

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

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ABSTRACT

We quantified the effects of four different protocols of Live-high Train-low altitude training on maximal aerobic capacity. A systematic search of PubMed for published studies, up to July 2010 was performed using appropriate search terms. Eleven studies met inclusion criteria. Combined analysis showed athletes exposed to hypoxia had higher maximal oxygen consumption compared to those undertaking normoxic training, Weighted Mean Difference (WMD) 1.51 ml. kg⁻¹.min⁻¹ [0.44, 2.58, p=0.006]; hemoglobin (WMD) 0.57 mg/dl⁻¹ [0.38, 0.75, p<0.00001], lower maximum heart rate (WMD) -1.77 beats.minute⁻¹ [-3.03, -0.50, p=0.006], and peak exercise blood lactate (WMD) -3.03 mmol.L⁻¹ [-4.57, -1.49, p=0.0001]. Studies utilizing minimum hypoxic exposure of 9.5 hours daily showed a significantly greater weighted mean difference in maximal oxygen consumption WMD 3.45 ml.kg⁻¹.min⁻¹[0.30, 6.60] p=0.03, in the hypoxic subjects. Protocols using altitudes between 2,500 to 3,500m for a minimum of 9.5 hours daily for at least 2 weeks elicited greatest performance effects.

Key words: Altitude Training, Hypoxia, Live-High Train-Low, Maximal Oxygen Consumption

INTRODUCTION

Athletes and coaches continue to debate the optimal method to deliver altitude training to better enhance endurance performance [1]. Recent interest has focused on live-high train-low (LHTL) altitude training, leading to the development of nitrogen houses, hypobaric chambers, altitude tents and hypoxic inhalers. These devices provide athletes with a convenient means to adapt to hypoxia and they are able to train normally without having to travel back and forth between low and high altitudes. The LHTL approach has proved effective in terms of performance enhancements [2]. In addition to natural LHTL methods, researchers have investigated varying approaches to artificial LHTL which can be grouped into three distinct categories (Figure 1): the artificial long continuous approach includes

studies in which participants are exposed to simulated moderate altitude (generally defined as 1,500m-2,500m) for 8 to 18 hours per day. The artificial short continuous approach includes studies in which participants are exposed to simulated moderate-high altitude (generally defined as 2,500m-5,300m) for 1.5 to 5 hours per day. The artificial brief intermittent approach includes studies in which participants are exposed to simulated high altitude (generally defined as 5,300m-8,848m) for less than 1.5 hours per day.

A recent review described improvements in sea-level exercise performance following adaptation to hypoxic exposure, although data pooling and meta-analysis were not conducted as all types of study design (e.g., uncontrolled and non-randomized) were included [2]. Our meta-analysis aimed to quantify the effects on endurance performance measures, of four different approaches of LHTL altitude training, using only randomized controlled trials of LHTL.

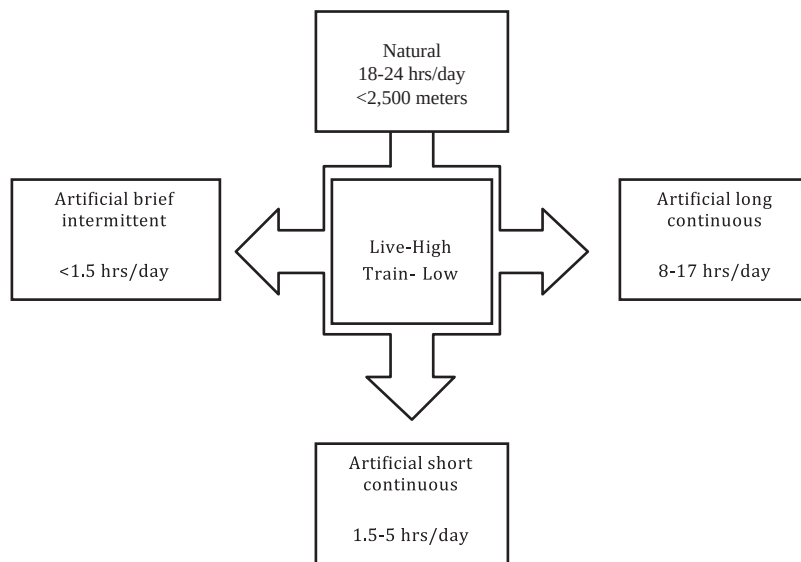


Figure 1. Methods of Live-High Train Low Altitude Training

METHODS

STUDY SELECTION

A systematic search of PubMed (1966-July 2010) for published studies, up to and including July 2010 was performed using the following search terms; *maximal oxygen consumption, altitude training, erythropoietin, heart rate, hypoxia and live-high train-low* (see Table 1). An advanced search strategy was used to identify randomized controlled trials. Reference lists of included articles were also examined by two reviewers against inclusion and exclusion criteria. Seventeen studies were excluded as they did not meet inclusion criteria (Figure 2). We recorded study details, including measures directly related to performance, specificity of performance tests, hypoxia treatment, altitude level and days, and time per day of exposure.

