Received: 10 September 2020 | Revised: 28 April 2021 | Accepted: 29 April 2021

DOI: 10.1002/tsm2.258

ORIGINAL ARTICLE

WILEY

Eucapnic voluntary hyperpnea challenge can support management of exercise-induced bronchoconstriction in elite swimmers

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Abstract

Introduction: This study investigated the use of eucapnic voluntary hyperpnea (EVH) to monitor efficacy of pharmacological therapy in elite swimmers with exercise-induced bronchoconstriction (EIB). Secondly, it evaluated the long-term test-retest repeatability of EVH in this population.

Methods: Twenty-seven elite international swimmers were included in this retrospective analysis of comprehensive respiratory assessments. Following an initial "withheld-therapy" assessment, athletes with EIB had been prescribed appropriate pharmacological therapy and returned twelve months later for a follow-up assessment to monitor EIB protection afforded by treatment. EIB-negative athletes had returned to confirm initial diagnosis, as were still reporting persistent respiratory symptoms. Athletes were retrospectively grouped into either "Therapy Adherent Group" (n = 12) or "Repeatability Group" (discontinued therapy at follow-up or EIB-negative, n = 15).

Results: Greatest fall in forced expiratory volume in 1 second ($\Delta FEV_1 max$) was significantly lower following therapy adherence (−11.8 ± 3.8%) compared to initial assessment (−24.0 ± 11.3%; $P < .01$). "Repeatability Group" $\Delta FEV_1 max$ did not differ significantly between initial assessment (−13.1 ± 4.5%) and follow-up (−12.3 ± 5.6%; $P = .32$), and showed good agreement (0.6%; −5.9%, 7.1%).

Conclusion: A follow-up assessment utilizing EVH is useful in the management of EIB and shows good test-retest repeatability over twelve months in elite swimmers who discontinue treatment or are EIB-negative.

KEYWORDS

asthma therapy, elite athletes, reproducibility, test-retest repeatability

1 | INTRODUCTION

Exercise-induced bronchoconstriction (EIB) is a transient airway disorder triggered by intense exercise stimuli.[1] By some, EIB could be considered an "occupational airway disorder" for elite athletes.[2] Prevalence is reported to be sport specific, with up to two-thirds of athletes demonstrating objective evidence of EIB in some sports.[3,4] Particularly at risk are elite swimmers, winter sports, and endurance athletes that require repeated exposure to high minute ventilation in asthmogenic environments (ie, cold dry-air, areas of high pollen, and pollution).[3-5]

Elite swimming provides a unique training and competition environment, as athletes are exposed to additional chlorination by-products.[3] Although highly specific, it can be difficult to adequately control a field-based exercise challenge to induce bronchoconstriction in elite swimmers. The inability to standardize protocol exercise intensity, minute ventilation, and environmental conditions can all contribute to poor EIB detection and add additional training load in this population.[5-7] The lack of standardization is problematic when reassessing athletes or monitoring efficacy of pharmacological therapy. While there is no "gold standard" assessment for EIB,[8] the American Thoracic Society (ATS) suggests an indirect bronchoprovocation assessment, the eucapnic voluntary hyperpnea (EVH) challenge, as a suitable surrogate for exercise.[9] The EVH has a high level of sensitivity and the ability to induce the pathogenic mechanisms associated with EIB.[5,10,11]

Our research group has previously demonstrated that EVH can provide objective evidence to support diagnosis of EIB in elite athletes.[3,4,12] It is not uncommon for athletes with EIB to demonstrate enhanced pulmonary function at baseline[13] and still report respiratory symptoms following treatment.[12,14] Therefore, when reviewing the efficacy of initiation or alteration in pharmacological therapy, one should incorporate the same indirect airway assessment used to support the initial diagnosis.

EVH has previously been used to objectively evaluate bronchoconstriction following specific acute pharmacological,[15-18] and short-term non-pharmacological therapy (eg, prebiotics).[19] Jackson et al[12] demonstrated EVH can be used to assess EIB severity following nine weeks of individualized pharmacological therapy in elite football players. Therefore, it may be suitable to use EVH to monitor EIB management over a longer time period (eg, at an annual assessment). Moreover, further research is required to investigate the utility of EVH to monitor EIB management in other elite sports, such as a swimming population, where athletes are exposed to additional asthmogenic stimuli.[3,6,20]

For EVH to be suitable for monitoring efficacy of EIB therapy, it requires good test-retest repeatability.[21] EVH has previously shown good short- ($\leq$7 days), and medium-term ($\leq$70 days) test-retest repeatability in elite and recreational athletes.[22-24] However, the repeatability of EVH on an annual basis, and when used within an athlete's annual medical assessment, has not been reported.

