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Personalised exercise prescription in the prevention and treatment of arterial hypertension: a Consensus Document from the European Association of Preventive Cardiology (EAPC) and the ESC Council on Hypertension

(Exercise and Hypertension)

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Key words: Physical activity; endurance training; resistance training; exercise prescription; blood pressure

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Abbreviation list

AT	Aerobic exercise training
BP	Blood pressure
CRF	Cardiorespiratory fitness
CT	Combined exercise training
CV	Cardiovascular
DBP	Diastolic blood pressure
DRT	Dynamic resistance training
HIIT	High intensity interval training
HRE	Hypertensive response to exercise
IRT	Isometric resistance Training
MAP	Mean arterial pressure
PA	Physical activity
RCT	Randomized controlled trial
1RM	1 Repetition maximum
RT	Resistance training
SBP	Systolic blood pressure

Abstract

Treatment of hypertension and its complications remains a major ongoing health care challenge. Around 25% of heart attacks in Europe are already attributed to hypertension and by 2025 up to 60% of the population will have hypertension. Physical inactivity has contributed to the rising prevalence of hypertension but patients who exercise or engage in physical activity reduce their risk of stroke, myocardial infarction and cardiovascular mortality. Hence, current international guidelines on cardiovascular disease prevention provide generic advice to increase aerobic activity, but physiological responses differ with blood pressure level, and greater reductions in blood pressure across a population may be achievable with more personalised advice. We performed a systematic review of meta-analyses to determine whether there was sufficient evidence for a scientific Consensus Document reporting how exercise prescription could be personalised for blood pressure control. The document discusses the findings of 35 meta-analyses on blood pressure lowering effects of aerobic endurance training, dynamic resistance training as well as isometric resistance training in patients with hypertension, high-normal and individuals with normal BP. As a main finding, there was sufficient evidence from the meta-review, based on the estimated range of exercise-induced blood pressure reduction, the number of randomized controlled trials and the quality score, to propose that type of exercise can be prescribed according to initial blood pressure level, although considerable research gaps remain. Therefore, this evidence-based Consensus Document proposes further work to encourage and develop more frequent use of personalised exercise prescription to optimise lifestyle interventions for the prevention and treatment of hypertension.

1 Introduction

1.1 Role of exercise in hypertension

The prevalence of hypertension across Europe is estimated to be 30-45%, with increasing blood pressure (BP) levels at higher age[1]. Hypertension is a major risk factor for cardiovascular (CV) disease such as coronary heart disease, myocardial infarction and stroke as well as hypertensive pathologies such as cardiomyopathy, retinopathy and nephropathy. Patients with hypertension present with additional CV disease risk factors, which often potentiate each other. About 25% of heart attacks in the European region have directly been attributed to hypertension in recent years and hypertension-induced CV disease is thought to be responsible for about 40% of all annual deaths in Europe[2]. Appropriate management of hypertension to prevent disease is critical and, by 2025, the number of people with hypertension globally is predicted to increase to 60%[3], making treatment of hypertension and its complications a major socio-economic and health care challenge.

A factor for the rise in prevalence of hypertension has been population changes in physical activity (PA). The Atherosclerosis Risk in Communities (ARIC) study demonstrated an inverse association between leisure time PA and risk of hypertension in white men[4]. In 2017, a meta-analysis of 29 studies including more than 330000 persons, assessed the quantitative dose-response association of PA and hypertension[5]. It showed that each reduction of leisure-time PA by 10 metabolic equivalent hrs/week increased the risk of hypertension by 6%. PA also determines progression of hypertension to end stage consequences including myocardial infarction and stroke. The National Health and Nutrition Examination Survey (NHANES) I epidemiological follow-up study between 1971- 1992[6] involving 14 000 adults, demonstrated that exercise was independently associated with decreased CV events in patients with hypertension in an exercise volume-dependent manner. In the prospective Life study, regular PA of at least 30 min twice per week in patients with hypertension and left ventricular hypertrophy was associated with reductions in CV death, stroke and myocardial infarction [7]. In a previous systematic review, including a total of 96 073 individuals with elevated BP, patients with hypertension engaged in different levels of PA had a reduced risk of CV mortality (16-67%), whereas sedentary patients had a twofold increased CV mortality risk[8].

1.2 Guideline advice for exercise and hypertension management

The association between PA and BP has been recognised in the 2016 European Guidelines on cardiovascular disease prevention in clinical practice[9] and its recent update[10], as well as statements from the American Heart Association (AHA)[11], American College of Sports Medicine (ACSM) [12] and updated recommendations from an American expert panel [13, 14]. The European 2016 guidelines recommend lifestyle interventions, including regular PA, for individuals receiving treatment for hypertension as well as those with high-normal BP (SBP: 130- 139 mmHg and/or DBP: 85- 89 mmHg) or grade 1 hypertension (SBP: 140-159 mmHg and/or DBP: 90- 99 mmHg), for whom it might be sufficient to reduce CV risk without the addition of anti-hypertensive medication[9]. Patients with hypertension are advised to engage in at least 30 min of moderate-intensity aerobic exercise such as walking, jogging, cycling or swimming on 5-7 days per week for at least 150 min a week[15, 16]. In addition, dynamic resistance exercises but not isometric exercises are recommended 2-3 days per week. Initiation of lifestyle and/or anti-hypertensive drug treatment depend on the grade of hypertension and the number of risk factors[1, 9]. For grade I hypertension, it is recommended to start with lifestyle and add BP medications if the target BP of < 140/90 mmHg is not reached after weeks or months (depending on the number of risk factors). In the presence of organ damage, chronic kidney disease or diabetes, patients with grade I hypertension need to combine lifestyle changes with antihypertensive medications from initial diagnosis. Further escalation of the grade of hypertension as well as the presence of risk factors, as can be assessed by risk scores such as the Systematic Coronary Risk Evaluation (SCORE), always imply an immediate start with BP drugs in combination with lifestyle changes[17].

Current recommendations have been re-evaluated based on findings of more recent studies. In particular there have been significant changes in how BP is diagnosed and managed. The Systolic Blood Pressure Intervention Trial (SPRINT), which showed reduced all-cause and CV mortality as well as heart failure (but not stroke and coronary heart disease) with lower SBP targets[18], resulted in significant changes in the 2017 American College of Cardiology (ACC)/AHA hypertension guidelines[19], which reduced hypertension diagnostic thresholds and treatment targets to <130/80 for all patients. Two recent meta-analyses have supported lower thresholds[20, 21] but the American Academy of Family Physicians (AAFP) recommended approaching hypertension treatment on an individualized basis, taking into account patients' histories, risk factors, preferences and resources (https://www.aafp.org/news/health-of-the-public/20171212notendorseaha-accgdlne.html).

The current European view recommends a BP target <130/80 mmHg in most patients, including those with type-2 diabetes, provided that treatment is well tolerated[22]. In older individuals, guidelines recommend treating physically active elderly patients aged >80 years with SBP ≥160 mmHg, and drug treatment can be considered in individuals aged <80 years with SBP >140 mmHg if well tolerated[1, 23]. In frail elderly individuals, the guidelines recommend that decision on treatment initiation be left to the treating physician[1]. The relevant emphasis put on PA and exercise in achieving these lower thresholds in different age groups is unclear. The 2017 AHCC/AHA hypertension guidelines emphasise diagnosis of hypertension and lower thresholds should result in greater focus on lifestyle interventions. Data from two meta-analyses[24, 25] and a randomised clinical trial[26] have shown significant treatment-induced reductions in CV events and mortality, even in patients with grade 1 hypertension and low-intermediate risk. For this reason, the 2018 European Guidelines for the management of arterial hypertension recommend starting anti-hypertensive drug treatment, in addition to life-style changes, in all patients with BP values >140/90 mmHg at any level of CV risk[27].

1.3 Aims and objectives

Hypertension is increasing globally with an expected rise in the associated CV and cerebrovascular sequelae. Sustainable strategies to manage BP are important and habitual PA as well as structured exercise are key parts of prevention and treatment strategies. Typically, guideline advice for PA implementation in BP management has been relatively limited to advice on amounts of aerobic exercise per week. However, changing international definitions and thresholds for hypertension have resulted in an increased awareness of BP and associated CV risk in individuals across a broader range of age groups and disease severities. Therefore, we performed an updated systematic review of meta-analyses (meta-review) to identify whether there is an evidence base for personalisation of exercise prescription across the range of blood pressures and hypertension severity thresholds within the population. This meta-review has been used to develop a scientific Consensus Document to inform how individualised exercise prescription could be incorporated into recommendations for individuals at risk of developing high BP and in patients with hypertension. Furthermore, we made use of the systematic review to identify areas of weakness in the evidence base that require further investigation.

