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Effect of aerobic exercise training on pulse wave velocity in adults with and without long-term conditions: a systematic review and meta-analysis

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ABSTRACT

Rationale There is conflicting evidence whether aerobic exercise training (AET) reduces pulse wave velocity (PWV) in adults with and without long-term conditions (LTCs).

Objective To explore whether PWV improves with AET in adults with and without LTC, to quantify the magnitude of any effect and understand the influence of the exercise prescription.

Data sources CENTRAL, MEDLINE and EMBASE were among the databases searched.

Eligibility criteria We included studies with a PWV measurement before and after supervised AET of at least 3 weeks duration. Exclusion criteria included resistance exercise and alternative measures of arterial stiffness.

Design Controlled trials were included in a random effects meta-analysis to explore the effect of AET on PWV. Uncontrolled studies were included in a secondary meta-analysis and meta-regression exploring the effect of patient and programme factors on change in PWV. The relevant risk of bias tool was used for each study design.

Results 79 studies (n=3729) were included: 35 controlled studies (21 randomised control trials (RCT) (n=1240) and 12 non-RCT (n=463)) and 44 uncontrolled (n=2026). In the controlled meta- analysis, PWV was significantly reduced following AET (mean (SD) 11 (7) weeks) in adults with and without LTC (mean difference −0.63; 95% CI −0.82 to −0.44; p<0.0001). PWV was similarly reduced between adults with and without LTC (p<0.001). Age, but not specific programme factors, was inversely associated with a reduction in PWV −0.010 (−0.020 to −0.010) m/s, p<0.001.

Discussion Short-term AET similarly reduces PWV in adults with and without LTC. Whether this effect is sustained and the clinical implications require further investigation.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ There is conflicting evidence whether aerobic exercise training (AET) reduces pulse wave velocity (PWV) in adults with and without long-term conditions (LTCs).

WHAT THIS STUDY ADDS

⇒ We found that PWV is significantly and similarly reduced following AET in adults with and without LTC.
⇒ Older age was associated with larger reductions in PWV following AET.
⇒ In the meta-analyses, different components of the exercise prescription did not affect PWV.
⇒ Whether these results are sustained in the longer term is unknown, but measures of future cardiac risk should be included as outcomes for exercise programmes in people with LTCs.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ AET should form an integral part of the management of people with a range of LTCs with the aim of reducing future cardiovascular risk.

INTRODUCTION

Arterial stiffness (AS) is a surrogate measure of cardiovascular risk that can be used to predict future cardiovascular events and all-cause mortality.[1 2] Pulse wave velocity (PWV) is a non- invasive measure of the speed of a pulse wave travelling between the two sites being assessed. A rise in AS is reflected by an increase in the velocity. The measurement of PWV from the carotid to the femoral, also known as carotid-femoral PWV (cfPWV), is the non-invasive clinical measure of PWV. An increase in aortic PWV of 1 m/s corresponds to an adjusted risk increase of 14% in cardiovascular events and 15% in cardiovascular mortality and all-cause mortality over a period of 7 years.[3]

Cardiovascular diseases are the leading cause of death globally.[4] Cardiovascular risk factors, including physical inactivity, high caloric intake and higher levels of adiposity, are shared among many long-term conditions (LTCs). Thus, identifying populations at highest risk of cardiovascular disease

using surrogate markers such as AS will ensure appropriate treatment is provided. However, there is minimal evidence regarding reducing increased cardiovascular risk in adults with and without LTCs.

Strategies to reduce cardiovascular risk have been proposed with aerobic exercise training (AET) shown to reduce AS in young healthy adults.[5] There are inconsistent conclusions as to whether AET improves central and peripheral PWV in adults with LTC.[6–8] It is also unclear how features of the exercise prescription (frequency, intensity, type of exercise and duration of intervention and sessions) impact the change in PWV.

To date, systematic reviews suggest that AET reduces PWV in a mixed cohort of adults with and without LTCs.[9–11] This approach prevents an understanding of how AET influences PWV in each separate cohort (healthy and LTC). These reviews have included studies that prescribe concurrent aerobic and resistance exercise training, and therefore, do not isolate the effects of AET on PWV. Thus, this systematic review and meta-analysis aims to extend previous work by assessing the effect of AET on PWV in each discrete adult population (eg, healthy, cardiometabolic risk factors and LTC), while also determining the magnitude of effect on a population level. In addition to this, we aimed to understand the impact of the exercise prescription and any participant factors on the influence of AET on PWV.

METHODS

This review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[12] This review was not registered on PROSPERO. The protocol was prospectively developed however it was not published.

Study eligibility

The inclusion criteria for this review were studies of adults, over 18 years, undergoing a supervised AET programme for a minimum of 3 weeks, with a PWV measurement before and after the intervention. Online supplemental material 1 includes the classification of the AET programmes. The exclusion criteria included trials with resistance exercise or combined aerobic and resistance/strength exercise training and interventions with no supervision (home-based exercise).

Literature search

The Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, EMCARE, Cumulative Index to Nursing and Allied Health Literature (CINAHL) and PeDRO databases were searched on 16 July 2021 from conception. The search terms included "pulse wave velocity", "exercise" and "adult" (see online supplemental material 1) for the full search terms. Eligible studies were selected by two independent reviewers.

Data extraction

The following information was extracted into a preformatted spreadsheet: (1) participant demographics, (2) disease/health characteristics, (3) exercise intervention characteristics, (4) method of the assessment of PWV and (5) outcome measures.

