



Home-based 'exergaming' was safe and significantly improved 6-min walking distance in patients with prostate cancer  
*a single-blinded randomised controlled trial*

Villumsen, Brigitta R; Jorgensen, Martin G; Frystyk, Jan; Hordam, Britta; Borre, Michael

*Published in:*  
B J U International (Print)

*DOI (link to publication from Publisher):*  
[10.1111/bju.14782](https://doi.org/10.1111/bju.14782)

*Publication date:*  
2019

*Document Version*  
Accepted author manuscript, peer reviewed version

[Link to publication from Aalborg University](#)

*Citation for published version (APA):*  
Villumsen, B. R., Jorgensen, M. G., Frystyk, J., Hordam, B., & Borre, M. (2019). Home-based 'exergaming' was safe and significantly improved 6-min walking distance in patients with prostate cancer: a single-blinded randomised controlled trial. *B J U International (Print)*, 124(4), 600-608. <https://doi.org/10.1111/bju.14782>

#### **General rights**

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal -

#### **Take down policy**

If you believe that this document breaches copyright please contact us at [vbn@aub.aau.dk](mailto:vbn@aub.aau.dk) providing details, and we will remove access to the work immediately and investigate your claim.

Article type : Original Article

Article Category: Urological Oncology

**Home-based exergaming was safe and significantly improved 6-min walking distance in prostate cancer patients: a single-blinded randomized controlled trial**

**Authors:**

*Brigitta R. Villumsen*<sup>1,2</sup>, *Martin G. Jorgensen*<sup>3</sup>, *Jan Frystyk*<sup>4,5</sup>, *Britta Hordam*<sup>6</sup> and *Michael Borre*<sup>2,7</sup>

**Affiliation**

1 Department of Urology, Regional Hospital Holstebro, Denmark

2 Department of Clinical Medicine, Faculty of Health, Aarhus University, Aarhus, Denmark

3 Center for PREDiction and prevention of FALLs (PREFALL), Department of Geriatrics, Aalborg University Hospital, Aalborg, Denmark.

4 Medical Research Laboratory, Department of Clinical Medicine, Faculty of Health, Aarhus University, Aarhus, Denmark;

5 Department of Endocrinology, Odense University Hospital & Institute of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark.

6 University of Copenhagen, Copenhagen, Denmark.

7 Department of Urology, Aarhus University Hospital, Aarhus, Denmark.

**Corresponding author**

Brigitta R Villumsen

Department of Urology, Regional Hospital Holstebro, Lægårdvej 12, 7500 Holstebro, Denmark.

E-mail: brigvill@rm.dk

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/bju.14782

This article is protected by copyright. All rights reserved.

## Abstract

**Objectives:** To explore the effects of 12 weeks of unsupervised home-based exergaming (i.e. technology-driven exercise) compared to usual care on physical function, body composition, quality of life (QoL) and fatigue in prostate cancer patients (PCa) on androgen deprivation therapy (ADT).

**Patients and methods:** In an assessor-blinded randomized controlled trial, 46 PCa patients (+65 years of age) with locally advanced or advanced stage disease undergoing ADT were randomized to 12 weeks of unsupervised home-based exergaming, or usual care from two hospitals in Denmark. The primary outcome of the study was 6-minute walking test (6MWT). Secondary outcomes were leg extensor power (LEP), body composition (lean- and fat- mass), self-reported physical functioning and global health status (EORTC QLQ-C30), QoL (FACT-P) and fatigue (FACT-F).

**Results:** Significant improvement was seen in the exergaming group compared to the usual care group in the primary outcome 6MWT (mean difference: 21.5 meters; 95% confidence interval (CI) 3.2 – 39.9;  $p=0.023$ ). No between group differences were seen for LEP ( $p=0.227$ ), lean body mass ( $p=0.100$ ), fat body mass ( $p=0.092$ ), self-reported physical functioning ( $p=0.084$ ) and global health status ( $p=0.113$ ), QoL ( $p=0.614$ ) and fatigue ( $p=0.147$ ).

**Conclusion:** 12 weeks of unsupervised home-based exergaming had an effect on the primary outcome 6MWT in PCa patients receiving ADT. However, no significant effects were found in secondary outcomes. The exergaming intervention appeared safe and could be an alternative to traditional aerobic and resistance training in this patient group.

Key words: Prostate cancer, Androgen deprivation therapy; Home-based exercise; Exergaming; Fatigue; Quality of life.

## Introduction

Androgen deprivation therapy (ADT) constitutes a central component in the treatment of metastatic prostate cancer (mPCa) and as adjuvant therapy to radiation in patients with intermediate or high-risk localized disease. Unfortunately, ADT has several adverse effects: reduced physical function shown by reduced grip strength, and decreased score on the Timed Up and Go test [1], Loss of muscle and bone mass [2], decreased (QoL) [3], and increased fatigue [4] are frequently observed. Fortunately many of these ADT related complaints appear to be counteracted by exercise interventions. Systematic reviews have documented beneficial effects of combined aerobic and resistance exercise interventions on ADT-related adverse effects in PCa patients [5–9]. However, the majority of exercise studies have been conducted in supervised facilities (i.e. a hospital clinic or a fitness centers), making the interventions inconvenient to patients due to travel distance and fairly costly due to the involved health professionals. Therefore, as an alternative, a few studies have explored home-based unsupervised walking interventions on PCa patients receiving ADT and have found positive results on vitality and body composition [10–12].

