Overview and Recommendations

Background

* Prostate cancer is the [second most common cancer in male persons](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#INCIDENCE_AND_MORTALITY__LI_ZYQ_2FV_PGB) worldwide (annual age-standardized incidence 30.7 per 100,000 persons per year) and the [most common cancer in male persons in the United States](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#INCIDENCE_AND_MORTALITY__LI_JPM_3M4_RNB) (annual age-adjusted incidence 113.4 per 100,000 persons per year).
* [Prostate cancer](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#DESCRIPTION) is most common among older adults ≥ 65 years old.
* Major [risk factors](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_V15_SJM_1KB) are older age, African descent, and family history of prostate cancer.
* Localized and locoregional prostate cancer generally has good prognosis, with 100% 5-year relative [survival](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_Y45_5QW_BKB) in United States.
* Most early prostate cancer may be asymptomatic. [Symptoms](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_HXT_5K4_DKB) associated with advanced disease may include lower urinary tract symptoms, hematuria, erectile dysfunction, and bone pain.

Evaluation

* Suspect prostate cancer based on digital rectal exam (DRE) and/or prostate-specific antigen (PSA) levels (see [Prostate Cancer Screening](https://dpa-pde-oxford.shinyapps.io/prevention/prostate-cancer-screening) for additional information).
* Definitive diagnosis of prostate cancer requires histopathologic analysis of biopsy.
* To avoid unnecessary biopsy, further risk assessment is necessary.
* For asymptomatic patients with normal DRE and PSA level 3-10 ng/mL, risk assessment includes risk calculators ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)), magnetic resonance imaging (MRI) ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)), and/or additional serum or urine biomarker testing ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* For patients with locally advanced prostate cancer suspected on DRE and/or PSA > 50 ng/mL, or for patients not pursuing definitive therapy, consider limited biopsy without MRI ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF))
* For all patients with localized prostate cancer, prior to biopsy, perform MRI ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + If MRI is positive, consider combined targeted biopsy with perilesional sampling ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + If MRI is indeterminate, and there is a very low clinical suspicion of prostate cancer (PSA density < 0.1 ng/mL/cm3, negative DRE, and no family history of prostate cancer), consider forgoing biopsy and consider PSA monitoring only ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)). Otherwise, consider targeted biopsy with perilesional sampling ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + If MRI is negative, and there is a low clinical suspicion of prostate cancer (PSA density < 0.2 ng/mL/cm3, negative DRE, and no family history of prostate cancer), consider forgoing biopsy and consider PSA monitoring only ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)). Otherwise, consider systematic biopsy ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* If MRI is not available, use risk calculator to help decide if systematic biopsy is necessary ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF))
* Estimate life expectancy and evaluate health status and comorbidity to determine testing strategies ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* See [Prostate Cancer Diagnosis and Staging](https://dpa-pde-oxford.shinyapps.io/evaluation/prostate-cancer-diagnosis-and-staging) for details.

Management

Management of Localized or Locally Advanced Prostate Cancer

* Risk stratification determines management strategies, and is based on a combination of clinical characteristics, biopsy results, and laboratory tests.

| Table 1: Risk Stratification of Localized and Locally Advanced Prostate Cancer | | | |
| --- | --- | --- | --- |
| **Risk Group** | **NCCN** | **EAU** | **AUA** |
| Very low risk | * + All of the following     - Clinical stage T1c     - ISUP Grade Group 1     - PSA < 10 ng/mL (10 mcg/L)     - PSA density < 0.15 ng/mL/g     - < 3 positive biopsy cores/fragments and ≤ 50% prostate cancer involvement in each core/fragment | NA | * + All of the following     - Clinical stage T1-T2a     - ISUP Grade Group 1     - PSA < 10 ng/mL (10 mcg/L)     - PSA density < 0.15 ng/mL/g     - < 34% of positive biopsy cores and no core with > 50% involved |
| Low risk | * + All of the following, but does not qualify for very low risk     - Clinical stage T1-T2a     - ISUP Grade Group 1     - PSA < 10 ng/mL (10 mcg/L) | * + All of the following     - Clinical stage T1-T2a based on DRE     - ISUP Grade Group 1     - PSA < 10 ng/mL (10 mcg/L) | * + All of the following     - Clinical stage T1-T2a     - ISUP Grade Group 1     - PSA < 10 ng/mL (10 mcg/L) |
| Intermediate risk | * + Has no high or very high risk features, and divided into favorable and unfavorable risk     - Favorable intermediate - has all the following       * Any 1 intermediate risk factor (clinical stage T2b-T2c, PSA 10-20 ng/mL [10-20 mcg/L], or ISUP Grade Group 2 or 3)       * ISUP Grade Group 1 or 2       * < 50% of biopsy cores is positive     - Unfavorable intermediate - has ≥ 1 of the following       * 2-3 intermediate risk factors (clinical stage T2b-T2c, PSA 10-20 ng/mL [10-20 mcg/L], or ISUP Grade Group 2 or 3)       * ISUP Grade Group 3       * ≥ 50% of biopsy cores is positive | * + Any 1 of the following     - Clinical stage T2b based on DRE     - ISUP Grade Group 2 or 3     - PSA 10-20 ng/mL (10-20 mcg/L) | * + 1 of the following: clinical stage T2b-T2c, PSA 10-20 ng/mL (10-20 mcg/L), or ISUP Grade Group 2 or 3; further divided into favorable and unfavorable risk     - Favorable intermediate risk has ≥ 1 of the following       * ISUP Grade Group 1 with PSA 10-20 ng/mL       * ISUP Grade Group 2 with PSA < 10 ng/mL     - Unfavorable intermediate risk has ≥ 1 of the following       * ISUP Grade Group 2 with either PSA 10-20 ng/mL or clinical stage T2b-T2c       * ISUP Grade Group 3 with PSA < 20 ng/mL |
| High risk | * + ≥ 1 of the following with no very-high-risk features     - Clinical stage T3a     - ISUP Grade Group 4 or 5     - PSA > 20 ng/mL (20 mcg/L) | * + Any 1 of the following     - Localized disease, with any 1 of the following       * Clinical stage T2c based on DRE       * ISUP Grade Group 4 or 5       * PSA > 20 ng/mL (20 mcg/L)     - Locally advanced disease (clinical stage T3-T4 based on DRE or positive lymph node involvement based on CT or bone scan) | * + 1 of the following     - Clinical stage ≥ T3     - ISUP Grade Group 4 or 5     - PSA > 20 ng/mL (20 mcg/L) |
| Very high risk | * + ≥ 1 of the following     - Clinical stage T3b-T4     - Primary Gleason pattern 5     - 2-3 high risk features     - > 4 cores with ISUP Grade Group 4 or 5 | NA | NA |
| Abbreviations: AUA, American Urological Association; CT, computed tomography; DRE, digital rectal examination; EAU, European Association of Urology; ISUP, International Society of Urological Pathology; NA, Not applicable; NCCN, National Comprehensive Cancer Network; PSA, prostate-specific antigen.  Reference - [NCCN 2024 Feb from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_1), [EAU 2023 Mar](https://uroweb.org/guidelines/prostate-cancer)[PDF](https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-EANM-ESTRO-ESUR-ISUP-SIOG-Guidelines-on-Prostate-Cancer-2023_2023-06-13-141145_owmj.pdf), [35536144J Urol 2022 Jul;208(1):10](http://pubmed.ncbi.nlm.nih.gov/35536144?dopt=Abstract), [35536148J Urol 2022 Jul;208(1):19](http://pubmed.ncbi.nlm.nih.gov/35536148?dopt=Abstract), [35536141J Urol 2022 Jul;208(1):26](http://pubmed.ncbi.nlm.nih.gov/35536141?dopt=Abstract). | | | |

* Decision between conservative management strategies and invasive definitive modalities should involve shared decision making, including discussion of complications and impact on quality of life related to each therapy ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* For patients with very-low-risk disease:
  + If life expectancy is ≥ 10 years, consider active surveillance only ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + If life expectancy is <10 years, consider watchful waiting only ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* For patients with low-risk disease:
  + If life expectancy is ≥ 10 years:
    - Offer active surveillance as the preferred option ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF))
    - Other options include
      * brachytherapy ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF))
      * external beam radiation therapy ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF))
      * radical prostatectomy ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF))
  + If life expectancy is ≤ 5-10 years, offer watchful waiting only, especially for patients with asymptomatic disease ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* For patients with favorable intermediate-risk disease:
  + If life expectancy is ≥ 10 years:
    - Primary management options include
      * radical prostatectomy ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)) plus extended pelvic lymph node dissection if patients have high risk of lymph node metastasis ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF))
      * external beam radiation therapy (EBRT) ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF))
      * brachytherapy ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF))
    - In select patients, consider active surveillance ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
    - Only consider cryotherapy, high-intensity focused ultrasound, or focal ablative therapy in the setting of a clinical trial or well-designed cohort study ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + If life expectancy is ≤ 5-10 years:
    - Offer watchful waiting as the preferred option, especially for patients with asymptomatic disease ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
    - Other management options include EBRT or brachytherapy monotherapy ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* For patients with unfavorable intermediate-risk disease:
  + If life expectancy is ≥ 10 years:
    - Primary management options include
      * radical prostatectomy ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)) with extended pelvic lymph node dissection if patients have high risk of lymph node metastasis ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF));
      * EBRT plus ADT for 4-6 months ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF));
      * EBRT plus brachytherapy with or without the addition of ADT for 4-6 months ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
    - Only consider cryotherapy or high-intensity focused ultrasound in the setting of a clinical trial or well-designed cohort study ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + if life expectancy is ≤ 5-10 years:
    - Offer watchful waiting as the preferred option, especially for patients with asymptomatic disease ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF))
    - Alternatively, consider EBRT and/or brachytherapy plus ADT for 4-6 months ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* For patients with high- or very-high-risk disease:
  + If the disease is symptomatic or if life expectancy is > 5 years, management options include
    - radical prostatectomy plus pelvic lymph node dissection as a part of multimodal therapy ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF));
    - EBRT plus ADT for 1-3 years ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF));
    - EBRT plus brachytherapy ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)) with the addition of ADT for 1-3 years ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + If the disease is asymptomatic and life expectancy is ≤ 5 years:
    - Offer watchful waiting ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
    - In select patients with complications such as hydronephrosis or if metastasis is expected within 5 years, consider monotherapy with either ADT or EBRT ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* For patients with locally advanced disease (including very high risk):
  + For patients with nodal negative disease (≥ cT3, cN0, cM0 disease):
    - If the disease is symptomatic or if life expectancy is > 5 years:
      * Offer external beam radiation therapy (EBRT) plus androgen-deprivation therapy (ADT) for 1 to ≥ 2 years ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)), with the possible addition of abiraterone acetate for 2 years for patients with very high risk ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
      * Consider EBRT plus brachytherapy with the addition of ADT for 1-3 years ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
      * For highly selected patients, radical prostatectomy plus extended pelvic lymph node dissection as a part of multimodal therapy may be a management option ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
    - If the disease is asymptomatic and life expectancy is ≤ 5 years:
      * Offer watchful waiting ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
      * In select patients with complications such as hydronephrosis or if metastasis is expected within 5 years, consider monotherapy with either ADT or EBRT ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + For patients with nodal positive disease (any T, cN1, cM0 disease):
    - Primary management options for patients with symptomatic disease or life expectancy > 5 years:
      * Offer external beam radiation therapy (EBRT) plus long-term androgen-deprivation therapy (ADT) plus abiraterone acetate ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
      * For highly selected patients, consider radical prostatectomy plus extended pelvic lymph node dissection as a part of multimodal therapy, with the addition of long-term ADT ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
    - Other options for patients with symptomatic disease or life expectancy > 5 years include
      * EBRT plus ADT ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF));
      * ADT with or without the addition of abiraterone acetate ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
    - For asymptomatic patients whose life expectancy is ≤ 5 years, consider either watchful waiting or ADT ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* See [Management of Localized or Locally Advanced Prostate Cancer](https://dpa-pde-oxford.shinyapps.io/management/management-of-localized-or-locally-advanced-prostate-cancer) for details.

Management of Biochemical Relapse of Localized Prostate Cancer

* Consider enrollment into a clinical trial ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* Management of prostate-specific antigen (PSA) recurrence/persistence after radical prostatectomy:
  + For patients with no pelvic nodal recurrence and no distant metastases, and life expectancy > 5 years:
    - Preferably consider salvage external beam radiation therapy with or without androgen deprivation therapy (ADT) ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
    - Alternatively, consider monitoring only, especially for patients with low risk ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + For patients with pelvic nodal recurrence but no distant metastases, and life expectancy > 5 years, consider salvage external beam radiation therapy plus ADT with or without abiraterone acetate ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
    - The STAMPEDE trial ([28578639N Engl J Med 2017 Jul 27;377(4):338](http://pubmed.ncbi.nlm.nih.gov/28578639?dopt=Abstract)) that studied the use of abiraterone acetate only contained a small subgroup of patients with recurrence. Therefore, the evidence on the use of abiraterone acetate on patients with pelvic recurrence may not be very robust.
  + For patients with no distant metastases, do not offer ADT routinely, especially for patients with low risk (PSA doubling time > 12 months) ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + Management of patients with disease progression after salvage therapy who have exhausted maximal pelvic salvage therapy:
    - Preferably consider monitoring ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
    - Alternatively, consider ADT only, possibly as intermittent ADT to reduce toxicity ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
    - TOPIC\_FTS\_CGL\_XNB\_\_LI\_Y2Q\_2YM\_S1CRU03122404/05/2024 11:44:00 AMrecommendationUpdateppcOncologic\_Disease Urologic\_DisordersFor patients with PSA doubling time ≤ 9 months and PSA ≥ 1 ng/mL after primary radical prostatectomy who have exhausted maximal pelvic salvage therapy, consider enzalutamide with or without ADT. For patients with PSA doubling time ≤ 9 months and PSA ≥ 1 ng/mL after primary radical prostatectomy, consider enzalutamide with or without ADT ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + For patients with life expectancy ≤ 5 years, consider watchful waiting ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* Management of PSA recurrence after radiation therapy:
  + For patients with no pelvic nodal recurrence, no distant metastases, and life expectancy > 5 years, consider monitoring, or ADT (possibly as intermittent ADT to reduce toxicity). For patients with biopsy-proven local recurrence, alternatively consider salvage radical prostatectomy plus pelvic lymph node dissection, cryotherapy, reirradiation, or high-intensity focused ultrasound ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)). Offer local therapy only in the setting of a clinical trial or a well-designed prospective cohort study ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + For patients with pelvic nodal recurrence, no distant metastases, and life expectancy > 5 years, management options include monitoring, ADT (possibly as intermittent ADT to reduce toxicity), pelvic lymph node irradiation or reirradiation with or without ADT, or pelvic lymph node dissection with or without ADT ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + For patients with no distant metastases, do not offer ADT routinely, especially for patients with low risk (PSA doubling time > 12 months) ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + Management of patients with disease progression after salvage therapy who have exhausted maximal pelvic salvage therapy:
    - Preferably consider monitoring ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
    - Alternatively, consider ADT only, possibly as intermittent ADT to reduce toxicity ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
    - TOPIC\_FTS\_CGL\_XNB\_\_LI\_B3F\_GYM\_S1CRU03122404/05/2024 11:44:00 AMrecommendationUpdateppcOncologic\_Disease Urologic\_DisordersFor patients with PSA doubling time ≤ 9 months and PSA ≥ 2 ng/mL after primary radiation therapy who have exhausted maximal pelvic salvage therapy, consider enzalutamide with or without ADT. For patients with PSA doubling time ≤ 9 months and PSA ≥ 2 ng/mL after primary radiation therapy, consider enzalutamide with or without ADT ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + For patients with life expectancy ≤ 5 years, consider watchful waiting ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* See [Management of Biochemical Relapse of Localized Prostate Cancer](https://dpa-pde-oxford.shinyapps.io/management/management-of-biochemical-relapse-of-localized-prostate-cancer) for details.

Management of Hormone-Sensitive Prostate Cancer

* For patients with life expectancy > 5 years who can tolerate combination therapy:
  + As the preferred management option, offer androgen deprivation therapy (ADT) in combination with any one of the following options:
    - abiraterone acetate and prednisone (regardless of disease volume) ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF))
    - apalutamide (regardless of disease volume) ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF))
    - enzalutamide (regardless of disease volume) ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF))
    - docetaxel plus either abiraterone with prednisone, or darolutamide (for high-volume synchronous or metachronous metastases, or low-volume synchronous metastases only) ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + For patients with synchronous metastases with low metastatic burden, consider ADT in combination with external beam radiation therapy to the primary tumor plus abiraterone and prednisone, or docetaxel ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* For patients with asymptomatic disease and life expectancy ≤ 5 years, consider either early ADT or observation ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* Primary options for ADT include orchiectomy , luteinizing-hormone releasing hormone (LHRH) agonist, or LHRH antagonist ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* Considerations for ADT:
  + For patients with evidence of impending spinal cord compression or bladder outlet obstruction, offer orchiectomy or LHRH antagonist ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + For patients initiating LHRH agonist, consider preceding with short-term first-generation antiandrogens to reduce the risk of testosterone flare ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + For ADT monotherapy, intermittent ADT may be considered to reduce toxicity. However, a randomized trial suggested that intermittent ADT may not have noninferior overall survival compared to continuous ADT.
* See [Management of Hormone-Sensitive Metastatic Prostate Cancer](https://dpa-pde-oxford.shinyapps.io/management/management-of-hormone-sensitive-metastatic-prostate-cancer-1) for details.

