

## Research

# Combined training is the most effective training modality to improve aerobic capacity and blood pressure control in people requiring haemodialysis for end-stage renal disease: systematic review and network meta-analysis

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## KEY WORDS

Chronic kidney failure  
Renal dialysis  
Exercise  
Network meta-analysis  
Physical therapy



## ABSTRACT

**Questions:** Do aerobic, resistance and combined exercise training improve aerobic capacity, arterial blood pressure and haemodialysis efficiency in people requiring haemodialysis for end-stage renal disease? Is one exercise training modality better than the others for improving these outcomes? **Design:** Systematic review with network meta-analysis of randomised trials. **Participants:** Adults requiring haemodialysis for end-stage renal disease. **Intervention:** Aerobic training, resistance training, combined training and control (no exercise or placebo). **Outcome measures:** Aerobic capacity, arterial blood pressure at rest, and haemodialysis efficiency. **Results:** Thirty-three trials involving 1254 participants were included. Direct meta-analyses were conducted first. Aerobic capacity improved significantly more with aerobic training (3.35 ml/kg/min, 95% CI 1.79 to 4.91) and combined training (5.00 ml/kg/min, 95% CI 3.50 to 6.50) than with control. Only combined training significantly reduced systolic (−9 mmHg, 95% CI −13 to −4) and diastolic (−5 mmHg, 95% CI −6 to −3) blood pressure compared to control. Only aerobic training was superior to control for haemodialysis efficiency (Kt/V 0.11, 95% CI 0.02 to 0.20). However, when network meta-analysis was conducted, there were some important different findings. Both aerobic training and combined training again elicited greater improvements in aerobic capacity than control. For systolic blood pressure, combined training was superior to control. For diastolic blood pressure, combined training was superior to aerobic training and control. No modality was superior to control for haemodialysis efficiency. Combined training was ranked as the most effective treatment for aerobic capacity and arterial blood pressure. **Conclusion:** Combined training was the most effective modality to increase aerobic capacity and blood pressure control in people who require haemodialysis. This finding helps to fill the gap created by the lack of head-to-head comparisons of different modalities of exercise in people with end-stage renal disease. **Registration:** PROSPERO CRD42015020531. [Scapini KB, Bohlke M, Moraes OA, Rodrigues CG, Inácio JFS, Sbruzzi G, Leguisamo CP, Sanches IC, Tourinho Filho H, Irigoyen MC (2019) Combined training is the most effective training modality to improve aerobic capacity and blood pressure control in people requiring haemodialysis for end-stage renal disease: systematic review and network meta-analysis. *Journal of Physiotherapy* 65:4–15]

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## Introduction

Chronic renal disease has been increasing in recent decades; it affects 8 to 16% of the population worldwide. This increase is mainly due to the increased prevalence of risk factors, such as diabetes mellitus and hypertension, and as result of aging of the population.<sup>1–3</sup>

People with end-stage renal disease present higher risk for cardiovascular disease and mortality,<sup>4</sup> which, as in other populations, may be aggravated by a sedentary lifestyle.<sup>5,6</sup> It is well documented that people with end-stage renal disease have reduced aerobic capacity, muscle strength and exercise tolerance, which are factors that contribute to

higher levels of physical inactivity. In two cohorts of people requiring haemodialysis for end-stage renal disease, 35% and 43% did not exercise at all, and only 5% and 6% exercised 4 to 5 times per week.<sup>6,7</sup>

Several trials have demonstrated that exercise training improves functional capacity, arterial blood pressure, lipid profile, heart rate variability, and quality of life in people with end-stage renal disease;<sup>8</sup> therefore, exercise interventions could be an interesting non-pharmacological strategy to improve cardiovascular health in this population. Furthermore, some studies have evaluated the effect of intradialytic exercise on haemodialysis efficiency, measured, in most cases, using Kt/V, and revealed conflicting results.<sup>9–11</sup>

Most published randomised clinical trials about the effects of exercise on people with end-stage renal disease have used aerobic exercise as the intervention. Resistance exercise or combined aerobic and resistance exercise have been investigated much less. Moreover, few randomised trials have compared the effects of different training modalities on the health outcomes of people with end-stage renal disease. The surveyed studies had small samples, short duration, different outcomes, and heterogeneous results.<sup>10,12,13</sup> This lack of solid and coherent evidence precludes any conclusion regarding the best training modality for people with end-stage renal disease.

While there is a broad consensus that exercise training promotes beneficial effects in end-stage renal disease, it is not routinely included in clinical practice and the comparative efficiency of different modalities of exercise training remains to be determined. To overcome the restrictions of limited available comparisons, this systematic review employed a network meta-analysis of randomised trials with the aim of assessing the effectiveness of different modalities of exercise training on aerobic capacity, arterial blood pressure and haemodialysis efficiency in adults with end-stage renal disease requiring haemodialysis treatment.

Therefore the research questions for this systematic review were:

1. Do aerobic, resistance, and combined exercise training improve aerobic capacity, arterial blood pressure and haemodialysis efficiency in people requiring haemodialysis for end-stage renal disease?
2. Is one exercise training modality better than the others for improving these outcomes?

## Methods

This systematic review is reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement.<sup>14</sup>

### Identification and selection of studies

The following electronic databases were searched in May 2018: PubMed, EMBASE, Cochrane CENTRAL (Wiley InterScience), Web of Science and LILACS (Bireme), for articles published up to 5 January 2018. The following MeSH terms were used: 'Exercise', 'Resistance Training', 'Kidney Failure, Chronic' and 'Renal Dialysis', as well as their synonyms. For the search of the LILACS database, the equivalent terms in Portuguese were used. All these search terms were combined with a highly sensitive search strategy for the retrieval of reports of controlled trials.<sup>15</sup> The complete search strategy used in PubMed is shown in Appendix 1 (see eAddenda for Appendix 1). There was no restriction on the language or the status of the publication. Further eligible studies were sought by manually searching the reference lists of eligible articles and of review articles on end-stage renal disease.

Eligibility criteria were defined a priori. The inclusion criteria are presented in Box 1. We excluded: studies in which people with end-stage renal disease were undergoing a type of renal replacement therapy other than haemodialysis; studies with randomised co-interventions besides haemodialysis; studies in which interventions consisted of guidelines and educational measures for exercise practice, rather than exercise training; and studies where only a single exercise session was delivered to assess acute effects.

Titles and abstracts of all articles identified by the search strategy were evaluated in duplicate by two investigators working independently. All abstracts that did not provide sufficient information regarding the eligibility criteria were selected for full-text evaluation. In the second phase, the same reviewers independently evaluated the full-text articles and made their selection in accordance with the eligibility criteria. Disagreements between reviewers were resolved by discussion.

### Box 1. Inclusion criteria.

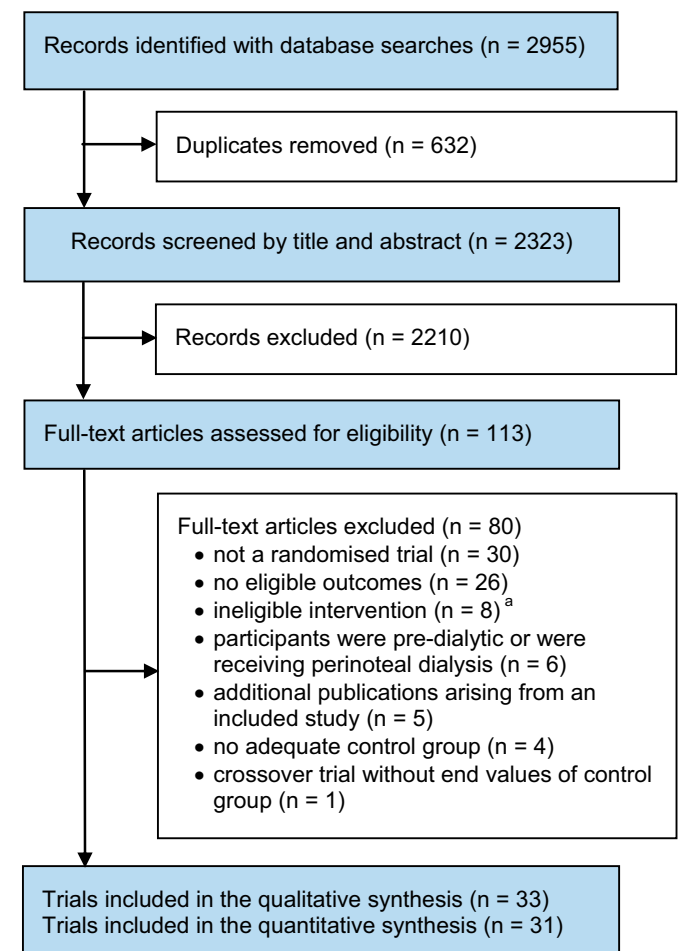
- Design
  - Randomised controlled trial
- Participants
  - People with chronic renal disease requiring haemodialysis
  - Adults (ie,  $\geq 18$  years old)
- Intervention
  - Aerobic training
  - Resistance training
  - Combined training (aerobic plus resistance training)
- Comparator
  - Control group (no exercise or placebo)
- Outcome measures
  - Aerobic capacity, measured by maximal oxygen uptake in ml/kg/min
  - Systolic and diastolic arterial pressures at rest in mmHg
  - Haemodialysis efficiency measured as single pool Kt/V<sup>a</sup>
- Comparisons
  - All interventions compared to the comparator and to each other

<sup>a</sup> See main text for explanation of Kt/V.

