Study Protocol

Title: A Soccer-based Lifestyle Intervention vs mHealth-based Physical Activity Intervention to Improve Bone Health and Metabolic Health in Prostate Cancer Survivors

NCT04144127

IRB Approval Date: 09/07/2021

A Soccer-based Lifestyle Intervention vs mHealth-based Physical Activity Intervention to Improve Bone Health and Metabolic Health in Prostate Cancer Survivors

Soccer in CA

Scientific Protocol

Principal Investigator - Felipe Lobelo, MD, Emory University Rollins School of Public Health, Global Health

Sponsor: Winship Cancer Institute

Protocol Version 4 08-17-2021

Background and Rationale

Prostate cancer (PCa) is the most common cancer in men in the U.S.(1, 2) and in other industrialized countries.(3) The lifetime probability of PCa in males is one in nine, and it has a high economic burden, with costs expected to rise.(4-6) Modern tailored treatment approaches, including androgen deprivation therapy (ADT), have resulted in longer life expectancy, but also longer treatment periods, which lead to significant adverse side effects.(7) These often include decreased bone mineral density (BMD), increased risk of fractures, low functional capacity, loss of lean body mass (LBM), increased fat mass, insulin resistance, psychological distress and pain.(8-12) Of particular concern is a sharp decline in bone health, with systemic bone loss caused by PCa-produced osteoclastogenic cytokines and drug interventions. Independent of disease stage, fractures in PCa patients are predictors of survival.(13, 14) In addition, concomitant physical inactivity and stress during and after treatment predispose PCa patients to elevated risk of deconditioning, BMD loss, cardiovascular and metabolic disease morbidity and mortality.(15-18)

Exercise-based lifestyle interventions aimed at counteracting treatment-induced adverse effects have been shown to be safe and effective in improving bone, functional and cardiometabolic health for patients with PCa.(19, 20) However, men, in general, are harder to engage in physical activity (PA) and lifestyle interventions.(3, 21) As an alternative to traditional exercise programs, recreational team sports provide a unique environment that may lead to increased physical activity participation and motivation to engage in other lifestyle changes.(22) Results from a recent meta-analysis by our group suggest that community-based, recreational team sports interventions lead to significant improvements in weight, waist circumference, body fat percentage, lipids, blood pressure and measures of fitness, with a greater change in males vs females.(23) More than any other sport, recreational soccer (RS) has been shown to be a successful health intervention in patients with, or at risk of chronic diseases,(24-26) including PCa.(27, 28) While soccer is extremely popular in many counties outside of the U.S. and has been found to dramatically improve health in PCa patients,(27, 29) soccer has only recently begun to gain popularity in the U.S., especially among men. Therefore, there is a need to develop implementation science strategies to adapt these interventions that can enhance adherence to lifestyle interventions in a population that stand to benefit greatly from a physical, phycological and mental health perspective.

Leveraging the growing enthusiasm around soccer in Atlanta and the U.S. may lead to increased interest, participation, retention and engagement in lifestyle change programming among PCa survivors. Therefore, this study seeks to directly test the implementation feasibility of a soccer-based lifestyle change intervention vs a low-cost mobile-health (mHealth) enabled lifestyle intervention and determine their effects on bone health, body composition, mental health, functional and cardiometabolic status among PCa survivors.

Bone health is of particular interest among PCa survivors given the ADT-related declines in BMD and increased risk of fractures, an independent factor inversely associated with disease survival independent of disease stage.(13) A recent meta-analysis that included five prospective cohort studies with a total of 533 patients, evaluated the change in BMD in patients with PCa receiving ADT, compared to those with PCa or other urologic conditions not receiving ADT.(14) The mean difference of percent change in BMD in the ADT treatment vs control group in the lumbar spine (BMD -3.60, 95% CI -6.72 to -0.47, P = 0.02) shows that there is a statistically and **clinically significant relationship between ADT and BMD reduction in patients with PCa** and that strategies to counteract BMD loss should be considered in patients with PCa undergoing ADT.(14) Further, changes in BMD have been detected with PA interventions within six months.(30, 31)

