Title: Recreational Football is Medicine against Non-Communicable Diseases: A systematic Review

Running title: Football is Medicine against NCD's

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Abstract

The purpose of this research was to conduct a systematic review of published articles related to the effect of recreational football on non-communicable diseases.

A systematic review of Web of Science, SPORTdiscus, MEDLINE and PubMed databases was performed according PRISMA guidelines. Only empirical studies were included. There were no restrictions on the types of study design eligible for inclusion. The primary outcome measures result from the potential effects of recreational football on non-communicable diseases (e.g., blood pressure, bone density, LDL-Cholesterol, fat mass, etc.).

A total of 44 articles met the inclusion criteria and were included. Recreational football is shown to: (1) decrease blood pressure and resting heart rate, improve cardiac structure and functioning, as well as increase maximal oxygen uptake in both sexes; (2) reduce cholesterol and triglycerides levels, increase insulin sensitivity, and have a positive impact on glycaemic control; (3) improve bone mineralization, increase both bone mineral density and content, as well as acting as a stimulus for osteogenesis; (4) be clearly beneficial for bone health, whilst slightly beneficial for body composition, muscle strength and maximal oxygen uptake in adults with prostate cancer.

The present systematic review demonstrated the benefits of recreational football practice on non-communicable diseases related to cardiovascular and bone health, body composition, type 2 diabetes and prostate cancer. The effectiveness of recreational

football on the aforementioned diseases may be related to age and gender; however, further research is required.

1 Introduction

Non-communicable diseases (NCDs), also known as chronic diseases, tend to be of long duration and are the result of a combination of diverse factors (e.g., genetic, physiological, environmental and behavioural). NCDs kill 41 million people each year (71% of all deaths globally). Of these people, 15 million are between the ages of 30 and 70 years old[1]. Cardiovascular diseases account for most NCD deaths (17.9 million people per year), followed by cancers (9.0 million), respiratory diseases (3.9 million), and diabetes (1.6 million)[2].

Physical inactivity has been identified as the fourth leading risk factor for global mortality, contributing to 6% of deaths worldwide[3]. In turn, overweight and obesity are responsible for 5% of global mortality, followed by high blood glucose (6%), tobacco use (9%) and high blood pressure (13%)[3]. Elimination of physical inactivity could reduce 6% and 10% of the major NCDs, i.e., coronary heart disease, type 2 diabetes mellitus (T2DM), and breast and colon cancers; subsequently increasing life expectancy[4]. In this context, the urgent need to create and develop intervention programs that are effective in promoting active lifestyles have been emphasized by different entities (e.g., WHO, UNESCO). As one of the most popular and most widely played sports in the world, football can have an important role in promoting active lifestyles.

The use of randomised controlled trials (RCT) to investigate recreational football (RF) as a strategy to improve health and well-being has increased exponentially in the last decade. Moreover, several special issues, systematic reviews and meta-analyses have confirmed that RF is an adequate exercise intervention for health promotion[5,6] including women's

fitness and health adaptations and mechanisms[7,8], as well as for disease prevention and treatment in untrained men[9]. Additionally, RF effectively improves cardiorespiratory fitness[10,11] and produces broad-spectrum physical fitness benefits which are all related to NCDs. Based on the aforementioned comprehensive research, FIFA (the Fédération Internationale de Football Association) introduced the slogan "Playing football for 45 minutes twice a week – best prevention of NCDs". However, conclusions are based on RCT trials which have separately investigated the effects of RF on the most common NCDs such as cardiovascular disease, type 2 diabetes, obesity, osteoporosis, cancer etc. Therefore, an overall conclusion based on the use of RF in the prevention and treatment of NCDs, based on a systematic literature review, remains elusive.

It is important that the current available evidence be identified and appraised, so that interventions on RF that are effective in managing NCDs may be identified and put into practice. The purpose of this systematic review was to systematically review the results of the published scientific papers concerning the effects of RF on NCDs.

2. Methods

2.1 Protocol and Registration

This systematic review protocol was registered at the International Prospective Register of systematic Reviews (PROSPERO) under number CRD42018107448.

2.2 Search Strategy: Databases and Inclusion Criteria

A systematic review of the available literature was conducted according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines [12].

The electronic databases Web of Science, SPORTdiscus, MEDLINE and PubMed were searched for relevant publications prior to the 31th of August 2018 by using the keywords

"football" OR "soccer" each one associated with the terms: "disease*" OR "cancer" OR "cardiovascular" OR "blood pressure" OR "hypertension" OR "overweight" OR "obesity" OR "tobacco" OR "smoking" OR "diabetes" OR "insulin" OR "cholesterol" OR "hyperglycemia" OR "hyperlipidemia" OR "dyslipidemia" OR "triglycerides" OR "osteoporosis" OR "bone health" OR "bone density" OR "chronic respiratory" OR "pulmonary disease" OR "asthma" OR "kidney disease" OR "prostatic hyperplasia" OR "renal failure" OR "kidney failure". The publications included in the first search round met the following criteria: (1) contained relevant data concerning NCDs; (2) were performed on RF male/female participants (all ages); and (3) were written in the English Language. Studies were excluded if they: (1) were performed in the context of competitive football; and (2) did not contain any relevant data about RF and NCDs.

Two reviewers (HS, FC) independently screened citations and abstracts to identify articles potentially meeting the inclusion criteria. For those articles, full text versions were retrieved and independently screened by those reviewers, to determine whether they met inclusion criteria. Any disagreement regarding study eligibility was resolved by consensus including a third reviewer (ZM).

2.3 Quality of the Studies and Extraction of Data

The overall methodological quality of the studies was assessed by two independent reviewers using the Physiotherapy Evidence Database (PEDro) scale. Agreement between reviewers was assessed using *k* statistics (k=0.96) for full-text screening and rating of relevance and risk of bias. In the event of disagreement about the risk of bias, the third reviewer checked the data and took the final decision on it.

A data extraction sheet (from Cochrane Consumers and Communication Review Group's data extraction template[13]) was adapted to this review's study inclusion requirements and

then tested on ten randomly selected studies (pilot test). One author extracted the data and another verified it.