### Assessment of characteristics of studies

#### Quality

Study quality assessment was conducted using the Cochrane Collaboration's tool for assessing risk of bias<sup>16</sup> and included random sequence generation, allocation concealment, blinding of outcome



**Figure 1.** Flow of studies through the review.

<sup>a</sup> Reasons for ineligibility of interventions included: provision of only guidelines and educational measures for exercise practice; delivery of a single exercise session only; use of an ineligible modality of exercise; and inclusion of a co-intervention as part of the randomised intervention.

**Table 1**  
Characteristics of the studies included in the review.

| Study                       | Country        | Group (n) | Interventions |        |  |                  |                | Loss (%) |
|-----------------------------|----------------|-----------|---------------|--------|--|------------------|----------------|----------|
|                             |                |           | Type          | Period | Prescription   | Program duration | Compliance (%) |          |
| Abreu 2017 <sup>26</sup>    | Brazil         | Exp = 32  | RT            | ID     | 3/week; 30 min: 3 sets of 10 reps, four lower limb exercises with ankle cuffs and elastic band resistance; intensity based on an adaptation of the 1RM test with the initial intensity set at 60% of 1RM   | 12 weeks         | NR             | 19       |
|                             |                | Con = 29  | –             | –      | No exercise  | 12 weeks         | –              | 35       |
| Frih 2017 <sup>27</sup>     | Tunisia        | Exp = 28  | CT            | ND     | 4/week; 60 min: 10 min warm up, dynamic closed- and open-chain strengthening exercises (quadriceps, pectoral, triceps, biceps and hamstrings, start at 50% 1RM and 12 to 15 reps for each exercise, load increased by 5% of the 1RM monthly), ergometer cycling and treadmill walking for 20 min at 5 to 6 RPE, 10 min cool down | 16 weeks         | NR             | 25       |
|                             |                | Con = 22  | –             | –      | No exercise  | 16 weeks         | –              | 9        |
| Liao 2016 <sup>28</sup>     | Taiwan         | Exp = 20  | AT            | ID     | 3/week; 30 min: 5 min warm up, 20 min ergometer cycling at 12 to 15 RPE, 5 min cool down   | 12 weeks         | NR             | NR       |
|                             |                | Con = 20  | –             | –      | No exercise  | 12 weeks         | –              | NR       |
| Thompson 2016 <sup>29</sup> | Canada         | Exp1 = 8  | AT            | ID     | 3/week; 5 min warm up, 15 min ergometer cycling at 12 to 14 RPE increased by 2.5 min/week, 5 min cool down   | 12 weeks         | 87             | 13       |
|                             |                | Exp2 = 7  | RT            | ID     | 3/week; 3 sets of 10 to 15 reps, knee extension, knee flexion and hip flexion (with ankle weights) and hip abduction (with elastic resistance band) at 12 to 14 RPE  | 12 weeks         | 84             | 14       |
|                             |                | Exp3 = 8  | CT            | ID     | 3/week; Exp1 followed by Exp2 at each session  | 12 weeks         | 88             | 13       |
|                             |                | Con = 8   | –             | –      | Stretching exercise  | 12 weeks         | –              | 25       |
| Groussard 2015 <sup>9</sup> | France         | Exp = 10  | AT            | ID     | 3/week; 30 min ergometer cycling at 50 rpm and 55 to 60% of peak power output  | 12 weeks         | NR             | 20       |
|                             |                | Con = 10  | –             | –      | No exercise  | 12 weeks         | –              | 0        |
| Mohseni 2013 <sup>30</sup>  | Iran           | Exp = 25  | AT            | ID     | 3/week; 15 min aerobic movement exercise of range of motion (rotating wrist 40 rpm, 20 times flexion and extension of the wrist, 20 times full flexion and extension of the elbow, 40 rpm of rotating the ankles, 20 times flexion and extension of the ankles)  | 8 weeks          | NR             | 8        |
|                             |                | Con = 25  | –             | –      | No exercise  | 8 weeks          | –              | 4        |
| Dobsak 2012 <sup>11</sup>   | Czech Republic | Exp = 11  | AT            | ID     | 3/week; 2 sets of 20 min ergometer cycling at 60% of individual Wpeak determined by ergometric test  | 20 weeks         | NR             | NR       |
|                             |                | Con = 10  | –             | –      | No exercise  | 20 weeks         | –              | NR       |
| Reboredo 2011 <sup>21</sup> | Brazil         | Exp = 14  | AT            | ID     | 3/week; 35 min supervised ergometer cycling at 4 to 6 modified RPE   | 12 weeks         | 77             | 14       |
|                             |                | Con = 14  | –             | –      | No exercise  | 12 weeks         | –              | 14       |
| Afshar 2010 <sup>12</sup>   | Iran           | Exp1 = 7  | AT            | ID     | 3/week; 10 to 30 min ergometer cycling at 12 to 16 RPE   | 8 weeks          | NR             | NR       |
|                             |                | Exp2 = 7  | RT            | ID     | 3/week; 3 sets of 8 reps at 60% of 3RM of knee extension-flexion and hip abduction-flexion at 15 to 17 RPE with ankle weights  | 8 weeks          | NR             | NR       |
|                             |                | Con = 7   | –             | –      | No exercise  | 8 weeks          | –              | NR       |
| Koh 2010 <sup>31</sup>      | Australia      | Exp = 27  | AT            | ID     | 3/week; 45 min ergometer cycling at 12 to 13 RPE   | 24 weeks         | 75             | 44       |
|                             |                | Con = 22  | –             | –      | Usual care   | 24 weeks         | –              | 27       |
| Kouidi 2010 <sup>32</sup>   | Greece         | Exp = 25  | CT            | ID     | 3/week; 60 min ergometer cycling and 20 min strengthening exercises; 11 to 13 RPE; RT initially consisted of 2 sets of exercises for the lower limbs using elastic bands and free weights. The workload was gradually increased by increasing the number of reps (8 to 12) and the number of sets.                               | 12 months        | 82             | 4        |
|                             |                | Con = 25  | –             | –      | No exercise  | 12 months        | –              | 20       |

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Table 1 (Continued)

