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Importance of characteristics and modalities of physical activity and exercise in the management of cardiovascular health in individuals with cardiovascular risk factors: recommendations from the EACPR (Part II)

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Abstract

In a previous paper, as the first of a series of three on the importance of characteristics and modalities of physical activity (PA) and exercise in the management of cardiovascular health within the general population, we concluded that, in the population at large, PA and aerobic exercise capacity clearly are inversely associated with increased cardiovascular disease risk and all-cause and cardiovascular mortality and that a dose–response curve on cardiovascular outcome has been demonstrated in most studies. More and more evidence is accumulated that engaging in regular PA and exercise interventions are essential components for reducing the severity of cardiovascular risk factors, such as obesity and abdominal fat, high BP, metabolic risk factors, and systemic inflammation. However, it is less clear whether and which type of PA and exercise intervention (aerobic exercise, dynamic resistive exercise, or both) or characteristic of exercise (frequency, intensity, time or duration, and volume) would yield more benefit for each separate risk factor. The present paper, therefore, will review and make recommendations for PA and exercise training in the management of cardiovascular health in individuals with cardiovascular risk factors. The guidance offered in this series of papers is aimed at medical doctors, health practitioners, kinesiologists, physiotherapists and exercise physiologists, politicians, public health policy makers, and individual members of the public. Based on previous and the current literature overviews, recommendations from the European Association on Cardiovascular Prevention and Rehabilitation are formulated regarding type, volume, and intensity of PA and regarding appropriate risk evaluation during exercise in individuals with cardiovascular risk factors.

Keywords

Physical activity, exercise, prevention, cardiovascular, risk factors, physical training

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Introduction

Over the last decades, researchers have given increased attention to the effects of physical activity (PA) on health and disease, morbidity and mortality.

Numerous epidemiological studies have provided strong evidence that there are inverse associations between PA and the risk for cardiovascular mortality

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and morbidity. We have reviewed these studies in a previous paper on the importance of characteristics and modalities of PA and exercise in the management of cardiovascular health within the general population in part I.¹ We concluded that in the population at large PA and aerobic exercise capacity clearly are inversely associated with increased cardiovascular disease risk and all-cause and cardiovascular mortality and that a dose–response curve on cardiovascular outcome has been demonstrated in most studies.¹

Several studies have also shown the importance of engaging in regular PA for reducing the severity of cardiovascular risk factors, such as obesity and abdominal fat, high blood pressure (BP), metabolic risk factors, and systemic inflammation.^{2–7} However, at present it is not clear if the type of PA or exercise intervention (endurance exercise, dynamic resistive exercise, or both) or characteristic of exercise (frequency, intensity, time, volume, and duration) would yield more benefit for each separate risk factor.

The present paper, therefore, will review and make recommendations for PA and exercise training in the management of cardiovascular health in individuals with cardiovascular risk factors (part II). After some exercise physiological definitions and background, this paper will focus on the current literature regarding the influence of type and characteristics of exercise on the various cardiovascular risk factors. Part III will then deal with the importance of exercise characteristics in the management of individuals with cardiovascular disease. The guidance offered in this series of papers is aimed at medical doctors, health practitioners, kinesiologists, physiotherapists and exercise physiologists, but also politicians, public health policy makers, and individual members of the public.

Definition and characteristics of exercise interventions

This section briefly covers the various types and characteristics of exercise training interventions. For a more complete definition of PA and physical fitness, we refer the reader to part I of this series of papers.

Aerobic exercise training

The most common modes of exercise are walking, jogging, cycling, and swimming, which, when carried out at moderate intensity, represent good examples of aerobic activity. To achieve a safe exercise training effect, the appropriate intensity, duration, and frequency of exercise should be chosen.

Exercise intensity. Submaximal prolonged walking, jogging, cycling, and swimming are representative types of exercise, usually called aerobic or endurance. Of all the basic elements of exercise prescription, exercise intensity is recently claimed to be an important factor in the development of aerobic fitness and reversion of risk factors.^{8,9} Absolute intensity refers to the rate of energy expenditure during exercise and is usually expressed in kcal/min or metabolic equivalent tasks (METs).^{1,10} Relative exercise intensity refers to a portion of maximal power (load) that is maintained during exercise and is usually prescribed as a percentage of maximal aerobic capacity ($\text{VO}_{2\text{max}}$) on the basis of a cardiopulmonary stress test.¹⁰ Training intensity can also be expressed as a percentage of maximal heart rate (HR_{max}) recorded in a stress test¹¹ or predicted on the basis of an equation stating that HR_{max} equals 220 minus age.^{12,13} We do not recommend the use of prediction equations of HR_{max} for individuals, because of the large standard deviation.¹⁴ Alternatively, exercise intensity can be expressed relative to a percentage of a person's HR reserve (HRR) which uses a percentage of the difference between HR_{max} and resting HR and adds it to the resting HR (Karvonen's formula).¹⁵ There are caveats and cautions to the use of HR for prescribing and evaluating exercise intensity in persons under β -blocker medication.¹⁶ Ideally, the HR derived for training should only be used if the functional capacity (or stress test) was performed under actual medication. Intensity could also be easily monitored using the rate of perceived exertion scale or the breathing rule – 'to be able to talk while exercising'¹⁴ – or arterialized blood lactate concentration^{1,17–19} (Table 1).

Exercise training zones. According to Galen (180 AD), not all movement constitutes exercise but only vigorous movement, which is indicated by remarkable alteration in respiration.²⁰ Nowadays it is accepted that, to enhance cardiorespiratory fitness, exercise should be sufficiently intense to overload the aerobic system. Aerobic fitness is improved when exercise intensity is above the aerobic threshold²¹ and within the aerobic training zone, the boundaries of which are indicated in Table 1. The first aerobic threshold, measured by gas exchange or by lactate levels, is indicative of everyday activities and presumably corresponds to 2 mmol/l lactate, while the second anaerobic threshold emerges from more intense aerobic activities which usually lead to a blood lactate accumulation of 4 mmol/l.^{21,22} For both primary and secondary cardiovascular disease prevention, the target intensity is usually recommended to be close to the second anaerobic threshold.^{11,23} Subsequent to the aerobic threshold is the anaerobic training

Table 1. Relationship among indices of exercise intensity and training zones

Intensity	Lactate (mmol/l)	METs	VO _{2max} (%)	HRR (%)	HR _{max} (%)	RPE scale	Training zone
Low intensity, light effort	2–3	2–4	28–39	30–39	45–54	10–11	Aerobic
Moderate intensity, moderate effort	4–5	4–6	40–59	40–59	55–69	12–13	Aerobic
High intensity, vigorous effort	6–8	6–8	60–79	60–84	70–89	14–16	Lactate, aerobic, anaerobic
Very hard effort	8–10	8–10	>80	>84	>89	17–19	Lactate, aerobic, anaerobic

HR_{max}, maximum heart rate; HRR, heart rate reserve; METs, metabolic equivalents, 1 MET = individual metabolic resting demand, when sitting quiet, about 3.5 ml oxygen/kg/min or 1 kcal (4.2 kJ/kg/h in the general population; RPE, Borg rating of perceived exertion (6–20 scale).

zone (Table 1).^{19,21,22} Cardiorespiratory endurance is also effectively improved as far as training stimulus is applied within this zone (6–10 mmol/l lactate and 14–20 rate of perceived exertion scale), but indicated more for athletic purposes.^{21,22}

Training volume. Exercise intensity is inversely related to exercise time. Their product (in kcal or kJ) defines the volume of each training unit which in turn multiplied by frequency of occurrence results into the energy expenditure of the training bout or session. The rate of applying training sessions and the duration of training period provide total energy expenditure of a training programme. Training volume should increase every week either by 2.5% in intensity⁷ or by 2 min in duration²⁴ although progressiveness of exercise dose is prudent to be tailored according to the biological adaptation of the individual. Training adaptation is also influenced by genetic potential²⁵ and environmental factors, such as dehydration, heat, cold, and high-altitude hypoxia.^{26–28}

Mode of training. Aerobic exercise training can either be continuous or interval. There is a huge amount of evidence and guidance on continuous aerobic exercise which this paper will distil in the following sections. There is also strong evidence emerging for the benefits of interval-type training. The interval design enables the individuals to complete short work periods at high intensities, which are assumed to challenge the pumping ability of the heart.^{29,30} Since intermittent training exposes subjects to near maximal capacity, long-enough rest intervals, preferably active ones, are recommended.³¹ The exercise to rest ratio would ideally be one to one.³² Moreover, interval training is reported to be motivating, since there is a varied procedure during each training session instead of a continuous boring exercise mode and mimics everyday activities.^{29,30} Interval training does not appear to be less safe than continuous training since the higher power output and blood lactate levels in the former type of exercise are accompanied by lower cardiac

stress (rate-pressure product), rate of perceived exertion, and plasma catecholamines.^{33,34}

Resistance training

Exercise intensity. The intensity of resistance exercise is prescribed relatively to 1 repetition performed at maximum weight (1RM). Even though, the performance of 1RM appears to be a safe approach for evaluating strength stimulus^{35,36} and no significant cardiovascular events were reported during it,³⁷ for convenience and compliance reasons the prediction of 1RM from multiple (usually 5) repetition testing (5RM) is suggested.³⁷ It is found that 5RM data produced the greatest prediction accuracy and that 1RM can be accurately estimated from multiple repetition testing.³⁸

Exercise training zones. Training with less than 20% 1RM is considered aerobic endurance training. With more than 20% 1RM, the muscular capillaries start to become compressed during muscle contraction resulting in a cyanotic stimulus responsible for training effects. The number of repetitions should be inverse to the training intensity. A moderate training intensity of 30–50% 1RM with 15–30 repetitions is considered muscular endurance training. Higher training intensities of 50–70% 1RM with 8–15 repetitions are optimal for strength gain.

Training volume. Exercise resistance design could follow a station or a circuit approach. In the former approach, individuals have to finish all the sets for a given exercise per muscle group first and then to move on to another exercise and muscle group. In the second approach, individuals have to perform 1 set of exercise per muscle group and then move on to another exercise and muscle group until completing 1 set. Afterwards, the circuit is followed again until trainees have completed the prescribed sets of each exercise. One to three sets of 8–15 repetitions should be performed for the flexion and extension of each

muscle group. Multiple sets are superior to a single set.^{39,40} A variety to 8–10 resistance exercises should be prescribed to cover most of the muscular groups.¹⁰ Muscular power is best maintained when prescribing 3–5 min rest intervals instead of short rest intervals (<1 min).⁴¹

Mode of training. Resistance training can either be isometric (i.e. unchanged muscle length without joint movement) or dynamic. Isometric (static) muscle actions may, at moderate to high loads, induce Valsalva manoeuvre, if not intentionally avoided by regular breathing, and may lead to an unnecessary fluctuation of BP. Contraction with shortening of the muscle and movement of the joint throughout a range of motion is referred to as dynamic. Dynamic training may include constant or variable resistance through the range of motion using either free weights or weight machines. In both these modes, the type of contraction and the velocity of movement vary throughout the range of motion. This type of muscle activity mirrors muscle loading faced in daily activity. There is one other mode of resistance training and muscle assessment, called isokinetic exercise, where the angular velocity remains constant. Isokinetic muscle action does not exist in daily life but the modality remains popular as a means of assessing muscle strength. Muscles can contract concentrically, when during the movement shortening is exhibited or eccentrically when a lengthening of the muscle occurs. Plyometric resistance training is an advanced application of resistance training where participants carry out a series of rapid concentric and eccentric muscle actions often at a relatively high load. Plyometric training is often used to improve sports-related performance and is beyond the scope of this paper.

It is well known that resistance exercise can result in an extreme increase in BP, but it is also recognized that this does not necessarily have to be the case if an appropriate training volume (weight, number of repetitions, sets) is chosen. The actual BP response to resistance exercise is dependent on the amount of static (isometric) muscle contraction, the actual load (% of individual's 1RM) and the amount of muscle mass involved, the number of repetitions, and total duration of muscular contraction. The highest BP response is reached when multiple repetitions are performed at 70–95% of 1RM to exhaustion.³⁸ Dynamic resistance training with low-to-moderate intensity allows a high number of repetitions (muscular endurance training (15–30 reps); moderate hypertrophy training (10–15 reps) without evoking any major rise in BP. The BP response during this type of training is lower compared to

the increase in BP seen during moderate endurance training. If the Valsalva manoeuvre is carried out during resistance exercise the rise in BP is more pronounced.

Effective exercise training for bodyweight control

Effects of exercise intervention on bodyweight loss in overweight/obesity

In obese individuals, fat mass loss can be achieved with endurance training.^{42–46} As a result of 16 weeks of endurance training without diet, an average weight loss of ~3 kg can be achieved.⁴² A decline of approximately 5–10% of initial bodyweight is associated with significant health benefits, such as a decreased risk for insulin resistance, type 2 diabetes mellitus (T2DM), cardiovascular disease, an improvement in lipid profile, bone metabolism, and BP.^{43–46} However, a different selection of training modalities might be instrumental to further optimize exercise intervention effectiveness. In overweight/obese patients, it is important to reduce fat mass as effectively as possible. The effect of different training modalities during exercise interventions on changes in fat mass in overweight/obese patients, as well as the maintenance of bodyweight loss will be examined and recommendations made in the following section.

Weight loss and characteristics of aerobic exercise training.

The impact of training frequency on fat mass loss during endurance exercise intervention in obese patients was assessed in one study with 23 females: a greater exercise frequency (5 vs. 3 days/week) had the desired effect with a greater fat mass loss (16 ± 4 vs. 13 ± 4 kg, respectively) when following a 12-week exercise intervention.⁴⁷ When comparing low- vs. high-intensity continuous exercise training programmes (with matched energy expenditure between trials), three studies unequivocally report no difference in fat mass loss in obese subjects.^{48–50} In a study comparing the effects of a 12-week high-intensity interval vs. a moderate-intensity continuous exercise regimen (matched for energy expenditure) in obese adults,⁸ it was demonstrated that fat mass declined to a similar extent (by 2.2 vs. 2.5%, respectively). A large number of studies indicate that prolonged exercise intervention results in a significantly greater reduction in fat mass in obese patients, as opposed to short exercise intervention.⁵¹ Studies targeting <150 min/week of PA do not yield a significant change in bodyweight in obese subjects,⁵² >150 min/week of PA reveal modest bodyweight loss of approximately 2–3 kg, whereas PA

between 224 and 420 min/week induce a bodyweight loss of approximately 5–7.5 kg. Extreme amounts of PA result in substantial greater weight loss.^{53,54}

Weight loss and characteristics of resistance training. Resistance training is reported to be medically safe in people with obesity^{52,55,56} and may affect positively cardiovascular disease risk factors,^{57–59} fat-free mass, muscle function, and resting energy expenditure,^{57,59–64} especially when diet is implemented.^{64–66} However, some studies have reported reductions in fat mass after resistance training,^{57,63,67–74} while others failed to reproduce such finding.^{8,52,55,64,75–81} It seems that resistance training in obese people primarily improves body composition by increasing fat-free mass.⁵¹ The contradiction in the literature regarding the impact of resistance training on fat mass in the overweight/obese might, at least in part, be related to the selection of training modalities.

No study has examined the effects of different resistance training frequencies (days/week) during exercise intervention on fat mass in obese subjects.^{8,67,68,80,82} Regarding intensity of resistance training used in the literature, they vary from 50% 1RM⁶⁸ up to 90% 1RM.⁸ In older men, neither moderate- nor low-intensity resistance training, added to endurance training, for 20 weeks affected body composition.⁸³ As to whether isometric, concentric, or eccentric resistance training exercises should be applied to reduce fat mass in the obese remains to be studied. Short-term resistance training (6–8 weeks) significantly improves body composition in overweight or obese subjects.^{73,74,84} Prolonged resistance training intervention results in greater muscle hypertrophy in obese people.^{66,85–87} There seems to be a dose–response relationship between resistance training intensity and biochemical and functional adaptation.^{80,87,88} Multiple resistance training sets were found to be associated with significantly greater strength gains than a single set per exercise during a resistance exercise programme. However, no further benefits for volumes greater than 3 sets were observed.^{89,90}

Combination of types of exercise training and/or diet. The addition of endurance training on top of diet increases bodyweight loss in the long term,⁴² as well as improves cardiovascular disease risk factors and insulin sensitivity.⁹¹ It has been suggested that the combination of resistance training and diet is needed to reduce fat mass in obese subjects.^{84,92,93} In combined interventions even low-volume high-intensity resistance training protocols are found to cause reductions in total and regional fat mass.^{69,94} The effect of implementation of resistance training within an

endurance exercise training programme generally does not induce greater fat mass loss in obese patients.⁵¹

Prevention of bodyweight gain after weight loss as result of exercise intervention

It is reported that individuals who engage in greater amounts of PA after bodyweight loss experience less bodyweight regain than individuals with low-to-moderate PA volumes.^{52,95,96} For general health and disease prevention⁸² or prevention of overweight,⁹⁷ 30 min of accumulated moderate-intensity activity on most, preferably all days of the week is recommended. However, in previously obese subjects, greater exercise volumes might be required to effectively prevent weight regain. Further studies on the impact of exercise modalities to prevent weight regain in the obese are required.⁹⁸

Mini summary

In general, exercise training has positive effects on bodyweight in the overweight/obese. However, it is still debated which PA is most effective e.g. mode, duration or intensity, for reducing fat mass in obesity. Endurance exercise intensity, and addition of resistance training to endurance training intervention, seems not to modulate fat mass loss, while an increase in exercise volume and programme prolongation are effective strategies to augment fat mass loss. The impact of resistance training modalities on fat mass in the obese remains obscure. Further investigation for the prevention of weight and fat mass regain after exercise intervention in the obese seems warranted.