Management of Castration-Resistant Prostate Cancer

* For patients with nonmetastatic castration-resistant prostate cancer:
  + Continue androgen deprivation therapy (ADT) to maintain castration level of testosterone, regardless of decisions on further therapies ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + Initial treatment depends on prostate-specific antigen (PSA) doubling time
    - If PSA doubling time > 10 months, consider observation as the preferred option ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
    - If PSA doubling time ≤ 10 months, offer one of the following preferred options: apalutamide, darolutamide, enzalutamide ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* Management of metastatic castration-resistant adenocarcinoma:
  + Continue ADT to maintain castration level of testosterone, regardless of decisions on further therapies ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + Preferred first-line therapy options include abiraterone acetate plus prednisone, enzalutamide, docetaxel, or radium-223 (for patients with symptomatic bone metastases but no visceral metastases) ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* Management of metastatic castration-resistant small cell or neuroendocrine tumor:
  + First and subsequent lines of chemotherapy include cisplatin plus etoposide, carboplatin plus etoposide, docetaxel plus carboplatin, or combination of atezolizumab, carboplatin, and etoposide ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF))
  + Consider systemic therapy options similar to small cell lung cancer. See Systemic Therapy for Extensive Stage Disease in [Management of Small Cell Lung Cancer](https://dpa-pde-oxford.shinyapps.io/management/management-of-small-cell-lung-cancer#CHEMOTHERAPY_FOR_EXTENSIVE_DISEASE) for additional information.
* For patients with bone metastases:
  + Offer denosumab ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)) or consider zoledronic acid ([Conditional recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)) to prevent osseous complications. For patients receiving either bone protective agents, monitor serum calcium level and provide supplemental calcium and vitamin D ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + Offer palliative radiation therapy and analgesics for painful disease ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* See [Management of Castration-Resistant Prostate Cancer](https://dpa-pde-oxford.shinyapps.io/management/management-of-castration-resistant-prostate-cancer-1) for details.

Screening

* The decision to offer testing for prostate cancer should be based on each individual’s estimated life expectancy as well as the probability that a clinically significant cancer may be present.
* Engage patients in shared decision-making for an informed choice regarding prostate cancer screening based on benefits and harms of prostate-specific antigen (PSA) testing ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
  + The potential benefits of screening include a small reduction in prostate cancer-specific mortality, but this effect is uncertain and inconsistent across trials.
  + The potential harms of screening include possible emotional distress with false positive results, the detection of clinically unimportant cancer and the risk for bleeding, infection, and urinary retention from a potentially unnecessary prostate biopsy, and a delayed diagnosis due to false negative results.
  + The potential harms of treatment for screen-detected prostate cancer are the same as for symptomatic patients diagnosed by workup and include urinary incontinence, erectile dysfunction, sarcopenia, osteoporosis, and bowel dysfunction, vs. risk of tumor growth and metastatic spread with watchful waiting.
* For patients with average risk, age for prostate cancer screening based on shared decision-making differs among professional organizations:
  + age 45-75 years according to the National Comprehensive Cancer Network (NCCN)
  + age 50-69 years according to the American College of Physicians (ACP)
  + age 55-69 years according to the American Urological Association (AUA) and the United States Preventive Services Task Force (USPSTF)
  + age 50 years according to the American Cancer Society (ACS)
  + age 50 also for patients at elevated risk not of African American ethnicity and without family history of prostate cancer according to the European Association of Urology (EAU)
* For patients with high risk (including African American patients, patients with germline *BRCA1* or *BRCA2* mutation, or patients with family history in first-degree relatives), start prostate cancer screening based on shared decision-making at age ≥ 40 years ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF))
* For patients ≥ 70 years old or with life expectancy < 10-15 years, prostate cancer screening is not recommended ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* For patients < 40 years old, prostate cancer screening is not recommended ([Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-AB58B260-1753-4538-BF37-4EAF1FF7B5BF)).
* See [Prostate Cancer Screening](https://dpa-pde-oxford.shinyapps.io/prevention/prostate-cancer-screening) for details.

Background Information

General InformationGeneral Information

Description

* Prostate cancer is the [second most common cancer in male persons](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#INCIDENCE_AND_MORTALITY__LI_ZYQ_2FV_PGB) worldwide and the [most common cancer in male persons in the United States](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#INCIDENCE_AND_MORTALITY__LI_JPM_3M4_RNB).[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__NCCN),[2](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__EAU2023)

Also Called

* Prostatic cancer
* Prostatic carcinoma

Definitions

* Definitions of biochemical recurrence and prostate-specific antigen (PSA) persistence:
  + Definitions of biochemical recurrence and PSA persistence after radical prostatectomy:
    - National Comprehensive Cancer Network (NCCN) defines biochemical recurrence as either detectable and increasing PSA on ≥ 2 subsequent measurements (after prior undetectable PSA), or PSA increase to > 0.1 ng/mL (0.1 mcg/L).
    - European Association of Urology (EAU) defines biochemical recurrence as detectable and increasing PSA to > 0.4 ng/L (0.4 mcg/L).
    - NCCN and EAU both define PSA persistence as failure of PSA to fall to undetectable level (typically < 0.1 ng/mL [0.1 mcg/L] after 4-8 weeks).
  + Radiation Therapy Oncology Group/American Society for Therapeutic Radiology and Oncology (RTOG/ASTRO) Phoenix definition of biochemical recurrence after radiation therapy is PSA rising ≥ 2 ng/mL (2 mcg/L) above the lowest PSA achieved.
  + The definition of PSA level for biochemical recurrence after high-intensity focused ultrasound or cryotherapy is not well established.
  + References - [NCCN 2024 Mar from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_1), [EAU 2024 Apr](https://uroweb.org/guidelines/prostate-cancer)[PDF](https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-EANM-ESTRO-ESUR-ISUP-SIOG-Guidelines-on-Prostate-Cancer-2024.pdf)
* Definitions of hormone-sensitive (castration-sensitive) disease
  + NCCN defines castration-sensitive prostate cancer as either of the following:
    - Patients who are not on androgen-deprivation therapy (ADT) at the time of progression and who have received no prior ADT
    - Patients who have recovered testicular function after prior ADT before, during, or after definitive radiation therapy
    - Reference - [NCCN 2024 Mar from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_1)
  + AUA/SUO defines hormone-sensitive prostate cancer as either a disease which is naive to ADT, or a disease which is still responsive to ADT, that is, a disease with no clinical or radiographic progression, and a disease with no rising prostate-specific antigen [PSA] levels ≥ 2 ng/mL above the nadir. ([37096583J Urol 2023 Jun;209(6):1082](http://pubmed.ncbi.nlm.nih.gov/37096583?dopt=Abstract))
* Castration-resistant prostate cancer (CRPC) is defined as disease progression despite castrate serum testosterone < 50 ng/dL (1.7 nmol/L).
  + National Comprehensive Cancer Network (NCCN) defines disease progression as biochemical, radiographic, and/or clinical progressions.
  + European Association of Urology (EAU) defines disease progression as biochemical and/or radiographic progressions.
    - Biochemical progression is defined as prostate-specific antigen (PSA) > 2 ng/mL, and there are 3 consecutive increases in PSA level ≥ 1 week apart, of which 2 increases are 50% over nadir.
    - Radiographic progression is defined as either the presence of ≥ 2 new bone lesions on bone scan, or the presence of new soft tissue lesions using the Response Evaluation Criteria in Solid Tumors (RECIST) criteria.
  + AUA/SUO definitions of disease progression:
    - AUA/SUO defines disease progression as biochemical progression, radiographic progression of new or pre-existing disease, and/or clinical, symptomatic progressions.
    - Biochemical progression is defined as PSA > 2 ng/mL, there are continuous increases in PSA, measured at ≥ 1 week apart, and the PSA doubling time has been estimated at least 3 times measured at ≥ 4 weeks apart.
  + References - [NCCN 2024 Mar from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_1), [EAU 2024 Apr](https://uroweb.org/guidelines/prostate-cancer)[PDF](https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-EANM-ESTRO-ESUR-ISUP-SIOG-Guidelines-on-Prostate-Cancer-2024.pdf), [37096583J Urol 2023 Jun;209(6):1082](http://pubmed.ncbi.nlm.nih.gov/37096583?dopt=Abstract)

Types

* Most prostate cancers are spontaneous cancers.[2](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__EAU2023)
* Hereditary prostate cancers, with ≥ 3 cases within the same family, cases in 3 successive generations, or ≥ 2 cases within the family with an age of presentation of < 55 years, are less common. Compared to spontaneous cancers, hereditary cancers may have earlier onset but they are mostly similar in other aspects.

Epidemiology

Epidemiology

Incidence and Prevalence

* The prevalence of prostate cancer was the highest in adults aged 65-74 years in the United States during 2016-2020, representing 41.8% of all cases.
  + The median age of diagnosis for prostate cancer was 67 years.
  + Only 0.3% of prostate cancer cases happened in persons < 45 years old.
  + Reference - [SEER Cancer Stat Facts, accessed 2024 Apr 5](https://seer.cancer.gov/statfacts/html/prost.html)
* PubMed32151466Critical reviews in oncology/hematologyCrit Rev Oncol Hematol20200401148102861102861About 75% of prostate cancer cases have been reported in adults ≥ 65 years old in Europe ([Crit Rev Oncol Hematol 2020 Apr;148:102861](http://pubmed.ncbi.nlm.nih.gov/32151466)).
* INCIDENCE\_AND\_MORTALITY\_\_LI\_ZYQ\_2FV\_PGB04/05/2024 11:41:57 AMevidenceUpdatestandardOncologic\_Disease Urologic\_Disordersglobally, prostate cancer was the second most commonly diagnosed cancer in male persons (excluding basal cell carcinoma) in 2022, with annual age-standardized incidence 29.4 per 100,000 persons per year (Global Cancer Observatory: Cancer Today, accessed 2024 Apr 5)

**globally, prostate cancer was the second most commonly diagnosed cancer in male persons (excluding basal cell carcinoma) in 2022, with annual age-standardized incidence 29.4 per 100,000 persons per year**

Population-based Surveillance[Global Cancer Observatory: Cancer Today, accessed 2024 Apr 5](https://gco.iarc.fr/today/en/dataviz/tables?mode=cancer&group_populations=1&multiple_populations=1&cancers=27&sexes=1&include_nmsc=1)

studySummary

* + based on population-based surveillancePopulation-based Surveillance
  + global population-based surveillance information on prostate cancer during 2022 from 185 countries or territories in Global Cancer Observatory: Cancer Today database was evaluated
  + estimated global new prostate cancer cases 1,467,854 in 2022 (14.2% of all new cancer cases and second most commonly diagnosed cancer in male persons, excluding basal cell carcinoma)
  + cumulative global lifetime risk of development of prostate cancer until the age of 74 years was 3.7%
  + age-standardized rates (ASRs) of prostate cancer incidence in 2022
    - overall ASR 29.4 per 100,000 persons per year

| Estimated Age-Adjusted Global Prostate Cancer Incidence by Global Region, 2022 | |
| --- | --- |
| **Region** | **ASRs per 100,000 Persons per Year** |
| Africa | 30.3 |
| Asia | 12.6 |
| Europe | 59.9 |
| Latin America and the Caribbean | 58 |
| Northern America | 73.5 |
| Oceania | 71.9 |
| Abbreviations: ASR, age-standardized rates. | |

* + CA: a cancer journal for clinicians20181101CA Cancer J Clin686394394References - [Global Cancer Observatory: Cancer Today, accessed 2024 Apr 5](https://gco.iarc.fr/today/en/dataviz/tables?mode=cancer&group_populations=1&multiple_populations=1&cancers=27&sexes=1&include_nmsc=1), [Global Cancer Observatory: Cancer Today, accessed 2024 Apr 5](https://gco.iarc.fr/today/en/dataviz/tables?mode=population&group_populations=0&multiple_populations=1&cancers=27&sexes=0&include_nmsc=1)
* INCIDENCE\_AND\_MORTALITY\_\_LI\_JPM\_3M4\_RNB04/05/2024 11:41:47 AMevidenceUpdatestandardOncologic\_Disease Urologic\_Disordersin the United States, prostate cancer is the most commonly diagnosed cancer (excluding basal cell and squamous cell skin carcinomas) in male persons in 2023, with annual age-adjusted incidence 113.4 per 100,000 persons per year during 2016-2020 (SEER Explorer, accessed 2024 Apr 5)

**in the United States, prostate cancer is the most commonly diagnosed cancer (excluding basal cell and squamous cell skin carcinomas) in male persons in 2023, with annual age-adjusted incidence 113.4 per 100,000 persons per year during 2016-2020**

Population-based Surveillance[SEER Explorer, accessed 2024 Apr 5](https://seer.cancer.gov/statistics-network/explorer/application.html?site=66&data_type=1&graph_type=10&compareBy=age_range&chk_age_range_1=1&chk_age_range_9=9&chk_age_range_141=141&chk_age_range_157=157&series=race&chk_race_1=1&chk_race_6=6&chk_race_5=5&chk_race_4=4&chk_race_9=9&chk_race_8=8&hdn_sex=2&stage=101&advopt_precision=1&advopt_show_ci=on&hdn_view=1)

studySummary

* + based on population-based surveillancePopulation-based Surveillance
  + annual population-based surveillance information on prostate cancer during 2016-2020 in the United States from the Surveillance, Epidemiology, and End Results (SEER) database was evaluated
  + incidence rates were age-adjusted to United States standard population in 2000
  + estimated 288,300 new prostate cancer cases in 2023
  + prostate cancer is the most commonly diagnosed cancer in male persons in the United States, excluding basal cell and squamous cell skin carcinomas
  + 5-year age-adjusted incidence during 2016-2020
    - overall, 113.4 per 100,000 persons per year
    - by age
      * 596.7 per 100,000 persons per year for age ≥ 65 years
      * 235.9 per 100,000 persons per year for age 50-64 years
      * 3.6 per 100,000 persons per year for age < 50 years
    - incidence varies by race/ethnicity

| Age-Adjusted Prostate Cancer Incidence Rates by Race/Ethnicity in 2016-2020 | |
| --- | --- |
| **Race/Ethnicity** | **Incidence Rate (per 100,000 Persons per Year)** |
| Hispanic | 86.9 |
| Non-Hispanic American Indian/Alaska Native | 73.2 |
| Non-Hispanic Asian/Pacific Islander | 59.3 |
| Non-Hispanic Black | 184.2 |
| Non-Hispanic White | 111.5 |

* + References - [SEER Explorer, accessed 2024 Apr 5](https://seer.cancer.gov/statistics-network/explorer/application.html?site=66&data_type=1&graph_type=10&compareBy=age_range&chk_age_range_1=1&chk_age_range_9=9&chk_age_range_141=141&chk_age_range_157=157&series=race&chk_race_1=1&chk_race_6=6&chk_race_5=5&chk_race_4=4&chk_race_9=9&chk_race_8=8&hdn_sex=2&stage=101&advopt_precision=1&advopt_show_ci=on&hdn_view=1), [SEER Cancer Stat Facts, accessed 2024 Apr 5](https://seer.cancer.gov/statfacts/html/prost.html)

Risk Factors

Overview of Risk Factors

* Major risk factors of prostate cancer include [increased age](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_C5P_HZN_3NB__LI_EFK_XJS_VNB), [African](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_C5P_HZN_3NB__LI_KGD_VKM_VNB) descent, and [family history (especially first-degree relatives)](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_XK2_4P4_BKB).
* Other risk factors include:
  + [Genetic mutations](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_A3Q_WZ4_BKB)
  + [Metabolic syndrome and obesity](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_EPQ_FKP_BKB)
  + [Smoking](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_D53_N4P_BKB)
  + [Dietary factors](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_DDL_TLV_BKB), including consumption of dairy products, high calcium intake, processed food intake, and heavy alcohol intake
  + [Environmental and occupational exposure](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_XW1_2MP_BKB)
  + [History of infections](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_YXN_K3Q_3NB), including human papillomavirus (HPV), and gonorrhea
  + [In vitro fertilization (IVF) and intra-cytoplasmic sperm injection (ICSI)](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_ILM_LMP_BKB)

Demographic Factors

* **increasing age associated with increased risk of prostate cancer**

Systematic Review[Int J Cancer 2015 Oct 1;137(7):1749](http://pubmed.ncbi.nlm.nih.gov/25821151)[Full Text](https://onlinelibrary.wiley.com/doi/10.1002/ijc.29538)

studySummary

* + Systematic Review based on systematic review of observational studies
  + systematic review of 29 case series evaluating worldwide prevalence of incidental prostate cancer at autopsy in 8,776 patients who died of non-prostate cancer-related causes
  + mean prevalence of incidental prostate cancer
    - 5% at age < 30 years
    - 15% at age 40-50 years
    - 59% at age > 79 years
  + each 10-year increase in age associated with increased risk of incidental prostate cancer (adjusted odds ratio 1.71, 95% CI 1.62-1.81)
  + PubMed25821151International journal of cancerInt J Cancer2015100113771749-571749Reference - [Int J Cancer 2015 Oct 1;137(7):1749](http://pubmed.ncbi.nlm.nih.gov/25821151)[full-text](https://onlinelibrary.wiley.com/doi/10.1002/ijc.29538)
* **African American and Latino adults may have higher risk of prostate cancer compared to White adults**

Cohort Study[Cancer Causes Control 2015 Oct;26(10):1507](http://pubmed.ncbi.nlm.nih.gov/26243447)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4567936/)

studySummary

* + Cohort Study based on prospective cohort study
  + 75,216 male adults (aged 45-75 years) from Hawaii and California, United States were followed for mean follow-up of 13.9 years
  + racial and ethnic groups included in study included African Americans, Native Hawaiians, Japanese Americans, Latino Americans, and White Americans
  + 7,115 adults (9.5%) developed incident prostate cancer
    - 4,113 adults (57.8%) had [International Society of Urological Pathology (ISUP)](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_RVM_VBD_XLB) grade group 1 disease
    - 2,710 adults (42.2%) had ISUP grade group ≥ 2 disease
  + in multivariate analysis
    - compared to White persons, increased risk of prostate cancer in
      * African American (relative risk [RR] 2.08, 95% CI 1.93-2.25)
      * Latinos (RR 1.16, 95% CI 1.07-1.26)
    - no significant differences in risk of prostate cancer comparing Native Hawaiian or Japanese Americans to White persons
  + PubMed26243447Cancer causes & control : CCCCancer Causes Control2015100126101507-151507Reference - [Cancer Causes Control 2015 Oct;26(10):1507](http://pubmed.ncbi.nlm.nih.gov/26243447)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4567936/)
* WCRF/AICR Continuous Update Project (CUP) on diet, nutrition, and physical activity and prostate cancer:
  + Increased adult attained height associated with increased risk of prostate cancer ([WCRF/AICR Probable evidence](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__WCRFGRADE)).
  + Attained height is unlikely to directly influence risk, but it is likely a marker for genetic, environmental, hormonal, and nutritional factors that are associated with growth.
  + Reference - [WCRF/AICR 2018 PDF](https://www.aicr.org/wp-content/uploads/2020/01/2014-prostate-cancer-cup.pdf)

