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ORGINAL ARTICLE

Influence of immune and nutritional biomarkers on illness risk during interval training

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Abstract

Intensive training periods may negatively influence immune function, but the immunological consequences of specific high-intensity training (HIT) prescriptions are not well defined. **Purpose:** This study explored whether three different HIT prescriptions influence multiple health-related biomarkers and whether biomarker responses to HIT were associated with upper respiratory illness (URI) risk. **Methods:** Twenty-five male cyclists and triathletes were randomised to three HIT groups and completed twelve HIT sessions over four weeks. Peak oxygen consumption ($\dot{V}O_{2peak}$) was determined using an incremental cycling protocol, while resting serum biomarkers (cortisol, testosterone, 25(OH)D and ferritin), salivary immunoglobulin-A (s-IgA) and energy availability (EA) were assessed before and after the training intervention. Participants self-reported upper respiratory symptoms during the intervention and episodes of URI were identified retrospectively. **Results:** Fourteen athletes reported URIs, but there were no differences in incidence, duration or severity between groups. Increased risk of URI was associated with higher s-IgA secretion rates (odds ratio=0.90, 90% CI:0.83-0.97). Lower pre-intervention cortisol and higher EA predicted a 4% increase in URI duration. Participants with higher $\dot{V}O_{2peak}$ reported higher total symptom scores (incidence rate ratio=1.07, 90% CI:1.01-1.13). **Conclusions:** Although multiple biomarkers were weakly associated with risk of URI, the direction of associations between s-IgA, cortisol, EA and URI risk were inverse to previous observations and physiological rationale. There was a cluster of URIs within the first week of the training intervention, but no samples were collected at this time-point. Future studies should incorporate more frequent sample time-points, especially around the onset of new training regimes, and include athletes with suspected or known nutritional deficiencies.

Key words: Endurance athletes, HIT, immunity, training load, URTI

Introduction

Trained endurance athletes often undertake a training intensity distribution including large volumes (≥80%) of low intensity training (LIT) with smaller volumes of moderate-intensity training near the lactate threshold (5-15%) and high-intensity training (HIT; <10%), typically distributed in a pyramidal or polarized model.[1] HIT encompasses training prescriptions where up to nine variables can be manipulated, including work interval intensity and duration, intensity and duration of recovery between bouts and series, number of repetitions and series as well as exercise modality.[2] Consequently, different HIT prescriptions induce different physiological, perceptual and performance responses. For example, four weeks of longer accumulated HIT duration (4 × 16 min) has been shown to elicit greater improvements in peak power output and peak oxygen consumption ($\dot{V}O_{2peak}$) compared to shorter duration HIT (4 × 4 min), despite lower heart rates (HR), blood lactate concentrations, ratings of perceived exertion (RPE) and a less pronounced steroid hormone response.[3] However, it is unclear how different interval training prescriptions influence athletes' health and immune status.

Training availability is critical for athletic performance[4] since being free from illness and injury permits athletes to maintain consistent, heavy training loads throughout the year. Intensified training periods[5,6] and sharp increases in training load[6,7] are risk factors that may increase the incidence of self-reported upper respiratory symptoms (URS) or upper respiratory illness (URI) in athletes. High training loads are commonly associated with immunological disturbances such as decreases in salivary secretory IgA (s-IgA) secretion rate,[7,8] and elevated cortisol levels.[7] Furthermore, low energy availability (LEA), vitamin D and iron deficiency may compromise immune function in athletes.[9] Although studies have explored the relative importance of multiple training- and lifestyle-related risk factors for illness in athletes,[10,11] to

our knowledge no studies have modeled nutritional risk factors such as LEA, low vitamin D- and iron status in combination with traditional markers such as cortisol and s-IgA.

The purpose of this study was therefore to compare the cumulative effects of a four-week HIT intervention, performed either as short or long intervals totaling the same accumulated work duration (AWD), on URI incidence and biomarkers of immunity, stress and nutritional status. We then aimed to explore the relationship between baseline immune, stress and nutritional biomarkers and URI incidence during HIT in well-trained male cyclists and triathletes. We hypothesized that there would be no difference between the groups' immune responses to the three different HIT protocols, but that either low salivary s-IgA, high cortisol, LEA, poor vitamin D and iron status before the training intervention or a combination of these markers would be associated with a higher incidence of URI during four weeks' HIT.