2 Exercise and Blood Pressure: A Systematic Review

2.1 Methods

Search Strategy

The systematic review is an updated version of the search performed by Johnson et al. in 2013[28]. Meta-analyses from 2000 until 2013 were retrieved from Johnson et al.[28]. Multiple databases were searched from June 2013 until June 2019 (PubMed (https://www.ncbi.nlm.nih.gov/pubmed), Scopus (https://www.scopus.com), Web of Science (http://apps.webofknowledge.com), and Cochrane Library (https://onlinelibrary.wiley.com). The search strategy for the PubMed search is shown in the supplements (Supplement Text S1). The search string was adapted for each database. After removal of duplicates, HH and AD searched titles, abstracts and full texts for eligible meta-analyses as depicted in the flow chart (Figure1). Disagreements were resolved through discussion and mutual agreement. We included meta-analyses with randomized controlled trials on regular aerobic training (AT), dynamic resistance training (DRT) and isometric resistance training (IRT) as well as combined exercise interventions with a duration ≥ 4 weeks in individuals with normal BP, high-normal BP and hypertension.

Inclusion Criteria

Since implementation of standards for the conduction of systematic reviews and meta-analysis (PRISMA[29]), significant quality progression has become evident[28]. We therefore included more recent meta-analysis performed from the year 2000 or after. Further inclusion criteria were: Systematic reviews and meta-analyses on exercise-based randomized controlled intervention trials; exercise qualified as either endurance (AT), resistance (DRT and IRT) or combined exercise regimes; adults (older than 18 years) with and without CV factors; BP changes as primary or secondary outcome.

Exclusion Criteria

Exclusion criteria were: Analysis of cohorts with a focus on specific diseases (for example type 2 diabetes or chronic kidney disease); inclusion of only children or adolescents; analysis of interventions with little or unclear CV effects; forms of neuromotor exercise including Tai-Chi or Yoga interventions; interventions on acute effects of exercise; non-randomized controlled trials; morbidity or mortality reduction as primary endpoint.

Study Quality

The Assessment of Multiple Systematic Reviews (AMSTAR) is a standard quality assessment tool for systematic reviews and meta-analyses[30, 31]. We used an augmented version of the AMSTAR tool that was adopted to focus on the effect of exercise on BP (AMSTAREXBP)[28]. An overview on the study quality of the included meta-analyses is shown in the supplements (Supplement Table S2). AMSTAREXBP refers to the number of items fully satisfied and the numbers of items applicable for the respective study. Meta-analyses already coded were adopted from Johnson et al.[28] For recent studies, the AMSTAREXBP scale was used.

Tables with Characteristics of Meta-analyses

Characteristics were extracted for the eligible meta-analyses in duplicate and agreement was assessed between coders. The tables with the overview of the meta-analyses included in the systematic review can be found in the online supplements (Supplement Table S3-S5). These contained the year of publication, the topic of the analysis, sample size, number and types of trials included, sex distribution, frequency, intensity, time and type of the performed exercise, BP change following the intervention. Mean values were extracted from the meta-analysis. If sample size and female percentage were reported we calculated the corresponding male percentage. The effects of AT, resistance (DRT and IRT) and combined exercise on BP reduction reported from eligible meta-analyses are discussed in the following three separate sections of this chapter.

2.2 Aerobic Exercise

Twenty-four meta-analyses on the effects of regular AT and BP reduction were identified since the year 2000 (Supplement Table S3). Seven of these investigated the effects of exercise on BP in patients with hypertension separately[32-38] and only two differentiated between all three BP categories[33, 34].

The overall effects of AT training across all BP categories were reductions in systolic BP (SBP) of -4.1 and diastolic BP (DBP) of -2.2 mmHg. In persons with normal BP, the mean BP lowering effects of AT were found to be -2.4/-2.6 mmHg for systolic and DBP, respectively[33-37]. In individuals with high-normal BP, the mean BP effects of AT were -1.9/-1.7 mmHg[33, 34]. Most strikingly, the BP lowering effects of AT in patients with hypertension were considerably larger with BP reductions of -7.6/-4.7 mmHg[32-37]. Of note, fewer data are available in individuals with high-normal BP (94 RCTs) and hypertension (92 RCTs) compared to normotension (140 RCTs).

A meta-analysis by Cornelissen et al. in 2013, including 105 AT groups and almost 4000 participants across all BP groups, revealed that regular AT can reduce office SBP, on average, by -3.5 mmHg and DBP by -2.5 mmHg[33]. In the analysis, BP reduction varied with BP categories and was most pronounced in patients with hypertension (-8.3/-5.2 mmHg), compared to high normal BP (-2.1/-1.7 mmHg) and normal BP (-0.8/-1.1 mmHg). Similar results were reported in an older meta-analysis including similar original articles with a lower AMSTAR Score[34]. Conceicao et al. performed a meta-analysis of four RCTs investigating the effects of dance therapy on BP in patients with hypertension[32]. Only 216 patients were included and the AMSTAR Score was low (47%). They found a BP reduction of -12.0/-3.4 mmHg in these patients. From these meta-analyses, and an additional one in low to middle-income countries including four RCTS[39], it seems evident that smaller sample sizes tend to have larger effect sizes.

Several other lessons on the effects of AT on BP are seen from this meta-review. Two studies looked at the effects of AT on BP in previously sedentary older individuals[40, 41]. In both meta-analyses, including more than 2000 persons, the age ranged from 65-70 years with BP at rest in the high-normal range on average. Taken together, the BP reductions after AT were -3.7/-1.9 mmHg. Therefore, AT in the elderly seems to yield BP reductions of similar magnitude compared to younger individuals. Moreover, the BP lowering effect of regular AT appears to be evident across White and Asian ethnic groups[35] with less evidence for Black ethnicity, and in both men and women[33]. In a subgroup meta-analysis of RCTs, the greatest reductions in BP were seen in studies where the exercise intervention was supervised rather than self-directed[35, 36].

In a recent meta-analysis by Batacan et al. including 25 RCTs, high-intensity interval training (HIIT) with a duration of more than 12 weeks showed significant effects on BP with reductions of -4.6/-2.9 mmHg in patients with overweight and obesity without differentiating across the range of BP categories[42]. The overall BP lowering effects of HIIT appear to be small, however, no meta-analyses on the BP lowering effects of HIIT in patients with hypertension are available. Costa et al., without reporting absolute values for exercise-induced BP reductions, compare HIIT with moderate continuous aerobic exercise training in patients with high-normal BP and hypertension[43]. It was concluded that both exercise modalities induced similar reductions in resting BP in both groups of patients. It remains to be elucidated whether HIIT can be recommended for patients with hypertension at high CV risk. To avoid overtraining and ensure sufficient recovery periods, HIIT should be performed periodically in conjunction with moderate continuous training at lower intensities. No data are currently available on how to perform periodization of HIIT long-term.

In summary, the systematic review of meta-analyses demonstrates the efficacy of AT in lowering BP, with larger mean BP reductions in patients with hypertension (SBP-7.6/DBP-4.7 mmHg) compared to high-normal BP (-1.9/-1.7 mmHg) and individuals with normal BP (-2.4/-2.6 mmHg).

2.3 Resistance Exercise

Several meta-analyses have examined the effects of chronic DRT and IRT on BP (Supplement Table S4). Of those qualifying for this review, six meta-analyses investigated the effects of DRT[33, 44-48] and another six looked at the effects of IRT on BP[33, 46, 49-52] (Supplement Table S4).

The BP lowering effects of DRT (SBP/DBP) were -3.7/-2.7 mmHg across the range of BP categories[33, 44-48]. In individuals with normal BP, DRT reduced BP by -1.8/-3.1 mmHg[33, 45-47], and in individuals with high-normal BP[33, 45, 46] and hypertension[33, 45-47] the BP lowering effects were -3.9/-3.3 mmHg and -2.6 mmHg/-2.1 mmHg, respectively. A recent meta-analysis with a high AMSTAR quality score (89%) including 64 RCTs assessed the efficacy of DRT as a stand-alone antihypertensive treatment strategy[45]. The greatest BP reductions for DRT were seen in patients with hypertension (-5.7/5.2 mmHg), arguably in the range of BP reductions reported for AT in high-quality meta-analyses (AMSTAR Score > 70%), including more than 10 RCTs in patients with hypertension[33, 35, 38].

Several moderators of the SBP response to DRT were defined. A greater number of exercises per session (≥8 vs. <8) was significantly associated with greater SBP reduction. Studies that had a BP-focused primary outcome reported greater BP lowering effects compared to non-BP focused outcomes. Most interestingly, non-white individuals had significantly greater BP lowering effects of DRT compared to whites. In non-whites with hypertension, the BP reductions (-14/-10 mmHg) were considerably higher than the effects previously reported for AT[45]. Other moderators of the BP lowering effects of DRT such as age, sex and exercise volume had significant influence[33, 46].

The mean BP lowering effects of IRT independent of the initial BP categories (33 RCTs, mean AMSTAR Score 73%) were -10.0/-5.8 mmHg[33, 46, 49-52]. In individuals with normal BP (17 RCTs, 76 %), IRT reduced BP by -6.6/3.0 mmHg[49, 50, 53]. In patients with hypertension (9 RCTs, 76%) the reduction of BP following IRT was -4.3/-5.0 mmHg[49, 50, 53]. There are no meta-analyses available on the effects of IRT in persons with high-normal BP. A meta-analysis by Inder et al. was the only study that assessed potential moderators of the BP response to IRT[49]. Older individuals (≥45 vs. <45 years) demonstrated larger reductions in mean arterial BP (MAP: -5.5 vs. -2.7 mmHg) and longer duration (≥8 vs. <8 weeks) induced larger reductions of SBP (-7.3 vs. -3.0 mmHg), independent of weight loss. IRT of the arm seemed to induce superior effects on SBP reduction compared to IRT of the leg (-6.9 vs. -4.2 mmHg). The amount of BP reduction reported depends on the number of participants, and meta-analyses that showed greater BP lowering effects included smaller and fewer RCTs. It needs to be mentioned that the presented data on IRT in normotension and hypertension are based on 27 RCTs, whereas the data on DRT for these BP categories are based on 126 RCTs. More data are available on DRT compared to IRT and, therefore, the effects of IRT may be overestimated. Nonetheless it is clear, that the BP lowering effects of IRT are greater in individuals with normal BP compared to patients with hypertension.