The primary aim of this research was to investigate the use of EVH to annually monitor the efficacy of individualized pharmacological therapy for EIB in elite swimmers. The secondary aim was to evaluate the long-term test-retest repeatability of EVH in elite swimmers who had discontinued therapy or without EIB diagnosis but persistent symptoms.

2 | METHODS

2.1 | Study overview

This study involved retrospective analysis of data collected from a subsection of the British Swimming Team at annual medical assessments between 2017 and 2019. Sixty-three swimmers were assessed during this period. However, twenty-seven athletes had multiple assessments during this time due to receiving pharmacological intervention or having persistent respiratory symptoms. In brief, athletes presented in this study initially underwent a comprehensive respiratory assessment, then twelve months later returned for a follow-up assessment to monitor EIB protection afforded by therapy, or to confirm a negative test. The study was approved by the University of Kent School of Sport and Exercise Sciences Research Ethics Committee (Prop 86_2018_19). All participants provided written informed consent to anonymized data analysis.

2.2 | Initial respiratory assessment

Prior to the initial assessment, all participants were asked to withhold use of any previously prescribed EIB or asthma medication to determine baseline EIB severity. Most notably, short-acting β_2-agonists (SABA) were withheld for at least 8 hours, inhaled corticosteroids (ICS) for 24 hours, long-acting β_2-agonists (LABA) for 24 hours, and leukotriene receptor antagonists (LTRA) for 96 hours. Athletes were also asked to avoid caffeine and exercise for $\geq$4 hours before assessments in accordance with EVH guidelines.[25]

Airway inflammation was assessed via fraction of exhaled nitric oxide (FeNO) at a flow rate of 50 mL s^{-1} against 16cmH_2O of resistance (NIOX VERO, NIOX, Aerocrine, Sweden) in accordance with ATS recommendations.[26] Participants then completed baseline maximal flow-volume maneuvers in triplicate using a turbine transducer spirometer (Spiro USB, Micro Medical LTD, Rochester, UK). Predicted values were calculated using the equations of Kuster et al[27] Within and between maneuver criteria were met in accordance to ATS/ERS

guidelines.[28] Participants then completed an EVH challenge; inhaling medical-grade dry-air at a target ventilation rate of 85% predicted maximum voluntary ventilation (MVV) (30 × baseline forced expiratory volume in 1 s [FEV_1]) for six minutes. The gas composed of 21% O_2, 5% CO_2, and 74% N to prevent syncope. Expired air passed through a dry-gas meter (Harvard Apparatus, Kent, UK) to measure minute ventilation (V_E) and calculate percentage of MVV achieved (%MVV). Maximal flow-volume maneuvers were then completed in duplicate at 3, 5, 7, 10, and 15 minutes post-EVH. An EVH challenge result was deemed positive (EIB-positive) if an athlete displayed a fall in FEV_1 of ≥10% from baseline at two consecutive timepoints,[10] with the maximum change defined as $\Delta FEV_1 max$. EIB severity was classified as: mild (≥10% but <25%), moderate (≥25% but <50%), and severe (≥50%).[9,25] To reverse bronchoconstriction, EIB-positive athletes inhaled 200 μg or 400 μg salbutamol depending on EIB severity and performed maximal flow-volume maneuvers 10 minutes post-inhalation.

2.3 | EIB therapy

EIB-positive swimmers were prescribed pharmacological therapy by the team physician. Treatment was guided by EIB severity in a stepwise approach and within World Anti-Doping Agency regulations.[9,25,29]

2.4 | Follow-up assessment

Twelve months after the initial visit, athletes returned for a follow-up and completed the same respiratory assessments. Athletes diagnosed EIB-positive at the initial assessment were asked to continue using therapy as prescribed to evaluate attenuation of EIB provided by pharmacological treatment. Complete protection against EIB was defined as <10% $\Delta FEV_1 max$ at the follow-up assessment or clinical attenuation if $\Delta FEV_1 max$ reduced by 50% compared to the initial test.[1] Minimally important reduction in airway inflammation was defined as ≥20% reduction in FeNO (if >50 ppb), or a 10 ppb reduction (if <50 ppb).[26]

EIB-negative athletes were required to adhere to the same criteria as at the initial test. EIB-negative athletes were retested on the follow-up assessment as they were still reporting persistent respiratory symptoms or had a previous differential diagnosis of EIB.

2.5 | Data analysis

Athletes were retrospectively grouped according to whether they had arrived to the follow-up assessment using prescribed EIB therapy or not, as evaluated by a pre-assessment medical questionnaire. The groups were defined as: those who had arrived using EIB therapy (Therapy Adherent Group) and those who had discontinued therapy or were EIB-negative (Repeatability Group) (Figure 1).