Methods

Study design

In a randomized design, participants were allocated to three groups who each undertook a four-week training intervention. In groups, participants completed three HIT sessions each week supplemented with *ad libitum* LIT. We measured $\dot{V}O_{2peak}$, energy availability (EA) and blood and salivary biomarkers before and after the intervention. To analyse the relationship between baseline biomarkers and risk of URI, the three groups were treated as one cohort.

Participants

Twenty-seven well-trained male cyclists and triathletes participated in the study of whom twenty-five were included in the data analyses (age: 29.9 ± 9.1 y, $\dot{V}O_{2peak}$: 64.0 ± 6.4 $mL \cdot kg^{-1} \cdot min^{-1}$; 'performance level' 3-4[12]). Participants were free from chronic disease and injury and performed at least three cycling sessions per week. One participant did not complete the study and one participant was excluded from data analysis due to non-compliance. The study was approved by the ethics committee of the Faculty for Health and Sports Science,

University of Agder, Norway. Participants provided written, informed consent and all testing complied with the Declaration of Helsinki.

Baseline and follow-up measurements

Participants visited the lab for two consecutive days before and after the HIT intervention (Figure 1). On day 1, participants provided a rested, fasted venous blood sample and passive drool saliva sample to assess immune, stress and nutritional biomarkers. Samples were collected between 06:00-08:00. On day 2, participants completed a battery of exercise tests including determination of $\dot{V}O_{2peak}$ according to a protocol previously described.[13]

Energy availability

On days 3-6 pre- and post-training, participants registered their energy intake (EI) using a digital kitchen scale and Dietist Net software (Kost och Näringsdata, Bromma, Sweden), and exercise energy expenditure (EEE) in their home environment mirroring their typical food patterns and training regime according a protocol previously described.[13] Participants recorded all training sessions using a HR monitor (Polar M400), and EEE was calculated using the equations described by Crouter et al.[14] EA was calculated by subtracting EEE from daily EI relative to fat-free mass (FFM) assessed by Dual-energy X-ray absorptiometry (Lunar Prodigy, EnCore v. 15, GE Medical Systems, 3030 Ohmeda Drive, Madison, WI, USA).

Training intervention

The four-week training intervention took place in Agder, Norway in November-December. Participants completed twelve supervised HIT sessions in groups, and were permitted to perform additional *ad libitum* LIT. For the duration of the intervention, participants were assigned to one of three HIT groups:

- LI – 4 × 8 min intervals with 2-min recovery periods (32 min AWD).
- SI1 – 4 × (12 × 40/20 s) intervals with 2-min recovery periods (32 min AWD if the 20-s recovery is not included in the total HIT duration).
- SI2 – 4 × (8 × 40/20 s) intervals with 2-min recovery periods (32 min AWD if the 20-s recovery is included in the total HIT duration).

The short interval sessions were designed to match the AWD of the long interval group, depending on whether the brief 20 s recovery period was included (SI2) or not (SI1) in the overall calculation of AWD. This design enabled the evaluation of the role of both interval modality and AWD on immune responses to training. Participants completed the HIT sessions on their own bikes mounted on electromagnetic rollers (Computrainer LabTM ergometers, Race Mate, Seattle, WA, USA). HR was monitored continuously throughout each session. Sessions started with a 20-30-min low-intensity warm up (55-70% maximum HR [HR_{max}]) interspersed by self-paced progressive sprints, and ended with 15-20 min cool down (55-70% HR_{max}). Participants were instructed to perform each HIT session at their maximal sustainable intensity (isoeffort).[15] RPE for the previous series (Borg 6-20 scale) was reported during the 2-min recovery periods. Power output during the recovery periods was 50% of the power output used during work intervals. If participants were unwell they were instructed to perform the session within the week in their own time at home. Two participants in the SI1 group missed a full week of training due to URI and completed an extra training week at the end of the intervention period.

Interim measures

During the intervention period, participants recorded the volume of *ad libitum* LIT undertaken in addition to the HIT sessions, and completed a Norwegian translation of the Jackson Common Cold questionnaire[16] (JCCQ) daily.

Questionnaire analysis

The JCCQ consists of one global question *'Do you think you have a common cold today'* followed by eight symptom items scored from 0-3.[16] One day of URI was defined as a day where participants had answered *'yes'* to the global question for two consecutive days[17] or reported a cumulative symptom score ≥14 during the previous seven days.[16] A new episode of URI was counted after seven consecutive days without URI.[11] Total symptom score represents the sum of all symptom scores recorded during the four-week training intervention. Peak severity represents the highest seven-day cumulative symptom score during the intervention. Participants who did not satisfy the criteria for URI during the training intervention were determined 'healthy'.

