contradict the results of the intention-to-treat analysis.

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


DOI: 10.1056/NEJMc1515007

The editorialists reply:
With respect to the comments by Schäfer and colleagues: we think that further investigation in this area is required, albeit with appropriate informed consent. There are at least two major unanswered questions. First, we do not know whether the results of the SERVE-HF trial were influenced by the specific adaptive servo-ventilation algorithm for adjustment of positive pressure. An ongoing trial (Effect of Adaptive Servo Ventilation on Survival and Hospital Admissions in Heart Failure [ADVENT-HF]; ClinicalTrials.gov number, NCT01128816) has different inclusion and exclusion criteria (it includes patients with both obstructive and central apneas) and uses a different adaptive servo-ventilation device with a less aggressive adjustment of positive pressure. The data and safety monitoring board for the ADVENT-HF trial has performed two interim analyses subsequent to the initial notification of the results of the SERVE-HF trial, and it has concluded that there are no safety concerns (Bradley TD: personal communication).

Second, we do not know whether the risks and benefits of adaptive servo-ventilation are different in specific subgroups of patients with sleep-disordered breathing and congestive heart failure. Thus, we continue to think that further investigation of this topic is required.

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DOI: 10.1056/NEJMc1515007

A Randomized, Controlled Trial of Total Knee Replacement

To the Editor: In the study reported by Skou and colleagues (Oct. 22 issue),1 patients were excluded if they had symptomatic knee osteoarthritis with pain scores higher than 60 mm on a visual-analogue scale (on which scores range from 0 to 100, with higher scores indicating worse pain). We are unclear as to the rationale for excluding patients with this level of pain, who are commonly seen in orthopedic practice. We agree with the conclusion that total knee replacement is superior to the nonsurgical regimen investigated. However, we are concerned that the exclusion of 117 of 244 otherwise eligible patients (48%) because of severity of symptoms may have led to substantial underestimation of the effect sizes of treatments in both groups, especially in the surgical group because of potentially increased crossover rates among the more severely symptomatic patients.

Reported serious adverse events (stiffness requiring manipulation of the knee while the patient was under anesthesia and deep venous thrombosis requiring anticoagulation) both occurred among 6% of patients in the total-knee-replacement group. These rates were higher than the respective rates (1.3%2 and 1.5%3) reported elsewhere for much larger cohorts. The authors did not report the time-to-event end points, care
protocols (such as prophylaxis against deep venous thrombosis), and criteria for manipulation of the knee while the patient was under anesthesia. Collectively, these factors may lead to misinterpretation of the complications associated with total knee replacement.

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Dr. Lieberman reports receiving consulting fees and intellectual-property royalties from DePuy Synthes, holding stock options in Hip Innovation Technology, and receiving royalties and financial and material support from Elsevier. No other potential conflict of interest relevant to this letter was reported.


DOI: 10.1056/NEJMc1514794

THE AUTHORS REPLY: We agree with Teuscher and Lieberman that our results cannot be generalized to patients with a pain-intensity rating higher than 60 mm on a 100-mm visual-analogue scale during the previous week. However, at baseline, 42% of the patients reported pain higher than 60 mm when asked about worst pain during the previous 24 hours, and 22% reported, on average, at least severe pain during activities of daily living in the previous week. As stated in our article, the mean baseline Knee Injury and Osteoarthritis Outcome Score pain subscale score of 49 (on a scale ranging from 0 to 100, with lower scores indicating more severe pain) was similar to previously reported scores in studies involving cohorts of patients who underwent total knee replacement.

In our study, patients who had severe knee stiffness during the rehabilitation period received manipulation of the knee while they were under anesthesia. A recent Danish multicenter study that included investigators from our department showed that among patients who underwent total knee replacement, 2.2% required manipulation of the knee while they were under anesthesia.1

At admission to the hospital, all patients in our study received prophylaxis against deep venous thrombosis with 10 mg of rivaroxaban orally once daily for 1 to 3 days. Cases of deep venous thromboses were diagnosed on day 2, day 3, and day 184 after total knee replacement (the third case of deep venous thrombosis occurred in a patient after surgery for femoral-neck fracture during the follow-up period). Our trial was too small to provide reliable rates of adverse events associated with total knee replacement.

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


DOI: 10.1056/NEJMct1514794

Pediatric Outcome after Maternal Cancer Diagnosed during Pregnancy

TO THE EDITOR: Amant et al. (Nov. 5 issue)1 report on a study of outcomes in children exposed in utero to maternal cancer. Despite the importance of this study, we are concerned about some basic methodologic flaws.2

Although this study is presented as a "pro-