The measure of variability of the change in PWV (SDchange) was not reported in 47 of the 79 included studies. This was calculated using the test statistic (p value) (k=13) or using a correlation coefficient specific (k=34) for this review, as recommended by the Cochrane Handbook of systematic reviews.[13]

The risk of bias was assessed independently by two reviewers using the relevant tool; the Revised Cochrane risk-of-bias tool for randomised trials (RoB 2) for randomised control trials (RCTs), the Risk Of Bias In Non-randomised Studies of Interventions tool for the non- RCTs and the Quality Test Tool for Observational Cohort and Cross-sectional studies for the uncontrolled studies.

Outcomes

The primary outcome was central and peripheral PWV measured by applanation tonometry, oscillometry, cardiac MRI or ultrasound. The secondary outcomes were aspects of the exercise prescription. The participant factors include age, sex at birth, body mass index, systolic blood pressure, cholesterol, Hbin A1c and exercise capacity.

Statistical analysis

The analysis was performed using the 'metafor' package in R (V.4.1.1). The prescribed exercise intensity was reported in different manners and thus, classified into four categories as described previously[14] (online supplemental e-Table 4).

Meta-regression was performed including participant factors, programme factors and methods measuring PWV, to explore the relationships between these factors and changes in PWV following AET. The meta-regression was controlled for age, sex-at-birth and baseline cfPWV. An increase in cfPWV has been linked with an increased risk of cardiovascular events, thus, this measure was used in the meta regression. An 'estimate' was produced representing the change in mean difference (MD) for one-unit change in the variable of interest. All the subanalyses were run twice; once unadjusted and once adjusted for the participant factors (see online supplemental material 1).

Publication bias was evaluated using funnel plots and Egger's regression test.[15] The heterogeneity of studies was assessed using the Cochrane Q statistics; $p>0.1$ signifies significant heterogeneity. Additionally, an I^2 test can be used to evaluate the heterogeneity of the studies; <25% shows low risk of heterogeneity, 25%–75% shows moderate risk of heterogeneity, >75% specifies high risk of heterogeneity.[16] A $p<0.05$ was considered statistically significant.

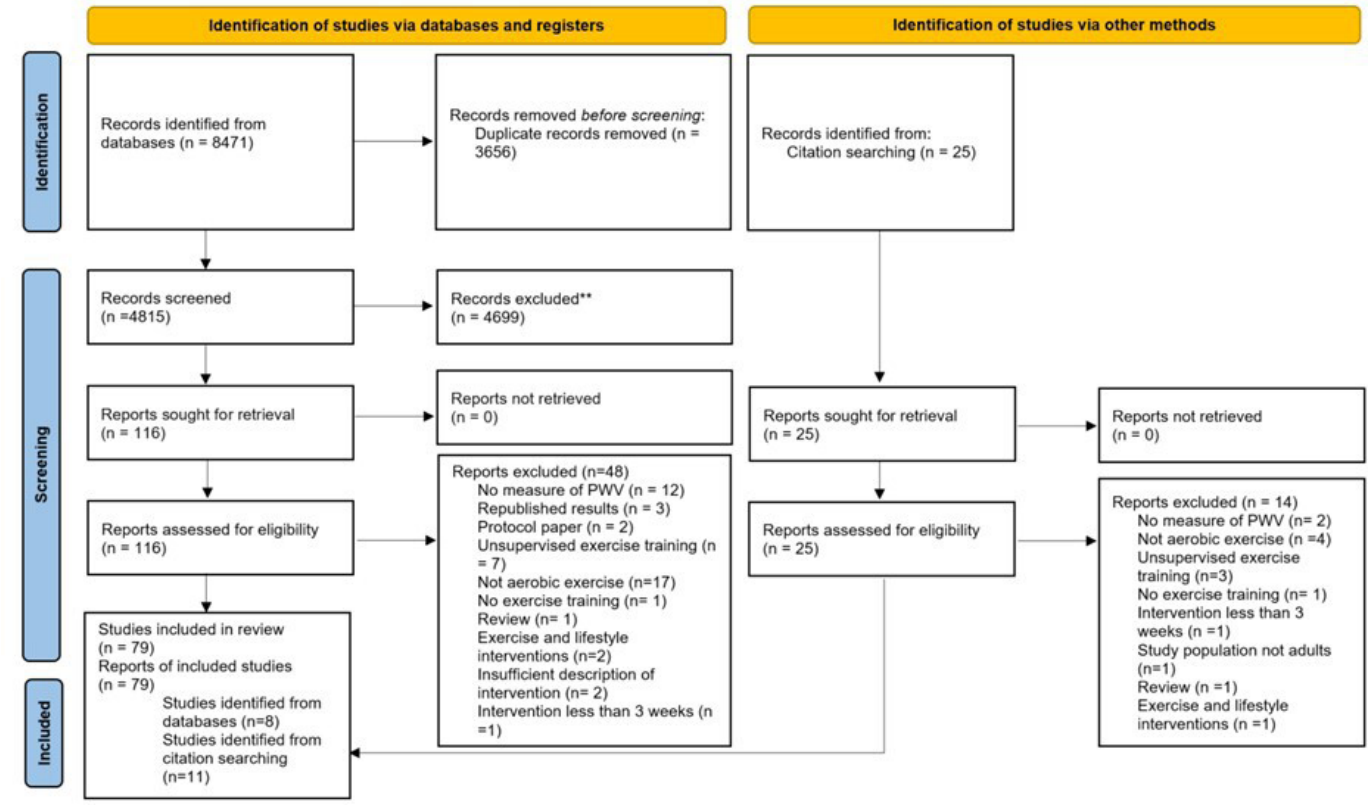

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2009 diagram of study selection. **Reasons for exclusion are detailed in online supplemental file 1.