Blood sample collection, handling and analysis

Venous blood samples collected before and after the four-week training intervention were analyzed to assess changes in hormones, iron and vitamin D levels. 10 mL whole blood was drawn from a cephalic vein into a vacutainer tube (CAT, BD, Franklin Lakes, USA), allowed to clot for 30 min then centrifuged at 3100 × *g* for 10 min at room temperature to separate the serum supernatant. Samples were frozen at -80°C and later analyzed for their content of cortisol, testosterone, iron, ferritin, transferrin and 25(OH)D using standard laboratory methods.

Saliva sample collection, handling and analysis

Unstimulated saliva samples were collected using a 5-min passive drool technique.[17] Saliva samples were frozen at -80°C before analysis for s-IgA in duplicate using commercially available ELISA kits (1602, Salimetrics, CA, USA; intra-assay CV = 5.3%). We calculated s-IgA secretion rate as the product of salivary flow rate and s-IgA concentration.

Statistical analysis

Statistical analyses were performed using Prism software (v7, GraphPad, CA) and the R statistical programming language (R Core Development Team, 2016). Data are reported as mean ± SD unless otherwise stated. Ninety percent confidence intervals (90% CI) denote the imprecision of point estimates. Two-tailed, statistical significance was accepted at $P<0.05$.

Differences in session HR and RPE between HIT groups were explored using a one-way ANOVA and Kruskal-Wallis test, respectively. A mixed ANOVA was used to explore differences in *ad libitum* training volume between HIT groups each week. Differences in training characteristics between participants with and without URI were examined using unpaired *t*-tests. Post-intervention differences in $\dot{V}O_{2peak}$ and serum and saliva biomarkers were examined between HIT groups, controlling for baseline measures, using the *nlme* package. Mean changes in $\dot{V}O_{2peak}$ and health-related biomarkers from pre- to post-intervention within each HIT group are reported with corresponding Cohen's *d* effect sizes and interpreted using qualitative descriptors: ≥0.2, small; ≥0.5, moderate; ≥0.8, large.

Due to the zero-inflated distribution of URS, differences between interval groups were explored using Kruskal-Wallis tests. Furthermore, owing to overdispersion, a zero-inflated negative binomial model, with a logit link function, was fit using the *pscl* package to analyse the relationship between pre-intervention s-IgA-secretion rate, vitamin D, ferritin, cortisol, testosterone, EA, $\dot{V}O_{2peak}$ and the count of days with URI between interval groups. Total symptom score, which was used to indicate global URS severity, was represented by zero-inflated continuous data and was analysed using a Tweedie distribution and logit link using a *glm* function. Parsimonious models were chosen using information theory. The model with the lowest Bayesian Information Criteria[18] value was considered parsimonious for URI incidence and model with the lowest residual deviance was considered parsimonious for URS severity. Model parameter estimates for URI incidence are reported as incidence rate ratios (IRR) for

the count section of the negative binomial model and as odds ratios (OR) for the zero-inflated section.

Results

Influence of HIT duration on URI incidence and duration and URS severity

During the training period, there was no difference in the duration of *ad libitum* training undertaken by the three HIT groups each week (F[6, 66]=0.757, P=0.606). Mean exercise intensity (represented by HR_{max} [%]) and RPE attained over the twelve sessions were not different between interval groups (all P>0.05; Table 1).

Fourteen of the 25 participants (56%) reported an episode of URI during the four-week training intervention, with episode duration ranging from 3-22 days (Figure 2). There were no differences in the duration, global or peak severity of URS between HIT groups (Table 2). Eleven (79%) of the participants with URI reported the first day of illness within the first eight days of the training intervention.

There were no differences in estimated annual training hours prior to the intervention, nor key training variables during the intervention (mean session RPE, mean session $\%HR_{max,}$ and *ad-libitum* training hours) between participants who reported URI and those who did not (all P>0.05).