2.6 | Statistical analysis

Data are presented as mean ± standard deviation unless stated. Normality was assessed through Shapiro-Wilk test. Differences between initial assessment and the follow-up assessment for main outcome measures (baseline spirometry, FeNO and $\Delta FEV_1 max$) were analyzed using paired-samples *t* test. The level of test-retest repeatability between "Repeatability Group" assessments was expressed as mean bias with 95% limits of agreement (LOA) and interpreted by Bland-Altman plot. Proportional bias was analyzed using linear regression. Correlation between "Repeatability Group" assessments was calculated using Pearson's correlation coefficient (r_p). Significance level was set at $P \leq .05$ for all analysis and performed using statistical package SPSS (SPSS v25, IBM, New York, USA).

3 | RESULTS

3.1 | Participant characteristics

Twenty-seven elite swimmers, competing regularly at international level, were included in this retrospective data analysis of comprehensive respiratory assessments (Table 1). Prior to the initial assessment, twelve athletes (44%) self-reported a history of asthma or EIB, and thirteen (48%) reported allergenic environments worsened their respiratory symptoms. No athlete had evidence of significant airflow obstruction at baseline (ie, FEV_1 >80% predicted & FEV_1/FVC >70%; Tables 2 and 3).

From the initial assessment, twenty-three athletes (85%) were diagnosed as EIB-positive. At the time of the follow-up assessment, all EIB-positive athletes were prescribed SABA therapy for emergency use. All EIB-positive athletes were also prescribed a form of maintenance therapy, with eleven (48%) using daily ICS monotherapy, and twelve (52%) requiring a combination of ICS and LABA therapy. In addition, two (9%) were prescribed add-on LTRA therapy. The remaining four EIB-negative athletes were not prescribed any treatment for EIB.

3.2 | Therapy adherent group

Twelve EIB-positive athletes returned to the follow-up assessment having used prescribed therapy as instructed