| Study                            | Country     | Group (n) | Interventions |        |  |                  |                | Loss (%) |
|----------------------------------|-------------|-----------|---------------|--------|--|------------------|----------------|----------|
|                                  |             |           | Type          | Period | Prescription   | Program duration | Compliance (%) |          |
| Reboredo 2010 <sup>33</sup>      | Brazil      | Exp = 14  | AT            | ID     | 3/week; 35 min supervised ergometer cycling at 4 to 6 modified RPE   | 12 weeks         | 75             | 22       |
|                                  |             | Con = 14  | –             | –      | Usual care   | 12 weeks         | –              | 22       |
| Wilund 2010 <sup>34</sup>        | USA         | Exp = 8   | AT            | ID     | 3/week; 45 min ergometer cycling at 12 to 14 RPE   | 16 weeks         | NR             | 13       |
|                                  |             | Con = 9   | –             | –      | Usual care   | 16 weeks         | –              | 11       |
| Kouidi 2009 <sup>35</sup>        | Greece      | Exp = 32  | CT            | ID     | 3/week; 40 min ergometer cycling and 30 min isotonic and isometric flexibility and strengthening exercises for the abdomen and lower limbs, with 3 sets of 15 reps using elastic bands and free weights; 13 RPE and 60 to 70% HRmax  | 10 months        | 88             | 6        |
|                                  |             | Con = 31  | –             | –      | Usual care   | 10 months        | –              | 6        |
| Ouzoni 2009 <sup>36</sup>        | Greece      | Exp = 20  | CT            | ID     | 3/week; 30 min ergometer cycling, 30 min of strengthening and flexibility exercises with elastic bands and limb weights; 13 to 14 RPE  | 10 months        | NR             | 5        |
|                                  |             | Con = 15  | –             | –      | No exercise  | 10 months        | –              | 7        |
| Petraki 2008 <sup>37</sup>       | Greece      | Exp = 26  | CT            | ID     | 3/week; 60 min of cycling and 30 min strengthening and flexibility exercises at 13 RPE; RT consisted of sets of reps of isotonic and isometric exercises and the workload was gradually increased by using elastic bands and limb weights  | 7 months         | NR             | 15       |
|                                  |             | Con = 24  | –             | –      | No exercise  | 7 months         | –              | 13       |
| Toussaint 2008 <sup>38</sup>     | Australia   | Exp = 10  | AT            | ID     | 3/week; 30 min ergometer cycling without exercise velocity, target HR or supervision   | 12 weeks         | NR             | 10       |
|                                  |             | Con = 10  | –             | –      | No exercise  | 12 weeks         | –              | 0        |
| Cheema 2007 <sup>19</sup>        | Australia   | Exp = 24  | RT            | ID     | 3/week; 2 sets of 8 reps; five upper limb exercises using free-weight dumbbells, five lower limb exercises using ankle weights or elastic resistance bands, and one abdominal exercise; 15 to 17 RPE   | 12 weeks         | 85             | 16       |
|                                  |             | Con = 25  | –             | –      | No exercise  | 12 weeks         | –              | 4        |
| Kopple 2007 <sup>10</sup>        | USA         | Exp1 = 20 | AT            | ID     | 3/week; 40 min ergometer cycling at ~50% of maximal oxygen uptake  | 20.7 weeks       | NR             | 50       |
|                                  |             | Exp2 = 20 | RT            | ND     | 3/week; apparatus for combined leg extension and flexion, and leg press and plantar flexion; 3 sets of 6 to 8 reps at 80% of 5RM   | 21.2 weeks       | NR             | 25       |
|                                  |             | Exp3 = 20 | CT            | ID/ND  | 3/week; CT group performed a combination of approximately one half of the AT and RT work effort  | 21.5 weeks       | NR             | 40       |
|                                  |             | Con = 20  | –             | –      | No exercise  | 21 weeks         | –              | 20       |
| Van Vilsteren 2005 <sup>39</sup> | Netherlands | Exp = 60  | CT            | ID/ND  | 2 to 3/week; 5 to 10 min warm up, 20 min of calisthenics exercises, step aerobics, flexibility and low-intensity resistance exercises, 5 to 10 min cool down, 20 to 30 min of cycling on pedals coupled to the haemodialysis chair; 12 to 16 RPE and ~60% of VO <sub>2</sub> max | 12 weeks         | NR             | 12       |
|                                  |             | Con = 43  | –             | –      | No exercise  | 12 weeks         | –              | 0        |
| Molsted 2004 <sup>40</sup>       | Denmark     | Exp = 22  | CT            | ND     | 2/week; 10 min warm up, 20 to 30 min of strength exercises and aerobic exercises (such as step and circuit training), 15 to 20 min ergometer cycling; 14 to 17 RPE   | 20 weeks         | 74             | 50       |
|                                  |             | Con = 11  | –             | –      | No exercise  | 20 weeks         | –              | 18       |
| Parsons 2004 <sup>41</sup>       | Canada      | Exp = 9   | AT            | ID     | 3/week; 3 bouts of 15 minute cycle ergometry exercise at 40 to 50% of maximum work load  | 8 weeks          | NR             | 33       |
|                                  |             | Con = 9   | –             | –      | No exercise  | 8 weeks          | –              | 22       |
| Tsuyuki 2003 <sup>42</sup>       | Japan       | Exp = 17  | AT            | ND     | 2 to 3/week; 30 min ergometer cycling, walking and running at 50 to 60% HRmax  | 20 weeks         | NR             | NR       |
|                                  |             | Con = 12  | –             | –      | No exercise  | 20 weeks         | –              | NR       |

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**Table 1** (Continued)

| Study                             | Country | Group (n) | Interventions |        |   |                  |                | Loss (%) |
|-----------------------------------|---------|-----------|---------------|--------|---|------------------|----------------|----------|
|                                   |         |           | Type          | Period | Prescription  | Program duration | Compliance (%) |          |
| De Paul 2002 <sup>43</sup>        | Canada  | Exp = 20  | CT            | ID/ND  | 3/week; 20 min egometer cycling at 13 to 14 RPE, at around 50 rpm; 3 sets of 10 reps of hamstring and quadriceps exercises on weight machines in the ND period, at 125% of 5RM  | 12 weeks         | NR             | 25       |
|                                   |         | Con = 18  | –             | –      | Sham (range of motion) exercises  | 12 weeks         | –              | 22       |
| Konstantinidou 2002 <sup>13</sup> | Greece  | Exp1 = 12 | CT            | ID     | 3/week; 30 min ergometer cycling, 30 min of stationary bike; 30 min of flexibility and strength exercises for the lower limbs. Progression via reps, sets, and elastic bands and limb weights; 70% HRmax  | 24 weeks         | NR             | 17       |
|                                   |         | Exp2 = 21 | CT            | ND     | 3/week; 10 min warm ergometer cycling or treadmill, 50 min intermittent aerobic exercise program, including calisthenics, steps and flexibility exercises, and 10 min cool down at 60 to 70% HR max. At 2 months, 10 min stretching and low-weight resistance program was added | 24 weeks         | NR             | 28       |
|                                   |         | Exp3 = 12 | AT            | ND     | 5/week; 30 min home ergometer cycling at 50 to 60% HRmax  | 24 weeks         | NR             | 17       |
|                                   |         | Con = 13  | –             | –      | No exercise   | 24 weeks         | –              | 8        |
| Painter 2002 <sup>44</sup>        | USA     | Exp = 10  | AT            | ID     | 3/week; 30 min ergometer cycling at 12 to 14 RPE and 70% HRmax  | 20 weeks         | NR             | NR       |
|                                   |         | Con = 14  | –             | –      | No exercise   | 20 weeks         | –              | NR       |
| Deligiannis 1999 <sup>45</sup>    | Greece  | Exp = 30  | CT            | ND     | 3 to 4/week; 50 min aerobic exercise (calisthenics exercises, step aerobics, swimming, or ball games); 20 min stretching and low-intensity resistance exercises; 60 to 70% HRmax  | 24 weeks         | NR             | NR       |
|                                   |         | Con = 30  | –             | –      | No exercise   | 24 weeks         | –              | NR       |
| Frey 1999 <sup>46</sup>           | USA     | Exp = 11  | AT            | ID     | 3/week; 45 min ergometer cycling 60 to 80% HRmax and 11 to 16 RPE   | 8 weeks          | NR             | 0        |
|                                   |         | Con = 11  | –             | –      | No exercise   | 8 weeks          | –              | 0        |
| Kouidi 1997 <sup>47</sup>         | Greece  | Exp = 24  | AT            | ND     | 3 to 4/week; 90 min of ergometer cycling, walking/jogging, calisthenics and aerobics, with swimming and/or ball sports in the last 8 to 12 weeks; 50 to 60% VO <sub>2</sub> max or 60 to 70% HRmax  | 24 weeks         | 78             | 17       |
|                                   |         | Con = 12  | –             | –      | No exercise   | 24 weeks         | –              | 8        |
| Akiba 1995 <sup>48</sup>          | Japan   | Exp = 10  | AT            | ND     | 3/week; 20 min on a cycle ergometer at 16 RPE   | 12 weeks         | NR             | 10       |
|                                   |         | Con = 10  | –             | –      | No exercise   | 12 weeks         | –              | 40       |
| Moros 1995 <sup>25</sup>          | Spain   | Exp = 9   | AT            | NR     | Frequency NR; dynamic aerobic exercises adapted individually according to the individual capacity   | 18 weeks         | NR             | 33       |
|                                   |         | Con = 7   | –             | –      | No exercise   | 18 weeks         | –              | 43       |
| Carney 1987 <sup>49</sup>         | USA     | Exp = 11  | AT            | ND     | 3/week; 45 to 60 min at 70 to 80% VO <sub>2</sub> max including calisthenics exercises, ergometer cycling, walking and jogging  | 24 weeks         | NR             | 9        |
|                                   |         | Con = 10  | –             | –      | Psychosocial support  | 24 weeks         | –              | 30       |
| Goldberg 1983 <sup>24</sup>       | USA     | Exp = 14  | AT            | ND     | 3/week; 45 to 60 min at 70 to 75%VO <sub>2</sub> max including cycling on a stationary bicycle ergometer, walking and jogging   | 12 months        | NR             | NR       |
|                                   |         | Con = 11  | –             | –      | No exercise   | 12 months        | –              |          |

AT = aerobic training, Con = control group, CT = combined training, Exp = experimental group, HR = heart rate, HRmax = maximum heart rate, ID = intradialytic, min = minutes, ND = non-dialytic, NR = not reported, RM = repetition maximum, RPE = Borg rating of perceived exertion, rpm = rotations per minute, RT = resistance training, VO<sub>2</sub>max = maximal oxygen uptake.

assessment, incomplete outcome data, and selective reporting. The same two reviewers independently performed the assessment. Disagreements between reviewers were resolved by discussion and, if necessary, the opinion of a third reviewer was sought.