Family History

* Family history (particularly first-degree relatives) of prostate cancer has been reported to increase risk of prostate cancer.
  + There is 2-fold increase in risk if there is a history of prostate cancer in 1 first-degree relative.
  + There is a 4-fold increase in risk if there is a history of prostate cancer in ≥ 2 first-degree relatives.
  + PubMed28681029Investigative and clinical urologyInvestig Clin Urol20170701584217-219217Reference - [Investig Clin Urol 2017 Jul;58(4):217](http://pubmed.ncbi.nlm.nih.gov/28681029)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5494343/)
* **family history of prostate cancer associated with increased risk for prostate cancer**

Cohort Study[23257063BMJ 2012 Dec 20;345:e8076](http://pubmed.ncbi.nlm.nih.gov/23257063?dopt=Abstract)[Full Text](http://www.bmj.com/content/345/bmj.e8076.long)

studySummary

* + based on prospective population-based cohort study Cohort Study
  + 7,904,092 persons aged 0-76 years in Sweden and their biological parents were analyzed
  + 36,878 persons had prostate cancer
  + compared to having no affected parent, having parent with prostate cancer associated with increased risk of prostate cancer (adjusted hazard ratio 2.3, 95% CI 2.2-2.4)
  + having parent diagnosed with prostate cancer at younger age (40-49 years) associated with highest familial risk
  + PubMed23257063BMJ (Clinical research ed.)20121220BMJ345e8076e8076 Reference - [23257063BMJ 2012 Dec 20;345:e8076](http://pubmed.ncbi.nlm.nih.gov/23257063?dopt=Abstract)[full-text](http://www.bmj.com/content/345/bmj.e8076.long), commentary can be found in [23734355J R Coll Physicians Edinb 2013;43(2):134](http://pubmed.ncbi.nlm.nih.gov/23734355?dopt=Abstract)
* **first-degree family history of prostate cancer associated with increased risk for overall prostate cancer, but not aggressive prostate cancer**

Randomized Trial[mnh26332304paph113705957t pa9h113705957t pbyh113705957t pcxh113705957t pmdc26332304pBJU Int 2016 Apr;117(4):576](http://pubmed.ncbi.nlm.nih.gov/26332304?dopt=Abstract)

studySummary

* + based on cohort analysis of data from randomized trial Randomized Trial
  + 4,932 Swiss persons (mean age 61 years) from ERSPC trial were assessed for family history of prostate cancer
  + 6.8% had positive first-degree family history of prostate cancer
  + comparing persons with positive family history vs. persons without family history
    - overall prostate cancer incidence 18% vs. 12% (p < 0.001)
    - aggressive prostate cancer incidence 5.1% vs. 4% (not significant)
  + PubMed26332304BJU international20160401BJU Int1174576576 Reference - [mnh26332304paph113705957t pa9h113705957t pbyh113705957t pcxh113705957t pmdc26332304pBJU Int 2016 Apr;117(4):576](http://pubmed.ncbi.nlm.nih.gov/26332304?dopt=Abstract)
* **family history of prostate cancer in first-, second-, or third-degree relatives each associated with increased risk of prostate cancer**

Cohort Study[Prostate 2015 Mar 1;75(4):390](http://pubmed.ncbi.nlm.nih.gov/25408531)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4293302/)

studySummary

* + Cohort Study based on retrospective population-based cohort study
  + 635,443 persons from Utah Population Data Base with ancestral data on prostate cancer were linked to Utah Cancer Registry and evaluated for association of risk of prostate cancer with family history
    - 201,791 persons (32%) had no family history (first-, second or third-degree relatives) of prostate cancer
    - 18,105 persons (2.85%) had prostate cancer
      * 15,180 persons had family history of prostate cancer
      * 2,925 persons did not have family history of prostate cancer
  + compared to persons with no family history, any family history of prostate cancer associated with increased risk of prostate cancer development

| Risk of Prostate Cancer by Degree of Relatives Affected | | | |
| --- | --- | --- | --- |
|  | **Number of Degree Relatives Affected** | **Number of Persons With Family History** | **Relative Risk** |
| First-degree relative\* | ≥ 1 | 6,439 | 2.76 (95% CI 2.69-2.82) |
| ≥ 3 | 453 | 5.76 (95% CI 5.24-6.32) |
| Second-degree relative\*\* | ≥ 1 | 3,981 | 1.51 (95% CI 1.47-1.56) |
| ≥ 3 | 411 | 2.21 (95% CI 2-2.43) |
| Third-degree relative\*\*\* | ≥ 1 | 4,759 | 1.15 (95% CI 1.12-1.19) |
| ≥ 3 | 1,451 | 1.32 (95% CI 1.25-1.39) |
| \* First-degree relatives included parents, children, or siblings; second- and third-degree relative histories were ignored.  \*\* Second-degree relatives included grandparents, grandchildren, avunculars; no first-degree relative family history of prostate cancer, and third-degree relative history was ignored.  \*\*\* Third-degree relatives included great grandparents or grandchildren, great avunculars, or first cousins; no first-degree or second-degree relative history of prostate cancer. | | | |

* + PubMed25408531The ProstateProstate20150301754390-8390 Reference - [Prostate 2015 Mar 1;75(4):390](http://pubmed.ncbi.nlm.nih.gov/25408531)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4293302/)

Genetic Factors

* Hereditary breast and ovarian cancer syndrome, and Lynch syndrome are 2 hereditary syndromes that are associated with an increased risk of prostate cancer.[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__NCCN),[2](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__EAU2023)
  + Hereditary breast and ovarian cancer syndrome is caused by germline mutations in homologous DNA repair genes. See also [Hereditary Breast and Ovarian Cancer (HBOC) Syndromes](https://dpa-pde-oxford.shinyapps.io/condition/hereditary-breast-and-ovarian-cancer-hboc-syndromes).
  + Lynch syndrome is caused by germline mutations in DNA mismatch repair genes, including *MLH1*, *MSH2*, *MSH6*, and *PMS2*. See also [Lynch Syndrome](https://dpa-pde-oxford.shinyapps.io/condition/lynch-syndrome).
* Persons with *BRCA1* and *BRCA2* mutations may be at increased risk of prostate cancer.
  + TOPIC\_A3Q\_WZ4\_BKB\_\_LI\_SMQ\_2BK\_PSBEU02162202/16/2022 03:51:53 PMevidenceUpdatestandardGenetic\_Disorders Oncologic\_Disease Urologic\_Disorders*BRCA1* and *BRCA2* mutations each associated with increased risk of prostate cancer and aggressive prostate cancer (Br J Cancer 2022 Apr)

***BRCA1* and *BRCA2* mutations each associated with increased risk of prostate cancer and aggressive prostate cancer**

Systematic Review[Br J Cancer 2022 Apr;126(7):1067](https://pubmed.ncbi.nlm.nih.gov/34963702)

studySummary

* + - Systematic Review based on systematic review of observational studies
    - systematic review of 27 studies (20 case-control and 7 cohort) evaluating association between *BRCA1* and/or *BRCA2* mutations and risk of prostate cancer
    - increased risk of prostate cancer associated with
      * *BRCA1* mutation
        + overall (relative risk [RR] 1.69, 95% CI 1.3-2.2) in analysis of 20 studies
        + in patients < 65 years old (RR 2.19, 95% CI 1.21-3.98) in analysis of 4 studies
      * *BRCA2* mutation
        + overall (RR 3.94, 95% CI 2.79-5.56) in analysis of 21 studies, results limited by significant heterogeneity
        + in Ashkenazi Jewish population (RR 2.08, 95% CI 1.38-3.12) in analysis of 6 studies
        + in non-Ashkenazi European ancestry population (RR 3.69, 95% CI 2.71-5.04) in analysis of 7 studies, results limited by significant heterogeneity
        + in patients < 65 years old (RR 5.28, 95% CI 3.1-9) in analysis of 5 studies, results limited by significant heterogeneity
        + in patients ≥ 65 years old (RR 3.74, 95% CI 2.82-4.96) in analysis of 3 studies
    - consistent results for association between *BRCA1* and *BRCA2* mutations and aggressive prostate cancer
    - no significant association between *BRCA1* mutation and prostate cancer in Ashkenazi Jewish population or non-Ashkenazi European ancestry population, or in patients ≥ 65 years old in analyses of 3-8 studies
    - PubMed34963702British journal of cancerBr J Cancer20211228Reference - [Br J Cancer 2022 Apr;126(7):1067](https://pubmed.ncbi.nlm.nih.gov/34963702)
  + ***BRCA1* and *BRCA2* mutations each associated with increased risk of prostate cancer**

Cohort Study[Eur Urol 2020 Jan;77(1):24](http://pubmed.ncbi.nlm.nih.gov/31495749)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6926480/)

Oncologic\_Disease Urologic\_DisordersBRCA1 and BRCA2 mutations each associated with increased risk of prostate cancer (Eur Urol 2020 Jan)12/22/2020 04:06:45 PMstudySummary

* + - Cohort Study based on prospective cohort study
    - 823 persons (median age 51-54 years) with either *BRCA1* or *BRCA2* mutation from United Kingdom and Ireland were evaluated for incidence of prostate cancer
      * 376 persons had *BRCA1* mutation
      * 447 persons had *BRCA2* mutation
    - median follow-up 5.9 years for patients with *BRCA1* mutation was and 5.3 years for patients with *BRCA2* mutation
    - 16 persons (4.3%) with *BRCA1* mutation and 26 persons (5.8%) with *BRCA2* mutation developed incident prostate cancer
    - compared to general population
      * *BRCA1* mutation associated with
        + increased risk of

any prostate cancer (standardized incidence ratio [SIR] 2.35, 95% CI 1.43-3.88)

[International Society of Urological Pathology (ISUP)](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_RVM_VBD_XLB) grade group 1 prostate cancer (SIR 3.5, 95% CI 1.67-7.35)

* + - * + nonsignificant increase in risk of ISUP grade group ≥ 2 prostate cancer (SIR 1.8, 95% CI 0.89-3.65)
      * *BRCA2* mutation associated with increased risk of
        + any prostate cancer (SIR of 4.45, 95% CI 2.99-6.61)
        + ISUP grade group 1 prostate cancer (SIR 3.03, 95% CI 1.24-7.44)
        + ISUP grade group ≥ 2 prostate cancer (SIR 5.07, 95% CI 3.2-8.02)
    - estimated absolute risk of any prostate cancer by age of 85 years
      * 29% (95% CI 17%-45%) for persons with *BRCA1* mutation
      * 60% (95% CI 43%-78%) for persons with *BRCA2* mutation
    - PubMed31495749European urologyEur Urol2020010177124-3524Reference - [Eur Urol 2020 Jan;77(1):24](http://pubmed.ncbi.nlm.nih.gov/31495749)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6926480/)
  + ***BRCA2*, and possibly *BRCA1*, may be associated with increased risk of prostate cancer**

Cohort Study[Cancer 2015 Jan 15;121(2):269](http://pubmed.ncbi.nlm.nih.gov/25224030)[Full Text](https://onlinelibrary.wiley.com/doi/full/10.1002/cncr.29041)

studySummary

* + - Cohort Study based on cohort study
    - 1,072 persons (mean age 49.3 years) from Texas, United States with either deleterious *BRCA1* or *BRCA2* mutation were evaluated for incidence of cancers and compared to general population of United States
    - persons excluded if
      * mutations in both *BRCA1* and *BRCA2* genes
      * presence of another known cancer-predisposing mutation or genetic condition
    - 3 persons with *BRCA1* mutation and 7 persons with*BRCA2* mutation developed prostate cancer
    - comparing persons with BRCA mutations to general population
      * persons with *BRCA2* mutation associated with increased risk of prostate cancer (standardized incidence ratio 4.89, 95% CI 1.96-10.08)
      * persons with *BRCA1* mutation associated with nonsignificant increase in risk of prostate cancer (standardized incidence ratio 3.81, 95% CI 0.77-11.13)
    - PubMed25224030CancerCancer201501151212269-75269 Reference - [Cancer 2015 Jan 15;121(2):269](http://pubmed.ncbi.nlm.nih.gov/25224030)[full-text](https://onlinelibrary.wiley.com/doi/full/10.1002/cncr.29041)
* ***HOXB13* G84E variant associated with increased risk of hereditary prostate cancer**

Case-Control Study[22236224N Engl J Med 2012 Jan 12;366(2):141](http://pubmed.ncbi.nlm.nih.gov/22236224?dopt=Abstract)

studySummary

* + based on case-control study Case-Control Study
  + 94 persons from families with hereditary prostate cancer (≥ 3 first-degree relatives with prostate cancer), 5,083 additional persons with prostate cancer, and 1,401 persons without prostate cancer were genotyped for 202 genes within 17q21-22 region of genome and evaluated for association with prostate cancer
  + all 18 persons with prostate cancer from families with hereditary prostate cancer had *HOXB13* G84E allele
  + compared to persons without prostate cancer, persons with prostate cancer were more likely to have *HOXB13* G84E allele (odds ratio 20.1, p < 0.0001)
  + in persons with prostate cancer
    - persons with family history were more likely to have *HOXB13* G84E allele (odds ratio [OR] 2.8, 95% CI 1.6-5.1)
    - persons with diagnosis age ≤ 55 years were more likely to have *HOXB13* G84E allele (OR 2.7, 95% CI 1.6-4.7)
  + PubMed22236224The New England journal of medicine20120112N Engl J Med3662141141 Reference - [22236224N Engl J Med 2012 Jan 12;366(2):141](http://pubmed.ncbi.nlm.nih.gov/22236224?dopt=Abstract), commentary can be found in [22271088Nat Rev Clin Oncol 2012 Jan 24;9(3):127](http://pubmed.ncbi.nlm.nih.gov/22271088?dopt=Abstract)
* ***CHEK2* 1100delCmutation may be associated with increased risk of prostate cancer**

Cohort Study[J Clin Oncol 2016 Apr 10;34(11):1208](http://pubmed.ncbi.nlm.nih.gov/26884562)

studySummary

* + Cohort Study based on prospective cohort study
  + 86,975 persons from Copenhagen General Population Study were evaluated for association between *CHEK2* 1100delC and risk of cancer from 2003 to 2010
  + *CHEK2* genotype evaluated with polymerase chain reaction on peripheral blood
  + median follow-up 42 years
  + in 39,014 persons
    - 289 persons (0.7%) were heterozygous for *CHEK2*1100del C mutation
    - 1,340 persons (3.4%) developed prostate cancer
  + compared to no mutations, heterozygous *CHEK2*1100delC mutation associated with increased risk of prostate cancer (adjusted hazard ratio 1.6, 95% CI 1-2.56)
  + PubMed26884562Journal of clinical oncology : official journal of the American Society of Clinical OncologyJ Clin Oncol2016041034111208-161208Reference - [J Clin Oncol 2016 Apr 10;34(11):1208](http://pubmed.ncbi.nlm.nih.gov/26884562)
* Prevalence of germline variants in a cross-sectional study of 3,607 patients with prostate cancer:
  + 620 patients (17.2%) were positive for germline pathogenic variants.
  + The most common pathogenic variants were in following genes:
    - *BRCA2* (4.74%)
    - *CHEK2* (2.88%)
    - *MUTYH* (2.37%)
    - *ATM* (2.03%)
    - *APC* (1.28%)
    - *BRCA1* (1.25%)
    - *HOXB13* (1.12%)
    - *MSH2* (0.69%)
    - *TP53* (0.66%)
    - *PALB2* (0.56%)
  + PubMed30730552JAMA oncologyJAMA Oncol2019040154523-528523Reference - [JAMA Oncol 2019 Apr 1;5(4):523](http://pubmed.ncbi.nlm.nih.gov/30730552)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6459112/)
* Prevalence of germline mutations in DNA repair genes in a cross-sectional study of 692 patients with metastatic prostate cancer:
  + 11.8% had germline mutations in DNA repair genes.
  + The most commonly mutated genes were as follows:
    - *BRCA2* (5.3%)
    - *CHEK2* (1.9%)
    - *ATM* (1.6%)
    - *BRCA1* (0.9%)
    - *RAD51D* (0.4%)
    - *PALB2* (0.4%)
  + PubMed27433846The New England journal of medicineN Engl J Med201608043755443-53443Reference - [N Engl J Med 2016 Aug 4;375(5):443](http://pubmed.ncbi.nlm.nih.gov/27433846)
* PubMed33106584British journal of cancerBr J Cancer20201027Review of genetic aberrations in DNA repair pathways can be found in [Br J Cancer 2021 Feb;124(3):552](http://doi.org/10.1038/s41416-020-01114-x)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7851123/).

