

NZHTA EVIDENCE TABLES

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In adults without clinical cardiovascular disease what is the dose, intensity and type of physical activity required to produce an effect on the risk factors of blood pressure, lipid profiles and weight?

*A critical appraisal of the literature presented in Evidence Tables*

Peter Day

New Zealand  
Health Technology Assessment

Department of Public Health and General Practice  
Christchurch School of Medicine  
Christchurch, NZ.

Division of Health Sciences, University of Otago

NEW ZEALAND HEALTH TECHNOLOGY ASSESSMENT (NZHTA)  
THE CLEARING HOUSE FOR HEALTH OUTCOMES AND  
HEALTH TECHNOLOGY ASSESSMENT

Department of Public Health and General Practice  
Christchurch School of Medicine, Christchurch, New Zealand

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## CONTACT DETAILS

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New Zealand Health Technology Assessment (NZHTA)  
The Clearing House for Health Outcomes and Health Technology Assessment  
Department of Public Health & General Practice  
Christchurch School of Medicine  
PO Box 4345  
Christchurch  
New Zealand  
Tel: +64 3 364 1152                      Fax: +64 3 364 1152

Email: [nzhta@chmeds.ac.nz](mailto:nzhta@chmeds.ac.nz)

Web Site: <http://nzhta.chmeds.ac.nz/>

## LIST OF ABBREVIATIONS AND ACRONYMS

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BIA	–	Bio-electrical impedance analysis
BP	–	Blood pressure
BMI	–	Body Mass Index
CI (95%)	–	Confidence Interval
CCT	–	Controlled Clinical trial
CVD	–	Cardiovascular Disease
DARE	–	Database of Abstracts of Reviews of Effects
DBP	–	Diastolic Blood Pressure
FE	–	Fixed Effects Model
HDL-C	–	High-density Lipoprotein Cholesterol
HDL <sub>2</sub> -C	–	High-density Lipoprotein Cholesterol sub-fraction
HDL <sub>3</sub> -C	–	High-density Lipoprotein Cholesterol sub-fraction
HR <sub>max</sub>	–	Maximal heart rate
HR <sub>res</sub>	–	Heart rate reserve
LDL-C	–	Low-density Lipoprotein Cholesterol
LTPA	–	Leisure Time Physical Activity
METs	–	Metabolic equivalents
MOH	–	Ministry of Health (NZ)
NZGG	–	New Zealand Guidelines Group
NZHTA	–	New Zealand Health Technology Assessment
RCT	–	Randomised Controlled Trial
RE	–	Random Effects Model
SBP	–	Systolic Blood Pressure
SCI	–	Science Citation Index
TC	–	Total Cholesterol
TG	–	Triglycerides
VO <sub>2max</sub>	–	Maximal volume of oxygen uptake

## GLOSSARY

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**Blinded study** - A study in which observers and/or subjects are kept ignorant of the group to which they are assigned. When both observers and subjects are kept ignorant, the study is referred to as double blind.

**Confidence interval** - The computed interval with a given probability, e.g. 95%, that the true value of a variable such as a mean, proportion, or rate is contained within the interval. The 95% CI is the range of values in which it is 95% certain that the true value lies for the whole population.

**Confounder** - A third variable that indirectly distorts the relationship between two other variables, because it is independently associated with each of the variables.

**Confounding** - A situation in which the measure of the effect of an exposure on risk is distorted because of the association of exposure with other factor(s) that influence the outcome under study.

**Fixed Effects model** – Used to combine study results in meta-analyses where summary statistics are averaged, studies are weighted according to a measure of the quantity of information they contain to produce a common effect.

**Grey literature** - That which is produced by all levels of government, academics, business and industry, in print and electronic formats, but which is not controlled by commercial publishers.

**Meta-analysis** - The process of using statistical methods to combine the results of different studies. The systematic and organised evaluation of a problem, using information from a number of independent studies of the problem.

**Random Effects model** - Used to combine study results in meta-analyses where summary statistics are combined inclusive of an estimate of between-study variation to estimate a total effect.

**Randomised controlled trial** - An epidemiologic experiment in which subjects in a population are randomly allocated into groups to receive or not receive an experimental preventive or therapeutic procedure, manoeuvre, or intervention. Randomised controlled trials are generally regarded as the most scientifically rigorous method of hypothesis testing available in epidemiology.

**Risk factor** - An exposure or aspect of personal behaviour or lifestyle, which on the basis of epidemiologic evidence is associated with a health-related condition.

**Selection bias** - Error due to systematic differences in characteristics between those who are selected for inclusion in a study and those who are not (or between those compared within a study and those who are not).

**Systematic review** - Literature review reporting a systematic method to search for, identify and appraise a number of independent studies.

# Methodology

## BACKGROUND

The Ministry of Health is funding a collaborative venture between the New Zealand Guidelines Group, the Stroke Foundation of New Zealand and the National Heart Foundation to develop an integrated set of best practice, evidence-based guidelines for cardiovascular disease. To inform this work, the New Zealand Health Technology Assessment (NZHTA) research unit has prepared Evidence Tables reporting on the critical appraisals of research studies relevant to specific aspects of the Guideline.

This topic provides the evidence base for the Guideline on the health effects of physical activity on commonly associated cardiovascular disease (CVD) risk factors in those without clinical cardiovascular disease. These results, as well as details on the study design, sample, measures, limitations and study quality are described and presented in the form of an Evidence Table.

Following the US Surgeon General's 1996 report on physical activity and health, the National Health Committee (NHC) undertook work based on this landmark document to report on the health benefits of physical activity and the means for best achieving these in a New Zealand context (1998). One of the key findings of the report was that "significant health benefits can be obtained from 30 minutes of moderate physical activity on all or most days". The report also cited numerous research, mainly from longitudinal cohort studies, showing the benefits to health from physical activity, where an inverse dose-response relationship exists between the level of physical activity and the risk of dying from coronary heart disease, the incidence of major coronary events, developing diabetes, developing high blood pressure, weight, and improvement in lipid profiles.

The evidence referenced from the NHC report, which relied upon the earlier US Surgeon General's report, indicated that health benefits are directly related to the amount of physical activity, defined as the combination of frequency, intensity, duration and type. The exact quantitative dose-response between the physical activity required (kilocalories required) and health benefits is not fully known as many early studies were not designed to demonstrate a dose-response gradient between the two. The NHC report did identify several studies where estimates of average caloric expenditure by activity categories enabled quantification of the amount of physical activity associated with improved health outcomes. The intensity of physical activity is usually described as light/low, moderate/mild, hard/vigorous, or very hard/strenuous. Moderate physical activity associated with health benefits was defined as 150 kilocalories of energy expended per day or 1,000 per week. Shorter durations of more vigorous activity were also associated with health benefits. The NHC report also identified evidence that showed health benefits from the accumulation of intermittent episodes of physical activity (three or more bouts of 10 minutes duration daily) that may have benefits over remaining sedentary.

The exact dose to achieve favourable outcomes that reduce cardiovascular disease and its risk factors was not clearly determined from the literature referenced in the NHS report. Gaps in the evidence were highlighted in the earlier 1996 US Surgeon General's report. It stated that future research was needed to adequately define the most important features of physical activity (total amount, intensity, duration, frequency, type, pattern) that confer specific health benefits, which in this context is cardiovascular disease risk reduction. Issues remain around the exact nature and trend of the dose-response and whether or not a bigger dose of physical activity is required for higher risk groups.

This review of the evidence that has become available since the publication of US Surgeon General's report on physical activity and health addresses the research question:

*"In adults without clinical cardiovascular disease what is the dose, intensity and type of physical activity required to produce an effect on the risk factors of blood pressure, lipid profiles and weight?"*

## SELECTION CRITERIA

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### *Study inclusion criteria*

#### Publication type

Studies published between 1996 and August, 2002 inclusive in the English language, including primary (original) research (published as full original reports) and secondary research (systematic reviews and meta-analyses) appearing in the published literature.

#### Study design

Peer reviewed studies were considered if they used one of the following study designs:

- systematic review or meta-analysis
- randomised controlled trials
- cohort studies (measuring harm/benefit).

Note: Any identified unpublished or 'grey' literature were included for New Zealand specific studies only where they meet the selection criteria.

#### Population

- study population are cardiovascular disease free adults (aged 25-75 years) from the general population but inclusive of people with risk factors (lipid profiles, BP, clotting profiles and weight).

#### Intervention

- studies are primary prevention interventions, measuring some or all of frequency, intensity, duration and type of physical activity and cardiovascular disease risk factor response
- studies where physical activity interventions are in Leisure Time Physical Activity (LTPA) settings, including organised team/individual sport, organised recreation or walking groups, gym classes and non-organised recreational sport, physical activity and walking for exercise or recreation, in occupational and active commuting settings and domestic settings.

#### Sample size

Studies with samples of at least 30 participants.

#### Outcomes

Outcomes considered included:

- blood pressure (systolic, diastolic)
- blood plasma lipid/lipoprotein profiles: High and Low-Density Lipoprotein (HDL, LDL), Triglycerides
- atherosclerosis
- obesity, BMI, distribution of fat, body weight.

### *Study exclusion criteria*

The following criteria were used to **exclude** studies from appraisal:

- outcomes reported for rehabilitation or treatment of a study population with clinical cardiovascular disease, diabetes
- outcomes reported from a study population including 50% or more outside the age range of 25-75 years
- outcomes reported from an atypical population group such as elite athletes, military, police, firefighter personnel, pregnant women, and the physically disabled

- outcomes reported from studies of physical activity interventions combined with dietary, smoking, alcohol, and pharmacological interventions for cardiovascular disease risk factor reduction
- studies evaluating physical activity health promotion campaigns, education programs, counseling, support group and individual advice programs – e.g., the platform/delivery mode of population-based physical activity interventions
- studies where the physical activity intervention is resistance exercise to increase muscle tone and strength, relaxation techniques, psychological therapies
- studies with fewer than 30 persons included in reported outcomes for RCTs and 100 for cohort studies
- citations that are narrative reviews, expert opinion, letters to the editor, comments, editorials, conference proceedings, abstract only, books and book chapters.

## SEARCH STRATEGY

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A systematic method of literature searching and selection was employed by an Information Specialist in the preparation of this review.

Searches were limited to English language material published from 1990 onwards. The searches were completed on 15 October, 2002.

### *Principal sources of information*

The following databases were searched (using the search strategy outlined in **Appendix 1**):

Bibliographic databases

Medline

Embase

Cinahl

Current Contents

Science/Social Science Citation Index

Cochrane Library Controlled Trials Register

Index New Zealand

Review databases

Evidence-based medicine reviews

Cochrane Database of Systematic Reviews

DARE

NHS Economic Evaluation Database

Health Technology Assessment Database

Other sources

National Guidelines Clearing House

Scottish Intercollegiate Guidelines Network

American College of Cardiology

National Heart, Lung, and Blood Institute

American Heart Association

### *Search terms used*

- index terms from Medline (MeSH terms): Physical Fitness, exercise, walking, yoga, running, jogging, swimming, exp Sports, exp Cardiovascular diseases, diabetes mellitus, diabetes mellitus – insulin-dependent, diabetes mellitus - non-insulin-dependent, Lipids, exp Lipoproteins, Blood Pressure, Glucose Intolerance, meta-analysis, randomized controlled trials, exp clinical trials, exp Cohort Studies
- index terms from Embase: fitness, walking, exp exercise, physical activity, cycling, jogging, running, stretching, swimming, exp cardiovascular disease, diabetes mellitus, insulin dependent

diabetes mellitus, non insulin dependent diabetes mellitus, lipid, Lipoprotein, lipid blood level, lipoprotein blood level, cholesterol blood level, Glucose Intolerance, blood pressure, clinical trial, randomized controlled trial, exp meta-analysis, cohort analysis

- the above index terms were used as keywords in databases where they were not available and in those databases without controlled vocabulary
- additional keywords (not standard index terms) were used in all databases: meta analy\*, metaanaly\*, systematic adj3 (review or overview), clinic\* adj3 trial\*, cohort adj (study or studies)
- Various subheadings were used in conjunction with some of the subject heading searches, these included: mo [mortality], pc [prevention and control], bl [blood], ph [physiology], ec [endogenous compound]. Some publication type searches were also used: meta analysis.pt, clinical trial.pt, randomized controlled trial.pt.

## STUDY SELECTION

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Studies were selected for appraisal using a two-stage process. Initially, the titles and abstracts (where available) identified from the search strategy were scanned and excluded as appropriate. The full text articles were retrieved for the remaining studies and these were appraised if they fulfilled the study selection criteria outlined above.

## APPRAISAL OF STUDIES

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Articles were formally appraised using the NZGG's GATE FRAME checklists for Systematic Reviews and Randomised Controlled Trials. There were four gradings applied, as follows:

1. quality of review design (minimising bias)
2. quality of results (understandable, precise, and/or sufficient power)
3. quality of study applicability: could applicability be determined?
4. quality of study applicability: are findings applicable in usual practice/settings?

Each Grade was coded as one of the following: Very well (+), Okay (Ø), Poorly (-) or as a combination of these.

## EVIDENCE TABLES

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Evidence tables for primary research studies present key information summaries described below:

- study source including authors, year published, and country of origin
- study design and setting, inclusion and exclusion criteria
- sample characteristics including sample size, sample characteristics including demographic variables, any comparisons between intervention groups on these variables at baseline, definitions
- methods (including search strategy for systematic reviews and meta-analyses)
- results including statistically tested comparisons and reporting relevant statistical data
- study quality gradings (applying GATE FRAME criteria as described above), specific study limitations and reviewer's conclusions.

## LIMITATIONS OF THE REVIEW

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This study used a structured approach to review the literature. However, there were some inherent limitations with this approach. Namely, systematic reviews are limited by the quality of the studies included in the review and the review's methodology.

This review has been limited by the restriction to English language studies. Restriction by language may result in study bias, but the direction of this bias cannot be determined. In addition, the review has been limited to the published academic literature, and has not appraised unpublished work.

