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SYSTEMATIC REVIEW

Sex Dimorphism of VO_{2max} Trainability: A Systematic Review and Meta-analysis

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Abstract

Background Increases in maximal oxygen uptake (VO_{2max}) are strongly associated with improved cardiovascular health.

Objective The aim was to perform a systematic review and meta-analysis to determine whether VO_{2max} responses to endurance training (ET), the most effective intervention to improve VO_{2max}, are influenced by sex.

Methods We conducted a systematic search of MEDLINE and Web of Science since their inceptions until February 2019 for articles assessing the VO_{2max} response to a given sex-matched dose of ET in healthy age-matched men and women. Meta-analyses were performed to determine the mean difference between VO_{2max} responses in men versus women. Subgroup and meta-regression analyses were used to assess potential moderating factors.

Results After systematic review, eight studies met the inclusion criteria. All studies implemented common modalities of ET in healthy untrained individuals, comprising a total of 175 men and women (90 ♂, 85 ♀). ET duration and intensity were sex-matched in all studies. After data pooling, ET induced substantially larger increases in absolute VO_{2max} in men compared with women (mean difference = + 191 ml·min^{-1}, 95% CI 99, 283; $P < 0.001$). A greater effect of ET on relative VO_{2max} was also observed in men versus women (mean difference = + 1.95 ml·min^{-1}·kg^{-1}, 95% CI 0.76, 3.15; $P = 0.001$). No heterogeneity was detected among studies ($I^2 = 0\%$, $P \geq 0.59$); the meta-analytical results were robust to potential moderating factors.

Conclusion Pooled evidence demonstrates greater improvements in VO_{2max} in healthy men compared with women in response to a given dose of ET, suggesting the presence of sexual dimorphism in the trainability of aerobic capacity.

Key Points

- Aerobic capacity, determined by maximal oxygen uptake (VO_{2max}), is improved to a greater extent in men compared with women in response to a given dose of endurance training.
- The consistency of this finding against potential confounding factors suggests the presence of a sexual dimorphism regarding VO_{2max} trainability.

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1 Introduction

Maximal oxygen uptake (VO_{2max}), a hallmark of aerobic capacity, lies within 30–85 ml·min^{-1}·kg^{-1} in healthy adults, encompassing a spectrum of aerobic capacities from untrained to elite endurance athletes [1–3]. Importantly, the higher is the VO_{2max}, the greater the likelihood to be free of cardiovascular disease (CVD), the main cause of mortality worldwide [4, 5]. Every gain in VO_{2max} counts; indeed, one metabolic equivalent increase in VO_{2max} (+ 3.5 ml·min^{-1}·kg^{-1}) is independently associated with ≥ 13% reduction in cardiovascular events and all-cause mortality [6]. The mortality benefit of high VO_{2max} seems to be slightly enhanced in women compared with men, possibly due to sex-specific adaptations underlying VO_{2max} improvement [4, 5]. Efforts to enhance VO_{2max} are commendable from functional and clinical standpoints in men and women.

The most effective intervention to improve VO_{2max} in humans is endurance training (ET), with typical increases ranging from 1 to 3 metabolic equivalents after 6 weeks or longer ET programs [2, 3, 7]. Analogous to the dose-response of pharmacological interventions, VO_{2max} responses to ET (thus termed VO_{2max} trainability) primarily depend on the total training dose, a function of exercise intensity, frequency and duration [7–9]. As a matter of fact, the extreme VO_{2max} levels reported in endurance athletes are underpinned by massive doses of ET sustained over several years [1, 10]. This observation is common to both male and female endurance athletes, albeit women frequently present with ~ 10 ml·min^{-1}·kg^{-1} less VO_{2max} compared with men of similar training status [1, 10]. Key determinants of VO_{2max} improvement such as cardiac adaptations are also attenuated in women versus men in response to the same ET dose [11]. On the other hand, skeletal muscle adaptations may be augmented in women relative to men matched by VO_{2max} and running performance [12]. Taken together, it has been suggested that women must be subjected to a higher ET dose than men to achieve a given VO_{2max} [12], a notion entailing a new variant of sex dimorphism with potential prognostic implications. Yet, very few studies have been specifically designed to elucidate sex differences in training responsiveness [11, 13]. Likewise, the identification of ET interventions separately reporting men and women VO_{2max} responses to the same training dose requires a systematic search of small sample size studies with seemingly conflicting results [11, 13–19]. Therefore, the primary purpose of this analysis was to systematically review and meta-analyze the effect of sex-matched doses of ET on VO_{2max} in healthy men and women, as well as to determine the influence of potential moderating factors.