Using standardised forms, the same two reviewers independently conducted data extraction regarding the methodological characteristics

of the studies, interventions, and outcomes. Disagreements were again resolved by discussion.

#### Participants

The country of recruitment was extracted for each study. The initial sample sizes and the percentage of dropouts were extracted for

**Table 2**  
Risk of bias of the included studies.

| Study<br>(Author, year)           | Selection bias             |                        | Detection bias                 | Attrition bias          | Reporting bias      | Other bias             |
|-----------------------------------|----------------------------|------------------------|--------------------------------|-------------------------|---------------------|------------------------|
|                                   | Random sequence generation | Allocation concealment | Blinding of outcome assessment | Incomplete outcome data | Selective reporting | Other sources of bias  |
| Abreu 2017 <sup>26</sup>          | Unclear                    | Unclear                | Unclear                        | Low risk                | Low risk            | None                   |
| Frih 2017 <sup>27</sup>           | Low risk                   | Unclear                | Low risk                       | Low risk                | Unclear             | None                   |
| Liao 2016 <sup>28</sup>           | Unclear                    | Unclear                | Unclear                        | Low risk                | Unclear             | None                   |
| Thompson 2016 <sup>29</sup>       | Low risk                   | Low risk               | Unclear                        | Low risk                | Low risk            | None                   |
| Groussard 2015 <sup>9</sup>       | Unclear                    | Unclear                | High risk                      | Low risk                | Unclear             | None                   |
| Mohseni 2013 <sup>30</sup>        | Low risk                   | High risk              | Low risk                       | Low risk                | Low risk            | None                   |
| Dobsak 2012 <sup>11</sup>         | Unclear                    | Unclear                | Low risk                       | Unclear                 | Unclear             | None                   |
| Reboredo 2011 <sup>21</sup>       | Unclear                    | Unclear                | Low risk                       | High risk               | Low risk            | None                   |
| Afshar 2010 <sup>12</sup>         | Unclear                    | Unclear                | Low risk                       | Unclear                 | Unclear             | High risk <sup>a</sup> |
| Koh 2010 <sup>31</sup>            | Low risk                   | Low risk               | Unclear                        | High risk               | Low risk            | None                   |
| Kouidi 2010 <sup>32</sup>         | Unclear                    | Unclear                | Unclear                        | High risk               | Unclear             | None                   |
| Reboredo 2010 <sup>33</sup>       | Unclear                    | Unclear                | Low risk                       | High risk               | Unclear             | None                   |
| Wilund 2010 <sup>34</sup>         | Unclear                    | Unclear                | Low risk                       | Low risk                | Unclear             | None                   |
| Kouidi 2009 <sup>35</sup>         | Low risk                   | Unclear                | Low risk                       | Low risk                | Low risk            | None                   |
| Ouzoni 2009 <sup>36</sup>         | Unclear                    | Unclear                | Unclear                        | Low risk                | Unclear             | None                   |
| Petraki 2008 <sup>37</sup>        | Unclear                    | Unclear                | Unclear                        | Low risk                | Unclear             | None                   |
| Toussaint 2008 <sup>38</sup>      | Low risk                   | Low risk               | Unclear                        | Low risk                | Low risk            | High risk <sup>b</sup> |
| Cheema 2007 <sup>19</sup>         | Low risk                   | Low risk               | Unclear                        | Low risk                | Low risk            | None                   |
| Kopple 2007 <sup>10</sup>         | Low risk                   | Unclear                | Unclear                        | High risk               | Unclear             | None                   |
| van Vilsteren 2005 <sup>39</sup>  | Unclear                    | Unclear                | Unclear                        | High risk               | Unclear             | None                   |
| Molsted 2004 <sup>40</sup>        | Low risk                   | Low risk               | Low risk                       | High risk               | Unclear             | None                   |
| Parsons 2004 <sup>41</sup>        | Unclear                    | Unclear                | Unclear                        | Low risk                | Unclear             | None                   |
| Tsuyuki 2003 <sup>42</sup>        | Unclear                    | Unclear                | Unclear                        | Unclear                 | Unclear             | High risk <sup>c</sup> |
| De Paul 2002 <sup>43</sup>        | Low risk                   | Low risk               | Low risk                       | Low risk                | Unclear             | None                   |
| Konstantinidou 2002 <sup>13</sup> | Unclear                    | Unclear                | Unclear                        | Low risk                | Unclear             | None                   |
| Painter 2002 <sup>44</sup>        | Unclear                    | Unclear                | Unclear                        | Unclear                 | Unclear             | None                   |
| Deligiannis 1999 <sup>45</sup>    | Unclear                    | Unclear                | Unclear                        | Unclear                 | Unclear             | None                   |
| Frey 1999 <sup>46</sup>           | Unclear                    | Unclear                | Unclear                        | Low risk                | Unclear             | None                   |
| Kouidi 1997 <sup>47</sup>         | Unclear                    | Unclear                | Unclear                        | Unclear                 | Unclear             | None                   |
| Akiba 1995 <sup>48</sup>          | Unclear                    | Unclear                | Unclear                        | Unclear                 | Unclear             | None                   |
| Moros 1995 <sup>25</sup>          | Unclear                    | Unclear                | Unclear                        | Unclear                 | Unclear             | None                   |
| Carney 1987 <sup>49</sup>         | Unclear                    | Unclear                | Unclear                        | Low risk                | Unclear             | None                   |
| Goldberg 1983 <sup>24</sup>       | Unclear                    | Unclear                | Unclear                        | Unclear                 | Unclear             | None                   |

<sup>a</sup> No women participants due to religious beliefs.

<sup>b</sup> Exercise was not supervised and there was no specific goal to duration and intensity.

<sup>c</sup> The primary cause of chronic kidney disease in all patients was chronic glomerulonephritis.

each group. The participants' compliance with the prescribed intervention was also noted.

### Intervention

To characterise the experimental intervention, the following information was extracted: the modality of exercise training (aerobic, resistance or combined) including further details where available; the duration, frequency and intensity of the training sessions; when the exercise sessions occurred in relation to haemodialysis (intradialytic, non-dialytic or both); and the progression and total duration of the training.

### Outcome measures

Exercise capacity data were extracted from formal cardiopulmonary exercise test results as maximum or peak oxygen uptake ( $\text{VO}_2\text{max}$ ), with conversion to  $\text{ml/kg/min}$  where necessary. Blood pressure data were extracted as systolic and diastolic arterial pressure at rest, in  $\text{mmHg}$ . Haemodialysis efficiency was extracted as  $\text{Kt/V}$ , which is an index comprised of  $\text{K}$  (dialyser clearance of urea),  $t$  (dialysis time), and  $V$  (volume of distribution of urea, approximately equal to patient's total body water. A patient's average  $\text{Kt/V}$  should be at least 1.2.

