Response by Ellingsen et al to Letters Regarding Article, “High-Intensity Interval Training in Patients With Heart Failure With Reduced Ejection Fraction”

In Response:
These letters focus on 3 potentially important factors for training effects in the SMARTEX trial (The SMARTEX Heart Failure Study): (1) adequate load increase, (2) control of exercise intensity, and (3) inherent patient characteristics. In addition, adherence to exercise seems crucial for long-term outcomes after a supervised program.

Iellamo and Volterrani rightly point out that the success of an aerobic training program depends on regularly adapting load to individual improvement in exercise capacity. Adjustments are typically based on a combination of time and intensity of the training, which can be performed at different levels of technical complexity, from teaching participants to exercise according to the Borg scale of perceived exertion, to following sophisticated measures based on oxygen uptake, external mechanical load, heart rate, and lactate measurements. SMARTEX applied a simple procedure from a previous study by Wisløff et al to compare the effect of high-intensity interval training (HIIT) with moderate continuous training (MCT), by training at 90% to 95% versus 60% to 70% of maximal heart rate throughout the study. According to the Wisløff study, load in terms of estimated calorie expenditure would be equalized by shorter exercise time per session in HIIT than in MCT (38 versus 47 minutes, including warm-up and cool-down).

As detailed in the letter from Wisløff et al, the SMARTEX data demonstrate that the tight control of prescribed exercise intensity and intended load increase was somehow lost in the translation from a small proof-of-principle study to a larger multicenter trial of the efficacy under conditions closer to standard clinical practice. Both factors may have reduced the effect of HIIT, and, thus, the differences between the training groups. If the prescribed combinations of exercise intensity and duration per session with HIIT and MCT yielded similar load, then the marked deviations in observed intensity in SMARTEX probably led to lower load in HIIT, higher load in MCT, and reduced differences in outcome.

At hindsight, we can only speculate whether larger increases in workload and smaller deviations from target heart rate could have been achieved with even more intensive monitoring and testing, or whether outcomes resulted from different patient characteristics in the study cohorts. In comparison with SMARTEX, participants in the Wisløff study were 15 years older, had been clinically stable for 1 year versus 3 months, had solely ischemic background versus ischemic and nonischemic pathogenesis, and may have had different comorbidities and other unknown background variables.

Bianchi’s letter discusses whether reduced training response could result from impaired skeletal muscle function associated with low body mass index and testosterone deficiency. We do not have testosterone data that confirm or exclude this mechanism, whereas age and body mass would act in the opposite direction. In SMARTEX, body mass index was 27 kg/m², versus 25 kg/m² in the previous study, which had the largest training effects in HIIT. Median age was 60 versus 75, re-
spectively, and there were no differences in body mass index or age between the interventions in either study. A final lesson from SMARTEX comes from comparing follow-up data of HIIT and MCT versus the control group that just got a recommendation of regular exercise. After the 3-month supervised intervention period, all participants were encouraged to continue on their own by monthly phone calls. At retest 9 months later, there were no differences in primary or secondary outcomes, indicating that subsequent physical activity did not maintain initial improvements. This is a reminder of the need to integrate measures to enhance motivation and adherence in exercise interventions. A major challenge in cardiac rehabilitation is helping those who need it most to implement and maintain lifestyle changes over time.

**DISCLOSURES**

Dr Halle reports grants from the Else-Kröner-Fresenius Foundation for the present work and is on the advisory board of Novartis, Sanofi-Aventis, and MSD outside the present study. Dr Linke reports grants and personal fees from Medtronic and from Claret Medical, and personal fees from Edwards, SJM, Bard, and Symetis, all outside the present study.

**AFFILIATIONS**

From Department of Cardiology, St. Olavs Hospital, Trondheim University Hospital, Norway (O.E.); K.G. Jebsen Center for Exercise in Medicine, Department of Circulation and Medical Imaging, Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology, Trondheim (O.E.); Department of Prevention, Rehabilitation and Sports Medicine, Technische Universität München, Klinikum rechts der Isar, Germany (M.H.); DZHK (German Center for Cardiovascular Research), partner site Munich Heart Alliance, Germany (M.H.); Else-Kröner-Fresenius Prevention Center, Klinikum rechts der Isar, Munich, Germany (M.H.); Department of Cardiology, Bispbjerg Hospital, University of Copenhagen, Denmark (E.P.); and Department of Cardiology, Herzzentrum, Universität Leipzig, Germany (A.L.).

**REFERENCES**


AUTHOR QUERIES

Authors please note: Authors are responsible for any page charges as outlined in the acceptance letter or as indicated on the Instructions for Authors (http://circ.ahajournals.org/content/accepted-manuscripts). Unless you have selected open access for your article, or it is otherwise noted on the acceptance letter, page charges are as follows: $70 per black and white page (print articles only) or $35 per page (online-only articles only). For each color page (print only), please add $653/page. If there are any concerns regarding these charges, these should be addressed within 48 hours of receiving the s-proof. Author(s) will be invoiced for all color and page charges post publication. If you have selected open access for your article, please refer to details in the queries below.

AUTHOR PLEASE ANSWER ALL QUERIES

AQ1—Please confirm that all authors are included in the correct order in the byline and that all names are spelled correctly, including special characters, accents, middle initials, and degrees, if applicable. For indexing purposes, confirm author names have been correctly identified as given names (blue) and surnames (red). Color in the byline will not appear on the final published version. Note that journal style discourages listing all honorary degrees in the byline; such degrees are deleted during editing.

AQ2—Please carefully review any Acknowledgments, Sources of Funding, and/or Disclosures listed at the end of the manuscript (before the References), and confirm that they are accurate and complete for all authors.

AQ3—Please confirm that all authors’ institutional affiliations (including city/state/country locations) are correct as shown in the affiliations footnote.

AQ4—No more than 5 references can appear in this type of article, per journal style. References to the letters to which you are responding do not have to be listed in the reference list; referral in the text is sufficient since these letters and the response accompany each other in the issue. Please check all related changes for accuracy.

AQ5—Reference 3: If possible, please supply the authors for this chapter.