95% CI, 1080.1 to 2260.5) in the high-dose group (Fig. 1A). A neutralizing-antibody response (an increase in reciprocal titer by a factor of ≥2) occurred in 21% (95% CI, 5 to 51) of the low-dose recipients and in 50% (95% CI, 23 to 77) of the high-dose recipients (Fig. 1B). The results in the per-protocol population were consistent with those in the full analysis population. iEvac-Z also induced IgG responses against nucleoprotein and VP40, with higher responses occurring among the high-dose recipients (Fig. S2). This multiantigen response distinguishes iEvac-Z from single-antigen vaccines. Furthermore, glycoprotein-specific antibodies persisted in 39% (95% CI, 14 to 68) of the high-dose recipients at 52 weeks (Fig. 1A), a finding that suggests a potential for longer-term immunologic memory.

Cytokine analysis after vaccination revealed generally modest responses (an increase in cytokine level by a factor of less than 2), with RANTES (regulated on activation, normal T-cell expressed and secreted) showing the largest increase (an increase in the RANTES level by a factor of 2.84; 95% CI, 2.09 to 3.86) and clustering with glycoprotein-specific antibodies (Figs. S3 and S4), findings that indicate mild, balanced immune activation.

Limitations of the study include the male-only Japanese population, the small sample size, and the lack of a T-cell response assessment. These results establish proof-of-concept for the inactivated EBOVΔVP30 platform, showing multiantigen immunogenicity in humans without evident safety concerns. The sustained antibody responses, manufacturing advantages under biosafety level 2 conditions, and multiantigen profile support continued development. Future adjuvanted formulations will be explored to enhance neutralizing-antibody responses while maintaining a favorable safety profile.

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A Regional Measles Outbreak — South Carolina, 2025–2026

TO THE EDITOR: Despite the elimination of measles in the United States in 2000, resurgence has occurred in regions with declining vaccination coverage.[1] Since October 2025, sustained community transmission of measles has been identified in upstate South Carolina. By the end

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Table 1. Characteristics of Patients in the Prisma Health System Who Had a Positive Test for Measles.

Characteristic	No. of Patients (N = 81)
Age	
<12 mo	6
1–4 yr	26
5–10 yr	21
11–17 yr	8
≥18 yr	20
Vaccination status	
Unvaccinated	59
Vaccinated (at least one vaccine)	19
Unknown	3
Presumed location of exposure	
Church	4
Home	32
School	4
Work	2
Other	11
Unknown	28
Evaluation location	
Emergency department	44
Primary care office	8
Telehealth	17
Urgent care facility	12
Duration of hospitalization*	
<24 hr	2
24 to <72 hr	7
≥72 hr	4
Symptoms	
Fever	78
Nasal symptoms	45
Eye symptoms	26
Cough or other respiratory symptoms	58
Koplik spots	21
Rash	69
Gastrointestinal symptoms	25
Categories of laboratory abnormalities	
Complete blood count	21
Electrolytes	18
Liver-function tests	22
Inflammatory markers	16

* A total of 13 patients were hospitalized.

of the outbreak, which was declared to be April 26, 2026, a total of 997 cases had been reported statewide, with the highest concentration in Spartanburg County, where measles–mumps–rubella (MMR) vaccination coverage was 88.9%.[2,3]

Measles typically manifests with fever, cough, coryza, conjunctivitis, and a rash that spreads in a cephalocaudal manner.[4] Because this outbreak occurred during the respiratory virus season, distinguishing measles from other viral illnesses, such as influenza, was essential.

Our health care system — Prisma Health, the tertiary referral center of the region — evaluated hundreds of patients for measles. A retrospective review was performed with approval from the investigational review board. Among more than 400 patients in whom measles tests were performed, 81 had a positive test; most of the cases were identified with a measles (also known as rubeola) polymerase-chain-reaction (PCR) test developed by LabCorp. Pediatric patients comprised a majority of the cases; 20 adults were affected. The characteristics of the patients are shown in Table 1.

Most of the patients (≥73%) were unvaccinated, and the most commonly identified presumed transmission location was the home. Five patients with a positive test had received the MMR vaccine within the previous 2 weeks; their PCR test results may have been related to the vaccine, given that commercially available PCR tests cannot distinguish between the vaccine virus and the wild-type virus. Patients were evaluated across emergency, urgent care, primary care, and telehealth settings.

The most common presenting features included fever, cough or other respiratory symptoms, and the characteristic rash. Koplik spots were observed more frequently than has generally been reported in patients with measles, since Koplik spots are often resolved by the time a patient presents with fever and rash. Although not classically identified as symptoms of measles, gastrointestinal symptoms were reported in more than one fourth of the patients. Some of the patients had a pruritic rash, which is atypical for measles. Laboratory abnormalities included cytopenias, hyponatremia, and elevated levels of liver enzymes and inflammatory markers.

A total of 13 patients were hospitalized, most often for less than 72 hours, primarily for dehydration, respiratory support, or pneumonia.

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Most of these patients had recovered by the time of discharge. Measles encephalitis developed in 2 patients and resulted in prolonged hospitalization; 1 of these patients was subsequently discharged to an inpatient rehabilitation facility and as of the time of this report is receiving ongoing outpatient therapy, and the other patient recovered but continues to have headaches and a vocal tic. Among the 13 hospitalized patients, 10 were children and 3 were adults.

A total of 24 patients had concurrent infections or subsequent infections within 1 month after the diagnosis of measles. The most common infections were otitis media, pneumonia, and sinusitis. No deaths were reported.

This outbreak highlights the reemergence of measles in the United States since its elimination in 2000. Most of the patients had typical clinical features, although severe complications — including encephalitis — were reported, along with substantial secondary infections. Moreover, the outbreak resulted in an increased burden on the health care system.

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Leucovorin Dispensing to U.S. Children in 2025

TO THE EDITOR: In a press release on September 22, 2025, the U.S. Department of Health and Human Services announced that the Food and Drug Administration would update the leucovorin label to include cerebral folate deficiency, which is sometimes accompanied by symptoms of autism.[1,2] Although the update applied only to cerebral folate deficiency, the press release indicated that the update would authorize the use of leucovorin in children with autism.[1]

Subsequently, a study suggested that the press release increased leucovorin prescribing to children in several U.S. health systems, but the generalizability of the findings was unclear.[3] Using the IQVIA Longitudinal Prescription Database, we evaluated nationwide changes in leucovorin dispensing among children 0 to 17 years of age after that press release. This database captures 93% of prescriptions from retail pharmacies, a factor that underscores the representativeness of the study population (Table S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org).

For each week from December 29, 2024, through December 14, 2025, we calculated the leucovorin dispensing rate (the number of children for whom leucovorin was dispensed, per 100,000 children). Using segmented regression models,[4] we assessed whether this outcome changed during the week of the press release (level change) and whether the weekly rate of change increased or decreased (slope change). We repeated these analyses among adults and in subgroups defined according to age and U.S. Census region among children. The widths of the confidence intervals have not been adjusted for multiplicity and should not be used for hypothesis testing.

During the study period, 150,026 leucovorin prescriptions were dispensed to 47,394 children. Between the weeks of December 29, 2024, and September 14, 2025, the leucovorin dispensing rate rose from 1.0 per 100,000 children to 4.6 per 100,000 children (Fig. 1A). Between the weeks of September 21, 2025, and December 14, 2025, the rate rose from 6.7 per 100,000 children to 8.0 per 100,000 children. During the week of September 21, 2025, the level change was 3.0 (95% confidence interval [CI], 2.5 to 3.6) per 100,000 children. The slope change was 0.04

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