Metabolic Syndrome and Obesity

* WCRF/AICR Continuous Update Project (CUP) on diet, nutrition, and physical activity and prostate cancer showed that increased body fatness, evidenced by waist circumference and waist-hip ratio, is associated with increased risk of advanced prostate cancer ([WCRF/AICR Probable evidence](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__WCRFGRADE)), but not non-advanced cancer ([WCRF/AICR 2018 PDF](https://www.aicr.org/wp-content/uploads/2020/01/2014-prostate-cancer-cup.pdf)).
* **adult weight gain associated with increased risk of developing high-risk and fatal prostate cancer**

Systematic Review[26356247Int J Cancer 2016 Feb 15;138(4):866](http://pubmed.ncbi.nlm.nih.gov/26356247?dopt=Abstract)

studySummary

* + based on a systematic review of observational studies Systematic Review
  + systematic review of 9 case-control and cohort studies evaluating the association between adult weight gain and risk of prostate cancer in 497,634 patients
  + 4.5% (22,338) developed prostate cancer
  + follow-up ranged from 3 to 29 years
  + adult weight gain was calculated as weight at baseline age minus weight at early adulthood (approximately 20 years of age)
  + positive linear relationship for each 5 kg increment of weight gain and
    - risk of developing high-risk prostate cancer (relative risk (RR) 1.02, 95% CI 1-1.04) in analysis of 5 studies with 463,786 patients
    - risk of developing fatal prostate cancer (RR 1.49, 95% CI 1.09-2) in analysis of 3 studies with 306,891 patients
  + PubMed26356247International journal of cancer20160215Int J Cancer1384866866 Reference - [26356247Int J Cancer 2016 Feb 15;138(4):866](http://pubmed.ncbi.nlm.nih.gov/26356247?dopt=Abstract)
* **higher body mass index associated with increased risk of advanced prostate cancer**

Systematic Review[22228452Ann Oncol 2012 Jul;23(7):1665](http://pubmed.ncbi.nlm.nih.gov/22228452?dopt=Abstract)[Full Text](https://www.annalsofoncology.org/article/S0923-7534(19)38023-8/fulltext)

studySummary

* + based on systematic review of observational studies
    - systematic review of 13 prospective cohort studies evaluating association of obesity and risk of prostate cancer
      * 13 studies with 1,080,790 persons had 7,067 cases of advanced prostate cancer
      * 12 studies with 1,033,009 persons had 19,130 cases of localized prostate cancer

Systematic Review

* + each increase in body mass index (BMI) of 5 kg/m2 associated with
    - increased risk of advanced prostate cancer (relative risk 1.09, 95% CI 1.02-1.16)
    - decreased risk of localized prostate cancer (relative risk 0.94, 95% CI 0.91-0.97)
  + PubMed22228452Annals of oncology : official journal of the European Society for Medical Oncology20120701Ann Oncol23716651665 Reference - [22228452Ann Oncol 2012 Jul;23(7):1665](http://pubmed.ncbi.nlm.nih.gov/22228452?dopt=Abstract)[full-text](https://www.annalsofoncology.org/article/S0923-7534(19)38023-8/fulltext)
* **presence of 3-4 metabolic syndrome-like components (obesity, hypercholesterolemia, diabetes, or hypertension) associated with increased risk of high-grade prostate cancer**

Randomized Trial[mnh24931061paph103386213t pa9h103386213t pbyh103386213t pcxh103386213t pmdc24931061pBJU Int 2015 May;115(5):736](http://pubmed.ncbi.nlm.nih.gov/24931061?dopt=Abstract)

studySummary

* + based on cohort analysis of data from randomized trial Randomized Trial
  + 6,426 persons from [REDUCE trial](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_TFJ_JZK_CKB__LI_Z1B_DYC_SNB) with prior negative prostate biopsy and prostate-specific antigen level 2.5-10 ng/mL were analyzed
  + metabolic syndrome-like components included obesity (body mass index > 30 kg/m2) and self-reported hypercholesterolemia, diabetes, or hypertension
  + 34% had 1 metabolic syndrome-like component, 11% had 2 components, and 3% had 3-4 components
  + compared to no metabolic syndrome-like components, 3-4 metabolic syndrome-like components associated with increased risk of high-grade prostate cancer (odds ratio 1.94, 95% CI 1.13-3.33)
  + no significant association between number of metabolic syndrome-like components and risk of low-grade prostate cancer
  + PubMed24931061BJU international20150501BJU Int1155736736 Reference - [mnh24931061paph103386213t pa9h103386213t pbyh103386213t pcxh103386213t pmdc24931061pBJU Int 2015 May;115(5):736](http://pubmed.ncbi.nlm.nih.gov/24931061?dopt=Abstract)
* **diabetes associated with reduced risk of prostate cancer in adults aged ≥ 50 years**

Cohort Study[Diabet Med 2018 Jan;35(1):107](http://www.ncbi.nlm.nih.gov/pubmed/29078006?dopt=Abstract)

studySummary

* + based on retrospective cohort studyCohort Study
  + 237,860 persons with diabetes from Canadian database were assessed
  + 80, 565 adults ≥ 50 years with incident diabetes and without cancer were age-matched to 80,001 adults without diabetes or cancer
  + median follow-up 9 years
  + incident prostate cancer per 1,000 person years 177.4 with diabetes vs. 216 without diabetes (adjusted hazard ratio [HR] 0.82, 95% CI 0.78-0.86)
  + Diabetic medicine : a journal of the British Diabetic Association20180101Diabet Med351107107Reference - [Diabet Med 2018 Jan;35(1):107](http://www.ncbi.nlm.nih.gov/pubmed/29078006?dopt=Abstract)

Smoking

* **current cigarette smoking associated with increased risk of high-grade prostate cancer in adults with elevated PSA**

Randomized Trial[25139338Clin Cancer Res 2014 Oct 15;20(20):5331](http://pubmed.ncbi.nlm.nih.gov/25139338?dopt=Abstract)[Full Text](https://clincancerres.aacrjournals.org/content/20/20/5331.long)

studySummary

* + based on cohort analysis of data from randomized trial Randomized Trial
  + 6,420 adults aged 50-75 years from [REDUCE trial](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_TFJ_JZK_CKB__LI_Z1B_DYC_SNB) with prior negative prostate biopsy and elevated prostate-specific antigen level (2.5-10 ng/mL) who had ≥ 1 on-study biopsy and cigarette smoking status data available were analyzed
  + 45.8% were never smokers, 39.8% former smokers, and 14.5% current smokers
  + tobacco exposure such as cigars, pipes, chewing tobacco, and second-hand smoke not assessed
  + low-grade disease defined as Gleason score 4-6, and high-grade disease as Gleason score 7-10
  + 17.2% had cancer at time of first on-study biopsy, 11.6% low-grade, 6% high-grade
  + analyses adjusted for age, race, geographic region, PSA, prostate volume, digital rectal examination findings, BMI, and treatment arm
  + comparing current smoking to never smoking
    - among all adults
      * current cigarette smoking associated with increased risk of high-grade disease (adjusted odds ratio [OR] 1.45, 95% CI 1.04-2.04)
      * no significant difference in risk of low-grade disease
    - among adults with BMI < 25 kg/m2
      * current cigarette smoking associated with increased risk of low-grade disease (adjusted OR 1.54, 95% CI 1.01-2.34)
      * current cigarette smoking associated with increased risk of high-grade disease (adjusted OR 2.45, 95% CI 1.39-4.32)
    - among adults with BMI ≥ 25 kg/m2, no significant association between current smoking and low-grade or high-grade cancer risk
  + PubMed25139338Clinical cancer research : an official journal of the American Association for Cancer Research20141015Clin Cancer Res202053315331 Reference - [25139338Clin Cancer Res 2014 Oct 15;20(20):5331](http://pubmed.ncbi.nlm.nih.gov/25139338?dopt=Abstract)[full-text](https://clincancerres.aacrjournals.org/content/20/20/5331.long), commentary can be found in [25201623Nat Rev Urol 2014 Nov;11(11):601](http://pubmed.ncbi.nlm.nih.gov/25201623?dopt=Abstract)

Dietary Factors

* WCRF/AICR Continuous Update Project (CUP) on diet, nutrition, and physical activity and prostate cancer reported limited evidence on the following dietary risk factors for prostate cancer:
  + Consumption of dairy products ([WCRF/AICR Suggestive evidence](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__WCRFGRADE))
  + High-calcium diet ([WCRF/AICR Suggestive evidence](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__WCRFGRADE))
  + Low plasma alpha-tocopherol concentrations ([WCRF/AICR Suggestive evidence](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__WCRFGRADE))
  + Low plasma selenium concentrations ([WCRF/AICR Suggestive evidence](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__WCRFGRADE))
  + Reference - [WCRF/AICR 2018 PDF](https://www.aicr.org/wp-content/uploads/2020/01/2014-prostate-cancer-cup.pdf)
* **dairy product intake associated with slight increase in prostate cancer risk**

Systematic Review[cxh100094724pmdc25527754pAm J Clin Nutr 2015 Jan;101(1):87](http://pubmed.ncbi.nlm.nih.gov/25527754?dopt=Abstract)

studySummary

* + based on systematic review of observational studies Systematic Review
  + systematic review of 32 prospective cohort studies evaluating effect of dairy products or calcium intake on risk of prostate cancer
  + slight increase in prostate cancer risk associated with intake of
    - total dairy products (relative risk [RR] per 400 g/day 1.07, 95% CI 1.02-1.12) in analysis of 15 studies with 848,395 persons
    - milk (RR per 200 g/day 1.03, 95% CI 1-1.06 per 200 g/day) in analysis of 14 studies with 539,676 persons
    - cheese (RR per 50 g/day 1.1, 95% CI 1.03-1.18) in analysis of 11 studies with 887,759 persons
    - low-fat milk (RR per 200 g/day 1.06, 95% CI 1.01-1.11) in analysis of 5 studies with 374,664 persons
  + no significant difference in risk of prostate cancer with intake of whole milk, yogurt, ice cream, or butter
  + PubMed25527754The American journal of clinical nutrition20150101Am J Clin Nutr10118787 Reference - [cxh100094724pmdc25527754pAm J Clin Nutr 2015 Jan;101(1):87](http://pubmed.ncbi.nlm.nih.gov/25527754?dopt=Abstract)
* Processed food:
  + **processed meat but not fresh red meat intake associated with increased risk of prostate cancer**

Systematic Review[mnh26689289paph111927701pa9h111927701pafh111927701pcxh111927701pmdc26689289pNutr J 2015 Dec 21;14:125](http://pubmed.ncbi.nlm.nih.gov/26689289?dopt=Abstract)[Full Text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4687294/)

studySummaryprocessed meat but not fresh red meat intake associated with slight increase in risk of prostate cancer (Nutr J 2015 Dec 21)06/13/2016 03:06:00 PMNutritionOncologic\_DiseasePrevention\_and\_ScreeningPrimary\_CareUrologic\_DisordersNutrition Oncologic\_Disease Prevention\_and\_Screening Primary\_Care Urologic\_Disordersprocessed meat but not fresh red meat intake associated with slight increase in risk of prostate cancer (Nutr J 2015 Dec 21)06/13/2016 03:06:00 PM26689289

* + - based on systematic review of observational studies Systematic Review
    - systematic review of 19 prospective cohort studies evaluating association between red or processed meat intake and risk of prostate cancer in 787,772 persons
    - fresh red meat defined as fresh or unprocessed beef, pork, or lamb
    - processed meat typically defined as smoked, cured, or dried beef, pork, or lamb
    - follow-up ranged from 6 to 22 years
    - compared to lowest category of processed meat consumption, highest category of processed meat consumption associated with increased risk of prostate cancer (risk ratio 1.05, 95% CI 1.01-1.1) in analysis of 11 studies
    - no significant association between prostate cancer risk and high fresh red meat consumption in analysis of 9 studies
    - PubMed26689289Nutrition journal20151221Nutr J14125125 Reference - [mnh26689289paph111927701pa9h111927701pafh111927701pcxh111927701pmdc26689289pNutr J 2015 Dec 21;14:125](http://pubmed.ncbi.nlm.nih.gov/26689289?dopt=Abstract)[full-text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4687294/)
  + **higher fried food intake associated with increased risk of prostate cancer**

Systematic Review[Int J Food Sci Nutr 2015;66(5):587](http://pubmed.ncbi.nlm.nih.gov/26114920)

studySummary

* + - Systematic Review based on systematic review of observational studies
    - systematic review of 4 case-control studies evaluating association between fried food and risk of prostate cancer in 2,579 persons with cancer and 2,277 controls
    - definition of amount of intake of fried food varied by studies
    - larger intake of fried food was associated with increased risk of prostate cancer (odds ratio 1.35, 95% CI 1.17-1.57) in analysis of all studies
    - PubMed26114920International journal of food sciences and nutritionInt J Food Sci Nutr20150101665587-9587Reference - [Int J Food Sci Nutr 2015;66(5):587](http://pubmed.ncbi.nlm.nih.gov/26114920)
  + **increased consumption of ultra-processed foods may not be associated with risk of prostate cancer**

Cohort Study[29444771BMJ 2018 Feb 14;360:k322](http://pubmed.ncbi.nlm.nih.gov/29444771?dopt=Abstract)[Full Text](http://www.bmj.com/content/360/bmj.k322.long)

studySummaryincreased consumption of ultra-processed foods may not be associated with risk of prostate cancer (BMJ 2018 Feb 14)03/08/2018 03:55:00 PMGeriatricsOncologic\_DiseaseSurgery\_and\_ProceduresUrologic\_DisordersGeriatrics Oncologic\_Disease Surgery\_and\_Procedures Urologic\_Disordersincreased consumption of ultra-processed foods may not be associated with risk of prostate cancer (BMJ 2018 Feb 14)03/08/2018 03:55:00 PM29444771

* + - based on prospective population-based cohort study Cohort Study
    - 104,980 adults (mean age 42 years, 78% women) in France completed 3 web-based 24-hour dietary records every 6 months to assess processed food consumption
    - food was categorized based on degree of processing by NOVA classification
      * minimally or unprocessed food includes fruits, vegetables, pulses (such as beans, peas, and lentils), rice, pasta, eggs, meat, fish, or milk
      * ultra-processed food includes mass-produced breads and desserts, packaged snacks, sweetened drinks, frozen or shelf-stable ready meals, reconstituted meat products, and food products made mostly from sugar, oils and fats, as well as hydrogenated oils, modified starches, flavoring agents, artificial sweeteners, and other cosmetic additives
    - ultra-processed food intake consisted mainly of sugary products (26%) and drinks (20%), starchy foods and breakfast cereals (16%), and ultra-processed fruits and vegetables (15%)
    - hazard ratios were adjusted for other dietary characteristics (such as lipid, sodium, and carbohydrate intake) as well as other biological factors
    - 2,228 adults developed cancer during median follow-up of 5 years (33% breast cancer, 13% prostate cancer, 7% colorectal cancer)
    - every 10% increase in proportion of ultra-processed foods in diet associated with increased risk of cancer overall (adjusted hazard ratio 1.13, 95% CI 1.07-1.18)
    - no significant association between increased consumption of ultra-processed food and risk of prostate cancer
    - PubMed29444771BMJ (Clinical research ed.)20180214BMJ360k322k322 Reference - [29444771BMJ 2018 Feb 14;360:k322](http://pubmed.ncbi.nlm.nih.gov/29444771?dopt=Abstract)[full-text](http://www.bmj.com/content/360/bmj.k322.long)
* Vitamins and minerals:
  + **calcium intake associated with increased risk of prostate cancer**

Systematic Review[cxh100094724pmdc25527754pAm J Clin Nutr 2015 Jan;101(1):87](http://pubmed.ncbi.nlm.nih.gov/25527754?dopt=Abstract)

studySummary

* + - based on systematic review of observational studies Systematic Review
    - systematic review of 32 prospective cohort studies evaluating effect of dairy products or calcium intake on risk of prostate cancer
    - slight increase in prostate cancer risk associated with intake of
      * total calcium (relative risk [RR] per 400 mg/day 1.02, 95% CI 1.01-1.03) in analysis of 9 studies with 750,275 persons
      * dietary calcium (RR per 400 mg/day 1.05, 95% CI 1.02-1.09) in analysis of 15 studies with 800,879 persons
      * dairy calcium (RR per 400 mg/day 1.06, 95% CI 1.02-1.09) in analysis of 6 studies with 475,774 persons
    - no significant difference in risk of prostate cancer with intake of nondairy calcium or supplemental calcium
    - PubMed25527754The American journal of clinical nutrition20150101Am J Clin Nutr10118787 Reference - [cxh100094724pmdc25527754pAm J Clin Nutr 2015 Jan;101(1):87](http://pubmed.ncbi.nlm.nih.gov/25527754?dopt=Abstract)
  + **increased serum folate levels, but not dietary folate intake, associated with increased risk of prostate cancer**

Systematic Review[mnh25543518paph101019679pa9h101019679pafh101019679pcxh101019679pmdc25543518pBMC Public Health 2014 Dec 29;14(1):1326](http://pubmed.ncbi.nlm.nih.gov/25543518?dopt=Abstract)[Full Text](http://www.biomedcentral.com/1471-2458/14/1326)

studySummary

* + - based on systematic review of observational studies Systematic Review
    - systematic review of 10 observational studies (5 cohort and 5 nested case-control studies) evaluating effect of serum folate levels and dietary folate intake on risk of prostate cancer in 202,512 persons
    - 5 nmol/L increase in serum folate levels associated with increased risk of prostate cancer (relative risk 1.04, 95% CI 1-1.07) in analysis of 5 nested case-control studies with 9,810 persons
    - no significant difference in risk of prostate cancer with 100 mcg/day intake of dietary folate in analysis of 5 cohort studies with 192,702 persons
    - PubMed25543518BMC public health20141229BMC Public Health14113261326 Reference - [mnh25543518paph101019679pa9h101019679pafh101019679pcxh101019679pmdc25543518pBMC Public Health 2014 Dec 29;14(1):1326](http://pubmed.ncbi.nlm.nih.gov/25543518?dopt=Abstract)[full-text](http://www.biomedcentral.com/1471-2458/14/1326)
  + **elevated 25-hydroxyvitamin D levels may be associated with increased risk of prostate cancer**

Systematic Review[mnh24838848pcxh97444876pmdc24838848pJ Cancer Res Clin Oncol 2014 Sep;140(9):1465](http://pubmed.ncbi.nlm.nih.gov/24838848?dopt=Abstract)

studySummary

* + - based on systematic review of observational studies Systematic Review
    - systematic review of 21 observational studies (3 cohort studies and 18 case-control studies) evaluating association between circulating 25-hydroxyvitamin D levels and risk of prostate cancer in 52,811 persons
    - 46% had prostate cancer
    - cutoffs for stratification of circulating 25-hydroxyvitamin D levels varied across studies
    - elevated circulating 25-hydroxyvitamin D levels associated with increased risk of prostate cancer (odds ratio 1.17, 95% CI 1.05-1.3) in analysis of all studies
    - PubMed24838848Journal of cancer research and clinical oncology20140901J Cancer Res Clin Oncol140914651465 Reference - [mnh24838848pcxh97444876pmdc24838848pJ Cancer Res Clin Oncol 2014 Sep;140(9):1465](http://pubmed.ncbi.nlm.nih.gov/24838848?dopt=Abstract)
* Alcohol intake:
  + **binge and heavy drinking associated with increased risk of prostate cancer**