Marked advances in gaming technology, e.g. the introduction of the Nintendo Wii balance board in 2008 and the Microsoft Kinect Camera in 2010, has led to a new way of controlling and playing games. This new way is by standing up and moving the body in order to control an avatar displayed on a television screen and has been labeled “exergaming”. Through history computer games have been controlled while sitting down using a handheld controller or a keyboard. This new way of exercising called exergaming has already been studied in other cancer patients than PCa patients and have shown alleviating fatigue, improving

functional performance [13], maintaining physical performance during chemotherapy [14] and increasing physical activity during hospitalization [15]. One home-based exergaming study in post-surgical lung cancer patients showed reduced fatigue, improved functional status and QoL [16]. Thus, in the present study we aimed to explore the effects of 12 weeks of unsupervised home-based exergaming in PCa patients receiving ADT compared to usual care. The effects were evaluated between the groups primarily through the 6MWT and secondary through leg extensor power (LEP), body composition (lean- and fat- mass), physical functioning and global health status (EORTC QLQ-C30), and QoL (FACT-P), and fatigue (FACT-F).

## **Material and Methods**

### *Study Design and Recruitment*

In an assessor-blinded randomized controlled trial 23 patients were assigned to the intervention group (Exergaming) and 23 patients to a usual care group. Eligible patients were Danish speaking PCa patients receiving continuous ADT for at least three months prior to inclusion, cognitively well-functioning and able to answer questionnaires and comply with the exercise program according to instruction, and performance status 0-1. For safety reasons, progression of PCa disease or development or progression of bone pain due to bone metastases during the intervention period would discontinue patients. Between February 2015 and January 2017 we included 46 patients from the urological outpatient clinics at Regional Hospital Holstebro, ( $n=32$ ) and Regional Hospital Viborg ( $n=14$ ), Denmark. All study procedures were conducted at Regional Hospital Holstebro. The study was registered at Clinical trial.gov, ID: NCT01762241 and approved by the Regional ethical committee Central Denmark Region, protocol no. 1-10-72-195-14 as well as by the Danish Data Protection Agency protocol no. 1-16-02-536-14.

Written informed consent was obtained from all patients prior to inclusion in the study.

The study protocol has previously been published [17]. Remaining outcomes stated in the protocol paper will be published elsewhere.

#### *Sample size calculation*

Based on pilot testing our sample size calculation assumed that the exergaming intervention would lead to a between group difference of 100 meter with a standard deviation of 84.5 in the 6MWT at 12 weeks follow-up favoring the exergaming group (one-way). Further, we based our sample size calculation on an alfa level of 5 % and a beta level of 90 % and a dropout rate of 30%. With these assumptions 48 patients needed to be enrolled to attain 34 completed patients.

#### *Randomization and blinding*

The principal investigator enrolled each subject. Randomization in blocks of 8-10 patients was used to secure a balanced allocation of patients (1:1) to either intervention or usual care. For randomization purposes, sealed, opaque envelopes with equal allocation to each group were used in an amount consistent to the number of subjects randomized in each block. The research assistant supervised each subject picking an envelope. All physical and functional outcomes were assessed by an experienced physiotherapists blinded to the group allocation.

#### *Intervention*

The intervention group received 90 minutes individual instruction by a physiotherapist prior to the homebased exergaming with the Xbox 360 Kinect system (Microsoft, Redmond, WA, USA). Patients were instructed to do aerobic and strength exercise for one hour, including a warm up and cool down period, three times a week for 12 weeks using the Your Shape

Fitness Evolved 2012, Sport and Adventure games at their own convenience. Free weights of 0.5, 1.0 and 2.0 kg were used to support the gradually increasing exercise intensity of the Fitness Evolved 2012 game. Throughout the study, i.e. from baseline to week24 (w24), each patient kept a diary of his self-reported exercise. No other study procedures were scheduled between w12 and w24.

Until the post-intervention assessments at w12 the research assistant contacted the intervention group by telephone every second week to ensure compliance, registration of adverse events, and changes in medication. Between w12 and w24 the patients were not contacted by the research assistant.

#### *Usual care*

Usual care group patients were instructed to continue their normal daily activities throughout the study and each patient kept a diary of his self-reported exercise. As the usual care group was not expected to increase activity level until the post-intervention assessments at w12, the research assistant contacted this group by telephone every fourth week to ensure compliance, registration of adverse events, and changes in medication. Between w12 and w24 the patients were not contacted by the research assistant.

At w24 patients in the usual care group were given advice on exercise according to existing guidelines, recommending 150 minutes of aerobic exercise of moderate intensity or 75 minutes of vigorous intensity every week, combined with two sessions of resistance exercise and stretching[18].

#### *Primary and secondary Outcomes*

Primary and secondary outcomes were measured at baseline and at w12 (Table 1).

The validated 6MWT was used to assess physical function, which was the primary outcome.