Restriction to the published literature is likely to lead to bias since the unpublished literature tends to consist of studies not identifying a significant result.

Papers published pre-1997 were not considered as these predated the publication of the US Surgeon General's 1996 report.

The studies were initially selected by examining the abstracts of these articles. Therefore, it is possible that some studies were inappropriately excluded prior to examination of the full text article.

All studies included in this review were conducted outside New Zealand, and therefore, their generalisability to the New Zealand population and context may be limited and needs to be considered.

This review was confined to an examination of the effectiveness of the interventions and did not consider the acceptability, or any ethical, economic or legal considerations associated with these interventions. Interventions were not assessed in terms of their impact on general quality of life.

The included secondary research (meta-analyses and systematic reviews) contain a relatively high degree of overlap in included studies. Successive meta-analyses and systematic reviews include studies that were covered in earlier reviews. The degree of overlap is as follows: Halbert et al. 1997 has 28/29 studies included in other appraised meta-analyses or systematic reviews; Kelley and Kelly, 1999 has 9/19 studies; Oja, 2001, has 20/36 studies; Fagard, 2001, has 34/44 studies; and Whelton et al. 2002 has 26/38 studies included elsewhere.

The evidence tables describe in detail the specific limitations of each included study. In summary, the appraised secondary research studies were limited by the high degree of heterogeneity of the included studies, the overall poor quality of the included studies or no appraisal of included studies, inadequate descriptions of methodology and publication bias. The included primary research studies (RCTs) were limited by inadequate descriptions of randomisation, concealment and blinding, subject selection bias, inadequate study power, inadequate controlling for confounders on outcomes related to physical exercise and the short exercise programme duration of many of the included RCTs.

Overall the clinical importance of changes in CVD risk factors was questionable, as these were generally small at the individual level although the public health benefit would be arguably more significant.

Most studies considered only the benefits of physical activity as an intervention in CVD risk factor modification. Harms and injury related to physical activity were generally not reported, although most studies reported warm-up and warm-down regimens, and the progressive implementation to the desired exercise intensity for the intervention protocol.

There was a lack of studies specifically designed to address the dose-response relationship between physical activity (defined as the frequency, intensity, program duration, exercise session duration and type of exercise activity) and CVD risk factor reduction.

For a detailed description of interventions and evaluation methods, and results used in the studies appraised, the reader is referred to the original papers cited.

Data extraction, critical appraisal and report preparation was performed by a single reviewer.

This review was conducted over a limited timeframe (October, 2002 – December, 2002).



## Results

From the search strategy, we identified over 1,700 potentially relevant articles/abstracts of which 75 were eligible for retrieval. Of these, 64 were excluded for the following reasons: expert opinion/narrative review/guideline/background (n=13), small sample size (n=5), outside age range (n=1), subjects are rehabilitating from CVD or have existing CVD (n=3), no physical exercise intervention or multiple interventions (n=3), eligible outcomes not measured (n=11), subset of, or already included in, appraised MAs or SR's (n=8), before and after study (no control group) (n=4), cross-sectional design/descriptive (n=6), not directly relevant to the topic (n=5), published pre 1996 (n=3), methodological problems (n=1), published in non-English language (n=1). These excluded papers, annotated with the reason for exclusion, are listed in **Appendix 2**.

Eleven retrieved articles were appraised, comprising of five meta-analyses, one systematic review and five randomised controlled trials (listed in **Appendix 3**). **Table 1 (pages 8-17)** comprises of four meta-analyses and one systematic review on the effectiveness of physical activity in lowering blood pressure and **Table 2 (pages 18-20)** comprises of one meta-analysis on the effectiveness of physical activity in modifying blood lipids. **Table 3 (pages 21 and 22)** comprises of one RCT on the effectiveness of physical activity in lowering blood pressure and modifying lipids. **Table 4 (pages 23-26)** comprises of two RCTs on the effectiveness of physical activity in modifying blood lipids and **Table 5 (pages 27-30)** two RCTs which examine the effectiveness of physical activity on body-weight. Full details of these papers, including methods, key results, limitations and conclusions, are provided in the evidence tables below. Papers within each Table are presented in decreasing order of quality (based on four quality gradings given equal weighting), and papers of equal quality are presented in reverse chronological order (i.e., more recently published first).

**Table 1. Evidence table of meta-analyses and systematic reviews examining the effectiveness of physical exercise in lowering blood pressure**

Authors Country	Study design, setting, comparisons	Sample characteristics, inclusion and exclusion criteria	Methods	Results and authors conclusions	Quality gradings and limitations
Halbert et al. (1997)  Australia	<p>Meta-analysis of RCTs.</p> <p>Study parameters Twenty-nine trials were included. Five trials had cross-over designs, the others had parallel designs. Studies compared type, intensity, frequency of exercise to maximise decreases in systolic and diastolic BP.</p> <p>Most studies used combination exercise training programmes. Walking, jogging, running were in 13 trials, cycling (bike or ergometer) in 10 trials, cycling/running/jogging in three trials, and resistance training in two trials.</p>	<p>Participants Twenty-nine trials with 1,533 participants. Eleven trials had participants of both sexes, four had women only, 13 men only and one unspecified. Across the trials: mean number of participants: 53 per trial, range 7-300, age range 18-79 years.</p> <p>Study inclusion criteria</p> <ul style="list-style-type: none"> <li>▪ RCTs involving aerobic or resistance training programme of at least four weeks duration</li> <li>▪ trials with cross-over design where treatments randomised with no significant order effects</li> <li>▪ primary or secondary outcomes include systolic and diastolic BP</li> <li>▪ hypertensive or normotensive subjects</li> <li>▪ otherwise healthy sedentary adults.</li> </ul>	<p>Search strategy English only studies from 1980-1995 in Medline, Embase, SCl, previous reviews, references from included studies.</p> <p>Appraisal of study internal validity using Cochrane Collaboration handbook (1995).</p> <p>Assessment of the degree of selection bias using a graded scale of: (A) where high degree of effort to control selection bias, (B) some effort to control selection bias, and (C) where little or no effort to control selection bias.</p> <p>BP effects measured as difference between the mean change in BP (mm Hg) (baseline-final value) between the exercise and control groups.</p>	<p>A total of 39 trials met preliminary inclusion criteria, of these 10 were excluded because of incomplete results or co-interventions (e.g., sodium reduction). Data presented for 27 trials (982 training subjects, 790 controls), excluded two trials with resistance training as per review exclusion criteria.</p> <ul style="list-style-type: none"> <li>▪ mean exercise intensity 62% VO<sub>2</sub> max (range 30-87% (% VO<sub>2</sub> max)</li> <li>▪ mean duration of exercise programme 18.9 weeks (4-52 weeks)</li> <li>▪ mean frequency of exercise sessions 3.2 (+/- 0.8) times per week.</li> </ul> <p>Pooled Effects Decrease in systolic BP (mm Hg) 95% CI Effects model, Fixed (FE), Random (RE)</p> <ul style="list-style-type: none"> <li>▪ aerobic activity -4.7 (-5.0, -4.4) FE, -4.6 (-5.7, -3.5) RE</li> <li>▪ training intensity (% VO<sub>2</sub> max) &lt;70% -4.6 (-5.0, -4.2) FE, -5.9 (-7.4, -4.3) RE &gt;70% -4.8 (-5.2, -4.4) FE, -3.1 (-4.9, -1.2) RE</li> <li>▪ training frequency (sessions per week) &lt;3 -4.7 (-5.0, -4.4) FE, -4.5 (-5.6, -3.4) RE &gt;3 -4.2 (-5.3, -3.2) FE, -5.0 (-8.8, -1.2) RE</li> <li>▪ BP status Hypertensive -4.0 (-4.7, -3.3) FE, -5.0 (-7.3, -2.7) RE Normotensive -4.2 (-5.3 -3.2) FE, -4.4 (-8.8, -1.2) RE</li> </ul>	<p>Quality gradings</p> <ul style="list-style-type: none"> <li>▪ quality of design? +</li> <li>▪ quality of results? +</li> <li>▪ could applicability be determined? ⌀</li> <li>▪ are findings applicable in usual practice? ⌀</li> </ul> <p>Specific limitations</p> <ul style="list-style-type: none"> <li>▪ high degree of heterogeneity in comparisons between included studies. Variability in gender, age of subjects, pre-training BP, sample sizes, exercise programmes. Also see Random Effect (RE) model results</li> <li>▪ criteria used to categorise trials and present results may be compromised due to lack of study power in sub groups; i.e., training frequency of &gt;3 sessions per week with only 99 subjects in training and 85 in control group</li> <li>▪ overall poor quality of included studies. Authors graded all studies with C grades, except two that were assigned B grades. Reported lack of information on method of randomisation, blinding, BP measurement methodologies. Inadequate data available from studies on associated body weight changes, programme adherence</li> <li>▪ funnel plots indicate publication bias as plots skewed towards large number of very small trials showing larger reductions in BP and absence of small trials showing no effect.</li> </ul>

**Table 1. Evidence table of meta-analyses and systematic reviews examining the effectiveness of physical exercise in lowering blood pressure (continued)**

Authors Country	Study design, setting, comparisons	Sample characteristics, inclusion and exclusion criteria	Methods	Results and authors conclusions	Quality gradings and limitations
Halbert et al. (1997)  Australia  (Continued)	Control groups were mostly non-exercise groups.	Study exclusion criteria <ul style="list-style-type: none"> <li>intensity of exercise programme could not be determined</li> <li>multi-faceted co-intervention.</li> </ul>	Pooled results with fixed and random effects models estimating systolic and diastolic BP effects sizes.  Funnel plots comparing the change in BP with number of trial participants to assess publication bias.	Decrease in diastolic BP (mm Hg) 95% CI Effects model, Fixed (FE), Random (RE) <ul style="list-style-type: none"> <li>aerobic activity -4.7 (-4.4, -5.0) FE, -4.6 (-3.5, -5.7) RE</li> <li>training intensity (% VO<sub>2max</sub>) <ul style="list-style-type: none"> <li>&lt;70% -4.6 (-4.2, -5.0) FE, -5.9 (-4.3, -7.4) RE</li> <li>&gt;70% -4.8 (-4.4, -5.2) FE, -3.1 (-1.2, -4.9) RE</li> </ul> </li> <li>training frequency (sessions per week) <ul style="list-style-type: none"> <li>&lt;3 -4.7 (-4.4, -5.0) FE, -4.5 (-3.4, -5.6) RE</li> <li>&gt;3 -4.2 (-3.2, -5.3) FE, -5.0 (-1.2, -8.8) RE</li> </ul> </li> <li>BP status <ul style="list-style-type: none"> <li>Hypertensive -4.0 (-3.3, -4.7) FE, -5.0 (-2.7, -7.3) RE</li> <li>Normotensive -4.2 (-3.2, -5.3) FE, -4.4 (-1.2, -8.8) RE</li> </ul> </li> </ul>	Conclusion Meta-analysis provides evidence that aerobic exercise produces significant but small decreases in systolic BP and diastolic BP. This may not be clinically significant for hypertensive subjects. Training programmes of high intensity >70% (% VO <sub>2max</sub> ) to lower BP may not have benefit over lower intensity regimens.

**Table 1. Evidence table of meta-analyses and systematic reviews examining the effectiveness of physical exercise in lowering blood pressure (continued)**

Authors Country	Study design, setting, comparisons	Sample characteristics, inclusion and exclusion criteria	Methods	Results and authors conclusions	Quality gradings and limitations
Oja (2001)  Finland	<p>Systematic review of studies examining dose-response between the volume of physical activity and health and fitness.</p> <p>Study types Overall 36 studies were included. Six cross-sectional, one case-control, 13 cohort, four randomised studies with no control group, one non-randomised study, and 11 Randomised Controlled Trials (RCT).</p> <p>Physical activity groups comprised of leisure time physical activity (LTPA) covering most daily physical activities; e.g., aerobic activity such as walking, jogging, cycling, occupational activities and more structured exercise regimen interventions.</p>	<p>Participants Individual study descriptions by study design. No aggregate descriptions of study demographics.</p> <p>Study inclusion criteria</p> <ul style="list-style-type: none"> <li>▪ randomised and non-randomised controlled trials, cohort studies, case-control and cross-sectional studies</li> <li>▪ studies with primary prevention focus</li> <li>▪ subjects were middle-aged and elderly adults and relatively inactive</li> <li>▪ quantitative description of the volume of physical activity</li> <li>▪ outcomes inclusive of cardiovascular risk factors</li> <li>▪ for experimental studies quantitative specification of intervention duration, frequency, session duration, and intensity of exercise programme. Intensity had to be described as either walking pace or percent maximal effort.</li> </ul>	<p>Search strategy Studies published from 1995 for observational studies and from 1990 for experimental studies. Studies published in English.</p> <p>Databases searched Medline, Sport Discus, Ebsco Academic Search Elite, Cochrane Systematic Reviews, and DARE.</p> <p>Descriptive analysis of individual studies by study design.</p> <p>For observational studies, tables presented study source, subjects, design, physical activity, outcome variables, results.</p> <p>For experimental studies, tables presented study source, subjects, programme duration, exercise groups, frequency per week, session duration, intensity (<math>VO_{2max}</math> or <math>HR_{max}</math>), exercise volume METs (metabolic equivalents) minutes per session/week (estimated from study data).</p>	<p>The number of search citations identified and number of abstracts meeting preliminary inclusion criteria not specified. Overall 36 studies included in the review.</p> <p>The 19 observational studies indicated a consistent inverse relationship between physical activity and CVD risk factors and incidence and mortality. A graded dose-response is indicated from individual studies presented. Note that many of the studies included examined CVD outcomes not within the scope of this review.</p> <p>The five randomised without control group studies and non-randomised studies showed no clear dose-response of exercise volume and CVD risk factor outcome response. Most studies showed an increase up to 10% in <math>VO_{2max}</math>. Four studies showed decreases in body weight, only one was significant. Two studies reported decreased SBP, one reported no change. Blood lipids were reported in three studies, all of which reported increases in HDL cholesterol. Other changes were small and non-significant.</p> <p>The 11 RCTs reported intervention duration, frequency, session duration, and intensity of exercise programme. No studies specifically examined the effects of different total volumes of exercise.</p>	<p>Quality gradings</p> <ul style="list-style-type: none"> <li>▪ quality of design? <math>\emptyset</math></li> <li>▪ quality of results? <math>\emptyset</math></li> <li>▪ could applicability be determined? <math>\emptyset</math></li> <li>▪ are findings applicable in usual practice? -</li> </ul> <p>Specific limitations</p> <ul style="list-style-type: none"> <li>▪ study variability in gender, age of subjects, pre-training baseline risk factors, sample sizes, exercise programmes measures of the volume of physical activity and risk factor responses</li> <li>▪ no systematic critical appraisal of validity of included studies</li> <li>▪ search strategy with limited period coverage, incomplete information on search results, possible study selection bias if narrow search</li> <li>▪ no quantification of combined study results, as not possible given the inadequate dose-response assessment of included studies. Narrative analysis of results. Research question unable to be answered.</li> </ul>

