

## Platinum Priority – Prostate Cancer

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# Undertreatment of Men in Their Seventies with High-risk Nonmetastatic Prostate Cancer

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### Abstract

**Background:** Many elderly men with high-risk nonmetastatic prostate cancer (HRnMPCa) do not receive radical treatment, despite the high mortality associated with conservative management.

**Objective:** To investigate how age and comorbidity affect treatment of men with HRnMPCa.

**Design, setting, and participants:** This was an observational nationwide register study during 2001–2012. We identified 19 190 men of <80 yr of age diagnosed with HRnMPCa in the National Prostate Cancer Register of Sweden and 95 948 age-matched men without prostate cancer in the register of the total population.

**Outcome measurements and statistical analysis:** The outcome was the proportion of men with HRnMPCa receiving radical treatment (radical prostatectomy or radiotherapy). Vital status and the Charlson comorbidity index (CCI) were obtained from nationwide registers. The 10-yr survival of men without prostate cancer, stratified by age and CCI, was used as a measure of the life expectancy of the men with prostate cancer.

**Results and limitations:** The proportions receiving radical treatment varied with life expectancy among men younger than 70 yr, whereas use of these treatments did not match the long life expectancy of men in their seventies with CCI 0–1. Only 10% of men aged 75–80 yr with CCI 0 received radical treatment despite 52% probability of 10-yr life expectancy, compared with approximately half of the men younger than 70 yr with a similar life expectancy. The use of radical treatment for HRnMPCa increased with time in all Swedish counties, but a threefold difference between counties remained in 2009–2012 for patients aged 70–80 yr with CCI 0–1. Uncertain external validity is a study limitation, and the impact of physician versus patient preferences on treatment selection could not be assessed.

**Conclusions:** Otherwise healthy men in their seventies with HRnMPCa were less likely to receive radical treatment than younger men with a similar life expectancy, although increasing use of radical treatment was observed during the study period. Our findings highlight the need for improved methods for clinical decision-making, including improved assessment of life expectancy.

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**Patient summary:** We performed a nationwide register study that showed that many healthy men in their seventies live for at least another 10 yr. Despite this long life expectancy, men in their seventies with high-risk nonmetastatic prostate cancer were often not treated with radical prostatectomy or radiotherapy, possibly because their life expectancy was underestimated. Our study highlights the need for improved clinical decision-making, which should incorporate an assessment of the patient's life expectancy.

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## 1. Introduction

Radical prostatectomy and radiotherapy are commonly used in elderly men with low- or intermediate-risk prostate cancer [1–6] despite high-level evidence of the absence of a survival benefit within 10 yr [7–10]. Therefore, it is difficult to understand why so many men in their seventies with high-risk nonmetastatic prostate cancer do not receive treatment with curative intent [2,5,6,11]. Two randomised studies showed a survival benefit from radiotherapy in combination with androgen deprivation therapy for men with high-risk prostate cancer [12,13], with a similar effect for men younger and older than 67 yr [12]. The survival benefit is apparent within 6–8 yr after treatment [12,13]. Without curative treatment, the 10-yr cancer-specific mortality from high-risk prostate cancer is approximately 30%, including in men older than 75 yr at the time of their diagnosis [14].

It is possible that the results from the SPCG-4 study have contributed to the low use of treatment with curative intent among older men with high-risk prostate cancer [8,9]. Subgroup analysis in the first reports from the SPCG-4 study indicated that the positive treatment effect of radical prostatectomy was confined to men younger than 65 yr [8,9]. However, most men in the SPCG-4 study had intermediate-risk disease. Men with poorly differentiated or locally advanced prostate cancer were excluded, and the results from SPCG-4 can therefore not be used to guide treatment of men with high-risk disease [8]. Furthermore, in the final analysis of the SPCG-4 study, radical prostatectomy was associated with significantly lower risks of metastasis and androgen deprivation therapy for men older than 65 yr [10].

The number of elderly men affected by prostate cancer is rapidly increasing around the world [15,16], so optimisation of their treatment is essential. The International Society of Geriatric Oncology recently expressed concerns about undertreatment of healthy elderly men with high-risk prostate cancer [17]. They pointed out that individual health status rather than chronological age should guide treatment decisions [17].

One possible reason for the undertreatment of elderly cancer patients is that their life expectancy is underestimated [6,18]. The aim of the present study was to investigate how treatment decisions for men with high-risk nonmetastatic prostate cancer are influenced by age and comorbidity, and to determine whether the use of radical

prostatectomy and radiotherapy is in accordance with patients' life expectancy.

## 2. Patients and methods

The Prostate Cancer Data Base Sweden (PCBaSe) 3.0 was created through record linkages between the National Prostate Cancer Register (NPCR) of Sweden and several other population-based, nationwide health care registers and demographic databases. The database has previously been described in detail [19]. The capture rate of the NPCR is 98% compared to the Swedish Cancer Register, to which registration is mandated by law [20]. Demographic data for men in PCBaSe Sweden were obtained from the register of the total population. Information on underlying and contributing causes and on the date of death was obtained from the cause of death register, which captures all deaths in Sweden. The quality and completeness of the Swedish national registers and databases are high, and notifications are regularly reviewed by Statistics Sweden. The overall agreement between the cause of death register and reviewed medical records is approximately 86% (95% confidence interval [CI] 85–87%) [21].

High-risk nonmetastatic prostate cancer was defined as prostate cancer with no evidence of metastasis (NO or Nx, MO or Mx) and at least one of the following three criteria: Gleason score 8–10, local clinical stage T3, or prostate-specific antigen (PSA) 20–49 ng/ml. The upper PSA limit was chosen because the Swedish guidelines did not recommend radical treatment in men with PSA  $\geq$ 50 ng/ml during the time period studied. PCBaSe does not include information on subcategories T2a, T2b, and T2c for local clinical stage. Only 12 men registered in the NPCR aged  $>$ 80 yr at the time of diagnosis were treated with radical prostatectomy or radiotherapy. We therefore restricted the analysis to men aged  $<$ 80 yr. The study included men diagnosed between January 1, 2001 and December 31, 2012.

For each prostate cancer case in PCBaSe, we identified five men in the Swedish register of the total population who matched the cases for date of birth ( $\pm$ 1 yr) and county of residence, but who were not diagnosed with prostate cancer. A total of 95 948 men without prostate cancer were identified and included in PCBaSe. Of these, 3608 were subsequently diagnosed with prostate cancer during follow-up. These latter men were censored at the time of diagnosis and were included in the life expectancy estimates only before the date of their prostate cancer diagnosis. All men were followed until death, emigration, or to December 31, 2012, whichever occurred first.

For each man in PCBaSe, a Charlson comorbidity index (CCI) on the date of diagnosis was constructed by grouping International Classification of Diseases (ICD) codes in the discharge diagnoses in the inpatient register, as previously described [22,23]. The prostate cancer diagnosis was not included in the CCI. The term *healthy men* is used for men with no registered comorbidity (CCI 0).

Differences among the 21 counties of Sweden and temporal trends in the use of radical prostatectomy and radiotherapy were also analysed. Radiotherapy was recommended in the Swedish guidelines as the

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