In summary, these meta-analyses demonstrate the efficacy of DRT and IRT in lowering BP among adults with hypertension. In individuals with normal BP, moderate evidence suggests greater BP reductions in response to IRT as compared to DRT or even AT.

2.4 Combined Aerobic and Resistance Exercise

The overall effects of combined exercise training across all BP categories are reductions of -5-5/-4.1 mmHg[33, 39, 54, 55] (Supplement Table S5). Differentiation according to the individual BP status can be established on the basis of a single meta-analysis[54]. The meta-analysis by Corso and colleagues included the largest number of trials and reached the highest AMSTAR quality score (94%) of studies focusing on combined exercise [54]. They found a significant overall reduction of SBP and DBP (-3.2/-2.5 mmHg) after combined exercise training. In individuals with normal BP, BP was reduced by -0.9/-1.5 mmHg, whereas BP was reduced by -2.9/-3.6 mmHg in persons with high-normal BP. In patients with hypertension, BP was reduced by -5.3/-5.6 mmHg. Overall, the quality of the RCTs was moderate and higher quality of studies were associated with greater BP reductions compared to lower quality studies (-3.6/-4.8 mmHg vs. -1.9/-2.3 mmHg, respectively). Most strikingly, the BP reduction in patients with hypertension in the higher quality studies with BP as the primary outcome were -9.2/-7.7 mmHg, therefore challenging standalone AT as the first priority for anti-hypertensive exercise treatment in hypertension.

In summary, combined exercise training seems to be of lesser added value in individuals at risk of developing hypertension. In patients with manifested hypertension, however, combined exercise may be an efficient alternative treatment option, but more RCTS are necessary to determine the BP lowering effects of combined exercise with BP as the primary outcome in patients with hypertension.

3 Personalized Exercise Prescription by Blood Pressure Level

3.1 Choice of exercise priority by level of blood pressure

Based on the systematic review of meta-analyses, we developed a table of exercise priorities with exercise recommendations proposed for the type of exercise depending on the initial BP categories (Table 1). The expected range of mean BP reductions as estimates of the available meta-analyses are given for each type of exercise in different BP categories. All meta-analyses which reported findings in the subgroups of BP categories were included. In the following, the proposed exercise priorities based on the initial BP level are compared and discussed in detail. In principle, the available evidence suggests that the magnitude of BP reduction to AT and RT are greater in patients with hypertension compared to individuals with high-normal and normal BP. In the two latter BP categories, RT may be favoured over AT as discussed in detail in the following sections.

Exercise priorities in patients with hypertension

The evidence from our systematic analysis supports AT as first line exercise therapy in patients with hypertension. The mean expected BP reduction ranged from -4.9 to -12.0 mmHg systolic and -3.4 to -5.8 mmHg diastolic (Table 1). In patients with hypertension, low-to-moderate intensity RT, with equal priority for IRT (range: -4.3 to -6.6 mmHg systolic and -4.5 to -5.5 mmHg diastolic) and DRT (range: +0.5 to -6.9 mmHg systolic and -1.0 to -5.2 mmHg diastolic), can be recommended as part of primary and secondary prevention programs of arterial hypertension as a second line exercise treatment (Table 1). Of note, only looking at high-quality meta-analyses (AMSTAR Score > 70) with more than 10 RCTs included, the BP lowering effects of DRT [45] are arguably in the range of those expected for AT [33, 35, 38]. For non-white patients with hypertension, DRT needs to be considered as a first line therapy[45]. Although examined in a small number of trials only (14 interventions, AMSTAR Score 89%), DRT showed greater BP reductions than any other exercise modality in non-white patients[45]. A combination of AT with either IRT or DRT can be recommended individually in patients who may additionally benefit from the metabolic adaptations to resistance exercise. It cannot be concluded that combined exercise is principally equal or superior to AT alone with a mean expected BP reduction of -5.3/-5.6 mmHg derived from a single meta-analysis. The efficacy of combined exercise increases with higher initial BP status. In patients with hypertension, IRT (a total of 9 RCTs only) and DRT(45) as well as combined exercise[54] may be in the range comparable to standalone AT[33, 35, 38] (Table 1). However, more high-quality meta-analyses including more RCTs are necessary to confirm whether either exercise modality can challenge AT as the primary exercise therapy in patients with hypertension. The order of the performed combined exercise does not seem to have an effect on the magnitude of BP reduction[56]. More RCTs are necessary to examine the BP lowering effects of combined exercise on BP reduction as the primary outcome in patients with hypertension.

Exercise priorities in individuals with high-normal blood pressure

Dynamic RT can be recommended as first line exercise priority in individuals with high-normal BP (range: -1.7 to -4.7 mmHg systolic and -1.7 to 3.8 mmHg diastolic) with slightly greater BP reduction compared to AT (range: -1.7 to -2.1 systolic and-1.7 mmHg diastolic) (Table 1). Isometric RT is likely to elicit similar if not superior BP lowering effects as DRT, but the level of evidence is low and the available data are scarce. No meta-analysis exists on the BP lowering effects of IRT in patients with high-normal BP. With respect to combined exercise, a mean BP reduction of -2.9/3.6 mmHg can be expected, slightly lower than the expected range of BP reduction for DRT alone. The BP lowering effects of combined exercise are slightly higher compared to AT alone. For patients with a combination of CV risk factors it may be preferable to prescribe combined DRT and AT rather than DRT alone. This will have to be addressed in future research.

Exercise priorities in individuals with normal blood pressure

Isometric RT may be recommended as first line exercise intervention in individuals with normal BP with expected BP lowering effects in the range of -5.4 to -8.3 mmHg systolic and -1.9 to -3.1 mmHg diastolic (three meta-analyses, 17 RCTs, mean AMSTAR Score 76%) (Table 1). An indication for IRT in healthy individuals with normal BP may be given, for example, in persons with a family history of hypertension, a history of gestational hypertension or other reasons for an increased risk of developing hypertension later in life. Individuals at increased risk of developing hypertension should primarily engage in IRT, for example isometric handgrip or leg extension. IRT is easy to apply and involves minimal time commitment. In principle, patients with obesity or (pre-)diabetes may want to include DRT of larger muscle groups (range: ±0 to -2.4 systolic and -0.9 to -3.4 diastolic) to benefit from additional metabolic adaptations.

AT can also be recommended as an effective exercise therapy in individuals with normal BP (range: -0.8 to -4.1 mmHg systolic and -1.1 to -2.9 mmHg diastolic). More high-quality meta-analyses (AMSTAR Score > 70%) including more than 10 RCTs are available for AT in normal BP[33, 35, 38, 57] as compared to IRT (all meta-analyses less than 10 RCTs, Table 1). Hence, the BP lowering effects of IRT as compared to AT may be overestimated and both exercise modalities may have similar BP lowering effects in individuals with normotension.

In patients with additional CV risk factors, a combination of IRT with AT may be warranted, although BP lowering effects of combined exercise (mean: -0.9/-1.5 mmHg) are considerably smaller compared to IRT alone. It has to be pointed out that improving exercise capacity (maximum oxygen uptake) reduces CV and all-cause mortality and, therefore, prescription of AT should be recommended in most patients with multiple risk factors and increased CV risk independent of differences in the efficacy to lower BP.

Summary

In summary, AT is recommended in patients with hypertension with expected BP reductions in the range of -4.9 to -12 mmHg systolic and -3.4 to -5.8 mmHg diastolic. In patients with high-normal BP, DRT can be recommended with a BP reduction in the range of -3.0 to -4.7 mmHg systolic and -3.2 to -3.8 mmHg diastolic. In individuals with normal BP but with risk factors for the development of hypertension, IRT can be recommended with an expected BP reduction of -5.4 to -8.3 mmHg systolic and -1.9 to -3.1 mmHg diastolic. However, these findings are based on three meta-analyses with a total number of only 17 RCTs, but with sufficient AMASTAR Scores. Future research and stronger evidence are warranted to elucidate whether IRT can be recommended over AT in individuals with normal BP.

