

Effect of Warm-Up Exercise on Exercise-Induced Bronchoconstriction

MICHAEL K. STICKLAND¹, BRIAN H. ROWE², CAROL H. SPOONER³, BEN VANDERMEER³, and DONNA M. DRYDEN³

¹Department of Medicine, University of Alberta and Centre for Lung Health (Covenant Health), Edmonton, Alberta, CANADA; ²Department of Emergency Medicine and School of Public Health, University of Alberta, Edmonton, Alberta, CANADA; and ³Department of Pediatrics and University of Alberta Evidence-Based Practice Center, University of Alberta, Edmonton, Alberta, CANADA

ABSTRACT

STICKLAND, M. K., B. H. ROWE, C. H. SPOONER, B. VANDERMEER, and D. M. DRYDEN. Effect of Warm-Up Exercise on Exercise-Induced Bronchoconstriction. *Med. Sci. Sports Exerc.*, Vol. 44, No. 3, pp. 383–391, 2012. **Purpose:** Exercise-induced bronchoconstriction (EIB) occurs when vigorous exercise induces bronchoconstriction. Preexercise warm-up routines are frequently used to elicit a refractory period and thus reduce or prevent EIB. This study aimed to conduct a systematic review to evaluate the effectiveness of preexercise routines to attenuate EIB. **Methods:** A comprehensive literature search was performed, with steps taken to avoid publication and selection bias. Preexercise warm-up routines were classified into four groups: interval high intensity, continuous low intensity, continuous high intensity, and variable intensity (i.e., a combination of low intensity up to very high intensity). The EIB response was measured by the percent fall in the forced expiratory volume in 1 s (FEV₁) after exercise, and the mean differences (MDs) and 95% confidence intervals (CI) are reported. **Results:** Seven randomized studies met the inclusion criteria. The pooled results showed that high intensity (MD = -10.6%, 95% CI = -14.7% to -6.5%) and variable intensity (MD = -10.9%, 95% CI = -14.37% to -7.5%) exercise warm-up attenuated the fall in FEV₁. However, continuous low-intensity warm-up (MD = -12.6%, 95% CI = -26.7% to 1.5%) and continuous high-intensity warm-up (MD = -9.8%, 95% CI = -26.0% to 6.4%) failed to result in a statistically significant reduction in bronchoconstriction. **Conclusions:** The most consistent and effective attenuation of EIB was observed with high-intensity interval and variable intensity preexercise warm-ups. These findings indicate that an appropriate warm-up strategy that includes at least some high-intensity exercise may be a short-term nonpharmacological strategy to reducing EIB. **Key Words:** EXERCISE-INDUCED ASTHMA, SPIROMETRY, EXERCISE, ASTHMA, WARM-UP

Exercise-induced bronchoconstriction (EIB) is defined as a transient narrowing of the lower airway after exercise in the presence or absence of clinically recognized asthma (25). In subjects who develop EIB, acute airflow obstruction, as measured by the forced expiratory volume in 1 s (FEV₁), is typically most severe 3–15 min after exercise termination and then remits spontaneously within 20–60 min (11). In addition to pharmacological interventions, many athletes, trainers, and researchers advocate specific warm-up routines as a method to trigger a refractory period, that is, a period after warm-up exercise

during which further vigorous exercise results in significantly less severe or no EIB. Approximately 40%–50% of individuals who have an initial episode of EIB experience a refractory period of diminished responsiveness that can last 1–4 h after the initial warm-up exercise (19). The cause of this refractory period is not fully understood but may be due to the depletion of catecholamines, increased circulation of prostaglandin, or degranulation of mast cell mediators (4).

The use of a warm-up to induce a refractory period to limit the magnitude of EIB in subsequent vigorous exercise is appealing, as it could result in fewer symptoms, decreased medication use, and improved exercise performance. A variety of warm-up protocols have been used to elicit the refractory period, and the purpose of this systematic review was to summarize the evidence on the effectiveness of each protocol to cause a refractory period.

METHODS

This review was part of a larger report (7) conducted for the Agency for Healthcare Research and Quality (Bethesda, MD) that 1) assessed the diagnostic characteristics of six alternative tests for EIB, 2) examined the efficacy of a single

Address for correspondence: Michael K. Stickland, Ph.D., Division of Pulmonary Medicine, Department of Medicine, 8334B Aberhart Centre, University of Alberta, Edmonton, Alberta, Canada T6G 2B7; E-mail: michael.stickland@ualberta.ca.

Submitted for publication April 2011.

Accepted for publication July 2011.

0195-9131/12/4403-0383/0

MEDICINE & SCIENCE IN SPORTS & EXERCISE®

Copyright © 2012 by the American College of Sports Medicine

DOI: 10.1249/MSS.0b013e31822fb73a

prophylactic dose of four pharmacologic interventions and one nonpharmacologic intervention to attenuate EIB, and 3) determined whether regular daily treatment with short-acting or long-acting β -agonists causes patients with EIB to develop tachyphylaxis.