**Table 1. Evidence table of meta-analyses and systematic reviews examining the effectiveness of physical exercise in lowering blood pressure (continued)**

Authors Country	Study design, setting, comparisons	Sample characteristics, inclusion and exclusion criteria	Methods	Results and authors conclusions	Quality gradings and limitations
Oja (2001) Finland (Continued)	Comparison groups were dependent on study design. RCTs and CCTs had different intensity, frequency, structure, exercise type comparison groups with a control (non-intervention) group. Several clinical trials had no control group and compared exercise intervention programmes.	Study exclusion criteria <ul style="list-style-type: none"> <li>▪ none specified.</li> </ul>	Narrative analysis of dose-response relationship between physical activity volume and indicators of health and fitness.	<p>All RCT studies except one showed significant increases in <math>VO_{2max}</math>. Body weight changes reported in 8 studies were small and mostly non-significant in both directions. Small reductions or no change in BP was reported in 4 studies. Similarly blood lipids changes reported in 7 studies were small and mostly non-significant. Only one study showing consistent changes from fast-walking exercise.</p> <p>The experimental studies showed mostly small or non-existent and inconsistent changes in CVD risk factors. None were designed to analyse specifically the dose-response of total exercise volume and health and fitness outcomes.</p>	<p>Conclusion</p> <p>This systematic review did not identify any studies that were designed to specifically examine the dose-response of total exercise and health outcomes. Reported responses in risk factors were generally small and inconsistent.</p>

**Table 1. Evidence table of meta-analyses and systematic reviews examining the effectiveness of physical exercise in lowering blood pressure (continued)**

Authors Country	Study design, setting, comparisons	Sample characteristics, inclusion and exclusion criteria	Methods	Results and authors conclusions	Quality gradings and limitations
Whelton et al. (2002)  USA	<p>Meta-analysis of randomised clinical controlled trials.</p> <p>Study parameters Overall, 54 trial interventions from 38 reports were included, with parallel designs in 39 trials, cross-over designs in five trials, factorial designs in two trials and Latin-square designs in eight trials.</p> <p>Trials comparing the effect of aerobic physical exercise on systolic and diastolic BP change.</p>	<p>Participants Overall 54 trial interventions from 38 reports conducted between 1986 and 2000 were included with 2,419 participants with sedentary lifestyles. Study subject age ranged from 21 to 79 years. Of 51 trials reporting sex distribution, 10 trials had &gt;80% men and 17 trials included mostly women. Of 37 trials reporting ethnicity, over 80% of participants were white in 23 trials, Asian in six trials, black in four trials.</p> <p>Fifteen of the 47 trials reporting hypertensive status were conducted in hypertensive subjects, 28 trials on normotensive subjects.</p>	<p>Search strategy Studies published before September 2001 in English. Databases searched included Medline (1966-2001), Sport Discus, and references from included studies.</p> <p>Data from studies independently abstracted by three investigators. Discrepancies resolved by consensus.</p> <p>BP effects measured as difference between BP (mm Hg) (baseline-final value) between the exercise intervention group and control group.</p> <p>Pooled effect sizes calculated by assigning weights equal to inverse of the total variance for changes in SBP and DBP.</p> <p>Fixed and random effects models used to calculate mean effect of aerobic exercise on BP. A random effects model chosen to present results as trials had significant heterogeneity in effect size and characteristics.</p>	<p>Overall 121 trial interventions initially met preliminary inclusion criteria and 54 trial interventions from 38 reports were finally included.</p> <p>Overall results</p> <ul style="list-style-type: none"> <li>baseline median SBP 127 (mm Hg), DBP 77 (mm Hg)</li> <li>median duration of exercise programme 12 weeks, range three weeks to two years</li> <li>net mean body weight change -0.3 kg, weighted by sample size net change -0.42 kg, <math>p=0.09</math>.</li> </ul> <p>Systolic BP (mm Hg) Tr=number of trials 95% CI</p> <ul style="list-style-type: none"> <li>single intervention Tr=47, -4.4 (-5.7, -3.1), <math>p&lt;0.001</math></li> <li>study duration</li> <li>&lt;10 wk Tr=20, -5.2 (-7.4, 2.9), <math>p=0.16</math></li> <li>10-24wk Tr=19, -4.6 (-6.9, 2.3)</li> <li>&gt;24wk Tr=14, -2.0 (-3.1, 0.9)</li> </ul> <p>Diastolic BP (mm Hg) Tr=number of trials 95% CI</p> <ul style="list-style-type: none"> <li>single intervention Tr=36, -3.0 (-3.8, -2.1), <math>p&lt;0.001</math></li> <li>study duration</li> <li>&lt;10 wk Tr=17, -4.3 (-6.1, -2.9), <math>p=0.05</math></li> <li>10-24 wk Tr=19, -2.5 (-3.1, -2.0)</li> <li>&gt;24 wk Tr=14, -2.0 (-2.3, -0.6)</li> </ul>	<p>Quality gradings</p> <ul style="list-style-type: none"> <li>quality of design? <math>\emptyset</math></li> <li>quality of results? <math>\emptyset</math></li> <li>could applicability be determined? <math>\emptyset</math></li> <li>are findings applicable in usual practice? -</li> </ul> <p>Specific limitations</p> <ul style="list-style-type: none"> <li>broad inclusion criteria and study variability in gender, age of subjects, pre-training BP, body-weight, sample sizes, study duration, exercise programmes and BP responses</li> <li>sub-group analysis reveals significant differences in BP reduction effects by sample size and ethnicity such that smaller studies showed larger effects on BP, and Asian and black participants revealed significantly greater effects than whites</li> <li>CVD status not stated in inclusion or exclusion criteria. Contacted author, who reported that "most studies did not provide this information"</li> <li>results may include small number of studies that contained more than a single intervention and/or subjects on anti-hypertensive medication confounding actual exercise effects. Sub-group analysis was not conducted exclusive of these studies</li> <li>no appraisal of the validity of included studies.</li> </ul>

**Table 1. Evidence table of meta-analyses and systematic reviews examining the effectiveness of physical exercise in lowering blood pressure (continued)**

Authors Country	Study design, setting, comparisons	Sample characteristics, inclusion and exclusion criteria	Methods	Results and authors conclusions	Quality gradings and limitations
Whelton et al. (2002)  USA  (Continued)	Control groups in most trials had participants instructed not to adjust their usual lifestyle, including physical activity. Differences between intervention and control groups limited to aerobic physical exercise.	<p>Study inclusion criteria</p> <ul style="list-style-type: none"> <li>▪ subjects randomly assigned to intervention and control groups</li> <li>▪ trials of at least two weeks duration</li> <li>▪ reported changes in systolic and diastolic BP from baseline to follow-up, variances and data to estimate effect</li> <li>▪ trial participants were adults aged 18 years or over.</li> </ul> <p>Study exclusion criteria</p> <ul style="list-style-type: none"> <li>▪ none specified.</li> </ul>	<p>Sub-group analyses to examine the influence of covariates (exercise type, frequency, intensity, duration etc) on BP.</p> <p>Funnel plots comparing the net change in BP with number of trial participants to assess publication bias.</p>	<p>No significant difference between exercise programme characteristics based on groupings of net weight changes, exercise types, exercise frequencies, exercise intensities for both SBP and DBP reduction.</p> <p>Authors state that funnel plots of SBP and DBP to detect publication bias revealed that several large trials reported a moderate reduction in BP but that sensitivity analysis did not warrant removal of any studies.</p>	<ul style="list-style-type: none"> <li>▪ no clear dose-response to varying exercise regimens identified from analysis. The decrease in SBP and DBP may be of significance in terms of generalising these to general population health benefits.</li> </ul> <p>Conclusion This meta-analysis shows that aerobic exercise provides BP reduction effects. The results do not provide evidence of a clear dose-response relationship between exercise programme characteristics and reductions in BP.</p>

**Table 1. Evidence table of meta-analyses and systematic reviews examining the effectiveness of physical exercise in lowering blood pressure (continued)**

Authors Country	Study design, setting, comparisons	Sample characteristics, inclusion and exclusion criteria	Methods	Results and authors conclusions	Quality gradings and limitations
Kelley & Kelley (1999)  USA	<p>Meta-analysis of randomised and non-randomised controlled trials.</p> <p>Study parameters Overall 19 trials were included, involving 47 groups (28 exercise, 19 control) comparing effect of aerobic exercise on resting systolic and diastolic BP control.</p> <p>Aerobic exercise programmes comprised walking, jogging, aerobic dance, cycling, and circuit training.</p>	<p>Participants Overall 19 trials were included with 1,029 participants (663 exercise, 366 control). Mean age 46 years (exercise group), 45 years (control group), range 18-78 years.</p> <p>Study inclusion criteria</p> <ul style="list-style-type: none"> <li>▪ randomised and non-randomised controlled trials</li> <li>▪ aerobic activity interventions only</li> <li>▪ comparative parallel non-exercise control group</li> <li>▪ primary or secondary outcomes include assessment of systolic and diastolic BP changes</li> <li>▪ trial participants were sedentary women aged 18+.</li> </ul>	<p>Search strategy Studies published as journal articles or dissertations between January 1966 and January 1998 in English. Databases searched Medline, Current Contents, Sport Discus, Dissertation Abstracts International, references from included studies.</p> <p>Coding sheets independently abstracted by two authors. Discrepancies resolved by consensus.</p> <p>BP effects measured as difference between the mean change in BP (mm Hg) (baseline-final value) between the exercise and control groups.</p> <p>Pooled effect sizes calculated by assigning weights equal to inverse of the total variance for net changes in BP.</p> <p>Sensitivity analysis on overall results by removing each study from the model. Cumulative meta-analysis ranked by year on net changes in BP by adding one study at a time to assess changes in outcome measures over time.</p>	<p>Overall the search yielded 3,592 citations, 21 trials met preliminary inclusion criteria and 19 trials were finally included.</p> <p>Overall results in 19 studies with 28 exercise programmes</p> <ul style="list-style-type: none"> <li>▪ baseline mean SBP 120 (mm Hg), DBP 74 (mm Hg)</li> <li>▪ mean intensity (max oxygen consumption) 64%, range 41%-80%</li> <li>▪ mean duration of exercise programme 25 weeks, range 6-52 weeks</li> <li>▪ frequency of exercise sessions ranged from two to five times per week, on average 3.5 times per week</li> <li>▪ mean exercise session time, 39 minutes, range 15-60 minutes</li> <li>▪ compliance in exercise sessions, mean 79%, range 53%-91%</li> <li>▪ mean number of exercise subjects completing trial 34, range 8-102, controls 19, range 5-37. Drop-out rate: average 25% for exercise groups, 17% in control groups.</li> </ul> <p>Overall Pooled Effects Decrease in systolic BP (mm Hg) 95% CI</p> <ul style="list-style-type: none"> <li>▪ aerobic exercise activity -2.0 (-3.1, -0.9)</li> <li>▪ correlation analyses of SBP change and changes in fat (%) <math>r=0.78</math>, <math>p=0.001</math>.</li> </ul> <p>Decrease in diastolic BP (mm Hg) 95% CI</p> <ul style="list-style-type: none"> <li>▪ aerobic training activity -0.6 (-1.5, 0.2)</li> <li>▪ correlation analyses of DBP change and changes in fat (%) <math>r=0.36</math>, <math>p=0.21</math>.</li> </ul>	<p>Quality gradings</p> <ul style="list-style-type: none"> <li>▪ quality of design? +</li> <li>▪ quality of results? <math>\emptyset</math></li> <li>▪ could applicability be determined? -</li> <li>▪ are findings applicable in usual practice? -</li> </ul> <p>Specific limitations</p> <ul style="list-style-type: none"> <li>▪ study variability in gender, age of subjects, pre-training BP, sample sizes, exercise programmes and BP responses</li> <li>▪ CVD status not explicit inclusion or exclusion criteria. Contacted author who reported that "most subjects were CVD free"</li> <li>▪ no appraisal of validity of included studies. Data provided indicates very high study drop-out rates</li> <li>▪ most subjects in included studies were normotensive subjects, which may account for small reductions in BP, and questionable clinical significance of decreases in SBP and DBP. Effects of exercise on hypertensive women not examined</li> <li>▪ potential publication bias identified from funnel plots of sample size and resting SBP but not DBP. Reductions in SBP and DBP greater in studies published outside the USA.</li> </ul>

**Table 1. Evidence table of meta-analyses and systematic reviews examining the effectiveness of physical exercise in lowering blood pressure (continued)**

Authors Country	Study design, setting, comparisons	Sample characteristics, inclusion and exclusion criteria	Methods	Results and authors conclusions	Quality gradings and limitations
Kelley & Kelley (1999)  USA  (Continued)	Control groups were defined as parallel non-exercise groups.	Study exclusion criteria <ul style="list-style-type: none"> <li>▪ multi-faceted co-interventions confounding intervention of interest</li> <li>▪ abstract only, conference proceedings</li> <li>▪ multiple studies on the same group of subjects.</li> </ul>	Heterogeneity tests of net changes in SBP and DBP, fixed and random effects models.  Funnel plots comparing the change in BP with number of trial participants to assess publication bias.	Length of programme (weeks), frequency (days/week), intensity (% $\text{VO}_{2\text{max}}$ ), duration (min) not significantly correlated with net SBP change or net DBP change.  No statistically significant heterogeneity for net changes in SBP ( $Q=20.7, p=0.79$ ) or DBP ( $Q=25.3, p=0.45$ ).	Conclusion This meta-analysis shows that aerobic exercise can lead to small but possibly clinically insignificant reductions in BP in normotensive adult women.  The results do not provide evidence of a relationship between particular training programme characteristics and BP response. It was not possible to provide evidence of an optimal dose-response.