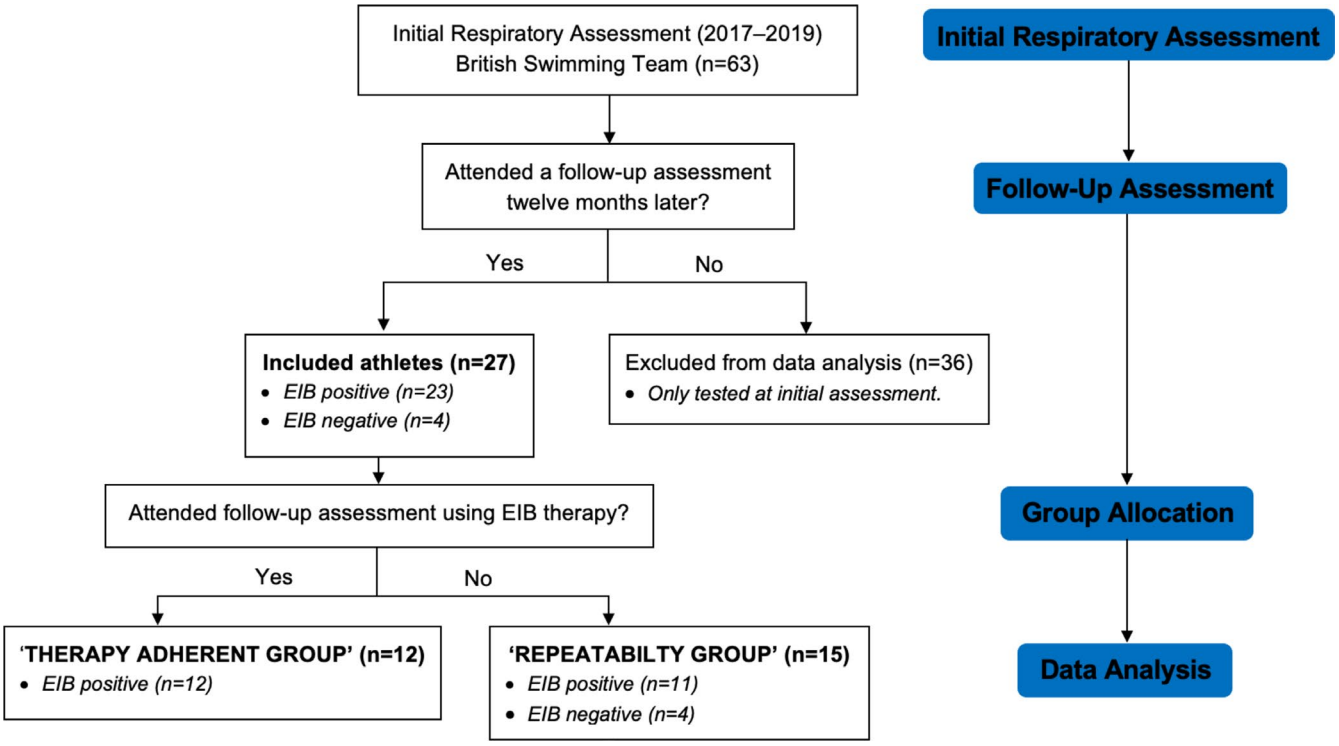

FIGURE 1 Schematic of retrospective data analysis. EIB, exercise-induced bronchoconstriction

TABLE 1 Participant characteristics (n = 27)

Sex	Males / Females	n = 14 / n = 13
Age (yrs)	20 ± 2	
Height (cm)	179.6 ± 7.1	
Body mass (kg)	71.3 ± 8.7	
Swimming training history (yrs)	11 ± 3	
Weekly pool training volume (hrs)	23 ± 4	

Note: Pooled data across both groups. Data presented as mean ± standard deviation.

(Therapy Adherent Group). No athlete reported acute use of SABA therapy on the day of the follow-up assessment. Baseline FEV_1 was significantly higher at the follow-up assessment compared to initial assessment ($P = .04$; Table 2). The group magnitude of change in baseline FEV_1 was 240 mL (±356 mL), with individual responses presented in Fig. S1. On a group level, FeNO was not significantly different between assessments ($P = .07$; Table 2). However, five athletes (42%) demonstrated a minimally important reduction in FeNO following use of therapy. Individual FeNO responses are presented in Fig. S2. Minute ventilation (V_E) during the EVH was not significantly different between assessments ($P = .40$); however, the %MVV achieved was significantly different ($P = .04$; Table 2). ΔFEV_1max was significantly lower at the follow-up assessment (−11.8 ± 3.8%) compared to the initial assessment (−24.0 ± 11.3%) ($P < .01$; Table 2; Figure 2). Use of therapy afforded complete protection to four athletes (33%) and provided clinical attenuation to a further four athletes (33%).

3.3 | Test-retest repeatability

Eleven EIB-positive athletes arrived to the follow-up assessment having discontinued EIB therapy (Repeatability Group). This group also included four EIB-negative athletes (total n = 15). Baseline pulmonary function, FeNO, V_E, and %MVV achieved did not differ significantly between assessments ($P > .05$; Table 3). There was no significant difference in ΔFEV_1max between initial assessment (−13.1 ± 4.5%) and follow-up assessment (−12.3 ± 5.6%; $P = .32$). Individual ΔFEV_1max responses are shown in Figure 3. Bland-Altman analysis indicated acceptable test-retest repeatability. The mean bias between assessments was 0.6% (95% LOA = −5.9, 7.1), with no data points outside the LOA (Figure 4). Linear regression analysis determined there was no proportional bias, as the distribution of agreement was not dependent on FEV_1max ($P = .61$). There was a statistically significant strong correlation in ΔFEV_1max between assessments (r_p =0.81, $P < .01$; Figure 5).

TABLE 2 Therapy adherent group (total n = 12: males n = 7, females n = 5)—baseline pulmonary function and EVH outcomes

Measure	Initial assessment	Follow-up	*P*-value
FEV_1 (L)	4.60 ± 0.68	4.84 ± 0.77	0.04*
FEV_1 (% of predicted)	110.2 ± 12.8	115.6 ± 15.3	0.03*
FVC (L)	5.98 ± 1.10	6.19 ± 1.10	0.07
FVC (% of predicted)	121.3 ± 14.0	124.3 ± 12.8	0.17
FEV_1/FVC (%)	77.6 ± 6.5	79.08 ± 8.3	0.17
Baseline FeNO	33.7 ± 23.2	22.2 ± 17.2	0.07
ΔFEV_1max (%)	-24.0 ± 11.3	-11.8 ± 3.8	<0.01*
Achieved V_E (L/min^{-1})	116.3 ± 20.6	112.9 ± 17.8	0.40
Achieved Ventilation %MVV (%)	72.4 ± 8.1	66.7 ± 8.15	0.04*

Note: Data presented as mean ±standard deviation.

Abbreviations: %MVV, percentage of maximum voluntary ventilation; FeNO, fraction of exhaled nitric oxide; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; V_E, minute ventilation; ΔFEV_1max, maximum fall in FEV_1 from baseline following eucapnic voluntary hyperpnea (EVH) challenge.