A power rig (University of Nottingham Medical School, Nottingham, UK) was used to assess leg extensor power (LEP). Body composition was assessed using the Bodystat® Quadscan 4000 bioelectrical impedance analyzer. The physical functioning and global health status subscales of the quality of life questionnaire EORTC QLQ-C30 and Functional Assessment of Cancer Therapy-Prostate (FACT-P) questionnaires were used to assess self-reported QoL. The fatigue subscale of the Functional Assessment of Cancer Therapy - Fatigue (FACT-F) questionnaire was used to assess fatigue using a fatigue-defining cut-off score of  $< 34$ [19]. Godin Leisure-Time Exercise Questionnaire score was used at baseline, w12 and follow-up at w24 (intervention group only) to track changes in physical activity level. High score is correlated with physical activity and low score reflects physical inactivity. Exercise intensity during exergaming as well as physical activity (i.e. accelerometry) was not measured.

#### *Statistical analysis*

Data were analyzed using Stata version 13. The primary analysis was a modified intention-to-treat (mITT) population consisting of individuals with both baseline and w12 measurements. We performed a complete case analysis comparing groups according to the original random allocation. For all outcome measures a linear regression analysis was conducted to evaluate differences in effects between groups adjusting for the baseline values as well as treatment duration below or above 365 days (ADT), BMI, and activity level based on the Godin Leisure-Time Exercise Questionnaire score. All values are shown as the mean and 95 % confidence interval (CI). A *P* value of less than 0.05 was considered to be statistically significant.

## Results

As shown in the CONSORT diagram (Figure 1), two patients in the intervention group and three patients in the usual care group did not complete the study, resulting in 91% completing patients in the intervention group and 87 % in the usual care group. One of the remaining 20 patients in the usual care group sustained a muscle strain during the physical tests at baseline and refused to repeat these tests at post-intervention.

There were no significant between-group differences at baseline (Table 2). A panel of biochemical routine measurements, including plasma potassium, sodium, calcium, albumin-adjusted calcium, albumin, creatinine, glomerular filtration rate, CO<sub>2</sub> and hemoglobin, were analyzed and remained stable during the study (data not shown).

Neither cardiovascular nor skeletal related events (i.e. pathologic fracture, spinal cord compression, necessity for radiation to bone (due to pain or impending fracture) or surgery to bone) were observed during the study.

### *Primary outcome*

At w12, the adjusted analysis for the 6MWT showed a statistically significant difference favoring the intervention group, with an estimated 4.2 % improvement of 21.5 meters (95 % CI 3.2 to 39.9,  $p=0.023$ ) compared to the usual care group (Table 3).

### *Secondary outcomes*

#### *LEP*

The LEP test showed no statistical significant improvement in the intervention group compared to the usual care group in the adjusted analysis (mean difference 20.3 w; 95 % CI -13.2 to 53.8  $p= 0.227$ ) (Table 3).

### *Body composition*

At w12 lean mass increased numerically (mean difference 0.91 %; 95 % CI -0.2 to 2.0;  $p=0.100$ ) and fat mass decreased numerically (mean difference -0.9 %; 95 % CI -2.0 to 0.2;  $p=0.092$ ) when comparing the groups (Table 3). However, neither difference reached the level of statistical significance.

### *Quality of life and Fatigue*

After 12 weeks the intervention group had the same QoL (FACT-P) as the usual care group (mean difference 2.1 points; 95 % CI -6.3 to 10.6  $p=0.614$ ). Numerical, but insignificant increases were observed in physical functioning (+7.7 %; mean difference 6.2 points; 95 % CI -0.9 to 13.3;  $p=0.084$ ) and global health status compared to the usual care group (mean difference +8.8 points; 95 % -2.2 to 19.7  $p=0.113$ ) (Table 3).

Fatigue did not improve in the intervention group compared to the usual care group at w12 (mean difference 2.4 points; 95 % CI -0.9 to 5.7  $p=0.155$ ) (Table 3).

The intervention was well-tolerated by all patients. However, when exercising one patient in the intervention group experienced severe non-heart-related chest pain due to surgical clips in thorax leading to discontinuation from the trial. No other adverse events from the intervention led to withdrawal or discontinuation of patients from the study.

### *Physical activity level*

The Xbox Kinect, games and dumbbells were given to the intervention group to keep, and thus we investigated any change in physical activity level in this group after the w12 assessments. Figure 2 shows that the intervention group voluntarily continued to increase physical activity level throughout the study displayed by an increase of 8.5 points on the

Godin Leisure-Time Exercise score at w12 and an increase of 15.2 points at w24 compared to baseline. However, the increase was not statistically significant.

Compliance to the intervention is shown in Figure 3. Each patient reported exergaming on average 153.5 minutes per week between baseline and w12; however, the protocolled exercise duration was 180 minutes per week.

## **Discussion**

This is the first study to examine the effects of 12 weeks of unsupervised home-based exergaming using a Microsoft Xbox 360 Kinect system in PCa patients receiving ADT compared to usual care. Our main finding was that the exergaming intervention significantly improved the six minutes walking ability compared to the usual care group. Surprisingly, in all of our secondary outcomes, we found no significant change between groups. However, we did see trends favoring the exergaming group as LEP increased by 7.6 % and fat mass decreased by 3.0 % compared to the usual care group. In addition, during the post-intervention period (from week 12 to 24) we did not expect the exergaming group to continue to be physically active, however the Godin score proved otherwise and peaked at week 24. Finally, the current exergaming intervention appeared safe in PCa patients on ADT, as no incidents of cardiovascular or skeletal related events were reported.