The certainty of evidence was rated using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach[17] using the GRADEPro online tool.

RESULTS

Study screening

The database searches identified 8471 publications of which 79 studies were included in the quantitative analysis (figure 1). Reasons for exclusion can be found in online supplemental e-Table 1. Characteristics of included studies are shown in table 1 for controlled trials and online supplemental e-Table 2 shows the uncontrolled studies. Uncontrolled studies (USs) were defined as studies without a control group such as cohort studies. From the 79 included studies, 30 were randomised controlled trials (RCTs), 12 were non-randomised controlled trials (non-RCTs), 2 were cross-over studies and 35 were USs.

Study characteristics

The total number of participants was 3076 (47% male) with a mean age of 48 (range 20–76) years. The sample sizes ranged from 6 to 71 participants and the mean duration of the intervention was 11 weeks (range: 4–52 weeks). The studies had measures of cfPWV (k=47; n=1813), aortic PWV (k=10; n=306) brachial-ankle PWV (k=13; n=363), carotid-brachial PWV (k=3; n=76), unspecified PWV (k=6; n=157) or radial PWV (k=1; n=11). Significant reductions were observed in studies that had measures of carotid-femoral, brachial ankle and carotid-brachial PWV following short-term AET (online supplemental e-Table 5). There was no difference in the method of assessing PWV (online supplemental e-Table 6).

Of the 79 studies, 25 had 2 intervention groups of which 7 were controlled studies. The studies were divided into two categories according to their population: healthy adults (k=50) and adults with LTC (k=55). Three studies possessed two intervention groups whereby one group consisted of adults with LTC and the other group included healthy adults.[18–20]

For the controlled meta-analysis, the LTCs were classified into cardiometabolic risk factors and disease groups. The cardiometabolic risk factors contained study populations of prehypertension and stage I hypertension,[21–23] isolated systolic hypertension,[24] metabolic syndrome[18 25 26] and hypertension complicated by type II diabetes and hyperlipidaemia.[1 6] The disease groups can be seen in figure 2.

Table 2 compares the demographics of the studies conducted in adults with and without LTC. The mean cfPWV of the studies conducted in healthy populations and adults with LTC were 8.04 and 9.23 m/s, respectively. Details of the training programmes for the controlled trials are shown in online supplemental e-Table 3.

Effect of AET on PWV

The meta-analysis of controlled studies (RCTs, non-RCTs and crossover studies) also showed a significant

Table 1 Description of included randomised and non- randomised controlled trials

Study	Country	Participant's characteristics	Intervention group					Control group			
			N	Age (years)	Sex at birth (% male)	BMI (kg/m^2)	Type of PWV measured	N	Age (years)	Sex at birth (% male)	BMI (kg/m^2)
Randomised controlled trials											
Adams *et al*,[28] 2017	Canada	Testicular cancer survivors	35	44 (12)	100	27.2 (5.0)	cfPWV	27	43 (10)	100	27.9 (4.2)
Beck *et al*,[23] 2013	USA	Prehypertension	13	20 (1)	69	28.7 (1.4)	cfPWV	15	22 (1)	67	27.0 (1.1)
Bouaziz *et al*,[42] 2019	France	Healthy	27	73 (3)	30	28.7 (5.3)	cfPWV	29	74 (3)	23	28.8 (5.0)
Ciolac *et al*,[43] 2010	Brazil	Healthy	32	26 (5)	0	23.9 (4.6)	cfPWV	15	25 (4)	0	25.3 (3.1)
Deiseroth *et al*,[44] 2019	Switzerland	Healthy	38	58 (5)	82	33.3 (3.0)	cfPWV	30	57 (6)	37	33.1 (5.1)
Graham-Brown *et al*,[27] 2021	UK	Haemodialysis	51	56 (16)	82		aPWV	50	59 (15)	65	
Greenwood *et al*,[45] 2015	UK	Kidney transplant recipients	13	54 (11)	77	26.6 (4.7)	cfPWV	20	50 (11)	50	27.3 (3.6)
Goldberg *et al*,[46] 2012	Australia	Healthy	15	21 (2)	100	23.3 (1.9)	cfPWV	15	21 (2)	100	23.4 (2.3)
Ha *et al*,[47] 2018	Korea	Healthy	11	74 (2)	0	23.9 (1.8)	cbPWV	8	76 (6)	0	29.1 (12.5)
Hannemann *et al*,[48] 2020	Germany	Healthy	12	34 (9)	42	26.8 (5.6)	PWV	12	37 (14)	25	27.8 (6.9)
Hanssen *et al*,[49] 2017	Switzerland	Episodic migraine	25	36 (10)	20	23.0 (6.9)	aPWV	12	37 (12)	17	23.4 (2.8)
Hasegawa *et al*,[50] 2018	Japan	Healthy	26	68 (7)	50	23.5 (3.5)	cfPWV	26	66 (9)	50	24.7 (4.7)
Hasegawa *et al*,[51] 2018	Japan	Healthy	14	24 (5)	100	21.9 (1.6)	aPWV	7	21 (1)	100	24.8 (3.4)
Headley *et al*,[52] 2014	USA	Chronic kidney disease	25	58 (8)	64	34.9 (8.0)	aPWV	21	57 (9)	67	36.5 (8.9)
Heydari *et al*,[7] 2013	Australia	Healthy	20		100	28.4 (2.4)	cfPWV	21		100	29.0 (3.9)
Ho *et al*,[53] 2020	Australia	Healthy	30	54 (3)	0	28.2 (3.5)	baPWV	30	53 (3)	0	27.4 (3.5)
Kang *et al*,[25] 2016	Korea	Metabolic syndrome	12	49 (11)	0	26.7 (2.1)	baPWV	11	51 (9)	0	25.4 (3.1)
Kim *et al*,[54] 2017	USA	Healthy	27	65 (6)	20	28.4 (4.0)	cfPWV	11	63 (7)	36	25.3 (4.6)
Koh *et al*,[55] 2010	Australia	Haemodialysis	15	52 (11)	67	27.6 (7.2)	cfPWV	16	51 (14)	50	28.6 (7.3)
Madden *et al*,[6] 2013	Canada	Hypertension complicated by type two diabetes and hyperlipidaemia	25	69 (5)	52	30.9 (5.0)	cfPWV	27	70 (63)	63	28.6 (4.2)
Madden *et al*,[1] 2009	Canada	Hypertension complicated by type 2 diabetes and hyperlipidaemia	17	72 (5)		30.1 (4.5)	cfPWV	17	71 (4)		27.7 (4.1)
Mora-Rodriguez *et al*,[26] 2018	Spain	Metabolic syndrome	23	53 (9)	83	32.8 (3.3)	cfPWV	23	54 (9)	83	32.9 (3.4)
Nualnim *et al*,[21] 2012	USA	Prehypertension or stage 1 hypertension	24	58 (10)	29	29.0 (1.0)	cfPWV	19	61 (9)	21	31.0 (1.0)
Oliveira *et al*,[56] 2015	Portugal	Acute myocardial infarction	37	55 (11)	87	26.5 (3.2)	cfPWV	41	59 (11)	81	27.1 (2.8)
Oudegeest-Sander *et al*,[57] 2013	The Netherlands	Healthy	11	68 (3)	73	27.0 (2.6)	cfPWV	11	71 (5)	27	24.3 (3.3)
Pascoalino *et al*,[58] 2015	Brazil	Heart transplant recipients	31	45 (17)	74	26.7 (5.0)	cfPWV	9	45 (18)	56	25.1 (7.5)
Sugawara *et al*,[59] 2011	Japan	Healthy	11	59 (7)	0	23.4 (1.0)	cfPWV	11	59 (7)	0	21.6 (0.8)
Oliveira e Silva *et al*,[60] 2019	Brazil	Chronic kidney disease on haemodialysis	15	50 (17)	47	25.7 (3.6)	cfPWV	15	58 (15)	53	26.7 (4.6)
Yoshizawa *et al*,[61] 2009	Japan	Healthy	12	47 (7)	0	24.6 (3.8)	cfPWV	12	49 (10)	0	21.8 (3.5)

