



**HAL**  
open science

## Do male athletes with already high initial haemoglobin mass benefit from ‘live high-train low’ altitude training?

Anna Hauser, Severin Troesch, Thomas Steiner, Franck Brocherie, Olivier Girard, Jonas J Saugy, Laurent Schmitt, Grégoire P Millet, Jon P. Wehrlin

### ► To cite this version:

Anna Hauser, Severin Troesch, Thomas Steiner, Franck Brocherie, Olivier Girard, et al.. Do male athletes with already high initial haemoglobin mass benefit from ‘live high-train low’ altitude training?. *Experimental Physiology*, 2018, 103 (1), pp.68-76. 10.1113/EP086590 . hal-02544357

**HAL Id: hal-02544357**

**<https://insep.hal.science//hal-02544357>**

Submitted on 16 Apr 2020

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L’archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d’enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

## Do male athletes with already high initial hemoglobin mass benefit from ‘live high–train low’ altitude training?

Anna Hauser<sup>1,2</sup>, Severin Troesch<sup>1</sup>, Thomas Steiner<sup>1</sup>, Franck Brocherie<sup>2,3</sup>, Olivier Girard<sup>2,4</sup>, Jonas J. Saugy<sup>2</sup>, Laurent Schmitt<sup>2,5</sup>, Grégoire P. Millet<sup>2\*</sup> and Jon P. Wehrlin<sup>1\*</sup>

<sup>1</sup>Swiss Federal Institute of Sport, Section for Elite Sport, Magglingen, Switzerland

<sup>2</sup>ISSUL, Institute of Sport Sciences, Faculty of Biology and Medicine, University of Lausanne, Switzerland

<sup>3</sup>INSEP, Institut National du Sport de l'Expertise et de la Performance, Paris, France

<sup>4</sup>Aspetar, Orthopaedic and Sports Medicine Hospital, Athlete Health and Performance Research Centre, Doha, Qatar.

<sup>5</sup>National School of Mountain Sports/National Ski-Nordic Centre, Prémamanon, France

\*These authors contributed equally to this work.

### Corresponding author:

Anna Hauser, PhD

Swiss Federal Institute of Sport, Section for Elite Sports

Alpenstrasse 16, 2532 Magglingen, Switzerland

E-mail: [anna.hauser@baspo.admin.ch](mailto:anna.hauser@baspo.admin.ch)

Phone: +41 58 467 64 89

**Running title:** Athletes, initial Hb<sub>mass</sub> and altitude training

**Total word count:** 3506

**Reference count:** 39

This is an Accepted Article that has been peer-reviewed and approved for publication in the Experimental Physiology, but has yet to undergo copy-editing and proof correction. Please cite this article as an Accepted Article; [doi: 10.1113/EP086590](https://doi.org/10.1113/EP086590).

This article is protected by copyright. All rights reserved.

## What is the central question of this study?

It has been assumed that athletes embarking on an LHTL camp with already high initial  $Hb_{mass}$  have a limited ability to further increase their  $Hb_{mass}$  post-intervention. Therefore, the relationship between initial  $Hb_{mass}$  and post-intervention increase were tested with duplicate  $Hb_{mass}$  measures and comparable hypoxic doses in male athletes.

## What is the main finding and its importance?

There were trivial to moderate inverse relationships between initial  $Hb_{mass}$  and percentage  $Hb_{mass}$  increase in endurance and team-sport athletes after LHTL camp, indicating that even athletes with higher initial  $Hb_{mass}$  can reasonably expect  $Hb_{mass}$  gains post-LHTL.

## Abstract

It has been proposed that athletes with high initial values of hemoglobin mass ( $Hb_{mass}$ ) will have a lower  $Hb_{mass}$  increase in response to 'live high-train low' (LHTL) altitude training. To verify this assumption, the relationship between initial absolute and relative  $Hb_{mass}$  values and their respective  $Hb_{mass}$  increase following LHTL in male endurance and team-sport athletes was investigated. Overall, 58 male athletes (35 well-trained endurance athletes and 23 elite male field hockey players) undertook an LHTL training camp with similar hypoxic doses (200-230 h).  $Hb_{mass}$  was measured in duplicate pre- and post-LHTL with the carbon monoxide rebreathing method. While there was no relationship ( $r = 0.02$ ,  $P = 0.91$ ) between initial absolute  $Hb_{mass}$  (g) and percentage increase in absolute  $Hb_{mass}$ , a moderate relationship ( $r = -0.31$ ,  $P = 0.02$ ) between initial relative  $Hb_{mass}$  ( $g \cdot kg^{-1}$ ) and percentage increase in relative  $Hb_{mass}$  was detected. Mean absolute and relative  $Hb_{mass}$  increased to a similar extent ( $P \geq 0.81$ ) in endurance (from  $916 \pm 88$  to  $951 \pm 96$  g, +3.8%,  $P < 0.001$  and from  $13.1 \pm 1.2$  to  $13.6 \pm 1.1$   $g \cdot kg^{-1}$ , +4.1%,  $P < 0.001$ ) and team-sport (from  $920 \pm 120$  to  $957 \pm 127$  g, +4.0%,  $P < 0.001$  and from  $11.9 \pm 0.9$  to  $12.3 \pm 0.9$   $g \cdot kg^{-1}$ , +4.0%,  $P < 0.001$ ) athletes following LHTL. The direct comparison study using individual data of male endurance and team-sport athletes and strict methodological control (duplicate  $Hb_{mass}$ -measures, matched-hypoxic dose) indicated that even athletes with higher initial  $Hb_{mass}$  can reasonably expect  $Hb_{mass}$  gain post-LHTL.

