



## Reply to Senefeld et al: Comment on “Sex Dimorphism of $VO_{2max}$ Trainability: A Systematic Review and Meta-analysis”

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Dear Editor,

We firmly believe that critical rather than laudatory observations positively contribute to scientific endeavors. Even if wrongly founded, sharp remarks spur scientists to progress forward, an effect seldom triggered by praise. For the sake of brevity, we thank but omit to elaborate on complimentary comments by Senefeld et al. [1]. The point of consideration is the potential effect of age on sex differences in trainability on the basis of isolated subgroup analyses. According to established meta-analytical guidelines [2], we performed subgroup and meta-regression analyses to assess potential moderating factors, including age [3]. Neither subgroup nor meta-regression analyses detected any influence of age on sex differences in  $VO_{2max}$  responses. Furthermore, no heterogeneity was found among studies ( $I^2 = 0\%$ ), confirming the consistency of the findings [3]. Of note, even if  $I^2 > 0\%$ , investigations of heterogeneity when there are very few studies are of questionable value [2]. Let us not forget that subgroup analyses are prone to the limitations of any observational investigation, e.g., plausible bias through confounding by other study-level characteristics.

Why do Senefeld et al. assert an effect of age based on subgroup analyses, specifically isolated subgroup analyses? As the Cochrane guidelines explicitly warn, “*it is tempting to compare effect estimates in different subgroups by considering the meta-analysis results from each subgroup*

*separately. This should only be done informally by comparing the magnitudes of effect. Noting that either the effect or the test for heterogeneity in one subgroup is statistically significant whilst that in the other subgroup is not statistically significant does not indicate that the subgroup factor explains heterogeneity. Since different subgroups are likely to contain different amounts of information and thus have different abilities to detect effects, it is extremely misleading simply to compare the statistical significance of the results*” [2]. Still more inaccurate is to present the isolated result of a given subgroup without statistically comparing the magnitude of effect between opposing subgroups (young vs. old), notably when as a matter of statistical fact there is no heterogeneity. The concern of Senefeld et al. vanishes when proper methodology is not overlooked [2]. The correspondents should have at the very least noticed and acknowledged the lack of significance between the magnitude of effect in age subgroups—if needed, they could have asked for guidance about standard meta-analytical procedures. Ultimately, as a minor point beyond methodology, it would have been comforting that, before asserting that certain mechanisms of adaptation were not suggested, they had read in detail the manuscript as well as the references provided in the letter. Caution and thoroughness are essential to avoid giving misleading directions for future research [2].

Notwithstanding these comments, we appreciate the enduring contributions of Joyner’s group to integrative physiology.

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### Compliance with Ethical Standards

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## References

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