# Comparative effectiveness of different types of exercise reducing arterial stiffness in children and adolescents 

## Supplementary material

Table S1. Characteristics of the included studies

|  |  |  | Sample |  |  | Intervention |  | Outcome |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Reference | Country | Study design | Sample size (\%women) | Age (years) | Type of population | Type of exercise | Intervention characteristics | Type of PWV | Measuring device | Basal values (m/s) |
| Bharath et al. 2018 | United States | RCT | $\begin{gathered} \hline \mathrm{IG}=20 \\ (100 \%) \\ \mathrm{CG}=20 \\ (100 \%) \end{gathered}$ | $\begin{gathered} \text { IG: } \\ 14.8 \pm 1 \\ \text { CG: } \\ 14.6 \pm 1 \end{gathered}$ | Obese adolescents | Combined exercise | IG: Resistance training $+30^{\prime}$ treadmill walking <br> - 60 min <br> - 5 times/wk <br> - 12 weeks | baPWV | Tonometry SphygmoCor | $\begin{gathered} \text { IG: } \\ 8.5 \pm 1.2 \\ \text { CG: } 8.3 \pm 1 \end{gathered}$ |
| Bruyndonckx et al. 2015 | Belgium | Quasi experiment al study | $\begin{gathered} \mathrm{IG}=33 \\ (72.7 \%) \\ \mathrm{CG}=28 \\ (78.5 \%) \end{gathered}$ | $\begin{gathered} \text { IG: } \\ 15.4 \pm 1.5 \\ \text { CG: } \\ 15.1 \pm 1.2 \end{gathered}$ | Obese adolescents | Combined exercise | IG: Resistance training + aerobic exercise (running, cycling or swimming) <br> - 40 min <br> - 3 times/wk <br> - 40 weeks | aPWV | Oscillometric <br> Arteriograph | $\begin{gathered} \text { IG: } \\ 5.9 \pm 0.4 \\ \text { CG: } \\ 6.1 \pm 0.5 \end{gathered}$ |
| Chuensiri et al. 2017 | Thailand | RCT | $\begin{gathered} \mathrm{IG}=16 \\ (0 \%) \\ \mathrm{CG}=16 \\ (0 \%) \end{gathered}$ | $\begin{gathered} \text { IG: } \\ 11.0 \pm 0.3 \\ \text { CG: } \\ 10.6 \pm 0.3 \end{gathered}$ | Obese children | HIIT | IG: Cycling at $90 \%$ of peak power output <br> - 8 sets of $2^{\prime}$ -1 ' rest <br> - 3 times/wk <br> - 12 weeks | baPWV | Oscillometric VP-1000plus | $\begin{gathered} \text { IG: } \\ 10.0 \pm 0.3 \\ \text { CG: } \\ 10.0 \pm 0.4 \end{gathered}$ |
| Davis et al. $2019$ | United States | RCT | $\begin{gathered} \mathrm{IG}=90 \\ (67 \%) \\ \mathrm{CG}=85 \\ (55 \%) \end{gathered}$ | $\begin{gathered} \text { IG: } \\ 9.6 \pm 0.2 \\ \text { CG: } \\ 9.7 \pm 0.2 \end{gathered}$ | Overweight children | Aerobic exercise | IG: Instructor-led aerobic exercise <br> - 40 min <br> - 5 times/wk <br> - 32 weeks | cfPWV | Tonometry SphygmoCor | $\begin{gathered} \text { IG: } \\ 5.1 \pm 0.2 \\ \text { CG: } \\ 5.1 \pm 0.1 \end{gathered}$ |
| Hacke et al. $2017$ | Germany | RCT | $\begin{gathered} \hline \mathrm{IG}=92 \\ (54.3 \%) \\ \mathrm{CG}=43 \\ (49.8 \%) \end{gathered}$ | $\begin{gathered} \text { IG: } \\ 4.7 \pm 0.2 \\ \text { CG: } \\ 5.1 \pm 0.3 \end{gathered}$ | Healthy preschoolers | Sensorymotor training | IG: Psychomotor play and functional gymnastics <br> - 60 min <br> - 2 times/wk <br> - 24 weeks | aPWV | Oscillometric Mobil-O-Graph | $\begin{gathered} \text { IG: } \\ 4.3 \pm 0.3 \\ \text { CG: } \\ 4.3 \pm 0.2 \end{gathered}$ |