3 Results

3.1 Search, Selection, and Inclusion of Publications

The initial search identified 1537 titles in the aforementioned databases and an additional 17 papers were selected on the basis of their references. These data were then exported to reference manager software (EndNote™X8, Clarivate Analytics, Philadelphia, PA, USA). Any duplicates (1147 references) were eliminated either automatically or manually. The remaining 407 articles were then screened for relevance based on their title and abstract, resulting in 317 studies being eliminated from the database. The full text of the remaining 90 articles was examined in more detail; 46 were rejected because they did not meet the inclusion criteria. At the end of the screening procedure, 44 articles were selected for in depth reading and analysis (Figure 1). The main factor for study exclusion (n=18) was their lack of relevance to the research topic of this review. Other studies were excluded because they contained data from other sports (n=13) or were developed in the context of competitive football.

****Insert_Figure_1****

3.3 General description of the studies

In this review, we grouped the studies according to the most common NCDs, namely: (1) Cardiovascular health; (2) Type 2 diabetes; (3) Overweight/Obesity; (4) Cancer; (5)

Osteoporosis (Figure 2). Nevertheless, some papers included topics that studied multiple NCDs and other health-related measures. Thus, an article included in a specific 'disease', could also be classified in another 'disease' whenever its content justified it[14-16].

****Insert_Figure_2****

3.3.1 Cardiovascular Health

RF interventions have been conducted to analyze the effects of regular exercise in the management of some markers associated with cardiovascular diseases or cardiovascular risk (Table 1). RF was commonly based on small-sided games played for 1-hour twice or three times a week, depending on the studies design.

The unique pathology used as inclusion criterion during RCT was mild-to-moderate hypertension (n=4)[17-20]. The majority of the studies were conducted in adult untrained participants (n=14), however, there were studies conducted on youth (<18 years old) (n=3) and elderly (>65 years old) (n=3) populations. Men (n=12), women (n=6) and both studied at the same time (n=2) were analyzed across the studies.

The majority of the studies were conducted as RCT (n=16), however some of them were cross-sectional (n=4) and one of the studies was a controlled training study without randomization[21]. The period of RCT was between 12 weeks[22,23] to 12-[17,24] and 16-months[25]. Usually, the RCT compared a football intervention against a passive control group (n=8). However, some studies also compared football against running-based intervention (n=6) or strength training (n=2).

The variables more commonly studied during the articles related to cardiovascular health were: (1) arterial blood pressure; (2) systolic and diastolic function (measured by echocardiography); (3) resting heart rate; (4) maximal oxygen uptake; and (5) cholesterol

and triglyceride concentrations. However, the reviewed studies tested other variables such as fitness status, body composition, bone health or blood metabolites such as glucose.

****Insert_ Table_1****

3.3.2 Type 2 diabetes

In all reviewed studies (Table 2) it was verified that RF has a positive effect against type 2 diabetes[26-29]. All studies screened were with adults and it was clear that football practice lowered cholesterol and triglycerides levels[27,29], increased insulin sensitivity[27,28], and positive impacted on glycaemic control[26]. Altogether, it seems that RF practice of at least 1-hour duration, twice a week has the potential to prevent type 2 diabetes, long-term morbidity, and may be used in the treatment of T2DM.

****Insert_ Table_2****

3.3.3 Overweight/Obesity

Five of the seven articles (all intervention studies), performed in several different countries with sample sizes range from 12 to 742 reported positive associations between football practice and reductions in body mass[15,30-33] (Table 3). The two studies that reported no changes in body mass index and percentage of body fat among participants, after 5- and 6-month intervention, were performed with children and adolescents[34,35]. A third study with children and adolescents showed that lean body mass (4.3%, ES = 0.40; 95% CI: −0.48, 1.29; P = .382) and muscle mass 4.4% (ES = 0.40; 95% CI: −0.48, 1.29; P = .378) very likely increased in the RF group[33]. All the studies with adults and older adults were consistent in showing that at least a 40-week RF intervention significantly

reduced body mass index, total body fat mass and made positive changes to other biomarkers of health risk, lifestyle behaviours and psychological outcomes[15,30-32].

****Insert_ Table_3****

3.3.4 Cancer

The reviewed studies on RF as part of the treatment on cancer or post-cancer patients (Table 4) only analyzed the effects of football on men with prostate cancer[36-38]. All of the studies were RCT's comparing RF intervention to control groups, during periods that ranged from 12 to 32-weeks[36-38]. The main aim of these studies was to analyse the effects of RF intervention on the androgen deprivation that usually leads to decreases in bone mass. Based on that, bone mineral density was one of the common variables measured across the cancer studies. Other variables such as maximal oxygen uptake, muscle strength, body composition or postural balance were also analysed.

****Insert_ Table_4****

3.3.5 Osteoporosis

The results from the reviewed studies[15,16,39-45] showed that there is a beneficial relationship between football practice and bone health (Table 5) in children[42], adolescents[45], adults[15,41,44], and older adults[16,39,40]. Among children and adolescents, a 10-month to 1-year intervention significantly improves bone mineralisation, bone mineral content and bone stiffness[42,45]. The effect of football on bone health was more pronounced than in other activities such as swimming and cycling[45]. Among adults and older adults, regular football practice twice or three times per week is related to an increase in bone mineral density[15,16,39-41] and bone mineral content[15,44]. These studies presented consistent

results. However, most were performed in Scandinavian countries with a sample size across studies ranged from 22 to 295 participants.

****Insert_ Table_5****

4. Discussion

The aim of this paper was to systematically review the results of the published scientific evidence concerning the effects of RF on NCDs. After in-depth analysis, it was decided that the most appropriate way to discuss the results would be to categorize research topics according to the most common NCDs.

4.1 Cardiovascular Health

The impact of RF interventions on blood pressure is one the most researched topics in the literature. Results of short periods of RF intervention (12 to 16 weeks) revealed that, generally, blood pressure decreases more in healthy or mild-to-moderate arterial hypertensive men[20,22,23] and women[46,47] when compared to a control group. Similar evidence can be found ≥1 year interventions[17,25,48]. These responses may be caused by a reduction in sympathetic tone and an increase in parasympathetic activity as verified by heart rate variability and heart rate measurements[20,22,23]. It is also possible that improvements in the flexibility of the heart and vascular system and a reduced resistance due to higher muscular vascularization may explain the benefits seen by participating in RF[23,47].

