Focused questions (PICOs) selected for updating of the national clinical guideline rehabilitation of patients with prostate cancer
Approved June 25. 2020

Content

PICO 1 (2016 and 2020) *Should all patients with prostate cancer undergo systematic assessment for depression instead of usual care?*

The guideline panel recommend updating the recommendation and the recommendation will be updated in 2020. See www.sst.dk for more information.

PICO 2 (2016) *Should patients with prostate cancer who starts on androgen deprivation therapy receive supervised exercise therapy of moderate or high intensity instead of usual care?*

PICO 3 (2016) *Should patients with prostate cancer who had been on androgen deprivation therapy for at least 6 months receive supervised exercise therapy of moderate or high intensity instead of usual care?*

The guideline panel recommend that the recommendations for PICO 2 and PICO 3 should be updated in 2020. The guideline panel recommends that the two original PICOs from 2016 should be merged to one new focused question I 2020.

(New PICO 2) New merged focused question 2020: *Should patients with prostate cancer on androgen deprivation therapy receive supervised exercise therapy of moderate or high intensity instead of usual care?*

Background and reasons for merging and updating the focused questions:

Androgen deprivation therapy is an important part of the treatment of prostate cancer (1). The treatment lowers the level of the male hormone testosterone significantly. This leads to negative side effects including reduced muscle mass, increases in fat mass and higher risk of fractures. At the same time androgen deprivation therapy can negatively affect quality of life for the patient (1,2,3), Among healthy older patients, moderate to high intensity exercise therapy have shown to increase muscle mass, bone mineral density and reduce fat mass (4,5).

The two original focused questions (PICO 2 and 3) from 2016 are almost identical. The only difference is the small distinction in populations: patients with prostate cancer who starts supervised exercise therapy within one month after starting on androgen deprivation therapy, and patients with prostate cancer who have been on androgen deprivation therapy for at least six months, respectively.

In the original guideline from 2016, the two focused questions were included to investigate the effect of both early and later onset of supervised exercise therapy after starting androgen deprivation therapy. This distinction proved to be arbitrary, as a part of the included trials in the original guideline included patients who had started exercise therapy 1-6 months after starting androgen deprivation therapy. On this background, the guideline panel suggested the two focused questions to be merged. By this, it is possible to give one overall recommendation for the entire population of men with prostate cancer who receives androgen deprivation therapy.

Since the publications of the original guideline from 2016, several new RCTs have investigated the effect of supervised exercise therapy in patients with prostate cancer receiving androgen deprivation therapy. Thus,

the guideline panel determined that the question of supervised exercise therapy for patients with prostate cancer on androgen deprivation therapy should be updated.

To explain potential heterogeneity in the results, a sub group analysis of timing of supervised exercise therapy after starting on androgen deprivation therapy is planned (e.g. start >2 months vs <2 months)

Population
Patients with prostate cancer currently receiving androgen deprivation therapy

Data will be extracted for the timing of the start of the exercise intervention. By this it will be possible to investigate potential heterogeneity in the results by performing a subgroup analysis of trials with early onset of exercise therapy vs later onset of exercise therapy after starting androgen deprivation therapy (e.g. start >2 months vs <2 months)

Intervention

Supervised exercises involving the whole body at a moderate to high intensity e.g. supervised resistance training involving the upper and/or lower extremity with an intensity of minimum 60% of one repetition maximum (RM) and/or supervised aerobic (cardiovascular) exercise at a minimum of 60% of the estimated maximum heart rate. Supervised exercise therapy is defined as a regimen of physical exercises that is instructed, supervised, and monitored by a health care professional. Supervision should be given at least twice per week. Only interventions with a duration of exercise therapy of least 2 months will be included.

Data will be extracted for the duration of the interventions and exercise modalities (e.g. resistance, aerobic or other) and information of group or individual training. By this, it will be possible to investigate potential heterogeneity in the results with sub group analyses of different training modalities, group vs individual training and intervention duration (e.g. > 8 weeks vs < 8 weeks). These results might allow us to elaborate the recommendation regarding to exercise modality, intervention duration and form of administration (group or individual)

Comparison
Usual care (No exercise therapy)

The recommendation for group based vs individual rehabilitation (see PICO 8) will be deleted in 2020.

Instead, the aspect of group based rehabilitation vs individual rehabilitation will be investigated by sub group analyses in the other focused questions selected for updating (assessment for depression, supervised exercise therapy and sexual counselling).