Walking speed has a potential to predict future health status, functional decline, and mortality[20], and as PCa patients can live for decades due to new therapies, the 6MWT could be used as a reliable measure in the clinical setting as well as in clinical research when health promoting interventions are evaluated. We found a significant difference of 21.5 meters ( $p=0.023$ ) between groups favoring the exergaming group in the 6MWT, but a *post hoc* effect size calculation (cohen's *d*) showed a small to medium effect. Unfortunately, no studies on minimal clinically important difference (MCID) have been performed on PCa

patients to place our results in context. However, a recent systematic review by Bohannon *et al* explored MCID in adults with different pathology and found the MCID distance on the 6MWT to be somewhere between 14.0 to 30.5 meters [21]. With this in mind our 21.5 meters might have had a clinical impact on our patients. On the other hand, when comparing our results to other studies which have looked at supervised and unsupervised aerobic and/or resistance exercise [7,11,22–26] our results appear fairly modest. In example, Gaskin *et al* found a significant increase of 49.98 meters in the intervention group compared to the control group [25], and in the study by Hojan *et al* [23] the intervention group increased walking distance while the control group gradually decreased walking distance leading to an improvement of 27.39 meters favoring the intervention group. Thus, the exergaming intervention did not reach the same effect on walking distance as supervised aerobic and resistance. This might be explained by the design of the study, as there was no supervision after the instructions at baseline, and thus the patients did not get any feed-back on their exercise level and performance other than what the technology provided. Exergaming technology offers some sort of feed-back, reward system and goal-setting and thus motivates PCa patients to exercise, which is considered important in cancer rehabilitation [27]. However, exertion is a self-perceived phenomenon, and it is unclear whether patients performed at their maximum during exergaming without supervision. Nevertheless, patients were in contact with a research assistant on regularly basis, and thus the effort put in to exergaming could have been influenced positively.

The lack of ability to show any significant improvement in self-reported physical functioning, general health status and FACT-P was supported by findings in previous studies, where supervised exercise was demonstrated to be more efficient than home-based exercise [23,28]. However, previous conflicting results have been reported with regards to this outcome measure [29]. The exergaming intervention showed an improvement of 1.74 % on the FACT-

P total score, which is less than previous shown 3-10 % improvements in adjusted between group differences in aerobic and resistance exercise interventions [28]. As the most beneficial exercise intervention to improve the FACT-P score has yet to be clarified, exergaming needs further investigations as the technology offers both single-player and multiplayer games, where patients can have fun while exergaming together. Thus, it can be investigated whether increase in QoL is dependent on, whether patients do exergaming together or alone as football due to its group-based nature has shown positive results on mental and social well-being [30].

The fatigue score was generally high in our patients, implying the absence of fatigue at baseline and this may explain that exercise was unable to improve it any further. Most likely, the high baseline fatigue score is explained by a selection bias when recruiting study participants. We believe the physically demanding intervention attracted primarily physically fit patients, as 78 eligible patients refused to participate.

Contrary to previous findings [31,32] the effect on body composition was negligible. We believe this reflects an insufficient intervention with regard to resistance exercise as well as the lack of continually reminding the patients about the progressive demand to perform moderate to high intensity exercise. In addition, exercise intensity is a subjective experience and some patients might not have challenged themselves as much as an exercise physiologist or physiotherapist would have done in a supervised setting. Especially the patients with bone metastases might have exercised more careful in respect of sustaining a fracture or injury when left on their own.

The observed numerically increase in leg muscle power in the intervention group was less than reported in supervised exercise studies [28], presumably due to factors as described above.

The documented average minutes spent exergaming per week did not comply with the protocolled 180 minutes. Thus it is unknown whether the reporting was unreliable or a true inadequate compliance explained by lack of interest, priority or a too demanding intervention.

As previously published [33] and recommended by Kahan *et al* [34], our analysis were adjusted to minimize any confounding impact on the outcomes, since randomization does not guarantee balance in important baseline covariates. In particular, we had expected physical activity to be a pronounced prognostic factor, however, this covariate turned out to be balanced at baseline (Table 2).

The very low attrition rate, with 91% completing patients in the intervention group and 87% in the usual care group, implies an applicable study design for use in future studies.

Nevertheless, a few limitations need to be taken into account in this study. The true effect of 21.5 meters was less pronounced than the estimated 100 meters increase in the intervention group compared to the usual care group. However, this estimate was unrealistic to reach as it presumably would have demanded changes in walking technique (i.e. posture, stride and arm motion) in addition to exergaming. Though, the statistical significant result of the 6MWT needs to be confirmed in larger multicenter studies, as the risk of type II error increased in this study. The sample size of 46 patients was based on the expectation that it would be unrealistic to recruit a significantly large study population within the actual time frame.