OUTCOME MEASURES

The outcome measures were maximal oxygen consumption, serum erythropoietin, maximum heart rate and blood lactate concentration.

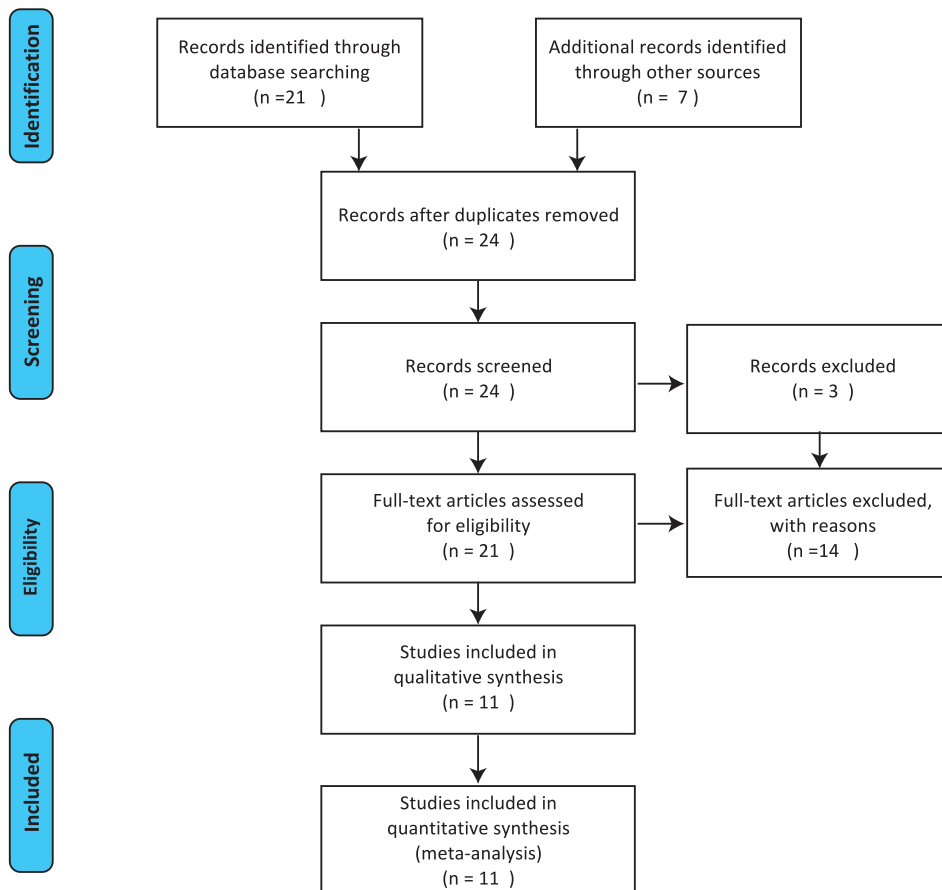


Figure 2. PRISMA 2009 Flow Diagram

Table 1. MEDLINE Search Strategy

#1 (altitude training*):ti,ab,kw
#2 MeSH descriptor Hypoxia, this term only
#3 MeSH descriptor Live high train low, explode all trees
#4 MeSH descriptor Hypoxic, this term only
#5 "erythropoietin":ti,ab,kw
#6 "maximal oxygen consumption":ti,ab,kw
#7 (VO2 Max):ti,ab,kw
#8 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8)

INCLUSIONS

Randomized controlled trials of natural and artificial LHTL altitude training studies were included. Studies integrated subjects from triathlons, running, cycling, swimming and cross-country skiing from both elite and subelite competitive levels. Studies included both male and female subjects. There were no language restrictions. Only data from the first part of crossover studies was included.

