dle minor ailments, maybe checking blood pressure and hemoglobin levels occasionally. After all, the retail clinic chains have been saying for years that they will expand significantly into chronic care management; if the value were so compelling (or access to new patients so likely), that should have happened already. Insurers could have created joint ventures with retail clinics or benefit designs that more strongly encouraged use of those clinics. The fact that they haven't could indicate that clinics have less potential than the framers of NewCo claim. Providers can return to business as usual.

The less cynical might observe that health care is ripe for change, and NewCo is well positioned to capitalize on the demand for that change. Patients are now accustomed to high-quality, digitally enabled services and are growing weary of the antiquated way they access primary care. It's hard to park at the doctor's office, one still can't usually book an appointment online, the wait is impossible to predict, and those are just tips of the iceberg of health care dysfunction. Seamless communication among insurers, pharmacies, and prescribers would save a lot of time and misery. Some of the healthiest and most profitable patients might gladly embrace CVS as a primary care provider, particularly if they're offered lower copayments and easy scheduling.

An audio interview with Dr. Dafny is available at NEJM.org

I would argue that providers' reaction should be the same whether they believe CVS–Aetna is a game changer or merely a pocket liner for executives and their advisors. The battle to take medical risk for patients and to manage and deliver the products and services they require is heating up. If CVS–Aetna cannot lure patients away with lower prices and convenient services, some other player will surely try.

Providers will have to figure out how to provide better, more convenient, less costly care — to offer the best affordable pathway to good health. They can choose to team up with NewCo if they believe total cost and quality of care will be improved that way, or work with other insurers to design products that minimize interactions with NewCo if they believe otherwise.

Competition can cut both ways for providers, but as long as it's not diminished by this megadeal — a question to be sorted out by antitrust investigators — patients stand to gain. Let the games begin.

Disclosure forms provided by the author are available at NEJM.org.

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Medical Devices in the Real World

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When it comes to medical devices, the Food and Drug Administration (FDA) is tasked with the herculean balancing act of ensuring efficacy and safety while accelerating access to new technologies for patients most likely to benefit from them. These two goals are inherently in conflict, but the FDA must make decisions daily, with imperfect information, regarding the approval and continued use of devices. The approval process has been criticized for being burdensome and slow, and new medical devices are frequently available for use outside the United States well before FDA review and clearance occur. Yet the FDA has also been criticized for inadequate evaluation of medical devices, and there have been notable recalls due to serious and occasionally fatal consequences of device failures. Further challenging this balancing act is the dynamic nature of medical devices, which, unlike drugs, undergo continuous iteration and design improvements.

The recently passed 21st Century Cures Act provides guidance in balancing these competing priorities by directing the FDA to consider how best to use real-world evidence (RWE) for reasonable assurance of device safety and effectiveness while accelerating access to important new tech-

nologies.[1] RWE includes information generated through routine health care delivery, including electronic health records (EHRs), billing data, clinical registries, and other data sources. Unfortunately, this information is inherently flawed by inconsistency, incompleteness, and bias from the very treatment decisions we might wish to elucidate. For these reasons, rigorous observational statistical methods are required to mitigate the limitations of real-world data.

As EHRs are adopted ever more broadly, RWE will become a more accessible and lower-cost source of detailed clinical information that could help clinicians and regulators understand the performance of medical devices in real-world practice. The recently implemented FDA regulations requiring use of a structured unique device identifier (UDI) will also help to unlock RWE for medical devices. Whereas drugs have had a standardized coding system for many years, the lack of a UDI for devices has greatly hampered use of RWE for evaluation of medical devices after market release. As UDIs become used routinely throughout our purchasing, inventory, clinical documentation, and billing systems, the ability of RWE to associate a particular device with a particular patient at a specific point in time will make it an ever more powerful resource.

As clinicians with responsibility for our patients' well-being, we should carefully consider how RWE could be used, and potentially misused, in support of complex regulatory decisions regarding medical devices. The FDA recently published guidance on potential use of RWE for supporting initial decisions to approve or clear devices for use in the United States as well as postmarketing assurance of medical device safety and performance.[2] Although there are substantial opportunities for applying RWE to both these domains, we believe that such evidence will be most valuable in the near future for postmarketing, since it is particularly in this setting that our current systems are inadequate for ensuring the safety and evaluating the performance of modern medical devices. The largest gaps in our understanding of devices relate to use outside the context of controlled clinical trials, and it is there that the majority of RWE will be collected.