Effective physical activity and exercise training for control of insulin/glucose dynamics

Several studies have clearly shown that regular PA and exercise training is associated with improved insulin sensitivity and a reduced incidence of T2DM.^{99–102} Very few studies compared the different modalities of exercise training on insulin/glucose dynamics.¹⁰³

Control of insulin/glucose dynamics and aerobic exercise training

Sixt et al.¹⁰⁴ assessed the effects of intensive endurance training (4 weeks of 6 × 15 min/day of cycle ergometry followed by 5 months of daily 30-min cycle ergometry at 70% of the maximum HR in addition to supervised group exercise sessions for 1 hour twice a week) as

compared to an antidiabetic, insulin sensitizer drug (rosiglitazone) or usual care on glucose metabolism and endothelial function in patients with established coronary artery disease and impaired glucose tolerance. Four weeks of exercise training, but not rosiglitazone or usual care, improved endothelium-dependent flow-mediated vasodilation. After 6 months of follow up, similar effects were observed.¹⁰⁵ There was a significant improvement in fasting glucose but not in HbA_{1c} both in the exercise as well as the rosiglitazone group, suggesting an independent effect of exercise training on the vessel wall.¹⁰⁶ In a further study, Sixt et al.¹⁰⁷ applied the same protocol as previous outlined and demonstrated, in patients with T2DM, that 6 months of multifactorial intervention led to a significant improvement in coronary endothelial function. There was no correlation between improved markers of acute or chronic hyperglycaemia and improved coronary endothelial dysfunction, suggesting that chronic hyperglycaemia is not the primary factor linking T2DM to endothelial dysfunction. Fasting insulin plasma concentrations and values of the Homeostatic Model Assessment (HOMA) for insulin resistance (IR) and beta-cell function (HOMA-IR) correlated with attenuated coronary vasoconstriction in response to acetylcholine. This suggests that beneficial effects may be primarily mediated by improved insulin sensitivity. In accordance with these findings, there was a continuous increase in the expression of glucose transporters in skeletal muscle (GLUT-4 mRNA) in response to training.

The STENO-2 study called for light-to-moderate exercise of at least 30 min from 3–5 times/week. After an average study period of 7.8 years of intensified therapy, fasting glucose levels as well as glycated haemoglobin (HbA_{1c}) were significantly better in the intervention group than in the control group. Most importantly, a reduction of cardiovascular and microvascular events by 50% was observed.^{108,109}

Control of insulin/glucose dynamics and resistance training

Several study protocols assessed resistance training of all major muscle groups at an intensity of 70–80% 1RM for 2–4 sets per muscle group performed 2–3 times/week.^{110,111} Castaneda et al.¹¹⁰ performed progressive resistance training 3 times/week for 16 weeks in addition to usual care in T2DM. They observed improvements in glycaemic control (HbA_{1c}, muscle glycogen storage), lean body mass, abdominal fat mass, and systolic BP. Fasting plasma glucose, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) levels did not significantly change between groups. Furthermore, progressive resistance training coincided

with a reduction in the dosage of antiglycaemic medication as compared with the control group.

Dunstan et al.¹¹² reported that HbA_{1c} decreased significantly during 6 months of supervised resistance training, but this effect was not maintained after 6 months of home-based training. Increases in upper and lower body muscle bulk were maintained over 12 months. There were no between-group differences for changes in bodyweight, fat mass, fasting glucose, or insulin at 6 or 12 months.

Ishii et al.¹¹³ examined the effect of resistance training on insulin sensitivity in non-obese, T2DM patients. The training programme consisted of nine exercises, 5 times/week (2 sets, 10–20 repetitions) for 4–6 weeks. After training intervention, glucose disposal rate during the hyperinsulinemic euglycaemic clamp increased in the training group but remained unchanged in the control group. No significant change in body composition was observed, whereas quadriceps strength increased as anticipated in the intervention group. Similarly, a 20-week resistance training that induced an overall improvement in glucose tolerance did not lower fasting glucose.¹¹⁴

Contrary to the above studies, Dela and Kjaer¹¹⁵ reported improved insulin-stimulated glucose uptake and improved muscle strength induced by resistance training in both elderly healthy individuals and elderly individuals with chronic diseases like T2DM. Recent data from Sato et al.¹¹⁶ have suggested that the improved effectiveness of insulin on skeletal muscle tissue following resistance training is attributable, at least in part, to increases in local expression of GLUT-4, IRS-1, and PI3 kinase.

Control of insulin/glucose dynamics and the combination of dynamic and resistance exercise training

Praet et al.¹¹⁷ used a combined training protocol of progressive resistance and interval exercise training and reported an increase in muscle strength and exercise performance whereas mean arterial BP, fasting plasma glucose, and non-esterified fatty acids decreased significantly. No significant changes were observed in VO_{2peak}, muscle oxidative capacity, intramyocellular lipid or glycogen storage, and blood glycosylated haemoglobin, adiponectin, tumour necrosis factor α and/or cholesterol concentrations.

Baldi and Snowling¹¹⁸ reported that 10 weeks of resistance training leads to improved glycaemic control, fasting glucose, HbA_{1c}, insulin, fat free mass, muscle strength, and endurance.

Cuff et al.¹¹⁹ compared combined aerobic and resistance training with aerobic training alone and found no

differences in HbA_{1c} levels between groups. The Diabetes Aerobic and Resistance Exercise Study¹²⁰ randomized 251 T2DM patients into one of four groups: aerobic training, resistance training, combined exercise training, and a sedentary control group. Patients in the training groups trained 3 times/week for 22 weeks. The absolute change in HbA_{1c} in the combined exercise training group was superior to changes documented in the control, aerobic, or resistance training groups. Both aerobic or resistance training alone improved glycaemic control, but improvements were greatest with combined aerobic and resistance training.

Marcus et al.¹²¹ compared a 16-week intervention of combined aerobic and high-force eccentric resistance exercise with aerobic exercise only and reported similar improvements in HbA_{1c}, glycaemic control, thigh composition, and physical performance in both training modalities, whereas changes in thigh lean tissue and body mass index were more pronounced in the combined training protocol.

Cauza et al.¹²² reported that resistance training was superior to endurance training with regard to improved HbA_{1c}, blood glucose, and insulin resistance.

Egger et al.¹²³ compared the effects of endurance training combined with either hypertrophy strength training (70–80% of 1RM; 2 sets of 10–12 repetitions) or endurance strength training (40–50% of 1RM; 2 sets of 20–30 repetitions). Hypertrophy strength training led to a significant reduction in fasting glucose levels and fructosamine, whereas no significant differences were detected in the endurance strength training group. A recent review summarized the current evidence about the effects of resistance training on glycaemic control¹²⁴ (Table 2).

Mini summary

Aerobic and resistance exercise alone have beneficial effects on glycaemic control, while a combination of both appears to be superior. If current guidelines on

exercise prescription are being followed (Table 3),^{125–128} beneficial effects on glycaemic control seems to be guaranteed.

Effective physical activity and exercise training for control of blood lipids

Physical activity and exercise in normolipidaemic subjects

It has been demonstrated that increase in PA and exercise training can improve lipid profile, primarily by increasing HDL-C and decreasing triglycerides (TG).^{129–134}

Short-term effects. A single session of exercise in sedentary individuals does not have any effects on lipids. By contrast, athletes display a reduction in plasma TG and an increase in HDL-C following prolonged a single intensive competition, such as marathon running or Nordic skiing. However, these effects last only a few days.^{135,136} It seems that more short-term exercise periods on the same day have a modestly greater effect for achieving transient increases in the HDL-C compared to a continuous similar duration of exercise.^{137,138} Both intermittent and continuous exercise in sedentary subjects decrease TC and LDL-C and increase HDL₂-C as well as the LDL particle size, which are all favourable.¹³⁹

Long-term effects of aerobic activity. Studies on athletes involved in aerobic or endurance activities, such as marathon running, Nordic skiing, and cycling, showed slightly lower levels of TC and LDL-C, markedly lower TG, and significantly higher HDL-C due to a selective increase in the HDL₂-C.^{136,140–142} With regard to plasma apolipoproteins, athletes display higher levels of apoA-I and slightly lower levels of apoB, resulting in a higher apoA-I/apoB ratio while no difference in apoA-II, apoC-II, apoC-III, and

Table 2. Effects of resistance training on glycaemic control – review of the current literature

	Studies	Pre training	Post training	ΔPre/Post
HbA _{1c} (%)	27	8.2 ± 0.8	7.1 ± 0.6	–1.1
Glucose (mg/dl)	17	158.8 ± 23.8	138.6 ± 28.3	–20.3
Insulin sensitivity (clamp) (mg/kg LBM min)	1	6.9 ± 2.8	10.1 ± 3.2	+3.3
Muscle glycogen storage (mmol glucose/kg muscle)	1	60.3 ± 0.0	79.1 ± 5.0	+18.8
Insulin resistance (HOMA)	6	8.1 ± 1.4	4.7 ± 2.2	–3.4
Insulin (pmol/l)	9	131.6 ± 30.8	103.7 ± 15.1	–27.9

Values are mean ± SD; HOMA, Homeostatic Model Assessment; LBM, lean body mass.

Table 3. Exercise prescription in the prevention and management of diabetes: recommendations of selected international associations

	Training mode	Intensity range	Exact intensity	Duration/sets/repetitions
ACSM (2000)	Endurance training	Low – moderate	40–60% $\text{VO}_{2\text{max}}$, RPE 11–13	40–60 min, 3–5 days/week
	Strength training			
	Circuit training	Low–moderate		8–10 repetitions (up to 20), 1–3 sets, 2–3 days/week
	Interval training			
	Free weights			
ADA (2009)	Stretching	Moderate		10–30 s/exercise, 2–3 days/week
	Endurance training	Moderate–high	40–60% $\text{VO}_{2\text{max}}$, 50–70% HR_{max}	150 min/week, 3 days/week
			>60% $\text{VO}_{2\text{max}}$, >70% HR_{max}	90 min/week, 3 days/week
	Strength training	Moderate		8–10 repetitions, 1–3 sets, 3 days/week
AHA (2009)	Endurance training	Moderate–high	<70% $\text{VO}_{2\text{max}}$ >70% $\text{VO}_{2\text{max}}$	150 min/week 90 min/week
	Strength training	Moderate		8–10 repetitions, 3 sets, 3 days/week
ESC (2010)	Endurance training	Moderate		30 min, 5 days/week

ACSM, American College of Sports Medicine;¹²⁷ ESC, European Society of Cardiology;¹²⁸ ADA, American Diabetes Association;¹²⁵ AHA, American Heart Association.¹²⁶ HR_{max} , maximal heart rate; RPE, Borg rating of perceived exertion (6–20 scale); $\text{VO}_{2\text{max}}$, maximal oxygen uptake.

apoE has been reported.¹³⁹ Prospective controlled studies on sedentary subjects have also documented variable, slight reductions in LDL-C, significant reductions in TG, and increases in HDL-C induced by aerobic training.^{136–142} A threshold value of about 1000 kcal has been identified, which is the equivalent of running about 12 km/week, as the energy expenditure required in order to achieve a significant increase in HDL-C.¹⁴³

It can be concluded that aerobic activity in general has favourable effects on plasma lipoprotein profile.

Long-term effects of anaerobic activity. Data are conflicting. While some authors claim that the lipid profile of athletes engaging in anaerobic activities is similar to that seen in those who perform aerobic activities, others have reported no change or even a worsening profile.^{144–146}

It can be concluded that at the moment there are not enough data to claim that anaerobic activity exerts any favourable effects on the lipoprotein pattern.

Long-term effects of resistance training and combined aerobic and resistance training. A recent meta-analysis of the impact of progressive resistance training on lipids indicated that caution may be warranted.¹⁴⁷ Others suggest that combining aerobic and

resistance-type exercise may confer better effect on lowering TG and LDL-C, improving LDL particle size and increasing HDL-C in healthy subjects than aerobic exercise alone.^{148–151}

Physical activity and exercise in hyperlipidaemic patients

Hypertriglyceridaemia. Studies on the effects of exercise in subjects with mildly to moderately elevated TG showed a more marked and longer-lasting reduction of TG in the subjects on diet plus exercise.¹⁵² However, in patients with hypertriglyceridaemia who underwent training, a significant reduction in TG was shown in spite of the fact that the subjects' dietary intake of calories increased.¹⁵³ In moderately hypertriglyceridaemic patients, exercise reduces TG, VLDL, and TC/HDL-C ratio.¹⁵⁴ The degree of TG reduction seems to be independent of the weight loss that accompanied the training and is proportional to the TG level.^{155,156} By contrast, in patients with severe hypertriglyceridaemia, the effects of training are modest and variable.¹⁵⁷

It can be concluded that in moderate hypertriglyceridaemia aerobic physical exercise seems to reduce TG by about 30–40% and to increase HDL-C by about 20%, while only slightly modifying total and LDL-C.^{158,159} There is not enough data to make

clear recommendations about the effects of any type or form of exercise in patients with severe hypertriglyceridaemia.

Hypercholesterolaemia. In patients with moderate hypercholesterolaemia, exercise seems to increase HDL-C and decrease TG, while TC and LDL-C do not correlate with the amount of exercise.^{160–163} In patients with mild hypercholesterolaemia and ischaemic heart disease, exercise training within the framework of a programme of cardiovascular rehabilitation, in addition to exerting positive haemodynamic effects and improving physical performance also increases HDL-C^{164,165} but induces only a slight reduction in TG.¹⁶⁶ It seems that, in high-risk subjects, exercise induces a decrease in apoB and an increase in LDL-C/apoB ratio thus suggesting favourable changes in the size of LDL particles, i.e. less small dense LDL particles which are more atherogenic.¹⁶⁷

There are only a few studies on patients with severe hypercholesterolaemia and combined dyslipidaemia, i.e. with elevated cholesterol and TG.^{168,169} Such studies have often been non-controlled and have yielded somewhat conflicting results. Studies on familial hypercholesterolaemia and on combined familial dyslipidaemia are totally lacking.

In conclusion, exercise does not seem to substantially modify TC or LDL-C in hypercholesterolaemic patients. It does appear, however, to reduce TG by 6–18% and to increase HDL-C by 7–16% in patients with increased both TC and TG, i.e. in combined hyperlipidaemia.^{158,159}

Mini summary

It has not yet been established how much exercise is required in order to improve the lipid pattern and, more generally, to reduce cardiovascular risk. The data currently available seem to indicate that a moderately intense aerobic exercise programme is sufficient to improve TG and HDL-C, while a more demanding regimen does not offer further significant advantages. It seems that the amount of exercise, in terms of overall energy expenditure, is of greater importance than the intensity of training. A threshold value of about 1000 kcal/week has been identified as the energy expenditure required in order to achieve a significant increase in HDL-C. Moderate PA involving energy expenditure greater than 1000 kcal/week, and carried out at intensity equal to 75–85% of the HR_{max} would therefore prove efficacious, safe, and easily practicable for the majority of individuals. Recent data, however, seem to suggest that high-intensity aerobic interval training could increase HDL-C more than moderate-intensity continuous training in patients with metabolic

syndrome. Exercise training should be scheduled in 3–4 sessions/week of at least 20 min each and should involve aerobic activity, such as brisk walking, jogging, or cycling. Moderate-intensity resistance exercise can efficaciously be combined with this in order to improve musculoskeletal efficiency and to increase lean body mass.

Effective physical activity and exercise training for control of blood pressure and arterial compliance

Hypertension is defined as a systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg or being on antihypertensive treatment. BP in excess of 140/90 mmHg is further categorized in terms of severity, defined as stage 1–3.^{170,171} Although BP $< 140/90$ mmHg was once considered normal, the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High BP now includes the category of prehypertension, defined as the pressure range between 120/80–139/89 mmHg.¹⁷⁰ Only pressures below 120/80 mmHg are considered optimal¹⁷¹ or normal.¹⁷⁰ Further, a decrease in arterial compliance has been recognized as an important independent cardiovascular risk factor and has been implicated in the development and progression of hypertension.¹⁷² Lifestyle changes, including an increase in PA, are recommended in the prevention, treatment, and control of BP.