### Data analysis

For each outcome considered in this systematic review, effect sizes between different exercise modalities were calculated using mean and standard deviation of the outcome. When the data were unavailable in the required format (eg, number of participants, means and standard deviation), the authors of the primary studies were contacted. Pooled-effect estimates were obtained using the post-intervention values.<sup>16</sup> Calculations were performed using a random-effects model. A  $p$  value  $\leq 0.05$  was regarded as statistically

significant. Statistical heterogeneity of the treatment effects among studies was assessed using Cochran's  $Q$  test and the  $I^2$  inconsistency test, in which values from 0 to 40% might not be important, 40 to 60% represents moderate heterogeneity, 60 to 75% substantial heterogeneity, and 75 to 100% considerable heterogeneity.<sup>16</sup>

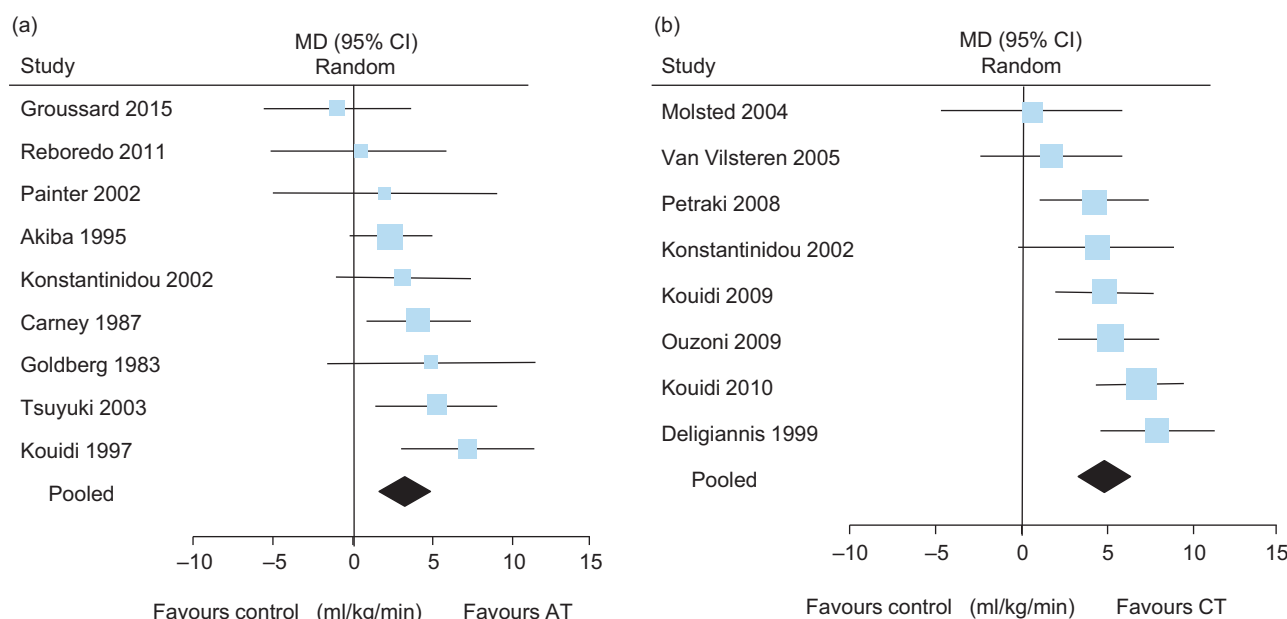
A network meta-analysis using a random-effects model was performed, allowing comparison of all modalities of exercise in a connected network of trials, making indirect comparison from trials that have at least one treatment in common. The Bayesian Markov-chain Monte Carlo method was used with RStudio statistical software<sup>a</sup> and the RJAGS package<sup>b</sup>. The network meta-analysis code used in RStudio is shown in Appendix 2 (see eAddenda for Appendix 2). Inconsistency in the network meta-analysis was verified by node-splitting analysis of inconsistency that is shown in Appendix 3 (see eAddenda for Appendix 3). The results were expressed with mean differences with 95% credible intervals (CrI). Also, rank probabilities for each outcome were obtained using Markov-chain Monte Carlo.

## Results

### Flow of studies through the review

The search strategy yielded 2955 articles, from which 113 were deemed potentially relevant and retrieved for detailed analysis. Of these articles, 75 were excluded based on the eligibility criteria. The excluded studies are listed under the reasons for exclusion in Appendix 4 (see eAddenda for Appendix 4). A further five articles were eliminated as they were found to be duplicate publications: Deligiannis et al<sup>17</sup> was included together with the study by Konstantinidou et al<sup>13</sup>, since the latter only added another intervention group to the former one; Cheema et al<sup>18</sup> was part of the study





**Figure 2.** Direct meta-analysis of the effect of (a) aerobic training compared to control and (b) combined training compared to control on aerobic capacity (VO<sub>2</sub>max). AT = aerobic training, CT = combined training, VO<sub>2</sub>max = maximal oxygen uptake.

Cheema et al<sup>19</sup>; Reboredo et al<sup>20</sup> duplicated the oxygen consumption data of Reboredo et al<sup>21</sup>; Goldberg et al<sup>22</sup> and Harter et al<sup>23</sup> were addressed together in Goldberg et al<sup>24</sup> in order not to duplicate data. Therefore, 33 studies were included in this review.<sup>9–13,19,21,24–49</sup> However, the study developed by Moros et al<sup>25</sup> was included only in the qualitative analyses because it did not present the values (mean and standard deviation) of control group for our outcomes of interest, and the authors did not respond to the request for data. Also, the study of Thompson et al<sup>29</sup> was not included in the meta-analysis because it presented values that not were similar between groups at baseline. Figure 1 shows the flow diagram of the studies included in this review and Table 1 summarises the characteristics of these studies.

### Characteristics of included studies

The studies comprised 1254 participants with end-stage renal disease and on haemodialysis; 703 were allocated to an experimental intervention (301 aerobic training, 312 combined training and 90 resistance training) and 551 were allocated to a control group.

The main characteristics of the included studies are shown in Table 1. Most studies (64%) evaluated the effects of aerobic training,<sup>9–13,21,24,28–31,33,34,38,41,42,44,46–49</sup> 37% evaluated combined training,<sup>10,13,27,29,32,35–37,39,40,43,45</sup> and 15% resistance training.<sup>10,12,19,26,29</sup> In most of the experimental groups (25/39, 64%), exercise sessions were scheduled during haemodialysis.<sup>9–13,19,21,26,28–38,41,44,46</sup> The duration of exercise protocol was 8 weeks in five groups (13%),<sup>12,30,41,46</sup> 12 weeks in 13 groups (33%),<sup>9,19,21,26,28,29,33,38,39,43,48</sup> 16 to 20 weeks in ten groups (26%),<sup>10,11,25,27,34,40,42,44</sup> and ≥24 weeks in 11 groups (28%).<sup>13,24,31,32,35–37,45,47,49</sup> The exercise training program was prescribed three times a week for most groups (80%).<sup>9–13,19,21,24,26,28–38,41,43,44,46,48,49</sup> Only nine studies (27%) reported compliance with the exercise training program,<sup>19,21,29,31–33,35,40,47</sup> with compliance being at least 74% in all experimental groups where it was reported.<sup>40</sup>

### Risk of bias

The data concerning the assessment of the risk of bias for each study are shown in Table 2. Most included studies had poor methodological quality. Adequate randomisation was reported in only 10

studies (30%),<sup>10,19,27,29–31,35,38,40,43</sup> and allocation concealment in only six studies (18%).<sup>19,29,31,38,40,43</sup> This review did not evaluate blinding of patients and investigators who delivered the interventions due to the characteristics of intervention. Ten trials (30%) blinded assessors.<sup>11,12,21,27,30,33–35,40,43</sup> Slightly more than half of the studies (52%) properly described losses and exclusions.<sup>9,13,19,26–30,34–38,41,43,46,49</sup>

### Synthesis of results – direct meta-analysis

#### Aerobic capacity

The effect of exercise training on aerobic capacity as estimated by direct meta-analysis is shown in Figure 2 (see Figure 3 on the eAddenda for a more detailed forest plot). Aerobic training significantly improved aerobic capacity (WMD 3.35 ml/kg/min, 95% CI 1.79 to 4.91,  $I^2 = 20\%$ ), as shown in Figure 2a. Combined training also significantly improved aerobic capacity (WMD 5.00 ml/kg/min, 95% CI 3.50 to 6.50,  $I^2 = 35\%$ ), as shown in Figure 2b.