Cohort Study[Cancer Causes Control 2016 Sep;27(9):1049](http://pubmed.ncbi.nlm.nih.gov/27351919)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5278639/)

studySummary

* + - Cohort Study based on prospective cohort study
    - 11,372 persons (mean age 40.1 years) from Older Finnish Twin Cohort were followed from 1981 to 2012 to evaluate association between alcohol use and risk of prostate cancer
    - 1 drink defined as 12 g of alcohol
    - alcohol consumption were classified as light (0.01-3 drinks/week), moderate (3.01-14 drinks/week), and heavy (> 14.01 drinks/week)
    - binge drinking defined as consumption of > 5 bottles of beer, 1 bottle of wine, or 4 drinks (≥ 18 mL of spirits) on one instance ≥ once/month
    - median follow-up 30 years
    - 601 persons developed incident prostate cancer
    - in multivariate analysis
      * compared to light drinking
        + heavy drinking associated with increased risk of prostate cancer (adjusted hazard ratio [HR] 1.46, 95% CI 1.12-1.91)
        + moderate drinking associated with nonsignificant increase in risk of prostate cancer (adjusted HR 1.2, 95% CI 0.99-1.46)
        + current abstinence of alcohol consumption associated with nonsignificant increase in risk of prostate cancer (adjusted HR 1.27, 95% CI 0.94-1.71)
      * compared to nonbinge drinking, binge drinking associated with increased risk of prostate cancer (adjusted HR 1.28, 95% CI 1.06-1.55)
    - in dose-response analysis, increase in each drink of alcohol intake associated with increased risk of prostate cancer (HR 1.1, 95% CI 1.05-1.15)
    - PubMed27351919Cancer causes & control : CCCCancer Causes Control201609012791049-581049Reference - [Cancer Causes Control 2016 Sep;27(9):1049](http://pubmed.ncbi.nlm.nih.gov/27351919)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5278639/)

Environmental and Occupational Exposures

* **night-shift work associated with increased risk of prostate cancer**

Systematic Review[Onco Targets Ther 2015;8:2817](http://pubmed.ncbi.nlm.nih.gov/26491356)[Full Text](https://www.dovepress.com/does-night-shift-work-increase-the-risk-of-prostate-cancer-a-systemati-peer-reviewed-fulltext-article-OTT)

studySummary

* + Systematic Review based on systematic review of observational studies
  + systematic review of 5 cohort studies and 3 case-control studies evaluating night-shift work and prostate cancer in 2,459,845 persons
  + 9,669 (0.4%) had prostate cancer
  + night-shift work associated with increased risk of prostate cancer (relative risk [RR] 1.24, 95% CI 1.05-1.46) in analysis of all studies, results limited by significant heterogeneity
  + in dose-response analysis of 3 studies, increase in every 5 years of night-shift work associated with 2.8% (95% CI 0.3%-5.4%) increase in risk of prostate cancer
  + PubMed26491356OncoTargets and therapyOnco Targets Ther2015100582817-262817Reference - [Onco Targets Ther 2015;8:2817](http://pubmed.ncbi.nlm.nih.gov/26491356)[full-text](https://www.dovepress.com/does-night-shift-work-increase-the-risk-of-prostate-cancer-a-systemati-peer-reviewed-fulltext-article-OTT)
* **agent orange exposure associated with increased risk of high-grade prostate cancer**

Cohort Study[23670242Cancer 2013 Jul 1;119(13):2399](http://pubmed.ncbi.nlm.nih.gov/23670242?dopt=Abstract)[Full Text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4090241/)

studySummary

* + based on prospective cohort study Cohort Study
  + 2,720 veterans having prostate biopsy were analyzed
  + 32.9% had prostate cancer and 16.9% had high-grade (Gleason score ≥ 7) prostate cancer
  + compared to no agent orange exposure, agent orange exposure associated with increased risk of
    - high-grade prostate cancer (adjusted odds ratio 1.75, 95% CI 1.12-2.74)
    - prostate cancer with Gleason score ≥ 8 (adjusted odds ratio 2.1, 95% CI 1.22-3.62)
  + no significant association between agent orange exposure and low-grade prostate cancer
  + PubMed23670242Cancer20130701Cancer1191323992399 Reference - [23670242Cancer 2013 Jul 1;119(13):2399](http://pubmed.ncbi.nlm.nih.gov/23670242?dopt=Abstract)[full-text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4090241/)
* **rescue and/or recovery work at World Trade Center site associated with increased risk of prostate cancer**

Cohort Study[23288447JAMA 2012 Dec 19;308(23):2479](http://pubmed.ncbi.nlm.nih.gov/23288447?dopt=Abstract)

studySummary

* + based on prospective cohort studyCohort Study
  + 55,778 residents of New York State who enrolled in World Trade Center Health Registry during 2003-2004 were followed through 2008
    - 39% were rescue and/or recovery workers at or near site of World Trade Center attacks from September 11, 2001 to June 30, 2002
    - 61% were not involved in rescue or recovery efforts but lived, worked, or attended school near World Trade Center site
  + 1,187 incident cancers were diagnosed during 253,269 person-years of follow-up (439 incident cancers in rescue and/or recovery workers)
  + compared to general population during 2007-2008, rescue and/or recovery work associated with increased risk of incident
    - prostate cancer (adjusted standardized incident ratio [SIR] 1.43, 95% CI 1.11-1.82)
    - multiple myeloma (adjusted SIR 2.85, 95% CI 1.15-5.88)
    - thyroid cancer (adjusted SIR 2.02, 95% CI 1.07-3.45)
  + no significant difference in cancer risk for persons not involved in rescue or recovery but exposed to World Trade Center site compared to general population during 2007-2008
  + intensity of World Trade Center exposure not associated with lung cancer, prostate cancer, thyroid cancer, non-Hodgkin lymphoma, or hematological cancer in either group
  + PubMed23288447JAMA20121219JAMA3082324792479Reference - [23288447JAMA 2012 Dec 19;308(23):2479](http://pubmed.ncbi.nlm.nih.gov/23288447?dopt=Abstract), commentary can be found in [23549571JAMA 2013 Apr 3;309(13):1344](http://pubmed.ncbi.nlm.nih.gov/23549571?dopt=Abstract)

Medical History of Infections

* **infection due to HPV-16, but not HPV-18, associated with increased risk of prostate cancer**

Systematic Review[Aging Male 2020 Jun;23(2):132](http://pubmed.ncbi.nlm.nih.gov/29571270)

Oncologic\_Disease Urologic\_Disordersinfection due to HPV-16, but not HPV-18, associated with increased risk of prostate cancer (Aging Male 2020 Jun)12/22/2020 04:09:21 PMstudySummary

* + Systematic Review based on systematic review of observational studies
  + systematic review of 31 observational studies evaluating association between human papillomavirus (HPV) infection and risk of prostate cancer
    - 31 studies evaluated association of HPV-16 infection in 6,478 persons, of whom 3,050 persons (47.1%) had prostate cancer
    - 7 studies evaluated association of HPV-18 infection in 6,545 persons, of whom 2,393 persons (36.6%) had prostate cancer
  + methods for detection of HPV infection varied among studies, and included polymerase-chain reaction (with type-specific and/or nonspecific primers), in situ hybridization, immunohistochemistry, and hybrid capture 2 (HC2) assay
  + HPV samples were from biopsy (26 studies) or serum or plasma (5 studies)
  + compared to no HPV infection, HPV-16 infection associated with increased risk of prostate cancer in analysis of 31 studies with 6,478 persons (odds ratio 1.38, 95% CI 1.16-1.64), results limited by significant heterogeneity
  + comparing HPV-18 infection to no infection, no significant difference in risk of prostate cancer in analysis of 7 studies with 6,545 persons
  + PubMed29571270The aging male : the official journal of the International Society for the Study of the Aging MaleAging Male20200601232132-138132Reference - [Aging Male 2020 Jun;23(2):132](http://pubmed.ncbi.nlm.nih.gov/29571270)
* **gonorrhea associated with increased risk of prostate cancer, especially in African Americans**

Systematic Review[Med Sci Monit 2015 Jul 1;21:1902](http://pubmed.ncbi.nlm.nih.gov/26126881)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4502545/)

studySummary

* + Systematic Review based on systematic review of observational studies
  + systematic review of 21 observational studies (19 case-control studies and 2 cohort studies) evaluating association between gonorrhea and risk of prostate cancer in 118,765 persons
  + 9,965 persons (8.4%) had prostate cancer
  + exposure or history of gonorrhea assessed by self-reports (18 studies), medical history (2 studies), or serology of *Neisseria gonorrhoeae* antibodies (1 study)
  + gonorrhea associated with
    - increased risk of prostate cancer (odds ratio 1.31, 95% CI 1.14-1.52) in analysis of all studies, results limited by significant heterogeneity
    - increased risk of prostate cancer in African Americans (odds ratio 1.32, 95% CI 1.06-1.65) in analysis of 6 studies with 8,920 persons, results limited by significant heterogeneity
    - no significant difference in risk of prostate cancer in White persons in analysis of 10 studies with 49,481 persons
  + PubMed26126881Medical science monitor : international medical journal of experimental and clinical researchMed Sci Monit20150701211902-101902Reference - [Med Sci Monit 2015 Jul 1;21:1902](http://pubmed.ncbi.nlm.nih.gov/26126881)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4502545/)

In Vitro Fertilization (IVF) and Intra-Cytoplasmic Sperm Injection (ICSI)

* **fathering children through in vitro fertilization (IVF) and intra-cytoplasmic sperm injection (ICSI) each associated with increased risk of prostate cancer before age 55 years**

Cohort Study[BMJ 2019 Sep 25;366:l5214](http://pubmed.ncbi.nlm.nih.gov/31554611?dopt=Abstract)[Full Text](https://www.bmj.com/content/366/bmj.l5214.long)

studySummary

* + based on population-based cohort studyCohort Study
  + 1,181,490 fathers who had live born children in Sweden during 1994-2014 were assessed
  + 1.7% fathered children by IVF, 1.5% fathered children by ICSI, and 97% fathered children by natural conception
  + total follow-up 14,389,198 person-years
  + diagnosis of prostate cancer in
    - 0.37% with IVF (adjusted hazard ratio [HR] 1.33, 95% CI 1.06-1.66 vs. natural conception)
    - 0.42% with ICSI (adjusted HR 1.64, 95% CI 1.25-2.15 vs. natural conception)
    - 0.28% with natural conception
  + compared to natural conception, increased risk of prostate cancer before age 55 years associated with
    - IVF (adjusted HR 1.51, 95% CI 1.09-2.08)
    - ICSI (adjusted HR 1.86, 95% CI 1.25-2.77)
  + PubMed31554611BMJ (Clinical research ed.)BMJ20190925366l5214l5214Reference - [BMJ 2019 Sep 25;366:l5214](http://pubmed.ncbi.nlm.nih.gov/31554611?dopt=Abstract)[full-text](https://www.bmj.com/content/366/bmj.l5214.long), editorial can be found in [BMJ 2019 Sep 25;366:l5525](http://pubmed.ncbi.nlm.nih.gov/31554620?dopt=Abstract)

Factors Associated With Decreased Risk

Overview of Factors Associated With Decreased Risk

* The following factors may be associated with decreased risk of prostate cancer:
  + [Chinese and Indian ethnicity](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_JVV_FVJ_SNB)
  + [Phytoestrogen intake](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_PJR_MLK_CKB__LI_ZDC_TVK_CKB)
  + [Lycopene, carotene, or tomato product intake](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_PJR_MLK_CKB__LI_IKV_TVK_CKB)
  + [Vegetable intake](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_PJR_MLK_CKB__LI_L2B_YBX_3NB)
  + [Higher selenium level](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_PJR_MLK_CKB__LI_P3Y_XCX_3NB), but not [selenium supplementation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_ZHM_GGQ_3NB)
  + [Coffee consumption](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_PJR_MLK_CKB__LI_BMH_TVK_CKB)
  + [Lower body mass index](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_OJ3_121_WNB__LI_WZT_C21_WNB)
  + [Lower free testosterone level](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_B2Q_ZHQ_3NB)
  + [Increased ejaculation frequency](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_QFP_CTJ_SNB)
  + Use of certain medications (see [Chemoprevention Strategies in Prostate Cancer](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_KLW_QWK_CKB) for medication use associated with reduced prostate cancer risk)
  + [Baseline prostate atrophy](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_DXF_MWJ_SNB)

Demographic Factors

* **Chinese and Indian ethnicity each associated with reduced risk of prostate cancer in adults ≥ 50 years old**

Cohort Study[Diabet Med 2018 Jan;35(1):107](http://www.ncbi.nlm.nih.gov/pubmed/29078006?dopt=Abstract)

studySummary

* + based on retrospective cohort studyCohort Study
  + 160,566 adults ≥ 50 years old from Canadian database were assessed
  + median follow-up 9 years
  + validated surname algorithms were used to identify ethnicity
  + 7.6% had Chinese ethnicity, 2.6% had Indian ethnicity, and rest classified as other
  + compared to other race or ethnicity, decreased risk of prostate cancer associated with
    - Chinese ethnicity (adjusted HR 0.54, 95% CI 0.46-0.63)
    - Indian ethnicity (adjusted HR 0.66, 95% CI 0.49-0.89)
  + Diabetic medicine : a journal of the British Diabetic Association20180101Diabet Med351107107Reference - [Diabet Med 2018 Jan;35(1):107](http://www.ncbi.nlm.nih.gov/pubmed/29078006?dopt=Abstract)

Dietary Factors

* Phytoestrogens:
  + **phytoestrogen consumption associated with reduced risk of prostate cancer**

Systematic Review[a9h108684301pcxh108684301pWorld J Surg Oncol 2015 Jul 31;13(1):231](http://pubmed.ncbi.nlm.nih.gov/26228387?dopt=Abstract)[Full Text](http://www.wjso.com/content/13/1/231)

studySummary

* + - based on systematic review of observational studies Systematic Review
    - systematic review of 16 observational studies evaluating association between phytoestrogen intake or serum phytoestrogen levels and risk of prostate cancer
    - higher phytoestrogen intake (highest category of intake) associated with reduced risk of prostate cancer compared to lower phytoestrogen intake (lowest category of intake) in analysis of 2 cohort studies and 9 case-control studies
      * odds ratio (OR) 0.8 (95% CI 0.7-0.91)
      * results limited by significant heterogeneity
    - higher phytoestrogen serum levels associated with reduced risk of prostate cancer compared to lower phytoestrogen serum levels (OR 0.83, 95% CI 0.7-0.99) in analysis of 8 case-control studies
    - in stratified analysis for individual types of phytoestrogens evaluated
      * high intake of genistein and daidzein, or high serum concentration of enterolactone associated with significantly reduced risk of prostate cancer
      * high intake of isoflavone or lignans, or high serum concentration of genistein, daidzein, or equol not associated with significantly reduced risk of prostate cancer
    - PubMed26228387World journal of surgical oncology20150731World J Surg Oncol131231231 Reference - [a9h108684301pcxh108684301pWorld J Surg Oncol 2015 Jul 31;13(1):231](http://pubmed.ncbi.nlm.nih.gov/26228387?dopt=Abstract)[full-text](http://www.wjso.com/content/13/1/231)
  + **soy intake associated with decreased risk of prostate cancer**

Systematic Review[Nutrients 2018 Jan 4;10(1):doi:10.3390/nu10010040](http://pubmed.ncbi.nlm.nih.gov/29300347)[Full Text](https://www.mdpi.com/2072-6643/10/1/40)

studySummary

* + - Systematic Review based on systematic review of observational studies
    - systematic review of 30 observational studies (8 cohort, 7 nested case-control, and 15 case-control studies) evaluating association of soy intake, or soy isoflavones (genistein and daidzein) with risk of prostate cancer in 266,699 persons
    - 21,612 persons (8.1%) had prostate cancer
    - decreased risk of prostate cancer associated with
      * total soy intake (risk ratio [RR] 0.71, 95% CI 0.58-0.85) in analysis of 16 studies, results limited by significant heterogeneity
      * unfermented soy intake (such as soy milk or tofu) (RR 0.65, 95% CI 0.56-0.83) in analysis of 11 studies, results limited by significant heterogeneity
      * genistein intake (RR 0.9, 95% CI 0.84-0.97) in analysis of 10 studies
      * daidzein intake (RR 0.84, 95% CI 0.73-0.97) in analysis of 10 studies, results limited by significant heterogeneity
    - no significant differences in risk of prostate cancer with fermented soy intake (such as miso or natto) in analysis of 8 studies, results limited by significant heterogeneity
    - PubMed29300347NutrientsNutrients20180104101 Reference - [Nutrients 2018 Jan 4;10(1):doi:10.3390/nu10010040](http://pubmed.ncbi.nlm.nih.gov/29300347)[full-text](https://www.mdpi.com/2072-6643/10/1/40)
  + **soy isoflavone supplements associated with reduced risk of prostate cancer**

Systematic Review[mnh24053483paph95683472t pa9h95683472t pbyh95683472t pcxh95683472t pmdc24053483pBJU Int 2014 May;113(5b):E119](http://pubmed.ncbi.nlm.nih.gov/24053483?dopt=Abstract)

studySummary

* + - based on systematic review limited by clinical heterogeneity Systematic Review
    - systematic review of 8 randomized trials evaluating soy foods or soy isoflavone supplements for prevention or treatment of prostate cancer in 1,025 persons
    - study populations, soy and soy isoflavone preparations, and dosage regimens varied across studies
    - soy isoflavone supplements associated with reduced risk of prostate cancer in analysis of 2 trials with 122 persons
      * risk ratio 0.49 (95% CI 0.26-0.95)
      * NNT 4-58 with 35% risk of prostate cancer in control group
    - no significant differences in levels of surrogate markers for prostate cancer
    - no significant differences in adverse events
    - PubMed24053483BJU international20140501BJU Int1135bE119E119 Reference - [mnh24053483paph95683472t pa9h95683472t pbyh95683472t pcxh95683472t pmdc24053483pBJU Int 2014 May;113(5b):E119](http://pubmed.ncbi.nlm.nih.gov/24053483?dopt=Abstract)
* Lycopene, carotene or tomato products:
  + **increased dietary alpha-carotene intake and increased lycopene blood levels each associated with slight decrease in prostate cancer risk**