Soccer has been shown to be a **successful vehicle to deliver health interventions**.(32, 33) **Soccer is the most popular** sport in the world and an important staple of social interaction globally, with over 500 million active registered participants worldwide and nearly 16 million in the US.(32, 33) Recreational soccer, can be effective to reduce cardio-metabolic risk in both children and adults through varied movement patterns and highly functional training.(26, 34) Generally, there are close to 100 high-intensity short runs and other specific intense actions over a 1-hour training session, with average heart rates around **80% of maximal heart rate, irrespective of age, fitness status and previous soccer training experience**.(35) These high intensity intervals (HIIT) reduce insulin resistance, chronic inflammation and arterial stiffness.(36) Proper screening and RS programming delivered by trained "**Football (soccer) Medicine**" coaches are **safely tolerated** by middle-aged and older adult participants with **hypertension, obesity, diabetes and cancer**.(28, 37-40) Despite the high heart rate, small-sided RS had the lowest perceived exertion rate compared to interval running.(41) This may contribute to the high **adherence rates (> 90%), long-term retention** and high enjoyment seen in RS

interventions.(35, 42) In addition, adding a functional warm-up program, has shown to reduce injuries by 40%.(43-46). RS also builds social capital and is associated with positive motivational factors.(47) The physiologic and behavioral aspects of RS associated with health improvements are summarized by the Football (soccer) is Medicine collaborative we belong to.(24)

Protocol Synopsis

Study Design: A randomized controlled trial to compare two lifestyle intervention deliveries and their effect on bone health and diet and physical activity related measures.

Planned Sample Size: 20 subjects

Subject population: Inclusion criteria: 1) Men aged 18-79 years; 2) PCa survivors that had at least 6 months of hormone therapy (i.e. ADT with testosterone lowering agents) within the past 10 years; 3) not engaged in soccer practice or other exercise or lifestyle intervention program for the past 12-months; 4) Availability of smartphone to receive text messages; 5) Treating Oncologist clearance 6) ability to read in English or Spanish and provide informed consent; **Exclusion criteria:** 1) BMI > 40 kg/m^2; 2) resting BP ≥170/100 at screening or uncontrolled hypertension; 3) any mobility issues or exercise program contraindications (48); 4) a recent (i.e., within 12 months) myocardial infarction, diagnosis of congestive heart disease, other active cancer 5) bone or organ metastases, 6) chemotherapy within past 6 months; 7) Therapies and diseases of bone unrelated to PCa e.g. systemic glucocorticoids, bisphosphonates, teriparatide, denosumab, osteomalacia; osteosarcoma; Paget's disease; systemic lupus erythematosus; inflammatory bowel diseases, rheumatoid arthitis; thyroid/parathyroid disorder or mental illness.8) Not COVID-19 vaccinated

Specific Aims

Aim 1: We will conduct a single-arm clinicaltrial over 3 months, among PCa survivors that had at least 6 months of hormone therapy (i.e. ADT with testosterone lowering agents) within the past 10 years. Participants (n=20) will be offered an intensive intervention including RS programming and lifestyle education. The group will receive RS, consisting of small-sided (5vs5) conditioning drills and games, adapted to the population (60-minute sessions twice/week). We will evaluate pre vs post differences over 3-months in:
(Aim 1a): Primary outcome: lumbar spine BMD at 3-months.
(Aim 1b): Secondary outcomes: impact on additional markers of bone health including total hip BMD and bone turnover markers (Osteocalcin (a marker of bone formation) and C-terminal telopeptide of collagen (CTx) a bone resorption marker), body composition (weight, BMI, % body fat, waist circumference, lean body mass), cardiometabolic markers (resting heart rate and blood pressure), functional markers (aerobic capacity, muscle strength), behavioral factors (diet and PA self-efficacy, dietary intake, smoking and alcohol habits, weekly steps, sedentary and sleep time) and patient-reported quality of life and depression symptoms.
Aim 2: To assess implementation feasibility and evaluate overall efficacy to increase engagement and adherence with PA, we will evaluate between-group differences over 3 months in:
(Aim 2a): compliance with recommendations of 150 minutes of moderate-to-vigorous PA/week.
(Aim 2b): To assess the RS program adherence and tolerance, we will monitor session attendance, attrition rates, injuries or adverse events, use surveys for assessing participant program satisfaction and behavior change self-efficacy