In the case of short period interventions, results seem to suggest that a short period of RF intervention can lead to meaningful decreases in blood pressure (5-12 mmHg) in healthy and mild-to-moderate hypertensive men and women [23,20,49,47]. Longer interventions (one

year or more) of RF training were associated with decreases of 5 mmHg in mean arterial pressure of mild hypertensive women while no changes were found in a control group[17]. Furthermore, despite a decrease in the volume of training completed by healthy male participants after an initial 12-week period, decreases in systolic and diastolic blood pressure of 8 and 3 mmHg, respectively were still observed[48]. Resting heart rate seems to be sensitive to RF intervention in short-[47] and long-term[19,24] interventions. Similar to blood pressure, resting heart rate seems to be more sensitive to the initial intervention turning stable after a short period (12 to 16-weeks) even in cases of longer interventions. The effects of RF interventions on cardiac structure and function have been reported[18,24,50]. Generally, results suggest an increase of the left ventricular posterior wall thickness and diameter[51,50]. These results are in line with previous studies that combined dynamic and static workloads[51]. Interestingly, such changes are not as apparent in sedentary participants that participated in regular physical training programs in similar time periods, suggesting that RF is more efficacious based on its specific demands and intermittent movement patterns[51].

Increases in left ventricular systolic and diastolic performances were found in RF and running-based interventions with improvements in the peak systolic velocity, respectively[51]. Differences were found between RF and running-based groups on isovolumetric relaxation with a decrease of 26% in the football group compared to only 14% in the running group[51]. It was also found that left ventricular diastolic mitral flow ratio and peak early diastolic velocity improved by 25% and 12%, respectively, during a RF intervention, while no meaningful changes were found in strength or control groups[24]. Therefore, RF interventions seem to elicit changes in both cardiac structure and function with meaningful improvements in comparison to strength interventions or control groups or with similar effects in comparison to running-based groups. However, none of the

studies revealed the intra- or inter-observer reliability of the technicians that executed the echocardiography.

Fitness was also an important parameter measured in the reviewed studies and maximal oxygen uptake (VO_{2max}) was the most studied fitness variable. Improvements between 8 and 15% of VO_{2max} have been observed following short-term RF programs[23,51]. The changes promoted by-short term programs remain almost unchanged until the 15th month[48]. In a longer period of intervention it was also found that RF also improved VO_{2max}, with changes of 7% and 8% in the 3th and 6th months, which was more than in the control group[18]. Considering the evidence, it is possible to suggest that RF interventions elicit improvements on maximal oxygen uptake in short and long-term periods, thus being beneficial for the participants. However, one of the limitations of all the studies is that no dose-response was studied regarding the quantification of load occurred and for that reason monitoring instruments should be used to better characterize the relationships between training stimulus and the variations in cardiovascular parameters.

4.2 Overweight/Obesity

Although football practice is an intensive physical activity, in two studies with children football participation did not significantly change body mass index[34,35]. On the other hand, in one study with children it was observed that football training reduces body mass index[33]. These contradictory results are in line with the general physical activity literature, that suggests that moderate to vigorous physical activity is not necessarily associated with lower body mass index or fat mass, and is part of a multifaceted relationship[52-54]. Nervtheless, we should be aware that the use of body mass index for establishing weight status in relation to health risk in children is problematic, particularly during the period

of peak growth velocity[55]. Results from previous studies[56] that evaluated effects of the school-based intervention "FIFA 11 for Health", warn for the necessary caution in the interpretation of these type of results.

Previously it was observed that although organized sports, such as football, contribute to children achieve their physical activity recommendations, participation in organised sports does reduce the likelihood of being classified as overweight or obese[57]. However, there is also evidence that moderate to vigorous physical activity is related with lower adiposity[58]. Nevertheless, prospective association between moderate to vigorous physical activity and adiposity does not equate to causality. There is evidence that physical activity is not strongly prospectively related with adiposity, and may not be a determinant of adiposity[60].

In adults, results were different than for children. The four reviewed studies showed that football intervention significantly reduced total body fat mass and fat percentage[15,30-32]. RF appears to be an effective activity to promote positive body composition changes, mainly due the high energy expenditure leading to greater energy consumption and consequently promoting body fat reduction[33]. Additionally, the multiple strength training elements and frequent performance of intense actions (e.g., dribbles, shots, tackles, turns, jumps) in training sessions can increase lean body mass[48].

4.3. Type 2 Diabetes

Diabetes is a metabolic disease characterized by hyperglycemia (increased blood glucose concentrations), as well as elevated non-esterified fatty acid concentrations. There is evidence to support that environmental influences are important determinant factors of T2DM risk[9]. These risk factors include physical inactivity[61,62]. Epidemiologial evidence suggests that physically active individuals have lower risk of developing T2DM than their

sedentary counterparts[63,64]. More specifically, T2DM is characterized by hyperglycemia, fasting hyperinsulinemia and insulin resistance in peripheral tissues[26]. The positive impact of RF on lowered total body and android mass in middle-aged men with T2DM was demonstated previously[26]. These changes in body composition can impact insulin sensivity and glycemic control, as changes in visceral adipose tissue are positively related to changes in homeostatic model assessment of diabetes insulin resistance. Aditionally, RF was associated (in middle age and older people) with decreased cholesterol and tryglycerides levels, plasma glucose and IGFBP-3 levels (contributing to higher insulin sensitivity), decreased ammoniagenesis, and increased lipolytic activity and IGF-1/IGFBP-3 ratio, all indicative of attenuated catabolism[27,28]. More recently, Skoradal et al.[65], also demonstrated that a program of 16 weeks of football training and dietary advice has positive effects on metabolic and cardiovascular health profiles, with greater overall effects than professional dietary advice *per se* for 55 to 70 year old women and men with prediabetes.

Diabetes mellitus is a worlwide health problem and the cost of treating this chronic disease and its related complications are high[27]. Because of its increasing prevalance, due to both aging and increasing levels of obesity, the prevention and treatment of this disease is urgent. The reviewed studies demonstrated that RF is a fun activity that can be an attractive contribution to the treatment and prevention of T2DM in adult, middle age, and elderly individuals.