2 Methods

The review is reported according to the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Group guidelines [20].

2.1 Data Sources and Searches

The systematic search included MEDLINE and Web of Science, since their inceptions until February 2019. We used combinations of the subject headings 'female', 'male', 'women', 'men', 'training', 'effect', 'adaptation', 'VO_{2max}' and 'VO_{2peak}'; the search strategy for MEDLINE is shown in Electronic Supplementary Material, Figure S1. We also performed hand searching in reference citations of identified reviews, personal article collections, articles included in meta-analysis and related citations in MEDLINE and Google Scholar.

2.2 Article Selection

To be included in the analysis, an original research article had to meet the following criteria: (1) ET intervention including healthy age-matched men and women, (2) definite sex-matched training dose, and (3) VO_{2max} reported prior to and after training. Studies following the above criteria but including additional interventions deemed likely to influence VO_{2max} were excluded. In the event of multiple publications pertaining to the same research, the most comprehensive report was included. Inclusion of articles was not limited by publication status or language.

2.3 Data Extraction and Quality Assessment

The following variables were summarized in a pre-formatted spreadsheet: authors, year of publication, characteristics of study participants (*n*, age, sex, height, body surface area, body mass index, weight, body fat percentage, heart rate, blood pressure, hematological profile, and health/fitness status), characteristics of the assessment of VO_{2max} (pre-testing conditions, test protocol, and criteria of VO_{2max}) and ET features (type, modality, frequency, intensity, session length, duration, and training dose). Given the observational design of the included studies, their methodological quality was assessed by a systematic appraisal of quality for observational research (SAQOR) [21] previously applied in meta-analyses evaluating VO_{2max} responses to exercise training [2, 3]. The SAQOR was adjusted to assess (1) the study sample, (2) quality of VO_{2max} assessment, (3) confounding variables and (4) data. Overall, the SAQOR was scored out of 14, quality deemed better with a greater score. Data extraction and quality assessment were performed independently and in duplicate by two investigators (D. M.) and (C. D).

2.4 Data Synthesis and Analysis

The meta-analysis was performed using Review Manager software (RevMan 5.3, Cochrane Collaboration, UK) and Comprehensive Meta-analysis software (CMA 2.0, Biostat, Englewood, USA). The primary outcomes were the mean difference between the effect of training on absolute VO_{2max} (ml·min^{-1}) or relative VO_{2max} (ml·min^{-1}·kg^{-1}) in men versus women. If the variability of change (i.e., standard deviation of change (SD_c)) for a given outcome was not reported, the formula $SD_c = \sqrt{[(SD_{pre})^2 + (SD_{post})^2 - (2 \times corr_{pre,post} \times SD_{pre} \times SD_{post})]}$ was applied [22]. SD_{pre}, SD_{post} and $corr_{pre,post}$ represent the standard deviation of the pre-training value, the standard deviation of the post-training value, and the correlation coefficient between pre- and post-training values, respectively. The $corr_{pre,post}$

was conservatively set at 0.5. Each mean difference was weighted by the inverse variance and they were pooled with a random-effects model [23].