**Key words:** LHTL, hypoxia, CO rebreathing method

This article is protected by copyright. All rights reserved.

## Introduction

**Paragraph Number 1** Many elite endurance athletes perform altitude training with the aim to enhance their oxygen-carrying capacity and eventually their sea-level performance (Wilber, 2007; Bonetti & Hopkins, 2009; Millet *et al.*, 2010). During the last decade, hypoxic/altitude training interventions have become increasingly popular in team sports and innovative methods fitting their physical requirements (combination of aerobic and anaerobic adaptations) have been introduced (McLean *et al.*, 2014; Brocherie *et al.*, 2017). Compared to endurance athletes, team-sport athletes are generally characterised by a lower maximal aerobic capacity (Girard *et al.*, 2013) and possess lower relative hemoglobin mass ( $Hb_{mass}$ ) (Heinicke *et al.*, 2001; Wachsmuth *et al.*, 2013a). The potential main benefit derived from the popular 'live high–train low' (LHTL) altitude training intervention seems to rely on an increase in  $Hb_{mass}$  (Levine & Stray-Gundersen, 2005; Gore *et al.*, 2013; Wehrlin *et al.*, 2016). In a particular sport (e.g. endurance or team sports), considerable individual variation in  $Hb_{mass}$  response to altitude training has been reported (Friedmann *et al.*, 2005; Garvican *et al.*, 2012; Siebenmann *et al.*, 2012; Garvican Lewis *et al.*, 2013; Wachsmuth *et al.*, 2013b) and quantified as a standard deviation (SD) from the mean change of  $\pm 1.7\%$  to  $\pm 2.2\%$  (McLean *et al.*, 2013; Hauser *et al.*, 2017). Although sources of this variability still remain unclear, aspects such as erythropoietic response to hypoxia (Chapman *et al.*, 1998; Friedmann *et al.*, 2005), genetic predisposition (Wilber *et al.*, 2007), residual fatigue and training history (Garvican *et al.*, 2007) and/or intra-individual conditions (Wachsmuth *et al.*, 2013b) likely play a role.

**Paragraph Number 2** Another suggested reason for this variability relies on the individual's initial  $Hb_{mass}$  level before embarking upon the altitude training camp. Hence, it has been proposed that athletes with already high initial  $Hb_{mass}$  have a limited ability to further increase (i.e. ceiling effect) their  $Hb_{mass}$  following altitude training (Gore *et al.*, 1998; Robach & Lundby, 2012; McLean *et al.*, 2013). A recent analysis of nine LHTL studies (Robach & Lundby, 2012) demonstrated a high correlation ( $r = 0.86$ ,  $P < 0.01$ ) between initial relative (expressed in  $g \cdot kg^{-1}$ )  $Hb_{mass}$  and post-intervention percentage increase in relative  $Hb_{mass}$ . However, this analysis had several important limitations, which limit the strength of comparison between the different LHTL training studies. First, different methods (Evans blue dye vs. CO-rebreathing methods) for the determination of  $Hb_{mass}$ , with different accuracy/reliability levels, have been used (Wehrlin *et al.*, 2016). Furthermore, these studies examined different genders - female athletes demonstrate a 10% lower level of  $Hb_{mass}$  compared to male athletes (Schmidt & Prommer, 2008), and 'hypoxic doses' varied greatly – between a total of 200–500 hours of hypoxic exposure. Lastly, the data analysis was based on averaged values and not on individual values. Nevertheless, one should be cautious when interpreting group mean data since considerable inter-individual variation in  $Hb_{mass}$  response to altitude training exists (Friedmann *et al.*, 2005; Garvican *et al.*, 2012; McLean *et al.*, 2013; Hauser *et al.*, 2016).

**Paragraph Number 3** Since LHTL is primarily used by elite endurance athletes typically presenting elevated  $Hb_{mass}$  values compared to team-sport athletes, the hypothesis that athletes embarking on an LHTL camp with already high initial  $Hb_{mass}$  have a limited ability to further increase their  $Hb_{mass}$  post-intervention (or at least to a lower extent than their team-sport counterparts) needs to be

tested with a more robust study design. Thus, the aim of the present study, which reanalyzed already existing data, was to examine the relationship between individual initial  $Hb_{mass}$  prior to LHTL (absolute and relative values) and percentage  $Hb_{mass}$  increase following a LHTL camp with comparable hypoxic doses in male endurance and team-sport athletes.

## Methods

### Ethical approval

**Paragraph Number 4** All altitude training studies were approved by the local ethical committees: Commission Cantonale Valaisanne d’Ethique Médicale, CCVEM (Agreement 051/09), French National Conference of Research Ethics Committees (N°CPP EST I: 2014/33; Dijon, France) and by the Anti-Doping Lab Qatar institutional review board (SCH-ADL-070; Doha, Qatar). All experimental procedures were conducted in accordance with the Declaration of Helsinki guidelines, and all athletes provided written informed consent to participate in the respective studies. The study was not registered in a database.

### Study design

**Paragraph Number 5** Data from three altitude training interventions (studies I, II and III), with similar hypoxic doses (200–230 h) and identical  $Hb_{mass}$  measurement procedures, were re-analysed to determine the nature of the association of individual  $Hb_{mass}$  increase the individual initial absolute and relative  $Hb_{mass}$ . The details of the experimental design of the three altitude training interventions have been published elsewhere (see Study I (Saugy *et al.*, 2014), Study II (Hauser *et al.*, 2016) and Study III (Brocherie *et al.*, 2015)).