| Horner et al. 2015 | United States | RCT | $\begin{gathered} \mathrm{IG} 1=30 \\ (50) \\ \mathrm{IG} 2=27 \\ (51.8) \\ \mathrm{CG}=24 \\ (50) \end{gathered}$ | $\begin{gathered} \text { IG1: } \\ 14.7 \pm 1.8 \\ \text { IG2: } \\ 14.6 \pm 1.9 \\ \text { CG: } \\ 14.9 \pm 1.8 \end{gathered}$ | Obese adolescents | IG1: Aerobic exercise IG2: <br> Resistance training | IG1: Moderate intensity exercise on a treadmill, elliptical or stationary bike <br> - 60 min <br> - 3 times/wk <br> - 24 weeks <br> IG2: Series of 10 whole body exercises ( 2 sets of 8-12 repetitions) <br> - 60 min <br> - 2 times/wk <br> - 24 weeks | aPWV | Piezoelectric Complior system | IG1: $6.5 \pm 1.4$ IG2: $6.6 \pm 1.7$ CG: $6.4 \pm 1.6$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Ketelhut et al. 2020 | Germany | RCT | $\begin{gathered} \mathrm{IG}=22 \\ (50 \%) \\ \mathrm{CG}=24 \\ (41.6 \%) \end{gathered}$ | $\begin{gathered} \text { IG: } \\ 10.8 \pm 0.6 \\ \text { CG: } \\ 10.7 \pm 0.7 \end{gathered}$ | Healthy children | HIIT | IG: Instructor-led HIIT <br> - 20 min <br> - 3 times/wk <br> - 12 weeks | aPWV | Oscillometric Mobil-O-Graph | $\begin{gathered} \text { IG: } \\ 4.8 \pm 0.3 \\ \text { CG: } \\ 4.4 \pm 0.3 \end{gathered}$ |
| Ketelhut et al. 2021 | Germany | RCT | $\begin{aligned} & \mathrm{IG}=51 \\ & (64.7 \%) \\ & \mathrm{CG}=54 \\ & (46.3 \%) \end{aligned}$ | $\begin{gathered} \text { IG: } \\ 8.1 \pm 0.6 \\ \text { CG: } \\ 8.3 \pm 0.6 \end{gathered}$ | Healthy children | HIIT | IG: Instructor-led HIIT <br> - 45 min <br> - 2 times/wk <br> - 36 weeks | aPWV | Oscillometric Mobil-O-Graph | $\begin{gathered} \text { IG: } \\ 4.8 \pm 0.3 \\ \text { CG: } \\ 4.6 \pm 0.3 \end{gathered}$ |
| Lee et al. 2020 | United States | RCT | $\begin{gathered} \text { IG1 }=38 \\ (66.8) \\ \text { IG2 }=40 \\ (62.5) \\ \text { IG3 }=40 \\ (65) \end{gathered}$ | $\begin{gathered} \text { IG1: } \\ 14.4 \pm 1.6 \\ \text { IG2: } \\ 14.4 \pm 1.6 \\ \text { IG3: } \\ 14.5 \pm 1.7 \end{gathered}$ | Obese adolescents | IG1: Aerobic exercise IG2: <br> Resistance training IG3: <br> Combined exercise | IG1: Progressive aerobic exercise (treadmills and/or ellipticals) IG2: whole-body resistance exercises IG3: 30' aerobic exercise+ 30'whole-body resistance exercises <br> - 60 min <br> - 3 times/wk | cfPWV | Piezoelectric Complior system | $\begin{gathered} \text { IG1: } \\ 5.96 \pm 0.7 \\ \text { IG2: } \\ 5.84 \pm 0.9 \\ \text { IG3: } \\ 5.99 \pm 0.9 \end{gathered}$ |


