Altitude Does Not Reduce Concussion Incidence: Response

Authors’ Response:
Thank you for allowing us to respond to the Letter to the Editor regarding our recently published study titled “Altitude Modulates Concussion Incidence Implications for Optimizing Brain Compliance to Prevent Brain Injury in Athletes.”

We agree with the author of the letter that this published study presents important findings that have the potential to influence the science related to concussion prevention strategies. We also thank him for his interest in this study, and we are encouraged that it is stimulating ongoing discussions in the field of concussion prevention. The Letter to the Editor makes 3 major points. We will respond to each in a point-by-point fashion.

We agree with the author that it is important to clarify the clinical relevance of our findings. As the authors of this article included basic scientists, public health researchers, and clinicians, we were very sensitive to the criteria required to demonstrate clinical significance and subsequently were very clear in this article that this was the first epidemiologic study to evaluate the novel hypothesis that a raised topographical altitude would be related to a reduction in concussion rates. Clinical significance must be demonstrated via a thorough line of research resulting in a progression of evidence, ideally culminating in clinical trials. Thus, we believe studies such as ours, which is in the very early stages of novel lines of research, should be used to generate hypotheses and drive additional research rather than to determine clinical significance. In addition, making determinations of clinical significance based on one statistic is inappropriate. Clinical significance should be determined only after a detailed examination of a potential clinical/public health problem, which requires an understanding of a wide range of factors: for example, the size of the population at risk; the prevalence, incidence, and/or rate of the negative health outcome in the population at risk; the seriousness/severity of the negative health outcome; and the effectiveness, availability, cost, and possible negative side effects of potential prevention and/or treatment options. When a large population is at risk for a negative health outcome (especially with potentially severe short- and/or long-term effects), even a modest rate decrease may eventually be determined to be clinically significant. The author’s claim of clinical meaningfulness” likely reflects a lack of understanding of the current evidence and the challenge that science has had in making any strides in preventing concussion in sport to date. Nevertheless, we sincerely hope that the author and clinician readers of this journal would not make clinical decisions based solely on the results of our single study.

While we made no claim of clinical significance from our study, having the author of the letter suggest that a 30% decrease in the rate of concussion among football players at higher altitude would be insignificant is simply irresponsible. In fact, our findings support the need for further research in this area specifically because the population at risk is large (1,116,739 US high school students played football in the 2012-2013 academic year), because the rate of concussion in this population has increased significantly over the past decade,1 and given the concerns regarding the potential severity of both short- and long-term outcomes for young athletes sustaining concussion. Contrary to the suggestions of the author, calculations of absolute risk are most appropriately reserved for studies much farther along in lines of research than pilot studies such as this. Again, studies of novel hypotheses, such as ours, are intended to drive discussion, generate more questions/hypotheses, and lead to additional research as we indicated in our original report—they are not intended to be used to determine clinical significance.

The authors also agree with the author of the Letter to the Editor that there should be a strong methodological rational for dichotomization of comparison groups. As clearly stated in our article, the 497 study schools were dichotomized by altitude using 600-ft elevation as the cut-off point because that was the median elevation for schools in our study sample. Researchers dichotomizing study samples traditionally utilize sample medians or means as cut-off points if a clear rationale for a physiologically driven cut-off point is not available (and frequently even when one is available). Utilizing a sample median as a cut-off point for dichotomization is a standard practice, not an arbitrary decision, and the author’s categorization of it as such is inaccurate. Furthermore, the mean altitude of the schools in the lower half of our dichotomized altitude variable was 244 ft while the mean altitude of schools in the upper half was 1689 ft (data not presented in the published article), which, coupled with the overall range of the study sample from 7 to 6903 ft in elevation, demonstrates this sample’s broad representation across the altitude continuum. Finally, the High School RIO surveillance system has, for the past 8 years, captured data from a large national sample of US high schools and the aggregate data set represents the largest database of high school sports–related injuries collected to date. We feel confident that our findings from the analyses of this large national sample are generalizable to the broader population of US high school athletes, and thus the author’s description of the findings being an “artifact” of the data set is another inaccurate categorization.

We acknowledge that the hydrodynamics of the intracranial space were not measured and therefore cannot confirm...
the mechanism by which reduction in concussion occurred. But, as speculated in the article, the physiological adaptation to higher altitude is one potential explanation for reduced concussion incidence at increased altitude. Cerebral blood flow rises in response to even mild hypoxemia (low oxygen levels), including hypoxic changes associated with increased elevations. Increased cerebral blood flow would also result in cerebral venous engorgement and a subsequent rise in intracranial pressure when the limits of cerebral compliance are reached. However, the relationship between increased altitude adaptation and mitigating concussive symptoms is unclear. While at extreme elevations, hypoxemia of the brain can have serious negative health effects (mountain sickness, high-altitude headache, and high-altitude cerebral edema), at lower altitudes, we still expect alterations of physical and physiological parameters as minor changes in air density, humidity, temperature, and oxygen levels occur, especially up to the maximum elevation of 7000 feet used in this study. However, the authors acknowledge that this relationship may be because of reasons other than the proposed physiological response to elevation, and further verification is needed.

In conclusion, while we welcome the discussion generated by our publication and appreciate the viewpoints raised in the Letter to the Editor, we respectfully disagree with the author’s critiques. We are confident in our work and our realistic valuation of it as the important first step in a novel line of research. Of interest, a recent investigation reported very similar results of a 32% reduction in risk of concussion in National Football League games played at higher altitudes. Regardless, it is clear that more work is needed to fully understand the potential reasons or mechanism(s) underlying the results of our published investigation.

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