Search Strategy

A comprehensive search was performed in the Cochrane Airways Register, which contains references to controlled clinical trials from systematic searches of the Cochrane Central Register of Controlled Trials, MEDLINE[®], Embase, CINAHL[®], AMED, and PsycINFO as well as results from hand searches of the top 20 respiratory journals and meeting abstracts. The original search was conducted on November 5, 2008, and was updated on August 4, 2009. To identify ongoing trials, we searched ClinicalTrial.gov and ClinicalStudyResults.org. In addition, we hand searched the following conference proceedings: American Academy of Asthma Allergy and Immunology (2007–2008), American Thoracic Society International Conference (2008), British Thoracic Society Winter Meeting (2008), Chest Meeting (2008), European Respiratory Society Annual Congress (2008), American College of Sports Medicine (2006–2008), and the Canadian Society for Exercise Physiology (2006–2008). We also hand searched the reference lists of included studies.

Search terms included a combination of subject headings and text words: (exerc* OR train* OR fitness OR physical OR athlete* OR sport*) AND (bronchoconstrict* OR asthma* OR antiasthma* OR wheeze* OR “Respiratory Sounds” OR “Bronchial Spasm” OR bronchospas* OR “Bronchial Hyperreactivity” OR “Respiratory Hypersensitivity” OR (bronch* AND spasm*) OR (bronch* AND constrict*) OR (bronchial* OR respiratory OR airway* OR lung*) AND (hypersensitiv* OR hyperreactiv* OR allerg* OR insufficiency)) OR EIB OR exercise-induced asthma. We did not apply language or date restrictions.

Study Selection

We selected randomized controlled trials (RCTs; parallel or crossover) that included adults and children (≥ 6 yr) with confirmed EIB. Both recreational and elite athletes were eligible for inclusion. The intervention was a preexercise warm-up period compared with no treatment or placebo. Outcomes of interest were the maximum percent fall in FEV₁ from preexercise baseline, symptoms, presence or absence of EIB (complete protection), clinical protection, and adverse effects. Two reviewers independently screened the search results (titles and abstracts) to determine whether a study met broad inclusion criteria. Two reviewers independently assessed the full-text of potentially relevant studies using a standard inclusion/exclusion form. Disagreements were resolved through discussion or third-party adjudication, as needed.

Data Extraction and Analysis

Data extraction, methodological quality assessment (using the scale of Jadad et al. (14)), and evaluation of the adequacy of allocation concealment (1,24) were completed independently in duplicate. Reviewers resolved discrepancies by consensus or in consultation with a third party.

In all studies, the mean maximum percent fall in FEV₁ measured after a control exercise challenge test (ECT) of 5–10 min with no warm-up was compared with the percent fall in an identical challenge after a designated warm-up routine. In one study, only peak flow was reported, and the change in peak flow was assumed to be equivalent to the change in FEV₁ (6). The pooled results are presented as a mean difference (MD) in the maximum percent fall in FEV₁ between the two challenges. All results are reported with 95% confidence intervals (CIs).

Most RCTs used a crossover design; therefore, SEM differences were either computed exactly using individual patient data or imputed using an estimated within-patient correlation of 0.5. Random-effects models were used for analyses in Review Manager 5.0 (The Cochrane Collaboration, Copenhagen, Denmark). The I^2 statistic was used to assess heterogeneity (13).

Where data were available, we also calculated the proportion of people who received complete protection from EIB with treatment compared with placebo. Results are reported as mean \pm 95% CI.

RESULTS

Literature Search

The search identified 1653 citations from electronic databases and 8 citations through hand searching (Fig. 1). Seven trials involving 128 participants met the inclusion criteria (Table 1) (6,8,16–18,20,22).

Study and Population Characteristics

Six of the seven trials used a crossover design (6,16–18,20,22); for one abstract, the specific design could not be determined (8). The studies were published between 1979 and 2007. EIB was defined in the trials as a fall in FEV₁ of at least 10% (8,17,18) or 15% (6,16,20). In three trials (6,8,20), it was not clear if the ECT that followed the warm-up met the American Thoracic Society criterion of a work rate equal to 80%–90% of an individually calculated HR_{max} (5). The time between warm-up and standardized ECT ranged from 1 to 49 min.

One study (6) included children only, three included adults only (16,17,20), and three included both children and adults (8,18,22). All participants were described as having mild stable asthma, except for one study (an abstract) where the asthma incidence and severity could not be determined (Table 2) (8).