4.4 Cancer

The reviewed studies[36,38] were focused exclusively on prostate cancer in elderly men who were undergoing treatment. The purpose of those studies was to investigate the potential benefits of RF intervention aiming to avoid or reduce the effects of androgen deprivation

treatment. Regarding the effects on cancer it was found that 12-weeks of RF intervention were enough to improve bone mineral density (BMD) and also to elevate markers of bone formation (P1NP and osteocalcin)[36,38]. Similar evidence was found in a longer period intervention (32-weeks) finding within-group improvements on femoral neck (~0.4 to ~0.7% for left and right, respectively) and lumbar spine (~0.6%) BMD after football intervention while decreases were found in the control group[37]. Therefore, shorter (12-weeks) or longer (32-weeks) interventions are beneficial to maintain or improve the BMD of patients under androgen deprivation treatment while control groups BMD decreases over time[36-38]. This evidence was supported by a 5-year follow-up study that found improvements of 2.8% and 4.7% in the right femoral neck and spine L2-L4, bone mineral density, respectively, while the control group (men's that not participating in football training) decreased by 2.0% and ~1.8%, respectively[16]. These improvements can be caused by a combination of exercise loading and internal body conditions, namely stimulating the role of osteocytes through mechanical stress. In particular, RF may provide some mechanical stress by its emphasis on accelerations/decelerations, jumping and speed running, thus contributing to an augmented mechanical stress and inducing the stimulation of the bone and thus osteogenesis.

4.5. Osteoporosis

Osteoporosis is characterized by decreased bone mineral density and increased risk of fractures[39]. The reviewed studies demonstrated a positive and significant association between bone health and RF among adolescents, adults and older adults. Football participation resulted in improved bone mineralization[42], increased bone mineral density[15,16,40,41], enhanced bone mineral content[15,45], and as a stimulus for osteogenesis[43]. These results are in line with previous findings, showing that active people have better

bone health than less active people[16]. Bone is a tissue that remodels during the course of life. Although skeletal characteristics are influenced by genetic factors[66], a healthy lifestyle including appropriate nutrition and regular physical activity helps to improve bone health[39,42,45], prevent age-related bone loss[67], and strengthen weak bone[68,69].

During activities that involve changes of direction, such as football, mechanical forces are exerted on bones in varied and unusual directions through reaction forces and contractile forces from muscles. The intense movements involved in football, characterized by accelerations, decelerations, jumps, change of directions, and rapid side-cutting movements contribute to the improvement of bone mineral content, bone mineral density, and osteogenesis[70,71].

For children and adolescents, football is an osteogenic activity that can augment bone mineral content and bone mineralization at the loaded sites of the skeleton[42,45,71]. For adults, football is also an osteogenic activity and can improve bone health whilst reducing the risk of age-related bone loss and osteoporosis[15,41,44]. For older adults, among other health outcomes, it can be a preventive strategy to reduce the risk of hospitalization because of traumas and fractures[16,39,40,43].

4.6 Limitations

A possible limitation of this systematic review is that it only includes studies in English from specific selected databases, thereby potentially overlooking other relevant publications, namely "grey literature". To reinforce the evidence observed in the present review, future studies should endeavour to perform meta-analytic analyses. This type of analyses was not possible herein, as the studies reviewed possessed a wide range of metrics and outcomes, which precluded the possibility of creating a coherent analytical strategy.

5. Perspectives

This systematic review demonstrates that RF interventions seem to decrease blood pressure and resting heart rate, improve cardiac structure and functioning, whilst increasing maximal oxygen uptake in both sexes. Additionally, football practice lowers cholesterol and triglyceride levels, increases insulin sensitivity, and has a positive impact on glycaemic control. Therefore, RF may have an important role in the prevention and treatment of T2DM.

There exists a significant association between improved bone health and RF among adolescents, adults and older adults. Football participation results in enhancements of bone mineralization, increases in bone mineral density and bone mineral content, whilst also being a stimulus for osteogenesis. In this sense, RF can play a role in osteoporosis prevention. In adults with prostate cancer, RF intervention seems to be beneficial for bone health, slightly beneficial for body composition, muscle strength and maximal oxygen uptake and without meaningful benefits for balance, although further studies are required. Moreover, further research on the health benefits of walking football is required, as this is a developing sport with an increasing participation rate.

NCDs have globally shown increasing impact on health status in populations and are the leading cause of mortality worldwide. An important way to control this type of diseases is to focus on reducing the associated risk factors (e.g. raised blood pressure, overweight/obesity, hyperglycemia, physical inactivity). The reviewed studies showed that RF, is an effective and engaging activity that presents itself as a low-cost solution in the prevention and treatment of some NCDs.

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Figure Legends

Figure 1 - Preferred reporting items for systematic reviews flow diagram

Figure 2 - Main Non-Communicable Diseases studied in the context of recreational football.

