whether dose-sparing vaccination was equivalent in children and adults.

Similarly, some experts have suggested using intradermal immunization rather than the traditional intramuscular or subcutaneous route.[5] Although that option seems promising, the limited studies that have been conducted included no comparison between intradermal and conventional subcutaneous immunization with the same dose of vaccine. Moreover, these studies have involved vaccine from only two of the six manufacturers.

A third approach is to shift manufacturing from embryonated chicken eggs to a continuous cell line. This possibility proved unsuccessful when it was investigated in the 1980s, but cell-culture technology has greatly improved in the past 30 years. Notably, Sanofi Pasteur manufactures its chimeric yellow fever 17D-dengue (Dengvaxia) and chimeric yellow fever 17D-Japanese encephalitis (Imojev) vaccines in monkey kidney Vero cells, which suggests that Vero cells could be used to manufacture 17D vaccine. Of course, the immunogenicity and safety profile of such a Vero-cell–derived vaccine would need to be compared with that of currently licensed egg-derived vaccines.

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

Finally, there have been no systematic studies investigating the genome sequences of wild-type yellow fever virus strains from outbreaks to elucidate the evolution of the virus and help model the potential for outbreaks. There are 40 genomic sequences of wild-type yellow fever virus isolates in GenBank, of which 12 are from Brazil and 14 from Senegal, though the virus is currently found in 44 other countries. We still have much to learn about wild-type yellow fever virus.

In the short term, there will be difficulties in ensuring that sufficient vaccine is available to fight this major public health problem, but we have the opportunity to avoid vaccine shortfalls in the future. Toward that end, the WHO periodically reviews "Recommendations to Assure the Quality, Safety and Efficacy of Live Attenuated Yellow Fever Vaccines." Now may be the time to revisit these requirements, which were last reviewed in 2010.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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This article was published on June 8, 2016, at NEJM.org.

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DOI: 10.1056/NEJMp1606997

United's Withdrawal from Exchanges — Much Ado about the Wrong Things?

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United Healthcare's announcement on April 19, 2016, that it would be withdrawing from most of the health insurance exchanges in which it had been participating has triggered another round of hand-wringing about the future of the exchanges, which were created under the Affordable Care Act (ACA). Detractors took it as further proof of the exchanges' flawed design, an enrollment pool that is sicker than can be supported, and a politicized rate-setting process that deters insurers. The exit of the health insurance giant is hardly the death knell for the ACA, but it will meaningfully reduce insurance competition in some markets, and it points to the challenges and limitations of maintaining insurer competition as a policy priority in small, fragmented lines of business.

United has not been a major player in the ACA exchanges. It

was a cautious entrant at the start, and only in the past year did it expand to 34 states. It's estimated that United had less than 6% of the 10.2 million "effectuated" enrollees (those who had applied for and paid for coverage) in exchanges at the end of last year's open enrollment in March.[1]

Competition produces losers as well as winners. Other national insurers are making money and expressing confidence in the market.[2] Nationally, exchange enrollment continues to increase. Federal subsidies and a slowly strengthening individual mandate continue to attract healthy people and to compel them to join the risk pool for insurers. As long as insurers in exchanges are granted rate increases sufficient to cover average costs, exchange health plans are not a failing line of business.

Locally, however, some markets will be hit hard by United's withdrawal. According to an analysis by the Kaiser Family Foundation (KFF),[3] in 17% of the counties in the United States, its departure will leave two or fewer insurers, affecting 1.8 million enrollees. This diminished choice will create political problems for ACA supporters, and more conservative cost assumptions for the remaining insurers as they price their products.

How likely are these markets to see new entrants? As a clinician might say, "It depends." Insurers crave stability. On the cost side, that means predictable populations with predictable medical expenses. The uncertainty associated with enrollment in the first few years of the exchanges made them a tough sell for some insurers.