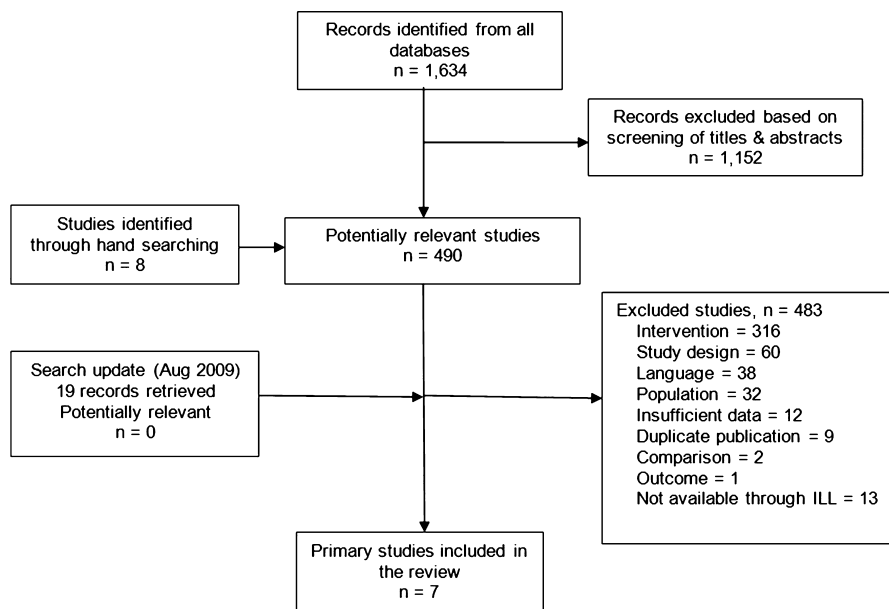


FIGURE 1—Flow diagram for study retrieval and selection.

Five studies investigated two or more warm-up protocols. The protocols were categorized into four subgroups based on the intensity of the routine. Four routines involved several short sprints and were designated “interval” warm-ups (6,16,17,22). Two studies involved two standardized challenges 45 min apart at 80%–90% of peak workload and were designated “continuous high-intensity” warm-ups (20,22). Three involved treadmill runs at work rates of 60% and were designated as “continuous low-intensity” warm-ups (16,18,20). The study by Eck et al. (8) and one arm of the study by Schnall and Landau (22) used a continuous routine followed by an interval routine and are reported separately as “variable-intensity” warm-ups. Study arms that involved drug therapy with or without a warm-up were not included in this analysis (17). See Table 1 for further description of warm-up protocols.

Overall, the methodological quality of the included studies was considered to be low with Jadad scores ranging from 1 to 2. No study described the randomization method. None stated that the assessors were blind. Concealment of allocation was unclear in all the trials.

Quantitative Results

Interval protocol. Four trials involving 52 patients compared the fall in FEV_1 in an ECT after an interval warm-up with the fall in an identical ECT with no previous warm-up (control challenge) (6,16,17,22). Spirometry was conducted up to 10 (6), 15 (17), 25 (16), and 80 min (22) after ECT. The interval warm-up protocols involved repetitive sprints of 26–30 s at 100% maximal oxygen consumption ($\dot{V}O_{2max}$) or higher. The mean difference in the maximum percent fall in FEV_1 in the subsequent ECT ranged from an improvement of 4.8%–16.1% over the control challenge. The pooled

results (Fig. 2) showed that a series of short, intense sprints attenuated the EIB response by a mean of -10.6% (95% CI = -14.7% to -6.5% , $I^2 = 15\%$). One study (16) reported that 1 of the 12 participants had falls in $FEV_1 < 15\%$ and would be classified as having obtained complete protection from EIB after the interval warm-up.

Continuous low-intensity protocol. Three trials involving 13 patients compared the fall in FEV_1 in an ECT after a continuous low-intensity warm-up that ranged from 3 (18) to 30 min (20) with an identical control challenge with no prior warm-up. The exercise intensity for the warm-up was 60% of HR_{max} (18), 60% of $\dot{V}O_{2max}$ (16), and reported as “low intensity” in the third study (20). Spirometry was conducted up to 25 (16), 30 (18), and 90 (20) min after ECT. The mean difference in the maximum percent fall in FEV_1 in the subsequent ECT ranged from no improvement to 20.6% over the control challenge. The pooled results (Fig. 2) showed that this type of warm-up failed to attenuate the EIB response (MD = -12.6% , 95% CI = -26.7% to 1.5% , $I^2 = 90\%$). One study also reported that 6 of the 12 participants had falls in $FEV_1 < 15\%$ and classified them as having obtained complete protection from EIB (16).

Continuous high-intensity protocol. Two trials involving 37 patients compared the fall in FEV_1 in an ECT after a continuous high-intensity warm-up with a control challenge with no warm-up (20,22). Exercise intensity for the warm-up was at $HR = 180$ bpm (22) and $98\% \pm 2\%$ of predicted maximum (20). Spirometry was conducted up to 80 (22) and 90 min (20) after ECT. The mean difference in the maximum percent fall in FEV_1 in the subsequent ECT ranged from very little improvement (0.99%) to 17.6% over the control challenge. The pooled results (Fig. 2) showed that this type of warm-up failed to attenuate the EIB response (MD = -9.8% , 95% CI = -26.0% to 6.4% , $I^2 = 89\%$).

TABLE 1. Description of RCTs included in the review.

