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THE AUTHORS REPLY: Our study was a pragmatic comparative-effectiveness trial evaluating functional testing versus coronary CTA in patients with stable chest pain and, as such, reflects actual care provided across its 193 North American sites. Each study site met current standards for imaging quality and was certified in all techniques. However, it is likely that testing at some sites reflects better available practices than at others. Whereas Bom et al. correctly point out that expert sites may use lower doses of radiation in performing CTA than were recorded for some patients in our study, this is also true for nuclear testing.

Pragmatic design principles also governed the selection of the type of functional test, which was at the discretion of the local care team. Although we did not record the appropriateness of testing according to technique, all patients were symptomatic and middle-aged or older, and more than 97% had at least one cardiovascular risk factor. Stress testing with the use of any technique is generally considered to be appropriate in such patients. We agree with Martin that many features of exercise stress testing predict the risk of death, and in our study, we compared the effect of all the information derived from testing on outcomes. Stratification of randomization according to the intended diagnostic test allowed for a comparison of outcomes in the approximately 1100 patients (a reasonably large cohort) who were assigned to undergo either exercise ECG or CTA, and the two strategies were found to be equivalent.

Blumenthal and Wasfy correctly point out that

many factors contribute to the decision to perform revascularization. In our study, we compared the effects of testing strategies on outcomes, but the study was not designed to assess care processes, including coronary revascularization or its appropriateness, nor was it powered to examine the effect of revascularization on clinical outcomes. Moreover, the higher revascularization rate in the CTA group is reflective of physician decisions, not the value of CTA itself. Economic analyses of our results have shown that the use of CTA did not significantly increase costs, despite the higher rate of revascularization in the CTA group.¹

Since the effect of testing data on clinical outcomes necessarily depends on changes in treatment, as noted by Nasir and Harper, tracking of differences in medical therapy and revascularization is helpful in understanding the observed outcomes. The differences in rates of revascularization have been reported, and we are currently analyzing the differences in medication use. However, although both of these factors are of substantial interest, they are intermediate end points, and the lack of improvement in clinical outcomes at 2 years in the CTA group remains, regardless of any differences in care.

Pamela S. Douglas, M.D.

Duke Clinical Research Institute
Durham, NC
pamela.douglas@duke.edu

Udo Hoffmann, M.D., M.P.H.

Massachusetts General Hospital
Boston, MA

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

1. Mark DB, Anstrom KJ, Cowper PA, et al. Economic comparison of anatomic versus functional diagnostic testing strategies in symptomatic patients with suspected CAD: results from the PROspective Multicenter Imaging Study for Evaluation of chest pain (PROMISE) Trial. Presented at the American College of Cardiology Annual Scientific Sessions, San Diego, CA, March 14–16, 2015.

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Vaccine against Pneumococcal Pneumonia in Adults

TO THE EDITOR: In their article on the efficacy of a 13-valent pneumococcal vaccine (PCV13) in the Community-Acquired Pneumonia Immunization Trial in Adults (CAPITA), Bonten et al. (March 19 issue)¹ interpret the outcome as a success. Yet the

other outcomes indicate the opposite. The relative risk of death from any cause is 1.00 (95% confidence interval [CI], 0.95 to 1.05), the relative risk of death from pneumococcal community-acquired pneumonia or invasive pneumococcal

disease is 0.86 (95% CI, 0.29 to 2.55), and the relative risk of pneumococcal community-acquired pneumonia is 0.95 (95% CI, 0.86 to 1.05). In this trial involving more than 84,000 participants, there was no significant reduction in any of the outcomes that are important to patients. Achieving only reductions in laboratory measurements (i.e., pneumococcal presence and strain) is unimpressive. The authors omit any mention of the number of hospitalizations. The trial design² states that all patients who were admitted or seen in an emergency department for suspected community-acquired pneumonia were checked for participation in the trial. Thus, the hospitalization data should be available. Given the importance of this outcome, the authors should report these data.

Andrew W. Swartz, M.D.

Yukon-Kuskokwim Health
Anchorage, AK

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TO THE EDITOR: The CAPITA trial of PCV13 touts a reduction in the relative risk of vaccine-strain-related pneumococcal pneumonia of 45.6% and in the relative risk of invasive pneumococcal disease of 75.0%. These seemingly impressive statistics, which helped to garner approval from the Food and Drug Administration and a recommendation by the Advisory Committee on Immunization Practices (ACIP) that PCV13 be used in all patients 65 years of age or older, ignore the paltry benefits of the vaccine versus its cost. The number needed to treat (NNT) would be 1030 to prevent one case of pneumonia over 3.97 years and 2011 to prevent one case of invasive pneumococcal disease, without any mortality benefit. At the current acquisition cost of \$150 per dose, this vaccine will cost the U.S. health care system up to \$6.3 billion to vaccinate the current population of persons 65 years of age or older and more than \$500 million per year thereafter.