### Participants

**Paragraph Number 6** For studies I and II, 35 well-trained male endurance athletes (age  $24.0 \pm 4.5$  years, height  $177.9 \pm 4.8$  cm, weight  $70.2 \pm 6.2$  kg, training 10–12 h per week) were recruited. For study III, 23 elite male field hockey players (age  $24.4 \pm 4.0$  years, height  $179.7 \pm 9.1$  cm, weight  $77.5 \pm 8.7$  kg, training 7–9 h per week) were included. A total of 58 athletes were included in the final sample. Inclusion criteria for analysis were as follows: initial ferritin levels  $>30 \mu\text{g}\cdot\text{L}^{-1}$  (sufficient ferritin stores), male (exclusion confounding factor ‘gender’), endurance or team sport athlete (guarantee high and low initial  $Hb_{mass}$  values within the data analysis) and completion of an LHTL altitude training camp with all  $Hb_{mass}$  measures done in duplicate by the same investigator prior to and after the intervention.

### Altitude interventions

**Paragraph Number 7** For studies I and II (normobaric groups), 24 endurance athletes performed an 18-d LHTL altitude training camp under normobaric hypoxic conditions ( $\sim 12.5 \text{ h}\cdot\text{day}^{-1}$  and  $225 \pm 9$  h total hypoxic dose), during which the athletes trained at  $<1200$  m and were exposed to normobaric

hypoxia equivalent to 2250 m (Wehrlin *et al.*, 2016) in hypoxic rooms ( $P_{iO_2}$   $111.9 \pm 0.6$  mm Hg;  $F_{iO_2}$   $18.1 \pm 0.1\%$ ;  $P_B$   $666.6 \pm 3.6$  mm Hg; 1150 m). For study II (hypobaric group), since normobaric and hypobaric hypoxia induces similar  $Hb_{mass}$  and endurance performance responses after LHTL altitude training (Saugy *et al.*, 2014; Hauser *et al.*, 2016), an additional 11 endurance athletes were included, who completed a 13-d LHTL camp under hypobaric hypoxic conditions with similar total hypoxic hours ( $230 \pm 1$  h,  $\sim 17.5$  h·day<sup>-1</sup>). Those athletes lived at 2250 m ( $P_{iO_2}$   $111.7 \pm 0.7$  mm Hg;  $F_{iO_2}$  20.9%,  $P_B$   $580.8 \pm 3.3$  mm Hg) and trained twice daily at < 1200 m. For study III, all 23 field hockey players performed a 14-d LHTL training camp under normobaric hypoxic conditions (> 14 h·day<sup>-1</sup> and  $\sim 198$  h total hypoxic dose); thereby they trained at sea level and slept in normobaric hypoxic rooms, and simulated altitude was gradually increased from 2500 m ( $P_{iO_2}$  108.3 mm Hg;  $F_{iO_2}$  15.1%,  $P_B$  768.0 mm Hg) up to 3000 m ( $P_{iO_2}$   $101.7 \pm 0.8$  mm Hg;  $F_{iO_2}$   $14.2 \pm 0.1\%$ ,  $P_B$   $765.3 \pm 1.5$  mm Hg) during the 14 days. In addition, they performed six repeated-sprints training sessions during the 14-d training camp either in normoxia ( $F_{iO_2}$  20.9%;  $n=12$ ) or normobaric hypoxic conditions (3000 m;  $F_{iO_2} \sim 14.5\%$ ;  $n=11$ ). In summary, according to the definition of Garvican-Lewis *et al.* (2016), the metrics for hypoxic dose (in km.h) between the LHTL groups were similar and differed within 6%, assuming that the present hypoxic doses were comparable (table 1).

\*\*\*Table 1 near here\*\*\*

## Hemoglobin mass

**Paragraph Number 8** In all athletes,  $Hb_{mass}$  was measured in duplicate using a slightly modified version (Steiner & Wehrlin, 2011) of the optimised carbon monoxide (CO)-rebreathing method described by Schmidt and Prommer (2005). For details, see Hauser *et al.* (2016) and Brocherie *et al.* (2015). Both measurements were performed on two consecutive days (12–24 h time lag between the measures), and the results were averaged. The typical error (TE) was calculated from duplicate measurements as the SD of the difference score divided by  $\sqrt{2}$  (Hopkins, 2000). In our mobile laboratories, the TEs ranged between 1.6% and 2.0%. Since duplicate measurements reduce the TE by a factor of  $1/\sqrt{2}$  (Hopkins, 2000), the TEs for averaged duplicate  $Hb_{mass}$  measurements ranged between 1.1% and 1.4%. For each athlete,  $Hb_{mass}$  measures were performed by the same investigator throughout the studies.