Continued

Table 1 Continued

Study	Country	Participant's characteristics	Intervention group N	Age (years)	Sex at birth (% male)	BMI (kg/m^2)	Type of PWV measured	Control group N	Age (years)	Sex at birth (% male)	BMI (kg/m^2)
Zempo-Miyaki *et al*,[29] 2016	Japan	Healthy	16	54 (8)	31	24.4 (4.4)	cfPWV	16	67 (6)	38	21.1 (2.0)
Non-randomised controlled trials											
Aghaei Bahmanbeglou *et al*,[22] 2019	Iran	Stage 1 hypertension	20	48 (5)	100	28.9 (5.0)	baPWV	10	47 (3)	100	29.5 (5.3)
Donley *et al*,[18] 2014	USA	Healthy	11	41 (13)	36	24.0 (3.3)	cfPWV	10	40 (13)	20	25.0 (3.2)
Donley *et al*,[18] 2014	USA	Metabolic syndrome	11	46 (13)	27	38.0 (6.6)	cfPWV	11	44 (10)	45	34.0 (6.6)
Fujie *et al*,[62] 2020	Japan	Healthy	27	21 (4)	56	21.1 (1.6)	cfPWV	9	21 (1)	56	21.8 (2.1)
Fujie *et al*,[62] 2020	Japan	Healthy	26	67 (7)	39	23.9 (3.6)	cfPWV	14	68 (6)	43	21.6 (4.1)
Holloway *et al*,[63] 2018	UK	Healthy	12	21 (2)	100	24.0 (3.0)	cfPWV	9	21(2)	100	23.0 (3.0)
Kim *et al*,[64] 2018	Korea	Healthy	28	67 (2)	0		cbPWV	12	66 (4)	0	
Mamen *et al*,[65] 2020	Norway	Healthy	19	43 (11)			PWV	37	38 (12)		
Shenouda *et al*,[66] 2017	Canada	Healthy	19	28 (8)	100	26.5 (5.4)	cfPWV	6	26 (8)	100	25.0 (7.0)
Soriano-Maldonado *et al*,[67] 2017	Spain	Systemic lupus erythematosus	26	43 (15)	0	25.9 (3.4)	PWV	32	45 (13)	0	24.7 (5.6)
Wong *et al*,[68] 2018	USA	Postmenopausal women with stage 2 hypertension	20	59 (4)	0	24.2 (3.6)	baPWV	21	59 (5)	0	23.8 (3.7)
Vivodtzev *et al*,[69] 2010	France	COPD	10	62 (9)	80	23.0 (5.0)	cbPWV	7	63 (6)	57	23.0 (4.0)

Cross-over trials

Study	Country	Participant's characteristics	N	Age (years)	Sex at birth (% male)	BMI (kg/m^2)	Type of PWV measured
Ferrier *et al*,[24] 2001	Australia	Isolated systolic hypertension	10	64 (7)	50	29.1 (3.2)	cfPWV
Toussaint *et al*,[70] 2008	Australia	End-stage kidney disease on haemodialysis	9	69 (8)	56	27.0 (4.0)	cfPWV
Toussaint *et al*,[70] 2008	Australia	End-stage kidney disease on haemodialysis	10	61 (16)	40	24.0 (4.0)	cfPWV