Heterogeneity among studies was assessed using the Chi-squared test for heterogeneity and I^2 statistics. Potential moderating factors influencing the mean difference in VO_{2max} were evaluated by subgroup analysis comparing studies grouped by qualitative variables related to the training program and methodology of exercise testing (e.g., use of continuous intensity versus interval training, assessment of VO_{2max} with cycle ergometer versus treadmill). In addition, meta-regression analyses were performed to determine the association between the mean difference in VO_{2max} and sex-related differences in potential moderating quantitative variables (age, height, weight, body surface area, body composition, maximal heart rate, training characteristics, baseline VO_{2max}, year of publication, and methodological quality score). In all meta-regression models, studies were weighted by the inverse variance of the dependent variable. Potential moderating factors were entered as independent variables in regression models with the mean difference in VO_{2max} as the dependent variable. Publication and/or other biases were evaluated by the Begg and Mazumdar's rank correlation test and Egger's regression test [24]. A P value < 0.05 was considered statistically significant.

3 Results

3.1 Study Selection and Characteristics

The flow diagram of the process of article selection is illustrated in Fig. 1, which resulted in the inclusion of 8 studies. Table 1 shows main characteristics of the included studies, comprising a total of 175 healthy individuals (90 ♂, 85 ♀). The mean age and weight ranged from 22 to 64 years and 59–82 kg, respectively. All the studies included untrained individuals, i.e., not engaged in regular exercise training and presenting with sedentary normal VO_{2max} levels. VO_{2max} was determined in all studies prior to and after ET with established incremental (cycle ergometer or treadmill) exercise protocols. The percentage change in VO_{2max} from pre- to post-training ranged from 5.0 to 27.5% in men and from 2.9 to 26.3% in women. With respect to ET characteristics (Table 2), cycling was a modality of endurance exercise in all studies, while 3 studies additionally comprised running, walking and/or swimming [11, 13, 17]. Average session length, frequency and duration of the training program ranged from 0.4 to 3 h, 3–6 sessions per week and 7–52 weeks. The overall training dose, defined by exercise intensity and total training time, was matched between men and women in all studies (Electronic Supplementary Material, Table S1).

The methodological quality of the studies was moderate-to-high (Electronic Supplementary Material, Table S2). The average score was 8.4 ± 1.8 out of a possible 14 points. With respect to the evaluation of potential biases for the mean difference in VO_{2max}, the Begg and Mazumdar's rank correlation test ($P = 0.71$) and Egger's regression test ($P = 0.48$) did not suggest the presence of publication bias and/or other biases in the studies included in the meta-analysis.

3.2 Effect of Endurance Training on VO_{2max} in Men Versus Women

ET induced significant increases in absolute ($ml \cdot min^{-1}$) and relative ($ml \cdot min^{-1} \cdot kg^{-1}$) VO_{2max} in all studies. After data pooling, ET induced a larger increase in absolute VO_{2max} in men compared with women ($n = 175$, mean difference = 191 $ml \cdot min^{-1}$, 95% CI 99, 283 $ml \cdot min^{-1}$; $P < 0.001$) (Fig. 2). No heterogeneity was detected among studies ($I^2 = 0\%$, $P = 0.69$). Likewise, the meta-analysis revealed a greater effect of ET on relative VO_{2max} in men versus women ($n = 175$, mean difference = 1.95 $ml \cdot min^{-1} \cdot kg^{-1}$, 95% CI 0.76, 3.15 $ml \cdot min^{-1} \cdot kg^{-1}$; $P = 0.001$) (Fig. 3), with null heterogeneity among studies ($I^2 = 0\%$, $P = 0.59$). Furthermore, subgroup and meta-regression analyses did not detect any significant influence of potential qualitative and quantitative moderating factors (main characteristics of study subjects, ET features, and study methodology) on the mean difference in $VO_{2max,}$ either in absolute or relative terms.

4 Discussion

In this systematic review and meta-analysis, we pooled and analyzed data from eight studies assessing the effects of sex-matched ET doses on VO_{2max} in a total of 175 healthy men and women. The main finding of this meta-analysis is that ET elicits greater increases in VO_{2max} in men compared with women, an outcome that was remarkably robust across potential moderating variables including baseline subject characteristics, ET features and exercise testing methodology.

