew a study that showed chloroquine and hydroxychloroquine increased mortality and cardiac arrhythmias in hospitalized patients with COVID-19. Both studies were compromised by poor quality EHR data. A study of 15 academic medical centers published in the Journal of the American Medical Informatics Association, showed "the current state of COVID-19 data reflects a patchwork of uncoordinated, temporary fixes to a historically neglected public safety function." There's still a great deal of work to be done.

**The need for updated methodology review and validation:** As the scale of RWD increased, so did the volume of studies generated. Observation studies are not immune to bias and the understandable rush to get a grip on the pandemic gave rise to some laxity in application of methodological rigor. This resulted in certain initial studies turning out to be, in hindsight, incorrect. The validation process is how scientific exploration works, but wrong conclusions may have been drawn and acted upon before the course correction could occur. Domain expertise is also vital but as many well-meaning groups rushed in to help, some lacked the vital context needed for these studies. Regulation guidance could help with this. With democratic access to data, if proper safeguards are not instituted, wrong or misleading conclusions from inexperienced talents as well as those with deliberately fraudulent intent, could have severe real-world implications.

We are about a year into this pandemic and are still learning, every day. However, some signs are clear: COVID-19 has accelerated the integration of big data into healthcare in the forms of RWD, RWE, and observational studies. This data-centric awareness, experiences, technologies, techniques, partnerships, and mindset are seeping rapidly into other areas in healthcare. It is catalyzing innovation and creative thinking from population health management, to drug manufacturing, hospital management, patient support, payer value models, and marketing and advertising. As practitioners in the healthcare space, we all got our data booster shot. PV