For the past 40 years, the FDA has relied extensively on physicians to report adverse events suspected to be related to a medical device. Unfortunately, clinicians significantly underreport such events: some estimates suggest that only 0.5% of all device-related adverse events are reported to the FDA. Meanwhile, traditional postapproval studies, frequently required as a condition of approval, are often far too small, lack adequate controls, are expensive to conduct, and rarely lead to actionable information regarding safety or performance of the device.

RWE from high-quality sources could supplement the adverse-event reporting process and might be able to replace many postapproval studies that are currently required, saving substantial expense and time. The routine use of RWE for active surveillance of devices, through routine monitoring of patients' experiences, offers tremendous opportunities for early identification of safety signals, which can inform clinicians, patients, and regulators about potential problems and inform manufacturers where they might focus redesign efforts to improve the device. Studies of active surveillance have demonstrated its ability to identify performance differences between approved devices and to save significant time as compared with traditional adverse-event reporting.

In contrast, we believe that the FDA should adopt a more cautious approach to using RWE to support device-approval decisions. Perhaps the best initial use of RWE in the premarketing setting is to leverage electronic clinical data resources to support pragmatic clinical trials by embedding the necessary data collection into ongoing registries or EHR systems. Such approaches could significantly reduce the cost and time required to complete a study as compared with traditional randomized clinical trials. Clinical follow-up through routine care or prespecified electronic patient contact could offer tremendous efficiencies, while also permitting broader patient populations to participate in trials of innovative therapies.

Another application of RWE could be to support expansion of the populations or conditions for which a device is approved. The value of RWE for this purpose has been borne out by recent experience with transcatheter aortic-valve replacement (TAVR) devices: the FDA broadened the indications for TAVR use on the basis of an analysis of the RWE from the national Transcatheter Valve Therapy registry. The first TAVR device was approved in 2011 for insertion either through the femoral artery or through a small chest incision and direct place-

ment through the apex of the heart. However, many patients who would benefit from TAVR could not be treated using these vascular access options. Within 2 years, the FDA leveraged the early national experience using the registry to expand the options to include access routes such as the subclavian artery and the thoracic aorta.[3] By all accounts, this approach cost substantially less and took significantly less time than the studies that would otherwise have been required to demonstrate efficacy in new groups of patients.

We believe, however, that there are important risks in basing initial market-approval decisions for high-risk medical devices on contemporary RWE. Even with the most stringent methods of statistical adjustment, RWE-based analyses are observational in nature, with inherent biases in treatment choice coloring the patterns and associations that might be observed. An example of the risks posed by reliance on imperfect clinical data can be found in the recently evaluated device designed for treating poorly controlled hypertension with radiofrequency ablation of the autonomic nerves supplying the kidneys. Although early European randomized, but unblinded, trials and extensive postapproval clinical studies had shown that this new technology had impressive efficacy, the pivotal FDA-mandated, U.S., blinded, sham-controlled study revealed no advantage of the device over the best medical therapy.[4] This example highlights the potential risks of basing regulatory approval on imperfect clinical evidence; reliance on the best available RWE for this device would probably have exposed many U.S. patients to an invasive procedure, with all its attendant risks, for no clinical benefit.

Over the next few years, the accelerating adoption of integrated EHR systems and information standards will undoubtedly provide us with many new opportunities to leverage RWE to elucidate which patients could benefit the most from medical devices, while assisting manufacturers in improving their products. The FDA and the clinical community can work together to maximize the impact of these emerging new sources of rich clinical information to support regulatory decisions and clinical choices. Our collective efforts can focus initially on active surveillance and other postapproval applications of RWE that can improve our understanding of the performance of medical devices, including which patients benefit the most from particular technologies. As experience grows with the application of RWE, extending its use into phases of the review process will become more reliable and appropriate.

Disclosure forms provided by the authors are available at NEJM.org.

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When the CHIPs Are Down — Health Coverage and Care at Risk for U.S. Children

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Despite bipartisan agreement on a 5-year plan in both the Senate and the House of Representatives, Congress failed to reauthorize the Children's Health Insurance Program (CHIP) last fall, causing uncertainty and worry for families and state CHIP directors alike. Families in several states, including Colorado and Virginia, received letters saying that their children could lose their CHIP coverage, and Alabama and Connecticut announced that they were going to stop new CHIP enrollments because of funding shortfalls.[1] Shortly before leaving town for the holidays, Congress