Author (yr)	Country	Source	Publication Status		Randomized (R)		Warm-up Protocol Description; Rest	ECT Type/Duration (min) after No Warm-up or Warm-up	ECT: Temp; RH	Definition EIB (% Fall FEV ₁)	
			Funding	Trial Design	Analyzed (A)	Withdrawals (W)				Outcomes:	Primary
de Bisschop et al. (1999) (6)	France	Journal article	NR	30	30	No warm-up or Protocol 1: interval: two sets of 5 × 26-s sprints, 1.5 min between, 5 min between sets (7.5% of the distance and 120% of the speed of FRAST)	FRAST: running as fast as possible × 7 min (mean distance = 1171 ± 142 m)	4°C ± 5°C; 1.5 ± 0.5 mm Hg	2; 1;	≥15% Primary: mean percent fall PEF	
Treatment center		Crossover		0	0	10-min rest		24 h, at mid day		Secondary: PEF (L·min ⁻¹); mean percent fall PEF predicted; PEF measured after each sprint, 5, and 10 min after sets; 5 and 10 min after FRAST NR ≥10% Primary: mean percent fall FEV ₁ Secondary: complete protection	
Eck et al. (2002) (8)	Germany, Switzerland	Abstract	NR	46	NR	No warm-up or 5-min stretching, no rest, plus Protocol 1: continuous: 10-min steady training	Treadmill × 10-min steady running	SABA × 12 h NR; NR 4; not clear; Not clear		NR ≥10% Primary: mean percent fall FEV ₁ Secondary: complete protection	
McKenzie et al. (1994) (16)	Canada	Journal article	NR	12	12	Protocol 2: interval: 10-min interval running Protocol 3: progressive: 10-min exercises with increasing intensity	Treadmill × 6 min at 90% VO _{2max}	20.7°C ± 1.2°C; ambient room humidity 3; not clear (three sessions);		≥15% Primary: max percent decrease FEV ₁	
Volunteers		Crossover		0	0	No warm-up or Protocol 1: continuous VO _{2max} separated by 1.5-min rest, 2-min rest		Not clear Caffeine and exercise × 4 h		Secondary: complete protection FEV ₁ measured at 0.5 min, then every 2 min to 25 min; NR ≥10%	
Mickleborough et al. (2007) (17)		Journal article		8	8	No warm-up or Protocol 1: interval: 8 × 30-s sprints with 45-s recovery between; 15-min rest (interval intensity equal to VO _{2max})	Treadmill × 8 min at 85%–90% predicted HR _{max} ; wore a noseclip	23°C; 50% 4; 1; ≥96 h		Primary: max percent decrease FEV ₁ ; AUC Secondary: NR	
United States, United Kingdom		NR		8	8	Protocol 1: interval: 8 × 30-s sprints with 45-s recovery between; 15-min rest (interval intensity equal to VO _{2max})		SABA × 12 h, caffeine/alcohol × 8 h, exercise × 24 h		FEV ₁ times measured at 1, 5, 10, 15 min	
University and local community		Crossover		0	0	Protocol 2: Sal 200 µg plus 8 × 30-s sprints with 45-s recovery between; 15-min rest; Protocol 3: Sal 200 µg; 15-min rest				NR	

Morton et al. (1979) (18)	Journal article Foundation Crossover	19 18 1	No warm-up or Protocol 1: continuous low-intensity: treadmill × 3 min at 60% predicted HR _{max} ; 1-min rest	Treadmill × 5 min at 85% predicted HR _{max}	Room temp, NR 2; 1; ≥8 d All med and exercise × 12 h	≥15% Primary: max percent decrease FEV ₁ Secondary: FVC percent change FEV ₁ times measured at 5, 10, 15, 20, and 30 min 1 AE ≥15%
Reiff et al. (1989) (20)	Journal article	7	Protocol 1: continuous high-intensity: treadmill at 15% incline; 6 km·h ⁻¹ × 6 min; 45-min rest HR = 98% ± 2% predicted max Protocol 2: continuous low-intensity: treadmill at 3% incline; 6 km·h ⁻¹ × 30 min; 21-min rest HR = 88% ± 32% predicted max	Treadmill × 6 min at 15% incline; 6 km·h ⁻¹ ; HR = 97% ± 3% predicted max	19.9°C ± 0.7°C; 39%–50% ± 4.0% 2; 1; Two sessions within 1 wk at same time of day ICS × 24 h; SABA × 8 h	Primary: max percent decrease FEV ₁ and PEF Secondary: mean percent fall FEV ₁ and PEF; AUC FEV ₁ /PEF measured at every 5 min to 90 min NR NR
Schnall and Landau (1980) (22)	Journal article	6	Protocol 1: continuous high-intensity: treadmill × 6 min at 10% incline (HR = 180 bpm), 49 min rest Protocol 2: progressive: treadmill × 6 min at 10% incline (HR = 180 bpm); 10-min rest; 7 × 30-s sprints with 2.5 min between (speed 120%–130% of first run); 20-min rest Protocol 3: interval: 7 × 30-s sprints with 2.5 min between (speed 120%–130% of first run) 20-min rest	Treadmill × 6 min at 10% incline; HR = 180 bpm	21°C–23.5°C ± 1.2°C; 0.55 3; 1;	Primary: max percent decrease FEV ₁ and PEF Secondary: FEV ₁ (L); PEF (L·min ⁻¹)
Australia	Government	6			SABA and SCG × 8 h	FEV ₁ /PEF measured at 0, 2, 5, 10, 15, 25 up to 80 min Yes
NR	Crossover	0			Three sessions in 4 wk	

AE, adverse events; AUC, area under the curve; FRAST, free-running asthma screening test; ICS, inhaled corticosteroid; NR, not reported; PEF, peak expiratory flow; RH, relative humidity; SABA, short-acting β-agonist; Sal, salbutamol; SCG, sodium chromoglycate; Temp, temperature; VO₂, oxygen consumption.