Research Design:

Organizational structure of study team: This study was investigator initiated and proposed to the Winship Cancer Institute prostate cancer funding opportunity at Emory University as part of an internal pilot grant. The funder's expectation was for the investigator to conduct feasibility or pilot research to support a larger grant. Funder will provide a speedtype for all expenses related to the study.

Setting: All assessments will be conducted at the Emory University Hosptial Georgia CTSA GCRC location (baseline and post intervention). Those randomized to the soccer intervention will attend soccer sessions at a local soccer field (either Dunwoody Elementary or the Atlanta Silverbacks indoor facility), no permission is

needed to conduct the study, but field owners are aware of the study be conducted. All data will be collected on paper and transferred to a REDCap database at Emory University Rollins School of Public Health.

Aim 1. Experienced soccer coaches will be identified and hired from the local area to deliver the soccer program. These coaches will be trained in two key aspects of the program: 1) leading small-sided recreational soccer training designed to safely engage participants in HIIT conditioning; 2) facilitate the lifestyle education by devoting time during each soccer training session to reviewing the material (based on Life's Simple 7 topics), fostering discussion and using the groups' social dynamics to promote sustained lifestyle behavior change and increase self-efficacy. These coaches will be the primary facilitator of the study, conducting both soccer specific activities and education discussion. The study staff will conduct consent and all measurements and assessments.

Recruitment: Participants will be recruited from the Emory Oncology clinics and if needed Georgia Urology through our Winship Cancer prostate cancer physicians and Kaiser Permanente and usingthe recruitment flyer. Interested participants will be screened over the phone to determine eligibility based on inclusion and exclusion criteria above. Those meeting inclusion criteria will be scheduled for baseline assessments at the Georgia CTSA research center. Participants meeting inclusion and exclusion criteria will be invited to participate in the study.

Study Assessments. Prior to testing, subjects will be asked to refrain from physical activity for 48 hours prior to test day, refrain from alcohol 24 hour prior to testing, and refrain from caffeinated drinks, smoking and other stimulants one hour prior to testing. Assessments will be conducted at baseline and post intervention at the Emory University Hospital Georgia CTSA research center (GCRC). Blood pressure, both systolic and diastolic blood pressure will be measured while sitting using a calibrated electronic blood pressure sphygmomanometer prior to any activity and after five minutes of rest., height and weight, waist circumference, aerobic and musculoskeletal fitness assessments will be performed. Bone mineral density will be measured by dual x-ray absorptiometry (DXA) scan at the lumbar spine (L2-L4) and total hip. Body composition will also be determined by DXA scan in the Bionutrition Unit of the GCRC. Venipuncture will be performed by the research nurse for bone turnover markers (Osteocalcin (a marker of bone formation) and C-terminal telopeptide of collagen (CTx) a bone resorption marker), a total testosterone level if not included in a recent clinic visit, and to bank one tube of plasma for future metabolomics studies. In addition, questionnaires will be used for self-reported physical and mental health, quality of life, PA and diet self-efficacy, program satisfaction and injuries. Dietary recalls will be conducted at baseline and 26 weeks by trained staff and analyzed using Nutrition Database System for Research.(49) In addition, both groups will also be asked to wear a Garmin fitness tracker for the duration of the study to measure steps and moderate and vigorous activity. Once baseline measurements are complete and 20 participants have completed they will be randomized to either the soccer group or the mobile health (mHealth) group. Participants in the soccer group will participate in soccer drills and other fitness routines (two 1-hour sessions per week). They will meet with the soccer coach after the soccer sessions to discuss the lifestyle education topics (Life's Simple 7 education topics). During the soccer sessions participants will be fitted with a wearable soccer-specific device to measure how much they move and their heart rate.