|  |  |  |  |  | - 24 weeks |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| McNarry et al. 2020 | United <br> Kingdom | RCT | $\begin{gathered} \text { IG }=16 \\ (40.7 \%) \\ C G=16 \\ (39.4 \%) \end{gathered}$ | $13.6 \pm 0.9$ | Healthy adolescents | HIIT | IG: Instructor-led HIIT <br> - 20 min <br> - 3 times/wk <br> - 12 weeks | cfPWV | Oscillometric Vicorder | $\begin{gathered} \text { IG: } \\ 5.7 \pm 0.7 \\ \text { CG: } \\ 5.4 \pm 0.5 \end{gathered}$ |
| Minghetti et al. $2022$ | Switzerland | RCT | $\begin{gathered} \mathrm{IG}=46 \\ (50 \%) \\ \mathrm{CG}=22 \\ (54.5 \%) \end{gathered}$ | $\begin{gathered} \text { IG: } \\ 5.2 \pm 0.6 \\ \text { CG: } \\ 5.4 \pm 0.5 \end{gathered}$ | Healthy preschoolers | Sensorymotor training | IG: Gross motor skills and locomotor exercises <br> - 45 min <br> - 1 times/wk <br> - 25 weeks | aPWV | Oscillometric Mobil-O-Graph | $\begin{gathered} \text { IG: } \\ 4.2 \pm 0.4 \\ \text { CG: } \\ 4.3 \pm 0.4 \end{gathered}$ |
| Son et al. 2017 | South <br> Korea | RCT | $\begin{gathered} \hline \mathrm{IG}=20 \\ (100 \%) \\ \mathrm{CG}=20 \\ (100 \%) \end{gathered}$ | $\begin{gathered} \text { IG: } \\ 15.0 \pm 1.0 \\ \text { CG: } \\ 15.0 \pm 1.0 \end{gathered}$ | Obese prehypertensive adolescents | Combined exercise | IG: Resistance exercise + badminton training <br> - 60 min <br> - 3 times/wk <br> - 12 weeks | baPWV | Tonometry SphygmoCor | $\begin{gathered} \text { IG: } \\ 8.2 \pm 0.8 \\ \text { CG: } \\ 7.9 \pm 0.3 \end{gathered}$ |
| $\begin{aligned} & \text { Sung et al. } \\ & 2019 \end{aligned}$ | South Korea | RCT | $\begin{gathered} \text { IG }=20 \\ (100 \%) \\ C G=20 \\ (100 \%) \end{gathered}$ | $\begin{gathered} \text { IG: } \\ 15.0 \pm 1.0 \\ \text { CG: } \\ 15.0 \pm 1.0 \end{gathered}$ | Prehypertensive adolescents | Aerobic exercise | IG: Aerobic exercise (jumping rope) <br> - 50 min <br> - 5 times/w <br> - 12 weeks | baPWV | Tonometry SphygmoCor | $\begin{gathered} \text { IG: } \\ 8.2 \pm 1.0 \\ \text { CG: } \\ 8.2 \pm 0.5 \end{gathered}$ |
| Wong et al. 2018 | United States | RCT | $\begin{gathered} \text { IG }=15 \\ (100 \%) \\ C G=15 \\ (100 \%) \end{gathered}$ | $\begin{gathered} \text { IG: } \\ 15.2 \pm 1.2 \\ \text { CG: } \\ 15.3 \pm 1.1 \end{gathered}$ | Obese adolescents | Combined exercise | IG: 20' resistance training $+30^{\prime}$ treadmill walking <br> - 60 min <br> - 3 times/w <br> - 12 weeks | baPWV | Tonometry SphygmoCor | $\begin{gathered} \text { IG: } \\ 8.4 \pm 0.8 \\ \text { CG: } \\ 8.5 \pm 0.7 \end{gathered}$ |