EXCLUSIONS

Studies that were published from conferences, abstracts, animal-based or non-controlled or non-randomized studies were excluded. Live-low train high (LLTH) and live-high train-high (LHTH) studies were also excluded.

DATA SYNTHESIS

Data relating to maximal oxygen consumption, serum erythropoietin, maximum heart rate, and blood lactate concentration were reviewed. Outcome measures for post values were recorded in a database. All data were continuous, so only post mean $\pm$ standard deviation values were used because the change in the standard deviation between pre and post values cannot be calculated, this method has been established previously [3].

STATISTICAL ANALYSIS

Results were obtained by calculating a weighted mean of outcome measures using (Norway) Review Manager 5.0 (The Nordic Cochrane Centre, Copenhagen, Denmark) and a weighted mean difference (WMD) between pooled data for hypoxic versus normoxic groups was reported for statistical analysis. The analysis used an inverse variance statistical method and random effects analysis model. The inverse variance method aggregates two or more random variables to minimize the variance of the sum. Each random variable in the sum is weighted in inverse proportion to its variance.

The weighted mean difference (WMD) was used where continuous scales of measurement were used to assess the effects of treatment. Instead of each of the data points contributing equally to the final average, with WMD some data points contribute more than others, depending on factors such as study size, or relative magnitude of reported standard deviations. Data was pooled and analysed using the fixed-effects model to ensure robustness of the chosen model and susceptibility to outliers. A 95% confidence interval and 5% level of significance was used. Heterogeneity was quantified by a Cochran Q test (a non-parametric statistical test of whether treatments have identical effects). The Cochran Q value is calculated as the weighted sum of squared differences between individual study effects and the pooled effect across studies, with the weights being those used in the pooling method. Q is distributed as a chi-square statistic with k (number of studies) minus 1 degrees of freedom. The I^2 statistic was also employed to describe the percentage of variation across studies that is due to heterogeneity rather than chance. $I^2 = 100\% \times (Q - df) / Q$ is an intuitive and simple expression of the inconsistency of studies' results. Unlike Q, I^2 does not inherently depend upon the number of studies considered. For the purposes of this study, I^2 values were classified as follows: <25% = low heterogeneity, 25-75% = moderate heterogeneity, >75% = high heterogeneity (data pooling between studies is not justified).

Meta-analyses are presented in forest plots. The p values associated with test for overall effect indicate level of significance. The WMD and 95% confidence intervals are plotted (green) for all studies and the diamond (black font) at the foot of the forest plot indicates the pooled (combined) overall effect of all studies for that analysis.

RESULTS

STUDY CHARACTERISTICS

The eleven randomized controlled trials that met our inclusion criteria had an aggregate of 160 participants, 106 (66%) males and 54 (34%) females (Table 2). The weighted mean age of participants in the hypoxic and normoxic groups was 26.7 ± 9.9 years for the hypoxic group and 26.2 ± 9.1 years for the normoxic group. Studies were conducted in Australia (3), Austria

(1), Finland (1), France (1), Japan (2), and the United States (3). The studies of Gore [4] and Rodriguez [5] shared data so these two papers are considered one data set as were the studies of Schmitt [6] and Robach [7].

Table 2. Study Design Characteristics Included Studies in Meta-Analysis

Study	Subjects	Competitive Level	Hypoxic (h/d)	Days Exposure	Altitude Level (m) Hypoxia/ Normoxia	Hypoxia Mechanism
Natural LH TL						
Dehnert [16]	Triathletes	Subelite	13	14	1956/800	Natural
Levine [8]	Runners	Subelite	18-24	28	1200-2500/150	Natural
Artificial LH TL						
i. Short Continuous						
Burtscher [17]	Runners	Elite	2	39	3200-5500	Simulated
Katayama [18]	Runners	Subelite	1.5	21	4500	Simulated
Katayama [19]	Runners	Subelite	3	14	4500	Simulated
Gore [4]#	Swim/Run	Subelite	3	28	4000-5500	Chamber
ii. Long Continuous						
Gore [20]	Endurance	Elite	9.5	23	3000	Simulated
Robertson [13]	Runners	Subelite	14	21	3000	Simulated
Saunders [21]	RaceWalkers	Elite	14	21	3000	Simulated
Schmitt [6]*	Skiers	Elite	11	18	2500-3500/1200	Simulated
iii. Brief Intermittent						
Julian [22]	Runners	Elite	0.75/1.5	20/26	3600-5000	Inhaler

Data shared with Rodriguez et al. [5]

*Data shared with Robach [7]

MAXIMAL OXYGEN CONSUMPTION

Nine studies reported changes in maximal oxygen consumption, those subjects who undertook hypoxic training showed significantly higher values Weighted Mean Difference (WMD) 1.51 ml. kg⁻¹.min⁻¹ [0.44, 2.58, p=0.006], compared to the normoxia group (Figure 3).