Another limitation, well-known in exercise trials, is that the current study was unavoidably affected by a selection bias. Firstly, the consent to participate required a surplus of mental and physical energy. This notion was supported by the high baseline score on the fatigue subscale and accordingly, our data cannot be extrapolated to more severely affected PCa patients. Secondly, all patients were from rural and urban areas, most of them married and holding a bachelor degree, making the study population quite homogenous but concurrently less representative for the entire background population of PCa patients.

## **Conclusions**

To the best of our knowledge, this is the first randomized study to investigate the effects of unsupervised home-based exergaming in PCa patients undergoing ADT. The study showed a significant but modest improvement in 6MWT favoring the exergaming group. In addition, results showed that the intervention group kept being physically active during the post-intervention period, where no influence from health care professionals was present. In addition, no significant effects in any of the secondary outcomes were found. The exergaming intervention appeared safe and could be an alternative to traditional aerobic and resistance training in this patient group.

## **Acknowledgement**

The authors would like to thank managers at Regional Hospital Holstebro, The Family Kjærsgaard, Sunds Foundation, Family Hede-Nielsen foundation, Mrs. Agnes Niebuhr Andersons Cancer Research Foundation and European Association of Urology Nurses in cooperation with Ferring Pharmaceuticals for financial support. Elgiganten, Gamestop and Sportsmaster Holstebro are thanked for delivering equipment at a reduced price. The Lundbeck Foundation Centre for Fast-track Hip and Knee Replacement for lending us the leg extensor power rig. Mölnlycke Health Care ApS for sponsor Visual Analog Scales, and the staff at Regional Hospital Holstebro and Regional Hospital Viborg for extensive support.

## **Conflict of interest**

No potential conflict of interest was reported by the authors.

## References

- [1] Alibhai SMH, Breunis H, Timilshina N, Naglie G, Tannock I, Krahn M, et al. Long-term impact of androgen-deprivation therapy on physical function and quality of life. *Cancer* 2015;121:2350–7. doi:10.1002/cncr.29355.
- [2] Walker LM, Tran S, Robinson JW. Luteinizing hormone-releasing hormone agonists: A quick reference for prevalence rates of potential adverse effects. *Clin Genitourin Cancer* 2013;11:375–84. doi:10.1016/j.clgc.2013.05.004.
- [3] Casey RG, Corcoran NM, Goldenberg SL. Quality of life issues in men undergoing androgen deprivation therapy: a review. *Asian J Androl* 2012;14:226–31. doi:10.1038/aja.2011.108.
- [4] Storey DJ, McLaren DB, Atkinson MA, Butcher I, Frew LC, Smyth JF, et al. Clinically relevant fatigue in men with hormone-sensitive prostate cancer on long-term androgen deprivation therapy. *Ann Oncol* 2012;23:1542–9. doi:10.1093/annonc/mdr447.
- [5] Teleni L, Chan RJ, Chan A, Isenring EA, Vela I, Inder WJ, et al. Exercise improves quality of life in androgen deprivation therapy-treated prostate cancer: Systematic review of randomised controlled trials. *Endocr Relat Cancer* 2016;23:101–12. doi:10.1530/ERC-15-0456.
- [6] Zopf EM, Newton RU, Taaffe DR, Spry N, Cormie P, Joseph D, et al. Associations between aerobic exercise levels and physical and mental health outcomes in men with bone metastatic prostate cancer: a cross-sectional investigation. *Eur J Cancer Care (Engl)* 2016;1–7. doi:10.1111/ecc.12575.
- [7] Østergren PB, Kistorp C, Bennedbæk FN, Faber J, Sønksen J, Fode M. The use of exercise interventions to overcome adverse effects of androgen deprivation therapy. *Nat Rev Urol* 2016;13:1–12. doi:10.1038/nrurol.2016.67.
- [8] Taaffe DR, Newton RU, Spry N, Joseph D, Chambers SK, Gardiner RA, et al. Effects of Different Exercise Modalities on Fatigue in Prostate Cancer Patients Undergoing Androgen Deprivation Therapy: A Year-long Randomised Controlled Trial. *Eur Urol* 2017;1–7. doi:10.1016/j.eururo.2017.02.019.
- [9] Bourke L, Smith D, Steed L, Hooper R, Carter A, Catto J, et al. Exercise for men with prostate cancer: A systematic review and meta-analysis. *Eur Urol* 2016;69:693–703. doi:10.1016/j.eururo.2015.10.047.
- [10] Phillips SM, Stampfer MJ, Chan JM, Giovannucci EL, Kenfield SA. Physical activity, sedentary behavior, and health-related quality of life in prostate cancer survivors in the health professionals follow-up study. *J Cancer Surviv* 2015;9:500–11. doi:10.1007/s11764-015-0426-2.
- [11] O’Neill RF, Haseen F, Murray LJ, O’Sullivan JM, Cantwell MM. A randomised controlled trial to evaluate the efficacy of a 6 month dietary and physical activity intervention for prostate cancer patients receiving androgen deprivation therapy. *J Cancer Surviv* 2015;9:431–40. doi:10.1186/1745-6215-11-86.
- [12] Tsianakas V, Harris J, Ream E, Van Hemelrijck M, Purushotham A, Mucci L, et al. CanWalk: A feasibility study with embedded randomised controlled trial pilot of a walking intervention for people with recurrent or metastatic cancer. *BMJ Open* 2017;7. doi:10.1136/bmjopen-2016-013719.
- [13] Hoffman AJ, Brintnall RA, Brown JK, Eye A von, Jones LW, Alderink G, et al. Too sick not to exercise: using a 6-week, home-based exercise intervention for cancer-related fatigue self-management for postsurgical non-small cell lung cancer patients. *Cancer Nurs* 2012;36:175–88. doi:10.1097/NCC.0b013e31826c7763.
- [14] Tsuda K, Sudo K, Goto G, Takai M, Itokawa T, Isshiki T, et al. A Feasibility Study of Virtual Reality Exercise in Elderly Patients with Hematologic Malignancies Receiving