Table S2. Search strategy for MEDLINE


#### Abstract

MEDLINE (via Pubmed) (("cardiovascular disease" OR "cardiovascular risk" OR "arterial stiffness" OR "pulse wave velocity" OR "PWV") AND ("physical activity" OR "physical exercise" OR "exercise" OR "training" OR "HIIT" OR "interval training" OR "intermittent exercise" OR "continuous exercise" OR "aerobic exercise" OR "endurance training" OR "resistance exercise" OR "strength" OR "stretching" OR "mind-body exercises" OR "Pilates" OR "yoga" OR "Tai Chi" OR sport) AND (child* OR pediatric OR infan* OR kids OR young OR adolescents OR teen*) AND (effectiveness OR "clinical trial" OR trials OR "controlled trial" OR random* OR "clinical trials"))


## Results: 614

Table S3. CINeMA confidence rating

| Comparison | Number of studies | Withinstudy bias | Reporting bias | Indirectness | Imprecision | Heterogeneity | Incoherence | Confidence rating |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| aer:comb | 1 | $\begin{gathered} \text { No } \\ \text { concerns } \end{gathered}$ | Some concerns | Some concerns | No concerns | $\begin{gathered} \text { Some } \\ \text { concerns } \end{gathered}$ | No concerns | High |
| aer:con | 3 | Some concerns | Some concerns | Some concerns | No concerns | Some concerns | No concerns | High |
| aer:res | 2 | Some concerns | Some concerns | Some concerns | Some concerns | Some concerns | No concerns | Moderate |
| comb:con | 4 | Some concerns | Some concerns | Some concerns | Some concerns | Some concerns | No concerns | Moderate |
| comb:res | 1 | $\begin{gathered} \text { No } \\ \text { concerns } \end{gathered}$ | Some concerns | Some concerns | Some concerns | Some concerns | No concerns | High |
| con:hit | 4 | Some concerns | Some concerns | No concerns | No concerns | Major concerns | No concerns | Low |
| con:res | 1 | Some concerns | Some concerns | Some concerns | Some concerns | Some concerns | No concerns | Moderate |
| con:sen | 2 | Some concerns | Some concerns | No concerns | Major concerns | No concerns | No concerns | Low |
| aer:hit | 0 | Some concerns | Some concerns | Some concerns | Some concerns | Some concerns | No concerns | Moderate |
| aer:sen | 0 | Some concerns | Some concerns | No concerns | No concerns | Some concerns | No concerns | High |
| comb:hit | 0 | Some concerns | Some concerns | Some concerns | $\begin{gathered} \text { Some } \\ \text { concerns } \end{gathered}$ | Some concerns | No concerns | Moderate |
| comb:sen | 0 | Some concerns | Some concerns | Some concerns | Some concerns | Some concerns | No concerns | Moderate |
| hit:res | 0 | Some concerns | Some concerns | Some concerns | Major concerns | No concerns | No concerns | Low |
| hit:sen | 0 | Some concerns | Some concerns | No concerns | Some concerns | Some concerns | No concerns | High |
| res:sen | 0 | Some concerns | Some concerns | Some concerns | Some concerns | Some concerns | No concerns | Moderate |

Table S4. Pooled SMD on types of PE. Upper right triangle gives the pooled mean differences from pairwise comparisons, lower left triangle pooled mean differences from the network meta-analysis (row intervention relative to column).
$\left.\begin{array}{cccccc}\hline \begin{array}{c}\text { Aerobic } \\ \text { exercise }\end{array} & \begin{array}{c}-1.36(-3.08 ; \\ 0.36)\end{array} & \text { NA } & -0.94(-2.16 ; & \text { NA } & -1.92(-2.95 ; \\ 0.29)\end{array}\right]$

Table S5. Analysis of the distribution of outcomes according to mean, standard deviation (SD) and Mean/SD ratio



Figure S1. Quality assessment


Figure S2. Forest plot of the pooled effect of each modality of exercise compared to the control group


Figure S3. Pairwise comparations (only comparisons with direct evidence are shown).