Examples of search terms:
Exercise, training, exercise therapy, supervised training, aerobic exercise, cardiovascular exercise, aerobic training, resistance exercise, resistance training, strength training, physical therapy modalities, physical therapy, physiotherapy.

Outcomes	Time point	Critical (primary) /Important (secondary)
Quality of life Disease-specific quality (1. priority, critical outcome) of life or health related quality of life (2. priority, important outcome) e.g. Functional Assessment of Cancer Therapy-Prostate (FACT-P) scale 0-156 EORTC QLQ-PR25/C30 SF 36, EQ-5D The Expanded Prostate Cancer Index Composite Short Form (EPIC-26)	End of treatment	Critical (disease specific) Important (health related)
Physical performance/activities of daily living e.g. walking performance (1. priority, critical outcome) Sit to stand performance (2. Priority, important outcome) Stair climbing (3. priority)	End of treatment	Critical (walking performance) Sit to stand performance (important)
Prevalence of cardiovascular diseases	Longest follow-up	Important
Prevalence of depression	Longest follow-up	Important
Prevalence of diabetes	Longest follow-up	Important
Muscle strength 1 RM, Kg e.g. Leg press (1. priority) Knee extension (2. priority) Hand grip strength (3. priority) Chess press (4. priority)	End of treatment	Important
Vo2 peak	End of treatment	Important
Fractures, number of persons with fractures	Longest follow-up	Important
Adverse events in form of training related injuries	End of treatment	Important
Dropouts of all causes	End of treatment	Important

Changes in outcomes from the original guideline from 2016:

Participation in everyday life: removed as an outcome. The outcome was critical in the original guideline from 2016, but no evidence was found for this outcome. The guideline panel judge that participation in everyday life is a part of the outcome quality of life and thus is investigated as a part of this outcome.

1) Attard G, Parker C, Eeles RA, Schröder F, Tomlins SA, Tannock I, et al. Prostate cancer. Lancet 2016;387(10013):70-82.
2) Nguyen PL, Alibhai SMH, Basaria S, D'Amico AV, Kantoff PW, Keating NL, et al. Adverse Effects of Androgen Deprivation Therapy and Strategies to Mitigate Them. Eur Urol 2014 Aug 2 [Epub].
3) Taylor LG, Canfield SE, Du XL. Review of major adverse effects of androgendeprivation therapy in men with prostate cancer. Cancer 2009;115(11):2388-2399.
4) Gómez-Cabello A, Ara I, González-Agüero A, Casajús JA, Vicente-Rodríguez G. Effects of training on bone mass in older adults: a systematic review. Sports Med 2012;42(4):301-325.
5) Taylor AH, Cable NT, Faulkner G, Hillsdon M, Narici M, Van DB. Physical activity and older adults: a review of health benefits and the effectiveness of interventions. J Sports Sci 2004;22(8):703-725.

PICO 4 (2016) *Should men who after prostatectomi is incontinent receive supervised pelvic floor muscle training?*

The guideline panel assesses that it is not necessary to update the recommendation in 2020.

PICO 5 (2016 and 2020) *Should patients with prostate cancer receive sexual counselling?*

The guideline panel recommend updating the recommendation and the recommendation will be updated in 2020. See www.sst.dk for more information.

PICO 6 (2016) *Should patients with prostate cancer receiving androgen deprivation therapy receive reguælar examination for cardiovascular risk factors?*

The guideline panel assesses that it is not necessary to update the recommendation in 2020.

PICO 7 (2016) *Should patients with prostate cancer starting on androgen deprivation therapy receive examination of bone mineral density?*

The guideline panel assesses that it is not necessary to update the recommendation in 2020.

The question is addressed in the publiction of the Danish Health Authority about treatment of primary osteoporosis in the primary sector (1). Here low level of testosterone in men is stated as an indication for DXA scanning.

1) Sundhedsstyrelsen. Behandling af primær osteoporose i almen praksis. Rationel Farmakoterapi, Sundhedsstyrelsen, februar 2019.

PICO 8 (2016) *Should patients with prostate cancer receive group based rehabilitation instead of individual rehabilitation?*

The guideline panel assesses that it is not necessary to update the recommendation in 2020. The recommendation will be deleted I 2020.

In the original guideline from 2016 no evidence was found for this focused question. A new updated search for guidelines and Cochrane reviews in 2020 did not identify literature, which investigated the question and the guideline panel did not know any literature investigating the question in this population.

The aspect of group based rehabilitation vs individual rehabilitation will be investigated by sub group analyses in the other focused questions selected for updating (supervised exercise therapy and sexual counselling).