**Table 1. Evidence table of meta-analyses and systematic reviews examining the effectiveness of physical exercise in lowering blood pressure (continued)**

Authors Country	Study design, setting, comparisons	Sample characteristics, inclusion and exclusion criteria	Methods	Results and authors conclusions	Quality gradings and limitations
Fagard (2001) Belgium	<p>Meta-analysis of RCTs.</p> <p>Study parameters Overall 44 trials were included, involving 68 training groups/ programmes comparing the effect of aerobic exercise on resting systolic and diastolic BP control.</p> <p>Exercise training programmes comprised of walking, jogging, or running in 69% of trials, and/or cycling (bike or ergometer) in 50% trials, swimming in 3% and "other" exercise in 23%.</p> <p>Control groups were defined as non-intervention groups</p> <p>Sub-analysis Across-study analysis involved 35 RCTs with 45 study groups or interventions that examined only one training intensity, median intensity 64% (range 43-87%).</p>	<p>Participants Overall, 44 trials were included with 2,674 participants. Twenty trials had participants of both sexes, four had women only, 19 had men only and one unspecified. Across studies, median age was 44 years, range 21-79 years.</p> <p>Study inclusion criteria</p> <ul style="list-style-type: none"> <li>RCTs involving dynamic aerobic or endurance exercise training programmes of at least four weeks duration</li> <li>trials where subjects were randomised to intervention and control groups or phases in cross-over designs</li> <li>primary or secondary outcomes include systolic and diastolic BP</li> <li>hypertensive or normotensive subjects, otherwise healthy</li> <li>if different training programmes were compared, randomisation to intervention groups or phases required</li> <li>published in peer-reviewed journal.</li> </ul>	<p>Search strategy English only studies, published pre-August 1998.</p> <p>BP effects measured as difference between the mean change in BP (mm Hg) (baseline-final value) between the exercise and control groups.</p> <p>Exercise intensity reported as either percent of maximal oxygen uptake (11 studies), maximal work load (7 studies), percent of heart rate reserve (8 studies), maximal heart rate (14 studies), lactate threshold (2 studies), not specified (2 studies). Adjusted where necessary.</p> <p>Net effects of training assessed by weighted pooled analysis of changes in the intervention group BP adjusted for control data (weighted by the number of participants in each study group). Reported as weighted means and 95% CI.</p>	<p>An unspecified number of trials met the preliminary inclusion criteria, but 44 were finally included.</p> <p>Overall results in 44 studies with 68 exercise programmes</p> <ul style="list-style-type: none"> <li>baseline mean SBP 126.5 (mm Hg), DBP 79.9 (mm Hg)</li> <li>mean intensity 65% (range 30%-87%)</li> <li>median duration of exercise programme 16 weeks (4-52 weeks)</li> <li>frequency of exercise sessions ranged from one to seven times per week, 66% of training programs had three sessions and all but five programmes had three to five sessions per week</li> <li>median exercise session time, 40 minutes, range 30-60 minutes in all but two programmes, these had 15 minute sessions.</li> </ul> <p>Overall Pooled Effects Decrease in systolic BP (mm Hg) 95% CI</p> <ul style="list-style-type: none"> <li>aerobic training activity -3.4 (-4.5, -2.3), <math>p &lt; 0.001</math></li> <li>BP status Hypertensive (16 groups) -7.4 (-10.5, -4.3)</li> <li>Normotensive (52 groups) -2.6 (-3.7, -1.5)</li> </ul> <p>Decrease in diastolic BP (mm Hg) 95% CI</p> <ul style="list-style-type: none"> <li>aerobic training activity -2.4 (-3.2, -1.6) <math>p &lt; 0.001</math></li> <li>BP status Hypertensive (16 groups) -5.8 (-8.0, -3.5)</li> <li>Normotensive (52 groups) -1.8 (-2.6, -1.1)</li> </ul>	<p>Quality gradings</p> <ul style="list-style-type: none"> <li>quality of design? -</li> <li>quality of results? -</li> <li>could applicability be determined? <math>\emptyset</math></li> <li>are findings applicable in usual practice? <math>\emptyset</math></li> </ul> <p>Specific limitations</p> <ul style="list-style-type: none"> <li>the degree of heterogeneity between included studies not quantitatively determined in analysis. Variability in gender, age of subjects, pre-training BP, sample sizes, exercise programmes and BP responses not adequately accounted for</li> <li>no information on BP measurement process of included studies. Variability in BP response may be linked to variable measurement processes</li> <li>search strategy not described, possible study selection bias if narrow search</li> <li>no appraisal of validity of included studies</li> <li>only a small subset of studies' characteristics individually described</li> <li>pooled analysis only included fixed effects method, does not account for heterogeneity in pooled results</li> <li>no funnel plots provided or able to be derived to assess degree of publication bias.</li> </ul>

**Table 1. Evidence table of meta-analyses and systematic reviews examining the effectiveness of physical exercise in lowering blood pressure (continued)**

Authors Country	Study design, setting, comparisons	Sample characteristics, inclusion and exclusion criteria	Methods	Results and authors conclusions	Quality gradings and limitations
Fagard (2001) Belgium (Continued)	Within-study analysis involving 14 RCTs where subjects were randomly allocated to different training regimens within each study design. Eleven studies examined different exercise intensities with four holding other characteristics constant, the other seven examined differences in frequency, time per session or type of exercise. Three studies examined changes in weekly frequency.	Study exclusion criteria <ul style="list-style-type: none"> <li>multi-faceted co-interventions confounding intervention of interest.</li> </ul>	Weighted meta-regression analysis to test whether variations in BP are related to variations in study group training characteristics.	<p>Decrease in BMI (kg-m<sup>2</sup>) in 64 groups or interventions: -0.34, (-0.46, -0.22) or -1.2% (-1.7%, -0.8%)</p> <p>Across study analysis of 35 trials with 45 groups/interventions of one training intensity, median 64%, (range 43%-87%) No significant relationships from meta-regression analysis of net training intensity and SBP (<math>r=0.19</math>, <math>p=0.21</math>) and DBP response (<math>r=-0.01</math>, <math>p=0.93</math>). BP not significantly related to weekly training frequency (<math>p&gt;0.44</math>) or to time per session (<math>p&gt;0.61</math>).</p> <p>Taken together explained only 4.9% of variance for SBP (<math>p=0.56</math>) and 1.1% for SBP (<math>p=0.92</math>).</p> <p>Duration of training programme significantly related to SBP <math>r=0.32</math>; <math>p&lt;0.05</math> but not DBP <math>p=0.37</math>.</p> <p>Within-study analysis of 14 trials assessing exercise intensities, differences in frequency, session time or type of exercise. No pooled analysis of these results due to wide variation in study design and interventions.</p> <p>Author concludes from narrative analysis of individual studies that there is no evidence that BP response to dynamic aerobic exercise differs according to exercise intensity between 40% and 70% of net maximal performance.</p> <p>BP response to dynamic aerobic exercise is similar for frequencies between three and five sessions per week and for session times between 30 and 60 minutes.</p>	<p>Conclusion This meta-analysis has major methodological limitations, the quality of results may be compromised by not allowing for heterogeneity across studies and by the unreported and possibly limited search strategy and unreported analysis.</p> <p>Study results (with above limitations) indicate that moderate to hard aerobic exercise of 40%-50% intensity or 60%-70% intensity produce similar reductions in BP, and training three to five times per week for 30-60 minutes per session reduces BP particularly in hypertensives.</p>

**Table 2. Evidence table of meta-analyses examining the effectiveness of physical exercise on blood lipids in hyperlipidemic and normolipidemic adults**

Authors Country	Study design, setting, comparisons	Sample characteristics, inclusion and exclusion criteria	Methods	Results and authors conclusions	Quality gradings and limitations
Halbert et al. (1999)  Australia	<p>Meta-analysis of RCTs.</p> <p>Study parameters Thirty-one trials included. One trial had a cross-over design, the others had parallel designs. Comparing type, intensity, frequency of exercise to modify blood lipids.</p> <p>Twenty-seven studies used aerobic exercise programmes only, three studies used resistance training and one study used both.</p> <p>Most programmes included walking, jogging, and/or running, three trials included cycling (bike or ergometer), three trials used resistance training, and one trial used both aerobic and resistance training. Seven trials compared programmes of differing intensity and frequency.</p>	<p>Participants Thirty-one trials with 1,833 participants. Five trials had participants of both sexes, ten had women only, 16 men only and one unspecified. Mean number of participants 59 per trial, range 16-300, age range 19-83 years.</p> <p>Study inclusion criteria</p> <ul style="list-style-type: none"> <li>RCTs involving aerobic or resistance training programme of at least four weeks duration</li> <li>trials with cross-over design where treatments randomised and these order effects not significant</li> <li>primary or secondary outcomes include reporting of blood lipids</li> <li>hyperlipidemic or normolipidemic subjects</li> <li>healthy sedentary adults other than having hyperlipidemia.</li> </ul>	<p>Search strategy English-only studies from 1975-1997 in Medline, Embase, SCl, previous reviews, references from included studies.</p> <p>Appraisal of study internal validity using Cochrane Collaboration handbook (1995).</p> <p>Assessment of the degree of selection bias using a graded scale of: (A) where high degree of effort to control selection bias, (B) some effort to control selection bias, and (C) where little or no effort to control selection bias.</p> <p>Effects of exercise on TC, TG, HDL-C, and LDL-C measured as the difference in (mmol/L) between the mean change in blood lipid (baseline-final value) in the training and control groups.</p>	<p>A total of 41 trials met preliminary inclusion criteria, of these, 10 were excluded because of incomplete data. Results presented are for 27 trials of aerobic exercise.</p> <ul style="list-style-type: none"> <li>mean exercise intensity 63% VO<sub>2</sub> max (range 30-84% (% VO<sub>2</sub> max)</li> <li>mean duration of exercise programme 26.0 weeks (9-52 weeks)</li> <li>mean frequency of exercise sessions 3.9 (+/-1.1) times per week.</li> </ul> <p>Pooled Effects Effect of aerobic exercise on lipid profile (mmol/L) 95% CI, Random Effects model (RE)</p> <p>TC 0.1 (0.02, 0.2) RE HDL-C -0.05 (-0.08, -0.02) RE LDL-C 0.1 (0.02, 0.19) RE TG 0.08 (0.02, 0.14) RE</p> <ul style="list-style-type: none"> <li>decrease in body-weight and BMI c.f. control group -0.95 kg (-1.4, -0.48) and -0.62 (-0.94, -0.31). These changes were not significantly correlated with changes in TC, HDL-C, LDL-C and TG</li> <li>the correlation between baseline lipid concentrations and post-training changes were low. No significant relationship between baseline lipids and the degree of changes with exercise.</li> </ul>	<p>Quality gradings</p> <ul style="list-style-type: none"> <li>quality of design? +</li> <li>quality of results? +</li> <li>could applicability be determined? ∅</li> <li>are findings applicable in usual practice? ∅</li> </ul> <p>Specific limitations</p> <ul style="list-style-type: none"> <li>high degree of heterogeneity in comparisons between included studies. Variability in gender, age of subjects, pre-training lipid concentrations, sample sizes, exercise programmes</li> <li>not clear if resistance training trials are also included in sub-group results for aerobic exercise training</li> <li>the status of trials with co-interventions (e.g., diet or medications) not explicitly stated in inclusion/exclusion criteria. Their inclusion would confound true effects of exercise interventions.</li> </ul>

**Table 2. Evidence table of meta-analyses examining the effectiveness of physical exercise on blood lipids in hyperlipidemic and normolipidemic adults (continued)**

Authors Country	Study design, setting, comparisons	Sample characteristics, inclusion and exclusion criteria	Methods	Results and authors conclusions	Quality gradings and limitations
Halbert et al. (1999)  Australia  (Continued)	Control groups were sedentary non-exercise groups.	Study exclusion criteria <ul style="list-style-type: none"> <li>▪ intensity of exercise programme could not be determined</li> <li>▪ study did not state that participants were randomly allocated.</li> </ul>	Pooled results with random effects model with a weighted average of the individual effects (inversely proportional to the variance of each effect) estimating changes in blood lipids  Funnel plots comparing the change in blood lipids with the number of trial participants to assess publication bias.	<ul style="list-style-type: none"> <li>▪ no significant correlation between changes in blood lipids and energy expenditure (intensity * duration*frequency of exercise session), and total volume of exercise (duration * frequency of exercise sessions).</li> </ul> <p>Effect of aerobic exercise training on TC</p> <ul style="list-style-type: none"> <li>▪ training intensity (% VO<sub>2 max</sub>)</li> <li>&lt;70% 0.08 (-0.04, 0.21) RE</li> <li>&gt;70% 0.14 ( 0.07, 0.21) RE</li> <li>▪ training frequency (sessions per week)</li> <li>3 0.18 (0.08, 0.28) RE</li> <li>&gt;3 0.04 (-0.09, 0.17) RE</li> <li>▪ blood lipid status</li> <li>Hyperlipidemic 0.03 (0.00, 0.07) RE</li> <li>Normolipidemic 0.08 (-0.05, 0.2) RE</li> </ul> <p>Effect of aerobic exercise training on HDL-C</p> <ul style="list-style-type: none"> <li>▪ training intensity (% VO<sub>2 max</sub>)</li> <li>&lt;70% -0.06 (-0.10, -0.02) RE</li> <li>&gt;70% -0.04 ( -0.09, 0.00) RE</li> <li>▪ training frequency (sessions per week)</li> <li>3 -0.06 (-0.09, -0.02) RE</li> <li>&gt;3 -0.04 (-0.10, 0.00) RE</li> <li>▪ blood lipid status</li> <li>Hyperlipidemic -0.07 (-0.1, -0.03) RE</li> <li>Normolipidemic -0.04 (-0.1, -0.02) RE</li> </ul>	<ul style="list-style-type: none"> <li>▪ overall included studies were of poor quality. Authors graded all studies with C grades, except five that were assigned B grades. Reported limitations included small sample sizes, lack of information on method of randomisation, blinding, variable blood lipid measurement methodologies. Inadequate data available from large number of studies on associated body weight changes.</li> </ul> <p>Conclusion This meta-analysis provides evidence that aerobic exercise produces small changes in blood lipids. Training programmes of high intensity &gt;70% (% VO<sub>2 max</sub>) produced larger changes in TC and LDL-C and programmes of lower intensity modified TG and HDL-C. Three exercise sessions per week produced greater changes in blood lipids than more frequent exercise.</p>