Systematic Review[aph109457240pa9h109457240pafh109457240pcxh109457240pmdc26372549pPLoS One 2015;10(9):e0137427](http://pubmed.ncbi.nlm.nih.gov/26372549?dopt=Abstract)[Full Text](http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0137427)

studySummary

* + - based on systematic review of observational studies Systematic Review
    - systematic review of 34 observational studies evaluating association between carotenoid intake and prostate cancer risk in 592,479 persons
      * carotenoids included alpha-carotene, beta-carotene, and lycopene
      * follow-up ranged from > 3 years to 30 years (21 studies) or was unspecified (13 studies)
    - 2.7% developed prostate cancer
    - decreased risk of prostate cancer associated with increased
      * dietary alpha-carotene intake (risk ratio [RR] 0.81, 95% CI 0.76-0.99) in analysis of 12 studies
      * lycopene blood levels (RR 0.81, 95% CI 0.69-0.96) in analysis of 15 studies
    - no significant differences in
      * risk of prostate cancer with increased
        + intake of dietary beta-carotene (19 studies) or lycopene (13 studies)
        + blood levels of beta-carotene (13 studies) or alpha-carotene (11 studies)
      * risk of advanced prostate cancer with increased blood levels of alpha-carotene (2 studies) or lycopene (4 studies)
    - PubMed26372549PloS one201501PLoS One109e0137427e0137427 Reference - [aph109457240pa9h109457240pafh109457240pcxh109457240pmdc26372549pPLoS One 2015;10(9):e0137427](http://pubmed.ncbi.nlm.nih.gov/26372549?dopt=Abstract)[full-text](http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0137427)
  + **increased intake of tomato products associated with modest decrease in prostate cancer risk**

Systematic Review[15006906Cancer Epidemiol Biomarkers Prev 2004 Mar;13(3):340](http://pubmed.ncbi.nlm.nih.gov/15006906?dopt=Abstract)[Full Text](http://cebp.aacrjournals.org/content/13/3/340.long)

studySummary

* + - based on systematic review of observational studies Systematic Review
    - systematic review of 21 studies (11 case-control studies, 5 cohort studies, and 5 nested case-control studies) evaluating effect of tomato, lycopene, or tomato products on prostate cancer risk
    - compared to lowest quintile of tomato product intake, highest quintile associated with
      * decreased risk of prostate cancer for
        + cooked tomato products (relative risk [RR] 0.81, 95% CI 0.71-0.92) in analysis of 6 studies
        + lycopene intake (RR 0.89, 95% CI 0.81-0.98) in analysis of 10 studies
      * nonsignificant reduction in risk of prostate cancer for raw tomato products (RR 0.89, 95% CI 0.8-1) in analysis of 9 studies
    - PubMed15006906Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology20040301Cancer Epidemiol Biomarkers Prev133340340 Reference - [15006906Cancer Epidemiol Biomarkers Prev 2004 Mar;13(3):340](http://pubmed.ncbi.nlm.nih.gov/15006906?dopt=Abstract)[full-text](http://cebp.aacrjournals.org/content/13/3/340.long)
  + **insufficient evidence from randomized trials to determine effect of lycopene on prostate cancer risk**

Cochrane Review[chhCD008007Cochrane Database Syst Rev 2011 Nov 9;(11):CD008007](http://www.ncbi.nlm.nih.gov/pubmed?term=22071840%5buid%5d%20AND%20CD008007%5bpg%5d)

studySummary

* + - based on Cochrane review Cochrane Review
    - systematic review of 3 randomized trials evaluating lycopene for prevention of prostate cancer in 154 persons
    - no significant difference in prostate cancer incidence comparing lycopene to no intervention (10% vs. 30%, p = 0.14) in 1 trial with 40 persons with high-grade prostatic intraepithelial neoplasia
    - no trials reported on prostate cancer-specific mortality
    - no significant difference in prostate-specific antigen (PSA) levels in meta-analysis
    - CochraneCD008007The Cochrane database of systematic reviews20111109Cochrane Database Syst Rev11CD008007CD008007 Reference - [chhCD008007Cochrane Database Syst Rev 2011 Nov 9;(11):CD008007](http://www.ncbi.nlm.nih.gov/pubmed?term=22071840%5buid%5d%20AND%20CD008007%5bpg%5d)
* Vegetable intake:
  + **vegetable intake does not appear associated with overall prostate cancer incidence, but may be associated with reduced risk for advanced prostate cancer in persons undergoing screening**

Cohort Study[17652276J Natl Cancer Inst 2007 Aug 1;99(15):1200](http://pubmed.ncbi.nlm.nih.gov/17652276?dopt=Abstract)[Full Text](http://jnci.oxfordjournals.org/content/99/15/1200.long)

studySummary

* + - based on nested cohort study Cohort Study
    - 29,361 persons in screening arm of Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO) evaluated for association of vegetable intake and overall prostate cancer incidence over average follow-up 4.2 years (limit 8 years)
    - 1,338 persons (4.6%) developed prostate cancer
    - no significant association found between vegetable and fruit consumption and overall risk of prostate cancer
    - compared with low intake, high intake associated with decreased risk of extraprostatic prostate cancer (defined as Stage III or IV tumors) (relative risk 0.41, 95% CI 0.22 - 0.74)
    - PubMed17652276Journal of the National Cancer Institute20070801J Natl Cancer Inst991512001200 Reference - [17652276J Natl Cancer Inst 2007 Aug 1;99(15):1200](http://pubmed.ncbi.nlm.nih.gov/17652276?dopt=Abstract)[full-text](http://jnci.oxfordjournals.org/content/99/15/1200.long)
  + **increased consumption of vegetables associated with decreased risk for prostate cancer in persons with previous exposure to asbestos**

Cohort Study[mnh17519926paph29388049pa9h29388049pmdc17519926pProstate Cancer Prostatic Dis 2008;11(1):61](http://pubmed.ncbi.nlm.nih.gov/17519926?dopt=Abstract)[Full Text](http://www.nature.com/pcan/journal/v11/n1/full/4500979a.html)

studySummary

* + - based on prospective cohort study Cohort Study
    - 1,985 persons previously exposed to asbestos and participating in cancer prevention program followed for median 12.7 years
    - 97 persons (4.9%) developed prostate cancer
    - compared with lowest tertile of intake, highest tertile (defined as > 4 servings per week) associated with decreased risk for prostate cancer (RR 0.53, 95% CI 0.29-0.99)
    - PubMed17519926Prostate cancer and prostatic diseases200801Prostate Cancer Prostatic Dis1116161 Reference - [mnh17519926paph29388049pa9h29388049pmdc17519926pProstate Cancer Prostatic Dis 2008;11(1):61](http://pubmed.ncbi.nlm.nih.gov/17519926?dopt=Abstract)[full-text](http://www.nature.com/pcan/journal/v11/n1/full/4500979a.html)
* Selenium:
  + **increasing toenail selenium concentration, but not blood selenium concentration, associated with reduced risk of prostate cancer**

Systematic Review[J Natl Cancer Inst 2016 Nov;108(11):doi:10.1093/jnci/djw153](http://pubmed.ncbi.nlm.nih.gov/27385803)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/27385803/)

studySummary

* + - Systematic Review based on individual patient data analysis from systematic review of observational studies
    - systematic review of 15 studies (8 nested case-control studies and 7 cohort analyses of randomized trials) evaluating association of selenium levels in toenail and blood with risk of prostate cancer in 14,604 persons (mean age range 55-69.1 years)
    - 6,497 persons (44.5%) had prostate cancer
    - every 80th percentile increase in toenail selenium concentration associated with reduced risk of prostate cancer (adjusted odds ratio 0.29, 95% CI 0.22-0.4) in analysis of 4 studies with 4,065 persons, results limited by significant heterogeneity
    - no significant difference in risk of prostate cancer for every 80th percentile increase in blood selenium concentration in analysis of 11 studies with 10,548 persons
    - PubMed27385803Journal of the National Cancer InstituteJ Natl Cancer Inst2016070610811Reference - [J Natl Cancer Inst 2016 Nov;108(11):doi:10.1093/jnci/djw153](http://pubmed.ncbi.nlm.nih.gov/27385803)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/27385803/)
* Coffee:
  + **high level of coffee consumption associated with reduced risk of prostate cancer**

Systematic Review[mnh21406107paph59743986pa9h59743986pafh59743986pcxh59743986pmdc21406107pBMC Cancer 2011 Mar 15;11:96](http://pubmed.ncbi.nlm.nih.gov/21406107?dopt=Abstract)[Full Text](http://www.biomedcentral.com/1471-2407/11/96)

studySummary

* + - based on systematic review of observational studies Systematic Review
    - systematic review of 40 prospective cohort studies evaluating coffee consumption on risk of cancers in 2,179,126 persons
    - compared with lowest amount of coffee consumption and nondrinkers, highest amount of coffee consumption associated with reduced risk of prostate cancer (relative risk 0.79, 95% CI 0.61-0.98) in analysis of 5 studies with 3,135 persons
    - PubMed21406107BMC cancer20110315BMC Cancer119696 Reference - [mnh21406107paph59743986pa9h59743986pafh59743986pcxh59743986pmdc21406107pBMC Cancer 2011 Mar 15;11:96](http://pubmed.ncbi.nlm.nih.gov/21406107?dopt=Abstract)[full-text](http://www.biomedcentral.com/1471-2407/11/96)

Lifestyle Factors

* **lower body mass index may be associated with reduced incidence of prostate cancer**

Cohort Study[Cancer 2007 Feb 15;109(4):675](http://pubmed.ncbi.nlm.nih.gov/17211863/)[Full Text](http://onlinelibrary.wiley.com/doi/10.1002/cncr.22443/full)

studySummary

* + Cohort Study based on prospective cohort study
  + 287,760 adults aged 50-71 years evaluated for (body mass index (BMI) and adult weight changes and followed for 5 years
  + adults in lowest BMI category (< 25 kg/m2) had reduced total prostate cancer incidence compared to
    - adults with BMI 35-39.9 kg/m2 (relative risk [RR] 0.86, 95% CI 0.75-0.98)
    - adults in highest BMI category (≥ 40 kg/m2) (RR 0.67, 95% CI 0.5-0.89)
  + no significant association of patient-reported adult weight gain from age 18 years to baseline with incident prostate cancer
  + PubMed17211863CancerCancer200702151094675-84675Reference - [Cancer 2007 Feb 15;109(4):675](http://pubmed.ncbi.nlm.nih.gov/17211863/)[full-text](http://onlinelibrary.wiley.com/doi/10.1002/cncr.22443/full)

Testosterone Level

* **very low free testosterone levels may be associated with reduced risk of prostate cancer, especially low-to-intermediate grade disease**

Systematic Review[Eur Urol 2018 Nov;74(5):585](http://pubmed.ncbi.nlm.nih.gov/30077399)[Full Text](https://www.sciencedirect.com/science/article/pii/S0302283818305463?via%3Dihub)

studySummary

* + Systematic Review based on individual patient data analysis from systematic review of observational studies
  + systematic review of 20 prospective studies (16 nested case-control studies and 4 cohort or case-cohort studies) evaluating association between free testosterone level and risk of prostate cancer in 19,021 persons (mean age 59.8 years)
  + 6,933 persons (36.4%) had prostate cancer
  + prostate cancers were mostly localized (55%) and low-grade (68%)
  + free testosterone levels were categorized into study-specific tenths with cutoffs defined by distribution in persons without prostate cancer
  + compared to higher concentrations, lowest 10th of free testosterone concentration associated with
    - lower risk of overall prostate cancer (odds ratio [OR] 0.77, 95% CI 0.69-0.86) in analysis of all studies
    - lower risk of International Society of Urological Pathology (ISUP) grade group ≤ 3 prostate cancer (OR 0.76, 95% CI 0.67-0.88) in analysis of 11,316 persons
    - nonsignificant increase in risk of ISUP grade group ≥ 4 prostate cancer (OR 1.56, 95% CI 0.95-2.57) in analysis of 919 persons
  + PubMed30077399European urologyEur Urol20181101745585-594585Reference - [Eur Urol 2018 Nov;74(5):585](http://pubmed.ncbi.nlm.nih.gov/30077399)[full-text](https://www.sciencedirect.com/science/article/pii/S0302283818305463?via%3Dihub), editorial can be found in [Eur Urol 2018 Nov;74(5):595](http://pubmed.ncbi.nlm.nih.gov/30195834)

Ejaculation Frequency

* **high ejaculation frequency associated with decreased risk of prostate cancer**

Cohort Study[Eur Urol 2016 Dec;70(6):974](http://pubmed.ncbi.nlm.nih.gov/27033442)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5040619/)

studySummary

* + Cohort Study based on prospective cohort study
  + 31,925 adults aged 40-75 years from Health Professionals Follow-up Study were evaluated for association of ejaculation frequency with risk of prostate cancer from 1992 to 2010
  + ejaculation frequency at age 20-29 years and 40-49 years were evaluated with questionnaires
  + total follow-up 480,831 person-years
  + 3,839 adults (12%) developed incident prostate cancer at ≥ T1b stage
  + comparing ejaculation frequency 4-7 times/month vs. ≥ 21 times/month
    - prostate cancer incidence 6.56 per 1,000 person-years vs. 8.95 per 1,000 person-years (adjusted hazard ratio 0.81, 95% CI 0.72-0.92) in analysis using ejaculation frequency data at age 20-29 years
    - prostate cancer incidence 6.74 per 1,000 person-years vs. 8.94 per 1,000 person-years (adjusted hazard ratio 0.78, 95% CI 0.69-0.89) in analysis using ejaculation frequency data at age 40-49 years
  + PubMed27033442European urologyEur Urol20161201706974-982974Reference - [Eur Urol 2016 Dec;70(6):974](http://pubmed.ncbi.nlm.nih.gov/27033442)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5040619/), editorial can be found in [Eur Urol 2016 Dec;70(6):983](http://pubmed.ncbi.nlm.nih.gov/27117750)

Baseline Prostate Atrophy

* **baseline prostate atrophy associated with decreased risk of prostate cancer at 2-4 years**

Cohort Study[26165588J Urol 2015 Nov;194(5):1241](http://pubmed.ncbi.nlm.nih.gov/26165588?dopt=Abstract)

studySummary

* + based on cohort analysis of data from [REDUCE trial](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_TFJ_JZK_CKB__LI_Z1B_DYC_SNB)Cohort Study
  + 3,965 adults aged 50-75 years with initial negative biopsy, prostate specific antigen levels 2.5-10 ng/mL, and complete baseline data from placebo arm in REDUCE trial were assessed
  + 54% had baseline prostate atrophy
  + 78% had prostate biopsy at 2 years and 55% at 4 years
  + comparing patients with baseline prostate atrophy vs. no atrophy in adjusted analyses
    - prostate cancer at 2 years in 14% vs. 22% (p < 0.001)
    - prostate cancer at 4 years in 10% vs. 13% (p = 0.03)
  + consistent results by severity of baseline prostate atrophy
  + PubMed26165588The Journal of urology20151101J Urol194512411241 Reference - [26165588J Urol 2015 Nov;194(5):1241](http://pubmed.ncbi.nlm.nih.gov/26165588?dopt=Abstract)

Etiology and Pathogenesis

Pathogenesis

Causes

* The exact cause of prostate cancer is unclear, but it likely involves [genetic predisposition](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_A3Q_WZ4_BKB).
  + Lynch syndrome, involving mutation in germline mutations in DNA mismatch repair genes, including *MLH1*, *MSH2*, *MSH6*, and *PMS2*, may predispose to prostate cancer. See also [Lynch Syndrome](https://dpa-pde-oxford.shinyapps.io/condition/lynch-syndrome).[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__NCCN)
  + Hereditary breast and ovarian cancer syndrome, involving germline mutations in homologous recombination repair genes, including *BRCA1*, *BRCA2*, *ATM*, *PALB2*, and *CHEK2*, may predispose to prostate cancer. See also [Hereditary Breast and Ovarian Cancer (HBOC) Syndromes](https://dpa-pde-oxford.shinyapps.io/condition/hereditary-breast-and-ovarian-cancer-hboc-syndromes).[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__NCCN),[2](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__EAU2023)
  + Germline mutations in *HOXB13* may predispose to prostate cancer.[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__NCCN),[2](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__EAU2023)