James D. Leo, M.D.

MemorialCare Health System
Fountain Valley, CA
jleo@memorialcare.org

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TO THE EDITOR: The ACIP recently recommended the routine use of PCV13 for all adults 65 years of age or older in the United States. This recommendation was based largely on the preliminary results of CAPITA and subsequent cost-benefit analyses.¹ However, we believe that the study and, subsequently, the ACIP recommendations focused on the wrong data from the trial. From a clinical or public health standpoint, the question should be not only whether the vaccine prevents community-acquired pneumonia caused by the serotypes targeted by PCV13 but also what fraction of all such cases could be prevented by PCV13. CAPITA clearly shows that PCV13 is not efficacious against noninvasive pneumococcal community-acquired pneumonia overall (regardless of serotype) and is not efficacious against all-cause pneumonia. Therefore, PCV13 may have only minimal benefits for older adults in the United States, despite its high cost (approximately \$100 per dose). These issues highlight the need for a different pneumococcal vaccine designed specifically for use in adults.²

Daniel M. Weinberger, Ph.D.

Christian A.W. Bruhn, Ph.D.

Yale School of Public Health
New Haven, CT
daniel.weinberger@yale.edu

Eugene D. Shapiro, M.D.

Yale School of Medicine
New Haven, CT

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1. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine among adults aged ≥65 years: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep* 2014;63:822-5.

2. Weinberger DM, Shapiro ED. Pneumococcal conjugate vaccines for adults: reasons for optimism and for caution. *Hum Vaccin Immunother* 2014;10:1334-6.

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THE AUTHORS REPLY: Swartz comments that patients in our study did not have a significant reduction in the rate of all-cause community-acquired pneumonia or death. Of note, our study was neither designed nor powered for those exploratory end points. Efficacy was shown for the prevention of confirmed community-acquired pneumonia by any pneumococcal strain, with a vaccine efficacy of 30.6% (95% CI, 9.8 to 46.7). Weinberger et al. suggest that the vaccination of adults 65 years of age or older will have minimal effects. The 5% reduction in the rate of all-cause community-acquired pneumonia, although not a significant change, is in line with the 12% prevalence of vaccine serotypes in all episodes of all-cause community-acquired pneumonia in the placebo group. The absolute numbers of infections that are prevented will depend on the burden of disease caused by PCV13 serotypes in elderly persons, and these data will influence the cost-effectiveness of routine use of PCV13 in this population. Naturally, such use may differ in various countries.

Given that vaccine-type pneumococci are estimated to be responsible for approximately 10% of all-cause community-acquired pneumonia in the United States,^{1,2} analysts at the Centers for Disease Control and Prevention have predicted that adding a dose of PCV13 to the current schedule for the 23-valent pneumococcal polysaccharide vaccine (PPSV23) for adults who are 65 years of age or older could prevent an estimated 230 cases of invasive pneumococcal disease and 12,000 cases of community-acquired pneumonia over the lifetime of a cohort of persons in this age group in the United States, assuming current indirect effects from child immunization and current PPSV23 vaccination coverage.^{3,4}

In our study, of the 3232 sentinel-center visits by patients with suspected pneumonia or invasive pneumococcal disease, 146 patients were not hospitalized. Of these patients, only 3 had a first episode of vaccine-type pneumococcal community-acquired pneumonia (2 in the PCV13 group and 1 in the placebo group).

Using our study data, Leo estimates the numbers of persons who would need to be treated to

prevent one case of pneumonia or one case of invasive pneumococcal disease. However, estimates of the NNT differ from estimates of the number needed to vaccinate (NNV), which can be biased, inaccurate, and therefore misleading when derived from a multiyear, event-driven study such as CAPITA.⁵ Despite our efforts to capture all events of community-acquired pneumonia, we would have missed some episodes, and in 7% of the episodes of suspected pneumonia, urine samples for antigen detection could not be obtained, thus reducing the likelihood of the detection of PCV13 serotypes as causative. Moreover, the NNV, a value that has no defined favorable threshold, is limited in its ability to independently predict a health benefit. Furthermore, participants in a large, randomized study may not be representative of the general population. Consequently, our study may not be the best one for a determination of the NNV.

Marc J.M. Bonten, M.D., Ph.D.

Susanne M. Huijts, M.D.

Marieke Bolkenbaas, M.D.

University Medical Center Utrecht

Utrecht, the Netherlands

mbonten@umcutrecht.nl

for the CAPITA Coauthors

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

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Chikungunya Virus Infections

TO THE EDITOR: Weaver and Lecuit's review (March 26 issue)¹ on chikungunya fever mentions that the disease may alter the quality of life for

up to 6 years.² On the basis of our clinical experience, two types of persistent post-chikungunya fever rheumatic disorders can be distinguished.²