TABLE 2. Baseline characteristics of patients in studies included in the review.

Author (yr)	Age (Mean ± SD)		Asthma Status	Pulmonary Function: Baseline FEV ₁ Percent Predicted (Mean ± SD)		Max Percent Fall FEV ₁ (Mean ± SD)		Smoking Status, n (%)	Atopic Status, n (%)	ICS History, n (%)
	Males, n (%)	n (%)		PEF: 99 ± 15%	NR	PEF: 37 ± 14.5	NR			
de Bisschop et al. (1999) (6)	12; range 8–15 21/30 (70)	NR	Stable, mixed severity	PEF: 99 ± 15%	NR	PEF: 37 ± 14.5	NR	NR	NR	≥8/30 (26.7)
Eck et al. (2002) (8)	Range 6–19	NR	NR	NR	NR	NR	NR	NR	NR	NR
McKenzie et al. (1994) (16)	26.5 ± 7.8 3/12 (33.3)	NR	Stable	3.42 ± 1.05 L	>30	>30	Nonsmokers	NR	NR	None
Mickleborough et al. (2007) (17)	19.5 ± 1.2	NR	Mild to persistent	92.4 ± 6.12 (3.5 ± 0.82 L)	18.25 ± 4.01	18.25 ± 4.01	Never smoked	NR	NR	8/8 (100)
Morton et al. (1979) (18)	19.7; range 11–33 10/18 (55.6%)	NR	Stable	100	38.1	38.1	NR	NR	NR	NR
Reiff et al. (1989) (20)	25.4 ± 6.6 5/7 (71.4)	NR	Stable, mild to persistent	80.6 ± 20.7	FEV ₁ : 46 ± 6.9; PEF: 51 ± 10.6	FEV ₁ : 46 ± 6.9; PEF: 51 ± 10.6	NR	7/7 (100)	7/7 (100)	2/7 (28.6)
Schnall and Landau (1980) (22)	Range 12–31 4/6 (66.7)	NR	Stable	84.1 (2.7 ± 0.71 L)	22.8 ± 8.08	22.8 ± 8.08	NR	NR	NR	None

NR, not reported.

Variable-intensity protocols. Eck et al. (8) failed to identify significant difference among the three protocols they investigated in 52 patients—10 min of continuous low-intensity running, 10 min of running in intervals, and 10 min of exercising with increasing intensity (8). No data on the intensity of each warm-up were reported. Schnall and Landau (22) performed spirometry up to 80 min after ECT; Eck et al. (8) did not report timing of post-ECT spirometry. When combined, the three protocols protected 79% (36/46) of participants from EIB (cut point not reported). The combined mean maximum percent fall in FEV₁ on the challenges after all warm-up protocols was compared with an ECT with no warm-up and indicated a mean improvement of -11.0% (95% CI = -14.6% to -7.37%, $I^2 = 0\%$; Fig. 2).

One of three protocols in the Schnall and Landau (22) trial involved a combination of continuous and interval segments: a 6-min treadmill run (HR = 180 bpm), a 10-min rest followed by 7 × 30-s sprints (treadmill speed increased 120%–130% during the first run), and then a 20-min rest before the final challenge of the same intensity as the original 6-min run. The mean difference in the maximum percent fall in FEV₁ compared with results of a no-warm-up ECT was an improvement of -10.4% (95% CI = -21.1% to 0.24%). The pooled results (Fig. 2) showed that variable-intensity warm-up protocols attenuated the EIB response by a mean of -10.9% (95% CI = -14.4% to -7.5%, $I^2 = 0\%$).

No data/results were presented for any preexercise routine for symptom relief, clinical protection, or adverse effects.

DISCUSSION

Using a comprehensive search strategy and concerted efforts to avoid publication and selection bias, this systematic review identified all the available evidence that compared various forms of warm-up activities with no warm-up in the preexercise treatment of EIB. A total of seven RCTs were identified, involving 128 patients with documented EIB after vigorous exercise. The evidence suggests that, compared with no warm-up, high-intensity intervalor variable-intensity warm-up exercise before vigorous exercise offers a statistically significant attenuation in the percent fall in FEV₁ for up to 80 min, with the response fairly consistent across studies.