Endurance exercise training, blood pressure and arterial compliance

A number of meta-analyses investigating the effect of endurance training on BP have been performed.^{173–177} The most recent meta-analysis, including 72 randomized controlled trials, 105 exercise training groups, and 3936 participants, showed that the average net change of systolic BP/diastolic BP was -3.0 (-4.0 to -2.0)/ -2.4 (-3.1 to -1.7) mmHg ($p < 0.001$). Further, net BP changes were greatest in the hypertensives compared to the normotensives. These results were obtained with training programmes that involved endurance exercises for an average of 40 min/session, 3 times/week, at an intensity of 65% of HRR.¹⁷⁷ The effect of endurance training on arterial compliance showed significant, clinically meaningful, positive effects in healthy individuals^{178,179} dominantly on central arterial compliance, but no impact on arterial compliance in hypertensive subjects.^{180,181}

Investigating the role of different exercise characteristics, it was shown that training frequencies of 3–7 times/week lowered BP to a similar extent.¹⁷⁷ However, Tully et al.¹⁸² observed a slightly larger,

although not significant, BP reduction in participants randomized to the 5-day walking group compared to those randomized to the 3-day walking group. Similarly, Jennings et al.¹⁸³ in normotensives and Nelson et al.¹⁸⁴ in hypertensives found that the fall in BP was significantly greater on a 7 times/week schedule than when the participants exercised 3 times/week. Importantly, during the last two decades, several investigators have shown that a single bout of exercise may result in immediate BP reductions that persist for a major portion of the day.¹⁸⁵

Current guidelines recommend endurance training at 'moderate intensity'.^{82,170,171,186} However, meta-regression analysis could not demonstrate a significant relation between changes in BP and training intensity.^{173,177} In addition it has recently been shown that exercise at lower intensity (30% of HRR) was as effective for reducing resting SBP (SBP during submaximal exercise and recovery from exercise) as an identical exercise training programme at higher intensity (66% of HRR), and this was in older sedentary subjects.¹⁸⁷

Given that a lack of time is a frequently cited barrier to PA a recommendation that allows individuals to perform short bouts of activity throughout the day rather than having to put aside a continuous time slot of 30–40 min seems attractive. Chronic intervention studies comparing continuous (e.g. 40 min) vs. intermittent exercise (e.g. 4 × 10 min) found similar decreases in BP, with no differences between the two patterns of exercise.¹⁸⁸ Furthermore, roughly similar BP reductions were observed following an acute session of 10, 15, 30, and 45 min of aerobic exercise at 70% of $\text{VO}_{2\text{peak}}$.¹⁸⁹

Finally, no difference in BP reduction has been observed between these different types of endurance training, like walking, jogging, cycling, or a combination of these.¹⁷⁷

Resistance training, blood pressure, and arterial compliance

Contrary to the large amount of evidence on the benefits of endurance training on BP, research on the effect of resistance training is less compelling. According to two different meta-analyses^{190,191} a distinction should be made with regard to type of resistance training, i.e. dynamic resistance training vs. isometric/static resistance training.

In a meta-analysis¹⁹⁰ involving mainly supervised progressive dynamic resistance training programmes which were performed on average 3 times/week at a mean intensity of 76% of 1RM and incorporated approximately eight exercises/session for arms, legs, and trunks and 3 sets/exercise, an overall weighted net change in resting systolic BP of -2.7 (-4.6 to

-0.78) mmHg and in diastolic BP of -2.9 (-4.1 to -1.7) mmHg was found. Though, contrary to dynamic endurance training, reductions in BP were smaller and not significant in the 101 hypertensive individuals.¹⁹⁰ Training intensity was not a significant determinant of the observed BP reductions after dynamic resistance training.¹⁹⁰ Similarly no significant difference could be observed after static or isometric leg exercise, 3 times/week for 8 weeks at low (10% of 1RM) or high intensity (20% of 1RM).¹⁹²

Results on the effect of dynamic resistance training on arterial compliance are heterogeneous. A 4-month dynamic resistance training programme (80% of 1RM) in 28 healthy men caused a significant decrease in carotid arterial compliance of 19% and an increase in stiffness index of 21% returning baseline levels during a 4-month detraining period.¹⁹³ By contrast, others could not demonstrate a significant change in arterial compliance after 3 months of concentric exercise of big muscle groups at 70% of 1RM¹⁹⁴ or 80% of 1RM¹⁹⁵ in healthy men and/or women, respectively.

No more than three randomized controlled trials, involving 81 men and women, could be included in the most recent meta-analysis on the effect of isometric resistance training on BP.¹⁹¹ The observed reduction in BP (-13.5 (-16.5 to -10.5)/ -6.1 (-8.3 to -3.9) mmHg) suggests that isometric handgrip exercise may be efficacious for reducing resting SBP and DBP; however, the generalization of these findings is limited given the small number of studies included. No data are available with regard to the effect of isometric resistance training on arterial compliance. High-intensity isometric exercise such as heavy weightlifting should be avoided.^{171,186}

With regard to the mode of dynamic resistance training, all dynamic resistance exercises involve movements of the arms, legs, and/or trunk, which is likely to introduce an aerobic component to the work out as suggested by the significant increase in $\text{VO}_{2\text{max}}$.¹⁹⁰ Furthermore, there were no differences in the BP reduction between conventional resistance training programmes or circuit protocols.¹⁹⁰

Mini summary

The recommendations in Table 4 are expected to result in a control and/or lowering of BP. Ideally, exercise prescription aimed at prevention or management of hypertension requires endurance exercise, supplemented by resistance exercise on most, preferably all days of the week. Exercise should be performed at moderate intensity for a minimum of 30 min of continuous or accumulated PA day. Given that a single bout of low-intensity exercise can cause acute reductions in BP that lasts several hours, augmenting or contributing

Table 4. Minimum exercise prescription recommendations in the prevention and management of hypertension

Mode	Intensity	Duration	Frequency
Aerobic (endurance) (walking, cycling, jogging, running)	Moderate: 40–60% of HRR or 12–13 RPE	30 min	5 days/week
	OR		
	Vigorous: 60–84% of HRR or 14–16 RPE	20 min	3 days/week
Resistance (strength) (progressive weight training using major muscles, bodyweight exercise, theraband exercise)	8–12 repetitions resulting in substantial fatigue	One set of 8–10 exercises (multiple sets if time allows)	2 or more non-consecutive days/week

HRR, heart rate reserve derived from individual maximal exercise testing; RPE, Borg rating of perceived exertion (6–20 scale). Combinations of moderate- and vigorous-intensity aerobic activity can be performed to meet the weekly recommendations (e.g. 2 × 30 min moderate sessions and 2 × 20 min vigorous sessions). Adapted from Sharman & Stowasser.¹⁹⁶

to the reductions in BP resulting from chronic exercise, daily exercise should be emphasized in the hypertensive patient. Furthermore, just as one BP drug and one dose are not suitable for all patients, one exercise prescription is unlikely to fit all individuals but requires individualization. With regard to arterial compliance, endurance training dominantly improves arterial stiffness while resistance exercise may have either a positive or a negative effect dependent on the intensity of exercise. However, clearly more research is needed before firm recommendation can be made on exercise and arterial compliance.

Effective physical activity and exercise training for control of new emerging cardiovascular risk factors (haemostasis, inflammation)

Inflammatory responses after acute and chronic endurance exercise are well documented^{197,198} while the evidence regarding the post-exercise haemostatic state is limited. Large variability in exercise protocols, training, and health status of studied populations and analytic methods may influence the expression of the circulating markers of inflammation and haemostasis and interfere with the objective interpretation of study results.¹⁹⁹ Interleukin-6 (IL-6) is the earliest and most marked cytokine response after strenuous exercise, which also triggers the hepatic C-reactive protein (CRP) synthesis exponentially.^{198,200–202} The increases in IL-6 with resistance training seem to be of a lesser magnitude than those seen in endurance exercise.²⁰³ A single bout of high-intensity exercise is also accompanied by a protective up-regulation of the anti-inflammatory cytokines including the IL-1 receptor antagonist, tumour necrosis factor

(TNF) receptors, IL-10, IL-8.¹⁹⁸ Similarly, bouts of resistance training produce an increase in IL-10^{204–205} but there were no changes in levels of TNF- α and IL-1 β .²⁰³ Studies comparing different levels of exercise intensities indicate that significant activity of factor VIII (FVIII) with concomitant variations of the von Willebrand Factor is observed only at the highest work intensities.^{206,207} Dynamic exercise is associated with shorter activated partial thromboplastin time whereas alterations of prothrombin time and plasma fibrinogen remain equivocal.^{208,209} A global increase in fibrinolytic activity has also been reported after acute exercise.²¹⁰

Accumulating data from cross-sectional studies point consistently to an inverse association between inflammatory markers and long-term PA.^{197,211–215} Individuals with high physical fitness level have CRP levels 25–40% lower than those of the least fit or least active individuals. The type of exercise (greater in swimmers than in rowers, in joggers than in cyclists) influences the effects of exercise training on CRP even after adjusting for confounding factors.^{197,212,216} Only few studies failed to confirm this inverse relationship, most likely because of the high proportion of sedentary subjects recruited.^{216,217} Physical activity decreases resting levels of IL-6 and TNF- α and, ultimately, CRP production, by reducing obesity and leptin, by increasing adiponectin and insulin sensitivity, and possibly by its antioxidative effects.^{198,202} The exercise-related anti-inflammatory effect is characterized by the modification of cytokine production from other sites besides adipose tissue, such as skeletal muscles and mononuclear cells, and by stimulating the production of atheroprotective mediators such as IL-10, IL-1 receptor antagonist, and TNF receptors.¹⁹⁷

The overall effect of long-term resistance training appears to attenuate inflammation but with unclear

effects on specific markers. Several studies demonstrated significant increases in anti- and in pro-inflammatory cytokines after resistance training, but the magnitude of the pro- to anti-inflammatory ratio is not yet well defined.²¹⁸ High-intensity work load appears to elicit a more favourable response of cytokine release whereas adaptations to training may be responsible for blunted cytokine responses.^{203,219} Limited research has examined the effects of different exercise training modalities or characteristics on inflammatory system in controls. One study assigned 87 older adults to cardiovascular, flexibility, and resistance exercises and showed reduced serum levels of IL-6, IL-8, and CRP post intervention in the cardiovascular exercise group but there were no differences in the flexibility and resistance exercise groups.²¹⁴

Regular PA is associated with lower levels of fibrinogen, von Willebrand Factor, coagulation FVIII and FIX, and D-dimer.^{216,220} Studies have shown that long-term exercise stimulates endogenous fibrinolysis, as expressed by dose-dependent reduced plasma tissue plasminogen activator antigen levels.^{216,220} Contradictory results on post-exercise coagulant and fibrinolytic responses may reflect differing adaptations with ageing and endothelial responses to exercise protocols.²⁰⁹

Consideration of age and sex

Exercise training is associated with reduced systemic inflammation also in the elderly but because of their physical or cognitive limitations the appropriate intensity is difficult to be determined.²¹⁶ Resistance training programmes may assist in improving age-related loss of muscle mass and muscle strength and reducing low-grade inflammation.²²¹ Advanced age appears also to influence the behaviour of many haemostatic parameters, by age-dependent endothelial dysfunction.^{207,209}

Gender-related differences in baseline inflammatory status are largely attributable to body fat. Some studies reporting on sex differences with respect to inflammation have shown an inverse association between PA level and CRP in men but not in women even after adjusting for menopausal status and hormone therapy use.^{222,223} The lack of association between CRP and PA in women may be due to the greater tendency of women vs. men to be inactive during leisure time or to the adaptation of different types of PA.²²⁴

Mini summary

Regular PA improves inflammatory profile and exerts antithrombotic effects, thereby contributing to the cardioprotective impact of exercise. Further research is required to identify the pathophysiological links

between inflammatory pathways and cardiorespiratory fitness along with the underlying genetic regulatory elements. Randomized controlled trials are warranted to investigate the type, dose, and intensity of PA needed to achieve beneficial effects.

Effective physical activity and exercise training for control of anxiety and depression

Anxiety

A level of anxiety exists in the general population and is particularly common in people with heart conditions, with prevalence up to 70% in patients who have experienced an acute cardiac event and long-term prevalence in up to 25% of patients with cardiovascular disease.^{225,226} Whether anxiety increases risk of coronary heart disease or leads to a poorer prognosis is still uncertain.^{225,227–231} Early meta-analyses have reported on the effect of exercise on anxiety symptoms in primarily healthy adults and in coronary patients.^{232,233} A recent systematic review and meta-analysis of exercise training of anxiety in patients with a chronic illness included 40 randomized controlled trials published between 1995 and 2007 with a total of 2914 patients (mean age 50 years, 59% women). The review compared exercise training with no treatment or as an addition to standard care and concluded that 3 or more weeks of exercise training resulted in significantly reduced anxiety symptoms.²³⁴ The overall mean effect was 0.29 SD (95% CI 0.23–0.36), i.e. a moderate effect. Effect did not differ with age, gender, or type of chronic disease, which were mainly cardiovascular disease, musculoskeletal disorders, cancer, chronic obstructive pulmonary disease, and psychological disorders. Also acute bouts of exercise have been demonstrated to result in a reduction in anxiety and panic symptoms, including in experimental settings.^{232,235–239}

Type and dosage of exercise. The intensity of exercise necessary to produce an anxiolytic effect is unclear. One study comparing six sessions of exercise at low-intensity (walking) with high-intensity (60–90% HR_{max}) exercise in 54 patients found that, whereas both reduced anxiety sensitivity, high intensity was more efficient.²⁴⁰ In contrast, a study of 80 healthy elderly patients found that light exercise improved anxiety scores but higher intensity did not have additional beneficial effect.²⁴¹ In the meta-analysis described above, effect did not differ with exercise intensity or whether intervention resulted in increased levels of fitness. There was, however, a significantly greater effect of exercise sessions that exceeded 30 min compared with shorter or unspecified durations and, surprisingly, also greater effect of programmes

running over 3–12 weeks than of longer duration. No difference with type of exercise (aerobic, resistance, or combined) could be found.²³⁴ However, few studies focused on exercise modality and further research is needed to clarify the dose–response relationship between exercise training and alleviation of anxiety.

Depression

Depression is a common condition affecting one in five over a lifetime. Major depression affects 15–20% of myocardial infarction patients²⁴² and is associated with poorer prognosis^{227,243–245}, although whether the association is directly causal or mediated/confounded by behavioural risk factors remains unclear.²⁴⁵ There is no clear evidence that pharmacological treatment of depression alters prognosis in coronary heart disease.^{246,247}

Exercise and depression have a bidirectional relationship: physically active persons are less likely to develop depression²⁴⁸ and, conversely, depression is a significant risk factor for development of a sedentary lifestyle.²⁴⁹ Regardless of causality, exercise may alleviate symptoms of depression and is part of established treatment of depression.²⁵⁰

A Cochrane systematic review and meta-analysis including 23 randomized controlled trials comparing exercise with no treatment or a control intervention comprising 907 patients found that exercise improved depression by SD -0.82 (95% CI -1.12 to -0.51), i.e. a large clinical effect.²⁵¹ There were more women than men in the studies and a wide range in mean ages (22–87.5 years). When including only the three highest quality studies comprising 216 patients, effect size was reduced to -0.42 SMD (95% CI -0.88 to -0.03), i.e. a moderate improvement of borderline significance. Other recent reviews have reached similar conclusions.^{237,252–256} Exercise training also appears to be a viable treatment option for elderly patients^{254,255} and medically ill patients with co morbid depression: exercise has been shown to reduce depressive symptoms in patients with coronary heart disease^{257–259} and pulmonary disease²⁶⁰ and may improve cognitive function in the elderly and patients with signs of dementia.^{261,262}

Type and dosage of exercise. Most studies showing effect of exercise have employed aerobic exercise (endurance training). In the systematic review, the SD for aerobic exercise indicated a moderate clinical effect (SD -0.63 , 95% CI -0.95 to -0.30), whilst the SDs for both mixed exercise (SD -1.47 , 95% CI -2.56 to -0.37) and resistance exercise (SD -1.34 , 95% CI -2.07 to -0.61) indicated large effect sizes, but confidence intervals were wide.²⁵¹ Studies directly comparing endurance training with resistance training in

patients with depression are lacking. Results, however, suggest that resistance training and mixed exercise may be substituted for aerobic training according to patient preference.

The Cochrane review could not determine the role of different intensity, duration, and frequency of exercise delivery.²⁵¹ Role of intensity of exercise was included in two studies. In one study, high- and low-energy exercise 3 or 5 times/week over a 12-week period were compared ($n=80$). The study showed superior effect of high-energy exercise on depressive symptoms whereas frequency (3 vs. 5 times/week) was not of importance. In another study of elderly depressed persons ($n=60$), high-intensity resistance training 3 days/week for 8 weeks was superior to low-intensity training.²⁶³ Higher-intensity exercise will lead to higher level of fitness. However, improved cardiovascular fitness may not be necessary to improve symptoms and correlations between level of fitness and effect on mood have not been consistent.²⁵¹ The meta-analysis has shown no clear relationship between duration of intervention and effect and no effect of whether exercise was supervised or not or whether it was performed indoor or outdoor.²⁵¹ These findings suggest that it is the effect of exercise itself, which is of benefit, rather than potential side-effects such as social support. However, concerns about methodological quality of trials leading to possible overestimation of treatment effects should be considered.^{251,255} Future research should also focus on defining the optimal dose of exercise training to achieve a favourable effect, as well as differences in effectiveness between aerobic exercise and other forms of training, such as resistance training, in individuals with depressive disorders.

Mini summary

Anxiety and depression have been linked to development of ischaemic heart disease and both are common in patients who have established heart disease. Based on randomized controlled trials, exercise training has been shown to alleviate both anxiety and depression. Most studies have used moderate-intensity aerobic exercise. At present there is insufficient data to give more specific recommendations on type, dosage, and intensity of exercise.

Lifestyle approaches to increase physical activity and exercise in persons with increased cardiovascular risk

Individuals with increased cardiovascular risk factors are targeted with lifestyle approaches to increase PA, as they constitute a high-risk group for future cardiovascular events.²⁶⁴ Different intervention methods are

needed, with the ultimate goal of all these lifestyle approaches is the increase in PA and the continued adherence to a higher level of activity.