## Data analysis

**Paragraph Number 9** Values are presented as means  $\pm$  SD. All data were checked for normality (Shapiro-Wilk test). A sample size estimation for a power of 0.8 (80%), a significance level at  $P = 0.05$  and a correlation coefficient of  $r = 0.4$  was performed and resulted in a minimal number of 46 subjects. Linear regressions were used to determine the Pearson's product-moment correlation coefficients ( $r$ ) between initial absolute and relative  $Hb_{mass}$  and their respective percent changes in  $Hb_{mass}$ , as well as for percent changes between body weight and  $Hb_{mass}$ . The standard error (SE) of the slope of the linear regression was calculated by bootstrapping. Correlation size was interpreted using the correlation classification of Hopkins (Hopkins *et al.*, 2009): trivial ( $r < 0.1$ ), small ( $0.1 < r <$

0.3), moderate ( $0.3 < r < 0.5$ ), large ( $0.5 < r < 0.7$ ), very large ( $0.7 < r < 0.9$ ), nearly perfect ( $r > 0.9$ ) and perfect ( $r = 1.0$ ). Multiple linear regression analysis was used to determine the effect of body weight changes and initial  $Hb_{mass}$  ( $g \cdot kg^{-1}$ ) on percent changes in relative  $Hb_{mass}$ . Paired *t*-tests were conducted to compare pre- and post-values in  $Hb_{mass}$  and body weight within the athlete group. An unpaired *t*-test was performed to compare percent changes between endurance and team-sport athletes. The level of significance was set at  $P < 0.05$ . All analyses were processed using Sigmaplot 11.0 (Systat Software, San Jose, CA) and the statistical software package R (Vienna, Austria).

## Results

### Relationship between initial $Hb_{mass}$ and $Hb_{mass}$ increase

**Paragraph Number 10** There was no relationship between the absolute initial  $Hb_{mass}$  (g) and the percentage increase in absolute  $Hb_{mass}$  ( $r = 0.02$ ,  $P = 0.91$ ) (Figure 1 A). The linear regression equation for absolute  $Hb_{mass}$  was  $y = -0.0004x + 3.5$  and the SE of the slope was  $\pm 0.003$ . A moderate negative correlation between the relative initial  $Hb_{mass}$  ( $g \cdot kg^{-1}$ ) and the percentage increase in relative  $Hb_{mass}$  ( $r = -0.31$ ,  $P = 0.02$ ) was observed (Figure 1 B). The linear regression equation for relative  $Hb_{mass}$  was  $y = -0.98x + 16.4$  and the SE of the slope was  $\pm 0.348$ . When, including body weight changes (%) to the multiple linear regression model (initial  $Hb_{mass}$  ( $g \cdot kg^{-1}$ )  $\times$  body weight changes (%)) the initial relative  $Hb_{mass}$  ( $g \cdot kg^{-1}$ ) was no longer significantly associated with percentage increase in  $Hb_{mass}$  ( $g \cdot kg^{-1}$ ) ( $P = 0.4$ ).

\*\*\*Figure 1 near here\*\*\*

### Mean $Hb_{mass}$ response

**Paragraph Number 11** Mean absolute  $Hb_{mass}$  increased to the same extent in endurance ( $916 \pm 88$  to  $951 \pm 96$  g,  $+3.8 \pm 2.9\%$ ,  $P < 0.001$ ) and team-sport ( $920 \pm 120$  to  $957 \pm 127$  g,  $+4.0 \pm 2.9\%$ ,  $P < 0.001$ ) athletes ( $P = 0.81$ ). Mean relative  $Hb_{mass}$  increased equally in endurance ( $13.1 \pm 1.2$  to  $13.6 \pm 1.1$   $g \cdot kg^{-1}$ ,  $+4.1 \pm 4.2\%$ ,  $P < 0.001$ ) and team-sport ( $11.9 \pm 0.9$  to  $12.3 \pm 0.9$   $g \cdot kg^{-1}$ ,  $+4.0 \pm 3.2\%$ ,  $P < 0.001$ ) athletes ( $P = 0.94$ ).

### Body weight

**Paragraph Number 12** The mean pre-body weight for endurance and team-sport athletes was  $70.2 \pm 6$  kg and  $77.5 \pm 9$  kg, respectively, while the mean post-body weight was  $70.0 \pm 6$  kg and  $77.4 \pm 8$  kg, respectively. The changes pre- to post-body weight did not differ between the groups ( $P \geq 0.53$ ). There was no relationship ( $r = -0.006$ ,  $P = 0.96$ ) between individual percent changes in body weight

and absolute  $Hb_{mass}$  (Figure 2 A). A large inverse relationship ( $r = -0.64$ ,  $P < 0.001$ ) occurred between individual percent changes in body weight and relative  $Hb_{mass}$  (Figure 2 B). Further, the multiple linear regression model for percent changes in relative  $Hb_{mass}$  (initial  $Hb_{mass}$  ( $g \cdot kg^{-1}$ )  $\times$  body weight changes (%)) showed that percent changes in body weight were significantly associated with percent changes in  $Hb_{mass}$  ( $g \cdot kg^{-1}$ ) ( $P < 0.001$ ).

\*\*\*Figure 2 near here\*\*\*

## Discussion

**Paragraph Number 13** To our knowledge, the present study is the first to demonstrate trivial (absolute values) to moderate (relative values) relationships between initial  $Hb_{mass}$  and percentage change in  $Hb_{mass}$  following LHTL altitude training in male endurance and team-sport athletes using individual data. Mean absolute and relative  $Hb_{mass}$  increased to the same extent in endurance and team-sport athletes following sport-specific LHTL interventions. Further, a large inverse relationship occurred between individual percent changes in body weight and relative  $Hb_{mass}$ .