| Study | TE seTE | Standardised Mean Difference | SMD | 95\%-CI |
| :---: | :---: | :---: | :---: | :---: |
| Combined vs Control |  |  |  |  |
| Bharath et al. 2018 | -0.20 0.4483 | $+$ | -0.20 | [-1.08; 0.68] |
| Bruyndonckx et al. 2015 | -0.68 0.2992 | $\dagger$ | -0.68 | [-1.27; -0.10] |
| Son et al. 2017 | -1.41 0.3410 | $+$ | -1.41 | [-2.08; -0.74] |
| Wong et al. 2018 | -0.39 0.3686 | $+$ | -0.39 | [-1.11; 0.33] |
| Random effects model (HK) |  |  | -0.71 | [-1.54; 0.13] |
| Heterogeneity: $I^{2}=52 \%, \tau^{2}$ | $389, p=0.10$ |  |  |  |
| HIIT vs Control |  |  |  |  |
| Chuensiri et al. 2017 | -2.84 0.6043 | $\pm$ | -2.84 | [-4.02; -1.66] |
| Ketelhut et al. 2020 | -0.85 0.2038 | + | -0.85 | [-1.24; -0.45] |
| Ketelhut et al. 2021 | -1.17 0.3192 | $+$ | -1.17 | [-1.79; -0.54] |
| McNarry et al. 2020 | 0.000 .3536 | $+$ | 0.00 | [-0.69; 0.69] |
| Random effects model (HK) |  |  | -1.09 | [-2.82; 0.65] |
| Heterogeneity: $I^{2}=83 \%, \tau^{2}=0.5219, p<0.01$ |  |  |  |  |
| Aerobic exercise vs Control |  |  |  |  |
| Davis et al. 2019 | -0.41 0.1528 | - | -0.41 | [-0.71; -0.11] |
| Horner et al. 2015 | -2.28 0.3726 | $\pm$ | -2.28 | [-3.01; -1.55] |
| Sung et al. 2019 | -3.50 0.5031 | $+$ | -3.50 | [-4.49; -2.51] |
| Random effects model (HK) |  |  | -2.02 | [-5.90; 1.86] |
| Heterogeneity: $I^{2}=96 \%, \tau^{2}=2.5957, p<0.01$ |  |  |  |  |
| Sensorymotor training vs Control |  |  |  |  |
| Hacke et al. 2017 | 0.000 .1847 |  | 0.00 | [-0.36; 0.36] |
| Minghetti et al. 2022 | 0.230 .2599 |  | 0.23 | $[-0.28 ; 0.74]$ |
| Random effects model (HK) |  |  | 0.08 | [-1.28; 1.43] |
| Heterogeneity: $I^{2}=0 \%, \tau^{2}=0, p=0.48$ |  |  |  |  |
| Resistance training vs Control |  |  |  |  |
| Horner et al. 2015 | -0.73 0.3316 | $+$ | -0.73 | [-1.38; -0.08] |
| Aerobic exercise vs Resistance training |  |  |  |  |
| Horner et al. 2015 | -1.55 0.3141 | $+$ | -1.55 | [-2.16; -0.93] |
| Lee et al. 2020 | -0.36 0.2309 | $+$ | -0.36 | [-0.81; 0.09] |
| Random effects model (HK)Heterogeneity: $I^{2}=89 \%, \tau^{2}=0.6$ |  |  | -0.94 | [-8.48; 6.61] |
|  |  |  |  |  |
| Aerobic exercise vs Combined |  |  |  |  |
| Lee et al. 2020 | -1.36 0.2494 | $+$ | -1.36 | [-1.85; -0.87] |
| Combined vs Resistance training |  |  |  |  |
| Lee et al. 2020 | 1.000 .2360 | + | 1.00 | [ $0.54 ; 1.46]$ |
|  |  | $\begin{array}{lll}-5 & 0 & 5\end{array}$ |  |  |

Figure S4. Pairwise comparations using Hartung-Knapp-Sidik-Jonkman random effects method (only comparisons with direct evidence are shown).