**Table 2. Evidence table of meta-analyses examining the effectiveness of physical exercise on blood lipids in hyperlipidemic and normolipidemic adults (continued)**

Authors Country	Study design, setting, comparisons	Sample characteristics, inclusion and exclusion criteria	Methods	Results and authors conclusions	Quality gradings and limitations
Halbert et al. (1999)  Australia  (Continued)				<p>Effect of aerobic exercise training on LDL-C</p> <ul style="list-style-type: none"> <li>▪ training intensity (% <math>VO_{2max}</math>)</li> </ul> <p>&lt;70% 0.07 (-0.04, 0.19) RE &gt;70% 0.16 ( 0.06, 0.25) RE</p> <ul style="list-style-type: none"> <li>▪ training frequency (sessions per week)</li> </ul> <p>3 0.16 (0.03, 0.29) RE &gt;3 0.06 (-0.07, 0.18) RE</p> <ul style="list-style-type: none"> <li>▪ blood lipid status</li> </ul> <p>Hyperlipidemic 0.05 (-0.07, 0.16) RE Normolipidemic 0.09 (0.00, 0.18) RE</p> <p>Effect of aerobic exercise training on TG</p> <ul style="list-style-type: none"> <li>▪ training intensity (% <math>VO_{2max}</math>)</li> </ul> <p>&lt;70% 0.10 (0.10, 0.19) RE &gt;70% 0.07 (0.07, 0.13) RE</p> <ul style="list-style-type: none"> <li>▪ training frequency (sessions per week)</li> </ul> <p>3 0.13 (0.06, 0.20) RE &gt;3 0.03 (-0.07, 0.13) RE</p> <ul style="list-style-type: none"> <li>▪ blood lipid status</li> </ul> <p>Hyperlipidemic 0.15 (0.7, 0.23) RE Normolipidemic 0.03 (-0.04, 0.11) RE</p> <p>Funnel plots did not indicate publication bias as equal number of trials showing no change, increase and decrease in blood lipids.</p>	

**Table 3. Evidence table of randomised controlled trials examining the effectiveness of physical exercise on blood pressure and blood lipids.**

Authors Country	Study design, setting, comparisons	Sample characteristics, inclusion and exclusion criteria	Methods	Results and authors conclusions	Quality gradings and limitations
Cox et al. (2001)  Australia	<p>Randomised Controlled Trial</p> <p>Study parameters Following a six week run-in period women were randomised to home-based (for initial 6 months) or centre-based exercise programmes (for initial six months) then a further 12 months of minimally supervised home-based exercise programme for all participants.</p> <p>Participants in the initial groups were further randomised to moderate intensity (40%-55% HR<sub>res</sub>) or vigorous intensity (65%-80% HR<sub>res</sub>).</p> <p>Study length was 18 months. During the first six months the centre-based group attended supervised exercise sessions three times per week. The home-based group attended exercise sessions 10 times in the first five weeks, then three times per week. Exercise comprised of 30-min sessions with four walks, one aerobics session and one circuit session every two weeks.</p>	<p>Participants Women were aged 40-65 years. Mean age was 48 years. Mean weight was 68 kg, BMI was 25 kg/m<sup>2</sup>. Ninety-seven percent were Caucasian, 69% post-menopausal and 28% taking oral contraceptives or HRT.</p> <p>Baseline mean SBP 111 mmHg, DBP 66 mmHg, mean TC 5.2 mmol/L, HDL-C 1.6mmol/L, LDL-C 3.2 mmol/L.</p> <p>Study inclusion criteria</p> <ul style="list-style-type: none"> <li>▪ sedentary lifestyle, no more than 20 min exercise twice per week over the last six months</li> <li>▪ non-smoking</li> <li>▪ BP less than 160/100 mmHg</li> <li>▪ alcohol consumption less than 210 ml/week.</li> </ul>	<p>Physical fitness assessments used VO<sub>2max</sub> oxygen consumption as the measure of aerobic capacity assessed at baseline and six, 12 and 18 months, 48-72 hours after the last exercise session using a progressive multistage exercise test on a cycle ergometer.</p> <p>BP was measured with a Dinamap 1846SX (Critikon Inc., Tampa Florida, USA) automatic oscillometric device. BP for each visit was estimated from 10 supine readings taken over 20 min and five standing readings over 5 min. At six, 12 and 18 months, BP measured as the mean from two separate visits over a two-week period.</p>	<p>The moderate intensity group exercised at 54, 56 and 55% of heart rate reserve HR<sub>res</sub>.</p> <p>The vigorous group at 61, 68 and 67% HR<sub>res</sub> at six, 12 and 18 months.</p> <p>SBP and DBP adjusted for age and baseline BP showed significant decreases in both SBP (-2.8 mmHg, p=0.049) and DBP (-2.7 mmHg, p=0.004) at 18 months for moderate intensity group but not for the vigorous intensity group (-0.2 mmHg, p=0.89 and -1.8 mmHg, p=0.07).</p> <p>Throughout the study, HDL-C, LDL-C and TG changes were unrelated to fitness levels, number of exercise sessions completed, distance walked or training intensity achieved.</p> <p>At 6 months, after adjusting for menopausal status, baseline lipids, and weight change there were small significant effects in subjects after vigorous compared with moderate intensity activity TC -0.23 mmol/L, p&lt;0.05 LDL-C -0.21 mmol/L, p&lt;0.05</p>	<p>Quality gradings</p> <ul style="list-style-type: none"> <li>▪ quality of design? Ø</li> <li>▪ quality of results? -</li> <li>▪ could applicability be determined? Ø</li> <li>▪ are findings applicable in usual practice? Ø</li> </ul> <p>Specific limitations</p> <ul style="list-style-type: none"> <li>▪ randomisation method not fully described</li> <li>▪ degree of concealment and blinding to outcome assessment not indicated</li> <li>▪ possible subject selection bias as study participants were respondents to media advertisements</li> <li>▪ participants lost to follow-up not included in analysis. Significantly lower retention rates in high intensity groups at 12 (76%) and 18 months (62%) when compared to moderate intensity group. Further undermining study power was adherence rates of those remaining in the study which were 77% versus 63% at 12 months and 79% versus 72% at 18 months. Difficulties with maintenance of vigorous activity regimen over a long period was the likely reason</li> <li>▪ interpreting changes in BP from baseline without a corresponding control group is problematic. Possible confounders on effects of exercise on lipids including differences in menstrual status, phase, use of oral contraceptives and HRT. These could not be completely controlled for.</li> </ul>

**Table 3. Evidence table of randomised controlled trials examining the effectiveness of physical exercise on blood pressure and blood lipids (continued)**

<b>Authors Country</b>	<b>Study design, setting, comparisons</b>	<b>Sample characteristics, inclusion and exclusion criteria</b>	<b>Methods</b>	<b>Results and authors conclusions</b>	<b>Quality gradings and limitations</b>
Cox et al. (2001)  Australia  (Continued)	Build-up during initial six weeks to moderate and vigorous intensity levels.  No control group.	Study exclusion criteria <ul style="list-style-type: none"> <li>▪ persons with musculoskeletal disorders</li> <li>▪ CVD history</li> <li>▪ mental incapacity</li> <li>▪ respiratory difficulty or other chronic illness.</li> </ul>	Body weight, skin-fold thickness and body fat measured at the same time as BP.	This difference did not persist at 12 and 18 months.  There were no significant changes in body-weight, percentage body fat and skin fold thickness between the two exercise intensity groups across the study period.	Conclusion This RCT provides limited evidence that moderate intensity (40%-55% HR <sub>res</sub> ) aerobic exercise rather than vigorous intensity (65%-80% HR <sub>res</sub> ) produces small decreases in SBP and DBP for middle-aged women. However, changes in lipid profiles were small. Large drop-out rates coupled with falling adherence rates in the vigorous exercise group is likely to have compromised comparative results.

**Table 4. Evidence table of Randomised Controlled Trials examining the effectiveness of physical exercise on blood lipids**

Authors Country	Study design, setting, comparisons	Sample characteristics, inclusion and exclusion criteria	Methods	Results and authors conclusions	Quality gradings and limitations
Kukkonen-Harjula et al. (1998)  Finland	Randomised Controlled Trial  Study parameters Subjects were randomised to an exercise and control group stratified by sex, and sub-maximal oxygen consumption.  The training group regimen consisted of walking training of four 50-minute sessions per week for 15 weeks. Other regular physical activity was also maintained. Target intensity for exercise was 74%-81% of HR <sub>max</sub> , equivalent to 65%-75% of VO <sub>2max</sub> .	Participants Adults mean age was 42 years in exercise group and 40 years in control group. Mean BMI 25 kg/m <sup>2</sup> in exercise group and 25.5 kg/m <sup>2</sup> in control group. Mean VO <sub>2max</sub> 2.9 l/min in exercise group and 3.0 l/min in control group, BIA % 24.0 and 25.0 respectively.  Subjects were advised to maintain their previous lifestyle throughout trial including diet, alcohol consumption, and any physical exercise.  Study inclusion criteria <ul style="list-style-type: none"> <li>▪ adults ages 30-55 years</li> <li>▪ non-smoking</li> <li>▪ pre-menopausal (women)</li> <li>▪ clinically healthy</li> <li>▪ no disabilities precluding exercise training.</li> </ul>	Body weight and height measurements. Fat proportion of the body weight was estimated using bio-electrical impedance analysis (BIA).  BP measurements were taken after subjects rested in sitting position for five minutes, using a random zero sphygmomanometer. Measured twice each time, mean values used.  Exercise VO <sub>2max</sub> was determined during an uphill walk on a treadmill and continued up to symptom free volitional maximum.  A metabolic analyser was used to collect and analyse expired air. ECG was monitored. Maximal effort defined as a plateau of VO <sub>2</sub> (increase less than 2 ml/min/kg between consecutive gas analyses every minute) and/or at least two of the following heart rate (HR) > 85% of age predicted maximum, respiratory quotient >1.05, post-capillary lactate >4 mmol/l. Continuous heart rate monitoring during exercise.	No substantive differences between the exercise and control groups (58 subjects each group) for age, BMI, VO <sub>2max</sub> , BIA).  On average walkers participated in 57 training sessions (92%) or 3.8 per week, with an average length of a session at 61 min and distance walked 7.2 km.  Outcomes Net differences (between pre-post-training in exercise and control groups) and 95% CI.  All statistically significant differences presented at p=<0.01.  VO <sub>2max</sub> 0.141 l/min (0.04, 0.23) TC -0.2 mmol/l (-0.34, -0.06) LDL-C -0.17 mmol/l (-0.29, -0.05) HDL-C/TC ratio 0.014 (0.005, 0.023) TG -0.15 mmol/l (-0.26, -0.04) Weight -1.7 kg (-2.5, -1.0) BMI -0.6 kg/m <sup>2</sup> (-0.8, -0.3)	Quality gradings <ul style="list-style-type: none"> <li>▪ quality of design? +</li> <li>▪ quality of results? +</li> <li>▪ could applicability be determined? ∅</li> <li>▪ are findings applicable in usual practice? ∅</li> </ul> Specific limitations <ul style="list-style-type: none"> <li>▪ randomisation method not described. Degree of concealment and blinding to outcome assessment was not indicated</li> <li>▪ possible subject selection bias as volunteers recruited from newspaper advertisements. No information on numbers screened and numbers meeting eligibility criteria</li> <li>▪ of study participants, 7% were lost to follow-up and not included in analysis. Five others had diminished participation but were included in the analysis</li> <li>▪ multiple potential confounding variables may have an effect on plasma lipid levels in association with a response to physical exercise; e.g., dietary changes</li> <li>▪ short duration of training programme.</li> </ul>

**Table 4. Evidence table of Randomised Controlled Trials examining the effectiveness of physical exercise on blood lipids (continued)**

Authors Country	Study design, setting, comparisons	Sample characteristics, inclusion and exclusion criteria	Methods	Results and authors conclusions	Quality gradings and limitations
Kukkonen-Harjula et al. (1998)  Finland  (Continued)	Control group did not perform any particular physical training over and above regular activities.	Study exclusion criteria <ul style="list-style-type: none"> <li>▪ subject doing physical exercise more than twice per week</li> <li>▪ subject on regular medication (except for hormonal contraception in women)</li> <li>▪ BMI &gt; 33 kg/m<sup>2</sup>.</li> </ul>	Dietary intake estimated on basis of food diaries recorded over three days, including one weekend day, at study beginning and end, with questionnaire and interview.  Biochemical analysis taken from an overnight fast before and after training. Subjects were to refrain from physical exercise and alcohol consumption 48 hours before. Mean lipoprotein results used from two blood samples taken within a week. Analysis from frozen samples, enzymatic cholesterol oxidase methodologies, enzymatic methods for triglyceride measurement, modified automated Clauss method fibrinogen test.	No significant changes in fibrinogen.  Food Intake increased slightly in exercise group men and decreased slightly in control group women.  No significant changes in mean energy intake ( $p=0.27$ ).  No changes in SBP during training, net difference for DBP was -2.7 mmHg (-5.3, 0.0).  Total study drop-out rate from study was 7%. One subject dropped out after randomisation due to arrhythmia during maximal exercise testing. Five others from exercise group and three from control group (two with severe injuries from training) dropped out during study. Another five had diminished participation but were included in analysis.	Conclusion This RCT provides some evidence of small but consistent modifications to lipid profiles and weight resulting from a moderate intensity walking programme in middle-aged adults of four 50-minute sessions per week for 15 weeks.