Informed Consent Process:

Adult consent forms will be prepared for this study. The consent form will describe the purpose of the study, the procedures and risks. Participant will be presented with the consent form by the trained study staff, in person and given time to read and ask questions. A signed consent form will be obtained from the participant. A copy of the consent form will be given to the participant and this process will be documented.

Risks:

There is minimal risk in this study. Potential risks are related to 1) Venipuncture and Finger sticks 2) Dual x-ray absorptiometry (DXA scan) 3) Physical injury related to sport and 4) Confidentiality. 1) A single-use finger stick device will be used during assessments along with alcohol to clean the site prior to stick to reduce chances of infection. Trained research nurses will be used for venipuncture in a clinical setting with proper antiseptic precautions 2) DXA involves exposure to small amounts of radiation. The radiation dose is equal to or less than the amount of background radiation received in a round-trip flight from New York to Los Angeles or the

natural environmental radiation the average person receives in the United States annually. The risk from radiation exposure of this magnitude is considered to be negligible when compared to everyday risks. 3) Exercise can cause muscle soreness, weakness and in some cases muscle strains, ligament sprains and rarely bone fractures can occur. In very rare cases exercise can induce chest pain or a heart attack or other medical emergency. The training program led by the soccer coach is designed to minimize risk of injuries or events by slowly progressing on the practice of soccer using soccer and exercise drills appropriate for your age and level of fitness. Soccer sessions will be led by trained professionals who are able to offer suggestions to limit and prevent these adverse events. They are trained to recognize medical emergencies, will have basic equipment available, and seek emergency care if needed. 4) There is a risk of loss of confidentiality. Efforts will be made to keep all personal information confidential. All data will be stored in locked offices and password-protected computers. Personal identity will be protected in any publication.
Benefits: There are no direct benefits of this study beyond opportunity to exercise and information about healthy behaviors.

Compensation:

Participants will receive a $20 gift card for each assessment visit plus a parking voucher (total compensation value $52). Subjects that complete the study will be allowed to keep the Garmin fitness tracker.

Data Analytics and Statistical Plan:
Descriptive analysis will be performed to assess the study primary aims. All statistical tests will be 2-sided, and the significance level will be set at 0.05. Data will be assessed for normality and reviewed for outliers and missing values. Mathematical transformations may be applied to meet normality assumptions. All primary analyses will be performed using the intention-to-treat principle to estimate the effects of the program. Moreover, we will estimate the intervention efficacy using as-treated analysis, where participants are classified according to the number of sessions actually attended (i.e. the dose-response will be evaluated). To assess the effect of the proposed intervention program between baseline and 3 months, to compare the differences in the changes of the primary outcome of BMD and secondary outcomes, multilevel longitudinal models (MLM) will be used to test for differences time effects while adjusting for attrition and the correlational structure within time (repeated measures). Potential covariates may include potential effects of age, smoking, alcohol use, and therapy type. Attention will also be paid to heterogeneity between subjects (random intercept effects). Given the sample size of 40 subjects, only large effect sizes will be detectable at 80% statistical power. However, the primary focus of the analysis will be to gather initial estimates on the effect sizes (group differences and intervention efficacy) to establish adequate statistical power for a future larger study. **All analysis will be conducted by Dr. Higgins.**

Training of study team:
As stated above all staff and soccer coaches will receive adequate training of all study procedures. All study staff and collaborators will take CITI training upon hire.