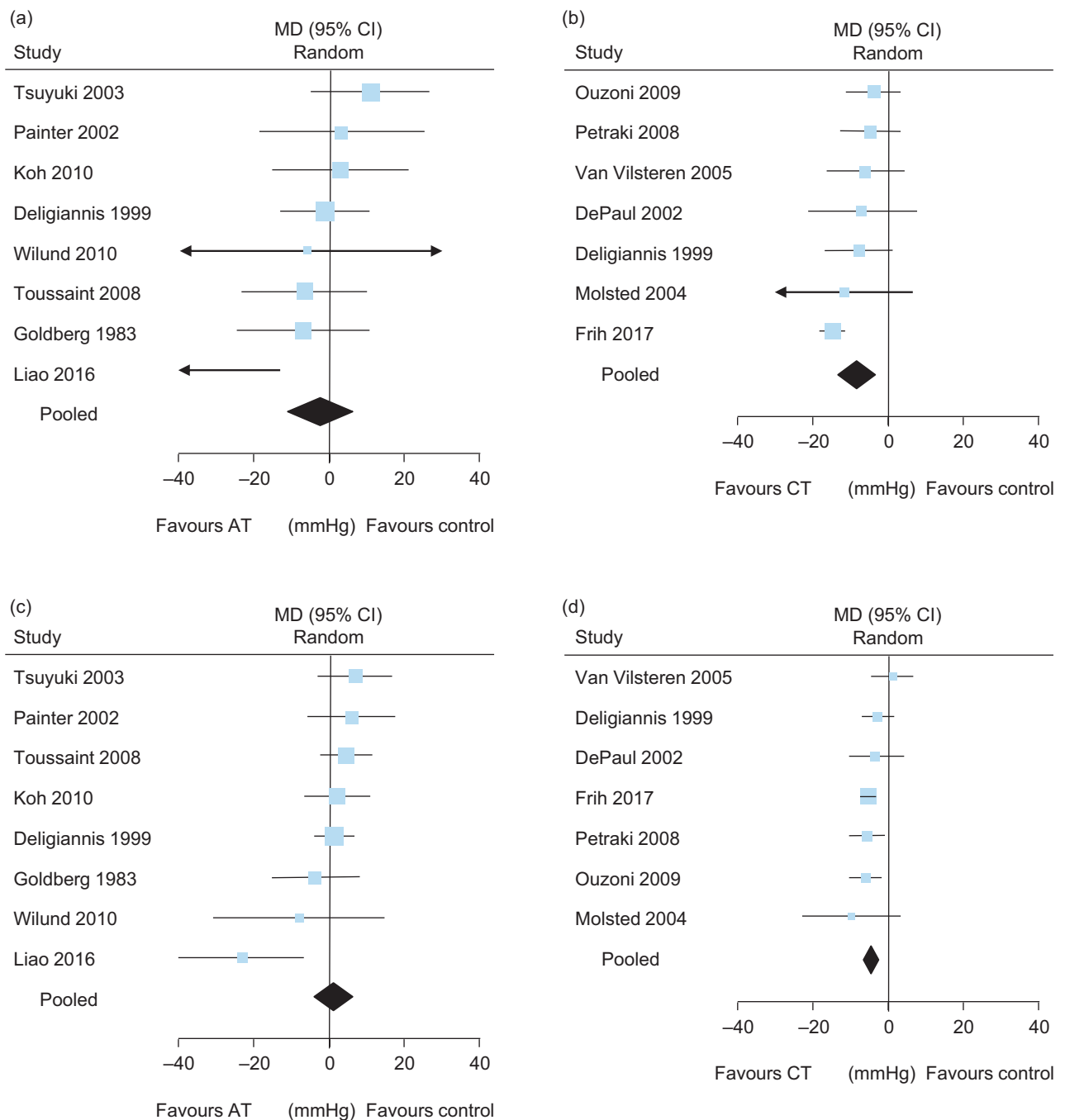
#### Blood pressure

The effect of exercise training on blood pressure as estimated by direct meta-analysis is shown in Figure 4 (see Figure 5 on the eAddenda for a detailed forest plot). Aerobic training did not significantly improve systolic blood pressure (WMD –3 mmHg, 95% CI –11 to 6,  $I^2 = 38\%$ ), as shown in Figure 4a. However, combined training did significantly reduce systolic blood pressure (WMD –9 mmHg, 95% CI –13 to –4,  $I^2 = 56\%$ ), as shown in Figure 4b.

The results were similar for diastolic blood pressure. Aerobic training did not significantly improve diastolic blood pressure (WMD 1 mmHg, 95% CI –4 to 5,  $I^2 = 45\%$ ), as shown in Figure 4c. However, combined training did significantly improve diastolic blood pressure (WMD –5 mmHg, 95% CI –6 to –3,  $I^2 = 8\%$ ), as shown in Figure 4d.

#### Haemodialysis efficiency

The effect of exercise training on haemodialysis efficiency as estimated by direct meta-analysis is shown in Figure 6 (see Figure 7 on the eAddenda for a detailed forest plot). Aerobic training improved haemodialysis efficiency (WMD 0.11, 95% CI 0.02 to 0.20,  $I^2 = 45\%$ ), as shown in Figure 6a. Haemodialysis efficiency was not significantly affected by resistance training (WMD –0.11, 95% CI –0.34 to 0.13,  $I^2 = 70\%$ ) or by combined training (WMD –0.01, 95% CI –0.18 to 0.16,  $I^2 = \%$ ), as shown in Figures 6b and 6c.



**Figure 4.** Direct meta-analysis of the effect of (a) aerobic training compared to control group on systolic arterial pressure, (b) combined training compared to control on systolic arterial pressure, (c) aerobic training compared to control on diastolic arterial pressure, and (d) combined training compared to control on diastolic arterial pressure. AT = aerobic training, CT = combined training.

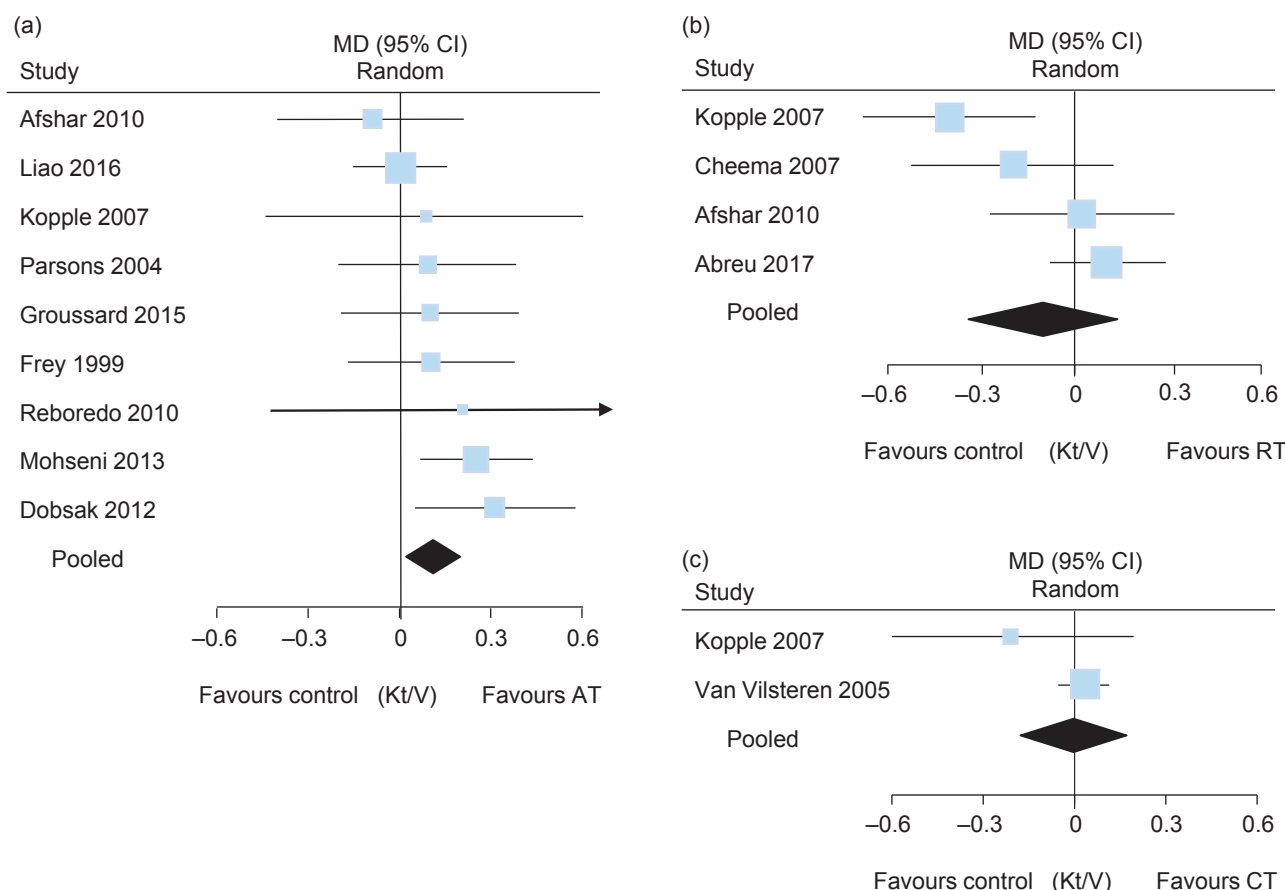
### Heterogeneity

No significant heterogeneity ( $I^2 > 60\%$ ) was observed for aerobic capacity and blood pressure; nevertheless, this review did investigate the possible reason for the heterogeneity amongst studies comparing the effects of combined training in aerobic capacity ( $I^2 = 35\%$ ) (Figure 2b). To explain the source of heterogeneity, we could identify two articles<sup>39,40</sup> that differed in the frequency of the intervention (twice per week) from the others (three or more per week). The exclusion of these trials eliminated heterogeneity and did not affect the evidence that combined training significantly increases  $\text{VO}_2\text{max}$  (WMD 5.79 ml/kg/min, 95% CI 4.52 to 7.06,  $I^2 = 0\%$ ).

