Observations from each trajectory are also interesting (Table 1). An FEV_1 that is normal at cohort inception without COPD at the final examination (trajectory 1) seems reasonable. An FEV_1 that is normal or low at cohort inception with concomitant COPD at the final examination (trajectories 3 and 4) does also, especially considering the authors' careful description of the participants assigned to trajectory 4. The long-term, 20% increase in FEV_1 reported for participants in trajectory 2, though, is noteworthy.[2] The stable ratio of FEV_1 to forced vital capacity (FVC) in participants in trajectory 2 (79±12 vs. 76±5) would imply a similar increase in FVC. Can the authors provide a second conclusion from their study?

Mark Moran, M.D.
55 Orinda View Rd.
Orinda, CA
mark@moranadvisors.com

No potential conflict of interest relevant to this letter was reported.

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THE AUTHORS REPLY: Moran focuses on the course of FEV_1 in participants in trajectory 2, the persons with small lungs in whom COPD did not develop during the approximately 22 years of follow-up. Yet, we disagree with Moran's conclusion. In this trajectory, there was no real increase in the FEV_1. The FEV_1 declined very little (approximately 2 ml per year, as shown in Fig. 1 of our article), and the mean FEV_1 was 2.6 liters both at baseline and at the end of the follow-up (Table 3 of our article). The impression of an increase of 20% is therefore erroneous, since it is not possible to assess the decline in FEV_1 according to the percentage of the predicted value. In other words, one can say that the "increased" FEV_1 in the percentage of the predicted value in this trajectory between the onset and the end of observation is caused by the fact that persons in this trajectory lost their FEV_1 much more slowly than would be expected according to prediction equations for normal FEV_1.

Peter Lange, M.D., Dr.Med.Sc.
University of Copenhagen
Copenhagen, Denmark
peter.lange@sund.ku.dk
Bartolome Celli, M.D.
Harvard Medical School
Boston, MA
Alvar Agustí, M.D., Ph.D.
Hospital Clinic Barcelona
Barcelona, Spain

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Adjuvanted Herpes Zoster Subunit Vaccine in Older Adults

TO THE EDITOR: Lal et al. (May 28 issue)[1] report on the efficacy of an adjuvanted subunit vaccine against herpes zoster. The case-definition algorithm included polymerase-chain-reaction (PCR) assays targeting varicella–zoster virus (VZV) and an ascertainment committee that reviewed digital photographs and clinical notes to classify each suspected case. The members of the committee were unaware of the PCR results and study-group assignments.

However, the primary efficacy end point could not be determined for 33 cases of suspected zoster (Fig. S1 in the Supplementary Appendix, available with the full text of the article at NEJM.org). It would be of interest to identify the proportion of participants who received vaccine in this group of 33 cases, since these data might provide evidence of a modified presentation of the rash. Milder, atypical (or modified) rashes have been described predominantly in previously vaccinated persons presenting with smallpox, measles, or primary VZV infection associated with partial immunity.[2-5] Could this phenomenon be associated with this zoster vaccine as well, albeit not a live one?

Ige A. George, M.D.
Steven J. Lawrence, M.D.
Washington University School of Medicine
St. Louis, MO
igeorge@dom.wustl.edu

Dr. Lawrence reports receiving consulting fees from Merck. No other potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: The Zoster Efficacy Study in Adults 50 Years of Age or Older (ZOE-50), a randomized, placebo-controlled, phase 3 study conducted by Lal and colleagues, showed 97.2% efficacy of a subunit vaccine containing VZV glycoprotein E and the $AS01_B$ adjuvant system (HZ/su) in preventing herpes zoster. We note that 337 participants (4.4%) received only one dose of vaccine, and 277 participants (3.6%) received only one dose of placebo. Can the authors provide the reasons why these participants did not receive a second dose?

Earlier findings from a phase 2 study showed significantly higher humoral and CD4+ T-cell responses to two doses of this vaccine than to a single dose.[1] In another study, the maximum humoral immune responses occurred in young adults after one dose; in other age groups, immunologic responses were higher after a second dose, but they were not statistically significant.[2]

Given previous immunologic responses to this vaccine and the high efficacy of two doses, it would be of interest to know the efficacy of a single dose. Although it was not a stated primary or secondary objective, and the precision is expected to be lower owing to the sample size, can the authors provide the efficacy of a single dose of this vaccine on the basis of data on the recipients of one dose in this study?

James E. Fielding, Ph.D.
Peter Doherty Institute for Infection and Immunity
Melbourne, VIC, Australia
james.fielding@mh.org.au

Stephen B. Lambert, M.B., B.S., Ph.D.
University of Queensland
Brisbane, QLD, Australia

No potential conflict of interest relevant to this letter was reported.