Interval exercise resulted in a mean attenuation in FEV₁ of 10.61%, ranging from -4.80% (16) to 16.10% (22). The warm-up exercise could be considered a physiological stress, and therefore, variations in warm-up protocol or environmental conditions may affect the stress on the airways and, correspondingly, the protective effect of the preexercise warm-up. The study by McKenzie et al. (16) showed the least protection for EIB, although the warm-up protocol and the environment conditions were similar to those described in the other included studies. Further, there were no apparent differences in subject characteristics among studies. It is unclear why the interval protocol used by McKenzie et al. (16) resulted in less attenuation of FEV₁ after the exercise challenge.

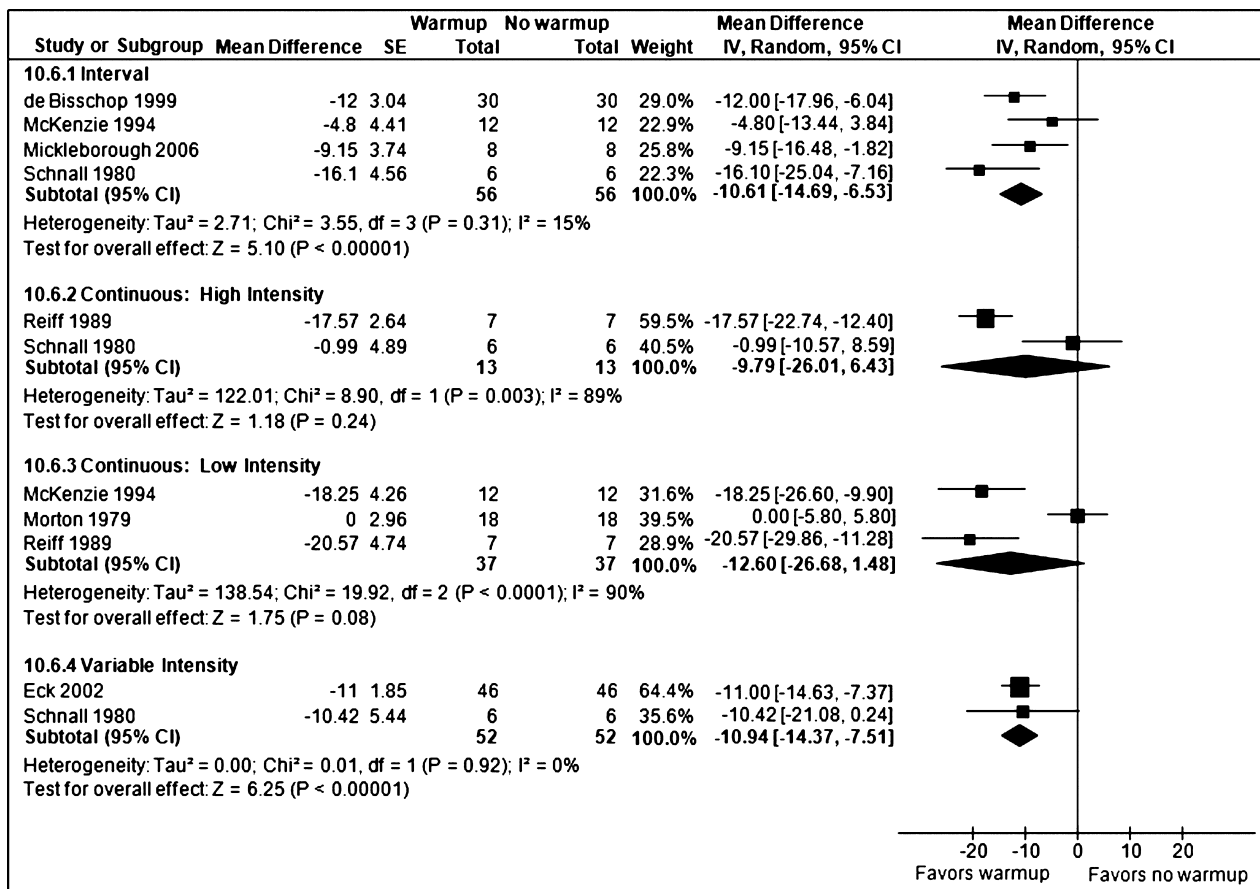


FIGURE 2—Warm-up versus no warm-up in preexercise treatment of EIB: maximum percent decrease in FEV₁ or peak expiratory flow.

In the two studies that examined continuous high-intensity warm-up, the mean attenuation in FEV₁ was -9.79%, with one study (20) showing significant protection (-17.57%), while the other study showing minimal protection (-0.99%) (22). In the study by Reiff et al. (20), the preexercise warm-up was 6 min at 98% of HR_{max}. In contrast, Schnall and Landau (22) had subjects exercise for 6 min at an absolute HR of 180 bpm. Schnall and Landau (22) report only an age range for their subjects (12–31 yr). Taking the median of the age range (22 yr), the predicted maximal HR would be ~198 bpm (220 - mean age), and therefore, 180 bpm represents ~91% of maximum. In addition, the relative humidity during all of the exercise conducted by Schnall and Landau (22) was 55%, which was higher than that reported by Reiff et al. (20) (range = 39%–50%). Taken together, the lack of protection for EIB observed by Schnall and Landau (22) may be explained by the reduced preconditioning airway stress during the warm-up, that is, lower exercise intensity and higher relative humidity.