Data are expressed as mean (SD) unless specified.
aPWV, aortic PWV; baPWV, brachial-ankle PWV; BMI, body mass index; cbPWV, carotid-brachial PWV; cfPWV, carotid-femoral PWV.COPD, chronic obstructive pulmonary disease; PWV, pulse wave velocity;

reduction in PWV (MD −0.63; 95% CI −0.82 to −0.44; p<0.0001) (figure 3). There was a reduction in PWV across all study designs (RCTs: MD −0.73; 95% CI −0.99 to -0.47, non-RCTs: MD −0.44; 95% CI −0.74 to -0.14, cross-over studies: MD −1.00; 95% CI −1.69 to −0.32). The larger meta-analysis combining all 79 controlled and USs showed AET significantly reduces PWV (MD −0.47; 95% CI −0.57 to −0.36; p<0.0001).

PWV was significantly reduced following AET in a meta-analysis of studies measuring PWV using carotid-femoral (MD −0.63; 95% CI −0.82 to −0.44; p<0.0001), brachial-ankle (MD −0.74; 95% CI −1.15 to −0.32; p<0.0005) and carotid-brachial (MD −0.97; 95% CI −1.62 to −0.32; p<0.005) (online supplemental e-Table 5).

Comparing adults with and without LTCs

In the meta-analysis of controlled and US, the effect of AET on PWV was not different between the studies conducted in healthy populations and those conducted in adults with LTC. Following AET, PWV was significantly reduced in adults with LTC (MD −0.86; 95% CI −1.36 to −0.37; p<0.0001) and healthy adults (MD −0.59; 95% CI −0.83 to −0.35; p<0.0001).

Subgroup and meta-regression analysis

The results of the meta-regression indicated that the population type (healthy or with LTC) did not reach statistical significance in the controlled studies (p=0.19). The meta-regression conducted in all studies also showed

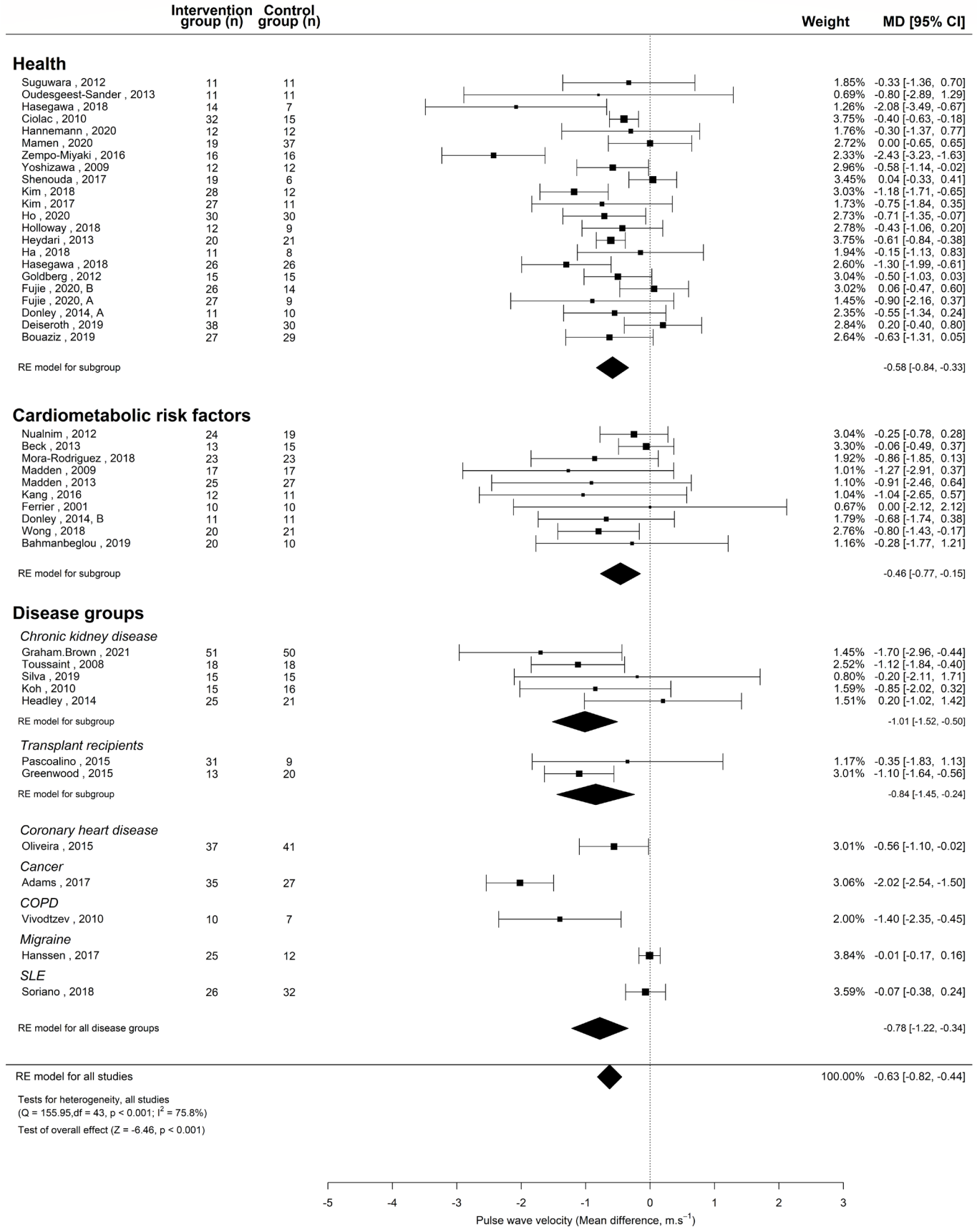

Figure 2 Meta-analysis of controlled trials assessing the effect of aerobic exercise training in health and long-term condition. MD, mean difference; RE model, random effects model.