*Statistically significant difference between assessments ($P \leq .05$).

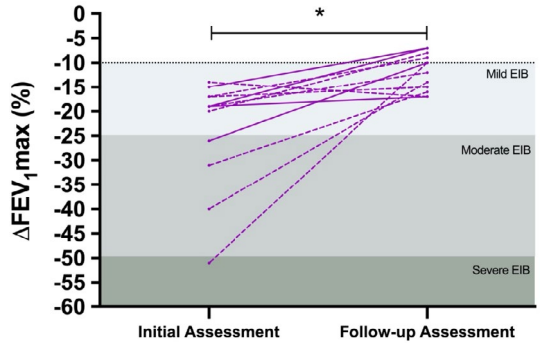

FIGURE 2 Individual ΔFEV_1max response in "Therapy Adherent Group." Solid line denotes inhaled corticosteroid (ICS) treatment only, broken line denotes ICS combined with long-acting β2-agonist (LABA). Dotted horizontal line denotes 10% fall in FEV_1 diagnostic threshold. * Statistically significant difference between time-points $P \leq .05$. FEV_1, forced expiratory volume in 1 s; EIB, exercise-induced bronchoconstriction

TABLE 3 Repeatability group (total n = 15: males n = 7, females n = 8)—baseline pulmonary function and EVH outcomes

Measure	Initial assessment	Follow-up	*P*-value
Baseline FEV_1 (L)	4.59 ± 0.60	4.57 ± 0.64	0.81
Baseline FEV_1 (% of predicted)	111.1 ± 16.4	112.1 ± 18.4	0.57
Baseline FVC (L)	5.74 ± 0.86	5.85 ± 0.90	0.15
Baseline FVC (% of predicted)	118.0 ± 13.3	122.3 ± 15.8	0.01*
Baseline FEV_1/FVC (%)	80.0 ± 7.7	78.27 ± 8.0	0.06
Baseline FeNO	21.6 ± 13.7	24.5 ± 11.4	0.98
ΔFEV_1max (%)	−13.1 ± 4.5	−12.3 ± 5.6	0.32
Achieved V_E (L/min^{-1})	105.23 ± 29.49	108.82 ± 28.74	0.31
Achieved Ventilation %MVV (%)	65.26 ± 15.79	67.71 ± 13.73	0.31

Note: Data presented as mean ±standard deviation.

Abbreviations: %MVV, percentage of maximum voluntary ventilation; FeNO, Fraction of exhaled nitric oxide; FEV_1, Forced expiratory volume in 1 second; FVC, Forced vital capacity; V_E, Minute ventilation; ΔFEV_1max, Maximum fall in FEV_1 from baseline following eucapnic voluntary hyperpnea (EVH) challenge.

*Statistically significant difference between assessments ($P \leq .05$).

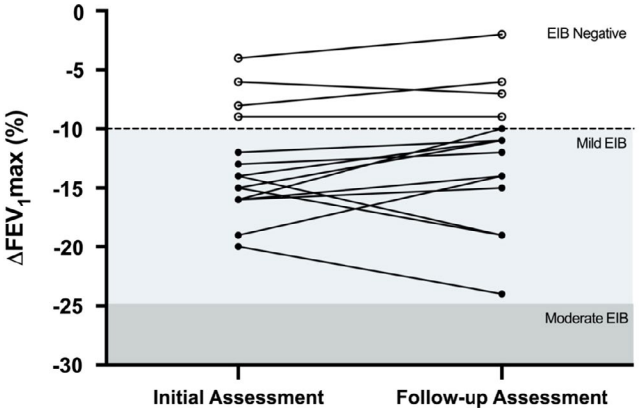

FIGURE 3 Individual ΔFEV_1max response in "Repeatability Group." [○ = EIB-negative ● = EIB-positive]. Broken horizontal line denotes 10% fall in FEV_1 diagnostic threshold. FEV_1, forced expiratory volume in 1 s; EIB, exercise-induced bronchoconstriction

4 | DISCUSSION

The present study is the first to report that a follow-up assessment utilizing EVH can be useful in the long-term management of EIB in elite swimmers. Our data from longitudinal respiratory assessments indicate that elite swimmers with EIB who maintain use of pharmacological therapy demonstrate improved pulmonary function at baseline, and attenuation of EIB induced by hyperpnea. We also demonstrated that elite swimmers who discontinue EIB therapy have a repeatable EVH challenge result after 12 months.