In the meta-analyses of the effect of aerobic training on arterial blood pressure, we observed heterogeneity of 38% for systolic pressure and 45% for diastolic pressure. To explain the

heterogeneity, we found that the study of Liao et al<sup>28</sup> showed a mean blood pressure reduction in the exercise group that was much higher than among the other studies: systolic pressure improved from 138 mmHg (SD 17) at baseline to 96 mmHg (SD 64) at the end of the training period; and diastolic pressure improved over the same period from 77 mmHg (SD 8) to 54 mmHg (SD 35). The study did not explain the reason for this major reduction and did not report whether the antihypertensive drug regimen was maintained during the protocol. The comparison between aerobic training and control group without the data of Liao et al<sup>26</sup> showed no heterogeneity for both the systolic and diastolic data, and did not affect the evidence that aerobic training does not improve systolic (0 mmHg, 95% CI -6 to 7,  $I^2 = 0\%$ ) or diastolic (2 mmHg, 95% CI -1 to 6,  $I^2 = 0\%$ ) arterial pressure.





**Figure 6.** Direct meta-analysis of the effect of (a) aerobic training compared to control, (b) resistance training compared to control, and (c) combined training compared to control on Kt/V. See main text for explanation of Kt/V.

AT = aerobic training, CT = combined training, RT = resistance training.

Substantial heterogeneity was found in the meta-analysis of the effect of resistance training on haemodialysis efficiency ( $I^2 = 70\%$ ) (Figure 6b); however, only four studies<sup>10,12,19,26</sup> were included in this comparison.

### Synthesis of results – network meta-analysis

Figure 8 shows the network of comparisons for each outcome measure in this review. Note that there is only one network of comparisons for blood pressure because all trials that measured blood pressure reported both systolic and diastolic data, so Figure 8b applies to both outcomes. The width of the lines is proportional to the number of trials comparing each pair of treatments, and the size of each node is proportional to the number of participants. Table 3 shows the results of the network meta-analysis.

In the network analysis for aerobic capacity, 199 participants were allocated to a combined training group, 113 to an aerobic training group, and 271 to the control group, summing to a total of 583 participants. As in the results obtained using direct meta-analysis, aerobic training (3.34 ml/kg/min, 95% CrI 1.55 to 5.11) and combined training (5.01 ml/kg/min, 95% CrI 3.26 to 6.57) were both superior to the control group for aerobic capacity, as presented in Table 3. Although no significant difference was found between aerobic training and combined training, combined training had 92% probability of being ranked as the most effective treatment, as presented in Figure 9a.

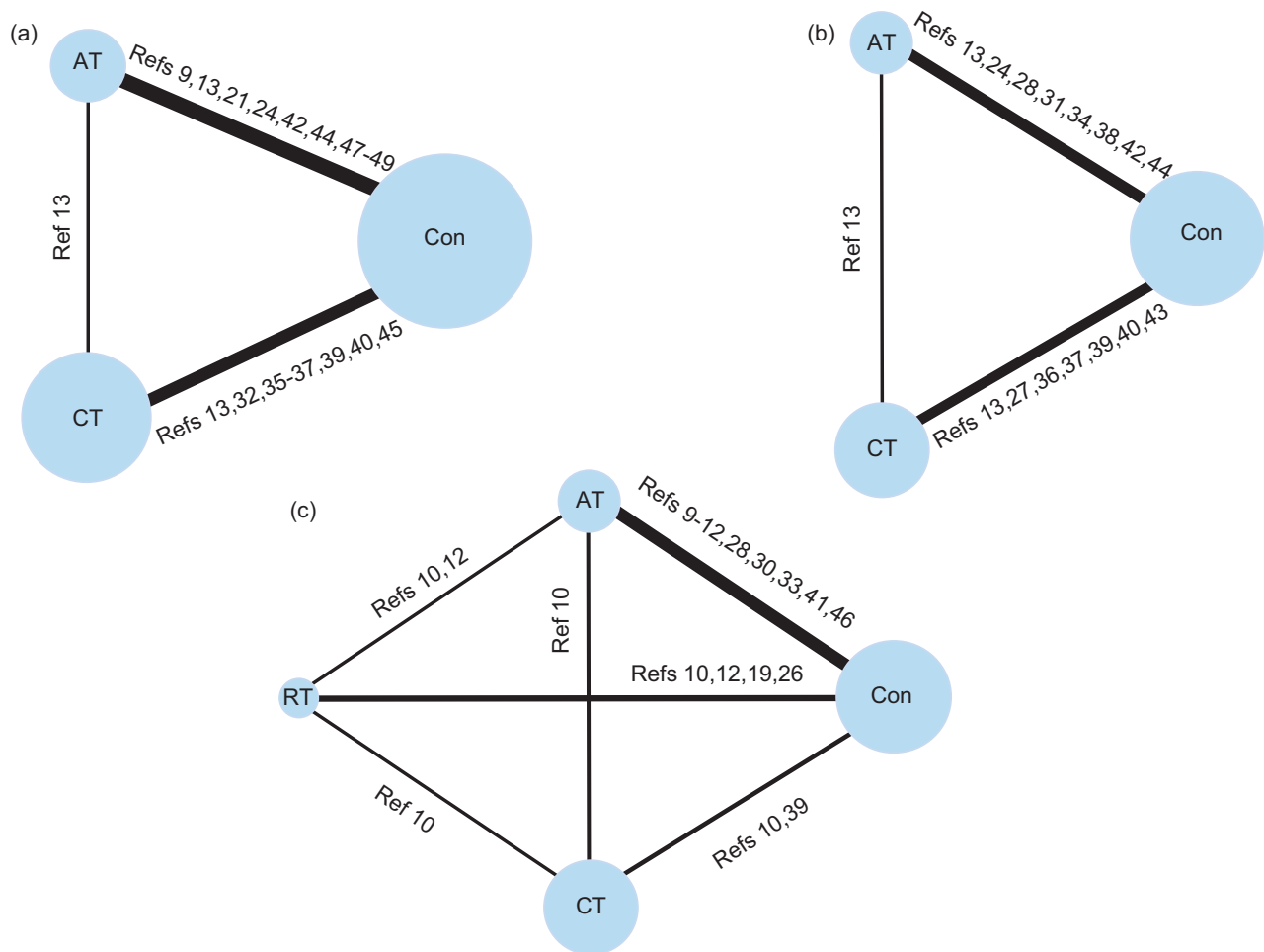
In network meta-analyses of arterial blood pressure, 157 participants were allocated to a combined training group, 102 to an aerobic training group, and 237 to the control group, summing to a total of 496 participants. In the network meta-analysis for systolic arterial blood pressure, only combined training was superior to the control group ( $-9$  mmHg, 95% CrI  $-14$  to  $-3$ ). In the network meta-analysis

for diastolic arterial blood pressure, combined training was superior to control ( $-4$  mmHg, 95% CrI  $-7$  to  $-2$ ) and to aerobic training ( $-6$  mmHg, 95% CrI  $-10$  to  $-1$ ), as presented in Table 3. Moreover, combined training presented 91% probability of being the best treatment for systolic arterial pressure and 99% for diastolic arterial pressure, as presented in Figures 9c and 9d.

In the network meta-analysis for haemodialysis efficiency, 100 participants were allocated to an aerobic training group, 71 to a resistance training group, 65 to a combined training group, and 230 to a control group, summing to a total of 466 participants. Unlike direct meta-analysis, which demonstrated that aerobic training improves haemodialysis efficiency when compared to control group, none of exercise training modalities were superior to control treatment, as shown in Table 3. Aerobic training had the highest probability (76%) of being the best treatment for this outcome, as presented in Figure 9b.

### Discussion

Network meta-analysis has been used to compare the effects of different exercise training modalities in a range of health conditions, such as overweight/obesity<sup>50</sup> and type 2 diabetes.<sup>51</sup> This is the first published network meta-analysis to compare exercise training modalities in people with end-stage renal disease who require haemodialysis. In doing so, it helps to overcome the absence of comparative data from head-to-head trials about the effects of different exercise modalities on aerobic capacity, blood pressure and dialysis efficiency in this population. The network meta-analysis results substantially progress understanding of the relative merits of the exercise training modalities beyond that obtained from the direct meta-analyses in this review and elsewhere.