3.2 Limitations and research gaps

Some limitations to the systematic review of meta-analyses and consequent recommendations need to be discussed. The differences in BP lowering effects between the different modes of exercise may appear small, however, they are in the range of several mmHg and can be considered clinically relevant[21]. BP lowering effects of AT in hypertension, for example, are in a range comparable to BP lowering effects reported for antihypertensive drug treatment[58]. Expected treatment efficacy with DRT or IRT can be expected to be about 3-4 mmHg lower. There is, in principle, less data available on the BP lowing effects of IRT for all BP categories. No meta-analyses exist for the BP lowering effects of IRT in high-normal BP. Only a single meta-analysis has investigated effects of combined exercise. No meta-analysis to date has investigated the BP lowering effects of different exercise modes in resistant hypertension. In order to give more precise exercise-prescriptions based on initial BP levels, more high-quality RCT are warranted to address these research gaps in the future. Sufficient data on alternative and complementary types of PA, such as for example Yoga or Tai Chi, are still lacking. Nonetheless, we believe it is time to think about individualisation of exercise prescription and the presented evidence supports this approach. We did not attempt to perform a meta-analysis of meta-analyses since the heterogeneity and the risk of bias between the meta-analyses are considerable. Of course, several RCTs have been included in more than one analysis and older RCTs tend to be included more often. To compare BP lowering effects of different exercise-modes on the basis of BP category we therefore reported the specific ranges of BP changes as estimates (section 3.1, Table 1). This Consensus Document focused on the evidence for personalisation of exercise prescription to lower BP. Here, we did not aim to give updated practical recommendations of "how to perform modes of exercise" such as frequency, intensity and time (FITT). A guide to the practical applications of AT, IRT and DRT can be found in the ACSM guidelines[59] and updated recommendations from an expert panel[13, 14]. In parallel to this European evidence-based statement on personalised exercise prescription in the prevention and treatment of arterial hypertension, the ACSM and its 2018 Physical Activity Guidelines Advisory Committee have recently updated their statements on exercise and hypertension [12, 14]. Similar research gaps were identified and addressed, but differences in the systematic analysis of the available evidence exist. This Consensus Document had a clear focus on validating the evidence for personalized exercise prescription depending on the initial BP level. In our statement, the meta-analyses varied in sample size and quality of evidence (AMSTAR Score), however, for the recommendations of exercise priorities based on the range of mean exercise-induced BP reductions, we decided to include the evidence from all meta-analyses, listing the number of RCTs and AMSTAR Score for every single meta-analysis (Table 1).

4 Conclusions

This consensus paper aimed to provide an evidence-based framework for exercise prescription guided by BP level. There is sufficient evidence from meta-analyses that AT is a useful and effective treatment option to lower BP in patients with hypertension and high-normal BP as well as individuals with normotension. This Consensus Document gives updated evidence for the BP lowering effects of exercise and is the first to focus on implementation of personalised exercise prescription. When prescribing exercise, age, sex, ethnicity and comorbidities as well as individual preferences and available infrastructure have to be taken into account. Most importantly, our systematic review of meta-analyses supports prioritising the choice of exercise based on the individual initial BP level. Patients with hypertension seem to benefit most from AT, whereas single high-quality meta-analyses each suggest that combined exercise[54] and DRT[45] may yield similar potential BP benefits (Table 1). Of note and as an exception, non-white patients with hypertension seem to benefit more from DRT. Patients with high-normal BP may need to implement DRT, with only few existing data on alternative exercise types. Individuals with normal BP with some degree of elevated CV disease risk should engage in IRT, even though the BP lowering effects may currently be slightly overestimated.

Both, AT and RT are therapeutic strategies known to be safe and effective for primary and secondary prevention of hypertension. Despite the unequivocal benefit of exercise in hypertension, it remains significantly underused, in part due to the lack of knowledge, fear and inertia of physicians. It may be possible to develop the use of exercise as an anti-hypertensive treatment strategy by motivational support to improve adherence, individualization of exercise prescription and close-meshed guidance by caretakers. From a socio-economic health perspective, it is a major challenge to develop, promote and implement individually tailored exercise programs for patients with hypertension under consideration of sustainable costs.

Conflict of interest:

AC received honoraria for lectures in symposia and educational activities sponsored by unrestricted grants from Abbott, Berlin-Chemie, Biolab, Boehringer-Ingelheim, Ferrer, Menarini, Merck and Sanofi-Aventis; MS reports personal fees from Novartis and Sanofi-Aventis. LP is lead author on the

American College of Sports Medicine recent Pronouncement[14]. All other authors have nothing to disclose.

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Figure 1: PRISMA Flowchart

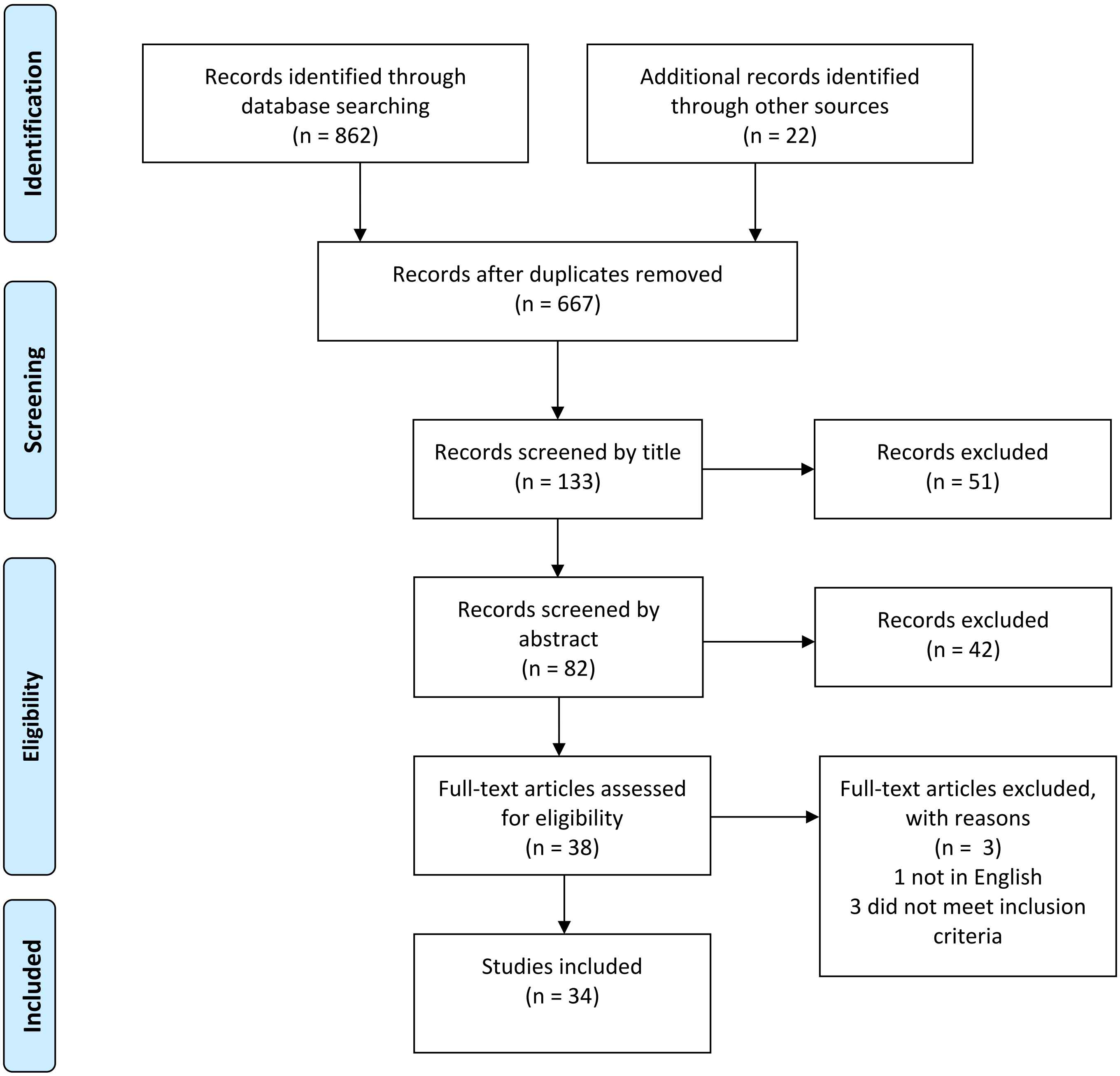

Table 1: Recommendations for exercise priorities based on range of mean exercise-induced blood pressure reductions in meta-analyses