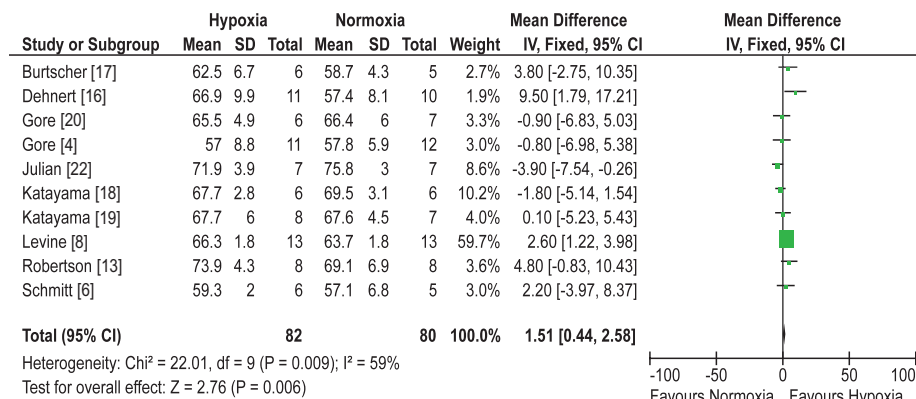


Figure 3. Maximal Oxygen Consumption

HEMOGLOBIN

Seven studies reported significantly higher serum hemoglobin levels in those subjects who undertook hypoxic training (WMD) 0.57 mg/dl⁻¹ [0.38, 0.75, $p < 0.00001$], compared to the normoxia group (Figure 4).

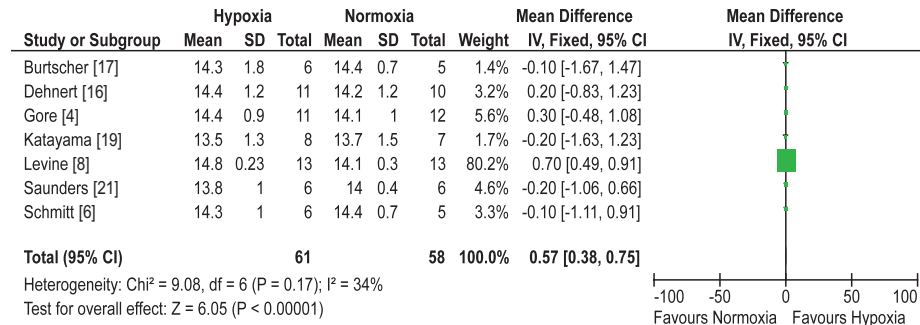


Figure 4. Serum Hemoglobin

MAXIMUM HEART RATE

Six studies reported significantly lower maximum heart rates in those subjects who undertook hypoxic training (WMD) -1.77 beats.minute⁻¹ [-3.03, -0.50, $p = 0.006$], compared to the normoxia group (Figure 5).

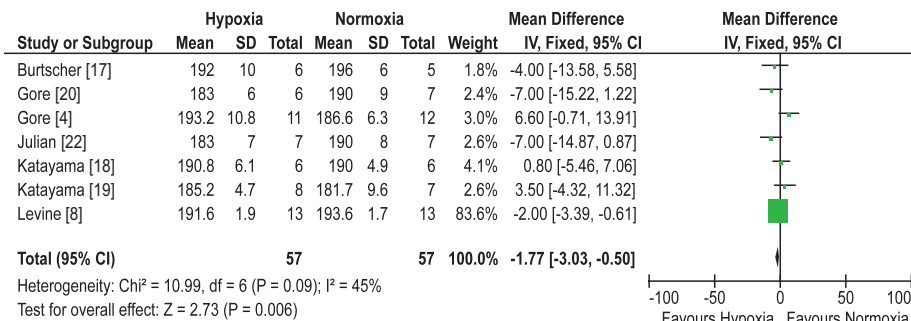


Figure 5. Maximum Heart Rate

HEMATOCRIT

Five studies reported no significant differences in serum hematocrit levels between subject groups (WMD) 0.60 % [-0.69, 1.88, $p = 0.36$], compared to the normoxia group (Figure 6).