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THE AUTHORS REPLY: George and Lawrence ask whether the inconclusive cases in our ZOE-50 study might indicate that there were modified presentations of zoster in persons who received the investigational HZ/su vaccine. Since this study is ongoing and treatment-group assignments remain blinded, we currently do not know whether inconclusive cases occurred in HZ/su recipients. However, cases of zoster may be inconclusive for reasons unrelated to the nature of the rash. For example, PCR testing, the primary method for verifying zoster cases, was not possible for 21 of 33 inconclusive cases because of the lack of samples. Also, for many inconclusive cases, inadequate clinical information, often because of the late presentation of participants at the study site, made case ascertainment difficult.

Fielding and Lambert note that a small proportion of participants in our study received a single dose of vaccine or placebo. Eighteen participants did not receive the second dose because a suspected zoster case occurred between the first and second doses. However, since the study remains blinded, we cannot yet provide reasons for nonreceipt of the second dose.

Fielding and Lambert further note that an earlier study showed strong humoral responses to a single dose of HZ/su in young adults.[1] Subsequent studies, however, provide a stronger basis for comparing one-dose immunogenicity with two-dose immunogenicity.[2,3] In these studies, HZ/su was assessed in larger, more representative older adult populations, and a second dose was shown to enhance both cellular and humoral responses. An ongoing parallel efficacy study, Zoster Efficacy Study in Adults 70 Years of Age or Older (ZOE-70), involves more than 14,000 older adults. When the study is completed, combined data from ZOE-50 and ZOE-70 can be used to provide an estimate of the efficacy of one dose. However, the power to evaluate the efficacy of one dose would be limited by the low number of zoster cases in participants receiving a single dose and the limited 2-month window in which most of these cases are likely to occur. We therefore expect that efficacy data based on this brief follow-up will provide only limited insight into the clinical value of single-dose vaccination.

Himal Lal, M.D.
GSK Vaccines
King of Prussia, PA

Anthony L. Cunningham, M.B., B.S., M.D.
Westmead Millennium Institute for Medical Research
Westmead, NSW, Australia
Thomas C. Heineman, M.D., Ph.D.
GSK Vaccines
King of Prussia, PA
thomas.c.heineman@gsk.com

Since publication of their article, the authors report no further potential conflict of interest.

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Short-Course Antimicrobial Therapy for Intraabdominal Infection

TO THE EDITOR: Sawyer and colleagues (May 21 issue)[1] report the findings of the Study to Optimize Peritoneal Infection Therapy (STOP-IT) trial. A strength of this study was the freedom afforded to clinicians in the selection of antibiotic regimens, as long as the choice met Surgical Infection Society–Infectious Diseases Society of America (SIS–IDSA) guidelines. International guidelines vary with respect to recommended regimens for intraabdominal infection[2,3]; this variation partly reflects differences in patterns of antimicrobial resistance worldwide.

Data on the most commonly used antimicrobial agents and culture isolates in the trial are presented in Table S1 in the Supplementary Appendix (available with the full text of the article at NEJM.org), but it would be of value to understand these in more detail, to help clinicians, in particular those outside North America, translate the findings of the trial into clinical practice.

Given the flexibility afforded with respect to first-line therapy, can the authors provide more details on which specific empirical regimens were used in the study? In particular, it would be informative to know the percentage of culture isolates that were susceptible to the initial antimicrobial regimen and how frequently therapy was switched because of resistance. Given the brief duration of treatment in the experimental group, was a mismatch between the choice of the initial antimicrobial drug and organism susceptibility associated with worse outcomes?

Michael Marks, M.B., B.S.
London School of Hygiene and Tropical Medicine
London, United Kingdom
michael.marks@lshtm.ac.uk
Gabriele Pollara, M.B., B.S., Ph.D.
University College London
London, United Kingdom

No potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: Sawyer et al. find that a short course of antimicrobial therapy (4±1 calendar days) was as efficient as an antibiotic treatment guided by a clinical approach with respect to the occurrence of surgical-site infections, recurrent intraabdominal infections, or death. We would like to focus on some points of concern. As designed in the study, this strategy cannot be extrapolated to patients with an inadequate source-control procedure. The authors did not report the proportion of included patients with severe sepsis, septic shock, or both; mortality among these patients is close to 25%.[1] The mortality in this study (0.8 to 1.2%) suggests that only patients with uncomplicated intraabdominal infections were involved. Can the study findings be extrapolated to antifungal therapy in *Candida albicans* infections (11.2% of the isolated pathogens in the control group and 7.0% of the isolated pathogens in the experimental group in this study), given that in such patients the isolation of candida has been considered to be a risk factor for death?[2] In any case, this study should lead physicians to be more cost-effective in their daily practice.