### Effect of absolute initial $Hb_{mass}$ on $Hb_{mass}$ response

**Paragraph Number 14** The observed trivial relationship ( $r = 0.02$ ) between absolute initial  $Hb_{mass}$  and percentage changes in absolute  $Hb_{mass}$  might suggest that absolute initial  $Hb_{mass}$  in our athlete cohort had no impact in regard to further  $Hb_{mass}$  improvements following LHTL. Thus far, no study has focused on this relationship using absolute  $Hb_{mass}$  values, with the rationale that absolute  $Hb_{mass}$  values are not an indicator for an individual's maximal aerobic capacity (Gore *et al.*, 1998; Lundby *et al.*, 2012; Robach & Lundby, 2012). However, to precisely evaluate the sole effect of initial  $Hb_{mass}$  on  $Hb_{mass}$  response to altitude training both absolute and relative  $Hb_{mass}$  values should be assessed to exclude the confounding factor 'body weight changes' during altitude training. Further, the average percentage increase in absolute  $Hb_{mass}$  was of a similar magnitude in endurance and team-sport athletes (+3.8 vs. +4.0%). This increase is in accordance with LHTL studies of similar total hypoxic hours (230–240 h), showing a measurable mean absolute  $Hb_{mass}$  increase in elite triathletes (+3.2%) (Humberstone-Gough *et al.*, 2013) and semi-professional Australian Footballers (+6.7%) (Inness *et al.*, 2016). Furthermore, to better fit the team sport's physical requirements, some team-sport athletes in the present study performed a combination of LHTL and repeated-sprints training sessions in hypoxia, the so-called 'live high–train low and high' method (Brocherie *et al.*, 2015). However, since mean  $Hb_{mass}$  response did not differ between the two hypoxic groups (LHTL vs. LHTL and high), it seems that the additional hypoxic sprints had no beneficial effect on mean  $Hb_{mass}$  response. Overall, in the present sample absolute initial  $Hb_{mass}$  demonstrated no adverse effect for further absolute  $Hb_{mass}$  improvement following LHTL.

## Effect of relative initial $Hb_{mass}$ on $Hb_{mass}$ response

**Paragraph Number 15** We found a moderate inverse correlation between initial relative  $Hb_{mass}$  and percentage increase in relative  $Hb_{mass}$  ( $r = -0.31$ ) following LHTL. Compared to the analysis of Robach and Lundby (2012) and a classic altitude training study on Australian footballers (McLean *et al.*, 2013), the present correlation coefficient was much smaller than in those studies ( $r = -0.51$  to  $-0.86$ ). The above mentioned studies suggested that athletes starting with high relative  $Hb_{mass}$  levels have smaller chances to further increase their relative  $Hb_{mass}$  following altitude training, with the rationale that those athletes would already have maximized their relative  $Hb_{mass}$  level by training at sea level (Robach & Lundby, 2012; McLean *et al.*, 2013). However, in the present study it seems that the moderate inverse relationship between initial relative  $Hb_{mass}$  and percent change in relative  $Hb_{mass}$  could not be attributed to the physiological limit of an athlete.

**Paragraph Number 16** Changes in an individual's body weight from pre- to post- intervention could explain the moderate relationship between initial relative  $Hb_{mass}$  and its percentage  $Hb_{mass}$  increase following LHTL. There was a large inverse relationship ( $r = -0.64$ ) between individual percent changes in body weight and relative  $Hb_{mass}$ , whereas no relationship between individual percent changes in body weight and absolute  $Hb_{mass}$  occurred. Further, percent changes in body weight were significantly associated with percent changes in relative  $Hb_{mass}$  ( $P < 0.001$ ) in contrast to initial relative  $Hb_{mass}$  ( $P = 0.4$ ). This assumes that, primarily, individual changes in body weight from pre- to post LHTL camp led to the moderate relationship between initial relative  $Hb_{mass}$  and percent change in  $Hb_{mass}$  following LHTL camp. Whether the body weight changes were due to alterations in fat and/or muscle mass or because of the weekly fluctuation in body weight/fluid (Orsama *et al.*, 2014) remains unclear. With a lack of significant relationship between individual changes in body weight and absolute  $Hb_{mass}$ , it can be assumed that body weight alterations did not negatively influence absolute  $Hb_{mass}$  response in the present study. Thus, we propose that lean body mass-adjusted relative  $Hb_{mass}$  values would be a better unit for future comparisons.

**Paragraph Number 17** A further point that must be considered when assessing the relationship between change and initial values, is the statistical phenomenon 'regression to the mean' (Galton, 1886; Bland & Altman, 1994). Although in the present study there was no relationship between initial absolute  $Hb_{mass}$  and percent changes in absolute  $Hb_{mass}$ , the 'regression to the mean' effect could have still appeared. Further, since individual changes in body weight from pre- to post-LHTL camp occurred, it could also be possible that the 'regression to the mean' effect arose within the relationship between initial body weight and body weight changes. This makes the speculation that part of the inverse relationship between initial relative  $Hb_{mass}$  and percent changes in relative  $Hb_{mass}$  following LHTL camp could be due to the statistical phenomenon 'regression to the mean'. However, this needs to be confirmed with a larger dataset, involving athletes of different performance levels and from various sport disciplines as well as using different altitude training paradigms with various characteristics (e.g., duration, altitude severity, hypobaric vs. normobaric hypoxia). Lastly, one should also keep in mind that the chosen metric for total 'hypoxic dose', i.e., 'kilometre hours' (Garvican Lewis *et al.*, 2016), is still debated in the literature (Millet *et al.*, 2016).

## Conclusion

**Paragraph Number 18** Our results indicate that trivial (absolute values) to moderate (relative values) relationships occurred between initial  $Hb_{mass}$  and  $Hb_{mass}$  increase following LHTL altitude training in endurance and team-sport athletes. This indicates that even athletes with higher initial  $Hb_{mass}$  can reasonably expect  $Hb_{mass}$  gains post-LHTL. Further, it seems that in the present study the moderate relationship between initial relative  $Hb_{mass}$  and percentage increase in relative  $Hb_{mass}$  following LHTL could be attributed to changes in body weight and possibly to the statistical phenomenon ‘regression to the mean’, rather than to a pure physiological effect.