Effect of HIT on health-related biomarkers

Following the training intervention, a moderate increase in $\dot{V}O_{2peak}$ occurred in the cohort (d=0.65, 90% CI: [0.16, 1.13], Fig. 3b), but the magnitude of improvement in $\dot{V}O_{2peak}$ was not significantly different between HIT groups (Fig. 3a). Serum cortisol concentration also increased moderately (d=0.60, 90% CI: [0.12, 1.08], Fig. 3f), and there was a large decrease in serum 25(OH)D concentration (d=-0.87, 90% CI: [-1.36, -0.37], Fig. 3j) during the training intervention. There were no differences in s-IgA secretion rate, testosterone or ferritin from

pre- to post-training (Fig. 3). When controlling for pre-test values, biomarker responses to the training intervention were not different between HIT groups (all $P>0.05$; Fig. 3).

Relationship between pre-training biomarkers and URI incidence/duration

The parsimonious model included EA ($P=0.02$) and cortisol ($P=0.02$) in the count section and s-IgA secretion rate ($P=0.03$) in the zero-inflated section. For the zero-inflated section, a one-unit increase in s-IgA secretion rate decreased the odds of remaining free from URI by 0.90 (90% CI: [0.83, 0.97]). For the count section, holding cortisol levels constant, for a one unit increase in EA the expected change in IRR for URI was 1.04 (90% CI: [1.01, 1.07]).

Relationship between pre-training biomarkers and URS severity

Global severity of URS during the monitoring period (represented by the total symptom score) was positively associated with relative $\dot{V}O_{2peak}$ ($P=0.03$). Specifically, each one unit increase in $\dot{V}O_{2peak}$ increased the odds of reporting more severe URS by 1.07 (90% CI: [1.01, 1.13]; Fig. 4).

Discussion

This study compared physiological responses to three HIT protocols and investigated whether HIT prescription influenced URI incidence. Over half (56%) of the cohort reported an episode of URI during the four-week training period that took place during the common cold season in Norway. Despite a high incidence of URI compared to seasonal norms,[19] mean $\dot{V}O_{2peak}$ increased across the cohort, and there were no differences in the magnitude of improvement between protocols. Serum cortisol increased, and vitamin D decreased following the training period, independent of HIT group. However, there were no differences in either URI incidence or the magnitude of changes in serum and saliva biomarkers from pre-to-post training between HIT groups. This is unsurprising given RPE and HR were similar between

groups, indicating that the HIT protocols elicited similar internal and external training loads. Biomarker responses to HIT did not differ between groups, which can be viewed as a positive finding for training planning, since it implies that neither short- nor long-intervals are preferable over the other with regard to illness risk.

It is notable that 79% of URI episodes occurred within the first eight days of commencing the HIT intervention, suggesting that commencing a new training regime may have been a risk factor for URI. We did not actively quantify participants' training load in the training block before commencing the study, although there was no difference in self-reported annual training hours between participants who reported URI and those who did not. However, spikes in training load have been identified as potential risk factors for illness.[6,7,20] For our participants, whether it was an increase in load *per se* or rather a change to their training regime that could have triggered this cluster of URIs following the first week of training is difficult to say. Alternatively, bringing athletes together for group training sessions may have facilitated transmission of infection.

We also examined the relationship between baseline biomarkers and subsequent URI incidence and duration. Similar to studies that have explored the influence of training on immune biomarkers,[7,21] resting salivary s-IgA was assessed pre- and post-HIT as a marker of immune competency. We observed that resting s-IgA was unaltered following 4 weeks' HIT and that there were no differences in s-IgA responses to HIT between groups. These observations concur with a recent study that also showed no influence of HIT on salivary s-IgA in recreational runners.[22] Absence of URI in the present study was associated with lower pre-training s-IgA secretion rate, an inverse relationship to previous observations.[5,8] Although salivary s-IgA has been widely accepted as a biomarker of URI susceptibility in athletes,[8,21] it's high biological variability, susceptibility to confounding variables and lack of correlation with clinical outcomes has led its utility as a marker of infection susceptibility to be

challenged.[17,23] Our findings further suggest that the relationship between s-IgA and URI risk remains unclear.

For participants who reported URI, longer illness duration was associated with lower pre-training cortisol. Similar to s-IgA, this relationship was inverse to previous observations, as high cortisol levels have been associated with increased risk of URI in several longitudinal studies.[7] More frequent sampling may have provided better resolution of cortisol responses to four-weeks' HIT. An alternative approach from recent studies is to assess the reactivity of biomarkers (such as cortisol and s-IgA) to standardized exercise stressors.[22,24,25] Ihalainen et al[25] recently observed differing salivary s-IgA responses to a single incremental exercise test in participants who developed URS during intensified training (acute increase) compared to participants who remained healthy (acute decrease). Therefore, examining changes in biomarkers in response to an exercise stressor could provide further insight into immunological and hormonal adaptations during the training period in future studies.