Pathogenesis

* The molecular mechanism for prostate cancer initiation and progression likely involves abnormalities in multiple signal pathways, genetic mutations, and epigenetic events.
  + Fusion of erythroblast transformation specific (ETS) transcription factor family:
    - Fusions of ETS transcription factor family genes are the most common gene fusions in prostate cancer, which have been reported in 50%-60% of the cases.
    - These abnormalities are the result of chromosomal rearrangements that fuse the *ETS* coding region with the 5' untranslated region of both androgen and non androgen regulated constitutively active genes.
      * *ETS* genes include *ERG* (most commonly involved in fusions), *ETV1*, *ETV4*, *ETV5*, and *FLI1*.
      * Androgen-regulated genes commonly involved in fusions include *TMPRSS2* and *SLC45A3*.
      * Constitutively active genes commonly involved in fusions include *HNRPA2B1*.
    - These fusions events are PubMed26074382Lancet (London, England)Lancet201601023871001370-8270likely early events in prostate cancer development, which is possibly initiated by the following mechanisms:
      * Androgen receptor-mediated DNA damage due to transcription at androgen receptor binding sites
      * Impairment of DNA repair due to genotoxic events (such as inflammation or infection) resulting in DNA double-stranded breaks
    - These fusions are associated with increased tumor aggressiveness.
    - Prostate cancers not containing *ETS* fusion represent distinct molecular subtypes, which may include the following abnormalities:
      * Mutations or homozygous deletions of *CHD1*, which has been reported in 5%-15% of the cases
      * *SPINK1* overexpression, which has been reported in 5%-10% of the cases
      * *SPOP* mutation, which has been reported in 5%-10% of the cases
      * Fusions or activating mutations of *RAF*, *RAS*, and *FGFR* gene family, which have been reported in 1%-2% of the cases
    - Tumors with unclear oncogenic drivers have reported in 25% of the cases.
    - References -
      * PubMed26074382Lancet (London, England)Lancet201601023871001370-8270[Lancet 2016 Jan 2;387(10013):70](http://pubmed.ncbi.nlm.nih.gov/26074382)
      * PubMed23806491Seminars in oncologySemin Oncol20130601403244-58244[Semin Oncol 2013 Jun;40(3):244](http://pubmed.ncbi.nlm.nih.gov/23806491)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3727396/)
  + Deletion of *PTEN*, which acts on phosphatidylinositol 3-kinase/AKT/mammalian target of rapamycin (PI3K/AKT/mTOR) pathway:
    - Normal regulation of the PI3K/AKT/mTOR pathway:
      * PI3K normally phosphorylates membrane-bound phospholipids, which activates AKT, and subsequently mTOR, through signal transduction, and ultimately leads to cell proliferation.
      * PTEN is a tumor suppressor which normally inhibits the PI3K/AKT/mTOR pathway.
      * PubMed23806491Seminars in oncologySemin Oncol20130601403244-58244Reference - [Semin Oncol 2013 Jun;40(3):244](http://pubmed.ncbi.nlm.nih.gov/23806491)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3727396/)
    - Effects of the loss of *PTEN*:
      * The loss of *PTEN* leads to an increased activity of the PI3K/AKT/mTOR pathway, which may initiate early stage of prostate cancer.
      * Most primary prostate cancers (70%) have been reported to be haploinsufficient in *PTEN*.
      * Loss of PTEN can occur in both *ETS* fusion-positive or -negative cancers, but it is more common in *ETS* fusion-positive diseases.
      * References -
        + PubMed26074382Lancet (London, England)Lancet201601023871001370-8270[Lancet 2016 Jan 2;387(10013):70](http://pubmed.ncbi.nlm.nih.gov/26074382)
        + PubMed23806491Seminars in oncologySemin Oncol20130601403244-58244[Semin Oncol 2013 Jun;40(3):244](http://pubmed.ncbi.nlm.nih.gov/23806491)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3727396/)
  + Mutations of *NKX3.1*:
    - *NKX3.1* is a prostate specific transcriptional repressor which is involved in all stages of prostate differentiation.
    - Mutations which inhibit *NKX3.1* ability to bind DNA or reduce its stability lead to an increased risk of prostate cancer development.
    - PubMed23806491Seminars in oncologySemin Oncol20130601403244-58244Reference - [Semin Oncol 2013 Jun;40(3):244](http://pubmed.ncbi.nlm.nih.gov/23806491)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3727396/)
  + Upregulation of *FOXA1*:
    - *FOXA1* is a transcription factor that is expressed in all stages of prostate development and maturation, and it regulates the expression of androgen receptor target genes.
    - Its upregulation increases androgen receptor accessibility to chromatin, promoting new gene expression profiles that can lead to cancer progression.
    - PubMed23806491Seminars in oncologySemin Oncol20130601403244-58244Reference - [Semin Oncol 2013 Jun;40(3):244](http://pubmed.ncbi.nlm.nih.gov/23806491)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3727396/)
  + Myc (oncogenic protein) overexpression:
    - Myc is a transcription factor that regulates growth and cell proliferation, as well as cell senescence or apoptosis.
    - Myc overexpression can immortalize prostate epithelial cells and lead to tumorigenesis.
    - *Myc* gene amplification has been reported in 30% of prostate cancers.
    - PubMed23806491Seminars in oncologySemin Oncol20130601403244-58244Reference - [Semin Oncol 2013 Jun;40(3):244](http://pubmed.ncbi.nlm.nih.gov/23806491)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3727396/)
  + Altered expression of BMI1 and EZH2:
    - BMI1 and EZH2 are histone modifiers which regulate cell differentiation.
    - Deregulated BMI1 and EZH1 expression can lead to cell dedifferentiation and an increase in oncogenic potential.
    - PubMed23806491Seminars in oncologySemin Oncol20130601403244-58244Reference - [Semin Oncol 2013 Jun;40(3):244](http://pubmed.ncbi.nlm.nih.gov/23806491)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3727396/)
  + Loss of retinoblastoma (RB) protein:
    - RB protein is a tumor suppressor which normally regulates cell cycle by suppressing E2F-mediated gene transcription.
    - The loss of RB protein leads to aberrant cell cycle and proliferation.
    - PubMed23806491Seminars in oncologySemin Oncol20130601403244-58244Reference - [Semin Oncol 2013 Jun;40(3):244](http://pubmed.ncbi.nlm.nih.gov/23806491)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3727396/)
* Cellular origin of prostate cancer is controversial.
  + Some proposed cellular mechanisms include the following:
    - Tumor origination from both luminal and basal epithelial cells
    - Tumor initiation by basal epithelial cells and later maintained by luminal-like cells
  + Overt basal cell differentiation in prostate cancer is extremely rare.
  + PubMed26074382Lancet (London, England)Lancet201601023871001370-8270Reference - [Lancet 2016 Jan 2;387(10013):70](http://pubmed.ncbi.nlm.nih.gov/26074382)
* Progression to castration-resistant prostate cancer:
  + Progression is typically caused by androgen receptor (AR) signaling pathway reactivation due to selective pressure from prolonged androgen deprivation therapy.
  + AR signaling pathway reactivation allows circumvention of therapeutic effects from AR antagonists and antiandrogens.
  + The mechanisms for AR reactivation in prostate tumor cells can include:
    - AR amplification or overexpression, which allows cell sensitization even to low androgen concentrations
    - Gain-of-function mutations of AR, which increase androgen sensitivity or decrease ligand specificity (increased ligand promiscuity)
    - Alternative splice variants of AR, which allow activation of AR without the need for a ligand binding domain, which is the usual target of AR antagonists
    - Altered posttranslational modifications that promote AR stability and increase its activity
    - Increased intratumoral androgen production by increasing expression of androgen precursors, such as CYP17A1 and HSD3B2, and enzymes that help convert precursors to androgen, such as AKR1C3 and SRD5A1/2
  + PubMed23806491Seminars in oncologySemin Oncol20130601403244-58244Reference - [Semin Oncol 2013 Jun;40(3):244](http://pubmed.ncbi.nlm.nih.gov/23806491)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3727396/)
* Most cancers arise in the periphery of the prostate gland, and they only cause symptoms when the tumor has grown to compress the urethra or invades the sphincter or neurovascular bundle ([15296564Br J Gen Pract 2004 Aug;54(505):617](http://pubmed.ncbi.nlm.nih.gov/15296564?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1324845/)).

History and Physical

History and Physical

History

Chief Concern (CC)

* In most patients with early prostate cancer, the disease PubMed32151466Critical reviews in oncology/hematologyCrit Rev Oncol Hematol20200401148102861102861may be asymptomatic ([Crit Rev Oncol Hematol 2020 Apr;148:102861](http://pubmed.ncbi.nlm.nih.gov/32151466)).
* Possible symptoms associated with advanced prostate cancer may be nonspecific, and may include the following:
  + Lower urinary tract symptoms, such as nocturia, voiding hesitancy, urinary retention, and urinary frequency/urgency ([Adv Ther 2018 Sep;35(9):1285](http://pubmed.ncbi.nlm.nih.gov/30097885/)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6133140/))
  + Hematuria ([Adv Ther 2018 Sep;35(9):1285](http://pubmed.ncbi.nlm.nih.gov/30097885/)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6133140/))
  + Hematospermia ([NCCN 2024 Mar from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_2))
  + Erectile dysfunction ([Adv Ther 2018 Sep;35(9):1285](http://pubmed.ncbi.nlm.nih.gov/30097885/))
  + Bone pain (in metastatic disease)[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__NCCN),[2](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__EAU2023)

Past Medical History (PMH)

* Ask about history of [metabolic syndrome and obesity](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_EPQ_FKP_BKB), and [medical history of infections](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_YXN_K3Q_3NB), including human papillomavirus (HPV) and gonorrhea.
* Ask about history of cancer.[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__NCCN)
* Ask about [hereditary syndromes](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_A3Q_WZ4_BKB) that may predispose prostate cancer, including [hereditary breast and ovarian cancer syndrome](https://dpa-pde-oxford.shinyapps.io/condition/hereditary-breast-and-ovarian-cancer-hboc-syndromes), which is caused by germline mutations in homologous DNA repair genes, and [Lynch syndrome](https://dpa-pde-oxford.shinyapps.io/condition/lynch-syndrome), which is caused by germline mutations in DNA mismatch repair genes, including *MLH1*, *MSH2*, *MSH6*, and *PMS2*.
* Ask about the results of prior germline genetic testing for [pathogenic variants](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_A3Q_WZ4_BKB) associated with increased risk of prostate cancer.[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__NCCN)

Family History (FH)

* Ask about [family history](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_XK2_4P4_BKB) of prostate cancer and other cancers[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__NCCN),[2](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__EAU2023)
* Ask about [family history of high-risk germline mutations](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_A3Q_WZ4_BKB), including genes associated with [Lynch syndrome](https://dpa-pde-oxford.shinyapps.io/condition/lynch-syndrome), such as *MLH1*, *MSH2*, *MSH6*, *PMS2*, and *EPCAM*, and genes associated with homologous recombination, such as *BRCA1*, *BRCA2*, *ATM*, *PALB2*, and *CHEK2*.[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__NCCN)
* Ask about Ashkenazi Jewish ancestry, due to the increased risk of germline *BRCA1* or *BRCA2* mutations.[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__NCCN)

Social History (SH)

* Ask about history of [smoking](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_D53_N4P_BKB), [alcohol consumption](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_DDL_TLV_BKB__LI_ZND_Z2S_SNB), and [environmental and occupational exposures](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_XW1_2MP_BKB).

Physical

* Digital rectal exam (DRE):
  + Abnormal DRE is a possible sign of prostate cancer, and has been reported to be associated with increased risk of higher [International Society of Urologic Pathologists (ISUP) grade](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_RVM_VBD_XLB). It is an indication for biopsy.[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__NCCN),[2](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__EAU2023)
  + DRE findings are helpful for determination of clinical T stage.[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__NCCN),[2](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__EAU2023)
  + See [Prostate Cancer Screening](https://dpa-pde-oxford.shinyapps.io/prevention/prostate-cancer-screening) for additional information.

Diagnosis and Staging

Diagnosis

Making the Diagnosis

* Testing strategies should balance overdiagnosis and overtreatment with the potential survival benefit of early diagnosis.
* Suspect prostate cancer based on digital rectal exam (DRE) and/or prostate-specific antigen (PSA) levels.
* Definitive diagnosis of prostate cancer requires histopathologic analysis of biopsy.
* Magnetic resonance imaging may also help detect prostate cancer prior to biopsy.
* To avoid unnecessary biopsy, further risk assessment is necessary. For asymptomatic patients with normal DRE and PSA level 3-10 ng/mL, risk assessment includes risk calculators ([EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE)), magnetic resonance imaging (MRI) ([EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE)), and/or additional serum or urine biomarker testing ([EAU Weak recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE)).
* See [Prostate Cancer Diagnosis and Staging](https://dpa-pde-oxford.shinyapps.io/evaluation/prostate-cancer-diagnosis-and-staging) for details.

Testing for Staging Evaluation

* Obtain personal and family history for any known high-risk germline mutations and any other suspicions to prompt genetic testing and genetic counseling ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)). Consider germline testing for patients with personal and/or family history of select cancers or known germline pathogenic or likely pathogenic variants ([EAU Weak recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE)).
* Use risk stratification to determine the need for staging workup.
* For patients in any risk group, consider using prebiopsy MRI for staging information ([EAU Weak recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE)).
* For patients with very-low-, low-, or intermediate-risk disease who are asymptomatic and have life expectancy ≤ 5 years, additional imaging workup for staging is not necessary until the patient becomes symptomatic.
* Staging for patients with very-low-risk, low-risk, or favorable intermediate-risk disease and life expectancy ≥ 10 years:
  + Consider confirmatory testing with prostate biopsy, multiparametric magnetic resonance imaging (mpMRI) (with determination of prostate-specific antigen density, and repeat biopsy if necessary), and/or tumor molecular and biomarker testing ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
  + Only for patients with symptoms consistent with bone metastases, consider bone imaging.
  + Do not offer additional imaging for staging ([EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE)).
* Staging for patients with unfavorable intermediate-risk, high-risk, or very-high-risk disease:
  + Consider abdominal plus pelvic mpMRI (preferred) or computed tomography (CT) plus chest CT, or prostate-specific membrane antigen-positron emission tomography/CT (PSMA-PET/CT) or PSMA-PET/MRI ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Weak recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE) for unfavorable intermediate-risk disease; [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE) for high-risk disease).
  + Consider bone imaging ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Weak recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE) for unfavorable intermediate-risk disease; [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE) for high-risk disease).
  + For patients with high-risk or very-high-risk disease, consider germline testing for high-risk pathogenic variants ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
* Staging for patients with locally advanced disease (N1, M0 disease):
  + Consider imaging studies ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
  + Consider tumor testing for homologous recombination repair gene mutations, and microsatellite instability (MSI) or mismatch repair deficiency (dMMR) ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
* Staging for patients with metastatic disease:
  + Consider biopsy of metastatic disease ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
  + Consider tumor testing for homologous recombination repair genes, MSI or deficient MMR (dMMR), and tumor mutational burden (TMB) ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
  + Consider germline testing for high-risk pathogenic variants, including homologous recombination repair genes ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Weak recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE)).
* See [Prostate Cancer Diagnosis and Staging](https://dpa-pde-oxford.shinyapps.io/evaluation/prostate-cancer-diagnosis-and-staging) for details.

Staging Systems

* See also Risk Assessment with [International Society of Urological Pathology (ISUP) Grading System](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_RVM_VBD_XLB).
* American Joint Committee on Cancer (AJCC) staging for prostate cancer, eighth edition:

| Table 2: Clinical Staging | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Stage** | **T** | **N** | **M** | **PSA\*** | **Grade Group\*** |
| Stage I | cT1a-cT1c | N0 | M0 | PSA < 10 | 1 |
| cT2a | N0 | M0 | PSA < 10 | 1 |
| pT2 | N0 | M0 | PSA < 10 | 1 |
| Stage IIA | cT1a-cT1c | N0 | M0 | PSA ≥ 10 but < 20 | 1 |
| cT2a | N0 | M0 | PSA ≥ 10 but < 20 | 1 |
| cT2b-cT2c | N0 | M0 | PSA < 20 | 1 |
| pT2 | N0 | M0 | PSA ≥ 10 but < 20 | 1 |
| Stage IIB | T1-T2 | N0 | M0 | PSA < 20 | 2 |
| Stage IIC | T1-T2 | N0 | M0 | PSA < 20 | 3-4 |
| Stage IIIA | T1-T2 | N0 | M0 | PSA ≥ 20 | 1-4 |
| Stage IIIB | T3-T4 | N0 | M0 | Any PSA | 1-4 |
| Stage IIIC | Any T | N0 | M0 | Any PSA | 5 |
| Stage IVA | Any T | N1 | M0 | Any PSA | Any grade |
| Stage IVB | Any T | N0 | M1 | Any PSA | Any grade |
| Abbreviations: cT, clinical tumor; M, metastasis; N, node; PSA, prostate-specific antigen; pT, pathologic tumor; T, tumor.  \* When either PSA or Grade Group is not available, grouping should be determined by T stage and/or either PSA or Grade Group as available. | | | | | |

* Definitions of staging abbreviations:
  + Primary tumor (T):
    - Clinical T (cT):
      * cTX: primary tumor cannot be assessed.
      * cT0: no evidence of primary tumor.
      * cT1: clinically inapparent tumor that is not palpable.
        + cT1a: incidental histologic finding of tumor in ≤ 5% of tissue resected.
        + cT1b: incidental histologic finding of tumor in > 5% of tissue resected.
        + cT1c: tumor identified by needle biopsy found in 1 or both sides but it is not palpable.
      * cT2: tumor is palpable and confined within prostate.
        + cT2a: tumor involves one-half of 1 side or less.
        + cT2b: tumor involves more than one-half of 1 side but not both sides.
        + cT2c: tumor involves both lobes.
      * cT3: extraprostatic tumor that is not fixed or does not invade adjacent structures.
        + cT3a: extraprostatic extension (unilateral or bilateral).
        + cT3b: tumor invades seminal vesicle(s).
      * cT4: tumor is fixed or invades adjacent structures other than seminal vesicles, such as external sphincter, rectum, bladder, levator muscles, and/or pelvic wall.
    - Pathologic T (pT):
      * pT2: organ confined.
      * pT3: extraprostatic extension.
        + pT3a: extraprostatic extension (unilateral or bilateral) or microscopic invasion of bladder neck.
        + pT3b: tumor invades seminal vesicle(s).
      * pT4: tumor is fixed or invades adjacent structures other than seminal vesicles, such as external sphincter, rectum, bladder, levator muscles, and/or pelvic wall.
  + Regional lymph nodes (N):
    - NX: regional lymph nodes were not assessed.
    - N0: no positive regional lymph node.
    - N1: metastases in regional lymph node(s).
  + Distant metastasis (M):
    - M0: no distant metastasis.
    - M1: distant metastasis.
      * M1a: nonregional lymph node(s).
      * M1b: bone(s).
      * M1c: other site(s) with or without bone disease.
* *Used with permission of the American College of Surgeons, Chicago, Illinois. The original source for this information is the AJCC Cancer Staging Manual, Eighth Edition (2017) published by Springer International Publishing.*