Table 1. Characteristics of included studies on cardiovascular health

Study	Gender	Age - years (mean±SD)	n	Country	Design	Observation	Main outcomes measured	Main results
Skoradal, Weihe, Patursson, Mortensen, Connolly, Krustrup, Mohr [72]	Male and female	61±6	50	Faroe Island	Randomized controlled trial; 16-week intervention; football + dietary vs. dietary.	Participants diagnosed with prediabetes. Participants that took part in regular physical activity were excluded.	Blood pressure; maximal oxygen uptake; oral glucose tolerance test; plasma parameters.	16-weeks of football training combined with dietary advice promoted improvements in metabolic and cardiovascular health compared to dietary advice alone.
Krustrup, Skoradal, Randers, Weihe, Uth, Mortensen, Mohr [17]	Female	E. G. - 45±6 C. G. -45±4	41	Faroe Island	Randomized controlled trial; 1-year intervention; soccer training group vs. inactive control group.	Sedentary lifestyle for the last 2 years; mild hypertension; body mass index > 25 $kg.m^{-2}$	Blood pressure; body fat; bone mineral content; physical performance; plasma profile.	1-year of recreational football training improved the cardiovascular, metabolic and muscle-skeletal health profile.
Hammami, Kasmi, Farinatti, Fgiri, Chamari, Bouhlel [73]	Male	15.8±0.6	12		Randomized counterbalanced design;2 experiments with 48-72 hours of interval; small-sided games group vs. repeated sprint running session.	Untrained healthy adolescents were included.	Heart rate; blood pressure.	Both training interventions resulted in similar exercise intensity without any changes in post-exercise blood pressure. Heart rate value declined after 20-minutes interventions were similar between interventions. However, heart rate were lower after small-sided games than repeated sprints at 30-minutes after intervention.
Reddy, Dias, Holland, Campbell, Nagar, Connolly, Krustrup, Hubball [14]	Male and female	E. G. - 61.1±N.S.; C. G. – 58.3±N.S.	20	England	24-week intervention; walking football vs. control group.	Warm-up + 45-50min/week for 12 weeks; small-sided games.	Body composition; blood pressure.	Only the measures for blood pressure improved more for players than for controls. This was significant for mean arterial blood pressure.
Wegmann, Steffen, Putz, Wurtz, Such, Faude, Bohm, Meyer [74]	Male	47.1±5.1	100	Germany	Cross-sectional study describing the prevalence of cardiovascular risk factors, fitness and real life physiological load characteristics of training and competition in veteran football players.	> 40 years old; veteran football players.	Body composition; electrocardiography; heart rate; blood pressure; Cholesterol and blood lipids.	Results obtained regarding cardiovascular risk were similar with previous data found in general population. Circulatory strain during veterans training and competition were considered high.

Schmidt, Andersen, Andersen, Randers, Hornstrup, Hansen, Bangsbo, Krustrup [75]	Male	68.1±2.1 68.2±3.2	54	Denmark	Randomized controlled trial; Veteran football players vs. untrained elderly health control subjects.	---	Body composition; heart rate; blood pressure; maximal oxygen uptake; cholesterol; triglyceride; fasting glucose.	Lifelong football training was associated with larger left ventricular end-diastolic volume and better left ventricular systolic function compared with untrained elderly health control subjects. Endothelial function and cardiovascular fitness were better in veteran football players. Body composition was also better (less fat mass) in veteran players.
Schmidt, Hansen, Andersen, Andersen, Hornstrup, Krustrup, Bangsbo [24]	Male	Football training Group – 68.0±4.0 Strength training Group 69.1 ±3.1 C.G. - 67.4 ±2.7	32	Denmark	Randomized controlled trial; 1-year intervention with three groups: football training vs. strength training vs. control group.	Healthy men aged 65-75 years without history of regular exercise.	Body composition; heart rate; blood pressure; maximal oxygen uptake; cholesterol; triglyceride.	Football training group had significant improvements in cardiac structure, left and right ventricular systolic functional and left ventricular diastolic function whereas strength group only improved systolic function. More time also increased the differences between groups. Football training group also reduced resting heart rate and meaningfully improved maximal oxygen uptake. Finally, body composition was also improved in the football group.
Randers, Andersen, Petersen, Sundstrup, Jakobsen, Bangsbo, Saltin, Krustrup [76]	Male	Soccer Players - 69.5±3.7 Endurance Trained - 71.3±3.4 Strength Trained- 76.3±5.1 Untrained – 71.3±3.9.	33	Denmark	Cross-sectional study. Comparison between four groups: soccer players; endurance-trained; strength-trained; untrained.	---	Incremental cycle test (minutes); maximal oxygen uptake; resting heart rate; blood pressure; body composition; muscle capillaries and muscle fibre type; muscle glycogen; fasting blood glucose.	Football players had more muscle capillaries per fibre than strength-trained and untrained participants. Moreover, football players also had meaningful lower values of resting heart rate than untrained. Football players had also a great exercise capacity, heart rate reserve and percentage of type IIx fibres than untrained.
Mohr, Lindenskov, Holm, Nielsen, Mortensen, Weihe, Krustrup [47]	Femal e	E.G. - 45±3 C.G. - 43±3	41	Faroe Islands	Randomized controlled trial. 15-weeks intervention group (football) and inactive control group.	Sedentary and premenopausal women.	Body composition; Incremental endurance test; heart rate; blood pressure; cholesterol; triglyceride concentration.	After 15-weeks, recreational football led to decreases in fat mass, blood pressure, total cholesterol and triglyceride and increased more endurance capacity compared to the inactive control group.
Andersen, Randers, Hansen,	Male	E.G. - 45.8±7.2	31	Denmark	Randomized controlled trial. 6-months football training intervention vs. control group.	Untrained males diagnosed with mild-	Blood pressure; sub- and maximal exercise test;	6-months of football training elicited improvements in cardiac structure and function. Moreover, decreases in blood pressure were found.

Hornstrup, Schmidt, Dvorak, Sogaard, Krustrup, Bangsbo [18]		C.G. - 46.9±7.6				to-moderate arterial hypertension.	Echocardiography; tissue Doppler imaging.	
Randers, Andersen, Orntoft, Bendiksen, Johansen, Horton, Hansen, Krustrup [46]	Female	E.G. - 24.4±4.0 C.G- 27.0±6.5	57	Denmark	Cross-sectional study. Comparison between elite football players and untrained women.	16-weeks intervention with untrained women.	Body composition; heart rate; blood pressure; lipid levels; cardiorespiratory, sprint and intermittent running performance; echocardiography.	Cardiac ventricular dimensions and systolic and diastolic functional parameters were better in elite players. It Improved maximal oxygen uptake, intermittent running, fat and lean mass, HDL cholesterol and resting heart rate was also observed in elite players. However, the 16-week intervention with untrained participants contributed to decrease the differences in cardiac function, systolic and diastolic blood pressures and fitness performance.
Krustrup, Randers, Andersen, Jackman, Bangsbo, Hansen [19]	Male	46±N.S.	33	Denmark	Randomized controlled trial. 6-months football training intervention. Comparison between training intervention and group receiving doctor's advice on a healthy lifestyle.	Diagnosed with mild-to-moderate hypertension.	Maximal oxygen uptake; blood pressure; incremental test; heart rate; peak lactate; blood glucose; plasma insulin; cholesterol; C-reactive protein.	Football training group improved physical fitness and had better results in the treatment of mild-to-moderate hypertension than traditional physician-guided advice group. Blood pressure decreased after 6-months of training while maximal oxygen uptake increased. Resting heart rate also decreased in football group.
Hansen, Andersen, Rebelo, Brito, Hornstrup, Schmidt, Jackman, Mota, Rego, Oliveira, Seabra, Krustrup [50]	Male and female	8-12	31	Portuguese	Randomized controlled trial. Two groups (3-months football group vs. control) were compared.	Overweight or obese participants.	Systolic and diastolic function; peripherical artery function; body composition; blood pressure; heart rate.	Football training intervention was associated with changes of left ventricular posterior wall diameter, tricuspid annular plane systolic excursion and global isovolumetric relaxation time and absence of the increase in systolic blood pressure that was observed in the control group.
Randers, Petersen, Andersen, Krustrup, Hornstrup, Nielsen,	Male	E.G. -37±10 C.G. - 43±9	55	Denmark	Controlled training study. Two-group were compared: 12-weeks intervention street-football training group and control group.	Not randomized. Homeless men.	Heart rate; activity profile in training and during daily life; maximal oxygen uptake and ventilation; body composition; blood lipoproteins and glucose; incremental cycle	Marked effects after 12-week football intervention were found on the cardiovascular risk profile, increased maximal oxygen uptake and decreased the fat percentage and LDL-cholesterol. Meaningful improvements were also found in endurance and intermittent exercise capacity in the 12-week football training intervention.