Table 2 Study demographics between studies in health and long-term conditions

Baseline demographics	Health (k=50; n=1666)	Long-term conditions (k=55; n=2063)
Age (years)	44±6	52±10
Male (%)	47	46
BMI (kg/m^2)	26.0±3.9	28.5±4.9
cfPWV (m/s)	8.17±2.15	9.23±2.48
BaPWV (m/s)	11.39±1.14	14.74±2.96
SBP (mm Hg)	123±13	132±21
DBP (mm Hg)	74±9	78±14
VO2max (mL/kg/min)	32.14±15.44	24.50±5.45
Heart rate (beats/min)	75±16	68±9
Glucose (mg/dL)	5.23±1.10	6.23±1.63
Cholesterol (mg/dL)	4.97±0.90	5.22±1.61
HDL cholesterol (mg/dL)	7.45±2.42	3.94±2.00
LDL cholesterol (mg/dL)	2.94±0.74	3.12±1.45
Triglycerides (mg/dL)	1.05±0.59	2.18±2.32

Data are expressed as mean±SD unless specified.
baPWV, brachial ankle pulse wave velocity; BMI, body mass index; cfPWV, carotid-femoral pulse wave velocity; DBP, diastolic blood pressure; HDL, cholesterol, high-density lipoprotein; K, number of studies in this category; LDL, cholesterol, low-density lipoprotein; PWV, pulse wave velocity; SBP, systolic blood pressure; VO2max, maximum rate of oxygen consumption.

that the presence of LTC does not affect the impact AET has on PWV (p=0.06) with and without adjustment for age, sex at birth and baseline PWV (p=0.77).

The meta-regression for programme and subject characteristics are shown in tables 3 and 4, respectively. Age was the strongest predictor of the improvement of PWV following AET, with an inverse relationship (table 3), and remained significant after controlling for sex at birth, presence of LTC and baseline PWV (table 3). The reduction in PWV following AET was independent of all aspects of the exercise prescription and health parameters reported (table 4).

Sensitivity analyses

In the meta-analysis of the controlled studies, three studies[27–29] had a significant influence on the results potentially due to these studies showing the biggest change in PWV in the intervention group. Thus, a sensitivity analysis excluding these studies showed an MD −0.52 m/s; (95% CI −0.68 to −0.37; p<0.0001) and there was no difference between this sensitivity analysis and main meta-analysis (p=0.34). Subgroup analysis of methods of calculating SD was statistically different (p=0.02), with the greatest change in PWV using presented test statistic (p values and CIs) (MD −1.03; 95% CI −1.34 to −0.73) and the smallest change seen in studies for which SD was imputed (MD −0.44; 95% CI −0.73 to −0.15).

Bias and heterogeneity

Across the studies, the risk of bias was low except for blinding of participants and personnel, for which the risk was high in 54 studies (68%). There was no difference (p=0.45) between the effect of AET on PWV in studies with a high risk of bias (MD −0.80; 95% CI −1.26 to −0.33) and studies with low risk of bias (MD −0.60; 95% CI −0.82 to −0.37).

Egger's regression test for publication bias was significant for the controlled and US (p=0.0014), however, there was no publication bias within the controlled studies (p=0.109). Heterogeneity was high for the meta-analysis of RCTs alone (I^2=74.1%), this is also seen in the meta-analysis of all studies (I^2=72.16%).

Certainty of evidence

The quality of evidence supporting the conclusion that AET reduces PWV in adults with and without LTC was assessed as very low.

DISCUSSION

After pooling data from 79 studies, this systematic review and meta-analysis suggests short-term AET significantly reduces PWV in adults with and without LTC by a similar magnitude. The participant factors were not associated with greater improvement in PWV, however, cohorts of older age had a greater reduction in PWV following AET than younger cohorts. The impact of PWV was independent of all recorded aspects of the exercise prescription. Similarly, the technique used to measure PWV, which includes cfPWV, brachial-ankle PWV and carotid-brachial PWV, did not affect the findings and neither did the equipment used to measure PWV.

The magnitude of the change in PWV from this review is −0.63 m/s across health and disease, which is potentially associated with a risk reduction of 9.3% for cardiovascular events, 10.0% for cardiovascular and all-cause mortality over 7 years, extrapolated from existing data.[3] The subanalyses showed that the presence of LTC does not impact the influence AET has on PWV. This implies that the beneficial effects of AET on vascular stiffness is not limited to healthy adults and exercise programmes incorporating AET could be of benefit for adults regardless of their health status to reduce the risk of cardiovascular events.