## Additional information

### Conflict of Interest

The authors have no conflicts of interest.

### Author Contributions

All authors performed the research and analysed or interpreted the data for the work. JPW, GPM, OG, LS and AH conceived and designed the research. AH, ST, JPW and GPM drafted the manuscript. All authors edited and revised the manuscript critically and approved the final version of the manuscript. All authors agree to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.

### Funding

This study was financially supported by the Federal Office of Sport (FOSPO; Switzerland), by the Ministère des Sports, de la Jeunesse, de l’Education Populaire et de la Vie Associative (MSJEPVA)/Institut National du Sport, de l’Expertise et de la Performance (INSEP, France) and by a grant awarded by Aspetar (Qatar Orthopedic and Sports Medicine Hospital) at the Aspire Zone Foundation, Qatar (AF/C/ASP1905/11).

### Acknowledgements

The authors thank the staff of the National Ski-Nordic Centre (Prémanon, France), of Aspetar and of the Fierendorf Center (Fiesch, Switzerland) for their administrative and technical support as well as providing their facilities. Last but not least, the authors acknowledge the dedicated participants, as well as their technical staff for their gracious compliance and cooperation during training and testing.

This article is protected by copyright. All rights reserved.

## References

- Bland JM & Altman DG (1994). Regression towards the mean. *BMJ (Clinical research ed.)* **308**, 1499.
- Bonetti DL & Hopkins WG (2009). Sea-level exercise performance following adaptation to hypoxia: a meta-analysis. *Sports Med* **39**, 107-127.
- Brocherie F, Girard O, Faiss R & Millet GP (2017). Effects of Repeated-Sprint Training in Hypoxia on Sea-Level Performance: A Meta-Analysis. *Sports Med*.
- Brocherie F, Millet GP, Hauser A, Steiner T, Rysman J, Wehrlin JP & Girard O (2015). "Live High-Train Low and High" Hypoxic Training Improves Team-Sport Performance. *Med Sci Sports Exerc* **47**, 2140-2149.
- Chapman RF, Stray-Gundersen J & Levine BD (1998). Individual variation in response to altitude training. *J Appl Physiol (1985)* **85**, 1448-1456.
- Friedmann B, Frese F, Menold E, Kauper F, Jost J & Bartsch P (2005). Individual variation in the erythropoietic response to altitude training in elite junior swimmers. *Br J Sports Med* **39**, 148-153.
- Galton F (1886). Regression towards mediocrity in hereditary stature. *The Journal of the Anthropological Institute of Great Britain and Ireland* **15**, 246-263.
- Garvican LA, Martin DT, Clark SA, Schmidt WF & Gore CJ (2007). Variability of erythropoietin response to sleeping at simulated altitude: a cycling case study. *Int J Sports Physiol Perform* **2**, 327-331.
- Garvican LA, Martin DT, Quod M, Stephens B, Sassi A & Gore CJ (2012). Time course of the hemoglobin mass response to natural altitude training in elite endurance cyclists. *Scand J Med Sci Sports* **22**, 95-103.
- Garvican Lewis LA, Clark SA, Polglaze T, McFadden G & Gore CJ (2013). Ten days of simulated live high:train low altitude training increases Hbmass in elite water polo players. *Br J Sports Med* **47 (Suppl 1)**, i70-73.
- Garvican Lewis LA, Sharpe K & Gore CJ (2016). Time for a new metric for hypoxic dose? *J Appl Physiol (1985)* **121**, 352-355.
- Girard O, Amann M, Aughey R, Billaut F, Bishop DJ, Bourdon P, Buchheit M, Chapman R, D'Hooghe M, Garvican-Lewis LA, Gore CJ, Millet GP, Roach GD, Sargent C, Saunders PU, Schmidt W & Schumacher YO (2013). Position statement--altitude training for improving team-sport

players' performance: current knowledge and unresolved issues. *Br J Sports Med* **47** (Suppl 1), i8-16.

Gore CJ, Hahn A, Rice A, Bourdon P, Lawrence S, Walsh C, Stanef T, Barnes P, Parisotto R, Martin D & Pyne D (1998). Altitude training at 2690m does not increase total haemoglobin mass or sea level VO<sub>2</sub>max in world champion track cyclists. *J Sci Med Sport* **1**, 156-170.

Gore CJ, Sharpe K, Garvican-Lewis LA, Saunders PU, Humberstone CE, Robertson EY, Wachsmuth NB, Clark SA, McLean BD, Friedmann-Bette B, Neya M, Pottgiesser T, Schumacher YO & Schmidt WF (2013). Altitude training and haemoglobin mass from the optimised carbon monoxide rebreathing method determined by a meta-analysis. *Br J Sports Med* **47** (Suppl 1), i31-39.

Hauser A, Schmitt L, Troesch S, Saugy JJ, Cejuela-Anta R, Faiss R, Robinson N, Wehrin JP & Millet GP (2016). Similar Hemoglobin Mass Response in Hypobaric and Normobaric Hypoxia in Athletes. *Med Sci Sports Exerc* **48**, 734-741.

Hauser A, Troesch S, Saugy JJ, Schmitt L, Cejuela-Anta R, Faiss R, Steiner T, Robinson N, Millet GP & Wehrin JP (2017). Individual hemoglobin mass response to normobaric and hypobaric "live high-train low": A one-year crossover study. *Journal of Applied Physiology* **123**, 387-393.