Nordentoft, Krustrup [21]							ergometer and Yo-Yo intermittent endurance test.	
Randers, Nielsen, Krustrup, Sundstrup, Jakobsen, Nybo, Dvorak, Bangsbo, Krustrup [48]	Male	20-43	22	Denmark	Randomized controlled trial. Two groups: 64-weeks football intervention and control group.	Healthy untrained male with no physical training in the last 2 years.	Body composition; maximal oxygen uptake; heart rate; blood pressure; cholesterol; blood glucose; glycogen content; muscle oxidative level; fiber size; lower-limb power; balance; incremental test; sprint.	Elevated lean body mass, maximal oxygen uptake, exercise performance and muscle oxidative level were found in 64-weeks of football intervention. Moreover, reduced blood pressure and fat mass were obtained immediately after 12-weeks of intervention and maintained during the intervention year. One year intervention was more beneficial than the first 12-weeks in the 30-meters sprint and reduction in blood lactate during submaximal exercise.
Krustrup, Hansen, Randers, Nybo, Martone, Andersen, Bune, Junge, Bangsbo [49]	Female	36±2	56	Denmark	Randomized controlled trial. Three groups: 16-weeks football group, 16-weeks running group and control group	Healthy untrained premenopausal women without prior experience of football	Cholesterol; triglycerides; resting blood glucose; fasting plasma insulin; systolic and diastolic blood pressure; body composition; heart rate.	16-weeks of recreational football resulted in reductions in blood pressure, resting heart rate and fat mass. Moreover, benefits for muscle capillarization and pulse pressure wave and increases in maximal oxygen uptake were found.
Krustrup, Hansen, Andersen, Jakobsen, Sundstrup, Randers, Christiansen, Helge, Pedersen, Sogaard, Junge, Dvorak, Aagaard, Bangsbo [25]	Female	E.G. - 40±3 C.G. - 40±2	28	Denmark	Randomized controlled trial. Three groups: 16-months football group, 16-months running group and control group.	---	Body composition; systolic and diastolic function; heart rate; blood pressure; fasting blood glucose; maximal oxygen uptake; 30-meters sprint; balance; isokinetic strength.	Bone mineral density, left and right ventricular end-diastolic diameter and right ventricular systolic function were marked improved after 4-months of recreational football. Improvements were better than in the running-group. Quadriceps peak force in slow and fast concentric and eccentric movements was higher after 16 than 4 months of recreational football intervention.
Knoepfli-Lenzin, Sennhauser, Toigo, Boutellier, Bangsbo, Krustrup,	Male	20-45	57	Switzerland	Randomized controlled trial. Three groups: 12-weeks football group, 12-weeks running group and control group.	----	Blood pressure; blood lipids and glucose; maximal oxygen uptake; resting heart rate and variability; body composition.	Recreational football decreased diastolic blood pressure, total cholesterol and fat mass. Improvements in cardiovascular fitness and maximal oxygen consumption were also found after football intervention.

Junge, Dvorak [22]								
Andersen, Randers, Westh, Martone, Hansen, Junge, Dvorak, Bangsbo, Krustrup [20]	Male	47±N.S.	25	Denmark	Randomized controlled trial. Two groups: 3-months football intervention and control group.	Mild-to-moderate arterial hypertension.	Blood pressure; fasting blood samples; DXA scanning; maximal oxygen uptake and peak ventilation; cholesterol; heart rate.	Blood pressure was reduced after 3-months of football intervention. Body fat, body mass, resting heart rate also decreased while cardio-pulmonary capacity increased.
Andersen, Hansen, Sogaard, Madsen, Bech, Krustrup [51]	Femal e	36.5±8.2	47	Denmark	Randomized controlled trial. Three groups: 16-weeks football intervention; 16-weeks running intervention and control group.	Healthy sedentary women	Maximal oxygen uptake; systolic and diastolic function; cardiac dimensions.	Cardiac dimensions and systolic and diastolic left ventricular function increased after rhe 16-week intervention. Maximal oxygen uptake also increased 16% after football training intervention.
Krustrup, Nielsen, Krustrup, Christensen, Pedersen, Randers, Aagaard, Petersen, Nybo, Bangsbo [23]	Male	20-43	36	Denmark	Randomized controlled trial. Three groups: 12-weeks football intervention; 12-weeks running intervention and control group.	Healthy untrained men	Maximal oxygen uptake; heart rate; cholesterol; blood pressure; body composition; muscle capillaries.	Blood pressure decreased after 12-weeks of the recreational football intervention. Lean body and leg bone mass were greater in recreational football than in running group. Fat oxidation and reductions in LDL cholesterol were also higher in recreational football than in running.
Castagna, Belardinelli, Impellizzeri, Abt, Coutts, D'Ottavio [77]	N.S.	E.G -16.7 ±1.2 C.G. -16.9 ±1.8	31	Italy	Cross-sectional study.	High school students	Maximal aerobic power; heart rate; perceived exertion.	The 5 vs. 5 format of play may be appropriate to enhance cardiovascular fitness in high school students. HRpeak was higher than recommended by ACSM to develop cardiovascular fitness. It was also found that heart rate during intermittent physical activities may have a lower predictive ability of the actual aerobic involvement if compared to continuous exercise.