Higher EA was associated with longer URI duration, and EA did not change from pre- to post-training. However, only five participants pre-training and three participants post-training registered EA <30 kcal·kg FFM^{-1}·d^{-1}, an accepted threshold for LEA in female athletes.[26] It is therefore possible that, for the majority of participants, EA was not low enough to compromise immunity. However, no consensus regarding a threshold for definition of LEA in males has been universally agreed. Additionally, concerns over the reliability and validity assessment of both EI and EEE have been raised,[26] so under- or over-reporting of the metrics included in the EA assessment may have occurred despite our efforts to reduce bias. Another possible explanation for the unexpected association between higher EA and longer URI duration, could be that LEA states may develop at different stages of training and competition due to varying physiological demands[26] and that a snap-shot of the condition only pre- and post-intervention may be insufficient to show whether the athletes had chronically reduced EA.

Vitamin D and iron status were not associated with the incidence or duration of URI. Although the study took place at a northern latitude in winter, no participants' 25(OH)D level was below the suggested vitamin D 'sufficiency' threshold of 50 nmol·L^{-1} upon commencing the HIT programme.[27] The decrease in 25(OH)D that occurred in all groups during the intervention can likely be attributed to seasonal variation.[27] Taken together, it is unlikely that vitamin D negatively influenced immune status in the present study. Similarly, no athletes were iron deficient at baseline (serum ferritin <20 μg·L^{-1}),[28] and iron status did not change during the training period. However, these findings are limited to male athletes. Understanding the influence of low iron status on risk of URI could be more important in female athletes where the incidence of iron deficiency is typically higher than in males.[28]

High $\dot{V}O_{2peak}$ was associated with increased global severity of URS during the training period. Since aerobic fitness was not associated with URI incidence or duration, this observation suggests that highly-trained athletes report more sub-clinical URS that do not reach the threshold for URI. It is possible that some URS reported during the training period may have arisen from non-infectious origins such as exercise-induced bronchoconstriction or airborne allergies.[29] This observation concurs with the findings of Spence et al., who reported a higher incidence of URI of unidentified (i.e. non-infectious) origin in elite athletes compared to recreationally active individuals, and observed that non-infectious URI episodes were typically less severe and of shorter duration than episodes of pathogen-confirmed upper respiratory tract infection (URTI).[30]

A limitation of this study is that we did not identify infectious pathogens during URI, an approach that has been used to confirm URTI in athletes and the general population.[17,30] However, detection of pathogens is impractical in elite sport, whilst longitudinal monitoring of self-reported URS has practical relevance for the athletic population since it is cost-effective, non-invasive and may allow practitioners to identify athletes who are prone to URS.

A second limitation of the study is that we only measured blood biomarkers at two time-points pre-and post-training. In investigating associations between pre-training biomarkers and subsequent incidence of URI, we can only draw conclusions about how baseline health status prior to commencing intensified training may relate to risk of URI. Moreover, the magnitude of the odds ratios were very small, with our identified risk factors potentially altering risk of URI by less than 10%. Thus, the clinical relevance of such risk factors is likely limited. It is also important to consider that any disturbances to biomarkers in the early phase of training may have resolved by the end of the training period when the post-samples were collected. We could hypothesize that incorporating more frequent sampling to detect changes in biomarkers that occurred in response to commencement of the training regime may have been able to further explain risk of URI in this cohort. This would have been especially pertinent for those biomarkers that are likely to respond acutely to training, such as s-IgA, cortisol and testosterone. Measuring these biomarkers at additional time-points during the first week of training may have given further insight into why the majority of participants who reported URI did so within the first eight days of the training intervention; this remains a potential avenue for further study.

Finally, the concept of exercise-induced immune suppression has been recently challenged by Campbell and Turner, who suggest that lifestyle factors rather than hard training may explain the high incidences of illness often reported by athletes.[23] Indeed, in this study we did not see any significant changes to immune biomarkers after four weeks' intensified training. Although we had no control group, we highlight that 56% of athletes reported an episode of URI in the four-week period, which is higher than has been reported in the general population during the Northern Hemisphere autumn-winter (~24%).[19] It is possible that the group-training interventions implemented during the study facilitated transmission of infection between individuals. However, we consider that the high incidence of URI in this study is a

strength, because cases of URI were not under-represented in the statistical model, and because of the increased likelihood that the participants who did not report URI were resilient to illness, rather than not exposed to pathogens. Nevertheless, it is possible that exposure to pathogens at home, in the workplace, or other life stressors[31] could have influenced infection risk besides the training intervention in this cohort.