In the promotion of PA in individuals with increased cardiovascular risk factors, the healthcare sector has a unique role. It reaches a large part of the population, and can offer individual expertise advice. About 65–70% of the population will meet a doctor at least once during a year,²⁶⁵ providing opportunities for lifestyle information. US figures are even higher.²⁶⁶ Healthcare professionals are considered as the most credible and respected source of health-related information²⁶⁷ and are recommended to routinely inform and counsel the patient on how to be regularly physically active,^{268–272} i.e. to ‘act in the best interest of the patient’ and ideally to involve activity counselling.²⁷³

Patients with increased risk of cardiovascular disease may be identified as part of a population screening strategy,²⁷² applying risk score stratification, or as opportunistic screening in a general practitioner setting.²⁶⁴ Patients with first degree relatives with early onset cardiovascular disease, patients with T2DM, hypertension, hypercholesterolaemia, and obesity, for example, should be targeted for intervention following existing guidelines,²⁶⁴ which include increased PA.

The evaluation of various approaches to increase PA in patients is difficult, because of the vast difference in the methods used, the type of activity prescribed, and the evaluation method chosen. Importantly, there is a gap between research in controlled conditions and the real life situation in everyday practice. Thus, the translation of health promotion research to practice remains a challenge.^{274,275} Furthermore, many of the suggested approaches to increase PA have been studied in the normal population, and not specifically in patients with increased risk.

General advice

The most common and the least complex approach to increase PA is general advice. Many physicians in primary care believe this is important, but advice is still underutilized,^{274,276–278} as only about 50% of them counsel sedentary patients on PA.^{277,279} In US studies, only 20% of consultations resulted in advice on increasing PA²⁸⁰ and only one-third of adults report exercise counselling at their last medical visit.²⁸¹

Most earlier reviews had shown a moderate increase in PA level in the short term (up to 8 weeks) by advice, but no significant long-term effects.^{282–284} The Swedish Council on Technology Assessment systematic review found that PA could be increased by 12–50% in 6 months by advice and counselling on PA only,²⁷¹ but the recent systematic review from the Swedish National Board of Health and Welfare found low efficacy of this

method for increasing PA in patients with cardiovascular risk factors.²⁸⁵

Advice on PA with additional support

In addition to oral advice on increasing PA, the physician may offer adjuvant therapy such as written advice, step counters, and follow ups. In a US study, only 40% of the individuals receiving oral advice, also received support in the form of a plan for PA or a follow-up visit.²⁷⁶ Counselling of PA supplemented by written prescription, diaries, pedometers, and information brochures may increase PA by another 15–50% in 6 months.²⁷¹ A Cochrane review²⁸⁶ found that advice on PA and continued support could increase PA in adults. A review of four systematic reviews found that brief advice from the general practitioner, supported by written materials, has a modest short-term effect on PA lasting 6–12 months.²⁸⁷ Importantly, the Swedish 2010 systematic review concluded that advice on PA with additional support (step counters, prescriptions, and follow up) had good efficacy for increasing the PA level in individuals with increased cardiovascular risk factors, giving this method a high priority within health care.²⁸⁵

Advice on PA using theoretical behavioural techniques

Additional support by cognitive and behavioural strategies in promoting PA have been tried.^{288,289} Most studies are based on the transtheoretical model or on similar models, with some positive effects.^{271,290} However, the US Preventive Services Task Force study concluded that there was insufficient evidence for the efficacy of behavioural counselling in the primary care setting,²⁹¹ as did the recent Swedish review of ‘methods to change lifestyle behaviour’.²⁸⁵

Exercise prescription and exercise referral

More complex methods or approaches for promotion of PA have also been tried. The most common methods are the ‘PA on prescription’ and the closely related method of ‘exercise referral schemes’.^{292–295}

Exercise referral scheme. The exercise referral scheme includes, by definition, referral of the individual by an appropriate professional to a service with a formalized process of assessment of the status and need of the patient, development of a individualized PA programme, and monitoring of the individual and follow up.²⁹⁶ This model is currently used in the UK and Denmark and often includes a referral to a 2–3-month exercise programme run by the local

exercise facilities.^{293,297,298} Exercise referral schemes have been evaluated in several (systematic) reviews^{293,297–300} showing an effect on the level of PA after 12 months²⁹⁹ and a small effect on the level of PA in sedentary people.³⁰⁰ Morgan²⁹³ found that exercise-related schemes may increase PA in slightly active individuals, older adults, and patients who are overweight. Sorensen et al.²⁹⁴ found a positive effect of PA counselling in six out of 12 studies. Exercise referral schemes in England and Wales resulted in a statistically significant increase in the proportion of sedentary people becoming moderately active.²⁸⁷

Physical activity on prescription

PA on prescription (PAP) involves counselling by the healthcare professional, resulting in a written prescription. However, the actual extent of the intervention may vary greatly in different countries and in different healthcare settings. PAP is used in Sweden,^{295,301,302} Australia, New Zealand, and Finland with variations on who gives the advice on PA, the use of written prescriptions or not, the actual PA prescribed, and the extent of additional support (pedometers, motivational support, and follow up), used.

A recent randomized controlled study in Spain³⁰³ showed a small, but significant increase in PA in physically inactive patients receiving information on PA and an exercise prescription, without other support. A more extensive approach of PAP has been evaluated in Sweden by several studies in the last years. Kallings et al.²⁹⁵ showed the efficacy of PAP in the setting of general practice, increasing the PA level after 6 months. In a randomized controlled setting, PAP was shown to increase the level of PA in overweight individuals and to reduce cardiovascular risk factors.³⁰⁴ Furthermore, the self-reported adherence to the PA prescribed was 65% at 6 months,³⁰¹ which is in line with earlier reports on adherence to medications (World Health Organization). Leijon et al.³⁰² subsequently showed that the efficacy of PAP to increase PA was extended to at least 12 months. Further studies are needed to explore the long-term effects of PAP over 24 months or longer.

Barriers to increased PA

Studies have shown that healthcare professionals think that the main obstacles to exercise advice is the low motivation of the patient,^{305,306} the lack of time, and support from the healthcare system (by reimbursements for example)^{307,308} as well as lack of knowledge and education on benefits of PA.^{308,309} Interestingly, the PA level of the healthcare professional themselves influence their counselling habits,³¹⁰ as recently reviewed by

Lobelo et al.,²⁶⁷ indicating the importance of the physicians own level of motivation. Unfortunately, the proportion of medical students perceiving PA counselling as highly relevant decreased significantly from the first year to the fourth year of medical school.³¹¹

Mini summary

Different lifestyle approaches to increase PA and exercise in persons with cardiovascular risk factors are needed in the healthcare system. The traditionally most common method, general advice without additional support, seems to have a low efficacy for increasing the PA level in persons with increased cardiovascular risk.

Systematic lifestyle approaches in health care, such as exercise referral schemes and exercise on prescription, have shown promising results in improving the level of PA and also on the reduction of cardiovascular risk factors. These approaches need further evaluation regarding long-term effects and cost–benefit aspects, as well as for external validity in routine clinical care in different countries and healthcare systems.

Precautions and safety for at risk individuals participating in PA and exercise

For the benefits of PA to be realized, the safe participation in exercise has to be ensured. In this perspective, requisite safety measures in the healthcare setting and at sports and exercise facilities are also part of the overall preventive strategy as recommended by the European Association for Cardiovascular Prevention and Rehabilitation (EACPR).

There is evidence that increasing PA is associated with a beneficial effect on the general health²⁶⁴ but also that vigorous physical exertion in risk individuals is associated with an increased risk for sudden cardiac death (SCD).^{312,313} In middle-aged male athletes, the incidence of SCD is around 6/100,000.³¹⁴ The appropriate precautions and safety measures will vary according to the individual (age, risk factors) as well as the setting (elite sports, exercise programme, type of activity).³¹⁵

Advice for safe exercise and sports participation in the young and apparently healthy individual

A higher rate of SCD has been reported (2.1 cases/100,000 athletes/year),³¹⁶ in young (<35 years) competitive athletes compared to non-athletes. The most common cause of death in younger athletes is inherited and/or unknown cardiac abnormalities,³¹⁷ the most common being hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, congenital

coronary artery anomalies,^{316,318} and to a lesser extent ion channelopathies (long QT-syndrome or Brugada syndrome).^{316,319,320}

Cardiovascular screening of athletes recommended by the European Society of Cardiology (ESC) to decrease SCD during sports consists of personal history (family history and alarming symptoms), physical examination, and resting electrocardiogram³²¹ and has shown promising results on mortality.³²² Cardiac screening programmes are now widely implemented by the sporting organizations.³²³

Advice for safe exercise and sports participation in adult/senior individuals

In untrained individuals that are subjected to high-intensity exercise, the acute physical stress is linked to an elevated risk for sudden cardiac arrest,^{312,313,324,325} with sedentary individuals with underlying coronary artery disease having the highest risk.^{312,326} Habitual exercise training may diminish the risk of acute myocardial infarction and SCD in patients with coronary artery disease.³²⁷

In adult and senior individuals (>35 years), silent or symptomatic coronary artery disease is by far the most common underlying cause of SCD. Advice for safe exercise participation must deal primarily with identification of individuals at increased risk of coronary-induced events, by means of systematic risk stratification before starting a training programme/leisure-time exercise.³¹⁵ The risk stratification includes:

1. Self assessment of risk and habitual exercise: the first step in the risk stratification may be self-assessment, using standardized protocols for example PAR-Q.³¹⁵ In case of a positive self-assessment, further evaluation by a physician should take place.
2. Medical history and physical examination: specific attention should be given to current discomforts (in particular if these are induced by exercise), pre-existing cardiovascular illness, risk factors, family history, and medication use.³²⁸ The individual risk profile could thus be estimated from:
The burden of known classical risk factors, age, sex, smoking, BP, and total cholesterol level together with diabetes, according to SCORE.²⁶⁴
The current level of habitual PA, undertaken by the individual as a marker of the cardio respiratory fitness.³²⁹
3. Exercise test: if risk stratification according to I-II identifies patients with increased risk, the next step is to rule out or confirm the presence of coronary artery disease.^{315,330} Based on the individual risk profile and the type/intensity of intended PA, different levels of cardiovascular evaluation are

recommended as appropriate for sedentary senior individuals and regularly active senior individuals, as outlined by the EACPR in 2010.³¹⁵

Safety at exercise facilities

The 'chain of survival', including early cardiopulmonary resuscitation, early defibrillation, and early advanced cardiac life support when needed, may increase the survival of out-of hospital sudden cardiac accidents from 2–5% to >50%.³³¹ The major determinant of survival is the time to defibrillation, the critical time being within 3–5 min.³³² Public access defibrillation using automated external defibrillator programmes may increase the number of patients receiving bystander cardiopulmonary resuscitation and early defibrillation,³³³ especially in locations where witnessed cardiac arrest is likely to occur³³⁴ at least once in every 2 years (e.g. sports arenas and exercise facilities).³³³ Automated external defibrillators are therefore recommended when normal access to defibrillation exceeds 5 min.³³⁵ European recommendations on cardiovascular preparedness at sports arenas were published in 2011.³³⁶

Mini summary

While PA is associated with a beneficial effect on the general health, vigorous physical exertion is associated with an increased risk for cardiac events, especially in risk individuals. Recently, practical and pragmatic algorithms for the cardiovascular evaluation of individuals (≥ 35 years) prior to engaging in regular PA and sports has been proposed, where appropriate precautions and safety measures will vary according to the individual's characteristics (age, risk factors, habitual exercise) as well as the setting of PA (elite sports, exercise programme, type and intensity of activity).

General conclusion

In general, there is strong evidence that a sufficient level of PA and exercise can have beneficial effects on various cardiovascular risk factors. For reducing fat mass in obesity, an increase in exercise volume and programme prolongation are effective strategies to augment fat mass loss but it is still debated which PA is most effective e.g. mode, duration, or intensity. Increasing endurance exercise intensity and addition of resistance training to endurance training intervention seem not to modulate fat mass loss. The impact of resistance training modalities on fat mass in the obese remains obscure. For glycaemic control, both aerobic and resistance exercise have beneficial effects while a combination of both appears superior. In order to

improve the lipid profile, the data currently available seem to indicate that a moderately intense aerobic exercise programme is sufficient to improve TG and HDL-C, while a more demanding regimen does not offer further significant advantages. It seems that the amount of exercise, in terms of overall energy expenditure, is of greater importance than the intensity of training. Exercise prescription aimed at prevention or management of hypertension requires endurance exercise, supplemented by resistance exercise on most, preferably all, days of the week. Exercise should be performed at moderate intensity for a minimum of 30 min of continuous or accumulated PA day. With regard to arterial compliance, endurance training dominantly improves arterial stiffness while resistance exercise may have either a positive or a negative effect dependent on the intensity of exercise. Regular PA improves the anti-inflammatory response and exerts antithrombotic effects. Moderate intense aerobic exercise has been shown to alleviate both anxiety and depression. At present there is insufficient data to give more specific recommendations on type, dosage, and intensity of exercise for prevention or treatment regarding new emerging risk factors or anxiety and depression.

Various lifestyle approaches to increase PA and exercise in persons with cardiovascular risk factors are needed in the healthcare system. General advice without additional support, the traditionally most common method, seems to have a low efficacy for increasing the PA level in persons with increased cardiovascular risk. Systematic lifestyle approaches in health care, such as exercise referral schemes and exercise on prescription, have shown promising results in improving the level of PA and also on the reduction of cardiovascular risk factors. With regard to safety, also appropriate individual exercise prescription, preferentially based on exercise testing, in patients with an increased risk profile and the presence of other safety measures, such as the availability of automated external defibrillators in fitness facilities, is mandatory.

It is clear that PA and exercise make a significant contribution to health and that the characteristics and mode of PA and exercise can be highly influential in defining the type and extent of impact in a range of cardiovascular disease risk factors.

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References

- Vanhees L, De Sutter J, Geladas N, Doyle F, Prescott E, Cornelissen V, et al. Importance of characteristics and modalities of physical activity and exercise in the management of cardiovascular health within the general population. Recommendations from the EACPR (Part I). *Eur J Cardiovasc Prev Rehabil* 2011 (submitted for publication).
- Ross R, Freeman JA and Janssen I. Exercise alone is an effective strategy for reducing obesity and related comorbidities. *Exerc Sport Sci Rev* 2000; 28(4): 165–170.
- Wei M, Gibbons LW, Kampert JB, Nichaman MZ and Blair SN. Low cardiorespiratory fitness and physical inactivity as predictors of mortality in men with type 2 diabetes. *Ann Intern Med* 2000; 132(8): 605–611.
- Church TS, Cheng YJ, Earnest CP, Barlow CE, Gibbons LW, Priest EL, et al. Exercise capacity and body composition as predictors of mortality among men with diabetes. *Diabetes Care* 2004; 27(1): 83–88.
- Kruger J, Galuska DA, Serdula MK and Jones DA. Attempting to lose weight: specific practices among U.S. adults. *Am J Prev Med* 2004; 26(5): 402–406.
- Maffiuletti NA, Agosti F, Marinone PG, Silvestri G, Lafortuna CL and Sartorio A. Changes in body composition, physical performance and cardiovascular risk factors after a 3-week integrated body weight reduction program and after 1-y follow-up in severely obese men and women. *Eur J Clin Nutr* 2005; 59(5): 685–694.
- Warburton DE, Nicol CW and Bredin SS. Health benefits of physical activity: the evidence. *CMAJ* 2006; 174(6): 801–809.
- Schjerve IE, Tyldum GA, Tjønnå AE, Stølen T, Loennechen JP, Hansen HE, et al. Both aerobic endurance and strength training programmes improve cardiovascular health in obese adults. *Clin Sci* 2008; 115(9): 283–293.
- Tjønnå AE, Stølen TO, Bye A, Volden M, Slørdahl SA, Odegård R, et al. Aerobic interval training reduces cardiovascular risk factors more than a multitreatment approach in overweight adolescents. *Clin Sci* 2009; 116(4): 317–326.
- Shephard RJ and Balady GJ. Exercise as cardiovascular therapy. *Circulation* 1999; 99(7): 963–972.
- Lavie CJ, Thomas RJ, Squires RW, Allison TG and Milani RV. Exercise training and cardiac rehabilitation in primary and secondary prevention of coronary heart disease. *Mayo Clin Proc* 2009; 84(4): 373–383.
- Lester M, Sheffield LT, Trammell P and Reeves TJ. The effect of age and athletic training on maximal heart rate during muscular exercise. *Am Heart J* 1968; 76: 370–376.
- Franckowiak SC, Dobrosielski DA, Reilley SM, Walston JD and Andersen RE. Maximal heart rate prediction in adults that are overweight or obese. *J Strength Cond Res* 2010; 25(5): 1407–1412.
- Vanhees L and Stevens A. Exercise intensity: a matter of measuring or of talking? *J Cardiopulm Rehabil* 2006; 26(2): 78–79.
- Myers J, Hadley D, Oswald U, Bruner K, Kottman W, Hsu L, et al. Effects of exercise training on heart rate recovery in patients with chronic heart failure. *Am Heart J* 2007; 153(6): 1056–1063.
- Tabet JY, Meurin P, Ben Driss A, Thabut G, Weber H, Renaud N, et al. Determination of exercise training heart rate in patients on beta-blockers after myocardial infarction. *Eur J Cardiovasc Prev Rehabil* 2006; 13(4): 538–543.
- American College of Sports Medicine Position Stand. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. *Med Sci Sports Exerc* 1998; 30(6): 975–991.
- Lavie CJ, Milani RV, Marks P and deGruiter H. Exercise and the heart: risks, benefits, and recommendations for providing exercise prescriptions. *The Ochsner J* 2001; 3(4): 207–213.
- O'Donovan G, Blazevich AJ, Boreham C, Cooper AR, Crank H, Ekelund U, et al. The ABC of Physical Activity for Health: a consensus statement from the British Association of Sport and Exercise Sciences. *J Sports Sci* 2010; 28(6): 573–591.
- Berryman JW. The tradition of the 'six things non-natural': exercise and medicine from Hippocrates through ante-bellum America. *Exerc Sport Sci Rev* 1989; 17: 515–559.
- Binder RK, Wonisch M, Corra U, Cohen-Solal A, Vanhees L, Saner H, et al. Methodological approach to the first and second lactate threshold in incremental cardiopulmonary exercise testing. *Eur J Cardiovasc Prev Rehabil* 2008; 15(6): 726–734.
- Faude O, Kindermann W and Meyer T. Lactate threshold concepts: how valid are they? *Sports Med* 2009; 39(6): 469–490.
- Milani RV, Lavie CJ, Mehra MR and Ventura HO. Understanding the basics of cardiopulmonary exercise testing. *Mayo Clin Proc* 2006; 81(12): 1603–1611.
- Glowacki SP, Martin SE, Maurer A, Baek W, Green JS and Crouse SF. Effects of resistance, endurance, and concurrent exercise on training outcomes in men. *Med Sci Sports Exerc* 2004; 36(12): 2119–2127.
- Gonzalez NC, Kirkton SD, Howlett RA, Britton SL, Koch LG, Wagner HE, et al. Continued divergence in