N.S.: not specified; E.G. – Experimental Group; C.G.- Control Group

Table 2. Characteristics of included studies on diabetes

Study	Gender	Age - years (mean±SD)	n	Country	Design	Observation	Main outcome measured	Main results
Paul, Bangsbo, Nassis [29]	Male	32.3±6.0	15	---	Cross-over design	Participants played a 60-min 9-a-side football match or rested (control group).	Body fat, heart rate, blood sample.	A single 60-min football match can attenuate the triglyceride response to a high-fat meal in normal and overweight individuals.
Vieira de Sousa, Fukui, Krustrup, Dagogo-Jack, Rossi da Silva [28]	Male and female	61.1±6.4	51	Brazil	RCT; 12-week intervention; football+diet vs. diet group.	40-min sessions 3 times/week.	VO2max, heart rate, blood sample, fat mass, lean mass.	Football was effective at lowering insulin-like growth factor binding protein-3 and glucose levels, which contribute to decreased insulin resistance and cardiovascular risks.

Reddy, Dias, Holland, Campbell, Nagar, Connolly, Krustrup, Hubball [14]	Male and female	E.G.- 61.1±N.S. C.G.- 58.3±N.S.	20	England	24-week intervention; walking football vs. control group.	Warm-up + 45-50min/week for 12 weeks; small-sided games.	BMI, Cholesterol, Glucose.	There were overall positive effects (e.g. for cholesterol) for both groups.
Andersen, Schmidt, Thomassen, Hornstrup, Frandsen, Randers, Hansen, Krustrup, Bangsbo [26]	Male	49.8±1.7	21	Denmark	24-week intervention; football vs. control group.	1 h twice a week. Small-sided (4-a-side, 5-a-side, 6-a-side) games.	BMI, blood lactate, plasma free fatty acids, heart rate.	Recreational football improved VO2peak, and lowered total body and android fat mass in men with type 2 diabetes. Positive impact of football training on glycaemic control was observed. Changes may be associated with reduced long-term morbidity and football may be use to the treatment of type 2 diabetes.
Vieira de Sousa, Fukui, Krustrup, Pereira, Silva, Rodrigues, de Andrade, Hernandez, da Silva [27]	Male and female	48-68	44	Brazil	RCT; 12-week intervention.	3×40 min/week for 12 weeks; small-sided games.	BMI, VO2max, heart rate, blood sample.	Football practice 2h/week and a calorie-restricted diet promoted much greater health benefits for T2D patients than a calorie-restricted diet alone. Football training lowered cholesterol and triglycerides levels and increased insulin sensitivity. It suggest that football is an effective way to reduce insulin resistance, beta cell dysfunction, and risk factors for cardiovascular disease in T2D patients.

N.S.: not specified; E.G. – Experimental Group; C.G.- Control Group

Table 3. Characteristics of included studies on overweight/obesity

Study	Gender	Age range (mean)	n	Country	Design	Observation	Main outcome measured	Main results
Cvetkovic, Stojanovic, Stojiljkovic, Nikolic, Scanlan, Milanovic [33]	Male	11-13	35		12-week intervention; football, high intensity interval training group vs. control group.	Recreational football and HIIT groups performed regular PE classes (2 times per week) plus the associated training intervention. Control group participated only in PE classes.	Total body fat, fat mass, muscle mass, lean mass, BMI.	Significant differences were found between football and control group in body mass and BMI. The magnitude of changes were higher with the football intervention compared to high intensity interval training group and control group for body composition.
Andersen, Schmidt, Pedersen, Krustrup, Bangsbo [32]	Male	68.1±2.1	27	Denmark	RCT; 52-week intervention; football, resistance groups vs. control group.	1h session 2 times/week for 16 weeks, and 3 times/week for the following 36 weeks.	Dietary intake, physical activity, fat mass, lean mass, blood sample.	Long-term football training reduces BMI and improves anti-oxidative capacity. Long-term resistance training impacts muscle protein enzyme expression and increases lean body mass.
Seabra, Seabra, Brito, Krustrup, Hansen, Mota, Rebelo, Rego, Malina [35]	Male	10.3±1.8	12	Portugal	5-month intervention; football vs, control group.	After school program, 4 days/week, 60–90 min/session.	BMI, body fat and lean mass.	Participants in the football group had significantly greater improvements in body image, self-esteem, and perceived physical competence compared with the control group. Changes in % body fat and lean body mass did not differ groups.
Hunt, Wyke, Gray, Anderson, Brady, Bunn, Donnan, Fenwick, Grieve, Leishman, Miller, Mutrie, Rauchhaus, White, Treweek [31]	Male	47.1±8.0	747	United Kingdom (Scotland)	RCT; 12-month intervention; football vs. control group.	Participants were football fans.	BMI, body fat, waist circumference.	Intervention helped men to achieve significant changes in weight, waist circumference, body fat, and BMI 12 months after baseline measurement. Mean weight loss in the intervention group fell almost 5%, and is likely to be of clinical benefit.

Barene, Krustrup, Brekke, Holtermann [15]	Male and female	45.8±9.3	118	Norway	RCT; 40-week intervention; football, Zumba vs. control group.	Participants were hospital employees. 1-2 session per week (1 h).	VO2max, blood-pressure, BMI, % body fat (DXA), heart rate, bone mineral content.	Intervention groups (football and Zumba) significantly reduced total body fat mass and fat percentage compared to the control group.
Gray, Hunt, Mutrie, Anderson, Treweek, Wyke [30]	Male	47.1±8.4	103	United Kingdom (Scotland)	RCT; 12-month intervention; intervention (football) vs. control group.	90 min/session/week	BMI, waist Circumference.	Intervention showed potential to support men in losing weight and making positive changes to other biomarkers of health risk, lifestyle behaviours and psychological outcomes.
Faude, Kerper, Multhaupt, Winter, Beziel, Junge, Meyer [34]	Male and female	10.8±1.2	39	Germany	RCT; 6-month intervention; football vs. standard training program	1 hour/3sessions/week	BMI	Body composition remained nearly unchanged.