The present meta-analysis of longitudinal studies indicates that for a given dose of ET, the VO_{2max} response differs between men and women. In response to ET, men exhibit almost + 200 $ml \cdot min^{-1}$ and + 2 $ml \cdot min^{-1} \cdot kg^{-1}$ in VO_{2max}, i.e., more than a half metabolic equivalent increase, compared with women, a gain associated with ~ 7–9% reductions in cardiovascular events and all-cause mortality [6]. Moreover, no significant heterogeneity was detected among studies. In line with our results, lower VO_{2max} in women relative to men of comparable training status has been reported in cross-sectional studies [12, 25, 26]. Likewise, sedentary women generally present lower VO_{2max} than men [27]. These

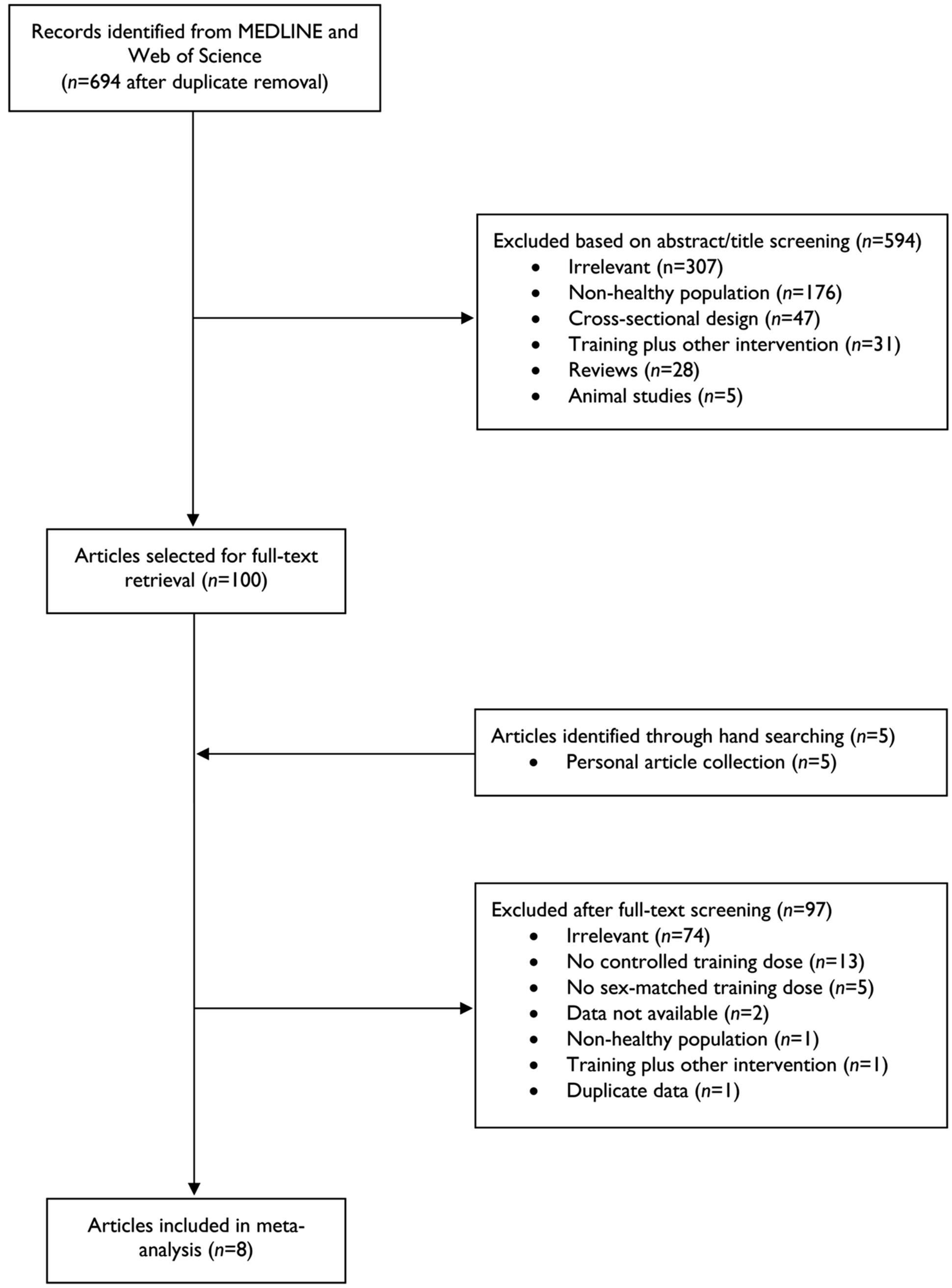

Fig. 1 Flow diagram of the process of article selection

differences could be explained by multiple factors, possibly assorted into two main categories: 'constitutional' and 'environmental'. Conforming to the first category, sex differences in VO_{2max} could primarily lie in sex-specific genetic traits. In contrast, distinct levels of physical activity/ET, possibly not discernible in cross-sectional studies, belong to the second class. The consistent results of this meta-analysis imply that 'constitutional', i.e., genetic factor(s) might underlie the sex-specific VO_{2max} trainability. We may thus suggest the presence of inherent differences between men and women in VO_{2max} responsiveness to ET, i.e., sex dimorphism of VO_{2max} trainability [28]. Whilst speculative, from an evolutionary perspective DNA variant facilitating adaptations in