Eleven conditions have been collated in this review to explore the effect of AET on PWV, however, it is evident that this association has not been investigated in various conditions, including inflammatory disorders and mental health conditions associated with high levels of sedentary behaviour. Considering inflammatory markers are associated with AS and patients with primary inflammatory disorders have increased vascular stiffness,[30] an AET programme could reduce the risk of cardiovascular events in adults with inflammatory conditions. AET programmes could also benefit conditions such as depression and anxiety that are associated with decreased levels

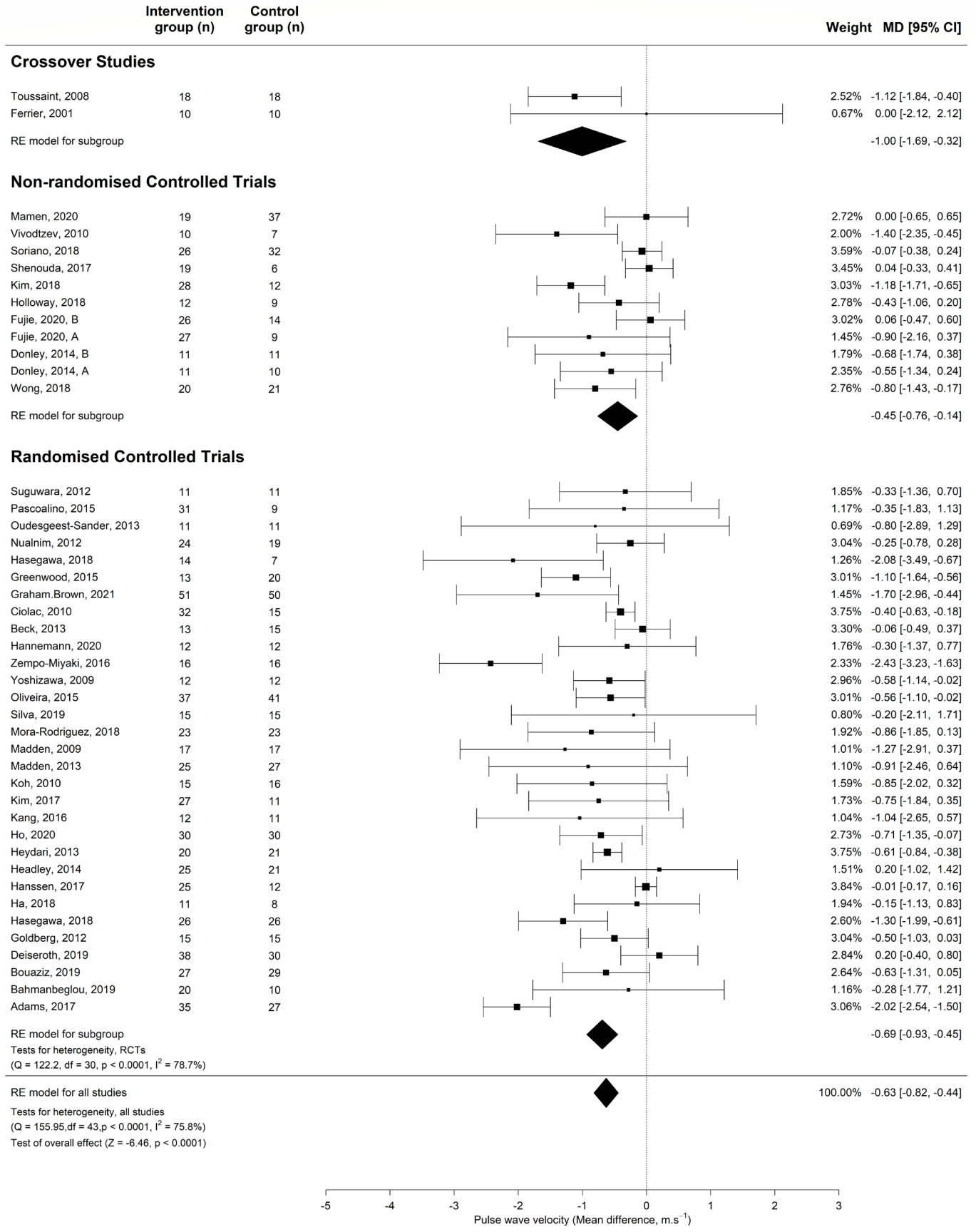

Figure 3 Meta-analysis of controlled trials assessing the effect of aerobic exercise training vs control on PWV in adults. MD, mean difference; PWV, pulse wave velocity. RE model, random effects model

Table 3 Meta-regression of participant characteristics

	Meta-regression ΔPWV (uncontrolled)			Meta-regression controlled for age, sex at birth, baseline PWV and presence of long-term conditions		
Variable	N=	Estimate (95% CI)	P value	N=	Estimate (95% CI)	P value
Age	100	0.01 (–0.02 to –0.005)	0.0005*	98	0.01 (–0.02 to –0.003)	0.008*
Sex at birth	99	0.001 (–0.004 to 0.002)	0.46	98	0.003 (–0.006 to 0.0004)	0.10
BMI	89	0.0003 (–0.03 to 0.03)	0.99	84	0.02 (–0.01 to 0.06)	0.22
Systolic blood pressure	97	0.01 (–0.02 to –0.0009)	0.03*	91	0.004 (–0.01 to 0.02)	0.59
Cholesterol	51	0.02 (–0.10 to 0.15)	0.74	46	0.03 (–0.18 to 0.12)	0.73
HbA1c	21	0.01 (–0.03 to 0.008)	0.26	18	0.007 (–0.25 to 0.26)	0.96
VO2 max	65	0.01 (–0.006 to 0.03)	0.23	61	0.004 (–0.03 to 0.02)	0.78

*p≤0.05.
BMI, body mass index; HbA1C, Glycosylated Haemoglobin; PWV, pulse wave velocity; VO2 max, maximum rate of oxygen consumption.

of physical activity, often linked to a rise in cardiovascular risk. Rehabilitation programmes for people with chronic obstructive pulmonary disease (COPD) and chronic heart failure (CHF) usually target improvements in exercise capacity and quality of life rather than improvements in cardiovascular risk, and therefore, the effect of AET on AS has rarely been studied in these populations.