Confidentiality: All participants will receive a study ID and this will be used on all paper and electronic forms. We will destroy all identifiers and any audio from key interviews after the study is complete.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA Cancer J Clin. 2019;69(1):7-34.
2. Noone AM, Howlader N, Krapcho M, Miller D, Brest A, Yu M, et al. SEER Cancer Statistics Review, 1975-2015 Bethesda, MD2018 [Available from: https://seer.cancer.gov/csr/1975_2015/.
3. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-424.
4. Roehrborn CG, Albertsen P, Stokes ME, Black L, Benedict A. First-year costs of treating prostate cancer: estimates from SEER-Medicare data. Prostate cancer and prostatic diseases. 2009;12(4):355-60.
5. Roehrborn CG, Black LK. The economic burden of prostate cancer. BJU Int. 2011;108(6):806-13.
6. Stokes ME, Black L, Benedict A, Roehrborn CG, Albertsen P. Long-term medical-care costs related to prostate cancer: estimates from linked SEER-Medicare data. Prostate cancer and prostatic diseases. 2010;13(3):278-84.

7. Meng MV, Grossfeld GD, Sadetsky N, Mehta SS, Lubeck DP, Carroll PR. Contemporary patterns of androgen deprivation therapy use for newly diagnosed prostate cancer. Urology. 2002;60(3 Suppl 1):7-11; discussion -2.
8. Galvao DA, Spry NA, Taaffe DR, Newton RU, Stanley J, Shannon T, et al. Changes in muscle, fat and bone mass after 36 weeks of maximal androgen blockade for prostate cancer. BJU Int. 2008;102(1):44-7.
9. Galvao DA, Taaffe DR, Spry N, Joseph D, Turner D, Newton RU. Reduced muscle strength and functional performance in men with prostate cancer undergoing androgen suppression: a comprehensive cross-sectional investigation. Prostate cancer and prostatic diseases. 2009;12(2):198-203.
10. Pin F, Couch ME, Bonetto A. Preservation of muscle mass as a strategy to reduce the toxic effects of cancer chemotherapy on body composition. Current opinion in supportive and palliative care. 2018;12(4):420-6.
11. Zabegalina NS, Henderickx M, Lamotte V, Segers B, Stassijns G, De Wachter S, et al. Effects of a six-month supervised physical exercise program on physical and cardio-metabolic profile and quality of life in patients with prostate cancer on androgen deprivation therapy: a pilot and feasibility study. Central European journal of urology. 2018;71(2):234-41.
12. Lotfi-Jam K, Gough K, Schofield P, Aranda S, Jefford M. A longitudinal study of four unique trajectories of psychological distress in cancer survivors after completing potentially curative treatment. Acta Oncol. 2019:1-8.
13. Oefelein MG, Ricchiuti V, Conrad W, Resnick MI. Skeletal fractures negatively correlate with overall survival in men with prostate cancer. J Urol. 2002;168(3):1005-7.
14. Kim DK, Lee JY, Kim KJ, Hong N, Kim JW, Hah YS, et al. Effect of Androgen-Deprivation Therapy on Bone Mineral Density in Patients with Prostate Cancer: A Systematic Review and Meta-Analysis. Journal of clinical medicine. 2019;8(1).
15. Keating NL, O'Malley AJ, Smith MR. Diabetes and cardiovascular disease during androgen deprivation therapy for prostate cancer. J Clin Oncol. 2006;24(27):4448-56.