The results of the three studies that examined continuous low-intensity warm-up showed a mean attenuation in FEV₁ of -12.60%, with two studies showing similar responses (-18.25% and -20.57%) (16,20), whereas one study showed no effect on FEV₁ (18). In the study by McKenzie et al. (16), subjects exercised for 15 min at 60% of $\dot{V}O_{2max}$, whereas in the study by Reiff et al. (20), subjects exercised for 30 min at

an average HR of 88% of maximum. In contrast, the study by Morton et al. (18), which showed no attenuation in the fall in FEV₁, had subjects exercise at 60% of maximum predicted HR for only 3 min. These results suggest that, in order for a continuous exercise warm-up to be effective in attenuating EIB, subjects may need to exercise longer (e.g., for at least 15 min).

Results of the variable intensity warm-up show a mean attenuation in FEV₁ of -10.94%. Of note, these studies need to be interpreted with caution. The study by Eck et al. (8) was a larger study (*n* = 46); however, it was a published abstract, and therefore, pertinent information such as EIB status and environmental conditions is absent. The “combination warm-up” arm of the study of Schnall and Landau (22) includes only six subjects and seems to have a high degree of variability in the change in FEV₁ (95% CI = -21.08% to 0.24%). In addition, because of the varying nature of the warm-up intensity, these protocols would be difficult to replicate as a standardized warm-up for subjects.

PHYSIOLOGICAL MECHANISM FOR REFRACTORY PERIOD

Potential physiological mechanisms have been proposed as to why exercise would cause a refractory period of EIB. Exercise is believed to result in dehydration of the airway

surface, which increases airway osmolarity, releasing inflammatory mediators (prostaglandins, leukotrienes, and histamine) from the mast cell, and it is the release of these mediators that causes bronchoconstriction (4). Of note, the pathophysiology of EIB in a patient with asthma may be different from bronchoconstriction in an athlete after exercise (4). The cause of this refractory period is not fully understood but may be due to depletion of catecholamines, increased circulation of prostaglandin, or degranulation of mast cell mediators. Depletion of mast cell mediator stores is a popular theory to explain refractory period after exercise (9,15,23). It has been hypothesized that warm-up causes a gradual discharge of mast cell mediators, and a time would be required for replenishment (10). If exercise is resumed within this period, then mediator stores would not be replenished, and therefore, EIB would not occur. McKenzie et al. (16) have suggested that if depletion of mast cell mediators explains the refractory period, then the duration of the warm-up would seem to be most critical. As the most consistent response was observed after high-intensity interval exercise, it would seem that duration of warm-up exercise is not most critical at attenuating EIB.

LIMITATIONS

The results from this review should be interpreted cautiously due to the relatively small sample sizes, low methodological quality of the RCTs, and the variability in the warm-up protocols studied. Importantly, because of the small number of studies reviewed, and the small sample sizes contained within the studies, the power to detect differences between the various types of warm-up protocol was limited. As a result, we were not able to conduct comparisons among protocols. As shown in Figure 2, both interval and variable-intensity protocols resulted in attenuation in FEV₁ of approximately 10%. Based on previous work, this magnitude of protection is likely clinically significant (2,3,12,21). Unfortunately, most studies did not report individual results, and therefore, individual clinical EIB protection could not be determined. Of note, studies performed spirometry up to 80 min after ECT, and therefore, preexercise warm-up should be considered a short-term strategy to prevent EIB.

REFERENCES

- Altman DG, Schulz KF. Statistics notes: concealing treatment allocation in randomised trials. *BMJ*. 2001;323(7310):446–7.
- Anderson SD, Brannan JD. Long-acting β_2 -adrenoceptor agonists and exercise-induced asthma: lessons to guide us in the future. *Paediatr Drugs*. 2004;6(3):161–75.
- Anderson SD, Brusasco V, Haahtela T, Popov T. *Criteria for Diagnosis of Asthma, EIB and AHR for Athletes: Lessons From the Olympic Games. Diagnosis, Prevention and Treatment of Exercise-Related Asthma, Respiratory and Allergic Disorders in Sport*. Wakefield (UK): European Respiratory Society Journals Ltd.; 2005. p. 44–66.
- Anderson SD, Holzer K. Exercise-induced asthma: is it the right diagnosis in elite athletes? *J Allergy Clin Immunol*. 2000;106(3):419–28.
- Crapo RO, Casaburi R, Coates AL, et al. Guidelines for methacholine and exercise challenge testing—1999. This official statement of the American Thoracic Society was adopted by the ATS Board of Directors, July 1999. *Am J Respir Crit Care Med*. 2000;161(1):309–29.
- de Bisschop C, Guenard H, Desnot P, Vergeret J. Reduction of exercise-induced asthma in children by short, repeated warm ups. *Br J Sports Med*. 1999;33(2):100–4.