**Table 4. Evidence table of Randomised Controlled Trials examining the effectiveness of physical exercise on blood lipids (continued)**

Authors Country	Study design, setting, comparisons	Sample characteristics, inclusion and exclusion criteria	Methods	Results and authors conclusions	Quality gradings and limitations
Sunami et al. (1999)  Japan	Randomised Controlled Trial  Study parameters Subjects were randomised to a training and control group matched for age, height, and weight.  The training group regimen used a bicycle ergometer at an intensity of 50% VO <sub>2max</sub> for 60 minutes, two to four times per week for 5 months. Other regular physical activity was maintained.	Participants Japanese adults mean age 67 years, age range 60-77 years. Mean weight 53 kg and BMI 22 kg/m <sup>2</sup> in exercise group and 55 kg and 23 kg/m <sup>2</sup> in control group. Baseline mean SBP 142 mmHg, DBP 83 mmHg in exercise group and SBP 145 mmHg, DBP 79 mmHg in control group. No one was taking medications known to influence lipid or lipoprotein metabolism. No significant differences in group body characteristics at baseline.  Exercise and control groups contained 20 subjects each (10 men and 10 women).  Subjects were advised to maintain their previous lifestyle throughout trial including diet, alcohol consumption, and physical training. For training group no change in regular physical activity was allowed.	Maximal oxygen consumption measured heart rate at three different sub-maximal workloads using electric bicycle ergometer.  After every session of 30 bouts of training each subject underwent a sub-maximal exercise test to readjust the VO <sub>2max</sub> intensity level.  Total exercise duration per week on mostly supervised bicycle ergometer exercise. Other regular supplementary low-intensity exercise (by four men and three women) continued.  Blood sampling for lipids collected early morning after 12 hours of fasting. Analyses completed within 48 hours.  TC and TG concentrations determined by the enzymatic method. HDL-C by the heparin-manganese precipitation method. HDL <sub>2</sub> -C sub-fraction calculated as difference between total HDL-C and HDL <sub>3</sub> -C. LDL-C calculated according to the method by Friedewald et al. 1972.	No participants lost to follow-up and all 40 included in analysis.  Mean total exercise duration at 50% VO <sub>2max</sub> in training group was 218 +/- 57 min/week.  There were no significant changes in body weight and percentage body fat, and BP in training group.  Significant increase in VO <sub>2max</sub> in training group, p<0.01.  No significant changes to any of these parameters in control group.  Serum lipids and lipoprotein concentrations: The training group showed a significantly higher HDL-C, HDL <sub>2</sub> -C and HDL <sub>2</sub> -C / HDL <sub>3</sub> -C ratio (p<0.05), compared with the control group after five months. No significant change was observed for any other parameters in the exercise and control groups.  Increase in weekly exercise duration positively correlated with change in HDL <sub>2</sub> -C (r=0.57, p<0.01) and HDL <sub>2</sub> -C / HDL <sub>3</sub> -C ratio (r=0.63, p<0.01). Also positively correlated with HDL-C, HDL <sub>2</sub> -C, and HDL <sub>2</sub> -C / HDL <sub>3</sub> -C ratio levels after training period.	Quality gradings <ul style="list-style-type: none"> <li>▪ quality of design? Ø</li> <li>▪ quality of results? Ø</li> <li>▪ could applicability be determined? Ø</li> <li>▪ are findings applicable in usual practice? Ø</li> </ul> Specific limitations <ul style="list-style-type: none"> <li>▪ randomisation method not described. Degree of concealment and blinding to outcome assessment not indicated</li> <li>▪ possible subject selection bias as no description of eligibility criteria. Only exercise and control group physical features were described, other demographic characteristics not described</li> <li>▪ programme adherence rates not described</li> <li>▪ multiple potential confounding variables may have an effect on plasma lipid levels in association with a response to physical exercise</li> <li>▪ dietary changes from questionnaires and interviews in training group were not reported in results.</li> </ul>

**Table 4. Evidence table of Randomised Controlled Trials examining the effectiveness of physical exercise on blood lipids (continued)**

<b>Authors Country</b>	<b>Study design, setting, comparisons</b>	<b>Sample characteristics, inclusion and exclusion criteria</b>	<b>Methods</b>	<b>Results and authors conclusions</b>	<b>Quality gradings and limitations</b>
Sunami et al. (1999)  Japan  (Continued)	Control group did not perform any particular physical training over and above regular activities.	<p>Study inclusion criteria</p> <ul style="list-style-type: none"> <li>▪ none specified.</li> </ul> <p>Study exclusion criteria</p> <ul style="list-style-type: none"> <li>▪ subjects with medical problems that could interfere with exercise programme.</li> </ul>	<p>Percent body fat estimated using methods and formulas described by Brozek et al. (1963).</p> <p>Training group required to record dietary intake for three days including one weekend before/after training period, with questionnaire and interview.</p>	Changes in body weight, % body fat and VO <sub>2max</sub> not significantly correlated with any lipid parameters.	<p>Conclusion</p> <p>This RCT provides some evidence that moderate intensity (50% VO<sub>2max</sub>) aerobic exercise in healthy elderly subjects may significantly increase HDL-C, HDL<sub>2</sub>-C levels and HDL<sub>2</sub>-C / HDL<sub>3</sub>-C ratio. Changes in weekly exercise duration were positively correlated with HDL<sub>2</sub>-C levels and HDL<sub>2</sub>-C / HDL<sub>3</sub>-C ratio.</p> <p>No relationship between body weight/percent body fat reduction and change in any lipid or lipoprotein was observed.</p>

**Table 5. Evidence table of Randomised Controlled Trials examining the effectiveness of physical exercise on body-weight**

Authors Country	Study design, setting, comparisons	Sample characteristics, inclusion and exclusion criteria	Methods	Results and authors conclusions	Quality gradings and limitations
Asikainen et al. (2002)  Finland	<p>Randomised Controlled Trial</p> <p>Study parameters Participants randomised into three parallel groups of one (W1) walking session per day, two (W2) walking sessions per day and no (C) walking sessions per day.</p> <p>Walking groups exercised five days per week for 15 weeks at an intensity of 65% <math>VO_{2max}</math> and energy expenditure of 300 kcal per session.</p> <p>Daily training (brisk walking) was continuous in group W1 and divided into two equal length sessions at least five hours apart in group W2.</p> <p>Two sessions per week were supervised on an indoor 100m track. The other sessions were (3 in W1 and 8 in W2) were unsupervised and took place as per participants preferences.</p>	<p>Participants Post-menopausal women with age range 47-64 years. Mean BMI per study group 26 kg/m<sup>2</sup>. Mean weight 68 kg. Percent fat 37% and mean <math>VO_{2max}</math> (ml/kg/min) 28 to 29.</p> <p>Subjects were asked to maintain their previous lifestyle throughout trial including diet and any exercise habits and HRT use.</p> <p>Study inclusion criteria</p> <ul style="list-style-type: none"> <li>▪ female, 48-63 years of age</li> <li>▪ at study beginning 2-10 years past onset of menopause</li> <li>▪ no chronic diseases</li> <li>▪ no regular medication</li> <li>▪ non-smoker</li> <li>▪ BMI &lt; 32 kg/m</li> <li>▪ resting BP &lt; 160/100 mmHg</li> <li>▪ not engaged in strenuous work or regular brisk leisure time exercise more than once per week, or light exercise three times per week.</li> </ul>	<p>Measurements were performed twice, that is before and after exercise intervention training.</p> <p>Sub-maximal exercise testing for screening and habituation using maximal exercise test on treadmill at 65% and 75% <math>VO_{2max}</math>.</p> <p><math>VO_2</math> measured using a metabolic cart, main criteria for reaching <math>VO_{2max}</math> was best possible effort of subject as judged by the test supervisor.</p> <p>Baseline and end of intervention questionnaire and interview for checking diet, daily exercise habits and HRT use.</p> <p>Body mass, BMI, skin-fold thickness measurements</p>	<p>Of 700 subjects replying to advertisements, 300 were screened by questionnaire, of these 236 screened by medical examination. Of these, 134 were included meeting eligibility criteria and were randomised into study groups. Number of subjects per group were W1: 46, W2: 43, C: 45.</p> <p>No differences between groups in baseline characteristics were identified.</p> <p>Training attendance compliance amongst exercise groups was 89% for group W1 (of 75 prescribed sessions) and 95% (of 150 prescribed sessions) for group W2. For supervised sessions attendance rates were 88% and 92% respectively.</p> <p>Mean duration of walking session was 48 min for group W1 and 25 min for group W2. Mean daily amount of walking according to pedometer readings (both prescribed and habitual exercise) was 9.2 km for group W1 and 10.4 km for group W2.</p>	<p>Quality gradings</p> <ul style="list-style-type: none"> <li>▪ quality of design? <math>\emptyset</math></li> <li>▪ quality of results? <math>\emptyset</math></li> <li>▪ could applicability be determined? <math>\emptyset</math></li> <li>▪ are findings applicable in usual practice? <math>\emptyset</math></li> </ul> <p>Specific limitations</p> <ul style="list-style-type: none"> <li>▪ uncertain of degree of concealment and blinding to outcome assessment also authors state subjects and testing personnel were informed about group results after baseline tests</li> <li>▪ possible subject selection bias as volunteers recruited by newspaper advertisements</li> <li>▪ calculations for adequate sample size yielded a minimum of 39 subjects per group at 90% power and type 1 error <math>\alpha=0.05</math> for a 10% change in <math>VO_{2max}</math>. Actual number of subjects ranged from 43-46 per group. Sufficient study power here generated greater effects than when compared to similar previous study by Asikainen et. al., 2002</li> <li>▪ of study participants, 97% completed the study, four (two from the exercise group and two controls) were lost to follow-up and not included in analysis. Three subjects of the exercise programme had diminished participation but were included in the analysis</li> <li>▪ short duration of the training programme (15 weeks) may have compromised the true effects of exercise on changes in body mass.</li> </ul>

**Table 5. Evidence table of Randomised Controlled Trials examining the effectiveness of physical exercise on body-weight**

<b>Authors Country</b>	<b>Study design, setting, comparisons</b>	<b>Sample characteristics, inclusion and exclusion criteria</b>	<b>Methods</b>	<b>Results and authors conclusions</b>	<b>Quality gradings and limitations</b>
Asikainen et al. (2002)  Finland  (Continued)	Supervised sessions also included a light muscle work out (10 exercises in one set with 10 repetitions using 5lb dumbbells).  HRT users and non-users were randomised separately in blocks of 15 into groups to ensure equal distribution of users and non-users in groups.  Control group attended a meeting once a month with health lectures and some light flexibility exercises.	Study exclusion criteria ▪ none specified.	Physical activity of all subjects during study recorded in diaries.	The net changes before and after intervention between each exercise groups and the control group were significant changes in body mass (approx 1 kg decrease, $p=0.001$ ) and BMI (approx 0.5 units, $p=0.001$ ) and percent fat which decreased by approximately 2% ( $p<0.001$ ).  $VO_{2max}$ net increase of 8.5% in both exercise groups compared with control group.  No changes in exercise were reported in control group. Six participants changed HRT status but were included in original group allocation.	Conclusion The evidence from this RCT indicates that walking exercise 5 days per week for a short 15 week period at an intensity of 65% $VO_{2max}$ and energy expenditure of 300 kcal per session produced significant changes in body mass with walking at a frequency of either one or two daily sessions.

**Table 5. Evidence table of Randomised Controlled Trials examining the effectiveness of physical exercise on body-weight (continued)**