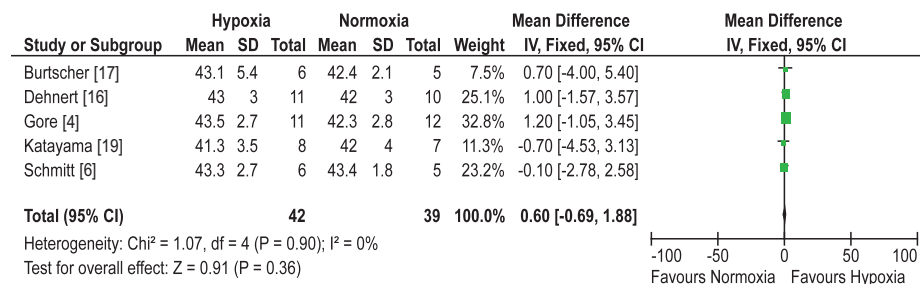


Figure 6. Hematocrit

PEAK EXERCISE BLOOD LACTATE CONCENTRATION

Two studies reported significantly lower peak exercise blood lactate levels in those subjects who undertook hypoxic training (WMD) $-3.03 \text{ mmol.L}^{-1}$ $[-4.57, -1.49, p=0.0001]$, compared to the normoxia group (Figure 7).

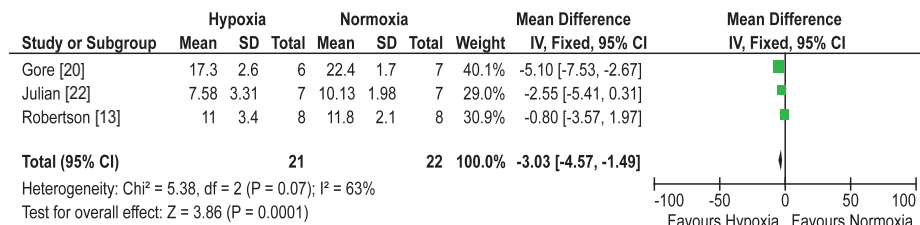


Figure 7. Hypoxia and Blood Lactate Concentration

STUDY HETEROGENEITY

All five analyses showed low to moderate heterogeneity, suggesting the analyses were justified. It was noted that the study of Levine [8] had remarkably lower standard deviations for reported outcome measures and this weighted the study heavily in the analyses. For this reason, sub-analyses were conducted by removing the study of Levine from maximal oxygen consumption, hemoglobin and peak exercise heart rate (other analyses did not use Levine data). When Levine's data was removed from the above three analyses, there was no longer a significant difference between hypoxic and normoxic groups.

MAXIMAL OXYGEN CONSUMPTION IN STUDIES WITH AT LEAST 9.5 HOURS DAILY EXPOSURE

Four studies utilised a minimum hypoxic exposure of 9.5 hours daily and showed a significantly greater weighted mean difference in maximal oxygen consumption of $3.45 \text{ ml.kg}^{-1}.\text{min}^{-1}$ $[0.30, 6.60] p=0.03$, in the hypoxic versus normoxic subjects (see Figure 8).

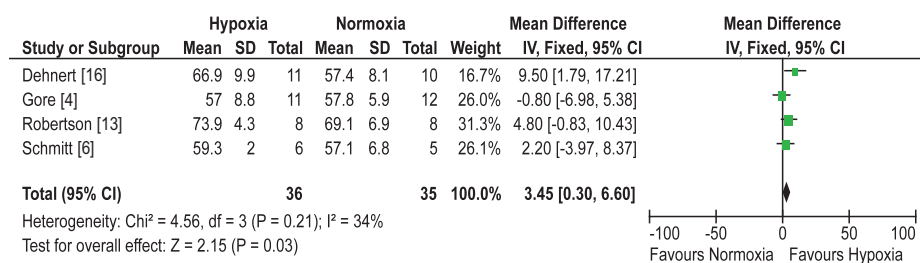


Figure 8. Maximal Oxygen Consumption in Studies with at Least 9.5 Hours Daily Altitude Exposure

RISK OF BIAS

Table 3 shows study quality assessment on a scale ranging from 2-5, with a median score of 3. Figure 9 shows an Egger plot (to assess risk of publication bias) relating to Figure 3, which was chosen as the analysis with the largest number of included studies. The Egger plot suggests risk of publication bias was low. Table 4 highlights the characteristics of excluded studies.