- Chemotherapy. *Intern Med* 2016;55:347–52. doi:10.2169/internalmedicine.55.5275.
- [15] Jahn P, Lakowa N, Landenberger M, Vordermark D, Stoll O. InterACTIV: an exploratory study of the use of a game console to promote physical activation of hospitalized adult patients with cancer. *Oncol Nurs Forum* 2012;39:E84-90. doi:10.1188/12.ONF.E84-E90.
- [16] Hoffman AJ, Brintnall RA, von Eye A, Jones LW, Alderink G, Patzelt LH, et al. Home-based exercise: promising rehabilitation for symptom relief, improved functional status and quality of life for post-surgical lung cancer patients. *J Thorac Dis* 2014;6:632–40.
- [17] Villumsen BR, Jørgensen MG, Frystyk J, Hørdam B, Borre M. Nursing and Health Care Patient Reported Outcomes in a New Home-Based Rehabilitation ClinMed. *Int Arch Nurs Heal Care* 2015;1:1–5.
- [18] Schmitz KH, Courneya KS, Matthews C, Demark-Wahnefried W, Galv??o DA, Pinto BM, et al. American college of sports medicine roundtable on exercise guidelines for cancer survivors. *Med Sci Sports Exerc* 2010;42:1409–26. doi:10.1249/MSS.0b013e3181e0c112.
- [19] Neefjes ECW, van den Hurk RM, Blauwhoff-Buskermolen S, van der Vorst MJDL, Becker-Commissaris A, de van der Schueren MAE, et al. Muscle mass as a target to reduce fatigue in patients with advanced cancer. *J Cachexia Sarcopenia Muscle* 2017;8:623–9. doi:10.1002/jcsm.12199.
- [20] Fritz S, Lusardi M. Walking speed : The sixth vital sign White Paper : “ Walking Speed : the Sixth Vital Sign .” *J Geriatr Phys Ther* 2009;32:110. doi:10.1519/00139143-200932020-00002.
- [21] Bohannon RW, Crouch R. Minimal clinically important difference for change in 6-minute walk test distance of adults with pathology: a systematic review. *J Eval Clin Pract* 2017;23:377–81. doi:10.1111/jep.12629.
- [22] 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;32:335–46. doi:10.1200/JCO.2013.49.5523.
- [23] Hojan K, Kwiatkowska-Borowczyk E, Leporowska E, Milecki P. Inflammation, cardiometabolic markers, and functional changes in men with prostate cancer: A randomized controlled trial of a 12-month exercise program. *Pol Arch Med Wewn* 2017;127:25–35. doi:10.20452/pamw.3888.
- [24] Culos-Reed SN, Robinson JL, Lau H, O’Connor K, Keats MR. Benefits of a physical activity intervention for men with prostate cancer. *J Sport Exerc Psychol* 2007;29:118–27.
- [25] Gaskin CJ, Fraser SF, Owen PJ, Craike M, Orellana L, Livingston PM. Fitness outcomes from a randomised controlled trial of exercise training for men with prostate cancer: the ENGAGE study. *J Cancer Surviv* 2016;10:972–80. doi:10.1007/s11764-016-0543-6.
- [26] Hansen PA, Dechet CB, Porucznik CA, LaStayo PC. Comparing Eccentric Resistance Exercise in Prostate Cancer Survivors On and Off Hormone Therapy: A Pilot Study. *PM R* 2009;1:1019–24. doi:10.1016/j.pmrj.2009.09.016.
- [27] Bourke L, Homer KE, Thaha MA, Steed L, Rosario D, Robb KA, et al. Interventions for promoting habitual exercise in people living with and beyond cancer (Review). *Cochrane Libr* 2018. doi:DOI: 10.1002/14651858.CD010192.pub3.
- [28] Keogh JW, MacLeod RD. Body composition, physical fitness, functional performance, quality of life, and fatigue benefits of exercise for prostate cancer patients: a systematic review. *J Pain Symptom Manage* 2012;43:96–110.