Hypertension *≥140/90 mmHg* *(no further differentiation)* *[mmHg]*	95% CI	No.	AS [%]	**High-Normal Blood Pressure** *≥130-139/85-89 mmHg* *[mmHg]*	95% CI	No.	AS [%]	**Normotension** *<130/84 mmHg* *(no further differentiation)* *[mmHg]*	95% CI	No.	AS [%]
1) AT				**1) DRT**				**1) IRT**			
-8.3/-5.2 (33)	-10,7/-6.0; -6.9/-3.4	26	76	**-3.0/-3.3** (45)	-5.1/-1.0; -5.3/-1.4	41*	89	**-5.4/-2.9** (49)	-6.3/-4.4; -3.6/-2.3	8	83
-7.4/-5.8 (36)	-10.5/-4.3; -8.0/-3.5	7	24	**-4.3/-3.8** (33)	-7.7/-0.9; -5.7/-1.9	13	76	**-7.8/-3.1** (50)	-9.2/-6.6; -3.9/-2.3	6	78
-4.9/-3.7 (35)	-7.2/-2.7; -5.7/-1.8	13	71	**-4.7/-3.2** (46)	-7.8/-1.6; -5.0/-1.4	14	67	**-8.3/-1.9** (53)	-10.4/-6.3; -4.0/0.2	3	67
-6.0/-3.4 (38)	-8.6/-3.3; -5.3/-1.6	14	71								
-6.9/-4.9 (34)	-9.1/-4.6; -6.5/-3.3	28	35	**2) and/or AT**				**2) and/or AT**			
-6/-5 (37)	-8/-3; -7/-3	NA	67	**-2.1/-1.7** (33)	-3.3/-0.8; -2.7/-0.7	50	76	**-0.8/-1.1** (33)	-2.2/0.7; -2.2/-0.1	26	76
-12.0/-3.4 (32)	-16.1/-7.9; -4.9/-1.9	4	47	**-1.7/-1.7** (34)	-3.1/-0.3; -2.6/-0.8	44	35	**-2.6/-1.8** (36)	-3.7/-1.5; -2.6/-1.1	7	24
								-4.0/-2.3 (35)	-5.3/-2.8; -3.1/-1.5	29	71
2) and/or IRT				**3) and/or IRT**				**-3.6/-2.9** (38)	-6.1/-1.2; -4.7/-1.1	17	71
-4.5/-4.5 (49)	-6.6/2.4; -6.9/-2.0	3	83	**No meta-**				**-2.4/-1.6** (34)	-4.2/-0.6; -2.4/-0.7	28	35
-4.3/-5.5 (50)	-6.4/-2.2; -7.9/-3.0	3	78	**analysis**				**-4.1/-1.8** (57)	NA	33	83
-6.6/-5.5 (53)	-11.7/-1.5; -7.9/-3.0	3	67								
								3) and/or DRT			
3) and/or DRT								**0.0/-0.9** (45)	-2.5/2.5; -2.1/2.2	16*	89
-5.7/-5.2 (45)	-9.0/-2.7; -8.4/-1.9	14*	89					**-0.6/-3.4** (33)	-3.1/2.0; -5.6/-1.2	12	76
+0.5/-1.0 (33)	-4.4/5.3; -3.9/1.9	4	76					**-1.2/-3.2** (46)	-3.5/1.0; -5.4/-0.9	12	67
-1.7/-1.1 (46)	-5.5/2.0; -3.1/0.9	4	67								
Combined exercise **-5.3/-5.6** (54)*	NA	11	94	**Combined exercise** **-2.9/-3.6** (54)*	NA	61	94	**Combined exercise** **-0.9/-1.5** (54)*	NA	3	94

Exercise priority depending on initial blood pressure level for hypertension, high-normal blood pressure and normotension.

*CI= confidence interval; No= number of studies included in the corresponding meta-analysis; AS= $AMSTAR_{EXBP}$ score of the corresponding meta-analysis; AT= aerobic training; IRT= isometric resistance training; DRT= dynamic resistance training; NA= not available; *number of intervention groups*

Supplement Text S1

Search Strategy

The systematic review is an updated version of the search performed by Johnson et al. in 2013 (1). Multiple databases were searched (PubMed (https://www.ncbi.nlm.nih.gov/pubmed), Scopus (https://www.scopus.com), Web of Science (http://apps.webofknowledge.com), Cochrane Library (https://onlinelibrary.wiley.com/). Table 1 contains the search terms for the Pubmed search. The search string was adapted for the other databases. Databases were searched from June 2013 until June 2019 (see Table 2). Meta-analysis from the year 2000 until 2013 were retrieved from Johnson et al. After removal of duplicates HH and AD searched titles, abstracts and full texts for eligible meta-analysis (Figure 1). Disagreements were resolved through discussion.

Inclusion criteria

Since implementation of standards for the conduction of systematic reviews and meta-analysis (such as PRSIMA (2)), significant quality progression is evident (1). We therefore included meta-analysis performed from the year 2000 or after. Further inclusion criteria were:

(1) Systematic-reviews and meta-analysis on exercise-based intervention studies.
(2) Exercise qualified as either endurance, resistance or combined training regimen.
(3) Human adults (older than 18 years) with and without cardiovascular risk factors.
(4) Blood pressure change as primary outcome.

Exclusion criteria were:

(1) Analysis of cohorts with specific diseases (e.g. type 2 diabetes only, chronic kidney disease)
(2) Only children or adolescents were included
(3) Analysis of interventions with little or unclear cardiovascular effect such as Tai-Chi or Yoga solely
(4) Interventions on acute effects of exercise bouts
(5) Primary endpoint was morbidity or mortality reduction

For the eligible meta-analysis characteristics were extracted (Supplement Tables 3-5). This contained the year of publication, the topic of the analysis, sample size, number and types of trials included, sex distribution, frequency, intensity, time and type of the performed exercise (FITT concept). BP change due to the intervention. Mean or median values were extracted from the meta-analysis. If not reported by the authors, a range of the values from the included studies was estimated. If sample size and female percentage were reported, we calculated the corresponding male percentage.

Study quality

The Assessment of Multiple Systematic Reviews (AMSTAR) is a standard quality assessment tool for systematic reviews and meta-analysis (3,4). We used an augmented version of the AMSTAR tool that was adopted to focus on the effect of exercise on BP ($AMSTAR_{EXBP}$) (1). Supplement five shows an overview of the included study quality. $AMSTAR_{EXBP}$ refers to the number of items fully satisfied of the numbers of items applicable for the respective study. Meta-analysis already coded were adopted from Johnson et al. (1). For recent studies the $AMSTAR_{EXBP}$ scale was calculated.

Table 1: Search strategy

(((("mean arterial" OR "blood pressure"[mesh] OR "blood pressure" OR "blood pressures" OR "arterial pressure" OR "arterial pressures" OR hypertension OR hypotension OR normotension OR hypertensive OR hypotensive OR normotensive OR "systolic pressure" OR "diastolic pressure" OR "pulse pressure" OR "venous pressure" OR "pressure monitor" OR hypotension OR "pre hypertension" OR "bp response" OR "bp decrease" OR "bp reduction" OR "bp monitor" OR "bp monitors" OR "bp measurement") AND ("exercise"[mesh] OR exercise OR exercises OR running OR bicycl* OR treadmill* OR "weight lifting" OR "weight training" OR "resistance training" OR "strength training" OR "endurance training" OR "speed training" OR "training duration" OR "training frequency" OR "training intensity" OR "aerobic endurance") AND ("Meta-Analysis" [Publication Type] OR meta-analysis[ti] OR metaanalysis[ti] OR systematic[sb] OR "systematic review"[ti]) NOT ("DASH"[tiab] OR cancer OR neoplasms OR fibromyalgia OR alzheimers OR alzheimer OR pregnant OR pregnancy OR "obesity/drug therapy"[mesh] OR "diet therapy"[mesh] OR "diet therapy"[subheading] OR caffeine OR "eating change" OR "activities of daily living" OR "dehydration" OR "dehydrate" OR "dehydrated" OR "dietary salt" OR sodium OR epilepsy OR influenza OR flu OR pneumonia OR septicemia OR arthritis OR hiv OR "Acquired Immunodeficiency Syndrome" OR meningitis OR "substance abuse" OR alcoholism OR "drug abuse" OR "epidemiology"[Subheading]))) AND ("2013/06/15"[Date - Publication] : "3000"[Date - Publication])) AND Humans[Filter]

Table 2: Results of database searches

Database	**Coverage**	**Date of search**	**Hits**
Pubmed	15/06/2013 - 03/06/2019	03/06/2019	257
Scopus	2013 - 03/06/2019	03/06/2019	166
Web of Science	2013 - 03/06/2019	03/06/2019	392
Cochrane Library	Oldest - 03/06/2019	03/06/2019	47
Sum			**862**

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2. Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7):e1000097.

3. Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol [Internet]. 2007 Dec [cited 2018 Mar 17];7(1). Available from: http://bmcmedresmethodol.biomedcentral.com/articles/10.1186/1471-2288-7-10

4. Shea BJ, Hamel C, Wells GA, Bouter LM, Kristjansson E, Grimshaw J, et al. AMSTAR is a reliable and valid measurement tool to assess the methodological quality of systematic reviews. J Clin Epidemiol. 2009 Oct;62(10):1013–20.