Heinicke K, Wolfarth B, Winchenbach P, Biermann B, Schmid A, Huber G, Friedmann B & Schmidt W (2001). Blood volume and hemoglobin mass in elite athletes of different disciplines. *Int J Sports Med* **22**, 504-512.

Hopkins WG (2000). Measures of Reliability in Sports Medicine and Science. *Sports Med* **30**, 1-15.

Hopkins WG, Marshall SW, Batterham AM & Hanin J (2009). Progressive statistics for studies in sports medicine and exercise science. *Med Sci Sports Exerc* **41**, 3-13.

Humberstone-Gough CE, Saunders PU, Bonetti DL, Stephens S, Bullock N, Anson JM & Gore CJ (2013). Comparison of Live High: Train Low Altitude and Intermittent Hypoxic Exposure. *J Sports Sci Med* **12**, 394-401.

Inness MWH, Billaut F & Aughey RJ (2016). Live-high train-low improves repeated time-trial and Yo-Yo IR2 performance in sub-elite team-sport athletes. *J Sci Med Sport* **20**, 190-195.

Levine BD & Stray-Gundersen J (2005). Point: positive effects of intermittent hypoxia (live high:train low) on exercise performance are mediated primarily by augmented red cell volume. *J Appl Physiol* (1985) **99**, 2053-2055.

Lundby C, Millet GP, Calbet JA, Bartsch P & Subudhi AW (2012). Does 'altitude training' increase exercise performance in elite athletes? *Br J Sports Med* **46**, 792-795.

- McLean BD, Buttifant D, Gore CJ, White K & Kemp J (2013). Year-to-year variability in haemoglobin mass response to two altitude training camps. *Br J Sports Med* **47 (Suppl 1)**, i51-58.
- McLean BD, Gore CJ & Kemp J (2014). Application of 'Live Low-Train High' for Enhancing Normoxic Exercise Performance in Team Sport Athletes. *Sports Med* **44**, 1275-1287.
- Millet GP, Brocherie F, Girard O, Wehrin JP, Troesch S, Hauser A, Steiner T, Peltonen JE, Rusko HK, Constantini K, Fulton TJ, Hursh DG, Noble TJ, Paris HL, Wiggins CC, Chapman RF, Levine BD, Kumar VH & Schmidt WF (2016). Commentaries on Viewpoint: Time for a new metric for hypoxic dose? *J Appl Physiol (1985)* **121**, 356-358.
- Millet GP, Roels B, Schmitt L, Woorons X & Richalet JP (2010). Combining hypoxic methods for peak performance. *Sports Med* **40**, 1-25.
- Orsama AL, Mattila E, Ermes M, van Gils M, Wansink B & Korhonen I (2014). Weight rhythms: weight increases during weekends and decreases during weekdays. *Obes Facts* **7**, 36-47.
- Robach P & Lundby C (2012). Is live high-train low altitude training relevant for elite athletes with already high total hemoglobin mass? *Scand J Med Sci Sports* **22**, 303-305.
- Saugy JJ, Schmitt L, Cejuela R, Faiss R, Hauser A, Wehrin JP, Rudaz B, Delessert A, Robinson N & Millet GP (2014). Comparison of "Live High-Train Low" in normobaric versus hypobaric hypoxia. *PLoS One* **9**, e114418.
- Schmidt W & Prommer N (2005). The optimised CO-rebreathing method: a new tool to determine total haemoglobin mass routinely. *Eur J Appl Physiol* **95**, 486-495.
- Schmidt W & Prommer N (2008). Effects of various training modalities on blood volume. *Scand J Med Sci Sports* **18 Suppl 1**, 57-69.
- Siebenmann C, Robach P, Jacobs RA, Rasmussen P, Nordsborg N, Diaz V, Christ A, Olsen NV, Maggiorini M & Lundby C (2012). "Live high-train low" using normobaric hypoxia: a double-blinded, placebo-controlled study. *J Appl Physiol (1985)* **112**, 106-117.
- Steiner T & Wehrin JP (2011). Does hemoglobin mass increase from age 16 to 21 and 28 in elite endurance athletes? *Med Sci Sports Exerc* **43**, 1735-1743.
- Wachsmuth NB, Kley M, Spielvogel H, Aughey RJ, Gore CJ, Bourdon PC, Hammond K, Sargent C, Roach GD, Sanchez RS, Claros JC, Schmidt WF & Garvican-Lewis LA (2013a). Changes in blood gas transport of altitude native soccer players near sea-level and sea-level native soccer players at altitude (ISA3600). *Br J Sports Med* **47 (Suppl 1)**, i93-99.

Wachsmuth NB, Volzke C, Prommer N, Schmidt-Trucksass A, Frese F, Spahl O, Eastwood A, Stray-Gundersen J & Schmidt W (2013b). The effects of classic altitude training on hemoglobin mass in swimmers. *Eur J Appl Physiol* **113**, 1199-1211.

Wehrlin JP, Marti B & Hallen J (2016). Hemoglobin Mass and Aerobic Performance at Moderate Altitude in Elite Athletes. *Adv Exp Med Biol* **903**, 357-374.

Wilber RL (2007). Application of altitude/hypoxic training by elite athletes. *Med Sci Sports Exerc* **39**, 1610-1624.

Wilber RL, Stray-Gundersen J & Levine BD (2007). Effect of hypoxic "dose" on physiological responses and sea-level performance. *Med Sci Sports Exerc* **39**, 1590-1599.