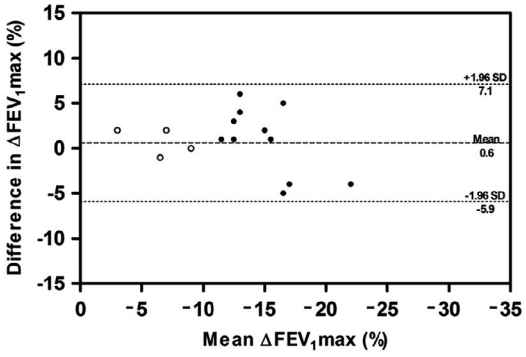

FIGURE 4 Bland-Altman plot for test-retest repeatability of maximum reduction in FEV_1 (ΔFEV_1max) between EVH assessments. [○ = EIB-negative ● = EIB-positive]. Broken horizontal line denotes mean bias, dotted lines indicate 95% upper and lower limits of agreement. FEV_1, forced expiratory volume in 1 s; EVH, Eucapnic voluntary hyperpnea; EIB, exercise-induced bronchoconstriction

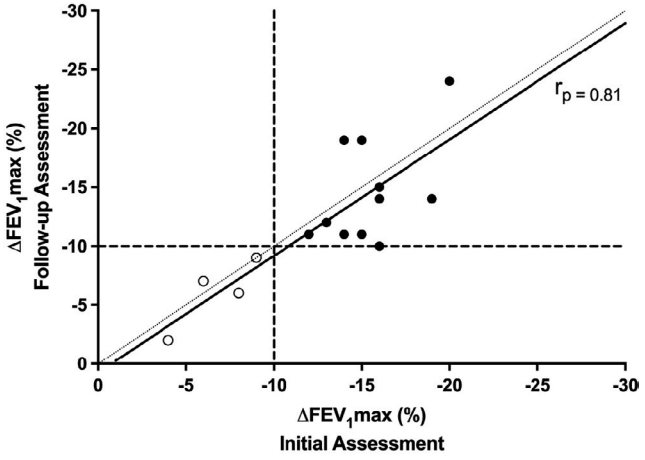

FIGURE 5 Correlation of maximum reduction in FEV_1 (ΔFEV_1max) between EVH assessment visits. [○ = EIB-negative ● = EIB-positive]. Broken horizontal and vertical lines denote 10% fall in FEV_1 diagnostic threshold. Solid line indicates line of equality, dotted line denotes dataset line of best fit. FEV_1, forced expiratory volume in 1 s; EVH, Eucapnic voluntary hyperpnea; EIB, exercise-induced bronchoconstriction

4.1 | Monitoring treatment

EIB management is achieved primarily through pharmacological intervention, with expert opinion driving the treatment of elite athletes.[30] Previous research has used EVH to objectively evaluate bronchial response following specific pharmacological treatments. In acute doses, 1500 μg beclomethasone,[15] 10 mg montelukast,[16] 0.5 mg terbutaline,[14,17] and 40 mg sodium cromoglycate [18] all reduced bronchoconstriction induced by EVH. Our results demonstrate that EVH is an effective tool to monitor the efficacy of long-term individualized pharmacological therapy in an elite swimming population, whom are uniquely exposed to additional chlorination by-products that EVH does not ordinarily induce.[3,6,20] As presented in previous literature, a standard EVH has greater sensitivity than a chlorinated inspirate-modified EVH, and also a field-based swimming exercise challenge.[20] Therefore, a standard EVH may be better suited to monitor therapy efficacy, especially if used to confirm the initial diagnosis.

There is a distinct lack of literature evaluating pharmacological therapy providing attenuation of bronchoconstriction in elite athletes with EIB. Similarly to the present study, Jackson *et al*[12] demonstrated reduced EIB severity following nine weeks use of pharmacological therapy in elite football players. However, the present study is the first to demonstrate reduced EIB severity following twelve-month use of pharmacological therapy in an applied elite athlete population. The ability to effectively monitor EIB therapy is vital for athlete health, as it has been suggested that there is an association between uncontrolled EIB and predisposition to an athlete developing respiratory tract infection (RTI),[31,32] which is reported to be a large burden on elite sport.[33] In addition, effective maintenance therapy management can reduce the frequency of SABA use, reduce the risk of tachyphylaxis development,[34] and respiratory condition exacerbation.[35]

Adherence to maintenance therapy provided complete protection to four athletes (33%), but provided clinical attenuation to a further four athletes (33%). Thus, eight (66%) of our adherent cohort demonstrated substantial reduction in EIB severity. Unfortunately, it is not possible to determine whether EIB attenuation is solely the result of long-term maintenance therapy, or by a dose administered by the athlete on the morning of the follow-up assessment (ie, this same effect would also be evident in acute use of ICS/LABA). Athletes using ICS/LABA combined therapy demonstrated the greatest reduction in EIB severity (Figure 1). However, one athlete using ICS monotherapy showed a substantial reduction in EIB severity (−25% to −10% ΔFEV_1max). The magnitude of EIB protection afforded by acute vs long-term use of maintenance therapy should be investigated further. In addition, as not all athletes showed reduction in EIB severity post-treatment, future studies should investigate how attenuation can be enhanced in athletes who do not respond adequately to standard treatment.