Practical Applications

This study indicates that choice of HIT protocol did not affect URI incidence in well-trained endurance athletes. However, athletes with high aerobic fitness may be slightly more likely to report URS during heavy training periods. Coaches should be mindful that URI incidence may be higher during intensified training, especially within the first week of a periodized HIT block. It would be worthwhile to investigate whether progressively increasing the frequency of HIT sessions can reduce URI incidence in the first week of a new training block.

Conclusion

Following four weeks' HIT, and despite a high overall incidence of URI, we observed no difference in URI incidence between groups that performed HIT interventions consisting of long (4 × 8 min) or short (4 × (8 or 12) × 40/20 s) intervals. Additionally, we observed no differences in immune and hormonal responses between HIT groups post-intervention. These observations are most likely a consequence of the similar external and internal training loads experienced by the participants; however, we did not assess interim biomarker responses to training during the intervention so are unable to conclude whether biomarker responses to specific phases of the training intervention differed between groups. It was notable that the majority of illnesses were reported within the first eight days of the training period, suggesting that a change of regime or increase in training load may have been a risk factor for illness. In addition, higher baseline $\dot{V}O_{2peak}$ was identified as a minor risk factor for URS. Contrary to

biological rationale, higher pre-intervention salivary s-IgA secretion rate, higher EA prior to training onset and lower pre-training cortisol were associated with slight increases in incidence or duration of URI across the athlete cohort. Future studies should aim to explore the relative importance of multiple risk factors for illness in well-trained and elite athlete cohorts including those at high risk of nutritional deficiencies, and incorporate more frequent monitoring of biomarker responses (e.g. to standardized exercise protocols) during intensified training periods.

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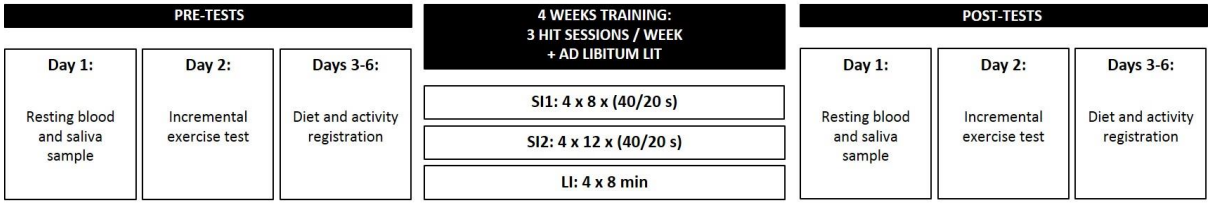

Figure 1. Schematic of study design. Pre- and post-test measures include rested, fasted blood and saliva biomarkers, an incremental exercise test for determination of peak oxygen uptake ($\dot{V}O_{2peak}$), and a four-day diet and activity registration. Participants were divided into three test groups for the four-week training intervention: short intervals 1 (SI1), short intervals 2 (SI2) and long intervals (LI). HIT, High intensity training; LIT, Low intensity training.