16. Keating NL, O'Malley AJ, Freedland SJ, Smith MR. Diabetes and cardiovascular disease during androgen deprivation therapy: observational study of veterans with prostate cancer. J Natl Cancer Inst. 2010;102(1):39-46.
17. Haque R, UlcickasYood M, Xu X, Cassidy-Bushrow AE, Tsai HT, Keating NL, et al. Cardiovascular disease risk and androgen deprivation therapy in patients with localised prostate cancer: a prospective cohort study. Br J Cancer. 2017;117(8):1233-40.
18. Sheill G, Brady L, Guinan E, Hayes B, Casey O, Greene J, et al. The ExPeCT (Examining Exercise, Prostate Cancer and Circulating Tumour Cells) trial: study protocol for a randomised controlled trial. Trials. 2017;18(1):456.
19. Gardner JR, Livingston PM, Fraser SF. Effects of exercise on treatment-related adverse effects for patients with prostate cancer receiving androgen-deprivation therapy: a systematic review. J Clin Oncol. 2014;32(4):335-46.
20. Cormie P, Galvao DA, Spry N, Joseph D, Chee R, Taaffe DR, et al. Can supervised exercise prevent treatment toxicity in patients with prostate cancer initiating androgen-deprivation therapy: a randomised controlled trial. BJU Int. 2015;115(2):256-66.
21. Hunt K, McCann C, Gray CM, Mutrie N, Wyke S. "You've got to walk before you run": positive evaluations of a walking program as part of a gender-sensitized, weight-management program delivered to men through professional football clubs. Health Psychol. 2013;32(1):57-65.
22. Pringle A, Zwolinsky S, McKenna J, Daly-Smith A, Robertson S, White A. Reducing CVD risk factors for men/hard-to-reach men using English premier league soccer clubs. Med Sci Sports Exerc. 2014;46(5):595.
23. Bellissimo MP, Arrendono KG, Paskert M, Lobelo F. A systematic review and meta-analysis of the reduction in cardiovascular disease through group sport inteventions in adults. Mayo Clin Proc. 2018;In Press.
24. Krustrup P, Williams CA, Mohr M, Hansen PR, Helge EW, Elbe AM, et al. The "Football is Medicine" platform-scientific evidence, large-scale implementation of evidence-based concepts and future perspectives. Scand J Med Sci Sports. 2018;28 Suppl 1:3-7.
25. Luo H, Newton RU, Ma'ayah F, Galvao DA, Taaffe DR. Recreational soccer as sport medicine for middle-aged and older adults: a systematic review. BMJ open sport & exercise medicine. 2018;4(1):e000336.
26. Bangsbo J, Hansen PR, Dvorak J, Krustrup P. Recreational football for disease prevention and treatment in untrained men: a narrative review examining cardiovascular health, lipid profile, body composition, muscle strength and functional capacity. Br J Sports Med. 2015;49(9):568-76.
27. Uth J, Fristrup B, Haahr RD, Brasso K, Helge JW, Rorth M, et al. Football training over 5 years is associated with preserved femoral bone mineral density in men with prostate cancer. Scand J Med Sci Sports. 2018;28 Suppl 1:61-73.
28. Uth J, Hornstrup T, Christensen JF, Christensen KB, Jorgensen NR, Schmidt JF, et al. Efficacy of recreational football on bone health, body composition, and physical functioning in men with prostate cancer undergoing androgen