**Figure 8.** Network of clinical trials comparing different modalities of exercise to (a) aerobic capacity, (b) arterial blood pressure, and (c) haemodialysis efficiency. AT = aerobic training, Con = control, CT = combined training, R = resistance training.

Our direct meta-analyses found that aerobic training increased aerobic capacity and haemodialysis efficiency compared to control, but had no effect on blood pressure. Combined training increased aerobic capacity and reduced both diastolic and systolic arterial pressure compared to control. Resistance training had no effect on the studied outcomes. These findings corroborate those of a 2011 Cochrane systematic review,<sup>8</sup> which found that aerobic training significantly improved aerobic capacity, but only combined training improved both aerobic capacity and blood pressure control. Although the Cochrane review<sup>8</sup> did not assess the effect of exercise on dialysis efficiency, this was estimated in a systematic review by Sheng et al,<sup>52</sup> which meta-analysed six studies with a total of 233 participants. That review found a significant effect of intradialytic exercise on haemodialysis efficiency (Kt/V 0.27, 95% CI 0.01 to 0.53), but they did not analyse that effect according to training modalities. Our direct meta-analysis is the first to separate the effects of different exercise

modalities on Kt/V and to find a significant effect only for aerobic training.

Our network meta-analysis revealed some interesting findings. First, it evidenced the superiority of combined training (aerobic exercise plus resistance training) in improving aerobic capacity and controlling blood pressure in people with end-stage renal disease. Increasing aerobic capacity in people with end-stage renal disease is a significant goal, given that exercise capacity, characterised as  $\text{VO}_{2\text{peak}}$ , has been considered a powerful predictor of survival in this clinical population.<sup>53</sup> Furthermore, a cross-sectional study including more than 10 000 haemodialysis patients found that subjective physical function was the strongest predictor of death among all health-related quality of life measures.<sup>7</sup> The positive effect of combined training on blood pressure is also a noteworthy finding, given that the risk of cardiovascular disease has a direct, strong and continuous correlation with blood pressure levels.<sup>54,55</sup>

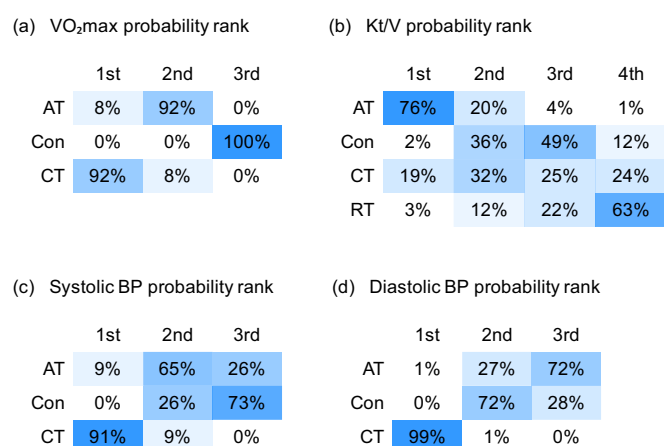
**Table 3**

Mean differences and credible intervals estimated from network meta-analysis model.

|               | $\text{VO}_{2\text{max}}$<br>(ml/kg/min) | Systolic arterial pressure<br>(mmHg) | Diastolic arterial pressure<br>(mmHg) | Haemodialysis efficiency<br>(Kt/V) <sup>a</sup> |
|---------------|--|--------------------------------------|---------------------------------------|---|
| AT versus Con | 3.34 (1.55 to 5.11)                      | -2 (-10 to 5)                        | 1 (-3 to 5)                           | 0.11 (-0.02 to 0.25)                            |
| CT versus Con | 5.01 (3.26 to 6.57)                      | -9 (-14 to -3)                       | -4 (-7 to -2)                         | 0.01 (-0.24 to 0.25)                            |
| RT versus Con | -  | -                                    | -                                     | -0.06 (-0.26 to 0.11)                           |
| CT versus AT  | 1.66 (-0.83 to 3.93)                     | -6 (-15 to 3)                        | -6 (-10 to -1)                        | -0.1 (-0.39 to 0.16)                            |
| AT versus RT  | -  | -                                    | -                                     | 0.17 (-0.03 to 0.39)                            |
| CT versus RT  | -  | -                                    | -                                     | 0.07 (-0.21 to 0.36)                            |

AT = aerobic training, Con = control, CT = combined training, RT = resistance training,  $\text{VO}_{2\text{max}}$  = maximal oxygen uptake.

<sup>a</sup> See main text for explanation of Kt/V.



**Figure 9.** Rankograms of aerobic training, control, combined training and resistance training for (a) aerobic capacity, (b) haemodialysis efficiency, (c) systolic arterial pressure, and (d) diastolic arterial pressure.

AT = aerobic training, BP = blood pressure, Con = control, CT = combined training, RT = resistance training.

The cell transparency is proportional to the probability of the treatment to be ranked in that column. The columns represent the ranks; the first column represents the best treatment and the last column represents the worst treatment.

Since combined training seems more effective in increasing functional capacity and decreasing blood pressure, it may play a role in survival rates. This hypothesis awaits testing in additional clinical trials assessing long-term outcomes.

The network meta-analysis for haemodialysis efficiency was inconclusive. This may mean that exercise has limited effect on haemodialysis efficiency or, alternatively, Kt/V-urea may not be the best way to measure the impact of exercise on dialysis efficiency. Kt/V is based on the clearance of urea, a small solute that is distributed in total body water and that passively distributes across plasma membranes. However, some trials have assessed haemodialysis efficiency through measurement of the removal of solutes of higher molecular weight or that are more hydrophilic than urea in dialysate; most of these studies found positive results.<sup>41,56–58</sup>

This systematic review had several methodological strengths, including: focused review questions; a comprehensive and systematic literature search; and the collaboration of a multidisciplinary team of health researchers and methodologists who used explicit and reproducible eligibility criteria. Furthermore, it employed network meta-analysis to indirectly compare different modalities of exercise training for each outcome analysed, which allowed new findings to be derived from the literature. Despite advancing knowledge on the issue, this network meta-analysis had some limitations due the characteristics of the included studies. Most trials included in the analysis have uncertain or high risk of bias. Regarding haemodialysis efficiency, the review was limited by the fact that these are small trials measuring only single pool Kt/V. Although the validity of Kt/V-urea as a prognostic factor has been questioned,<sup>59</sup> this measure was chosen because it has largely been used in previous studies on dialysis efficiency. Moreover, the analysis did not consider training details, such as intensity and duration.

The main contribution of this network meta-analysis is the ranking of the potential benefits of different exercise training modalities on health outcomes in people who required haemodialysis for end-stage renal disease. This ranking shows that combined aerobic and resistance training is the most effective modality to increase aerobic capacity and control blood pressure in this population. This knowledge helps physiotherapists and other clinicians to advise people with end-stage renal disease about which exercise training modality is likely to be most beneficial for them, despite the lack of head-to-head trials comparing the different modalities.

Future research could examine the influence of the duration and intensity of the exercise training regimen on its clinical effects, to further guide clinical exercise prescription in this setting. Despite the need for this

further evidence, the findings of this review support the prescriptions of combined exercise training regimens in haemodialysis centres.

**What was already known on this topic:** People with end-stage renal disease present higher risk for cardiovascular disease and mortality, which may be aggravated by a sedentary lifestyle. Exercise training improves functional capacity, arterial blood pressure, lipid profile, heart rate variability, and quality of life in people with end-stage renal disease, but few head-to-head comparisons between different exercise modalities have been published.

**What this study adds:** Using network meta-analysis, the review identified that combined training is the most effective modality to increase aerobic capacity and control blood pressure in people who require haemodialysis for end-stage renal disease.

**Footnotes:** <sup>a</sup> RStudio Inc, Boston, USA. <sup>b</sup> R package version 2.2.0-3, <http://CRAN.R-project.org/package=rjags>.

**eAddenda:** Figures 3, 5 and 7, and Appendices 1, 2, 3 and 4 can be found online at DOI: <https://doi.org/10.1016/j.jphys.2018.11.008>.

**Ethics Approval:** Nil.

**Competing interest:** Nil.

**Source of support:** Supported by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) - Brazil: 467 300/2014-3, 457 581/2013-1, 307 138/2015-1; Supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) - Brazil: 074/2012-PVE, CsF - PveS 1170/2013.

**Acknowledgements:** Nil.

**Provenance:** Not invited. Peer reviewed.

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