- doi:10.1016/j.jpainsymman.2011.03.006.
- [29] Vashistha V, Singh B, Kaur S, Prokop LJ, Kaushik D. The Effects of Exercise on Fatigue, Quality of Life, and Psychological Function for Men with Prostate Cancer: Systematic Review and Meta-analyses. *Eur Urol Focus* 2016;2:284–95. doi:10.1016/j.euf.2016.02.011.
- [30] Krustup P, Williams CA, Mohr M, Hansen PR, Helge EW, Elbe A-M, 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;28:3–7. doi:10.1111/sms.13220.
- [31] Cormie P, Galvão DA, Spry N, Joseph D, Taaffe DR, Newton RU. Functional benefits are sustained after a program of supervised resistance exercise in cancer patients with bone metastases: longitudinal results of a pilot study. *Support Care Cancer* 2014;22:1537–48. doi:10.1007/s00520-013-2103-1.
- [32] Uth J, Hornstrup T, Schmidt JF, Christensen JF, Frandsen C, Christensen KB, et al. Football training improves lean body mass in men with prostate cancer undergoing androgen deprivation therapy. *Scand J Med Sport* 2014;24:105–12. doi:10.1111/sms.12260.
- [33] Bourke L, Gilbert S, Hooper R, Steed LA, Joshi M, Catto JWF, et al. Lifestyle changes for improving disease-specific quality of life in sedentary men on long-term androgen-deprivation therapy for advanced prostate cancer: A randomised controlled trial. *Eur Urol* 2014;65:865–72. doi:10.1016/j.eururo.2013.09.040.
- [34] Kahan BC, Jairath V, Doré CJ, Morris TP. The risks and rewards of covariate adjustment in randomized trials: an assessment of 12 outcomes from 8 studies. *Trials* 2014;15:139. doi:10.1186/1745-6215-15-139.

#### **Legends to figures and tables:**

#### **Figure 1 - CONSORT diagram of recruitment and loss to follow-up through the trial**

One patient in the intervention group developed non-cardiac related chest pain during exercise and one withdrew consent. In the control group one patient violated the allocated intervention, one suffered a severe traffic accident, and another did not accept the allocated intervention.

#### **Figure 2 – Mean score on the Godin Leisure-Time Exercise Questionnaire**

Mean score on the Godin Leisure-Time Exercise questionnaire reflecting physical activity level throughout the study. Only data on the exergaming group at 24 weeks follow-up.

**Figure 3 – Average minutes spent exercising per week for all patients in the exergaming group.**

**Table 1 – Assessment schedule**

All assessments were conducted at three time points over the course of six months.

At baseline patients allocated to the intervention group attended the clinic an additional two times for instructions regarding the home-based exercise program.

**Table 2 – Baseline characteristics of study participants**

ADT=Androgen Deprivation Therapy.

Data for continuous variables were assessed as Mean (SD) using independent sample t-test.

Non-normal distributed continuous data were assessed as median (IQR) using Mann-Whitney test.

Data for categorical variables are presented as frequency (%) using Fisher's exact test.

There were no statistical significant differences between groups at baseline ( $p > 0.05$  for all variables).

T stage was determined at time of PCa diagnosis. The presence of metastases was determined when ADT was initiated.

**Table 3 – Between group changes adjusted for baseline score on the Godin Leisure-Time Exercise Questionnaire, ADT treatment duration  $\leq$  365 days and BMI**

\*Baseline data was not available from one withdrawn patient in the usual care group.

**Table 1 – Assessment schedule**

All assessments were conducted at three time points over the course of six months.

At baseline patients allocated to the intervention group attended the clinic an additional two times for instructions regarding the home-based exercise program.

|   | Week -2/baseline     | Week 0-12  | Week 12              | Week 24 |
|---|----------------------|------------|----------------------|---------|
| Inklusion and randomization   | x                    |            |                      |         |
| Assessments:<br>6MWT<br>LEP<br>Body composition   | x<br>x<br>x          |            | x<br>x<br>x          |         |
| Questionnaires:<br>EORTC QLQ C-30<br>scales: Physical<br>functioning and<br>General Health<br>status.<br>FACT-P<br>FACT-F | x<br><br>x<br>x<br>x |            | x<br><br>x<br>x<br>x |         |
| Godin Leisure-<br>Time exercise<br>questionnaire*   | x                    |            | x                    | x       |
| Exergaming three<br>times per week/180<br>min.<br>(intervention<br>group)   |                      | x<br><br>x |                      |         |
| Usual activity level<br>(usual care group)  |                      |            |                      |         |

\*At week 24 the Godin Leisure-Time exercise questionnaire was handed out to the intervention group only.

**Table 2 – Baseline characteristics of study participants**

|                                | Intervention group | Usual care group |
|--------------------------------|--------------------|------------------|
|                                | (n=23)             | (n=23)           |
|                                | mean $\pm$ (sd)    | mean $\pm$ (sd)  |
|                                | n (%)              | n (%)            |
|                                | median (IQR)       | median (IQR)     |
| Age                            | 67.6 (4.6)         | 69.8 (4.4)       |
| Marital status:                |                    |                  |
| Single                         | 4 (17 %)           | 3 (13 %)         |
| In relationship, not married   | 0 (0 %)            | 2 (9 %)          |
| Married                        | 18 (78 %)          | 18 (78 %)        |
| Divorced                       | 0 (0 %)            | 1 (4 %)          |
| Educational level:             |                    |                  |
| Primary school                 | 1 (4 %)            | 0 (0 %)          |
| High school                    | 1 (4 %)            | 2 (9 %)          |
| Short-length higher education  | 5 (22 %)           | 6 (26 %)         |
| Medium-length higher education | 14 (61 %)          | 14 (61 %)        |
| University degree              | 2 (9 %)            | 1 (4 %)          |
| Weight (kg)                    | 93.2 (11.4)        | 88.3 (12.1)      |
| BMI                            | 29.8 (0.6)         | 29.1 (0.7)       |
| Waist circumference (cm)       | 110.1 (8.4)        | 109.6 (9.6)      |
| Gleason score:                 |                    |                  |
| Gleason 6                      | 1 (4 %)            | 3 (13 %)         |
| Gleason 7                      | 11 (48 %)          | 5 (22 %)         |
| Gleason 8-10                   | 11 (48 %)          | 14 (61 %)        |

