# Live-High Train-Low Altitude Training on Maximal Oxygen Consumption in Athletes: A Systematic Review and Meta-analysis

## A Commentary

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## INTRODUCTION

Lancaster and Smart have provided us with an altitude training / hypoxic exposure meta-analysis, which includes a group of 11 studies utilizing a wide variety of hypoxia delivery mechanisms, exposure times, and subject cohorts. Meta-analysis is a quantitative analysis of the results of individual empirical studies [1] and is often used as a means to review previous studies, test theoretical propositions, and/or make generalizations about an entire population. Meta-analysis can be quite useful and is utilized in a number of fields, most prominently in medicine [2]. However, meta-analysis is not without limitations. With any meta-analysis, there is an underlying assumption that the combined studies share commonalities, particularly with regard to components such as treatments, subject characteristics, and measurements. If these components are quite similar, then a meta-analysis can be a helpful tool. However, if the studies under consideration have fundamental differences in experimental design or underlying physiological rationale, then a meta-analysis may in fact just be combining noise, ultimately comparing apples and oranges.

In giving weight to the Lancaster and Smart analysis, the reader should be fully aware of some of the many issues involved with training studies in general and altitude training / hypoxic exposure studies in particular [3], many of which go well beyond the limitations noted by the authors in their paper. Each of these issues, if not controlled for, can add substantial variability to the outcome measures being examined. Additionally, there are substantial differences in both the research methodologies and hypoxic doses used in the studies utilized in this particular meta-analysis. We question if it is useful and proper to compare the outcomes of these studies to each other under a global umbrella of "Live High – Train Low." Each of these theoretical issues is addressed below.

## ISSUES RELATED TO CONTROLS AND VARIANCE IN ALTITUDE TRAINING RESEARCH

Historically, studies that have examined the effect of altitude training or hypoxic exposure on sea-level performance have produced contradictory results with a wide variance in individual outcomes. A large number of these studies suffer from experimental design issues, most of which are in the area of adequate pre-altitude / hypoxia controls. With training based studies, proper controls are often difficult, time consuming, and expensive additions to a protocol. However, without them, it becomes difficult to partition out the variance in outcomes that is truly due to the effect of altitude training or hypoxic exposure, and what is due to some other factor. Below is a list of some common control issues with altitude training / hypoxic exposure studies, each of which may influence the meta-analysis of Lancaster and Smart.

## THE TRAINING CAMP AND GROUP TRAINING EFFECTS

The atmosphere of a training camp has many different qualities that differ from the living and training dynamic that most athletes experience in their daily lives. While at a training camp, the athlete normally does not have the added stressors of work, family, or other daily responsibilities and can focus solely on training. Additionally, when athletes complete a training camp as part of a group, the quality and quantity of training typically increase over pre-camp levels. Adequately controlling for this effect involves a burdensome and expensive step of completing a sea-level training camp for an extended period of time, prior to the altitude training camp. Of the 11 studies used by Lancaster and Smart in the meta-analysis, only the study by Levine and Stray-Gundersen [4] utilized a sea level training camp to control for the training camp and group training effects. How much these effects added to the overall variability in the physiological outcomes that the meta-analysis of Lancaster and Smart are trying to account for is unknown. Examination of the weights assigned in the meta-analysis to the study of Levine and Stray-Gundersen may help to illustrate the importance of a sea-level control group. The average weight assigned to Levine and Stray-Gundersen was 74.5%, and this disproportionate weight had a profound effect on the meta-analysis. So much so, that without the data of Levine and Stray-Gundersen, serum lactate was the only outcome variable to reach statistical significance. Weights are assigned based on the level of precision (i.e., small variability), which implies that Levine and Stray-Gundersen more rigorously controlled the experimental conditions compared to the other studies in the analysis.

## TRAINING LEVELS PRIOR TO THE ALTITUDE TRAINING CAMP / HYPOXIC EXPOSURE

In many published studies, a quantification of training of the subjects prior to the intervention of altitude or hypoxic exposure is not included. As a result, it is not known if, for example, an increase in $\dot{V}O_2$max after altitude training is due primarily to the adaptations specific to altitude or due to a change in the overall quantity or quality of training during the training camp. Again, the lack of this particular control is a significant issue for many of the 11 studies utilized in the Lancaster and Smart meta-analysis.

## IRON STORAGE LEVELS AND SUPPLEMENTATION

A high percentage of endurance athletes display clinically low levels of iron stored as ferritin [5]. This becomes an issue with chronic altitude exposure, as athletes with low serum ferritin levels prior to an altitude training camp have been shown to fail to display an increase in red cell mass after the camp. Athletes who had normal levels of serum ferritin demonstrated significant increases in both red cell mass and $\dot{V}O_2$max after four weeks of Live high – Train low altitude training [5]. How much the data of the studies utilized in the Lancaster and

Smart meta-analysis varies as a result of iron storage differences prior to hypoxic exposure and training is not known.

## ISSUES RELATED TO FUNDAMENTAL DIFFERENCES IN RESEARCH DESIGN OF INCLUDED STUDIES

In the analysis by Lancaster and Smart, four different types of hypoxic delivery mechanisms are grouped under the common umbrella of Live High – Train Low: "natural" or terrestrial exposure to the hypoxia of altitude, as well as three different forms of artificial hypoxic exposure of varying durations and intensities. The assumption is that each of these forms of hypoxic exposure is similar with regard to their physiological effects, and therefore would be legitimate to compare to one another. However, we would caution the reader that comparing terrestrial, full-day exposure to altitude with intermittent hypoxic exposure of short duration is akin to comparing apples with oranges — particularly in terms of the proposed mechanistic adaptations and published physiological adaptive outcomes.