- VO_{2max} of rats artificially selected for running endurance is mediated by greater convective blood O₂ delivery. *J Appl Physiol* 2006; 101(5): 1288–1296.
26. Glass RI and Zack Jr MM. Increase in deaths from ischaemic heart-disease after blizzards. *Lancet* 1979; 1(8114): 485–487.
 27. Pandolf KB, Cafarelli E, Noble BJ and Metz KF. Hyperthermia: effect on exercise prescription. *Arch Phys Med Rehabil* 1975; 56(12): 524–526.
 28. Hammoudeh AJ and Haft JJ. Coronary-plaque rupture in acute coronary syndromes triggered by snow shoveling. *N Engl J Med* 1996; 335(26): 2001–2002.
 29. Wisloff U, Stoylen A, Loennechen JP, Bruvold M, Rognmo O, Haram PM, et al. Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients: a randomized study. *Circulation* 2007; 115(24): 3086–3094.
 30. Tjønnå AE, Lee SJ, Rognmo Ø, Stølen TO, Bye A, Haram PM, et al. Aerobic interval training versus continuous moderate exercise as a treatment for the metabolic syndrome: a pilot study. *Circulation* 2008; 118(4): 346–354.
 31. MacDonald MJ and Currie KD. Interval exercise is a path to good health, but how much, how often and for whom? *Clin Sci* 2009; 116(4): 315–316.
 32. Helgerud J, Høydal K, Wang E, Karlsen T, Berg P, Bjerkaas M, et al. Aerobic high-intensity intervals improve VO_{2max} more than moderate training. *Med Sci Sports Exerc* 2007; 39(4): 665–671.
 33. Meyer K, Samek L, Schwaibold M, Westbrook S, Hajric R, Lehmann M, et al. Physical responses to different modes of interval exercise in patients with chronic heart failure—application to exercise training. *Eur Heart J* 1996; 17(7): 1040–1047.
 34. Meyer K, Samek L, Schwaibold M, Westbrook S, Hajric R, Beneke R, et al. Interval training in patients with severe chronic heart failure: analysis and recommendations for exercise procedures. *Med Sci Sports Exerc* 1997; 29(3): 306–312.
 35. Ratamess NA, Falvo MJ, Mangine GT, Hoffman JR, Faigenbaum AD and Kang J. The effect of rest interval length on metabolic responses to the bench press exercise. *Eur J Appl Physiol* 2007; 100(1): 1–17.
 36. Rydwik E, Karlsson C, Frändin K and Akner G. Muscle strength testing with one repetition maximum in the arm/shoulder for people aged 75 + – test-retest reliability. *Clin Rehabil* 2007; 21(3): 258–265.
 37. Gordon NF, Kohl 3rd HW, Pollock ML, Vaandrager H, Gibbons LW and Blair SN. Cardiovascular safety of maximal strength testing in healthy adults. *Am J Cardiol* 1995; 76(11): 851–853.
 38. Reynolds JM, Gordon TJ and Robergs RA. Prediction of one repetition maximum strength from multiple repetition maximum testing and anthropometry. *J Strength Cond Res* 2006; 20(3): 584–592.
 39. Bjarnason-Wehrens B, Mayer-Berger W, Meister ER, Baum K, Hambrecht R and Gielen S. Recommendations for resistance exercise in cardiac rehabilitation. Recommendations of the German Federation for Cardiovascular Prevention and Rehabilitation. *Eur J Cardiovasc Prev Rehabil* 2004; 11(4): 352–361.
 40. Rhea MR, Alvar BA and Burkett LN. Single versus multiple sets for strength: a meta-analysis to address the controversy. *Res Q Exerc Sport* 2002; 73(4): 485–488.
 41. Peterson MD, Rhea MR and Alvar BA. Applications of the dose–response for muscular strength development: a review of meta-analytic efficacy and reliability for designing training prescription. *J Strength Cond Res* 2005; 19(4): 950–958.
 42. Miller WC, Kocaja DM and Hamilton EJ. A meta-analysis of the past 25 years of weight loss research using diet, exercise or diet plus exercise intervention. *Int J Obes Relat Metab Disord* 1997; 21(10): 941–947.
 43. Khan K, McKay HA, Haapasalo H, Bennell KL, Forwood MR, Kannus P, et al. Does childhood and adolescence provide a unique opportunity for exercise to strengthen the skeleton? *J Sci Med Sport* 2000; 3(2): 150–164.
 44. Church TS, Finley CE, Earnest CP, Kampert JB, Gibbons LW and Blair SN. Relative associations of fitness and fatness to fibrinogen, white blood cell count, uric acid and metabolic syndrome. *Int J Obes Relat Metab Disord* 2002; 26(6): 805–813.
 45. Steele RM, Brage S, Corder K, Wareham NJ and Ekelund U. Physical activity, cardiorespiratory fitness, and the metabolic syndrome in youth. *J Appl Physiol* 2008; 105(1): 342–351.
 46. Brown T, Avenell A, Edmunds LD, Moore H, Whittaker V, Avery L, et al. Systematic review of long-term lifestyle interventions to prevent weight gain and morbidity in adults. *Obes Rev* 2009; 10(6): 627–638.
 47. Whitley JE, Gillespie WJ, Honig J, Walsh MJ, Blackburn AL and Blackburn GL. Does the amount of endurance exercise in combination with weight training and a very-low-energy diet affect resting metabolic rate and body composition? *Am J Clin Nutr* 1994; 59(5): 1088–1092.
 48. Ballor DL, McCarthy JP and Wilterdink EJ. Exercise intensity does not affect the composition of diet- and exercise-induced body mass loss. *Am J Clin Nutr* 1990; 51(2): 142–146.
 49. Leutholtz BC, Keyser RE, Heusner WW, Wendt VE and Rosen L. Exercise training and severe caloric restriction: effect on lean body mass in the obese. *Arch Phys Med Rehabil* 1995; 76(1): 65–70.
 50. van Aggel-Leijssen D, Saris WHM, Wagenmakers AJM, Senden JM and van Baak MA. Effect of exercise training at different intensities on fat metabolism of obese men. *J Appl Physiol* 2002; 92(3): 1300–1309.
 51. Hansen D, Dendale P, van Loon LJ and Meeusen R. The impact of training modalities on the clinical benefits of exercise intervention in patients with cardiovascular disease risk or type 2 diabetes. *Sports Med* 2010; 40(11): 921–940.
 52. Donnelly JE, Blair SN, Jakicic JM, Manore MM, Rankin JW and Smith BK. American College of Sports Medicine Position Stand. Appropriate physical activity intervention strategies for weight loss and

- prevention of weight regain for adults. *Med Sci Sports Exerc* 2009; 41(2): 459–471.
53. Pulfrey SM and Jones PJ. Energy expenditure and requirement while climbing above 6,000 m. *J Appl Physiol* 1996; 81(3): 1306–1311.
 54. Nindl BC, Barnes BR, Alemany JA, Frykman PN, Shippee RL and Friedl KE. Physiological consequences of U.S. Army Ranger training. *Med Sci Sports Exerc* 2007; 39(8): 1380–1387.
 55. Donnelly JE, Smith B, Jacobsen DJ, Kirk E, Dubose K, Hyder M, et al. The role of exercise for weight loss and maintenance. *Best Pract Res Clin Gastroenterol* 2004; 18(6): 1009–1029.
 56. Treserras MA and Balady GJ. Resistance training in the treatment of diabetes and obesity: mechanisms and outcomes. *J Cardiopulm Rehabil Prev* 2009; 29(2): 67–75.
 57. Hunter GR, Bryan DR, Wetzstein CJ, Zuckerman PA and Bamman MM. Resistance training and intra-abdominal adipose tissue in older men and women. *Med Sci Sports Exerc* 2002; 34(6): 1023–1028.
 58. Ibanez J, Izquierdo M, Martinez-Labari C, Ortega F, Grijalba A, Forga L, et al. Resistance training improves cardiovascular risk factors in obese women despite a significant decrease in serum adiponectin levels. *Obesity* 2010; 18(3): 535–541.
 59. van der Heijden GJ, Wang ZJ, Chu Z, Toffolo G, Manesso E, Sauer PJ, et al. Strength exercise improves muscle mass and hepatic insulin sensitivity in obese youth. *Med Sci Sports Exerc* 2010; 42(11): 1973–1980.
 60. Gillette CA, Bullough RC and Melby CL. Postexercise energy expenditure in response to acute aerobic or resistive exercise. *Int J Sport Nutr* 1994; 4(4): 347–360.
 61. Toth MJ, Beckett T and Poehlman ET. Physical activity and the progressive change in body composition with aging: current evidence and research issues. *Med Sci Sports Exerc* 1999; 31(Suppl 11): S590–S596.
 62. Hunter GR, McCarthy JP and Bamman MM. Effects of resistance training on older adults. *Sports Med* 2004; 34(5): 329–348.
 63. Maesta N, Nahas EA, Nahas-Neto J, Orsatti FL, Fernandes CE, Traiman P, et al. Effects of soy protein and resistance exercise on body composition and blood lipids in postmenopausal women. *Maturitas* 2007; 56(4): 350–358.
 64. Jabekk PT, Moe IA, Meen HD, Tomten SE and Hostmark AT. Resistance training in overweight women on a ketogenic diet conserved lean body mass while reducing body fat. *Nutr Metab Lond* 2010; 7: 17.
 65. Villareal DT, Banks M, Sinacore DR, Siener C and Klein S. Effect of weight loss and exercise on frailty in obese older adults. *Arch Intern Med* 2006; 166(8): 860–866.
 66. Frimel TN, Sinacore DR and Villareal DT. Exercise attenuates the weight-loss-induced reduction in muscle mass in frail obese older adults. *Med Sci Sports Exerc* 2008; 40(7): 1213–1219.
 67. Treuth MS, Ryan AS, Pratley RE, Rubin MA, Miller JP, Nicklas BJ, et al. Effects of strength training on total and regional body composition in older men. *J Appl Physiol* 1994; 77(2): 614–620.
 68. Treuth MS, Hunter GR, Kekes-Szabo T, Weinsier RL, Goran MI and Berland L. Reduction in intra-abdominal adipose tissue after strength training in older women. *J Appl Physiol* 1995; 78(4): 1425–1431.
 69. Ross R, Rissanen J, Pedwell H, Clifford J and Shragge P. Influence of diet and exercise on skeletal muscle and visceral adipose tissue in men. *J Appl Physiol* 1996; 81(6): 2445–2455.
 70. Sothorn MS, Loftin JM, Udall JN, Suskind RM, Ewing TL, Tang SC, et al. Inclusion of resistance exercise in a multidisciplinary outpatient treatment program for pre-adolescent obese children. *South Med J* 1999; 92(6): 585–592.
 71. Hagerman FC, Walsh SJ, Staron RS, Hikida RS, Gilders RM, Murray TF, et al. Effects of high-intensity resistance training on untrained older men. I. Strength, cardiovascular, and metabolic responses. *J Gerontol A Biol Sci Med Sci* 2000; 55(7): B336–B346.
 72. Benson AC, Torode ME and Fiatarone Singh MA. The effect of high-intensity progressive resistance training on adiposity in children: a randomized controlled trial. *Int J Obes* 2008; 32(6): 1016–1027.
 73. McGuigan MR, Tatasciore M, Newton RU and Pettigrew S. Eight weeks of resistance training can significantly alter body composition in children who are overweight or obese. *J Strength Cond Res* 2009; 23(1): 80–85.
 74. Sgro M, McGuigan MR, Pettigrew S and Newton RU. The effect of duration of resistance training interventions in children who are overweight or obese. *J Strength Cond Res* 2009; 23(4): 1263–1270.
 75. Hakkinen K, Pakarinen A, Kraemer WJ, Newton RU and Alen M. Basal concentrations and acute responses of serum hormones and strength development during heavy resistance training in middle-aged and elderly men and women. *J Gerontol A Biol Sci Med Sci* 2000; 55(2): B95–B105.
 76. Elliott KJ, Sale C and Cable NT. Effects of resistance training and detraining on muscle strength and blood lipid profiles in postmenopausal women. *Br J Sports Med* 2002; 36(5): 340–344.
 77. Teixeira PJ, Going SB, Houtkooper LB, Metcalfe LL, Blew RM, Flint-Wagner HG, et al. Resistance training in postmenopausal women with and without hormone therapy. *Med Sci Sports Exerc* 2003; 35(4): 555–562.
 78. Shaibi GQ, Cruz ML, Ball GD, Weigensberg MJ, Salem GJ, Crespo NC, et al. Effects of resistance training on insulin sensitivity in overweight Latino adolescent males. *Med Sci Sports Exerc* 2006; 38(7): 1208–1215.
 79. Bell LM, Watts K, Siafarikas A, Thompson A, Ratnam N, Bulsara M, et al. Exercise alone reduces insulin resistance in obese children independently of changes in body composition. *J Clin Endocrinol Metab* 2007; 92(11): 4230–4235.
 80. Orsatti FL, Nahas EA, Maesta N, Nahas-Neto J and Burini RC. Plasma hormones, muscle mass and strength in resistance-trained postmenopausal women. *Maturitas* 2008; 59(4): 394–404.