VO_{2max} could have been particularly selected in men [29]. Yet, the underpinning genetic basis of VO_{2max} trainability remains unresolved and candidate genes (e.g., ACE) thought to explain high levels of VO_{2max} have not been confirmed in population studies [30, 31]. Notwithstanding, the potential implications of the current findings in terms of sex-specific strategies to improve cardiovascular fitness and prevent CVD [4, 5, 30] will have to be addressed by future investigations.

The question arises as to which adaptations to ET could explain sex differences in VO_{2max} trainability. Previous

Table 1 Main characteristics of studies included in the meta-analysis

References	n		Age (year)		Weight (kg)		BSA (m^{-2})		VO_{2max} ($ml \cdot min^{-1} \cdot kg^{-1}$)		VO_{2max} (% change)[a]	
	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
Montero et al. [16]	5	6	26 ± 4	28 ± 5	73 ± 13	69 ± 24	1.92	1.77*	45.4 ± 9.7	30.9 ± 7.0*	10.3	10.3
Howden et al. [11]	7	5	26 ± 7	31 ± 6	78 ± 6	60 ± 3*	1.96	1.67*	43.4 ± 5.5	36.5 ± 1.1*	24.0	14.8
Tarnopolsky et al. [18]	5	7	24 ± 4	22 ± 1	80 ± 20	65 ± 6	1.98	1.71*	42.9 ± 7.3	36.9 ± 6.6	9.3	14.4
Weber et al. [19]	7	7	24 ± 4	23 ± 7	81 ± 6	64 ± 4*	1.98	1.74*	44.4 ± 6.3	39.6 ± 2.4	5.0	2.9
Carter et al. [14]	8	8	22 ± 3	22 ± 3	78 ± 7	67 ± 8*	1.95	1.74*	41.5 ± 6.8	32.3 ± 4.5*	17.3	26.3
McKenzie et al. [15]	6	6	27 ± 3	27 ± 2	79 ± 12	59 ± 9*	1.96	1.63*	45.9 ± 4.4	37.7 ± 6.1*	12.0	18.3
Seip et al. [17]	28	29	64 ± 3	64 ± 3	82 ± 12	67 ± 13*	n/a	n/a	28.2 ± 4.4	22.4 ± 3.2*	22.3	18.8
Kohrt et al. [13]	24	17	64 ± 3	64 ± 3	82 ± 12	64 ± 12*	1.99	1.70*	27.6 ± 4.6	22.1 ± 3.0*	27.5	20.8