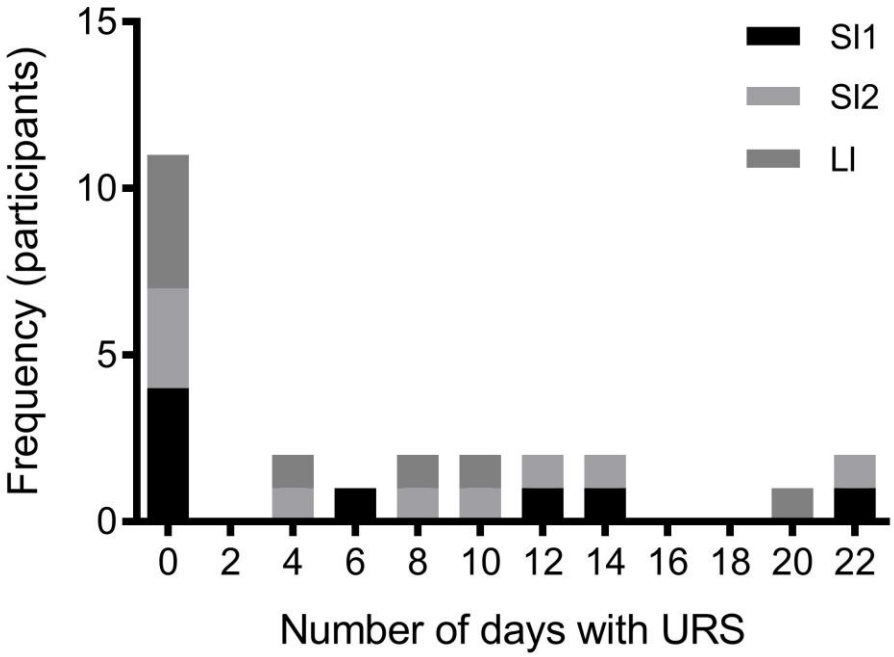

Figure 2. Frequency distribution of upper respiratory illness reported during the four-week intervention period.

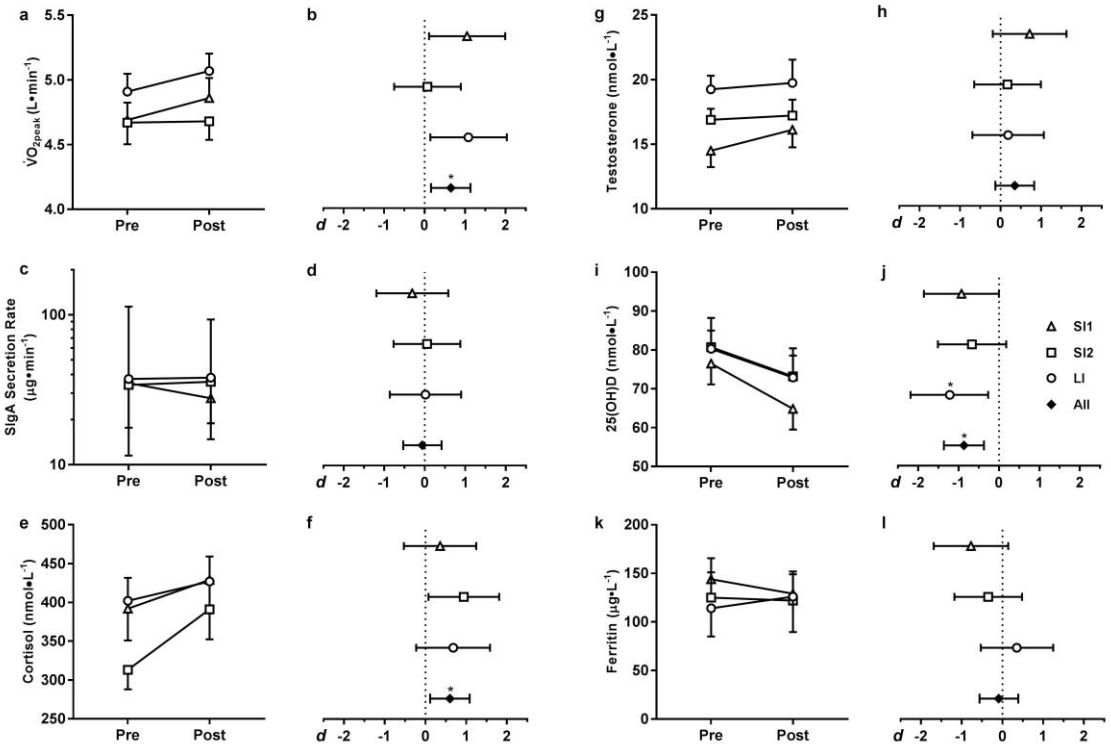

Figure 3. Biomarker responses to four-weeks high-intensity training with 4×(12×40/20 s) short intervals (SI1), 4×(8×40/20 s) short intervals (SI2) and 4×8 min long intervals (LI). Left panels indicate group mean and standard error, except for panel c which displays geometric mean and SD factor for SIgA secretion rate. Right panels indicate Cohen's *d* effect sizes from pre- to post-training with 90% confidence intervals of the difference. *, $P < 0.05$.