Supplement Table S2: Quality of included meta-analysis according to AMSTAR$_{EXBP}$ scoring

		Item																		Items completely satisfied	Items completely satisfied	Items partly satisfied	Items applicable
Author	Year	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18				
Zhang et al. (60)	2018	2	2	2	2	0	0	2	2	1	2	0	99	2	2	0	0	2	2	65%	11	1	17
Oja et al. (59)	2018	2	2	2	2	2	0	2	2	2	2	2	0	2	2	0	2	2	2	83%	15	0	18
Igarashi et al (38)	2018	2	2	2	2	0	0	2	2	2	2	0	99	2	2	0	1	2	2	71%	12	1	17
Herrod et al. (61)	2018	2	1	2	2	1	0	2	2	2	0	98	99	2	2	0	2	2	2	69%	11	2	16
De Sousa et al. (44)	2017	2	2	2	2	2	0	2	2	0	0	99	99	2	2	0	2	0	2	69%	11	0	16
Jin et al. (53)	2017	2	2	2	2	1	0	2	2	2	2	0	0	2	2	0	2	0	2	67%	12	1	18
Wen and Wang (62)	2017	2	2	2	2	2	0	2	2	0	0	0	99	2	2	0	0	2	0	59%	10	0	17
Batacan et al. (42)	2016	2	2	2	0	2	0	2	2	1	2	2	2	2	2	0	2	2	2	78%	14	1	18
Conceição et al. (32)	2016	2	1	2	2	1	0	2	1	0	2	1	98	2	0	0	2	0	2	47%	8	4	17
Corso et al. (54)	2016	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	94%	17	0	18
Inder et al. (49)	2016	2	2	2	2	2	0	2	2	2	2	2	0	2	2	0	2	2	2	83%	15	0	18
MacDonald et al. (45)	2016	2	2	2	2	2	0	2	2	2	2	2	2	2	2	0	2	2	2	89%	16	0	18
Goessler et al. (55)	2015	2	2	2	0	2	0	2	2	1	2	2	0	2	2	0	0	2	2	67%	12	1	18
Hanson et al. (63)	2015	2	2	1	2	2	2	2	2	1	0	99	99	2	2	0	2	2	2	75%	12	2	16
Murtagh et al. (64)	2015	2	2	2	2	2	0	2	2	2	2	2	0	2	2	0	2	2	2	83%	15	0	18
Baena et al. (39)	2014	2	2	2	2	2	0	2	2	0	2	2	98	2	2	0	2	1	2	76%	13	1	17
Carlson et al. (50)	2014	2	0	2	2	2	0	2	2	1	2	2	2	2	2	0	2	2	2	78%	14	1	18
Cornelissen et al. (65)*	2013	2	2	2	2	2	0	2	2	2	2	0	99	2	2	0	0	2	2	76%	13	0	17
Cornelissen and Smart (33)*	2013	2	2	2	2	2	0	2	2	0	2	0	99	2	2	0	2	2	2	76%	13	0	17
Huang et al. (40)	2013	2	2	1	2	0	0	0	0	0	1	0	0	2	2	0	2	2	2	44%	8	2	18
Cornelissen et al. (46)*	2011	2	2	2	2	0	0	0	2	2	2	2	0	2	2	0	0	2	2	67%	12	0	18
Thorogood et al. (66)*	2011	2	2	2	2	2	2	2	2	2	2	0	0	0	1	0	0	0	2	61%	11	1	18
Kelley and Kelley (51)*	2010	2	0	2	2	2	2	2	2	2	2	0	0	2	2	0	2	2	2	78%	14	0	18
Owen et al. (52)*	2010	2	0	2	0	2	0	2	2	2	0	99	99	2	0	0	0	2	2	56%	9	0	16
Murphy et al. (67)*	2007	2	2	98	2	0	2	0	2	2	2	0	0	2	2	0	2	2	0	65%	11	0	17
Dickinson et al. (68)*	2006	2	2	2	2	0	0	2	2	0	1	2	2	2	2	0	2	2	2	72%	13	1	18
Cornelissen and Fagard (47)*	2005	2	2	0	0	2	0	0	2	2	1	0	99	2	2	0	2	2	2	59%	10	1	17
Cornelissen and Fagard (34)*	2005	2	2	2	0	0	0	0	0	0	0	0	99	1	1	0	2	2	2	35%	6	2	17
Whelton et al. (35)*	2002	2	0	2	2	0	2	2	2	2	1	2	99	2	2	0	0	2	2	71%	12	1	17
Fagard (36)*	2001	2	0	0	0	0	0	0	0	2	1	0	99	0	2	0	2	0	0	24%	4	1	17
Kelley and Kelley (41)*	2001	2	2	2	2	0	0	0	0	2	2	0	98	1	2	0	0	2	2	53%	9	1	17
Kelly et al. (69)*	2001	2	2	2	2	0	2	2	0	0	2	2	0	2	2	0	2	2	0	67%	12	0	18
Kelly et al. (37)*	2001	2	2	2	2	0	2	2	0	0	2	0	2	2	2	0	0	2	2	67%	12	0	18
Kelley and Kelly (48)*	2000	2	2	2	2	0	2	0	0	0	2	0	0	2	2	0	2	2	2	61%	11	0	18

For each item, scores could be: 2=completely satisfied; 1=Partially satisfied; 0=Not satisfied; 98=Unknown; 99=Not applicable (not relevant).
*adopted from Johnson et al. (28)

Supplement Table S3: Characteristics of meta-analysis on effects of aerobic exercise on blood pressure

Authors	Year	Objective	Trials	Sample size	Sex (% males)	Age# [years]	Duration of intervention#	FITT#	BP change	$AMSTAR_{EXBP}$
Zhang et al. (60)*	2018	"to systematically assess effects of aerobic exercise at different durations on the cardiovascular health of untrained women"	7 RCTs	150	0	45-64	8-52 weeks	F: 2.3x/week I: - T: 60min T: football, walking, cycling, aerobic exercise	≤ 3month: SBP +2.71 mmHg (ns) 4-6 months: SBP +6.5 mmHg	65%
Herrod et al (61)**	2018	"all randomized controlled trials involving participants with a mean age of 65 or over investigating nonpharmacological strategies to reduce blood pressure"	24 RCTs	1709	-	65-85	6-52 weeks	F: 1-6x/week I: 40-90% HFmax T: 25-60min T: walking, jogging, cycling, swimming, stair climbing, trampolining	SBP -5.1 mmHg DBP -2.2 mmHg	69%
Oja et al. (59)**	2018	"to assess the changes in CVD risk factors and the dose-response-relationship between frequency, intensity, duration and volume of walking and cardivascualr risk factors"	35 RCTs	-	-	30-72	8-52 weeks	F: 1-15.4x/week I: - T: 10-325min/week T: walking	SBP -4.05 mmHg DBP -1.76 mmHg	83%
Igarashi et al. (38)	2018	"to evaluate the effects of regular aerobic exercise on blood pressure in East Asians."	26 RCTs	1994	37%	60	8-48 weeks	F: 2-6x/week I: 65-81% HFmax T: 30-60min T: walking, bicycle ergometer	SBP -4.7 mmHg DBP -3.2 mmHg	71%
Wen and Wang (62)	2017	"to explore the reductive effect of aerobic exercise on blood pressure of hypertensive patients"	13 intervention studies	802	-	21-83	4 weeks-6 months	-	SBP -0.79 (SMD) DBP -0.63 (SMD)	59%
Batacan et al. (42)**	2017	"to clarify the cardiometabolic health effects of HIIT in adults"	25 RCTs, non-RCTS and clinical trials (65 total)	1047	-	18-78	short-term: 2-10 weeks long-term: 12-24 weeks	F: 3x/week I: >85% VO_2max T: 30min to 4x4min T: *HIIT:* treadmill running, swimming and cycling	normal weight: *short-term (n=5):* ns *long-term (n=2):* SBP ns/DBP -4.7 overweight/obese: *short-term(n=6):* ns *long-term (n=11):* SBP -4.6/ DBP -2.9	78%
Conceição et al. (32)	2016	"to investigate the effects of dance therapy in hypertensive patients"	4 RCTs	216	-	44-55	4-12 weeks	F: 3x/week I: - T: 45-60min T: dancing	SBP -12.0 mmHg DBP -3.4 mmHg	47%

Hanson et al. (63)**	2015	"to assess the health benefits of outdoor walking groups"	14 intervention studies	440	-	20-82	6 weeks - 6 months	F: - I: - T: - T: walking	SBP -3.7 mmHg DBP -3.1 mmHg	75%
Murthagh et al. (64)**	2015	"to examine the effect of walking on risk factors for cardiovascular disease"	17 RCTs	816	-	20-84	8-24 weeks	F: 2-7x/week I: - T: 20-60min T: walking	SBP -3.6 mmHg DBP -1.5 mmHg	83%
Baena et al. (39)*	2014	"to summarize and quantify the available evidence on the effects of lifestyle-related interventions conducted in low-to-middle-income countries"	4 RCTs and clinical trials	-	-	49-70	2-12-months	F: - I: - T: - T: resistance, aerobicy, hydro gym, Tai Chi, Yoga	SBP -8.5 mmHg DBP -2.3 mmHg	76%
Cornelissen and Smart (33)*	2013	"[to examine] the effects of endurance […] training on resting BP in adults"	70 RCTs	3994	-	18-83	4-52 weeks	F: 1-7x/week I: 35-90 HFmax, 40-85% VO_2max T: 28-60min T: e.g. running, swimming, cycling, skiing, soccer	SBP -3.5 mmHg DBP -2.5 mmHg	76%
Cornelissen et al. (65)	2013	"to determine the effect of aerobic endurance training on daytime and night-time BP in healthy adults"	15 RCTs	633	-	47	15 weeks	F: 3x/week I: 50-85% Hfmax, 50-90% VO_2max T: 30-60min T: walking, jogging, swimming, cycling	Daytime BP: SBP -3.2 mmHg DBP -2.7 mmHg *(no effects on nighttime BP)*	76%
Huang et al. (40)	2013	"to determine effects of aerobic exercise training on resting systolic (SBP) and diastolic blood pressure (DBP) among previously sedentary older adults"	23 RCTs and non-RCTs	1226	-	68	8-42 weeks	F: 3x/week I: 50-90% HFmax T: 19-60min T: walking, jogging, running, cycling, stair-climbing, aerobic dance, outdoor aerobic performance, aerobic games	SBP -5.39 mmHg DBP -3.68 mmHg	44%
Thorogood et al. (66)	2011	"the efficacy of isolated aerobic exercise at promoting weight loss"	6 RCTs (2 studies 6-month intervention)	1083	57%	39-76	3-12 months	F: 2-7x/week I: 60-85% HFmax T: 135-225 min/week T: walking, cycling, jogging, cycle ergometry, mini-trampoline, rowing, treadmill	6-month intervention: SBP -2.9 mmHg DBP -1.8 mmHg	61%