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Table 4. Characteristics of included studies on cancer

Study	Gender	Age range (mean)	n	Country	Design	Main outcome measured	Main results
Uth, Fristrup, Haahr, Brasso, Helge, Rorth, Midtgaard, Helge, Krustrup [16]	Male	71.3±3.8	22	Denmark	Randomized controlled trial. Two groups were compared: football and control (5-year follow-up assessments).	Body composition; bone mineral density; blood pressure; resting heart rate; plasma cholesterol; flexibility; balance; maximal oxygen uptake; muscle strength.	Higher beneficial changes on right femoral neck bone mineral density in football group. It was also found that long-term adherence to self-organized recreational football in men with androgen deprivation therapy may better preserve bone mineral status. However, no associations were observed on body composition, fitness or physical functioning.
Uth, Hornstrup, Christensen, Christensen, Jorgensen, Schmidt, Brasso, Jakobsen, Sundstrup, Andersen, Rorth, Midtgaard, Krustrup, Helge [37]	Male	E.G. -67.1±7.1 C.G.- 66.5±4.9	57	Denmark	Randomized controlled trial. Two groups were compared: 32-weeks football group and control (usual care).	Bone mineral density; physical activity; body composition; physical functioning.	Football training group improved bone mineral density of the total hip and femoral shaft compared to control group. Moreover, greater improvements of femoral neck and lumbar spine bone mineral density and plasma osteocalcin were found in recreational football group. Greater improvements in lower limb power were found in recreational football group.
Uth, Hornstrup, Christensen, Christensen, Jorgensen, Helge,	Male	E.G. - 67±7 C.G.- 66±5	57	Denmark	Randomized controlled trial. Two groups were compared: 12-weeks football group and control (usual care).	Body composition; postural balance; activity profile; bone mineral density.	Recreational football promoted a high intermittent activity in participants. Moreover, the 12-weeks football intervention elevated markers of bone formation and helped to maintain body composition.

Schmidt, Brasso, Helge, Jakobsen, Andersen, Rorth, Midtgaard, Krustrup [36]							
Uth, Hornstrup, Schmidt, Christensen, Frandsen, Christensen, Helge, Brasso, Rorth, Midtgaard, Krustrup [38]	Male	E.G.- 67.1±7.1 C.G.- 66.5±4.9	57	Denmark	Randomized controlled trial. Two groups were compared: 12-weeks football group and control (usual care).	Body composition; heart rate during training intervention; maximal oxygen uptake; muscle strength; flexibility.	The 12-week football intervention resulted in improvements in lean body mass in comparison to control group. Moreover, an increase in knee-extensor muscle strength was also found in football group.

E.G. – Experimental Group; C.G.- Control Group

Table 5. Characteristics of included studies on osteoporosis

Study	Gender	Age range (mean)	n	Country	Design	Observation	Main outcome measured	Main results
Skoradal, Weihe, Patursson, Mortensen, Connolly, Krustrup, Mohr [72]	Male and female	60.5±8.5	50	Faroe Islands	RCT; 16-week intervention.	2 session/week (30-60 min).	BMI, bone mineral content, bone mineral density.	Football training provides a powerful osteogenic stimulus and improves bone health in people diagnosed with prediabetes.
Vlachopoulos, Barker, Ubago-Guisado, Ortega, Krustrup, Metcalf, Castro Pinero, Ruiz, Knapp, Williams, Moreno, Gracia-Marco [45]	Male and female	13.1±0.1	116	United Kingdom	RCT, 1-years intervention; football, swimming and cycling vs. active control group.	Adolescent involved in football, swimming and cycling.	Bone mineral content.	After 12 months footballers had significantly higher BMC and bone stiffness gains compared to swimmers and cyclists, and higher but non-significant BMC and bone stiffness compared to active controls.
Hagman, Helge, Hornstrup, Fristrup, Nielsen, Jørgensen, Andersen, Helge, Krustrup [39]	Male	Elite football players - 22.1±3.4; Football trained elderly -71.9±2.8; Lifelong football players.	140	Denmark	Cross-sectional; football vs. control group.	Participants were non-smoking men without chronic diseases.	Bone mineral density, bone mineral content, lean body mass.	Trained football players aged 65-80 years and young elite players aged 18-30 years have proximal femur and whole-body bone mineral density that are markedly higher than in age-matched untrained men.

Larsen, Nielsen, Helge, Madsen, Manniche, Hansen, Hansen, Bangsbo, Krustrup [42]	Male and female	8-10	295	Denmark	RCT; 10-month intervention; small-sided football game, circuit strength training group vs. control group.	3×40 min/week.	Bone mineral density, bone mineral content, lean body mass.	3×40 min/week of small-sided football game over a full school year improves bone mineralisation.
Helge, Andersen, Schmidt, Jorgensen, Hornstrup, Krustrup, Bangsbo [40]	Male	68.2±3.2	32	Denmark	RCT; 1-year intervention; football, resistance training vs. control group.	Physical inactive in the past 5 years.	Bone mineral density, bone turnover marker.	Football participation 2 times/week (45-60 min per section) resulted in an increase in BMD. Resistance training had no effect.
Helge, Randers, Hornstrup, Nielsen, Blackwell, Jackman, Krustrup [41]	Male	39.55±9.25	22	Denmark	RCT; 1-year intervention; football vs. control group.	Homeless people.	Bone mineral density, bone turnover marker, fat-free mass.	Football participation 3 times/week (45-60 min per section) modestly increased trunk BMD.
Mohr, Helge, Petersen, Lindenskov, Weihe, Mortensen, Jorgensen, Krustrup [44]	Female	45±6	83	Denmark (Faroe Islands)	RCT; 15-week intervention; football, swimming vs. control group	~3 sessions per week, 1 hr/session	Bone mineral content, bone turnover markers	Training for 15 weeks increases plasma turnover markers of bone formation, and increases total leg and femur bone mineral content.