Although many different mediating mechanisms have been proposed to explain the improved performance with altitude training or hypoxic exposure, the abundance of data (from adequately controlled studies) leads us to conclude that the erythropoietic effect of altitude / hypoxia acclimatization is of primary importance [6]. If so, the question then becomes one of a dose-response nature – i.e., what level of hypoxic exposure, and for what duration, is adequate enough to produce significant and substantial changes in red cell / hemoglobin mass?

## HOURS PER DAY OF HYPOXIC EXPOSURE

It has been well established that chronic moderate altitude exposure for 20-24 hours / day increases red cell mass in both untrained and highly trained individuals. However, lesser durations of hypoxic exposure are far from universal in their ability to increase red cell mass. For example, in one of the studies utilized in the Lancaster and Smart meta-analysis [7], there was no change in red cell mass, hemoglobin concentration, hematocrit, or reticulocytes with 3 hr / day exposure to a simulated altitude of up to 5,500m for 4 weeks. This outcome is despite a transient increase in erythropoietin after the hypoxic exposure. The lack of erythropoiesis with an intermittent hypoxia protocol appears to be a function more of the duration of the normoxic exposure than the duration of the hypoxic exposure. The principal activator of gene expression within hypoxic cells is HIF-$\alpha$, which is quite stable under hypoxic conditions, allowing for transcriptional activation and stimulation of protein synthesis [8]. However, as soon as oxygen becomes present, HIF-$\alpha$ is hydroxylated, rapidly degraded, and ultimately has one of the shortest half-lives of any known protein [9]. In addition, once oxygen levels return to normal in normoxia, erythropoietin is suppressed, causing a selective apoptosis of immature red blood cells termed "neocytolysis" [10]. Taken together, less-than-full-day exposure to hypoxia may not be sufficient time to cause the mechanistic adaptation (i.e., a significant increase in red cell mass) necessary to improve performance with altitude training / hypoxic exposure. If so, this brings into question whether studies of intermittent hypoxic exposure are comparable to studies utilizing full- or near-full-time residence at altitude.

## NUMBER OF DAYS OF HYPOXIC EXPOSURE

In the classic Live High – Train Low studies of Levine and Stray-Gundersen, a standard altitude camp duration of 28 days has been shown to be sufficient to significantly improve red cell mass, maximal aerobic capacity, and track performance. However, studies that have followed, including many in the Lancaster and Smart meta-analysis, have used much shorter durations of hypoxic exposure. Changes in red cell mass in both published and unpublished studies has been complied by Levine and Stray-Gundersen [6], which shows that studies with < 2 weeks of altitude / hypoxic exposure fail to significantly increase red cell mass. With exposure of 3 weeks and longer, significant increases in red cell mass are demonstrated, with a near doubling of red cell mass in studies with 4 weeks of altitude exposure compared to those with 3 weeks of exposure. Only 3 of the 11 studies included by Lancaster and Smart utilized 28 days or more of altitude exposure, therefore is the meta-analysis really comparing like studies?

### MECHANISM OF HYPOXIC DELIVERY

This meta-analysis generally assumes that there is no difference in the adaptive response to terrestrial altitude exposure, hypobaric chamber exposure, or normobaric hypoxia inhalation. Recent data suggests that this may not be a valid assumption. Work by US Army scientists (USARIEM) has shown that 6-15 days of either terrestrial moderate altitude residence or intermittent hypobaric chamber residence both resulted in improved exercise performance at high altitude [11, 12], but multiple studies using 7 days of intermittent normobaric hypoxia exposure did not enhance high-altitude exercise performance [13, 14]. While certainly not the same as utilizing altitude training / hypoxic exposure for the purpose of enhancing sea-level performance, the USARIEM data does bring in to question the assumption that all modes of hypoxic delivery are equivalent and thus whether it is appropriate to lump them collectively for a meta-analysis.

Taking each of these issues together, we would offer that not all methods of altitude training or hypoxic exposure are the same, noting the vast differences in outcomes based on hypoxic exposure lengths, lack of controls, hypoxia delivery methods, and more. As a result, we are not certain that it is appropriate to combine the 11 studies chosen by Lancaster and Smart together as being “Live High – Train Low” or comparable in nature. Clearly, an important assumption associated with meta-analysis is that the studies included possess commonalities with regards to treatment (type and duration), subjects, and measurements. Violation of this assumption makes it extremely difficult to interpret the results of a meta-analysis. Therefore, in this instance, it may be best to evaluate the scientific merit and practical applications of each study individually rather than using a combined statistical analysis.

## CONCLUSION

“Athletes and coaches continue to debate the optimal method to deliver altitude training to better enhance sea level performance” serves as the introductory sentence in the article by Lancaster and Smart. Ultimately, the authors conclude from their analysis that an altitude of 2,500 – 3,500m, utilized for a minimum of 9.5 hours daily, for a period of at least 2 weeks is the most beneficial application of altitude / hypoxic exposure for performance enhancement. We come to a different conclusion, and suggest that living at an altitude of 2,000 – 2,500m, for > 20 hours daily, for a period of no less than 28 days has repeatedly shown to be consistently effective in enhancing performance. We come to this conclusion not from a meta-analysis, but more from a careful and studious examination of the existing literature, taking into account the various issues involved with altitude training / hypoxic exposure research and the plausible physiological mechanisms by which performance can be enhanced. Clearly, we must add “scientists” to the list of people who will continue to debate the optimal method to deliver altitude training to better enhance sea-level performance.

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