deprivation therapy: 32-week follow-up of the FC prostate randomised controlled trial. Osteoporos Int. 2016;27(4):1507-18.
29. Uth J, Schmidt JF, Christensen JF, Hornstrup T, Andersen LJ, Hansen PR, et al. Effects of recreational soccer in men with prostate cancer undergoing androgen deprivation therapy: study protocol for the 'FC Prostate' randomized controlled trial. BMC cancer. 2013;13:595.
30. Wang A, Karunasinghe N, Plank L, Zhu S, Osborne S, Bishop K, et al. Effect of Androgen Deprivation Therapy on Bone Mineral Density in a Prostate Cancer Cohort in New Zealand: A Pilot Study. Clinical Medicine Insights Oncology. 2017;11:1179554917733449.
31. Cipriani C, Abraham A, Silva BC, Cusano NE, Rubin MR, McMahon DJ, et al. Skeletal changes after restoration of the euparathyroid state in patients with hypoparathyroidism and primary hyperparathyroidism. Endocrine. 2017;55(2):591-8.
32. Barriguete Melendez JA, Dvorak J, Cordova Villalobos JA, Juan Lopez M, Davila Torres J, Compean Palacios J, et al. FIFA 11 for Health in Mexico: a school-based intervention for the prevention of obesity and non-communicable diseases. Br J Sports Med. 2014;48(12):940-1.
33. Statista. Number of soccer players in the U.S. 2017 New York: Statista; 2017 [Available from: https://www.statista.com/statistics/227428/number-of-soccer-players-usa/.
34. de Sousa MV, Fukui R, Krustrup P, Pereira RM, Silva PR, Rodrigues AC, et al. Positive effects of football on fitness, lipid profile, and insulin resistance in Brazilian patients with type 2 diabetes. Scand J Med Sci Sports. 2014;24 Suppl 1:57-65.
35. Krustrup P, Dvorak J, Junge A, Bangsbo J. Executive summary: the health and fitness benefits of regular participation in small-sided football games. Scand J Med Sci Sports. 2010;20 Suppl 1:132-5.
36. Jelleyman C, Yates T, O'Donovan G, Gray LJ, King JA, Khunti K, et al. The effects of high-intensity interval training on glucose regulation and insulin resistance: a meta-analysis. Obesity reviews : an official journal of the International Association for the Study of Obesity. 2015;16(11):942-61.
37. Andersen LJ, Randers MB, Hansen PR, Hornstrup T, Schmidt JF, Dvorak J, et al. Structural and functional cardiac adaptations to 6 months of football training in untrained hypertensive men. Scand J Med Sci Sports. 2014;24 Suppl 1:27-35.
38. Andersen LJ, Randers MB, Westh K, Martone D, Hansen PR, Junge A, et al. Football as a treatment for hypertension in untrained 30-55-year-old men: a prospective randomized study. Scand J Med Sci Sports. 2010;20 Suppl 1:98-102.
39. Andersen TR, Schmidt JF, Thomassen M, Hornstrup T, Frandsen U, Randers MB, et al. A preliminary study: effects of football training on glucose control, body composition, and performance in men with type 2 diabetes. Scand J Med Sci Sports. 2014;24 Suppl 1:43-56.
40. Krustrup P, Randers MB, Andersen LJ, Jackman SR, Bangsbo J, Hansen PR. Soccer improves fitness and attenuates cardiovascular risk factors in hypertensive men. Med Sci Sports Exerc. 2013;45(3):553-60.
41. Randers MB, Nielsen JJ, Bangsbo J, Krustrup P. Physiological response and activity profile in recreational small-sided football: no effect of the number of players. Scand J Med Sci Sports. 2014;24 Suppl 1:130-7.
42. Nielsen G, Wikman JM, Jensen CJ, Schmidt JF, Gliemann L, Andersen TR. Health promotion: the impact of beliefs of health benefits, social relations and enjoyment on exercise continuation. Scand J Med Sci Sports. 2014;24 Suppl 1:66-75.
43. Thorborg K, Krommes KK, Esteve E, Clausen MB, Bartels EM, Rathleff MS. Effect of specific exercise-based football injury prevention programmes on the overall injury rate in football: a systematic review and meta-analysis of the FIFA 11 and 11+ programmes. Br J Sports Med. 2017;51(7):562-71.
44. Al Attar WS, Soomro N, Pappas E, Sinclair PJ, Sanders RH. How Effective are F-MARC Injury Prevention Programs for Soccer Players? A Systematic Review and Meta-Analysis. Sports Med. 2016;46(2):205-17.
45. Herrero H, Salinero JJ, Del Coso J. Injuries among Spanish male amateur soccer players: a retrospective population study. Am J Sports Med. 2014;42(1):78-85.
46. van Beijsterveldt AM, Steffen K, Stubbe JH, Frederiks JE, van de Port IG, Backx FJ. Soccer injuries and recovery in Dutch male amateur soccer players: results of a prospective cohort study. Clin J Sport Med. 2014;24(4):337-42.
47. Blatter JS, Dvorak J. Football for health - science proves that playing football on a regular basis contributes to the improvement of public health. Scand J Med Sci Sports. 2014;24 Suppl 1:2-3.
48. Riebe D, Franklin BA, Thompson PD, Garber CE, Whitfield GP, Magal M, et al. Updating ACSM's Recommendations for Exercise Preparticipation Health Screening. Med Sci Sports Exerc. 2015;47(11):2473-9.

49. Harnack L, Stevens M, van Heel N, Schakel S, Dwyer JT, Himes J. A computer-based approach for assessing dietary supplement use in conjuction with dietary recalls. Journal of Food Composition and Analysis. 2008;21:S78-82.