| Comparison | Number of Studies | p-value | 12 | Random eff | fects model | SMD | 95\%-Cl |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Aerobic exercise vs Combined |  |  |  |  |  |  |  |
| Direct estimate | 1 | 0.38 |  | $\ddagger$ |  | -1.36 | [-3.08; 0.36] |
| Indirect estimate |  |  |  | $\square$ |  |  | [-2.69; 0.03] |
| Network estimate |  |  |  | $\sim$ |  | -1.34 | [-2.41; -0.28] |
| Prediction interval |  |  |  |  |  |  | [-3.57; 0.89] |
| Aerobic exercise vs Control |  |  |  |  |  |  |  |
| Direct estimate | 3 | 0.78 | 0.96 | 1 |  | -1.92 | [-2.95; -0.89] |
| Indirect estimate |  |  |  |  |  |  | [-3.89, -0.03] |
| Network estimate |  |  |  | $\sim$ |  | -1.93 | [-2.84; -1.02] |
| Prediction interval |  |  |  |  |  |  | [-4.07; 0.21] |
| Aerobic exercise vs Resistance training |  |  |  |  |  |  |  |
| Direct estimate | 2 | 0.88 | 0.89 | , |  | -0.94 | [-2.16; 0.29] |
| Indirect estimate |  |  |  |  |  | -0.20 | [-3.55; 3.15] |
| Network estimate |  |  |  | = |  | -0.85 | $[-2.00 ; 0.30]$ |
| Prediction interval |  |  |  |  |  |  | $[-3.13 ; 1.43]$ |
| Combined vs Control |  |  |  |  |  |  |  |
| Direct estimate | 4 | 0.80 | 0.52 | $\cdots$ |  | -0.68 | [-1.58; 0.21] |
| Indirect estimate |  |  |  |  |  | -0.19 | $[-2.00 ; 1.62]$ |
| Network estimate |  |  |  | $\cdots$ |  | -0.59 | [-1.39; 0.22] |
| Prediction interval |  |  |  |  |  |  | [-2.67; 1.50] |
| Combined vs Resistance training ${ }^{\text {c }}$ |  |  |  |  |  |  |  |
| Direct estimate | 1 | 0.53 |  |  | 1 |  | [-0.71; 2.71] |
| Indirect estimate |  |  |  |  |  | -0.09 | [-1.92; 1.74] |
| Network estimate |  |  |  |  | $\bigcirc$ | 0.49 | $[-0.76 ; 1.74]$ |
| Prediction interval |  |  |  |  |  |  | [-1.86; 2.84] |
| Resistance training vs Control |  |  |  |  |  |  |  |
| Direct estimate | 1 | 0.45 |  | $\pm$ |  | -0.73 | [-2.50; 1.04] |
| Indirect estimate |  |  |  | $\square$ |  | -1.37 | [-2.98; 0.24] |
| Network estimate |  |  |  | $\cdots$ |  | -1.08 | [-2.27; 0.11] |
| Prediction interval |  |  |  | 1 | 1 |  | [-3.39; 1.23] |
|  |  |  |  | .) $n$ | $\bigcirc$ ? |  |  |

Figure S5. Node-splitting


Figure S6. Heatplot.


## Cumulative ranking probabilities

|  | $\mathbf{1}$ | $\mathbf{2}$ | $\mathbf{3}$ | $\mathbf{4}$ | $\mathbf{5}$ | $\mathbf{6}$ |
| ---: | :--- | :--- | :--- | :--- | :--- | :--- |
| Aerobic exercise | 0.9 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Combined | 0.0 | 0.1 | 0.4 | 0.9 | 1.0 | 1.0 |
| HIIT | 0.0 | 0.4 | 0.7 | 0.9 | 0.1 | 1.0 |
| Resistance training | 0.1 | 0.5 | 0.8 | 0.1 | 1.0 | 1.0 |
| Sensory motor training | 0.0 | 0.0 | 0.1 | 0.2 | 0.4 | 1.0 |
| Control | 0.0 | 0.0 | 0.0 | 0.1 | 0.6 | 1.0 |

Figure S7. Rankogram for each intervention of physical exercise.


Figure S8. Forest plot of the pooled effect of each modality of exercise compared to the control group without high risk of bias studies


Figure S9. Pairwise comparisons without high risk of bias studies


Figure S10. Contour-enhanced funnel plot for pooled mean differences.


Figure S11. Meta-regression by mean age of participants
$\beta=-0.91$ (95\%Cl: -2.06, 0.24)


Figure S12. Meta-regression by type of population.


Figure S13. Meta-regression by type of PWV measurement


Figure S14. Meta-regression by type of PWV measurement method