81. Bouchard DR, Soucy L, Senechal M, Dionne IJ and Brochu M. Impact of resistance training with or without caloric restriction on physical capacity in obese older women. *Menopause* 2009; 16(1): 66–72.
82. Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Med Sci Sports Exerc* 2007; 39(8): 1423–1434.
83. Delecluse C, Colman V, Roelants M, Verschueren S, Derave W, Ceux T, et al. Exercise programs for older men: mode and intensity to induce the highest possible health-related benefits. *Prev Med* 2004; 39(4): 823–833.
84. Yu CC, Sung RY, So RC, Lui KC, Lau W, Lam PK, et al. Effects of strength training on body composition and bone mineral content in children who are obese. *J Strength Cond Res* 2005; 19(3): 667–672.
85. Fielding RA. The role of progressive resistance training and nutrition in the preservation of lean body mass in the elderly. *J Am Coll Nutr* 1995; 14(6): 587–594.
86. Deschenes MR and Kraemer WJ. Performance and physiologic adaptations to resistance training. *Am J Phys Med Rehabil* 2002; 81(Suppl 11): S3–S16.
87. de Vos NJ, Singh NA, Ross DA, Stavrinou TM, Orr R and Fiatarone Singh MA. Optimal load for increasing muscle power during explosive resistance training in older adults. *J Gerontol A Biol Sci Med Sci* 2005; 60(5): 638–647.
88. Slentz CA, Houmard JA and Kraus WE. Exercise, abdominal obesity, skeletal muscle, and metabolic risk: evidence for a dose response. *Obesity* 2009; 17(Suppl 3): S27–S33.
89. Wolfe BL, LeMura LM and Cole PJ. Quantitative analysis of single- vs. multiple-set programs in resistance training. *J Strength Cond Res* 2004; 18(1): 35–47.
90. Krieger JW. Single versus multiple sets of resistance exercise: a meta-regression. *J Strength Cond Res* 2009; 23(6): 1890–1901.
91. Larson-Meyer DE, Redman L, Heilbronn LK, Martin CK and Ravussin E. Caloric restriction with or without exercise: the fitness versus fatness debate. *Med Sci Sports Exerc* 2010; 42(1): 152–159.
92. Villareal DT, Apovian CM, Kushner RF and Klein S. Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, The Obesity Society. *Am J Clin Nutr* 2005; 82(5): 923–934.
93. Davidson LE, Hudson R, Kilpatrick K, Kuk JL, McMillan K, Janiszewski PM, et al. Effects of exercise modality on insulin resistance and functional limitation in older adults: a randomized controlled trial. *Arch Intern Med* 2009; 169(2): 122–131.
94. Ross R and Rissanen J. Mobilization of visceral and subcutaneous adipose tissue in response to energy restriction and exercise. *Am J Clin Nutr* 1994; 60(5): 695–703.
95. Fogelholm M and Kukkonen-Harjula K. Does physical activity prevent weight gain—a systematic review. *Obes Rev* 2000; 1(2): 95–111.
96. Jeffery RW, Wing RR, Sherwood NE and Tate DF. Physical activity and weight loss: does prescribing higher physical activity goals improve outcome? *Am J Clin Nutr* 2003; 78(4): 684–689.
97. Saris WH, Blair SN, van Baak MA, Eaton SB, Davies PS, Di PL, et al. How much physical activity is enough to prevent unhealthy weight gain? Outcome of the IASO 1st Stock Conference and consensus statement. *Obes Rev* 2003; 4(2): 101–114.
98. Wareham N. Physical activity and obesity prevention. *Obes Rev* 2007; 8(Suppl 1): 109–114.
99. Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, et al. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. *N Engl J Med* 2001; 345(11): 790–797.
100. Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 2001; 344(18): 1343–1350.
101. Thomas DE, Elliott EJ and Naughton GA. Exercise for type 2 diabetes mellitus. *Cochrane Database Syst Rev* 2006; (3): CD002968.
102. Jeon CY, Lokken RP, Hu FB and van Dam RM. Physical activity of moderate intensity and risk of type 2 diabetes: a systematic review. *Diabetes Care* 2007; 30(3): 744–752.
103. Snowling NJ and Hopkins WG. Effects of different modes of exercise training on glucose control and risk factors for complications in type 2 diabetic patients. *Diabetes Care* 2006; 29(11): 2518–2527.
104. Sixt S, Rastan A, Desch S, Sonnabend M, Schmidt A, Schuler G, et al. Exercise training but not rosiglitazone improves endothelial function in prediabetic patients with coronary disease. *Eur J Cardiovasc Prev Rehabil* 2008; 15(4): 473–478.
105. Desch S, Sonnabend M, Niebauer J, Sixt S, Sareban M, Eitel I, et al. Effects of physical exercise versus rosiglitazone on endothelial function in coronary artery disease patients with prediabetes. *Diabetes Obes Metab* 2010; 12(9): 825–828.
106. Niebauer J and Cooke JP. Cardiovascular effects of exercise: role of endothelial shear stress. *J Am Coll Cardiol* 1996; 28(7): 1652–1660.
107. Sixt S, Beer S, Blüher M, Korff N, Peschel T, Sonnabend M, et al. Long- but not short-term multifactorial intervention with focus on exercise training improves coronary endothelial dysfunction in diabetes mellitus type 2 and coronary artery disease. *Eur Heart J* 2010; 31(1): 112–119.
108. Gæde P, Vedel P, Larsen N, Jensen GV, Parving HH and Pedersen O. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med* 2003; 348(5): 383–393.
109. Gæde P, Lund-Andersen H, Parving HH and Pedersen O. Effect of a multifactorial intervention on mortality in type 2 diabetes. *N Engl J Med* 2008; 358(6): 580–591.
110. Castaneda C, Layne JE, Munoz-Orians L, Gordon PL, Walsmith J, Foldvari M, et al. A randomized controlled trial of resistance exercise training to improve glycemic

- control in older adults with type 2 diabetes. *Diabetes Care* 2002; 25(12): 2335–2341.
111. Dunstan DW, Daly RM, Owen N, Jolley D, De Courten M, Shaw J, et al. High-intensity resistance training improves glycemic control in older patients with type 2 diabetes. *Diabetes Care* 2002; 25(10): 1729–1736.
 112. Dunstan DW, Daly RM, Owen N, Jolley D, Vulikh E, Shaw J, et al. Home-based resistance training is not sufficient to maintain improved glycemic control following supervised training in older individuals with type 2 diabetes. *Diabetes Care* 2005; 28(1): 3–9.
 113. Ishii T, Yamakita T, Sato T, Tanaka S and Fujii S. Resistance training improves insulin sensitivity in NIDDM subjects without altering maximal oxygen uptake. *Diabetes Care* 1998; 21(8): 1353–1355.
 114. Smutok MA, Reece C, Kokkinos PF, Farmer CM, Dawson PK, DeVane J, et al. Effects of exercise training modality on glucose tolerance in men with abnormal glucose regulation. *Int J Sports Med* 1994; 15(6): 283–289.
 115. Dela F and Kjaer M. Resistance training, insulin sensitivity and muscle function in the elderly. *Essays Biochem* 2006; 42: 75–88.
 116. Sato Y, Nagasaki M, Kubota M, Uno T and Nakai N. Clinical aspects of physical exercise for diabetes/metabolic syndrome. *Diabetes Res Clin Pract* 2007; 77(Suppl 1): S87–S91.
 117. Praet SF, Jonkers RA, Schep G, Stehouwer CDA, Kuipers H, Keizer HA, et al. Long-standing, insulin-treated type 2 diabetes patients with complications respond well to short-term resistance and interval exercise training. *Eur J Endocrinol* 2008; 158(2): 163–172.
 118. Baldi JC and Snowling N. Resistance training improves glycaemic control in obese type 2 diabetic men. *Int J Sports Med* 2003; 24(6): 419–423.
 119. Cuff DJ, Meneilly GS, Martin A, Ignaszewski A, Tildesley HD and Frohlich JJ. Effective exercise modality to reduce insulin resistance in women with type 2 diabetes. *Diabetes Care* 2003; 26(11): 2977–2982.
 120. Sigal RJ, Kenny GP, Boule NG, Wells GA, Prud'homme D, Fortier M, et al. Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes: a randomized trial. *Ann Intern Med* 2007; 147(6): 357–369.
 121. Marcus RL, Smith S, Morrell G, Addison O, Dibble LE, Wahoff-Stice D, et al. Comparison of combined aerobic and high-force eccentric resistance exercise with aerobic exercise only for people with type 2 diabetes mellitus. *Phys Ther* 2008; 88(11): 1345–1354.
 122. Cauza E, Hanusch-Enserer U, Strasser B, Ludvik B, Metz-Schimmerl S, Pacini G, et al. The relative benefits of endurance and strength training on the metabolic factors and muscle function of people with type 2 diabetes mellitus. *Arch Phys Med Rehabil* 2005; 86(8): 1527–1533.
 123. Egger A, Niederseer D, Ledl-Kurkowski E, Graf S, Patsch W, Forstner R, et al. Hypertrophy versus endurance strength training in patients with type 2 diabetes: effects on muscle mass, strength and glycemic control (submitted for publication).
 124. Steidle EM, Niederseer D and Niebauer J. Rationale, evidence and recommendations for resistance training in type 2 diabetes mellitus: a systematic review (submitted for publication).
 125. Lund SS and Vaag AA. Intensive glycemic control and the prevention of cardiovascular events: implications of the accord, advance, and VA diabetes trials: a position statement of the American Diabetes Association and a scientific statement of the American College of Cardiology Foundation and the American Heart Association: response to Skyler, et al. *Diabetes Care* 2009; 32(7): e90–e91.
 126. Marwick Th, Hordern Md, Miller T, Chyun DA, Bertoni AG, Blumenthal RS, et al. Exercise training for type 2 diabetes mellitus: impact on cardiovascular risk: a scientific statement from the American Heart Association. *Circulation* 2009; 119(25): 3244–3262.
 127. Albright A, Franz M, Hornsby G, Kriska A, Marrero D, Ullrich I, et al. American College of Sports Medicine position stand. Exercise and type 2 diabetes. *Med Sci Sports Exerc* 2000; 32(7): 1345–1360.
 128. Corrà U, Piepoli MF, Carré F, Heuschmann P, Hoffmann U, Verschuren M, et al. Secondary prevention through cardiac rehabilitation: physical activity counselling and exercise training: key components of the position paper from the Cardiac Rehabilitation Section of the European Association of Cardiovascular Prevention and Rehabilitation. *Eur Heart J* 2010; 31(16): 1967–1974.
 129. Tran ZV and Weltman A. Differential effects of exercise on serum lipid and lipoprotein levels seen with changes in body weight. A meta-analysis. *JAMA* 1985; 254(7): 919–924.
 130. Halbert JA, Silagy CA, Finucane P, Withers RT and Hamdorf PA. Exercise training and blood lipids in hyperlipidemic and normolipidemic adults: a meta-analysis of randomized, controlled trials. *Eur J Clin Nutr* 1999; 53(7): 514–522.
 131. Leon AS and Sanchez OA. Response of blood lipids to exercise training alone or combined with dietary intervention. *Med Sci Sports Exerc* 2001; 33(Suppl 6): S502–S515; discussion S528–S529. Review.
 132. Carroll S and Dudfield M. What is the relationship between exercise and metabolic abnormalities? A review of the metabolic syndrome. *Sports Med* 2004; 34(6): 371–418.
 133. Duncan GE, Anton SD, Sydesman SJ, Newton Jr RL, Corsica JA, Durning PE, et al. Prescribing exercise at varied levels of intensity and frequency: a randomized trial. *Arch Intern Med* 2005; 165(20): 2362–2369.
 134. Kelley GA, Kelley KS and Vu Tran Z. Aerobic exercise, lipids and lipoproteins in overweight and obese adults: a meta-analysis of randomized controlled trials. *Int J Obes* 2005; 29(8): 881–893.
 135. Haskell WL. Exercise-induced changes in plasma lipids and lipoproteins. *Prev Med* 1984; 13(1): 23–36.
 136. Durstine JL, Grandjean PW, Davis PG, Ferguson MA, Alderson NL and DuBose KD. Blood lipid and lipoprotein adaptations to exercise. *Sports Med* 2001; 31(15): 1033–1062.

137. Mosher PE, Ferguson MA and Arnold RO. Lipid and lipoprotein changes in premenstrual women following step aerobic dance training. *Int J Sports Med* 2005; 26(8): 669–674.
138. Mestek ML, Garner JC, Plaisance EP, Taylor JK, Alhassan S and Grandjean PW. Blood lipid responses after continuous and accumulated aerobic exercise. *Int J Sport Nutr Exerc Metab* 2006; 16(3): 245–254.
139. Altena TS, Michaelson JL, Ball SD, Guilford BL and Thomas TR. Lipoprotein subfraction changes after continuous or intermittent exercise training. *Med Sci Sports Exerc* 2006; 38(2): 367–372.
140. Giada F, Baldo-Enzi G, Baiocchi MR, Zuliani G, Vitale E and Fellin R. Specialized physical training programs: effects on serum lipoproteins cholesterol, apoproteins A-I and B and lipolytic enzyme activities. *J Sports Med Phys Fitn* 1991; 31(2): 196–203.
141. Giada F, Vigna GB, Vitale E, Baldo-Enzi G and Fellin R. Effect of age on the response of blood lipids, body composition, and aerobic power in physical conditioning and deconditioning. *Metabolism* 1995; 44(2): 161–165.
142. Kodama S, Tanaka S and Sito K. Effect of aerobic exercise training on serum levels of high-density lipoprotein cholesterol. *Arch Intern Med* 2007; 167(10): 999–1008.
143. Wood PD, Haskell WL, Blair SN, Williams PT, Krauss RM, Lindgren FT, et al. Increased exercise level plasma lipoprotein concentrations: a one-year, randomized, controlled study in sedentary middle-aged men. *Metabolism* 1983; 32(1): 31–39.
144. Shaw I and Shaw BS. Relationship between resistance training and lipoprotein profiles in sedentary male smokers. *Cardiovasc J Afr* 2008; 19(4): 194–197.
145. Arora E, Shenoy S and Sandhu JS. Effects of resistance training on metabolic profile of adults with type 2 diabetes. *Indian J Med Res* 2009; 129(5): 515–519.
146. Marques E, Carvalho J, Soares JM, Marques F and Mota J. Effects of resistance and multicomponent exercise on lipid profiles of older women. *Maturitas* 2009; 63(1): 84–88.
147. Kelley GA and Kelley KS. Impact of progressive resistance training on lipids and lipoproteins in adults: another look at a meta-analysis using prediction intervals. *Prev Med* 2009; 49(6): 473–475.
148. Wijndaele K, Duvigneaud N, Matton L, Duquet W, Thomis M, Beunen G, et al. Muscular strength, aerobic fitness, and metabolic syndrome risk in Flemish adults. *Med Sci Sports Exerc* 2007; 39(2): 233–240.
149. Igwebuike A, Irving BA, Bigelow ML, Short KR, McConnell JP and Nair KS. Lack of dehydroepiandrosterone effect on a combined endurance and resistance exercise program in postmenopausal women. *J Clin Endocrinol Metab* 2008; 93(2): 534–538.
150. Pitsavos C, Panagiotakos DB, Tambalis KD, Chrysohou C, Sidossis LS, Skoumas J, et al. Resistance exercise plus to aerobic activities is associated with better lipids' profile among healthy individuals: the ATTICA study. *QJM* 2009; 102(9): 609–616.
151. Tambalis K, Panagiotakos DB, Kavouras SA and Sidossis LS. Responses of blood lipids to aerobic, resistance, and combined aerobic with resistance exercise training: a systematic review of current evidence. *Angiology* 2009; 60(5): 614–632.
152. Lampman RM, Santiga JT, Hodge MF, Block WD, Flora JD and Bassett DR. Comparative effect of physical training and diet in normalizing serum lipids in men with type IV hyperlipoproteinemia. *Circulation* 1977; 55(4): 652–659.
153. Gynzelberg F, Brennan R, Holloszy JO, Schonefeld G, Rennie MJ and Weidman SW. Plasma triglyceride lowering by exercise despite increased food intake in patients with type IV hyperlipoproteinemia. *Am J Clin Nutr* 1977; 30(5): 716–720.
154. Lampman RM, Santiga JT, Savage PJ, Bassett DR, Hyndrick CR, Flora JD, et al. Effect of exercise training on glucose tolerance in vivo insulin sensitivity, lipid and lipoprotein concentrations in middle-aged men with mild hypertriglyceridemia. *Metabolism* 1985; 34(3): 205–211.
155. Wirth A, Diehm C, Hanel W, Welte J and Vogel I. Training-induced changes in serum lipids, fat tolerance, and adipose tissue metabolism in patients with hypertriglyceridemia. *Atherosclerosis* 1985; 54(3): 263–271.
156. Hanefeld M, Fischer S, Julius U, Leonhardt W, Schubert E and Beckert H. More exercise for the hyperlipidemic patients. *Ann Clin Res* 1988; 20(1–2): 77–83.
157. Oscai LB, Patterson JA and Bogard DL. Normalization of serum triglycerides and lipoprotein electrophoretic pattern by exercise. *Am J Cardiol* 1972; 30(7): 775–780.
158. Reiner Ž, Catapano AL, De Backer G, Graham I, Taskinen MR, Wiklund O, et al. ESC/EAS Guidelines for the management of dyslipidaemias: the Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). *Eur Heart J* 2011; 32(14): 1769–1818.
159. Chapman MJ, Ginsberg HN, Amarencu P, Andreotti F, Boren J, Catapano AL, et al. for the European Atherosclerosis Society Consensus Panel. Triglyceride-rich lipoproteins and high-density lipoprotein cholesterol in patients at high risk of cardiovascular disease: evidence and guidance for management. *Eur Heart J* 2011; 32(11): 1345–1361.
160. Holloszy JO, Skinner JS, Toro G and Cureton TK. Effects of a six month program of endurance exercise on serum lipids of middle-aged men. *Am J Cardiol* 1964; 14: 753–760.
161. Alterkruse EB and Wilmore JH. Changes in blood chemistries following a controlled exercise program. *J Occ Med* 1973; 15(2): 110–113.
162. Gordon DJ, Witztum JL, Hunninghake D, Gates S and Glueck CJ. Habitual physical activity and high density lipoprotein cholesterol in men with primary hypercholesterolemia. *Circulation* 1983; 68(3): 512–520.
163. Marti B, Suter E, Riesen WF, Tschopp A, Wanner HU and Gutzwiller F. Effects of long-term, self-monitored exercise on the serum lipoprotein and apolipoprotein profile in middle-aged men. *Atherosclerosis* 1990; 81(1): 19–31.

