TO THE EDITOR: We agree with Drs. Debevec and Millet (1) that a study with either a longer duration (>6 h) or intermittent hypoxic exposures might detect differences in certain outcomes between hypobaric hypoxia (NH) and normobaric hypoxia (HH).

Symptoms of acute mountain sickness (AMS) can develop within 1 hour (2) of continuous hypoxic exposure. Minute ventilation has been shown to achieve steady-state over 40 minutes (6) to a few hours (3), and changes in chemosensitivity are noticeable after a 3-hour hypoxic exposure (4). We selected to use a 6-h exposure to capture key, early changes in respiratory control and to cause AMS in approximately one-half of participants. One must also consider that when comparing different methods of inducing hypoxia (i.e., NH vs. HH) the influences of utilizing terrestrial altitude as opposed to a hypobaric chamber. Although terrestrial altitude can be more practical than chamber hypobaric hypoxia, it has the disadvantage of preventing blinding and being influenced by confounders such as weather patterns, travel stress, fatigue, and dehydration.

There are myriad experimental variables in addition to duration that should be considered when comparing multiple studies. For example, the degree of hypoxia or altitude, amount of exercise training at altitude, cardiorespiratory fitness, participant age, sex, and ascent profile could be experimentally manipulated. The parameters we assessed (5) were restricted to control of breathing and AMS susceptibility, and we did not generalize our findings to exercise and other outcomes.

As Drs. Debevec and Millet rightfully indicate, additional studies are necessary to comprehensively characterize the differences between hypobaric and normobaric hypoxia. We have shown, using a rigorous design that 6 h of continuous hypoxia is not sufficient to demonstrate cardiorespiratory or symptomatic differences between normobaric and hypobaric hypoxia at rest, yet we anticipate that this study will represent just one of many rigorously controlled studies comparing the two interventions to come.

DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS
Author contributions: N.A.R., A.W.S., and M.S.K. drafted manuscript; N.A.R., A.W.S., and M.S.K. edited and revised manuscript; N.A.R., I.S.S., N.W., S.F., A.W.S., and M.S.K. approved final version of manuscript.

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