Authors Country	Study design, setting, comparisons	Sample characteristics, inclusion and exclusion criteria	Methods	Results and authors conclusions	Quality gradings and limitations
Asikainen et al. (2002)  Finland	<p>Randomised Controlled Trial</p> <p>Study parameters Participants randomised into five parallel groups of four walking exercise groups (W) and one control group (C).</p> <p>Walking groups exercised (with brisk walking) five days per week for 24 weeks with different intensities (% of VO<sub>2max</sub> and energy expenditure kcal/week) ranging from W1, 55% /1500 kcal for 54 min, W2, 45% /1500 kcal for 65 min, W3, 55% /1000 kcal for 38 min and W4 45% /1000 kcal for 46 min.</p> <p>Two sessions per week were supervised.</p> <p>HRT users and non-users were randomised separately into groups to ensure equal distribution of users and non-users in groups.</p>	<p>Participants Post-menopausal women with age range 48-63 years. Mean BMI per study group ranged from 25 kg/m<sup>2</sup> to 27 kg/m<sup>2</sup>. Mean weight (kg) ranged from 66 to 70 per group. Percent fat ranged from 36% to 38% and mean VO<sub>2max</sub> (ml/kg/min) 29.3 to 30.8.</p> <p>Subjects were asked to maintain their previous lifestyle throughout trial including diet and any exercise habits and HRT use.</p> <p>Study inclusion criteria</p> <ul style="list-style-type: none"> <li>▪ female, 48-63 years of age</li> <li>▪ at study beginning 2-10 years past onset of menopause</li> <li>▪ no chronic diseases</li> <li>▪ no regular medication</li> <li>▪ non-smoker</li> <li>▪ BMI &lt; 32 kg/m</li> <li>▪ resting BP &lt; 160/100 mmHg</li> <li>▪ not engaged in strenuous work or regular brisk leisure time exercise more than once per week, or light exercise more than three times per week.</li> </ul>	<p>Measurements were performed before and after the exercise intervention training.</p> <p>Sub-maximal exercise testing for screening and habituation using maximal exercise test on treadmill. VO<sub>2</sub> measured using a metabolic cart, main criteria for reaching VO<sub>2max</sub> was best possible effort of subject as judged by the test supervisor</p> <p>Baseline and end of intervention questionnaires for checking diet, exercise habits and HRT use.</p> <p>Dietary intake estimated on basis of food diaries recording three days including one weekend day at study beginning and end.</p> <p>Physical activity of all subjects during study recorded in diaries.</p>	<p>Of 413 subjects replying to advertisements, 329 were screened. Of these 123 were included meeting eligibility criteria. Of this number 121 subjects were randomised into study groups. Number of subjects per group were W1: 21, W2: 21, W3: 18, W4: 21 and C: 40. No differences between groups in baseline characteristics.</p> <p>Training compliance amongst exercise groups for exercise intervention was 90%-98% for session duration, walking sessions per week 84%-89%, length of intervention 97%-99%. Habitual physical activity (min/day)</p> <p>The net changes before and after intervention between each exercise group and the control group were not significant, change in body mass (<math>p=0.53</math>) and BMI (<math>p=0.67</math>). Percent fat decreased by approximately 1% across all exercise groups (<math>p=0.007</math>).</p> <p>No clear dose-response relationship between exercise intensity and changes in body mass or fat.</p>	<p>Quality gradings</p> <ul style="list-style-type: none"> <li>▪ quality of design? -</li> <li>▪ quality of results? -</li> <li>▪ could applicability be determined? <math>\emptyset</math></li> <li>▪ are findings applicable in usual practice? <math>\emptyset</math></li> </ul> <p>Specific limitations</p> <ul style="list-style-type: none"> <li>▪ uncertain of degree of concealment and blinding to outcome assessment also authors state subjects and testing personnel were informed about group results after baseline tests</li> <li>▪ possible subject selection bias as volunteers were recruited by newspaper advertisements</li> <li>▪ calculations for adequate sample size yielded a minimum of 39 subjects per group at 90% power and type 1 error <math>\alpha=0.05</math> for a 10% change in VO<sub>2max</sub>. Actual number of subjects ranged from 18-21 per group. Analysis done at exercise group level, none were combined. Inadequate study power is likely to have contributed to null results</li> <li>▪ of study participants, 96% completed the study, five (three from exercise groups and two controls) were lost to follow-up and not included in analysis. Two others had diminished participation but were included in the analysis. The short duration of the training programme may have compromised the true effects of exercise on changes in body mass.</li> </ul>

**Table 5. Evidence table of Randomised Controlled Trials examining the effectiveness of physical exercise on body-weight (continued)**

<b>Authors Country</b>	<b>Study design, setting, comparisons</b>	<b>Sample characteristics, inclusion and exclusion criteria</b>	<b>Methods</b>	<b>Results and authors conclusions</b>	<b>Quality gradings and limitations</b>
Asikainen et al. (2002)  Finland	Control group was given instructions on starting exercise according to the American College of Sports Medicine (ACSM) recommendations.	Study exclusion criteria <ul style="list-style-type: none"> <li>▪ none specified.</li> </ul>	Body mass, BMI, skin-fold thickness measurements	<p><math>VO_{2max}</math> increase ranged from 7.3% in exercise group W4 to 9.5% in exercise group W1.</p> <p>According to questionnaires no significant quantitative and qualitative dietary changes were reported.</p> <p>A total of 25 subjects consulted a doctor with exercise-related problems, mostly mild lower limb or back problems. No difference in injury rates between exercise groups.</p>	<p>Conclusion</p> <p>This RCT has several methodological problems, particularly that of weak study power. Therefore the largely null results of no significant changes in body mass due to moderate walking activity intensity of 45% to 55% <math>VO_{2max}</math> (1000-1500 kcal) five days per week for 40-60 min cannot reliably be interpreted as a minimum exercise regimen for favourable responses in body weight.</p>

## References

*Active For Life: A Call For Action. The Health Benefits of Physical Activity.* (1998). Wellington: National Health Committee.

*Physical Activity and Health: A Report of the Surgeon General.* (1996). Atlanta, GA: US Department of Health and Human Services, Centres for Disease Control and Prevention, National Centre for Chronic Disease Prevention and Health Promotion.



# Appendix 1: Search strategies

## SEARCH STRATEGIES

### *Medline*

- 1 Physical Fitness/ (10751)
- 2 exercise/ or walking/ or yoga/ (28531)
- 3 running/ or jogging/ or swimming/ (12365)
- 4 exp Sports/ (43391)
- 5 or/1-4 (71763)
- 6 exp Cardiovascular Diseases/mo, pc [Mortality, Prevention & Control] (111860)
- 7 diabetes mellitus/pc, mo or diabetes mellitus, insulin-dependent/pc, mo or diabetes mellitus, non-insulin-dependent/pc, mo (4916)
- 8 Lipids/bl [Blood] (24037)
- 9 exp Lipoproteins/bl [Blood] (37289)
- 10 Blood Pressure/ph [Physiology] (17889)
- 11 Glucose Intolerance/ (1488)
- 12 or/6-11 (183759)
- 13 5 and 12 (4524)
- 14 limit 13 to yr=1996-2002 (2127)
- 15 meta-analysis/ (4536)
- 16 (meta analy\$ or metaanaly\$).tw. (8839)
- 17 meta analysis.pt. (7016)
- 18 (systematic adj3 (review or overview)).tw. (3308)
- 19 randomized controlled trials/ (25104)
- 20 clinical trial.pt. (338005)
- 21 exp clinical trials/ (135479)
- 22 (clinic\$ adj3 trial\$).tw. (68858)
- 23 randomized controlled trial.pt. (166066)
- 24 or/15-23 (438570)
- 25 14 and 24 (526)
- 26 limit 25 to (human and english language and all adult <19 plus years>) (418)
- 27 from 26 keep [SELECTED REFERENCES] (51)
- 28 exp Cohort Studies/ (434756)
- 29 (cohort adj (study or studies)).tw. (14398)
- 30 5 and 12 and (28 or 29) (566)
- 31 30 not 25 (476)
- 32 limit 31 to (human and english language and all adult <19 plus years> and yr=1996-2002) (203)
- 33 from 32 keep [SELECTED REFERENCES] (32)
- 34 27 or 33 (83)

### *Embase*

- 1 fitness/ (4955)
- 2 walking/ (5621)
- 3 exp exercise/ or physical activity/ or cycling/ or jogging/ or running/ or stretching/ or swimming/ (55710)
- 4 or/1-3 (62525)
- 5 exp cardiovascular disease/pc (39853)
- 6 diabetes mellitus/ or insulin dependent diabetes mellitus/ or non insulin dependent diabetes mellitus/ (84276)
- 7 lipid/ (17960)
- 8 Lipoprotein/ec [Endogenous Compound] (5071)

- 9 lipid blood level/ or lipoprotein blood level/ (15774)
- 10 cholesterol blood level/ (19050)
- 11 Glucose Intolerance/ (1968)
- 12 blood pressure/ (34027)
- 13 or/5-12 (190283)
- 14 4 and 13 (7042)
- 15 clinical trial/ (239280)
- 16 randomized controlled trial/ (68221)
- 17 exp meta-analysis/ (14168)
- 18 ((meta adj analys\$) or metaanaly\$.tw. (7912)
- 19 (systematic adj (review\$ or overview\$)).mp. (2986)
- 20 Cohort Analysis/ (11889)
- 21 or/15-20 (257814)
- 22 14 and 21 (932)
- 23 limit 22 to (human and english language and yr=1996-2002) (682)
- 24 limit 23 to adult <18 to 64 years> (349)
- 25 from 24 keep [SELECTED REFERENCES] (39)

### ***Current Contents***

- 1 (hypertension or stroke or myocardial infarction or diabetes).mp. (181093)
- 2 (blood pressure or clotting or lipid\$.tw. (142403)
- 3 cardiovascular disease\$.mp. (19536)
- 4 or/1-3 (295062)
- 5 randomi?ed controlled trial\$.tw. (12407)
- 6 (meta analys\$ or metaanaly\$.tw. (11519)
- 7 (systematic adj3 (review\$ or overview\$)).tw. (3638)
- 8 (clinic\$ adj3 trial\$.tw. (43189)
- 9 (cohort adj (analy\$ or study or studies)).tw. (12598)
- 10 or/5-9 (76252)
- 11 (physical adj (activity or fitness or exercise)).ti. (3144)
- 12 (walking or swimming or jogging or running or sport\$.ti. (10909)
- 13 11 or 12 (13971)
- 14 4 and 10 and 13 (89)
- 15 limit 14 to (english language and yr=1996-2002) (82)
- 16 from 15 keep [SELECTED REFERENCES] (15)

## **SEARCHES FROM OTHER SOURCES**

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In databases and all other sources without controlled vocabulary combinations of the index terms and additional keywords from the above strategies, were used in the search.

## Appendix 2: Excluded papers

### RETRIEVED STUDIES EXCLUDED FOR REVIEW

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Ades, P. A., & Coello, C. E. (2000). Effects of exercise and cardiac rehabilitation on cardiovascular outcomes. *Medical Clinics of North America*, 84, 251-265.

*Subjects rehabilitating from CVD or have existing CVD.*

Berlin, J. A., & Colditz, G. A. (1990). A meta-analysis of physical activity in the prevention of coronary heart disease. *American Journal of Epidemiology*, 132, 612-628.

*Pre-1996 systematic review (CVD reduction outcomes).*

Bernstein, M. S. (2002). Clinical trials for evaluating the benefits of increased levels of physical activity in adults. *Medecine et Hygiene*, 60, 281-288.

*Non-English language (French).*

Blair S. N., Cheng, Y., & Holder, J. S. (2001). Is physical activity or physical fitness more important in defining health benefits? *Medicine & Science in Sports & Exercise*, 33, S379-399; discussion S419-420.

*No relevant outcomes. Meta-analysis.*

Bouchard, C. (2001). Effects of endurance exercise training on plasma HDL cholesterol levels depend on levels of triglycerides: evidence from men of the Health, Risk Factors, Exercise Training and Genetics (HERITAGE) Family Study. *Arteriosclerosis, Thrombosis & Vascular Biology*, 21, 1226-1232.

*Before and after study ("Heritage" study).*

Byberg, L., Zethelius, B., McKeigue, P. M., & Lithell, H. O. (2001). Changes in physical activity are associated with changes in metabolic cardiovascular risk factors. *Diabetologia*, 44, 2134-2139.

*Cross-sectional study, dose-response not investigated adequately relevant to topic.*

Center for Reviews and Dissemination Reviewers. (2002a). Prescription and results of physical activity. *Database of Abstracts of Reviews of Effectiveness*, 4. Review of original article: Fagard R H. (1995). Prescription and results of physical activity. *Journal of Cardiovascular Pharmacology*, 25 (Suppl 1): S20-S27.

*Pre-1996 abstract.*

Center for Reviews and Dissemination Reviewers. (2002b). The role of exercise in blood pressure control: supportive evidence. *Database of Abstracts of Reviews of Effectiveness*, 4. Review of original article: Fagard R H. (1995). The role of exercise in blood pressure control: supportive evidence. *Journal of Hypertension*, 13, 1223-1227.

*Pre-1996 abstract.*

Couillard, C., Despres, J. P., Lamarche, B., Bergeron, J., Gagnon, J., Leon, A. S., Rao, D. C., et al. (2001). Effects of endurance exercise training on plasma HDL cholesterol levels depend on levels of triglycerides: evidence from men of the Health, Risk Factors, Exercise Training and Genetics (HERITAGE) Family Study. *Arteriosclerosis, Thrombosis & Vascular Biology*, 21, 1226-1232.

*Before and after study ("Heritage" study).*

Cox, K. L., Puddey, I. B., Burke, V., Beilin, L. J., Morton, A. R., & Bettridge, H. F. (1996). Determinants of change in blood pressure during S.W.E.A.T.: the sedentary women exercise adherence trial. *Clinical & Experimental Pharmacology & Physiology*, 23, 567-569.

*Study already included in appraised meta-analyses.*

Crouse, S. F., O'Brien, B. C., Grandjean, P. W., Lowe, R. C., Rohack, J. J., Green, J. S., & Tolson, H. (1997). Training intensity, blood lipids, and apolipoproteins in men with high cholesterol. *Journal of Applied Physiology*, 82, 270-277.

*Small sample size (n=26).*

Donnelly, J. E., Jacobsen, D. J., Heelan, K. S., Seip, R., & Smith, S. (2000). The effects of 18 months of intermittent vs. continuous exercise on aerobic capacity, body weight and composition, and metabolic fitness in previously sedentary, moderately obese females. *International Journal of Obesity & Related Metabolic Disorders*, 24, 566-572.

*Small sample size (n=22).*

Dunn, A. L., Marcus, B. H., Kampert, J. B., Garcia, M. E., Kohl, H. W., 3rd, & Blair, S. N. (1997). Reduction in cardiovascular disease risk factors: 6-month results from Project Active. *Preventive Medicine*, 26, 883-892.

*No relevant outcomes (comparing physical activity counseling with structured programmes).*

Durstine, J. L., Grandjean, P. W., Davis, P. G., Ferguson, M. A., Alderson, N. L., & DuBose, K. D. (2001). Blood lipid and lipoprotein adaptations to exercise: a quantitative analysis. *Sports Medicine*, 31, 1033-1062.

*Narrative, non-systematic review.*

Ebrahim, S., & Smith, G. D. (1997). Systematic review of randomised controlled trials of multiple risk factor interventions for preventing coronary heart disease. *British Medical Journal*, 314, 1666-1674.

*Multiple risk factor intervention (including exercise).*

Ebrahim, S., & Smith, G. D. (1998). Lowering blood pressure: A systematic review of sustained effects of non-pharmacological interventions. *Journal of Public Health Medicine*, 20, 441-448.

*Systematic review considering multiple interventions.*

Exercise and cardiovascular disease. *Bandolier*.

Available from: <http://www.jr2.ox.ac.uk/bandolier/booth/hliving/ExcerCVD.html> accessed on: 24.10.02.