**Table 1.** Characteristics of the altitude training interventions

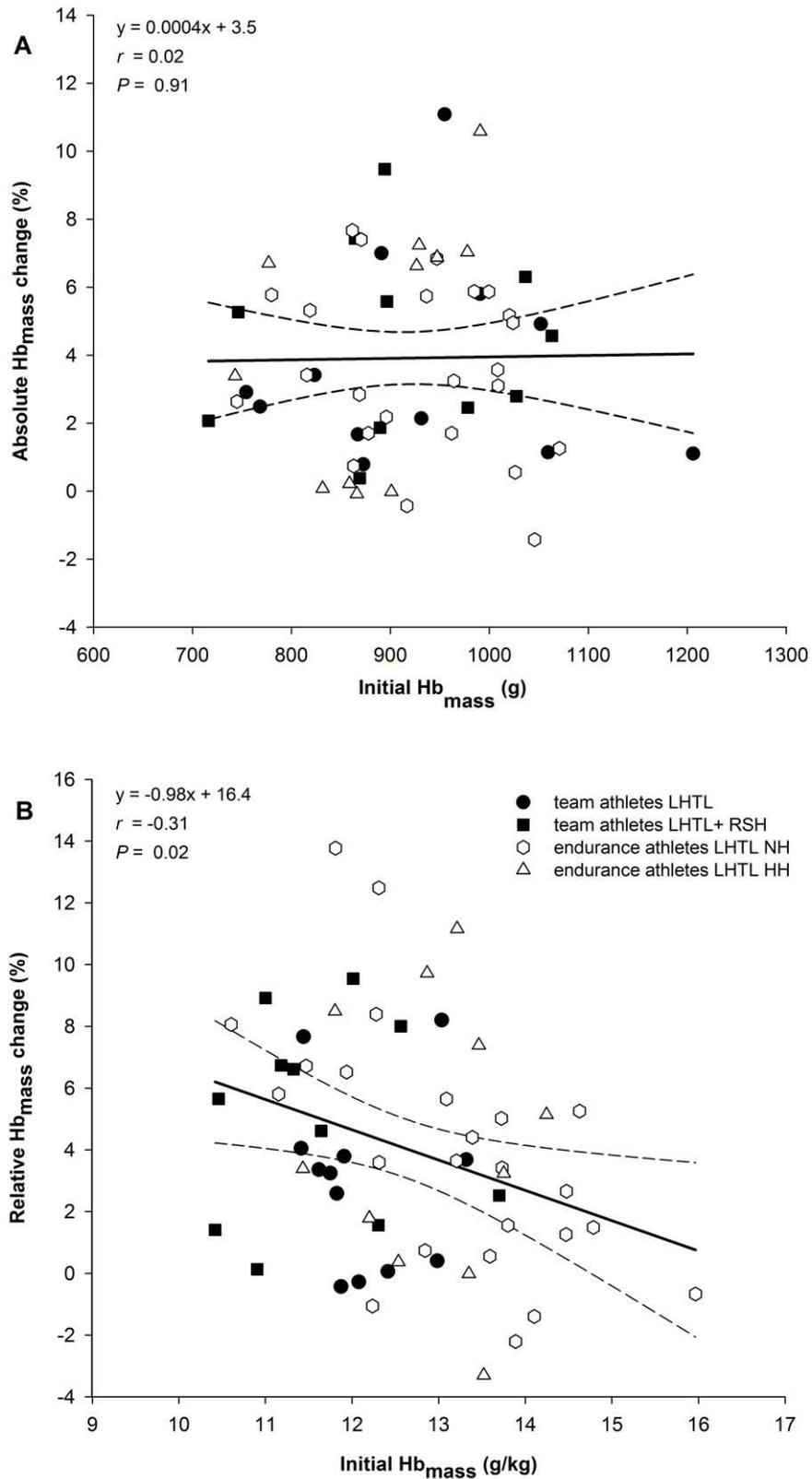
Data source	n	Sport	Altitude mode	Hypoxic mode	Altitude (m)	Duration (days)	Daily exposure (h)	Hypoxic dose (h)	Hypoxic dose (km.h)
Study I & II	24	triathlon	LHTL	NH	2250	18	12.5	225	506
Study II	11	triathlon	LHTL	HH	2250	13	17.5	230	518
Study III	11	hockey	LHTL	NH	2500-3000	14	14	200	545
	12	hockey	LHTL+RSH	NH	2500-3000	14	14	200	545

LHTL = live high-train low; RSH = repeated-sprints in hypoxia; NH = normobaric hypoxia; HH = hypobaric hypoxia.

## Figure legends

**Figure 1. (A)** Linear regression between the individual's initial absolute  $Hb_{mass}$  (g) and the individual's absolute  $Hb_{mass}$  change (%) following LHTL. **(B)** Linear regression between the individual's initial

relative  $Hb_{mass}$  (g/kg) and the individual's relative  $Hb_{mass}$  change (%) following LHTL. Regression slope (solid line) and 95% confidence limits (dashed lines) are shown.  $n = 58$ . LHTL = live high–train low, RSH = repeated-sprints in hypoxia, NH = normobaric hypoxia, HH = hypobaric hypoxia.



**Figure 2.** Linear regression between individual body weight change (%) and **(A)** individual absolute  $Hb_{mass}$  change (%) and **(B)** individual relative  $Hb_{mass}$  change (%) following LHTL. Regression slope (solid line) and 95% confidence limits (dashed lines) are shown.  $n = 58$ .