164. Kennedy C, Sprekeman RE and Markin HT. One-year graduated exercise program for men with angina pectoris. *Mayo Clinic Proc* 1976; 51(4): 231–236.
165. Hartung GH, Squires WG and Gotto AM. Effect of exercise training on plasma high-density lipoprotein cholesterol in coronary disease patients. *Am Heart J* 1981; 101(2): 181–184.
166. La Rosa JC, Cleary P and Muesing RA. Effect of long-term moderate physical exercise on plasma lipoprotein. The national exercise heart disease project. *Arch Intern Med* 1982; 142(13): 2269–2274.
167. Kawano M, Shono N, Yoshimura T, Yamaguchi M, Hirano T and Hisatomi A. Improved cardio-respiratory fitness correlates with changes in the number and size of small dense LDL: randomized controlled trial with exercise training and dietary instruction. *Intern Med* 2009; 48(1): 25–32.
168. Melish J, Bronstein D and Gross R. Effect of exercise training in type II hyperlipoproteinemia. *Circulation* 1978; 57: 38.
169. Sutherland WHF, Nye ER and Wodhouse SP. Red blood cell cholesterol levels, plasma cholesterol esterification rate and serum lipid and lipoproteins in men with hypercholesterolaemia and normal men during 16 weeks physical training. *Atherosclerosis* 1983; 47(2): 145–157.
170. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, et al.; National High Blood Pressure Education Program Coordination Committee. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure. *Hypertension* 2003; 42(6): 1206–1252.
171. Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G, et al. Management of Arterial Hypertension of the European Society of Hypertension; European Society of Cardiology. 2007 Guidelines for the Management of Arterial Hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens* 2007; 25(6): 1105–1187.
172. Laurent S and Boutouyrie P. Arterial stiffness: a new surrogate end point for cardiovascular disease? *J Nephrol* 2007; 20(Suppl 12): S45–S50.
173. Fagard RH. Exercise characteristics and the BP response to dynamic physical training. *Med Sci Sports Exerc* 2001; 33(Suppl 6): S484–S492.
174. Kelley GA, Kelley KA and Tran ZV. Aerobic exercise and resting BP: a meta-analytic review of randomized controlled trials. *Prev Cardiol* 2001; 4(2): 73–86.
175. Kelley GA and Kelley KS. Aerobic exercise and resting BP in older adults: a meta-analytic review of randomized controlled trials. *J Gerontol A Biol Sci Med Sci* 2001; 56(5): M298–M303.
176. Whelton SP, Chin A, Xin X and He J. Effect of aerobic exercise on blood pressure: a meta-analysis of randomized controlled trials. *Ann Intern Med* 2002; 136(7): 493–503.
177. Cornelissen VA and Fagard RH. Effects of dynamic aerobic endurance training on blood pressure, blood pressure-regulating mechanisms and cardiovascular risk factors. *Hypertension* 2005; 46(4): 667–675.
178. Hayashi K, Sugawara J, Komine H, Maeda S and Yokoi T. Effects of aerobic exercise training on the stiffness of central and peripheral arteries in middle-aged sedentary men. *Jpn J Physiol* 2005; 55(4): 235–239.
179. Maeda S, Tanabe T, Otsuki T, Sugawara J, Ajisaka R and Matsuda M. Acute exercise increases systemic arterial compliance after 6-month exercise training in older women. *Hypertens Res* 2008; 31(2): 377–381.
180. Ferrier KE, Waddell TK, Gatzaka CD, Cameron JD, Dart AM and Kingwell BA. Aerobic exercise training does not modify large-artery compliance in isolated systolic hypertension. *Hypertension* 2001; 38(2): 222–226.
181. Westhoff TH, Franke N, Schmidt S, Vallbracht-Israng K, Meissner R, Yildirim H, et al. Too old to benefit from sports? The cardiovascular effects of exercise training in elderly subjects treated for isolated systolic hypertension. *Kidney Blood Press Res* 2007; 30(4): 240–247.
182. Tully MA, Cupples ME, Hart ND, McEneny J, McGlade KJ, Chan WS, et al. Randomised controlled trial of home-based walking programmes at and below current recommended levels of exercise in sedentary adults. *J Epidemiol Community Health* 2007; 61(9): 778–783.
183. Jennings G, Nelson L, Nestel P, Esler M, Korner P, Burton D, et al. The effects of changes in physical activity on major cardiovascular risk factors, hemodynamics, sympathetic function, and glucose utilization in man: a controlled study of four levels of activity. *Circulation* 1986; 73(1): 30–40.
184. Nelson L, Esler MD, Jennings GL and Korner PI. Effect of changing levels of physical activity on blood pressure and haemodynamics in essential hypertension. *Lancet* 1986; 2(8505): 473–476.
185. Pescatello LS and Kulikowich JM. The aftereffects of dynamic exercise on ambulatory blood pressure. *Med Sci Sports Exerc* 2001; 33(11): 1855–1861.
186. Pescatello LS, Franklin BA, Fagard R, Farquhar WB, Kelley GA and Ray CA. Exercise and hypertension: position stand of the American College of Sports Medicine. *Med Sci Sports Exerc* 2004; 36(3): 533–553.
187. Cornelissen VA, Arnout J, Holvoet P and Fagard RH. Influence of exercise at lower and higher intensity on blood pressure and cardiovascular risk factors at older age. *J Hypertens* 2009; 27(4): 753.
188. Murphy MH, Blair SN and Murtagh EM. Accumulated versus continuous exercise for health benefit – a review of empirical studies. *Sports Med* 2009; 39(1): 29–43.
189. MacDonald JR. Potential causes, mechanisms, and implications of post exercise hypotension. *J Hum Hypertens* 2002; 16(4): 225–236.
190. Cornelissen VA, Fagard RH, Coeckelberghs E and Vanhees L. Impact of resistance training on blood pressure and other cardiovascular risk factors: a meta-analysis of randomized controlled trials. *Hypertension* 2011; 58(5): 950–958.

191. Kelley GA and Kelley KS. Isometric handgrip exercise and resting blood pressure: a meta-analysis of randomized controlled trials. *J Hypertens* 2010; 28(3): 411–418.
192. Wiles JD, Coleman DA and Swaine IL. The effects of performing isometric training at two exercise intensities in healthy young males. *Eur J Appl Physiol* 2010; 108(3): 419–428.
193. Miyachi M, Kawano H, Sugawara J, Takahashi K, Hayashi K, Yamazaki K, et al. Unfavorable effects of resistance training on central arterial compliance: a randomized intervention study. *Circulation* 2004; 110(18): 2858–2863.
194. Cortez-Cooper MY, Anton MM, DeVan AE, Neidre DB, Cook JN and Tanaka H. The effects of strength training on central arterial compliance in middle-aged and older adults. *Eur J Cardiovasc Prev Rehabil* 2008; 15(2): 149–155.
195. Fjeldstad AS, Bembien MG and Bembien DA. Resistance training effects on arterial compliance in premenopausal women. *Angiology* 2009; 60(6): 750–756.
196. Sharman JE and Stowasser M. Australian association for exercise and sports science position statement on exercise and hypertension. *J Sci Med Sport* 2009; 12(2): 252–257.
197. Kasapis C and Thompson PD. The effects of physical activity on serum C-reactive protein and inflammatory markers: a systematic review. *J Am Coll Cardiol* 2005; 45(10): 1563–1569.
198. Petersen AM and Pedersen BK. The anti-inflammatory effect of exercise. *J Appl Physiol* 2005; 98(4): 1154–1162.
199. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H and Kannel WB. Prediction of coronary heart disease using risk factors categories. *Circulation* 1998; 97(18): 1837–1847.
200. Weight LM, Alexander D and Jacobs P. Strenuous exercise: analogous to the acute-phase response? *Clin Sci* 1991; 81(5): 677–683.
201. Pedersen BK, Steensberg A, Fischer C, Keller C, Keller P, Plomgaard P, Febbraio M, et al. Searching for the exercise factor: is IL-6 a candidate. *J Muscle Res Cell Motil* 2003; 24(2–3): 113–119.
202. Bruunsgaard H. Physical activity and modulation of systemic low-level inflammation. *J Leukoc Biol* 2005; 78(4): 819–835.
203. Calle MC and Fernandez ML. Effects of resistance training on the inflammatory response. *Nutr Res Pract* 2010; 4(4): 259–269.
204. Hirose L, Nosaka K, Newton M, Laveder A, Kano M, Peake J, et al. Changes in inflammatory mediators following eccentric exercise of the elbow flexors. *Exerc Immunol Rev* 2004; 10: 75–90.
205. Smith LL, Anwar A, Fragen M, Rananto C, Johnson R and Holbert D. Cytokines and cell adhesion molecules associated with high-intensity eccentric exercise. *Eur J Appl Physiol* 2000; 82(1–2): 61–67.
206. Hansen JB, Wilsgard L, Olsen JO and Osterud B. Formation and persistence of procoagulant and fibrinolytic activities in circulation after strenuous physical exercise. *Thromb Haemost* 1990; 64(3): 385–389.
207. Van den Burg PJ, Hospers JE, Mosterd WL, Bouma BN and Huisveld IA. Aging, physical conditioning and exercise-induced changes in hemostatic factors and reaction products. *J Appl Physiol* 2000; 88(5): 1558–1564.
208. El-Sayed MS, El-Sayed Ali Z and Ahmadizad S. Exercise and training effects on blood haemostasis in health and disease: an update. *Sports Med* 2004; 34(3): 181–200.
209. Ribeiro J, Almeida-Dias A, Ascensão A, Magalhães J, Oliveira AR, Carlson J, et al. Hemostatic response to acute physical exercise in healthy adolescents. *J Sci Med Sport* 2007; 10(3): 164–169.
210. Rankinen T, Vaisanen S, Penttilä I and Rauramaa R. Acute dynamic exercise increases fibrinolytic activity. *Thromb Haemost* 1995; 73(2): 281–286.
211. Geffken DF, Cushman M, Burke GL, Polak JF, Sakkinen PA and Tracy RP. Association between physical activity and markers of inflammation in a healthy elderly population. *Am J Epidemiol* 2001; 153(3): 242–250.
212. King DE, Carek P, Mainous AG III and Pearson WS. Inflammatory markers and exercise: differences related to exercise type. *Med Sci Sports Exerc* 2003; 35(4): 575–581.
213. Lakka TA, Lakka HM, Rankinen T, Leon AS, Rao DC, Skinner JS, et al. Effect of exercise training on plasma levels of C-reactive protein in healthy adults: the HERITAGE Family Study. *Eur Heart J* 2005; 26(19): 2018–2025.
214. Kohut ML, McCann DA, Russell DW, Konopka DN, Cunnick JE, Franke WD, et al. Aerobic exercise, but not flexibility/resistance exercise, reduces serum IL-18, CRP, and IL-6 independent of beta-blockers, BMI, and psychosocial factors in older adults. *Brain Behav Immun* 2006; 20(3): 201–209.
215. Thompson D, Markovitch D, Betts JA, Mazzatti D, Turner J and Tyrrell RM. Time course of changes in inflammatory markers during a 6-mo exercise intervention in sedentary middle-aged men: a randomized-controlled trial. *J Appl Physiol* 2010; 108(4): 769–779.
216. Wannamethee SG, Lowe GD, Whincup PH, Rumley A, Walker M and Lennon L. Physical activity and hemostatic and inflammatory variables in elderly men. *Circulation* 2002; 105(15): 1785–1790.
217. Hammett CJ, Prapavessis H, Baldi JC, Varo N, Schoenbeck U, Ameratunga R, et al. Effects of exercise training on 5 inflammatory markers associated cardiovascular risk. *Am Heart J* 2006; 151(2): 367.e7–367.e16.
218. Izquierdo M, Ibañez J, Calbet JAL, Navarro-Amezqueta I, González-Izal M, Idoate F, et al. Cytokine and hormone responses to resistance training. *Eur J Appl Physiol* 2009; 107(4): 397–409.
219. Stewart LK, Flynn MG, Campbell WW, Craig BA, Robinson JP, Timmerman KL, et al. The influence of exercise training on inflammatory cytokines and C-reactive protein. *Med Sci Sports Exerc* 2007; 39(10): 1714–1719.
220. Eliasson M, Asplund K and Evrin PE. Regular leisure time physical activity predicts high activity of tissue plasminogen activator: the Northern Sweden

- MONICA Study. *Int J Epidemiol* 1996; 25(6): 1182–1188.
221. Ogawa K, Sanada K, Machida S, Okutsu M and Suzuki K. Resistance exercise training-induced muscle hypertrophy was associated with reduction of inflammatory markers in elderly women. *Mediators Inflamm* 2010; (Epub ahead of print).
 222. Albert MA, Glynn RJ and Ridker PM. Effect of physical activity on serum C-reactive protein. *Am J Cardiol* 2004; 93(2): 221–225.
 223. Majka DS, Chang RW, Vu TH, Palmas W, Geffken DF, Ouyang P, et al. Physical activity and high-sensitivity C-reactive protein: the multi-ethnic study of atherosclerosis. *Am J Prev Med* 2009; 36(1): 56–62.
 224. Bertoni AG, Whitt-Glover MC, Chung H, Le KY, Barr RG, Mahesh M, et al. The association between physical activity and subclinical atherosclerosis: the Multi-Ethnic Study of Atherosclerosis. *Am J Epidemiol* 2009; 169(4): 444–454.
 225. Moser DK. The rust of life: impact of anxiety on cardiac patients. *Am J Crit Care* 2007; 16(4): 361–369.
 226. Todaro JF, Shen BJ, Raffa SD, Tilkemeier PL and Niaura R. Prevalence of anxiety disorders in men and women with established coronary heart disease. *J Cardiopulm Rehabil Prev* 2007; 27(2): 86–91.
 227. Hemingway H and Marmot M. Evidence based cardiology: psychosocial factors in the aetiology and prognosis of coronary heart disease. Systematic review of prospective cohort studies. *BMJ* 1999; 318(7196): 1460–1467.
 228. Kuper H, Marmot M and Hemingway H. Systematic review of prospective cohort studies of psychosocial factors in the etiology and prognosis of coronary heart disease. *Semin Vasc Med* 2002; 2(3): 267–314.
 229. Scottish Intercollegiate Guidelines Network. *Risk estimation and the prevention of cardiovascular disease. A national clinical guideline*. Edinburgh: SIGN, 2007.
 230. Shen BJ, Avivi YE, Todaro JF, Spiro A III, Laurenceau JP, Ward KD, et al. Anxiety characteristics independently and prospectively predict myocardial infarction in men the unique contribution of anxiety among psychologic factors. *J Am Coll Cardiol* 2008; 51(2): 113–119.
 231. Kent LK and Shapiro PA. Depression and related psychological factors in heart disease. *Harv Rev Psychiatry* 2009; 17(6): 377–388.
 232. Petruzzello SJ, Landers DM, Hatfield BD, Kubitz KA and Salazar W. A meta-analysis on the anxiety-reducing effects of acute and chronic exercise. Outcomes and mechanisms. *Sports Med* 1991; 11(3): 143–182.
 233. Kugler J, Seelbach H and Kruskemper GM. Effects of rehabilitation exercise programmes on anxiety and depression in coronary patients: a meta-analysis. *Br J Clin Psychol* 1994; 33(Pt3): 401–410.
 234. Herring MP, O'Connor PJ and Dishman RK. The effect of exercise training on anxiety symptoms among patients: a systematic review. *Arch Intern Med* 2010; 170(4): 321–331.
 235. Rejeski WJ, Thompson A, Brubaker PH and Miller HS. Acute exercise: buffering psychosocial stress responses in women. *Health Psychol* 1992; 11(6): 355–362.
 236. Strohle A, Feller C, Onken M, Godemann F, Heinz A and Dimeo F. The acute antipanic activity of aerobic exercise. *Am J Psychiatry* 2005; 162(12): 2376–2378.
 237. Barbour KA, Edenfield TM and Blumenthal JA. Exercise as a treatment for depression and other psychiatric disorders: a review. *J Cardiopulm Rehabil Prev* 2007; 27(6): 359–367.
 238. Petruzzello SJ, Snook EM, Gliottoni RC and Motl RW. Anxiety and mood changes associated with acute cycling in persons with multiple sclerosis. *Anxiety Stress Coping* 2009; 22(3): 297–307.
 239. Strohle A, Graetz B, Scheel M, Wittmann A, Feller C, Heinz A, et al. The acute antipanic and anxiolytic activity of aerobic exercise in patients with panic disorder and healthy control subjects. *J Psychiatr Res* 2009; 43(12): 1013–1017.
 240. Broman-Fulks JJ, Berman ME, Rabian BA and Webster MJ. Effects of aerobic exercise on anxiety sensitivity. *Behav Res Ther* 2004; 42(2): 125–136.
 241. Katula JA, Blissmer BJ and McAuley E. Exercise intensity and self-efficacy effects on anxiety reduction in healthy, older adults. *J Behav Med* 1999; 22(3): 233–247.
 242. Thombs BD, Bass EB, Ford DE, Stewart KJ, Tsilidis KK, Patel U, et al. Prevalence of depression in survivors of acute myocardial infarction. *J Gen Intern Med* 2006; 21(1): 30–38.
 243. Barth J, Schumacher M and Herrmann-Lingen C. Depression as a risk factor for mortality in patients with coronary heart disease: a meta-analysis. *Psychosom Med* 2004; 66(6): 802–813.
 244. Van Melle JP, de Jonge P, Spijkerman TA, Tijssen JG, Ormel J, van Veldhuisen DJ, et al. Prognostic association of depression following myocardial infarction with mortality and cardiovascular events: a meta-analysis. *Psychosom Med* 2004; 66(6): 814–822.
 245. Nicholson A, Kuper H and Hemingway H. Depression as an aetiological and prognostic factor in coronary heart disease: a meta-analysis of 6362 events among 146 538 participants in 54 observational studies. *Eur Heart J* 2006; 27(23): 2763–2774.
 246. Glassman AH, O'Connor CM, Califf RM, Swedberg K, Schwartz P, Bigger Jr JT, et al. Sertraline treatment of major depression in patients with acute MI or unstable angina. *JAMA* 2002; 288(6): 701–709.
 247. Berkman LF, Blumenthal J, Burg M, Carney RM, Catellier D, Cowan MJ, et al. Effects of treating depression and low perceived social support on clinical events after myocardial infarction: the Enhancing Recovery in Coronary Heart Disease Patients (ENRICH) Randomized Trial. *JAMA* 2003; 289(23): 3106–3116.
 248. Teychenne M, Ball K and Salmon J. Physical activity and likelihood of depression in adults: a review. *Prev Med* 2008; 46(5): 397–411.
 249. Roshanaei-Moghaddam B, Katon WJ and Russo J. The longitudinal effects of depression on physical activity. *Gen Hosp Psychiatry* 2009; 31(4): 306–315.
 250. Davidson JR. Major depressive disorder treatment guidelines in America and Europe. *J Clin Psychiatry* 2010; 71(Suppl E1): e04.