Murphy et al. (67)	2007	"quantify the magnitude and direction of walking-induced changes that may alter selected cardiovascular risk factors"	24 RCTs (9 with BP measurement)	1128	17%	52	35 weeks	F: 4x/week I: 70% HFmax T: 38min T: walking	SBP ns DBP -1.5 mmHg	65%
Cornelissen and Fagard (35)	2005	"to perform a comprehensive meta-analysis including resting and ambulatory blood pressure"	72 RCTs and crossover studies	3936	-	47	16 weeks	F: 3x/week I: 65% HFmax T: 40 min T: walking, jogging, running, cycling	SBP -3.0 mmHg DBP -2.4 mmHg	35%
Whelton et al. (35)	2002	"to determine the effect of aerobic exercise on blood pressure"	54 RCTs and crossover studies	2419	-	21-79	12 weeks	F: 3-7x/week I: 60-95% HFmax, 40-82% VO_2max T: 20-60min T: biking, walking, jogging	SBP -3.8 mmHg DBP -2.6 mmHg	71%
Fagard (36)	2001	"to assess the influence of the characteristics of the exercise program (...) on the blood pressure response to dynamic physical training in otherwise healthy"	44 RCTs	1529	65%	44	16 weeks	F: 1-7x/week I: 65% of exercise performance T: 30-60 min T: walking, jogging, running, cycling, swimming	SBP -3.4 mmHg DBP -2.4 mmHg	24%
Kelley and Kelley (41)	2001	"to examine the effects of aerobic exercise for reducing resting SBP and DBP in older adults"	7 RCTs	802	-	68	35 weeks	F: 3x/week I: 63% VO_2max T: 40 min T: aerobic exercise	SBP -2 mmHg DBP ns	53%
Kelley et al. (69)	2001	"to examine the effects of aerobic exercise on resting systolic and diastolic blood pressure in adults"	47 RCTs	2543	51-56%	47-49	23 weeks	F: 3x/week I: 67% VO_2max T: 40 min T: walking, jogging, cycling, aerobic dance, swimming	SBP -2 mmHg DBP -2 mmHg	67%
Kelley et al. (37)	2001	"to examine the effects of walking on resting systolic and diastolic blood pressure in adults"	16 RCTs and non-RCTs	650	-	58	25 weeks	F: 4x/week I: 63% VO_2max T: 42 min T: walking	SBP -3 mmHg DBP -2 mmHg	67%

$AMSTAR_{EXBP}$ reflects the percentage of items fully satisfied.

* Analysis included the effects of various lifestyle interventions or training regimens. If provided by the authors data for physical activity or the specific training regimen are presented.

** BP was one of several outcomes. If provided data are presented for BP results only. *If not provided data are shown in italic letters.*

***Refers to all trials included in the meta-analysis

[#]If median or mean were not reported, range was estimated from included studies.

Abbreviations: FITT, frequency, intensity, time, type of exercise; bp, blood pressure, sbp, systolic blood pressure; dbp, diastolic blood pressure; HIIT, high-intensity-interval-training; ns, not significant; RCT, randomized controlled study; SMD standard mean difference; HFmax, maximum heart rate; VO_2max, maximal oxygen consumption; min, minutes; n, number of trials.

Supplement Table S4: Characteristics of meta-analysis on effects of resistance training on blood pressure

Authors	Year	Objective	Trials	Sample size	Sex (% males)	Age[#] [years]	Duration of intervention[#]	FITT[#]	BP change	$AMSTAR_{EXBP}$
Herrod et al. (61)*	2018	"all randomized controlled trials involving participants with a mean age of 65 or over investigating nonpharmacological strategies to reduce blood pressure"	2 RCTs	66	-	65-85	8-10 weeks	F: 3x/week I: 30-40% of MVC T: 4 x 2min T: isometric handgrip training	SBP -9.1 mmHg DBP -3.0 mmHg	69%
Herrod et al. (61)*	2018	"all randomized controlled trials involving participants with a mean age of 65 or over investigating nonpharmacological strategies to reduce blood pressure"	12 RCTs	514	-	65-85	12-52 weeks	F: 3x/week I: 50-90% of 1 RM T: 1-3 sets per session, 6-13 repititions, up to 40 mins T: resistance training	SBP -5.5 mmHg DBP -2.0 mmHg	69%
Jin et al. (53)	2017	"examine the effect of IH G training on resting BP in participants with different initial BP status"	7 RCTs	157	-	20-70	8-10 weeks	F: 3-5x/week I: 30-40% MVC T: 4 x 2min T: isometric handgrip training	SBP -8.3 mmHg DBP: -3.9 mmHg	67%
De Sousa et al. (44)	2017	"to evaluate the effects of resistance training alone on the systolic and diastolic blood pressure in prehypertensive and hypertensive individuals"	5 RCTs	201	-	18-88	12 weeks	F: 3x/week I: 40-80% of 1 RM T: 8-25 sets per session, 14-30 repetitions T: *DRT:* Progressive RT, Theraband	SBP -8.2 mmHg DBP -4.1 mmHg	69%
Inder et al. (49)	2016	"to examine the effects of IRT on resting blood pressure in adults"	11 RCTs	302	-	18-80	3-10 weeks	F: 3-5x/week I: 14-40% MVC T: 4x2min, 1-4min rest T: *IRT:* handgrip and leg exercise	SBP -5.2 mmHg DBP -3.9 mmHg	83%
MacDonald et al. (45)	2016	"to provide (…) estimates regarding the efficacy of dynamic RT as stand-alone antihypertensive therapy"	64 RCTs and non-RCTs	2374	52-54%	47	14 weeks	F: 3x/week I: 65% of 1 RM T: 8 exercises, 3 sets, 11 reps T: *DRT*	SBP -3 mmHg DBP -2.1 mmHg	89%
Baena et al. (39)*	2014	"to summarize and quantify the available evidence on the effects of lifestyle-related interventions conducted in low-to-middle-income countries"	3 RCTs and clinical trials	-	-	49-70	2-12-months	-	SBP -13.0 mmHg DBP -9.8 mmHg	76%
Carlson et al. (50)	2014	"to quantify the effects of isometric resistance training on the change in BP"	9 RCTs and crossover studies	223	-	18-80	4-10 weeks	F: 3-5x/week I: 30-40% MVC, 75-95% HFmax T: 4x2 minutes, 1-4 minutes rest T: *IRT:* handgrip and leg exercise	SBP -6.8 mmHg DBP -4.0 mmHg	78%

Cornelissen and Smart (33)*	2013	"[to examine] the effects of [..] dynamic resistance […] training on resting BP in adults"	25 RCTs	754	-	18-83	6-52 weeks	F: 1-7x/week I: 30-85% of 1 RM T: various T: *DRT*	SBP -1.8 mmHg DBP -3.2 mmHg	76%
Cornelissen and Smart (33)*	2013	"[to examine] the effects of […] isometric resistance training on resting BP in adults"	4 RCTs	114	-	18-83	8-10 weeks	F: 3x/week I: 10-40% MVC T: 4x2min, 1-3min rest T: *IRT:* handgrip and leg exercise	SBP -10,9 mmHg DBP -6,2 mmHg	76%
Cornelissen et al. (46)	2011	"[to review] the effect of resistance training on blood pressure […] in adults"	28 RCTs	1124	65%	54	DRT: 16 weeks IRT: 8 weeks	F: 3x/week I: *DRT:* 76% of 1 RM, *IRT* : 30% of 1 RM T: *DRT:* 8 exercises, 3 sets, 6-30 repetitions, *IRT:* 4x2min T: *DRT:* Circuit training, *IRT:* handgrip exercise	DRT: SBP -2.6 mmHg DBP -3.1 mmHg IRT: SBP -11.8 mmHg DBP -5.8 mmHg	67%
Kelley and Kelley (51)	2010	"to examine the efficacy of isometric handgrip exercise for reducing resting SBP and DBP in adult humans"	3 RCTs	81	-	20-69	8-10 weeks	F: 3x/week I: 30-40% MVC T: 4x2min contractions, 1 minute rest T: *IRT:* handgrip exercise	SBP -13.4 mmHg DBP -7.8 mmHg	78%
Owen et al. (52)	2010	"[to examine] the effect of isometric exercise on resting blood pressure"	5 RCTS and non-RCTs	122	-	21-80	5-10 weeks	F: 3x/week I: 20-40% MVC T: 4x2 contractions, 1-3min rest T: *IRT:* handgrip and lower body exercise	SBP -10.4 mmHg DBP -6.7 mmHg	56%
Cornelissen and Fagard (34)	2005	"to assess the influence of resistance training on resting blood pressure in healthy sedentary adults"	9 RCTs	341	61%	69	16.4 weeks	F: 3x/week I: 61% of 1 RM T: 9.9 exercises, 1.8 sets, 1-25 repetitions T: *DRT:* exercise of arms, legs and trunk	SBP -3.2 mmHg DBP -3.9 mmHg	59%
Kelley and Kelley (41)	2000	"to examine the effects of progressive resistance exercise on resting systolic and diastolic blood pressure in adult humans"	11 RCTs	320	-	47	14 weeks	F: 3x/week I: 35% of 1 RM T: 10 exercises, 2 sets, 4-50 reps T: *DRT:* circuit training	SBP -3 mmHg DBP -3 mmHg	61%

$AMSTAR_{EXBP}$ reflects the percentage of items fully satisfied.

