ventions are primarily due to improved skeletal muscle function.[3]

We agree with Brunner regarding heterogeneity of the patients with heart failure in our trial. Notably, patients with preserved ejection fraction and those with reduced ejection fraction were included in the trial. We recently reported that among these two phenotypes, the participants with heart failure with preserved ejection fraction had significantly worse physical dysfunction and frailty at baseline and appeared to receive much greater benefit from the intervention, including benefit in terms of improved physical functioning and quality of life and lower rates of frailty, rehospitalization, and death.[4]

Although the outcomes in our trial are clinically meaningful, we agree that a larger trial, adequately powered for clinical events and safety, will be needed to effect change in clinical practice and reimbursement. Ideally, such a trial would focus on patients with heart failure with preserved ejection fraction, given their worse baseline status, greater response to the intervention, and limited treatment options as compared with those with heart failure with reduced ejection fraction.

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

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Targeted Temperature Management after Cardiac Arrest

TO THE EDITOR: After the first trial involving targeted temperature management (TTM),[1] the guidelines called for a temperature between 32°C and 36°C in comatose patients following out-of-hospital cardiac arrest.[2] The authors of the TTM2 trial[3] are to be congratulated in determining that there was no significant difference in outcomes whether hypothermia or normothermia (with fever avoidance) was targeted. We wonder, however, about the generalizability of the TTM2 cohort in which 75% of patients had shockable rhythms, 90% had cardiac arrests, and 80% received bystander-initiated cardiopulmonary resuscitation (CPR). Outcomes following cardiac arrest are known to be superior in persons with shockable rhythms[4]; bystander-initiated CPR is associated with an increase in survival that is three times as high as that without it.[5] Unfortunately, recent European data indicate that only 20% of persons in cardiac arrest have a shockable rhythm, that 58% of such persons receive bystander-initiated CPR (with rates as low as 13% in some locations), and that the rate of survival to hospital discharge is only 8%.[4] Indeed, we wonder whether any intervention strongly affected the outcome in the setting of the TTM2 trial, which benefited from excellent local responses that may be unobtainable in most communities.

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THE AUTHORS REPLY: We thank Ristagno and colleagues for their comments on the TTM2 trial. When describing a cohort of patients who have had cardiac arrest, it is important to be clear about when and where the patients were assessed and what their characteristics were. Did assessment take place at the scene (outside of the hospital), in the emergency department, in the intensive care unit, or after the patients were discharged from the hospital? Demographics will differ at each time point because the denominator changes dramatically given factors such as unsuccessful resuscitation, early death, and eligibility for advanced care. Ristagno and colleagues refer to the EuReCa TWO study,[1] in which resuscitation was attempted at the scene by emergency medical services, whereas the TTM2 trial involved patients who had had a stable return of spontaneous circulation and were eligible for intensive care. The TTM2 trial recruited patients from a setting similar to that described in the EuReCa TWO study, but direct comparisons should probably be reserved for studies of patients admitted to intensive care. The overall mortality in the TTM2 trial was 50%, which indicates a severely ill group of patients and an appropriate setting for the study of a neuroprotective intervention.

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

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BNT162b2 Covid-19 Vaccine in Adolescents

TO THE EDITOR: Frenck et al. (July 15 issue)[1] report the outcomes of BNT162b2 vaccination in adolescents, and the Food and Drug Administration has authorized the expansion of Emergency Use Authorization for the BNT162b2 vaccine to include adolescents 12 to 15 years of age, with full approval of the vaccine in persons 16 years of age or older. However, because study protocols consistently separate the administration of the BNT162b2 vaccine from that of other, routine vaccines by a period of 14 to 28 days,[2] questions remain regarding the immunogenicity and safety of coadministration of the BNT162b2 vaccine with other vaccines. So far, no trial has been registered to evaluate the coadministration of the BNT162b2 vaccine and other routine vaccines in children. There has been one trial involving adults receiving pneumococcal vaccine coadministered with a booster dose of the BNT162b2 vaccine (ClinicalTrials.gov number, NCT04887948).

Although the Centers for Disease Control and Prevention (CDC) allows the concomitant use of Covid-19 vaccines and other vaccines on the same day,[3] no direct evidence supports such a recommendation. Furthermore, the known immunogenicity and safety issues associated with vaccine coadministration or vaccine combinations, such as the coadministration of the pneumococcal and meningococcal conjugate vaccines being linked with immune interactions and the combination measles–mumps–rubella and varicella vaccine being linked with fever and febrile seizure, are seen in children.[4] Given the low hospitalization rate among children with Covid-19 (13 cases per million patients as of April 2021),[5] are we in such an emergency as to skip