Table 3. Risk of Bias for Included Studies

Study	Allocation Concealment	Blinding	Incomplete Outcome Data*	Randomization Method	Selective Outcome Reporting*	Score /5
Dehnert [16]	No	No	No	Stratified by Fitness	No	3
Levine [8]	No	No	Yes	Unclear	No	2
Burtscher [17]	No	No	Yes	Unclear	No	1
Katayama [18]	No	No	No	Unclear	No	2
Katayama [19]	No	No	No	Unclear	No	2
Gore [4]	Yes	Double	No	Stratified by gender/fitness	Yes	4
Gore et al. [20]	No	No	No	Stratified by Fitness	No	3
Robertson [13]	No	No	No	Unclear	No	2
Saunders [21]	No	Single	No	Stratified by Performance	No	4
Schmitt [6]	Yes	No	No	Stratified by Fitness	No	4
Julian [22]	Yes	Double	Yes	Stratified by Fitness	No	4

*'No' answer scores 1 point, all other 'No' score zero. Higher score means lower risk of bias (scale 0-5).

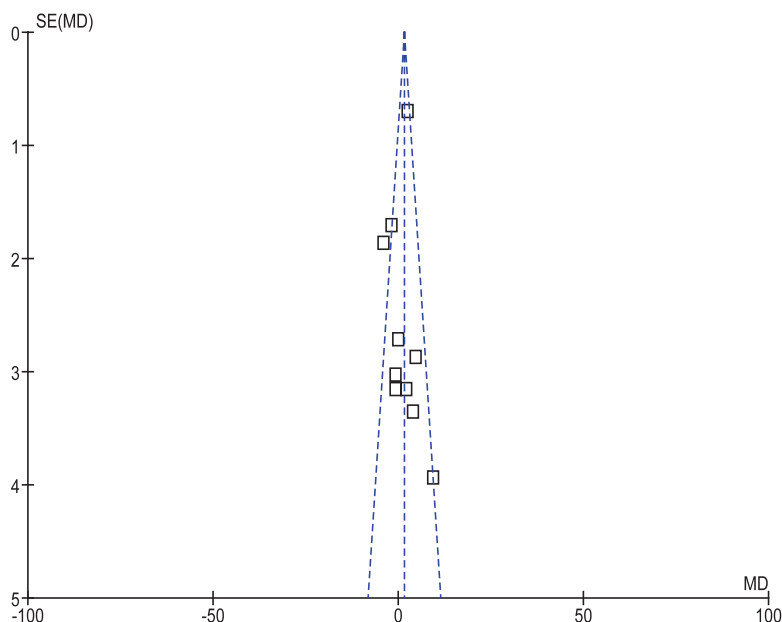


Figure 9. Egger (Funnel) Plot Assessment of Publication Bias for Analysis of Maximal Oxygen Consumption

DISCUSSION

This analysis of live-high train-low (LHTL) altitude training suggests that the hypoxic training method may be superior to sea level training for improving maximal oxygen consumption, serum hemoglobin, peak exercise heart rate, and peak serum lactate. The results must, however, be regarded with a degree of caution because when analyses containing data from the study of Levine [8] (the most heavily weighted study) is removed from the analyses, only change in blood lactate (which did not contain data from Levine) remains statistically significant.

Our sub-analysis demonstrates that the two studies with a minimum of 9.5 hours exposure daily effected the largest change in maximal oxygen consumption, but the small number of studies means this finding should be interpreted cautiously. Previous work suggested a minimum of 12 hours of daily exposure is necessary to produce significant changes in aerobic capacity [9, 10]. Brief intermittent LHTL for 1.5 hours or less per day may not allow improved $\dot{V}O_2$ max, even if exposure altitude is 6,000m [11, 12]. These data imply that performance improvements follow a dose-response relationship based upon hours of daily exposure.