4.2 | Improvement in baseline FEV_1

The present study showed a mean increase of 240 mL in baseline FEV_1 following long-term use of pharmacological maintenance therapy. To our knowledge, this is the first time this has been published in an elite athlete population, who already possess high baseline pulmonary function.[13] A change in FEV_1 of >200 mL would be considered minimal clinically important.[36] Our relative magnitude of change in baseline

FEV_1 (↑ of 5%) was similarly presented by Simpson et al,[17] who in a cohort of recreationally active athletes showed a smaller (but statistically significant) bronchodilator effect following acute 0.5 mg terbutaline (mean increase of 170 mL (↑ of 5%)). This finding was further enhanced to 194 mL when a larger cohort was later included in their analysis.[14] Eight of our adherent group were prescribed a LABA in combination with ICS. The inclusion of LABA therapy may have contributed to an increase in baseline FEV_1, as the largest magnitude of change came from those using concurrent therapy, rather than ICS alone (Fig. S1). Even though athletes would have been prescribed a SABA as needed, no athlete reported acute use of this prior to the follow-up assessment, suggesting the increase in baseline FEV_1 came from maintenance therapy (ie, ICS or ICS/LABA combined therapy). However, as previously stated, it is difficult to distinguish if this observation would also be evident in acute use of ICS/LABA maintenance therapy.

4.3 | Fraction of exhaled nitric oxide

Airway inflammation related to "clinical" asthma has been shown to reduce following regular use of ICS in the general population.[37] One would therefore expect this to occur in athletes with EIB actively using ICS, as has previously been reported in a cohort of elite footballers.[12] Despite no significant group effect in our cohort, five athletes (42%) did display a minimally important reduction in airway inflammation following adherent use of maintenance therapy.

EIB pathophysiology is heterogeneous in nature. Most notably, EIB is thought to present in two main phenotypes; atopic, and those without allergic features.[38] It is evident that six of our adherent athletes (50%) may fall into the latter group, displaying "normal" levels of FeNO at the initial assessment (Fig. S2). With inherently low levels of FeNO, these athletes would have affected the statistics at a group level. These findings provide further evidence of an individualized inflammatory profile associated with EIB, as such, FeNO could be useful in selected athletes to support the diagnosis of EIB [26] and monitor efficacy of pharmacological therapy. It may be appropriate to use FeNO in combination with other intermediate respiratory assessments (ie, monitoring of respiratory symptoms, pulmonary function at baseline and following exercise) once treatment has been initiated, especially in athletes who do not present allergic features.

4.4 | Test-retest repeatability of EVH

The present study showed good long-term test-retest repeatability of EVH in a cohort of elite swimmers. Good test-retest repeatability is essential for an assessment to be used as a clinical utility,[21] particularly over a long time period. These findings support previous research demonstrating that EVH produces repeatable results on a short [22-24] and medium-term [24] basis. The findings of the present study are consistent with a previous investigation on elite swimmers, where the authors demonstrated strong correlation between repeated EVH challenges, and good test-retest repeatability, albeit over a short time period (~1 day).[23] Moreover, the mean bias (0.7%) and LOA (~6%) reported by Stadelmann et al [23] were similar to our study. Medium-term (≤70 days) repeatability has been demonstrated previously in physically active individuals with EIB.[24]

In the present study, EIB-positive elite swimmers produced repeatable results, including those with mild EIB severity. Our results support findings by Williams and colleagues,[24] who reported reproducible ΔFEV_1max irrespective of EIB severity. However, Price et al [39] demonstrated wider limits of agreement in a cohort of recreationally active individuals, particularly those with a mild or borderline response. This inconsistency in literature may be due to the population investigated, and the severity of EIB within the group. The comparable low mean ΔFEV_1max ($10 \pm 8\%$), small cohort of physician-diagnosed asthmatics, and a non-elite athletic population may have contributed to wider limits of agreement seen by Price et al[39] It has previously been suggested that using EVH with elite athletes is more suitable than with recreationally active individuals, due to the ability to maintain high-ventilation rates and the stimulus closer mimics the demands of high-intensity exercise, at which elite athletes are more accustomed.[8] Moreover, as previously discussed, the heterogenous phenotypes of EIB may impact how EIB develops in recreational compared to elite athletes.

