Response to letter by Grendstad and Skattebo: Puberty, more important for cardiovascular adaptations than endurance training?

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We thank Grendstad and Skattebo (2022) for their recognition of our work and for stimulating discussion on the cardiovascular adaptations to endurance training in youth athletes. There are areas where we are in agreement with the authors, foremost the need for rigorous experimental designs to conclusively address whether enhanced remodelling occurs at different stages of development. The authors rightly point out that our study was cross-sectional in nature, the limitations of which are acknowledged in our manuscript, and discussed in depth with the reviewers. However, we differ in opinion on numerous points. The authors claim there is need for longitudinal design rationalised by the fact that dropout from endurance sport because of lack of ability may bias the post-pubertal group in a cross-sectional design. In support of their position, they reference multiple papers produced at their institution (Bjerring *et al.*, 2019; Landgraff & Hallen, 2020; Landgraff *et al.*, 2021) that have adopted a longitudinal design, but fail to acknowledge that longitudinal observational studies suffer in the same way from dropout. No longitudinal measures can be made in an athlete who is no longer training. Furthermore, the cited studies all lack any kind of control group, and instead just follow a cohort of athletes across puberty. In one study, athletes who dropout are categorised as 'former athletes' and compared to those who continued (Bjerring *et al.*, 2019), but these individuals will have benefitted from years of training in their younger lives that we can expect to have lasting effects on their cardiac phenotype (Asif *et al.*, 2018; Perkins *et al.*, 2018). The longitudinal nature alone does not allow any firmer conclusions to be drawn, especially without the use of a non-active control group followed across the maturational spectrum, as has been adopted recently (Unnithan *et al.*, 2022). Therefore, while the authors have encouraged us to embrace longitudinal designs, perhaps all of those working in the field of exercise physiology need to adopt prospective, randomised-controlled trials to truly elucidate the effects of endurance training on cardiovascular remodelling during maturation.

While we concluded that cardiovascular remodelling was more comprehensive post-puberty, we agree that cardiac remodelling is still possible to some extent pre-puberty. Grendstad and Skattebo (2022) again highlight findings from their institution, that demonstrated greater left and right ventricular chamber size in pre-pubertal cross-country skiers compared to age-matched non-competing controls (Bjerring *et al.*, 2018). However, this study suffers from two of the methodological issues the authors highlight in our study: (1) the cross-sectional nature and (2) the self-reporting of physical exercise volumes and durations. As such, the authors present a paradox where methodological flaws in our study render the conclusions dubious, with their contention supported by work from their institution with the same experimental design flaws. That said, we have acknowledged the limitations of cross-sectional designs, and are unconvinced that differences in physical activity would have altered the conclusions of either study given the training volumes were sufficient for both cardiac (Obert *et al.*, 2001) and haematological (Prommer *et al.*, 2018) adaptations in children. We also examined the potential impact of training history during the per review process, to attempt to account for the longer training years in the post-pubertal group as a product of their age. Our key outcome variables were analysed using sub-sets of our pre- and post-pubertal trained cohorts matched for training volumes and training history, and we found no significant differences in

our results. Moreover, both our study and the study by (Bjerring *et al.*, 2018) conducted incremental tests to exhaustion, and demonstrate clear differences in aerobic fitness between trained vs. untrained cohorts (~10-20 ml/kg/min). Importantly, the mean age of the mixed-sex cohort in the study of Bjerring *et al.* (2018) is 12 years old and no attempt was made to estimate maturity. Based on chronological age alone, it seems highly likely that a proportion of the cohort will be circa-pubertal, especially the females, meaning conclusions about the extent of pre-pubertal remodelling are better explained by other work in the area (Geenen *et al.*, 1982; Rowland *et al.*, 1987; Rowland *et al.*, 1994; Obert *et al.*, 1998; Rowland *et al.*, 2000; Obert *et al.*, 2001; Nottin *et al.*, 2002; Obert *et al.*, 2003; Nottin *et al.*, 2004; George *et al.*, 2005; Larsen *et al.*, 2018; Unnithan *et al.*, 2018; Beaumont *et al.*, 2020; Larsen *et al.*, 2020). The lack of quantification of pubertal status is problematic for the field as a whole, as highlighted by a recent meta-analysis of cardiac remodelling in youth athletes where only 33% of articles included made any attempt to quantify maturity status (McClean *et al.*, 2017).

We recognise and acknowledge that haematological parameters are closely associated with LBM, as highlighted by Prommer *et al.* (2018). Whilst we respect the important work completed in the studies cited by Grendstad and Skattebo (2022), Prommer *et al.* (2018) are the only other study to have tested children as young as 8 years old and thus more appropriate comparisons were able to be drawn with our study. Whilst training studies are to be commended, Eastwood *et al.* (2009) pooled a small sample of 7 males and 5 females with an age range of 11-15 years, thus negating any interpretation of a maturational effect. Landgraff and Hallen (2020) followed a mixed-sex sample from age 12 to 15 and quantified maturity status, but again did not include an age-matched control group rendering conclusions problematic. Instead, endurance athletes were compared with team sport athletes, both of which have an inherently high cardiovascular training load. The results from Steiner *et al.* (2019) are also intriguing, but their aim was to investigate haematological adaptations in late adolescence (e.g. 16-19 years old), where the vast majority of pubertal development and growth has already occurred. Additionally, although they found no significant difference between trained and untrained groups at 16 years old, the untrained group had a surprising high maximal oxygen consumption of 59.2 ± 5.4 mL/min/kg and no training history was reported. As such, we hope the authors can now appreciate our reasoning for not citing this work.

Over the last decade, our knowledge of the paediatric athlete's heart has advanced considerably via a combination of cross-sectional and longitudinal cohort studies. However, all lack the methodological rigour of a randomised-control trial to definitively accept or reject the hypothesis that adaptation to exercise training is more pronounced post-puberty. To do this will be extremely challenging in human research, as discreet periods of training will need to be applied in pre- and post-pubertal phases. We should, however, not shy away from the challenge, and instead take inspiration from recent examples of exemplary study design in exercise sciences (Marsh *et al.*, 2020) and work together as a discipline to address these important research questions.

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