The ACA's new rules for premium rating for small-group and individual insurance and for federally mandated risk-adjustment payments create substantial uncertainty regarding revenue. Insurers can vary premiums only on the basis of age and family size, and insurers who end up having better financial performance only because of healthier-than-expected enrolled populations must share their gains with their less-lucky competitors. These risk-adjustment payments and receipts can be sizable — for the 2014 benefit year, the Centers for Medicare and Medicaid Services reports that they amounted to as much as 17% of premiums for some carriers.[4] A tested and profitable strategy for insurers is to avoid risky populations if possible, and to price their products cautiously to account for them if not. The new rules of the road are less appealing for some carriers.

In the long run, competitive health insurance markets may deliver more political benefits than affordable health care benefits.

Even more than certainty, insurers need volume: the prospective number of enrollees in the exchange must be big enough to generate returns and to negotiate a provider network. The most logical entrants into an exchange are the insurers already doing business in the geographic market — and not necessarily commercial insurance. More than 40% of insurers participating in exchanges offer a Medicaid product in the same state.[5]

Deciding to enter an insurance market is a function of persuasion and politics as well as finances. State insurance commissioners generally guard those gates, and they can be friendly or foreboding to prospective applicants depending on their interpretations of regulatory standards for network adequacy, subscriber-contract compliance, and rate filings. Political leaders in the states that the KFF analysis indicates are at greatest risk for diminished competition in the event of a United pullout — Alabama, Florida, Kansas, North Carolina, and Oklahoma — are all noted foes of the ACA and its insurance exchanges. None of them have expanded Medicaid — which would create a larger insured market in the state to attract insurers.

United's departure from most exchange markets also underscores two larger points about health insurance in the United States. The first is that multiple lines of business exist for financing and administering health benefits in this country (see table). In addition to being a source of provider frustration, administrative overhead, and variable public oversight, these lines of business represent distinct opportunities for national insurers, many of which specialize in particular areas — Humana, for example, specializes in Medicare, as Centene does in Medicaid.

With subsidies available only through them, exchanges may crowd out the rest of the individ-

Lines of Business for Financing and Administering Health Benefits.

Line of Business	Geographic Market	No. of People Covered (millions)*	Who Sets Benefits and Oversees Premium Setting
Self-insured	National and regional	76.3	Employer
Large group	Regional	48.2	Employer and state insurance commissioner
Managed Medicaid	State and regional	40.0	State Medicaid agency
Small group	Regional	17.9	Federal floor, administered by state insurance commissioner
Managed Medicare	Regional	14.0	Centers for Medicare and Medicaid Services
Individual (nonexchange)	Regional	10.9	Federal floor, administered by state insurance commissioner
Health insurance exchanges	Regional	8.8	Federal floor, administered by state insurance commissioner

* Data are from Kaiser State Health Facts and are for 2013, except the figure for managed Medicaid and health insurance exchanges, which are for 2015.

ual insurance market and evolve in a fashion similar to the managed-care lines of business of Medicaid and Medicare. This may attract insurers that are comfortable with greater market constraints and government oversight.

Second, in the long run, competitive health insurance markets may deliver more political benefits than affordable health care benefits. A competitive exchange market will prevent carriers from shifting the costs of other, more competitive, lines of business to exchange plans. But health insurance is expensive because health care is expensive. Exchange markets need to be profitable for insurers to stay in them — as the 2017 rate requests for exchange products make clear — and profitability in health care (for insurers and providers) will continue to collide with affordability. Even large exchanges with robust insurer competition — based on service and innovation, not risk selection — will fail to deliver relief to enrollees facing increasing premiums and deductibles or to governments that are underfunding other services to pay their health care obligations.

In theory, price- and quality-based competition among providers could help, but addressing the duplication, waste, poor quality, and high prices that plague U.S. health care requires aligning efforts at measurement and provider-payment reform across payers and lines of business. The payment reforms being tested and implemented by Medicare must be joined by commercial payers and the growing self-insured sector in aligned, transparent, and publicly accountable ways at the state and federal levels. This process can be accelerated with public-sector requirements and standards in areas such as purchasing of benefits for public-sector employees, managed-care contracting in Medicaid and Medicare, and insurance rate review. The policy priority of competitive insurance markets is at best a necessary precondition to — and perhaps merely a distraction from — this much harder work.

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

From the Milbank Memorial Fund, New York.

This article was published on June 22, 2016, at NEJM.org.

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DOI: 10.1056/NEJMp1605841