Data are *n*, mean ± SD, mean or % change. *Significantly different from male group at $P < 0.05$

BSA, body surface area, *n/a* data not available, VO_{2max} maximal oxygen uptake

[a]Percentage change from pre- to post-training

Table 2 Endurance training (ET) characteristics of studies included in the meta-analysis

References	Modality	Intensity	Hrs/session	Frequency (#/week)	Duration (week)	Total training dose (♂ vs. ♀)[a]
Montero et al. [16]	CYC	50–70% W_{max}	1	3	8	Sex-matched intensity and total training time
Howden et al. [11]	CYC, RUN, SWM	5 levels according to HR_{max}	0.8–3	3–5	52	Sex-matched intensity and total training time
Tarnopolsky et al. [18]	CYC	60% VO_{2max}	1	5	7	Sex-matched intensity and total training time
Weber et al. [19]	CYC	82.5–100% W_{max}	0.4	3	8	Sex-matched intensity and total training time
Carter et al. [14]	CYC	60% VO_{2max}	1	5	7	Sex-matched intensity and total training time
McKenzie et al. [15]	CYC	60% VO_{2max}, 100% VO_{2max}	1.1	6	5	Sex-matched intensity and total training time
Seip et al. [17]	CYC, RUN, WLK	65–85% HR_{max}	0.8–1	4	39–52	Sex-matched intensity and total training time
Kohrt et al. [13]	CYC, RUN, WLK	60–85% HR_{max}	0.5–0.8	4	52	Sex-matched intensity and total training time

Data are *n*, mean ± SD, mean or range

CYC cycling, HR_{max} maximal heart rate, *Hrs* hours, *RUN* running, *SWM* swimming, VO_{2max} maximal oxygen uptake, *WLK* walking, W_{max} maximal power output

[a]Detailed information on training dose is presented in Electronic Supplementary Material, Table S1

experimental studies have demonstrated the fundamental role of increases in blood volume and hemoglobin mass for ET-induced improvements in VO_{2max} [7, 16, 32]. Blood volume expansion, comprising ~ 10% increments in plasma and red blood cell volume, is observed following approximately 4–6 weeks of ET in healthy previously untrained individuals [7, 16, 32–34]. As a result, cardiac preload, stroke volume and cardiac output are enhanced, collectively leading to increased capacity to deliver oxygen, the main determinant of VO_{2max} in healthy humans [30, 32]. In fact, VO_{2max} improvements are reverted to pre-training levels when hematological adaptations are abolished by means of phlebotomy [32, 35]. Yet, whether blood volume adaptations dictate cardiac function and aerobic capacity in women remains uncertain. The vast majority of previous experimental studies underpinning our current understanding of VO_{2max} determinants mainly comprise young men. Provided that blood volume–cardiac interactions are not altered by sex, reduced VO_{2max} trainability in women could be partly explained by blunted hematological adaptations

Study or Subgroup	Men Mean	Men SD	Men Total	Women Mean	Women SD	Women Total	Weight	Mean Difference IV, Random, 95% CI
1.1.1 Change in absolute maximal oxygen uptake (ml·min^{-1})								
Montero et al [16], 2017	362	270	5	208	16	6	15.1%	154.00 [-83.01, 391.01]
Howden et al [11], 2015	730	456	7	320	131	5	6.7%	410.00 [53.21, 766.79]
Tarnopolsky et al [18], 2007	300	457	5	310	340	7	3.8%	-10.00 [-483.18, 463.18]
Weber et al [19], 2002	270	478	7	70	261	7	5.2%	200.00 [-203.45, 603.45]
Carter et al [14], 2001	548	402	8	546	292	8	7.2%	2.00 [-342.30, 346.30]
McKenzie et al [15], 2000	300	557	6	300	265	6	3.5%	0.00 [-493.55, 493.55]
Seip et al [17], 1993	410	317	28	220	261	29	37.3%	190.00 [38.97, 341.03]
Kohrt et al [13], 1991	490	427	24	210	220	17	21.2%	280.00 [79.70, 480.30]
Subtotal (95% CI)			**90**			**85**	**100.0%**	**191.13 [98.91, 283.35]**