Neither hypoxic exposure duration in days nor altitude level was observed to affect maximal oxygen consumption. Data from two studies shows that it may be beneficial for athletes to go to altitudes between 2,500 to 3,500m for shorter periods (approximately 14 days) around 2-3 weeks before competition to elicit significant changes in maximal $\dot{V}O_2$, but again we reiterate the small number of studies in this analysis warrants caution [6, 13]. Our work confirms the positive effects on performance at exposure altitudes previously recommended (2,500-3,000 m). It is important to highlight that it is uncertain whether training intensity is sacrificed at these altitudes. Levine et al. [14] suggest training intensity

Table 4. Characteristics of Excluded Studies

Study	Organization	Country	No. of Subjects	Reason for Exclusion
Bonetti [2]	Sport Institute	New Zealand	N/A	Review
Clark [23]	University	Australia	33	No relevant data
Nummela [24]	Sport Institute	Finland	8	No relevant data
Hamlin [25]	University	New Zealand	22	No relevant data
Hahn [26]	Sport Institute	Australia	N/A	Review
Hinckson [11]	University	Australia/New Zealand	12	No Relevant data
Julian [22]	Sport Institute/University	US/Australia	14	5 minute hypoxia : normoxia intervals
Katayama [27]	Sport Institute/University	Japan	7	Acute exercise study
Racinais [28]	Sport Institute	Qatar	13	Only 2-day intervention used
Robach [7]	Sport Institute/University	France	11	Duplicate Schmitt [6]
Rodriguez [5]	Sport Institute/University	Europe/US/Australia	23	Duplicate Gore [4]
Robertson [29]	Sport Institute/University	Australia	17	Duplicate Robertson [13]
Robertson [30]	Sport Institute/University	Australia	18	Study design precluded analysis
Saunders [31]	Sport Institute/University	Australia	22	Study design precluded data analysis
Truijens [32]	Sport Institute/University	Europe/US/Australia	23	Sub-maximal data reported
Wehrlin [15]	Sport Institute	Switzerland	10	Non-Randomized, controlled Study
Wilber [1]	Sport Institute	US	N/A	Review
Wood [12]	University	New Zealand	29	No relevant data

is unaffected, but Wehrlin [15] found that in endurance trained athletes performance decrements may occur already at altitudes as low as ~800 m. So consideration may need to be given to living at 800m or below.

Data from the brief intermittent LHTL method was obtained from studies that were conducted at up to 5,500m and supports the suggestion from researchers that extremely high altitudes may prove detrimental in performance outcomes due to decreased training intensity.

As the study of Levine showed the smallest standard deviations in outcome measures, it was given the most weight. We took the approach of removing the study of Levine [8] from analysis, and the outcome measures maximal oxygen consumption, hemoglobin and peak exercise heart rate were no longer statistically significant for between-group comparisons.

Our analysis could not determine whether or not maximal oxygen consumption is the primary determinant of performance following adaptation to hypoxia. Moreover, it is unclear whether improvements in maximal oxygen consumption were due to changes in cardiac function, red cell mass, or respiratory control. It has been argued whether red cell volume is the primary mediator on exercise performance. Levine [8] first addressed individual manipulation with the example of blood doping and injection of erythropoietin, stating it improved maximal oxygen consumption laboratory-based performance and international competition outcomes. These same authors conclude that if maximal oxygen consumption does not increase, then performance does not increase. Red cell mass is the only effect of altitude acclimatization that can be manipulated independently, but changes in maximal oxygen consumption and red cell volume could be affected by non-altitude related reasons such as increased training volume or the participant's higher intensity of interval training [8].

LIMITATIONS

The search strategy was limited to PubMed. The reference lists of identified studies yielded further 'hits', but this was limited to six studies. Only one of four authors of an included study provided extra information. Combined with limited numbers of included studies, this precluded some subgroup analyses. Only post-intervention analyses were used, but there are flaws with this methodology as group data may not be matched at baseline. Randomized controlled trials were used for this analysis to reduce the possibility of a training camp effect in which subjects in an experimental group feed off each other and tend to work harder, leading to a potential for larger between-group effect estimates when compared with the control group. A controlled trial, however, may have a placebo effect meaning control group subjects perform worse and blinding of subjects is difficult in natural LHTL. It is worth noting that only 3 of 11 studies employed blinding, and only one of these was double blind. This highlights the difficulty of implementing blinding in the sport and exercise sciences. More research using a double blind design should be employed, because it would address placebo, placebo and training camp effects in addition to measurement error. As primary data were not available, outcome measures related to iron metabolism may lead to biased analysis, because of obvious gender variations (although studies were generally well matched for gender).

CONCLUSION

Natural and artificial long continuous protocols seem to elicit the greatest effects on performance measures when altitudes between 2,500 to 3,500m are utilized for a minimum of 9.5 hours daily for a period of at least 2 weeks prior to competition.

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