* Analysis included the effects of various lifestyle interventions or training regimens. If provided by the authors data for physical activity or the specific training regimen are presented.

** BP was one of several outcomes. If provided data are presented for BP results only.

If median or mean were not reported, range was estimated from included studies.

Abbreviations: FITT, frequency, intensity, time, type of exercise; bp, blood pressure, sbp, systolic blood pressure; dbp, diastolic blood pressure; ns, not significant; RCT, randomized controlled study; DRT, dynamic resistance training; IRT, isometrich resistance training; RM, repetition maximum; RT, resistance training; min, minutes; MVC, maximal voluntary contraction.

Supplement Table S5: Characteristics of meta-analysis based on effects of aerobic exercise and resistance training on blood pressure

Authors	Year	Objective	Trials	Sample size	Sex (% males)	Age# [years]	Duration of intervention#	FITT#	BP change	$AMSTAR_{EXBP}$
Herrod et al. (61)*	2018	"all randomized controlled trials involving participants with a mean age of 65 or over investigating nonpharmacological strategies to reduce blood pressure"	12 RCTs	1237	-	65-85	8-52 weeks	F: 2-6x/week I: ET: 50-90% HFmax; RT: 50-90% of 1RM T: ET: 30-60min; RT: 7-9 exercises, 2-3 sets, 8-15 repetitions T: cycling, walking; RT: (body weight) resistance training, circuit training	SBP -5.9 mmHg DBP -3.5 mmHg	69%
Corso et al. (54)	2016	"[to investigate the] influence of (...) concurrent exercise training, on resting BP"	68 RCTs and non-RCTs	4110	46%	55	20 weeks	F: 3x/week I: *ET:* 69% HFmax; *RT:* 64% of 1RM T: *ET:* 35min; *RT:* 8 exercises, 3 sets, 12 repetitions T: endurance and resistance training, circuit training	SBP -3.2 mmHg DBP -2.5 mmHg	94%
Goessler et al. (55)	2015	"to evaluate the effect of exercise training on parameters of the renin–angiotensin–aldosterone system in healthy adults, and to investigate the relation with training induced changes in blood pressure"	11 RCTs	375	37%	22-68	12 weeks	F: 3x/week I: *ET:* 50-65% VO_2max, 53-85% HFmax; *RT:* 70-75% of 1 RM T: *ET:* 30-60 min; *RT:* 12 repetitions, 1 set T: cycling, walking, jogging, resistance training	SBP -5.7 mmHg DPB -3.6 mmHg	67%
Baena et al. (39)*	2014	"to summarize and quantify the available evidence on the effects of lifestyle-related interventions conducted in low-to-middle-income countries"	7 RCTs and clinical trials	-	-	49-70	2-12-months	-	SBP -12.9 mmHg DBP -8.0 mmHg	76%
Cornelissen and Smart (33)*	2013	"[to examine] the effects of […] combined endurance and resistance training […] on resting BP in adults"	11 RCTs	252	-	18-83	4-52 weeks	F: 3x/week I: - T: - T: -	SBP ns DBP -2.2 mmHg	76%
Dickinson et al. (68)**	2006	"to quantify effectiveness of lifestyle interventions for hypertension"	21 RCTs	1518	57%	52	12 weeks	F: 3-5x/week I: - T: 30-60min T: walking jogging cycling, strength training	SBP -6.1 mmHg DBP -3.0 mmHg	72%

$AMSTAR_{EXBP}$ reflects the percentage of items fully satisfied.

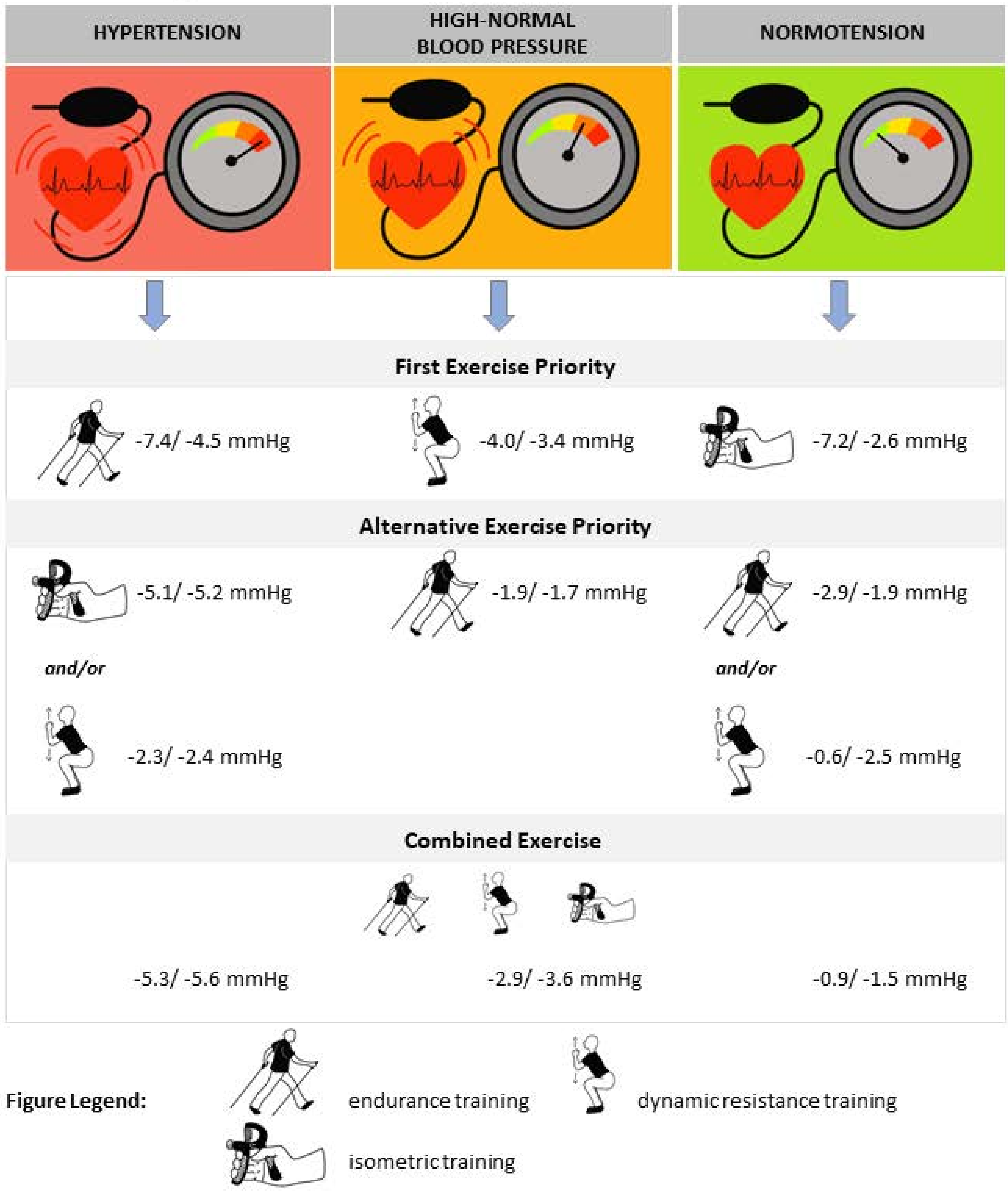
* Analysis included the effects of various lifestyle interventions or training regimens. If provided by the authors data for physical activity or the specific training regimen are presented.

** BP was one of several outcomes. If provided data are presented for BP results only. Sample size for the subpopulation not defined.

#If median or mean were not reported, range was estimated from included studies.

Abbreviations: FITT, frequency, intensity, time, type of exercise; nmr, no median or mean reported; bp, blood pressure, sbp, systolic blood pressure; dbp, diastolic blood pressure; ns, not significant; RCT, randomized controlled study; RM, repetition maximum; HFmax, maximum heart rate; VO_2max, maximal oxygen consumption; ET, endurance training; RT, resistance training; min, minutes

Conclusion Figure



Blood pressure levels represent mean range of expected systolic and diastolic blood pressure lowering effects of exercise modalities.