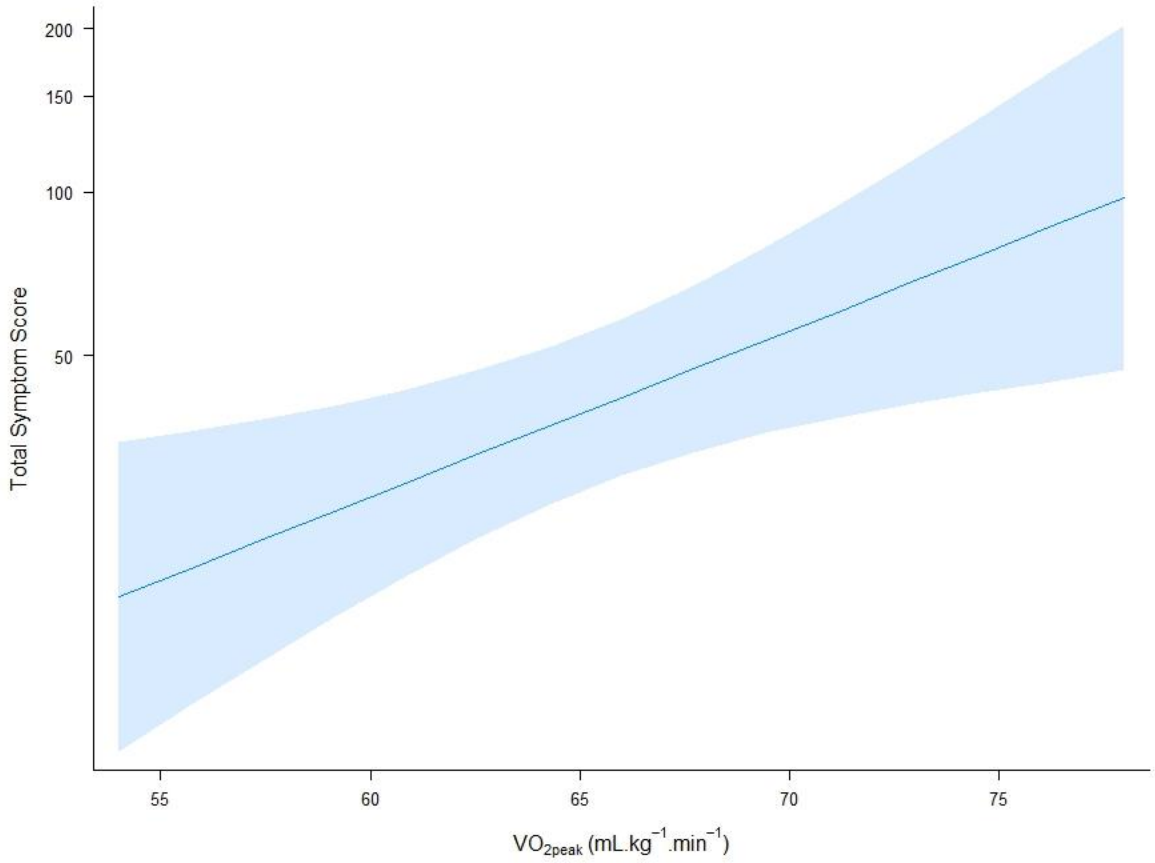

Figure 4. Relationship between $\dot{V}O_{2peak}$ and total self-reported upper-respiratory symptom scores during the four-week training period. Blue band represents 90% confidence interval.

Table 1. Mean percentage of maximum heart rate [HRmax (%)] and median Borg's rating of perceived exertion (RPE) attained during each of the twelve training sessions for each high-intensity training group.

Group	**HR_{max} (%)**		**RPE**	
	Mean	**SD**	**Median**	**Range**
SI1	86	4	17	16-18
SI2	87	1	17	16-17
LI	86	2	17	16-18

Abbreviations: SI1, short intervals 1 (4×(12×40/20 s); SI2: short intervals 2 (4×(8×40/20 s); LI, long intervals (4×8 min).

Table 2. Severity of upper respiratory symptoms between high-intensity interval training groups. Total symptom score represents the sum of self-reported symptom scores from the 4-week training period. Peak severity is the highest total symptom score reported in a continuous 7-day period. URI represents participants who reported at least one day of upper respiratory illness during the 4-week training period; Healthy refers to participants who did not report a day of illness. Data are median (range).

Group	Total Symptom Score		Peak Severity	
	URI	Healthy	URI	Healthy
SI1	83 (13-133)	7 (0-12)	60 (13-81)	5 (0-8)
SI2	44 (16-82)	8 (0-8)	20 (14-58)	4 (0-5)
LI	49 (12-184)	14 (3-37)	34 (7-95)	8 (1-13)

Abbreviations: SI1, short intervals 1 (4×(12×40/20 s); SI2: short intervals 2 (4×(8×40/20 s); LI, long intervals (4×8 min).