In addition, limitations associated with systematic reviews should be discussed. First, there is a possibility of publication bias (i.e., that only positive studies were published). Importantly, we conducted comprehensive and systematic searches of the published literature for potentially relevant studies; these were supplemented by hand searching for gray literature (i.e., unpublished or difficult to find studies). Despite these efforts, we recognize that we may have missed some studies. In addition, EIB literature is not indexed well, and authors do not use consistent terms. To control for this, the search strategy was designed to be highly sensitive to avoid missing potentially relevant articles and 18 electronic databases were searched to retrieve as many studies as possible. More high-quality studies examining the efficacy of warm-up strategies to reduce EIB are needed.

CONCLUSIONS

From the available evidence, the attenuation in the fall in FEV₁ was similar whether high-intensity interval or variable intensity warm-up exercise was used. The attenuation in FEV₁ seems consistent with either warm-up strategy; however, interval exercise may be superior as it is a more easily standardized for the athlete/coach, and there is more evidence for this strategy. These findings indicate that an appropriate warm-up strategy, which includes at least some exercise close to peak oxygen consumption or maximal HR, may be a short-term nonpharmacological alternative to reducing EIB.

This project was funded under contract no. 290-2007-10021-I from the Agency for Healthcare Research and Quality, US Department of Health and Human Services. The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by the Agency for Healthcare Research and Quality or the US Department of Health and Human Services. Dr. Stickland is supported by a Canadian Institutes for Health Research (Ottawa, Ontario) New Investigator Award. Dr. Rowe is supported by the 21st Century Canada Research Chair Program through the Canadian Institutes of Health Research from the Government of Canada (Ottawa, Ontario).

The authors have no conflicts of interest to disclose.

The authors thank the Cochrane Airways Group for their assistance and providing access to their database of articles.

Results of the present study do not constitute endorsement by the American College of Sports Medicine.

7. Dryden DM, Spooner CH, Stickland MK, et al. Exercise-induced bronchoconstriction and asthma. *Evid Rep Technol Assess (Full Rep)*. 2010;(189):1–154, v–vi.
8. Eck R, Lachtermann E, Pleyer K, Schmitz M, Jung K. Effect of standardized warm-up programs on the intensity and frequency of exercise induced asthma (EIA) in children and teenagers. *Int J Sports Med*. 2002;23:S86.
9. Edmunds AT, Tooley M, Godfrey S. The refractory period after exercise-induced asthma: its duration and relation to the severity of exercise. *Am Rev Respir Dis*. 1978;117(2):247–54.
10. Godfrey S. Exercise-induced asthma—clinical, physiological, and therapeutic implications. *J Allergy Clin Immunol*. 1975;56(1):1–17.
11. Godfrey S, Bar-Yishay E. Exercised-induced asthma revisited. *Respir Med*. 1993;87(5):331–44.
12. Helenius IJ, Tikkanen HO, Haahtela T. Occurrence of exercise induced bronchospasm in elite runners: dependence on atopy and exposure to cold air and pollen. *Br J Sports Med*. 1998;32(2):125–9.
13. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med*. 2002;21(11):1539–58.
14. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials*. 1996;17(1):1–12.
15. Lee TH, Assoufi BK, Kay AB. The link between exercise, respiratory heat exchange, and the mast cell in bronchial asthma. *Lancet*. 1983;1(8323):520–2.
16. McKenzie DC, McLuckie SL, Stirling DR. The protective effects of continuous and interval exercise in athletes with exercise-induced asthma. *Med Sci Sports Exerc*. 1994;26(8):951–6.
17. Mickleborough TD, Lindley MR, Turner LA. Comparative effects of a high-intensity interval warm-up and salbutamol on the bronchoconstrictor response to exercise in asthmatic athletes. *Int J Sports Med*. 2007;28(6):456–62.
18. Morton AR, Fitch KD, Davis T. The effect of “warm-up” on exercise-induced asthma. *Ann Allergy*. 1979;42(4):257–60.
19. Randolph C. Exercise-induced asthma: update on pathophysiology, clinical diagnosis, and treatment. *Curr Probl Pediatr*. 1997;27(2):53–77.
20. Reiff DB, Choudry NB, Pride NB, Ind PW. The effect of prolonged submaximal warm-up exercise on exercise-induced asthma. *Am Rev Respir Dis*. 1989;139(2):479–84.
21. Rundell KW, Im J, Mayers LB, Wilber RL, Szmedra L, Schmitz HR. Self-reported symptoms and exercise-induced asthma in the elite athlete. *Med Sci Sports Exerc*. 2001;33(2):208–13.
22. Schnall RP, Landau LI. Protective effects of repeated short sprints in exercise-induced asthma. *Thorax*. 1980;35(11):828–32.
23. Schoeffel RE, Anderson SD, Gillam I, Lindsay DA. Multiple exercise and histamine challenge in asthmatic patients. *Thorax*. 1980;35(3):164–70.
24. Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA*. 1995;273(5):408–12.
25. Weiler JM, Anderson SD, Randolph C, et al. Pathogenesis, prevalence, diagnosis, and management of exercise-induced bronchoconstriction: a practice parameter. *Ann Allergy Asthma Immunol*. 2010;105(6 suppl):S1–47.