AET was chosen as the intervention as this modality confers beneficial effects on the heart and increases exercise capacity. Reduction in central and peripheral stiffness has been reported following AET in healthy populations[31–35] and hypertensive adults.[36] The underlying mechanisms by which AET reduces vascular stiffness is unknown, however, evidence suggests it may be via arterial remodelling, improved endothelial function and decreased sympathetic tone.[31]

Previous systematic reviews comparing the influences of aerobic, resistance and combined (aerobic and resistance) exercise training on a range of measures of vascular stiffness collectively report that AET significantly improves vascular stiffness whereas resistance and combined exercise had no effect in a mixed cohort of adults with and without LTC.[9 11] A common hypothesis suggests the resistance exercise component of the combined exercise could limit the improvement in AS, as resistance training has been linked to increased PWV.[37] Despite the influence of resistance exercise on vascular stiffness, this mode of exercise is associated with many cardiometabolic benefits including reduction of resting blood pressure and prevention and management of type 2 diabetes.[38]

In contrast to previous systematic reviews,[9–11] this review collates studies with supervised AET rather than concurrent aerobic and resistance exercise training interventions. Despite the similar change in PWV after AET across the systematic reviews, updated studies have been added to this review alongside US enabling a clear understanding of the impact that AET has on PWV. This review also differs from the previous reviews as it explores whether any aspect of the exercise prescription or the population demographics influences the change in PWV.

The quality of evidence in this review was graded very low with the main reason being the inclusion of

Table 4 Meta-regression of programme factors

	Meta-regression ΔPWV			Meta-regression controlled for age, sex at birth, baseline PWV and presence of long-term conditions		
Variable	No of studies	Estimate (95% CI)	P value	No of studies	Estimate (95% CI)	P value
Duration programme of	104	0.01 (–0.03 to 0.01)	0.40	98	0.001 (–0.03 to 0.02)	0.94
Frequency	103	0.03 (–0.20 to 0.14)	0.73	97	0.01 (–0.18 to 0.16)	0.94
No of sessions	103	0.004 (–0.01 to 0.004)	0.34	97	0.0003 (–0.008 to 0.008)	0.94
Intensity	104	0.05 (–0.19 to 0.08)	0.44	98	0.09 (–0.22 to 0.04)	0.19
Duration of exercise session	102	0.001 (–0.007 to 0.01)	0.74	96	0.0006 (–0.009 to 0.008)	0.88
Total exercise duration	99	0.0007 (–0.01 to 0.009)	0.88	95	0.0005 (–0.01 to 0.01)	0.93

PWV, pulse wave velocity.

observational studies (non-RCTs) alongside the RCTs. The high heterogeneity may also contribute to the low grading.

Strengths and limitations

The main strength of this systematic review was the focus on AET in isolation to remove the possible confounding of resistance training, and the inclusion of US to provide a larger dataset for meta-regression, allowing exploration of the impact of patient and programme factors on change in PWV.

The main limitation of this study is that it explores the effect of an exercise intervention on PWV when it is unknown whether the reduction in cardiovascular events associated with AET is mediated by AS or an alternative mechanism.

The mean duration of the AET programmes in the included studies was 11 weeks. Although a reduction in PWV was observed, the long-term benefits of AET on PWV, cardiovascular health and the effect of detraining on PWV remain unknown. One trial reported that PWV returned to baseline levels after 1 month of detraining.[39]

Poor reporting of exercise interventions, specifically training intensity, potentially reduced the power of the meta-regression to detect an effect for patient and programme factors. There was a greater change in PWV observed in studies where SD was estimated using presented test statistics compared with using correlation coefficient. A potential explanation is that studies reporting test statistics often show significant results demonstrating precise results with greater effects.

The included studies possessed small sample sizes (number of participants range: 6–71), indicating the studies could be predominantly underpowered. High risk of bias was present in study designs other than RCTs due to a lack of participant blinding, potentially leading to performance bias, however, this is very difficult to avoid in studies of exercise training. The presence of publication bias could indicate successful trials are more likely to be published, supported by the three positive studies that had a large influence on the change in PWV. The number of studies in individual diseases was small, suggesting the need for further exploration in these diseases.

Narrowing the focus of this review to AET restricts the application of these results to interventions that combine AET with other factors (eg, resistance training or dietary modification). In turn, this excludes populations with LTC, such as COPD and CHF, for whom rehabilitation programmes lead to beneficial effects on symptoms often include resistance and AET.[40 41] Pharmacological interventions, includinganti-hypertensive and lipid-lowering medications, can influence PWV but were not taken into consideration in this review.

Finally, confining the measure of AS to PWV could limit the generalisability of the results. Although combining different measures of AS such as PWV, carotid-intima thickness and flow-mediated vasodilation would illustrate the overall picture of AS, these parameters cannot be compared as each measure assesses a different aspect of vascular stiffness.

CONCLUSION

PWV is reduced following short-term AET in both adults with and without LTC, and the overall magnitude of the change is −0.63 m/s, which is of prognostic importance. There was no difference between the effect of AET on PWV between healthy populations and populations with LTC, however, cohorts with older mean age showed greater improvement in PWV following AET. The exercise prescription did not influence the impact of AET on PWV. However, the overall quality of data was graded very low, with high heterogeneity and inclusion of observational studies. Despite the paucity of studies in specific LTC, AET should form an integral part of the management of people with a range of LTCs with the aim of reducing future cardiovascular risk.

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