*Expert opinion article, Guideline.*

Fagard, R. H. (1999). Physical activity in the prevention and treatment of hypertension in the obese. *Medicine & Science in Sports & Exercise*, 31, S624-630.

*Not directly relevant, and methods not clearly described.*

Fagard, R. H., Staessen, J. A., & Thijs, L. (1996). Advantages and disadvantages of the meta-analysis approach. *Journal of Hypertension - Supplement*, 14, S9-12; discussion S13.

*Background paper on methodological issues.*

Fahlman, M. M., Boardley, D., Lambert, C. P., & Flynn, M. G. (2002). Effects of endurance training and resistance training on plasma lipoprotein profiles in elderly women. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences*, 57, B54-60.

*Subjects are elderly.*

Fone, D. (1998). Primary prevention of cardiovascular disease. *Health Evidence Bulletins Wales*. Available from: <http://hebw.uwcm.ac.uk/cardio.chapter1.html> accessed on: 29.10.02.

*Narrative review.*

Friedman, G. D., Cutter, G. R., Donahue, R. P., Hughes, G. H., Hulley, S. B., Jacobs, D. R., Jr., Liu, K., & Savage, P. J. (1988). CARDIA: study design, recruitment, and some characteristics of the examined subjects. *Journal of Clinical Epidemiology*, 41, 1105-1116.

*Background paper on CARDIA study design.*

Guthrie, J. R., Dudley, E. C., Dennerstein, L., & Hopper, J. L. (1997). Changes in physical activity and health outcomes in a population-based cohort of mid-life Australian-born women. *Australian & New Zealand Journal of Public Health*, 21, 682-687.

*Cross-sectional study, dose-response not investigated adequately relevant to topic.*

Haennel, R. G., & Lemire, F. (2002). Physical activity to prevent cardiovascular disease - How much is enough? *Canadian Family Physician*, 48, 65-71.

*No relevant outcomes. Systematic review.*

Hayashi, T., Tsumura, K., Suematsu, C., Okada, K., Fujii, S., & Endo, G. (1999). Walking to work and the risk for hypertension in men: the Osaka Health Survey. *Annals of Internal Medicine*, 131, 21-26.

*Study already included in appraised systematic review.*

Hillsdon, M., Foster, C., & Thorogood, M. (2002). Interventions for promoting physical activity. *Cochrane Database of Systematic Reviews*, 3.

*No relevant outcomes. Health promotion evaluation.*

Jolliffe, J. A., Rees, K., Taylor, R. S., Thompson, D., Oldridge, N., & Ebrahim, S. (2001). Exercise-based rehabilitation for coronary heart disease. *Cochrane Database of Systematic Reviews*, 1.

*Subjects rehabilitating from CVD or have existing CVD.*

Katzmarzyk, P. T. (2001). Chair summary and contents. *Medicine and Science in Sports and Exercise*, S640-641.

*Expert opinion/narrative review.*

Katzmarzyk, P. T., Leon, A. S., Rankinen, T., Gagnon, J., Skinner, J. S., Wilmore, J. H., Rao, D. C., & Bouchard, C. (2001). Changes in blood lipids consequent to aerobic exercise training related to changes in body fatness and aerobic fitness. *Metabolism: Clinical & Experimental*, 50, 841-848.

*Before and after study ("Heritage" study).*

Kelley, G. A. (1999). Aerobic exercise and resting blood pressure among women: a meta-analysis. *Preventive Medicine*, 28, 264-275.

*Sub-set of Kelley and Kelley (1999), already appraised.*

Kelley, G. A., Kelley, K. S., & Tran, Z. V. (2001). Walking and resting blood pressure in adults: a meta-analysis. *Preventive Medicine*, 33, 120-127.

*Not directly relevant meta-analysis.*

Kelley, G. A., & Sharpe Kelley, K. (2001). Aerobic exercise and resting blood pressure in older adults: a meta-analytic review of randomized controlled trials. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences*, 56, M298-303.

*Not directly relevant meta-analysis.*

Ketola, E., Sipila, R., & Makela, M. (2000). Effectiveness of individual lifestyle interventions in reducing cardiovascular disease and risk factors. *Annals of Medicine*, 32, 239-251.

*No relevant outcomes. Systematic review.*

Kobayashi, Y., Hosoi, T., Takeuchi, T., & Aoki, S. (2001). Benefits of a convenient, self-regulated 6-month walking program in sedentary, middle-aged women. *Japanese Journal of Physical Fitness and Sports Medicine*, 50, 313-323.

*Small sample size (n=14).*

Lamb, S. E., Bartlett, H. P., Ashley, A., & Bird, W. (2002). Can lay-led walking programmes increase physical activity in middle aged adults? A randomised controlled trial. *Journal of Epidemiology & Community Health*, 56, 246-252.

*No relevant outcomes (comparing efficacy of delivery methods for advice on walking schemes).*

Lee, I. M., Rexrode, K. M., Cook, N. R., Manson, J. E., & Buring, J. E. (2001). Physical activity and coronary heart disease in women: Is 'No Pain, No Gain' passe? *Journal of the American Medical Association*, 285, 1447-1454.

*No relevant outcomes. CHD risk.*

Lee, C., & White, S. W. (1997). Controlled trial of a minimal-intervention exercise program for middle-aged working women. *Psychology & Health*, 12, 361-374.

*Methodological problems.*

Leon, A. S., Casal, D., & Jacobs Jr, D. (1996). Effects of 2,000 kcal per week of walking and stair climbing on physical fitness and risk factors for coronary heart disease. *Journal of Cardiopulmonary Rehabilitation*, 16, 183-192.

*Study already included in appraised meta-analyses.*

Leon, A. S., Gaskill, S. E., Rice, T., Bergeron, J., Gagnon, J., Rao, D. C., Skinner, J. S., et al. (2002). Variability in the response of HDL cholesterol to exercise training in the HERITAGE Family Study. *International Journal of Sports Medicine*, 23, 1-9.

*Before and after study ("Heritage" study).*

Manson, J. E., Greenland, P., LaCroix, A. Z., Stefanick, M. L., Mouton, C. P., Oberman, A., Perri, M. G., et al. (2002). Walking compared with vigorous exercise for the prevention of cardiovascular events in women. *New England Journal of Medicine*, 347, 716-725.

*No relevant outcomes (CHD risk).*

Mensink, G. B. M., Ziese, T., & Kok, F. J. (1999). Benefits of leisure-time physical activity on the cardiovascular risk profile at older age. *International Journal of Epidemiology*, 28, 659-666.

*Cross-sectional study, no intervention.*

Miller, T. D., Balady, G. J., & Fletcher, G. F. (1997). Exercise and its role in the prevention and rehabilitation of cardiovascular disease. *Annals of Behavioral Medicine*, 19, 220-229.

*Narrative, non-systematic review.*

Murphy, M. H., & Hardman, A. E. (1998). Training effects of short and long bouts of brisk walking in sedentary women. *Medicine and Science in Sports and Exercise*, 30, 152-157.

*Study already included in appraised meta-analyses.*

Murphy, M., Nevill, A., Neville, C., Biddle, S., & Hardman, A. (2002). Accumulating brisk walking for fitness, cardiovascular risk, and psychological health. *Medicine & Science in Sports & Exercise*, 34, 1468-1474.

*Small sample size (n=21).*

National Heart Lung and Blood Institute. (2001). *National Heart, Lung, and Blood Institute task force report on research in prevention of cardiovascular disease*. Bethesda MD: The Institute. Available from: <http://www.nhlbi.nih.gov/resources/docs/cvdrpt/htm> accessed on 29.10.02.

*Expert opinion article.*

Miyai, N., Arita, M., Miyashita, K., Morioka, I., Shiraishi, T., Nishio, I., & Takeda, S. (2002). Antihypertensive effects of aerobic exercise in middle-aged normotensive men with exaggerated blood pressure response to exercise. *Hypertension Research*, 25, 507-514.

*The meta-analyses included in the Evidence Tables provide coverage of the effects of aerobic exercise on blood pressure. Study does not add new additional evidence.*

Parkkari, J., Natri, A., Kannus, P., Manttari, A., Laukkanen, R., Haapasalo, H., Nenonen, A., et al. (2000). A controlled trial of the health benefits of regular walking on a golf course. *American Journal of Medicine*, 109, 102-108.

*Study already included in appraised meta-analyses.*

Rodriguez, C. J., Sacco, R. L., Sciacca, R. R., Boden-Albala, B., Homma, S., & Di Tullio, M. R. (2002). Physical activity attenuates the effect of increased left ventricular mass on the risk of ischemic stroke: The Northern Manhattan Stroke Study. *Journal of the American College of Cardiology*, 39, 1482-1488.

*Subjects have existing CVD.*

Sesso, H. D., Paffenbarger, R. S., Jr., & Lee, I. M. (2000). Physical activity and coronary heart disease in men: The Harvard Alumni Health Study. *Circulation*, 102, 975-980.

*No relevant outcomes (CHD risk).*

Spate-Douglas, T., & Keyser, R. E. (1999). Exercise intensity: its effect on the high-density lipoprotein profile. *Archives of Physical Medicine & Rehabilitation*, 80, 691-695.

*Small samples size (n=25).*

Sternfeld, B., Sidney, S., Jacobs, D. R., Jr., Sadler, M. C., Haskell, W. L., & Schreiner, P. J. (1999). Seven-year changes in physical fitness, physical activity, and lipid profile in the CARDIA study. *Annals of Epidemiology*, 9, 25-33.

*Cross-sectional study, dose-response not investigated adequately relevant to topic.*

Thune, I., Njolstad, I., Lochen, M. L., & Forde, O. H. (1998). Physical activity improves the metabolic risk profiles in men and women: the Tromso Study. *Archives of Internal Medicine*, 158, 1633-1640.

*Cross-sectional study, dose-response not investigated adequately relevant to topic.*

U.S. Department of Health and Human Services Office of the Assistant Secretary for Planning and Evaluation (2002). *Physical activity fundamental to preventing disease*. Washington, D.C.: The Department.

*Expert opinion article.*

U.S. Preventive Services Task Force (USPSTF) (2002). *Recommendations and rationale: behavioral counseling in primary care to promote physical activity*. Rockville, MD: U.S. Preventive Services Task Force. Available from: <http://www.ahrq.gov/clinic/3rduspstf/physactivity/physactrr.htm>. Accessed on 29.10.02.

*Expert opinion article, Guideline.*

University of Iowa Gerontological Nursing Interventions Research Center (2002). *Brief summary: evidence-based protocol exercise promotion: walking in elders*. Iowa City, IA.: University of Iowa Gerontological Nursing Interventions Research Center.

*Expert opinion article, Guideline.*

Van Dam, R. M., Schuit, A. J., Feskens, E. J., Seidell, J. C., & Kromhout, D. (2002). Physical activity and glucose tolerance in elderly men: the Zutphen Elderly study. *Medicine & Science in Sports & Exercise*, 34, 1132-1136.

*No relevant outcomes.*

Wannamethee, S. G., & Shaper, A. G. (2001). Physical activity in the prevention of cardiovascular disease: an epidemiological perspective. *Sports Medicine*, 31, 101-114.

*Narrative, non-systematic review.*

Wei, M., Macera, C. A., Hornung, C. A., & Blair, S. N. (1997). Changes in lipids associated with change in regular exercise in free-living men. *Journal of Clinical Epidemiology*, 50, 1137-1142.

*Cross-sectional study, dose-response not investigated adequately relevant to topic.*

Williams P. T. (2001). Physical fitness and activity as separate heart disease risk factors: a meta-analysis. *Medicine & Science in Sports & Exercise*, 33, 754-761

*No relevant outcomes. Meta-analysis.*

Wilmore, J. H. (2001). Dose response: variation with age, sex, and health status. *Medicine and Science in Sports and Exercise*, 33, S622-S634.

*Not directly relevant.*

Wilmore, J. H., Green, J. S., Stanforth, P. R., Gagnon, J., Rankinen, T., Leon, A. S., Rao, D. C., et al. (2001). Relationship of changes in maximal and submaximal aerobic fitness to changes in cardiovascular disease and non-insulin-dependent diabetes mellitus risk factors with endurance training: the HERITAGE Family Study. *Metabolism: Clinical & Experimental*, 50, 1255-1263.

*Before and after study ("Heritage" study).*

Wilmore, J. H., Stanforth, P. R., Gagnon, J., Rice, T., Mandel, S., Leon, A. S., Rao, D. C., et al. (2001). Heart rate and blood pressure changes with endurance training: the HERITAGE Family Study. *Medicine & Science in Sports & Exercise*, 33, 107-116.

*Not directly relevant (and methodologically inadequate systematic review) of confounding factors in relationship between BP and exercise.*

Young, D. R., Appel, L. J., Jee, S., & Miller, E. R., 3rd (1999). The effects of aerobic exercise and T'ai Chi on blood pressure in older people: results of a randomized trial. *Journal of the American Geriatrics Society*, 47, 277-284.

*Study comparing effects on blood pressure of two moderate intensity aerobic programs. The effects of these types of exercise programmes on blood pressure are sufficiently covered in the meta-analyses included in the evidence tables. Study does not add new additional evidence.*

Yu-Poth, S., Zhao, G., Etherton, T., Naglak, M., Jonnalagadda, S., & Kris-Etherton, P. M. (1999). Effects of the National Cholesterol Education Program's Step I and Step II dietary intervention programs on cardiovascular disease risk factors: a meta-analysis. *American Journal of Clinical Nutrition*, 69, 632-646

*No physical exercise intervention. Meta-analysis on dietary interventions on CVD risk factors.*

## Appendix 3: Included papers

### STUDIES INCLUDED FOR REVIEW AND APPRAISAL

Asikainen, T. M., Miilunpalo, S., Oja, P., Rinne, M., Pasanen, M., Uusi-Rasi, K., & Vuori, I. (2002a). Randomised, controlled walking trials in postmenopausal women: the minimum dose to improve aerobic fitness? *British Journal of Sports Medicine*, 36, 189-194.

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