Heterogeneity: Tau² = 0.00; Chi² = 4.73, df = 7 (P = 0.69); I² = 0%
Test for overall effect: Z = 4.06 (P < 0.0001)

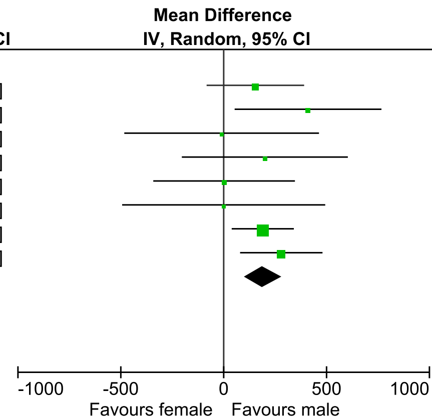

Fig. 2 Forest plot of the mean difference between the training effect on absolute VO_{2max} (ml·min^{-1}) in men versus women. Squares represent the mean difference for each study. Diamonds represents the pooled mean difference across studies. *CI* confidence interval, *df* degrees of freedom, *IV* inverse variance, *SD* standard deviation

Study or Subgroup	Male Mean	Male SD	Male Total	Female Mean	Female SD	Female Total	Weight	Mean Difference IV, Random, 95% CI
1.1.1 Change in relative maximal oxygen uptake (ml·min^{-1}·kg^{-1})								
Montero et al [16], 2017	4.67	3.05	5	3.18	0.71	6	19.1%	1.49 [-1.24, 4.22]
Howden et al [11], 2015	10.41	6.26	7	5.4	2.68	5	5.3%	5.01 [-0.19, 10.21]
Tarnopolsky et al [18], 2007	4	7.56	5	5.3	6.65	7	2.1%	-1.30 [-9.56, 6.96]
Weber et al [19], 2002	2.21	6.05	7	1.15	4.45	7	4.6%	1.06 [-4.50, 6.62]
Carter et al [14], 2001	7.2	5.99	8	8.5	4.01	8	5.7%	-1.30 [-6.30, 3.70]
McKenzie et al [15], 2000	5.5	5.52	6	6.9	6.2	6	3.2%	-1.40 [-8.04, 5.24]
Seip et al [17], 1993	6.3	4.45	28	4.2	3.46	29	33.1%	2.10 [0.03, 4.17]
Kohrt et al [13], 1991	7.6	4	24	4.6	3.47	17	27.0%	3.00 [0.70, 5.30]
Subtotal (95% CI)			**90**			**85**	**100.0%**	**1.95 [0.76, 3.15]**

Heterogeneity: Tau² = 0.00; Chi² = 5.56, df = 7 (P = 0.59); I² = 0%
Test for overall effect: Z = 3.21 (P = 0.001)

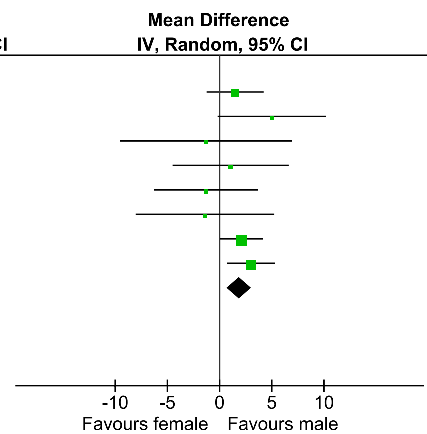

Fig. 3 Forest plot of the mean difference between the training effect on relative VO_{2max} (ml·min^{-1}·kg^{-1}) in men versus women. Squares represent the mean difference for each study. Diamonds represents the pooled mean difference across studies. *CI* confidence interval, *df* degrees of freedom, *IV* inverse variance, *SD* standard deviation