251. Mead GE, Morley W, Campbell P, Greig CA, McMurdo M and Lawlor DA. Exercise for depression. *Cochrane Database Syst Rev* 2009; (3): CD004366.
252. Strohle A. Physical activity, exercise, depression and anxiety disorders. *J Neural Transm* 2009; 116(6): 777–784.
253. Byrne A and Byrne DG. The effect of exercise on depression, anxiety and other mood states: a review. *J Psychosom Res* 1993; 37(6): 565–574.
254. Barbour KA and Blumenthal JA. Exercise training and depression in older adults. *Neurobiol Aging* 2005; 26(Suppl 1): 119–123.
255. Daley A. Exercise and depression: a review of reviews. *J Clin Psychol Med Settings* 2008; 15(2): 140–147.
256. Blake H, Mo P, Malik S and Thomas S. How effective are physical activity interventions for alleviating depressive symptoms in older people? A systematic review. *Clin Rehabil* 2009; 23(10): 873–887.
257. Milani RV, Lavie CJ and Cassidy MM. Effects of cardiac rehabilitation and exercise training programs on depression in patients after major coronary events. *Am Heart J* 1996; 132(4): 726–732.
258. Blumenthal JA, Sherwood A, Babyak MA, Watkins LL, Waugh R, Georgiades A, et al. Effects of exercise and stress management training on markers of cardiovascular risk in patients with ischemic heart disease: a randomized controlled trial. *JAMA* 2005; 293: 1626–1634.
259. Blumenthal JA. Depression and coronary heart disease: association and implications for treatment. *Cleve Clin J Med* 2008; 75(Suppl 2): S48–S53.
260. Coventry PA and Hind D. Comprehensive pulmonary rehabilitation for anxiety and depression in adults with chronic obstructive pulmonary disease: systematic review and meta-analysis. *J Psychosom Res* 2007; 63(5): 551–565.
261. Angevaren M, Aufdemkampe G, Verhaar HJ, Aleman A and Vanhees L. Physical activity and enhanced fitness to improve cognitive function in older people without known cognitive impairment. *Cochrane Database Syst Rev* 2008; (2): CD005381.
262. Deslandes A, Moraes H, Ferreira C, Veiga H, Silveira H, Mouta R, et al. Exercise and mental health: many reasons to move. *Neuropsychobiology* 2009; 59(4): 191–198.
263. Singh NA, Stavrinou TM, Scarbek Y, Galambos G, Liber C and Fiatarone Singh MA. A randomized controlled trial of high versus low intensity weight training versus general practitioner care for clinical depression in older adults. *J Gerontol A Biol Sci Med Sci* 2005; 60(6): 768–776.
264. Graham I, Atar D, Borch-Johnsen K, Boysen G, Burell G, Cifkova R, et al.; European Society of Cardiology (ESC) Committee for Practice Guidelines (CPG). European guidelines on cardiovascular disease prevention in clinical practice: executive summary. Fourth Joint Task Force of the European Society of Cardiology and other Societies. *Eur Heart J* 2007; 28(19): 2375–2414.
265. Aittasalo M. Physical activity counselling in primary health care. *Scand J Med Sci Sports* 2008; 18(3): 261–262.
266. Cherry DK, Woodwell DA and Rechtsteiner EA. National ambulatory medical care survey: 2005 summary. *Adv Data* 2007; (387): 1–39.
267. Lobelo F, Duperly J and Frank E. Physical activity habits of doctors and medical students influence their counselling practices. *Br J Sports Med* 2009; 43(2): 89–92.
268. Pate RR, Pratt M, Blair SN, Haskell WL, Macera CA, Bouchard C, et al. Physical activity and public health. A recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *JAMA* 1995; 273(5): 402–407.
269. World Health Organization. *Global strategy on diet, physical activity and health*. Geneva: WHO, 2004.
270. Jacobson DM, Strohecker L, Compton MT and Katz DL. Physical activity counseling in the adult primary care setting: position statement of the American College of Preventive Medicine. *Am J Prev Med* 2005; 29(2): 158–162.
271. Swedish Council on Technology Assessment. *Methods of promoting physical activity: A systematic review*. Stockholm: SBU, 2007 Report no. 181.
272. Cooper A and O'Flynn N. Risk assessment and lipid modification for primary and secondary prevention of cardiovascular disease: summary of NICE guidance. *BMJ* 2008; 336(7655): 1246–1248.
273. Chakravarthy MV, Joyner MJ and Brooth PW. An obligation for primary care physicians to prescribe physical activity to sedentary patients to reduce the risk of chronic health conditions. *Mayo Clin Proc* 2002; 77(2): 165–173.
274. Glasgow RE, Lichtenstein E and Marcus AC. Why don't we see more translation of health promotion research to practice? Rethinking the efficacy-to-effectiveness transition. *Am J Public Health* 2003; 93(8): 1261–1267.
275. Glasgow RE and Emmons KM. How can we increase translation of research into practice? Types of evidence needed. *Ann Rev Public Health* 2007; 28: 413–433.
276. Glasgow RE, Eakin EG, Fisher EB, Bacak SJ and Brownson RC. Physician advice and support for physical activity: results from a national survey. *Am J Prev Med* 2001; 21(3): 189–196.
277. Brotons C, Bjorkelund C, Bulc M, Ciurana R, Godycki-Cwirko M, Jurgova E, et al. Prevention and health promotion in clinical practice: the views of general practitioners in Europe. *Prev Med* 2005; 40(5): 595–601.
278. Van der Ploeg HP, Smith BJ, Stubbs T, Vita P, Holford R and Bauman AE. Physical activity promotion—are GPs getting the message? *Aust Fam Physician* 2007; 36(10): 871–874.
279. Walsh JME, Swangard DM, Davis T and McPhee SJ. Exercise counseling by primary care physicians in the era of managed care. *Am J Prev Med* 1999; 16(4): 307–313.
280. Anis NA, Lee RE, Ellerbeck EF, Nazir N, Greiner KA and Ahluwalia JS. Direct observation of physician

- counseling on dietary habits and exercise: patient, physician, and office correlates. *Prev Med* 2004; 38(2): 198–202.
281. Wee CC, McCarthy EP, Davis RB and Philips RS. Physician counseling about exercise. *JAMA* 1999; 282(16): 1583–1588.
 282. Eaton CB and Menard LM. Asystematic review of physical activity promotion in primary care settings. *Br J Sports Med* 1998; 32(1): 11–16.
 283. Eakin EG, Glasgow RE and Riley KM. Review of primary-care based physical activity intervention studies. *J Fam Pract* 2000; 49(2): 158–168.
 284. Lawlor DA and Hanratty B. The effect of physical activity advice given in routine primary care consultations: a systematic review. *J Public Health Med* 2001; 23(3): 219–226.
 285. Socialstyrelsen. *National guidelines for lifestyle-methods for disease prevention*. Stockholm: Swedish National Board of Health and Welfare, 2010.
 286. Hillsdon M, Foster C and Thorogood M. Interventions for promoting physical activity. *Cochrane Database Syst Rev* 2005; (1): CD003180.
 287. Williams NH. 'The wise, for cure, on exercise depend': physical activity interventions in primary care in Wales. *Br J Sports Med* 2009; 43(2): 106–108.
 288. Smith BJ. Promotion of physical activity in primary health care: update of the evidence on interventions. *J Sci Med Sport* 2004; 7(Suppl 1): 67–73.
 289. Smitherman TA, Kendzor DE, Grothe KB and Dubbert PM. State of the art review: promoting physical activity in primary care settings: a review of cognitive and behavioral strategies. *Am J Lifestyle Med* 2007; 1(5): 397–409.
 290. Spencer L, Adams TB, Malone S, Roy L and Yost E. Applying the transtheoretical model to exercise: a systematic and comprehensive review of the literature. *Health Promot Pract* 2006; 7(4): 428–443.
 291. Preventive Services Task Force US. Behavioural counseling in primary care to promote physical activity: recommendations and rationale. *Ann Intern Med* 2002; 137(3): 205–207.
 292. Elley CR, Kerse N, Arroll B and Robinson E. Effectiveness of counselling patients on physical activity in general practice: cluster randomised controlled trial. *BMJ* 2003; 326(7393): 793.
 293. Morgan O. Approaches to increase physical activity: reviewing the evidence for exercise-referral schemes. *Public Health* 2005; 119(5): 361–370.
 294. Sorensen JB, Skovgaard T and Puggaard L. Exercise on prescription in general practice: a systematic review. *Scand J Prim Health Care* 2006; 24(2): 69–74.
 295. Kallings LV, Leijon M, Hellénus ML and Stahle A. Physical activity on prescription in primary health care: a follow-up of physical activity level and quality of life. *Scand J Med Sci Sports* 2008; 18(2): 154–161.
 296. National Institute for Health and Clinical Excellence. Public Health Collaborating Centre for Physical Activity. A rapid review of the effectiveness of exercise referral schemes to promote physical activity in adults. London: National Institute for Health and Clinical Excellence; 2006.
 297. Kahn EB, Ramsey LT, Brownson RC, Heath GW, Howze EH, Powell KE, et al. The effectiveness of interventions to increase physical activity. A systematic review. *Am J Prev Med* 2002; 22(Suppl 4): 73–107.
 298. Sorensen JB, Kragstrup J, Kjaer K and Puggaard L. Exercise on prescription: trial protocol and evaluation of outcomes. *BMC Health Serv Res* 2007; 7: 36.
 299. Dugdill L, Graham RC and McNair F. Exercise referral: the public health panacea for physical activity promotion? *Ergonomics* 2005; 48(11–14): 1390–1410.
 300. Williams NH, Hendry M, France B, Lewis R and Wilkinson C. Effectiveness of exercise-referral schemes to promote physical activity in adults: a systematic review. *Br J Gen Pract* 2007; 57(545): 979–986.
 301. Kallings LV, Leijon ME, Kowalski J, Hellénus ML and Stahle A. Self-reported adherence: a method for evaluating prescribed physical activity in primary health care patients. *J Phys Act Health* 2009; 6(4): 483–492.
 302. Leijon ME, Bendtsen P, Nilsen P, Festin K and Stahle A. Does a physical activity referral scheme improve the physical activity among routine primary health care patients? *Scand J Med Sci Sports* 2009; 19(5): 627–636.
 303. Grandes G, Sanchez A, Sanchez-Pinilla RO, Torcal J, Montoya I, Lizaraga K, et al. Effectiveness of physical activity advice and prescription by physicians in routine primary care: a cluster randomized trial. *Arch Intern Med* 2009; 169(7): 694–701.
 304. Kallings LV, Sierra-Johnson J, Fischer RM, Faire U, Stahle A, Hemmingsson E, et al. Beneficial effects of individualized physical activity on prescription on body composition and cardiometabolic risk factors: results from a randomized controlled trial. *Eur J Cardiovasc Prev Rehabil* 2009; 16(1): 80–84.
 305. Reiner Z, Sonicki Z and Tedeschi-Reiner E. Public perceptions of cardiovascular risk factors in Croatia: the PERCRO survey. *Prev Med* 2010; 51(6): 494–496.
 306. Riegel B and Carlson B. Facilitators and barriers to heart failure self-care. *Pat Educat Counsel* 2002; 46(4): 287–295.
 307. Burack RC. Barriers to clinical preventive medicine. *Primary Care* 1989; 16: 245–250.
 308. McKenna J, Naylor PJ and McDowell N. Barriers to physical activity promotion by general practitioners and practice nurses. *Br J Sports Med* 1998; 32(3): 242–247.
 309. Douglas F, Torrance N, vanTeijlingen E, Meloni S and Kerr A. Primary staff's views and experiences related to routinely advising patients about physical activity. A questionnaire survey. *BMC Public Health* 2006; 6: 138.
 310. Abramson S, Stein J, Schaefele M, Frates E and Rogan S. Personal exercise habits and counseling practices of primary care physicians: a national survey. *Clin J Sport Med* 2000; 10(1): 40–48.
 311. Frank E, Tong E, Lobelo F, Carrera J and Duperly J. Physical activity levels and counseling practices of U.S. medical students. *Med Sci Sports Exerc* 2008; 40(3): 413–421.

312. Siscovick D, Weiss NS, Fletcher RH and Lasky T. The incidence of primary cardiac arrest during vigorous exercise. *N Engl J Med* 1984; 311(14): 874–877.
313. Albert CM, Mittleman MA, Chae CU, Lee IM, Hennekens CH and Manson JE. Triggering of sudden death from cardiac causes by vigorous exertion. *N Engl J Med* 2000; 343(19): 1355–1361.
314. Thompson PD. The cardiovascular complications of vigorous physical activity. *Arch Intern Med* 1996; 156(20): 2297–2302.
315. Börjesson M, Urhausen A, Koudi E, Dugmore D, Sharma S, Halle M, et al. Cardiovascular evaluation of adult/senior individuals engaged in leisure-time sport activities: position stand from the sections of Exercise Physiology and Sports Cardiology of the EACPR. *Eur J Cardiovasc Prev Rehabil* 2010; 18(3): 446–458.
316. Corrado D, Basso C, Rizzoli G, Schiavon M and Thiene G. Does sports activity enhance the risk of sudden death in adolescents and young adults? *J Am Coll Cardiol* 2003; 42(11): 1959–1963.
317. Borjesson M and Pelliccia A. Incidence and aetiology of sudden cardiac death in young athletes: an international perspective. *Br J Sports Med* 2009; 43(9): 644–648.
318. Maron BJ. Sudden death in young athletes. *N Engl J Med* 2003; 349(11): 1064–1075.
319. Burke AP, Farb A, Virmani R, Goodin J and Smialek JE. Sports-related and non-sports-related sudden cardiac death in young adults. *Am Heart J* 1991; 121(2 pt 1): 568–575.
320. Maron BJ, Doerer JJ, Haas TS, Tierney DM and Mueller FO. Profile and frequency of sudden death in 1463 young competitive athletes: from a 25 year US national registry: 1980–2005. *Circulation* 2006; 114(Suppl II): 830.
321. Corrado D, Pelliccia A, Bjornstad HH, Vanhees L, Biffi A, Borjesson M, et al. Cardiovascular pre-participation screening of young competitive athletes for prevention of sudden death: proposal for a common European protocol. *Eur Heart J* 2005; 26(5): 516–524.
322. Corrado D, Basso C, Pavei A, Michieli P, Schiavon M and Thiene G. Trends in sudden cardiovascular death in young competitive athletes after implementation of a preparticipation screening programme. *JAMA* 2006; 296(13): 1593–1601.
323. Corrado D, Basso C, Schiavon M, Pelliccia A and Thiene G. Pre-participation screening of young competitive athletes for prevention of sudden cardiac death. *J Am Coll Cardiol* 2008; 52(24): 1981–1989.
324. Mittleman MA, Maclure M, Tofler GH, Sherwood JB, Goldberg RJ and Muller JE. Triggering of acute myocardial infarction by heavy physical exertion. Protection against triggering by regular exercise. *N Engl J Med* 1993; 329(23): 1677–1683.
325. Willich SN, Maclure M, Mittleman M, Arntz H-R and Muller JE. Sudden cardiac death: support for a role of triggering in causation. *Circulation* 1993; 87(5): 1442–1450.
326. Maron BJ. The paradox of exercise. *N Engl J Med* 2000; 343(19): 1409–1411.
327. Taylor R, Brown A, Ebrahim S, Jolliffe J, Noorani H, Rees K, et al. Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomised controlled trials. *Am J Med* 2004; 116(10): 682–692.
328. Kodama S, Kazumi S, Tanaka S, Maki M, Yachi Y, Asumi M, et al. Cardiorespiratory fitness as quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women. A meta-analysis. *JAMA* 2009; 301(19): 2024–2035.
329. Saltin B. Physiological effects of physical conditioning. In: Hansen AT, Schnor P and Rose G (eds) *Ischaemic heart disease: The strategy of postponement*. Chicago: Year Book Medical Publishers, 1977, pp.104–115.
330. Borjesson M, Assanelli D, Carré F, Dugmore D, Panhuyzen-Goedkoop NM, Seiler C, et al. ESC Study Group of Sports Cardiology: recommendations for participation in leisure-time physical activity and competitive sports for patients with ischemic heart disease. *Eur J Cardiovasc Prev Rehabil* 2006; 13(2): 137–149.
331. Drezner JA. Contemporary approaches to the identification of athletes at risk of sudden cardiac death. *Curr Opin Cardiolol* 2008; 23(5): 494–501.
332. AHA. Exercise and acute cardiovascular events. Placing the risk into perspective. AHA Scientific statement. *Circulation* 2007; 115(17): 2358–2368.
333. Hallstrom A and Ornato JP. Public-access defibrillation and survival after out-of-hospital cardiac arrest. *N Engl J Med* 2004; 351(7): 637–646.
334. Becker L, Eisenberg M, Fahrenbruch C and Cobb L. Public locations of cardiac arrest: implications for public access defibrillation. *Circulation* 1998; 97(21): 2106–2109.
335. American College of Sports Medicine and American Heart Association. American College of Sports Medicine; American Heart Association joint position statement: automated external defibrillators in health/fitness facilities. *Med Sci Sports Exerc* 2002; 34(3): 561–564.
336. Börjesson M, Serratos L, Carré F, Corrado D, Drezner J, Dugmore DL, et al. Consensus document regarding cardiovascular safety at sports arenas. *Eur Heart J* 2011; 32(17): 2119–2124.