|                                      |               |               |
|--------------------------------------|---------------|---------------|
| Not available                        | 0 (0 %)       | 1 (4%)        |
| T-Stage:                             |               |               |
| T1c-T2a                              | 6 (26 %)      | 1 (4 %)       |
| T2b                                  | 5 (22 %)      | 2 (9 %)       |
| T2c-T3c                              | 12 (52 %)     | 19 (83 %)     |
| Tx                                   | 0 (0 %)       | 1 (4 %)       |
| Metastases                           |               |               |
| Bone metastases                      | 10 (43 %)     | 6 (26 %)      |
| Lymph node metastases                | 2 (9 %)       | 1 (4 %)       |
| M0, prior radiation<br>therapy + ADT | 11 (48 %)     | 16 (70 %)     |
| ADT < 365 days                       | 7 (30 %)      | 8 (35 %)      |
| ADT > 365 days                       | 16 (70 %)     | 15 (65 %)     |
| Cardiovascular disease               | 16 (70 %)     | 17 (74 %)     |
| PSA (µg/L)                           | 0,1 (0.1-0.3) | 0.1 (0.1-0.2) |
| Godin score                          | 29.3 (29.2)   | 27.3 (21.8)   |

ADT=Androgen Deprivation Therapy.

Data for continuous variables were assessed as Mean (SD) using independent sample t-test.

Non-normal distributed continuous data were assessed as median (IQR) using Mann-Whitney test.

Data for categorical variables are presented as frequency (%) using Fisher's exact test.

There were no statistical significant differences between groups at baseline ( $p > 0.05$  for all variables).

T stage was determined at time of PCa diagnosis. The presence of metastases was determined when ADT was initiated.

**Table 3 – Between group changes adjusted for baseline score on the Godin Leisure-Time Questionnaire, ADT treatment duration </> 365 days and BMI**

|                               | Baseline                           |                                  | Week 12                            |                                  | Adjusted group differences in mean change over 12 weeks |              |                 |
|-------------------------------|------------------------------------|----------------------------------|------------------------------------|----------------------------------|---|--------------|-----------------|
|                               | Intervention group ( <i>n</i> =23) | Usual care group ( <i>n</i> =23) | Intervention group ( <i>n</i> =21) | Usual care group ( <i>n</i> =20) | Mean  | 95%CI        | <i>p</i> -value |
|                               | Mean (SD)                          | Mean (SD)                        | Mean (SD)                          | Mean (SD)                        |   |              |                 |
| 6-min walk test (m)           | 526.8 (65.6)                       | 497.3 (79.8)                     | 556.1 (59.0)                       | 500.8 (80.6)                     | 21.5  | 3.2 – 39.9   | 0.023           |
| Leg extensor power (w)        | 319.3 (102.4)                      | 267.3 (108.2)                    | 349.2 (93.0)                       | 272.3 (95.8)                     | 20.3  | -13.2 – 53.8 | 0.227           |
| Lean mass (%)                 | 71.1 (3.6)                         | 70.6 (3.7)                       | 71.2 (3.9)                         | 70.0 (4.3)                       | 0.91  | -0.2 – 2.0   | 0.100           |
| Fat mass (%)                  | 28.9 (3.6)                         | 29.4 (3.7)                       | 28.8 (3.9)                         | 30.0 (4.3)                       | -0.9  | -2.0-0.2     | 0.092           |
| Physical functioning (points) | 89.3 (9.8)                         | 86.4 (12.0)                      | 93.7 (9.8)                         | 83.3 (18.8)                      | 6.2   | -0.9 – 13.3  | 0.084           |
| Global health status (points) | 67.0 (20.2)                        | 67.4 (23.4)                      | 81.4 (16.9)                        | 72.5 (20.4)                      | 8.8   | -2.2 – 19.7  | 0.113           |

|                                |              |              |              |              |     |             |       |
|--------------------------------|--------------|--------------|--------------|--------------|-----|-------------|-------|
| *FACT-P questionnaire (points) | 118.7 (14.2) | 119.4 (17.4) | 123.1 (13.9) | 120.7 (18.0) | 2.1 | -6.3 – 10.6 | 0.614 |
| FACT-F subscale (points)       | 43.8 (5.4)   | 41.1 (8.6)   | 45.9 (6.7)   | 40.0 (10.3)  | 2.4 | -0.9 - 5.7  | 0.155 |

\* Baseline data was not available from one withdrawn participant in the usual care group

**Figure 1 - CONSORT diagram of recruitment and loss to follow-up through the trial**

One patient in the intervention group developed non-cardiac related chest pain during exercise and one withdrew consent. In the control group one patient violated the allocated intervention, one suffered a severe traffic accident, and another did not accept the allocated intervention.