[36]. In this respect, cross-sectional studies in elite female endurance athletes (Olympic medalists) clearly show high blood volumes (5–6 l), albeit far lower than those of male athlete counterparts with similar anthropometric measures [1]. Otherwise, observational evidence from longitudinal studies is scarce and inconclusive with respect to sex differences in blood volume adaptations to ET [11, 16]. Exiguous, but more consistent results have been reported regarding cardiac structural and functional variables that may facilitate increases in stroke volume and cardiac output. Of note, cardiac adaptations seem to be enhanced with ET interventions comprising high-intensity ET and/or exercise modalities involving greater central hemodynamic loads [37–42]. A 1-year long-distance running program sex-matched by training stimuli, including high-intensity exercise, induced a less prominent increase in left ventricular (LV) mass and Frank–Starling curves in women versus men [11]. Similarly, in prepubertal children, 3 months of ET resulted in attenuated increases in LV internal chamber size in girls compared with boys, a cardiac adaptation linearly related to the effect of ET on stroke volume, cardiac output and VO_{2max} [43]. These adaptations are coherent with cross-sectional analyses in endurance athletes [44] and population studies, in that adult sedentary women commonly present with lower LV mass and volume for a given LV filling pressure compared with body size-matched men [45, 46]. The women's heart may thus be stiffer and less amenable to eccentric remodeling than in men [47], thus limiting central adaptations underlying VO_{2max} trainability.

In addition to central determinants of VO_{2max}, peripheral variables along the O_2 transport and utilization chain can be hypothesized to play a role in VO_{2max} trainability. With this regard, adaptations in systemic and skeletal muscle blood flow distribution, mitochondrial content and function might facilitate O_2 extraction. Yet, the fact that O_2 extraction is near peak levels at VO_{2max} in untrained (male) individuals limits the potential contribution of peripheral adaptations to enhanced VO_{2max} responses to ET in men relative to women [48, 49]. On the other hand, sex differences in specific peripheral adaptations such as skeletal muscle vasodilation leading to decreased systemic vascular resistance might contribute to central adaptations (augmented stroke volume) and VO_{2max} improvement [43]. Collectively considered, further research is needed to establish the mechanisms that explain the blunted VO_{2max} trainability in women.

4.1 Limitations and Strengths

We selected studies assessing ET interventions in healthy individuals to limit the influence of disease-related confounding factors. Further research will elucidate whether the present findings can be extrapolated to clinical populations. Second, a relatively few number of studies were included and the majority of them involved different intensities and doses of cycle ergometry ET; thus, our conclusions should be taken with caution and be primarily limited to this type of endurance exercise. Third, there might be sex differences in the lag time between ET and VO_{2max} responses. Yet, a reduced VO_{2max} trainability in women versus men was observed independently of the duration of ET, including in long-term studies, in that a plateau in VO_{2max} was plausibly achieved [11, 13, 17]. Fourth, the included studies did not report comprehensive information about lifestyle factors, which could differ between untrained men and women. Future studies and meta-analyses might take lifestyle factors into account to provide far-reaching insights. Finally, the mean methodological quality of the included studies was determined as moderate-to-high and no publication bias and/or other biases were detected.

5 Conclusions

The current meta-analysis provides evidence that VO_{2max}, a hallmark of aerobic capacity, is further improved in men compared with women healthy individuals in response to a given ET dose. The consistency of this finding against potential confounding factors suggests the presence of a sexual dimorphism regarding the main physiological adaptations determining VO_{2max} improvement with ET. The specific mechanisms underlying sex-specific VO_{2max} trainability are speculative at present and will have to be characterized in future experimental studies.

Data Availability Statement The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Compliance with Ethical Standards

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Conflict of interest David Montero and Candela Diaz-Canestro declare that they have no conflicts of interest relevant to the content of this review.

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