4.5 | Adherence

A pertinent observation of the present study is that cessation of therapy was high within our cohort, with eleven (48% of EIB-positive athletes) returning to the follow-up assessment having ceased treatment. However, our respiratory assessments were completed following a periodized recovery mesocycle, so it was often anecdotally reported that athletes had stopped EIB therapy due to cessation of training and competition, suggesting symptoms that normally would be present had reduced, thus negating the perceived requirement for therapy. It is likely that EIB-positive athletes within our "repeatability group" deployed an "on-off" relationship with therapy throughout the twelve-month period. The reasons as to why an individual adheres (or not) to therapy will be multifactorial, and further emphasizes the challenge of managing chronic medical conditions in elite athletes. We hope our findings highlight the need to investigate strategies aimed at improving adherence to therapy in elite athletes diagnosed

with asthma and/or EIB. Such interventions may incorporate athlete/coach education, closer monitoring of inhaler use by team physician, and more regular appraisal of respiratory symptoms.

4.6 | Limitations

The long-term monitoring of elite swimmers over a twelve-month period has valid strengths; including avoiding seasonal variation, and a consistent pre-season training state at each assessment. An elite performance environment is inherently time restricted due to volume of training and competition. Therefore, it can be troublesome to obtain access to this population for initial consultation, but more so for a follow-up assessment to investigate the response to a treatment.

A key limitation of this study is the retrospective, rather than prospective nature of the experimental design. More specifically, the athletes were not studied in a randomized double-blinded placebo-controlled manner, and thus our results must be interpreted with this in mind. In addition, we were not able to report or quantify exactly when therapy was used during the twelve-month period before the follow-up assessment (ie, athletes may have only ceased or recommenced therapy in the weeks preceding the scheduled follow-up, or not maintained therapy religiously over the twelve-month duration). The implication of this is it can take up to four weeks following the initiation of maintenance therapy to see maximal protection, particularly in outcome measures such as FeNO.[9]

Within our study, we were not able to conduct assessments of swimming performance alongside monitoring airway health. An important driving factor in elite sport is the impact of a medical condition or intervention on exercise performance. At present, the effect of treated and untreated EIB on overall health and exercise performance remains largely unknown.[40] While it is difficult to demonstrate the effect of uncontrolled EIB on exercise performance, attempts have been made to investigate the impact of EIB detection and treatment; however, samples are often small and results inconclusive.[12,41] This clearly warrants further investigation from both a health and anti-doping standpoint.

5 | PERSPECTIVE

The results of the present study provide support for EVH as a clinical utility to evaluate the efficacy of pharmacological EIB therapy. Moreover, the findings suggest that EVH challenges are repeatable over a twelve-month period in an elite swimming population. While not advocating the frequent use of EVH, our results demonstrate that a follow-up assessment after treatment initiation can be beneficial. Follow-up assessments provide an opportunity to ensure EIB therapy is adequate, reinforce inhaler technique, emphasize importance of adherence, and assist education to athletes / support staff.[9] Once treatment is deemed to provide clinical attenuation for EIB, intermediate baseline respiratory assessments (ie pulmonary function, FeNO and respiratory health questionnaires) could be implemented, unless an alteration in EIB therapy occurs or there is an emergence of respiratory symptoms.

As proposed by Hull et al,[33] our research supports a so-called "systematic approach to respiratory athlete health" (SARAH) to enhance the identification and management of respiratory disorders, such as EIB, exercise-induced laryngeal obstruction, dysfunctional breathing,[42] and RTI.[32] Failure to optimize respiratory care presents a risk of respiratory condition exacerbation, and subsequent reduction in exercise performance and/or health.

6 | CONCLUSION

Overall, this study provides evidence that a follow-up assessment incorporating EVH can be suitable to monitor the efficacy of pharmacological EIB therapy in an elite swimming population. Active use of appropriately prescribed therapy increased baseline FEV_1 and reduced EIB severity. Furthermore, EVH demonstrated good test-retest repeatability over a twelve-month period in elite swimmers who had discontinued EIB therapy, or were EIB-negative.

ACKNOWLEDGEMENTS

The authors would like to thank the athletes/support staff for participating and contributing to this research.

CONFLICT OF INTEREST

None.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Gowers W, Evans G, Carré J, et al. Eucapnic voluntary hyperpnea challenge can support management of exercise-induced bronchoconstriction in elite swimmers. *Transl Sports Med*. 2021;00:1–10. https://doi.org/10.1002/tsm2.258