International Society of Urological Pathology (ISUP) Grading System

* Gleason score is calculated by combining the most and second-most common tumor patterns (Gleason patterns) ([Am J Surg Pathol 2016 Feb;40(2):244](http://pubmed.ncbi.nlm.nih.gov/26492179)).
* ISUP grading system of prostate cancer:PubMed26492179The American journal of surgical pathologyAm J Surg Pathol20160201402244-52244

| Table 3: International Society of Urological Pathology (ISUP) Grading System | | |
| --- | --- | --- |
| **ISUP Grade** | **Gleason Score** | **Histologic Characteristics** |
| 1 | 2-6 | Individual discrete well-formed glands |
| 2 | 7 (3+4) | Predominately well-formed glands with lesser component of poorly formed/fused/cribriform glands |
| 3 | 7 (4+3) | Predominately poorly formed/fused/cribriform glands with lesser component of well-formed glands (if > 95% poorly formed/fused/cribriform glands or lacking of glands on a core or at radical prostatectomy, < 5% well-formed glands is not factored into grade) |
| 4 | 8 (4+4) | Only poorly formed glands |
| 8 (3+5) | Predominately well-formed glands with lesser component of lacking glands (poorly formed/fused/cribriform glands can be a minor component) |
| 8 (5+3) | Predominately lacking glands with lesser component of well-formed glands (poorly formed/fused/cribriform glands can be a minor component) |
| 5 | 9-10 | Lack gland formation or presence of necrosis, with or without poorly formed/fused/cribriform glands (if > 95% poorly formed/fused/cribriform glands or lacking of glands on a core or at radical prostatectomy, < 5% well-formed glands is not factored into grade) |
| Abbreviations: ISUP, International Society of Urological Pathology.  Reference - [Am J Surg Pathol 2016 Feb;40(2):244](http://pubmed.ncbi.nlm.nih.gov/26492179). | | |

Risk Stratification

* National Comprehensive Cancer Network (NCCN) risk stratification systems for local or locally advanced prostate cancer:

| Table 4: NCCN risk stratification system for local or locally advanced prostate cancer | |
| --- | --- |
| **Risk Group** | **Risk Group Criteria** |
| Very low | All of the following:   * + Clinical stage T1c   + ISUP Grade Group 1   + PSA < 10 ng/mL (10 mcg/L)   + PSA density < 0.15 ng/mL/g   + < 3 positive biopsy cores/fragments and ≤ 50% prostate cancer involvement in each core/fragment\* |
| Low | All of following, but does not qualify for very low risk:   * + Clinical stage T1-T2a   + ISUP Grade Group 1   + PSA < 10 ng/mL (10 mcg/L) |
| Intermediate | Intermediate risk has no high or very high-risk features, and is divided into favorable and unfavorable risk.   * + Favorable intermediate risk has all of following:     - Any 1 intermediate risk factor (clinical stage T2b-T2c, PSA 10-20 ng/mL [10-20 mcg/L], or ISUP Grade Group 2 or 3)     - ISUP Grade Group 1 or 2     - < 50% of biopsy cores is positive\*\*   + Unfavorable intermediate risk has ≥ 1 of following:     - 2-3 intermediate risk factors (clinical stage T2b-T2c, PSA 10-20 ng/mL [10-20 mcg/L], or ISUP Grade Group 2 or 3)     - ISUP Grade Group 3     - ≥ 50% of biopsy cores is positive\*\* |
| High | Exactly 1 of the following, with no very-high-risk features:   * + Clinical stage T3a   + ISUP Grade Group 4 or 5   + PSA > 20 ng/mL (20 mcg/L) |
| Very high | ≥ 1 of the following:   * + Clinical stage T3b-T4   + Primary Gleason pattern 5   + 2-3 high-risk features   + > 4 cores with ISUP Grade Group 4 or 5 |
| \*If an ultrasound-, magnetic resonance imaging-, or digital rectal examination-guided lesion that is biopsied more than once shows cancer, regardless of the percentage of core involvement or the number of involved cores, it is considered a single positive core.  \*\*The percentage of positive cores for favorable or unfavorable intermediate risk is based on systemic biopsies, with or without targeted magnetic resonance imaging-guided biopsies.  Abbreviations: ISUP, International Society of Urological Pathology; NCCN, National Comprehensive Cancer Network; PSA, prostate-specific antigen.  Reference - [NCCN 2024 Mar from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_1). | |

* + NCCN uses the above stratification to provide recommendations on management strategy, but acknowledges that there are other tools and stratification systems that may have better performance, but they may have not been routinely reported in clinical trials.
  + The NCCN risk stratification above only has moderate performance, and there is heterogeneity within each with group, so it may be appropriate to use management strategy designed for the adjacent risk groups if a more accurate risk stratification system is used.
  + The following is a list of additional stratification systems that may further help with personalized management:
    - D'Amico stratification system (original publication on the stratification system can be found in [9749478JAMA 1998 Sep 16;280(11):969](http://pubmed.ncbi.nlm.nih.gov/9749478?dopt=Abstract))
    - American Joint Committee on Cancer (AJCC) staging system
    - Cancer of the Prostate Risk Assessment (CAPRA) stratification, which is not appropriate for patients with cT3b-cT4 disease, or clinical lymph node involvement (original publication on the stratification system can be found in [15879786J Urol 2005 Jun;173(6):1938](http://pubmed.ncbi.nlm.nih.gov/15879786?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2948569/))
    - Memorial Sloan Kettering Cancer Center (MSKCC) stratification (tool can be found at [MSKCC website](https://www.mskcc.org/nomograms/prostate/pre_op))
    - STAR-CAP stratification (original publication on the stratification system can be found in [33090219JAMA Oncol 2020 Dec 1;6(12):1912](http://pubmed.ncbi.nlm.nih.gov/33090219?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7582232/))
  + Gene expression biomarkers, and artificial intelligence (A.I.) pathology are additional tools that provide independent risk stratification.
    - These tools should only be used if they may change management, and should not be used in patients with very-low-risk disease.
    - These tools are most useful in deciding among the following management strategies:
      * Active surveillance (and its intensity) vs. Active management
      * Whether short-term androgen deprivation therapy (ADT) should be used with radiation therapy
      * Whether radiation therapy should be used with short-term or long-term ADT
    - The following is a list of gene expression biomarkers, and A.I. Pathology tools
      * Decipher
      * Prolaris
      * Oncotype DX Prostate
      * ArteraAI Prostate tool (a tool based on artificial intelligence-derived digital histopathology biomarkers) (original publication on the tool can be found in [35676445NPJ Digit Med 2022 Jun 8;5(1):71](http://pubmed.ncbi.nlm.nih.gov/35676445?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9177850/))
      * Germline testing for homologous recombination repair gene deficiency
  + Reference - [NCCN 2024 Feb from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_1)
* European Association of Urology (EAU) risk stratification systems for local or locally advanced prostate cancer:

| Table 5: EAU risk stratification system for local or locally advanced prostate cancer | |
| --- | --- |
| **Risk Group** | **Risk Group Criteria** |
| Low | All of the following:   * + Clinical stage T1-T2a based on DRE   + ISUP Grade Group 1   + PSA < 10 ng/mL (10 mcg/L) |
| Intermediate | Any 1 of the following:   * + Clinical stage T2b based on DRE   + ISUP Grade Group 2 or 3   + PSA 10-20 ng/mL (10-20 mcg/L) |
| High | Any 1 of the following:   * + Localized disease, with any 1 of the following:     - Clinical stage T2c based on DRE     - ISUP Grade Group 4 or 5     - PSA > 20 ng/mL (20 mcg/L)   + Locally advanced disease (clinical stage T3-T4 based on DRE or positive lymph node involvement based on CT) |
| Abbreviations: CT, computed tomography; DRE, digital rectal examination; EAU, European Association of Urology; ISUP, International Society of Urological Pathology; PSA, prostate-specific antigen.  Reference - [EAU 2024 Apr](https://uroweb.org/guidelines/prostate-cancer)[PDF](https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-EANM-ESTRO-ESUR-ISUP-SIOG-Guidelines-on-Prostate-Cancer-2024.pdf) | |

* American Urological Association (AUA) risk stratification system for local or locally advanced prostate cancer:

| Table 6: AUA risk stratification systems for local or locally advanced prostate cancer | |
| --- | --- |
| **Risk Group** | **Risk Group Criteria** |
| Very low | All of the following:   * + Clinical stage T1-T2a   + ISUP Grade Group 1   + PSA < 10 ng/mL (10 mcg/L)   + PSA density < 0.15 ng/mL/g   + < 34% of positive biopsy cores and no core with > 50% involved |
| Low | All of the following:   * + Clinical stage T1-T2a   + ISUP Grade Group 1   + PSA < 10 ng/mL (10 mcg/L) |
| Intermediate | 1 of the following: clinical stage T2b-T2c, PSA 10-20 ng/mL (10-20 mcg/L), or ISUP Grade Group 2 or 3. It is further divided into favorable and unfavorable risk.   * + Favorable intermediate risk has ≥ 1 of the following:     - ISUP Grade Group 1 with PSA 10-20 ng/mL     - ISUP Grade Group 2 with PSA < 10 ng/mL   + Unfavorable intermediate risk has ≥ 1 of the following:     - ISUP Grade Group 2 with either PSA 10-20 ng/mL or clinical stage T2b-T2c     - ISUP Grade Group 3 with PSA < 20 ng/mL |
| High | 1 of the following:   * + Clinical stage ≥ T3   + ISUP Grade Group 4 or 5   + PSA > 20 ng/mL (20 mcg/L) |
| Abbreviations: AUA, American Urological Association; ISUP, International Society of Urological Pathology; PSA, prostate-specific antigen.  Reference - [AUA 2022](https://www.auanet.org/guidelines-and-quality/guidelines/clinically-localized-prostate-cancer-aua/astro-guideline-2022). | |

Intraductal Carcinoma

* An intraductal carcinoma is a variant of prostate cancer that is rarely detected.
* National Comprehensive Cancer Network recommendations for detection of intraductal carcinoma on initial prostate biopsy:
  + Consider initial management as prostate cancer ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)), due to the high risk of high-grade cancer.
  + If management as prostate cancer is not considered, consider careful evaluations with repeat biopsy with magnetic resonance imaging (MRI) guidance.
  + Reference - [NCCN 2024 Mar from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_2)
* Detection of solitary intraductal carcinoma is highly suggestive of the presence of high-grade prostate cancer.
  + Presence of intraductal carcinoma in biopsy is an adverse prognostic factor for biochemical recurrence, cancer-specific survival, survival after distant metastasis, and metastatic recurrence after radiation therapy.
  + Presence of intraductal carcinoma in radical prostatectomy sample is associated with other pathological features of invasive prostate cancer, including higher [International Society of Urological Pathology grade group](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_RVM_VBD_XLB), larger tumor volume, increased risk of extraprostatic extension, seminal vesicle invasion, and pelvic lymph node metastasis.
  + Reference - [NCCN 2024 Mar from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_2)
* Histological features of intraductal carcinoma:
  + The main diagnostic morphological features are as follows:
    - Expanded growth of atypical cells which form large dense cribriform and/or solid pattern
    - Atypical cells at intraductal and acinar sites with preservation of basal cells
  + Other diagnostic features include the following:
    - Nonfocal comedonecrosis with > 2 glands involvement
    - Pleomorphic nuclei ≥ 6 times the size of adjacent benign nuclei
  + Other possible features, include loose cribriform morphology, and variation in nuclear sizes, although they may not be diagnostic.
  + Reference - [Mod Pathol 2018 Jan;31(S1):S71](http://pubmed.ncbi.nlm.nih.gov/29297491)

Precancerous Prostate Lesions

High-Grade Prostatic Intraepithelial Neoplasia (PIN)

* TOPIC\_AVT\_5BW\_KNB\_\_LI\_QCS\_3HF\_Z1CGSU04052404/05/2024 11:42:23 AMguidelineSummaryUpdatestandardOncologic\_Disease Urologic\_DisordersNational Comprehensive Cancer Network (NCCN) recommendations on detection of precancerous lesions (NCCN 2024 Mar)National Comprehensive Cancer Network (NCCN) recommendations on detection of high-grade PIN on initial prostate biopsy:
  + Testing for patients with no prior high-quality multiparametric magnetic resonance imaging (MRI):
    - Consider further testing with biomarkers and/or multiparametric MRI ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
    - Biomarkers that improve specificity of screening include percent free prostate-specific antigen (PSA), Prostate Health Index (PHI), ConfirmMDx, 4Kscore, ExoDx Prostate Test, prostate cancer antigen 3 (PCA3), MyProstateScore (MPS), and IsoPSA ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)). See [Prostate Cancer Screening](https://dpa-pde-oxford.shinyapps.io/prevention/prostate-cancer-screening) for additional information.
    - For patients with atypia, consider repeat biopsy in 12-24 months with relative increase in sampling of atypical sites ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
  + Testing for patients with prior high-quality multiparametric MRI:
    - Consider repeat testing with PSA and digital rectal exam (DRE) at intervals of 12-24-months ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
    - Consider testing biomarkers that improve specificity of screening ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)), including percent free PSA, PHI, ConfirmMDx, 4Kscore, ExoDx Prostate Test, PCA3, MPS, and IsoPSA ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)). See [Prostate Cancer Screening](https://dpa-pde-oxford.shinyapps.io/prevention/prostate-cancer-screening) for additional information.
    - Consider repeat prostate biopsy with refined techniques ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)), such as imaging guidance from MRI/ultrasound fusion.
  + Reference - [NCCN 2024 Mar from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_2)
* High-grade PIN is the main precursor lesion to invasive prostate carcinoma ([Mod Pathol 2018 Jan;31(S1):S71](http://pubmed.ncbi.nlm.nih.gov/29297491)).
* For patients with high-grade PIN detected on initial biopsy, the risk of prostate cancer in subsequent repeat biopsy has been reported to be about 25% ([Mod Pathol 2018 Jan;31(S1):S71](http://pubmed.ncbi.nlm.nih.gov/29297491)).
* Prevalence of high-grade PIN:
  + High-grade PIN has been reported in about 5% of prostate biopsies ([Mod Pathol 2018 Jan;31(S1):S71](http://pubmed.ncbi.nlm.nih.gov/29297491)).
  + High-grade PIN has been reported in almost all radical prostatectomy samples ([Mod Pathol 2018 Jan;31(S1):S71](http://pubmed.ncbi.nlm.nih.gov/29297491)).
  + There is a PubMed29297491Modern pathology : an official journal of the United States and Canadian Academy of Pathology, IncMod Pathol2018010131S1S71-79S71greater prevalence of high-grade PIN in Black patients than White patients ([Mod Pathol 2018 Jan;31(S1):S71](http://pubmed.ncbi.nlm.nih.gov/29297491)).
* Hypoechogenicity in ultrasound is also associated with high-grade PIN, which is similar to prostate carcinoma. However, abnormal DRE or elevated serum PSA are not associated with high-grade PIN ([Mod Pathol 2018 Jan;31(S1):S71](http://pubmed.ncbi.nlm.nih.gov/29297491)).
* Histological features of high-grade PIN:
  + High-grade PIN shows cytological atypia of prostate glandular epithelial cells within prostatic ducts and acini.
    - At low microscopic magnification, atypia appear as dark amphophilic glands structurally resembling adjacent benign glands.
    - At high microscopic magnification, findings of atypia include the following:
      * Amphophilic cytoplasm in luminal cells
      * Irregular spacing
      * Nuclear crowding and stratification
      * Chromatin hyperchromasia and clumping
      * Prominent nucleoli
    - The main morphologies of high-grade PIN include flat, tufting, micropapillary, and cribriform morphologies.
    - Other rare morphologies include signet-ring, mucinous, inverted, and small-cell neuroendocrine morphologies.
  + Basal cells are often focal and discontinuous.
  + PubMed29297491Modern pathology : an official journal of the United States and Canadian Academy of Pathology, IncMod Pathol2018010131S1S71-79S71Reference - [Mod Pathol 2018 Jan;31(S1):S71](http://pubmed.ncbi.nlm.nih.gov/29297491)

Atypical Intraductal Proliferation (AIP)

* National Comprehensive Cancer Network (NCCN) suggests repeat magnetic resonance imaging (MRI)-targeted and systemic biopsy to detect invasive carcinoma ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)) ([NCCN 2024 Mar from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_2)).
* For patients with AIP detected on initial biopsy, the risk of prostate cancer has been reported to be 50% on subsequent repeat biopsy ([NCCN 2024 Mar from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_2)).
* Histologically, AIP may have higher degree of morphological complexity and/or cytologic atypia compared to [high-grade prostatic intraepithelial neoplasia](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_AVT_5BW_KNB), but it does not meet the diagnostic criteria of [intraductal carcinoma](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_XZL_ZBW_KNB) ([NCCN 2024 Mar from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_2)).

Atypical Glands Suspicious for Cancer/Atypical Small Acinar Proliferation

* National Comprehensive Cancer Network (NCCN) recommendations on detection of atypical glands suspicious for cancer detected on initial prostate biopsy:
  + Testing for patients with no prior high-quality multiparametric magnetic resonance imaging (MRI):
    - Consider further testing with biomarkers and/or multiparametric MRI ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
    - Biomarkers that improve specificity of screening include percent free prostate-specific antigen (PSA), Prostate Health Index (PHI), ConfirmMDx, 4Kscore, ExoDx Prostate Test, prostate cancer antigen 3 (PCA3), MyProstateScore (MPS), and IsoPSA([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)). See [Prostate Cancer Screening](https://dpa-pde-oxford.shinyapps.io/prevention/prostate-cancer-screening) for additional information.
    - For patients with atypia, consider repeat biopsy in 12-24 months with relative increase in sampling of atypical sites ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
  + Testing for patients with prior high-quality multiparametric MRI:
    - Consider repeat testing with PSA and digital rectal exam (DRE) at intervals of 12-24-months ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
    - Consider testing biomarkers that improve specificity of screening ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)), including percent free PSA, PHI, ConfirmMDx, 4Kscore, ExoDx Prostate Test, PCA3, MPS, and IsoPSA ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)). See [Prostate Cancer Screening](https://dpa-pde-oxford.shinyapps.io/prevention/prostate-cancer-screening) for additional information.
    - Consider repeat prostate biopsy with refined techniques ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)), such as imaging guidance from MRI/ultrasound fusion.
  + Reference - [NCCN 2024 Mar from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_2)
* For patients with atypical glands suspicious for cancer detected on initial prostate biopsy, the risk of prostate cancer has been reported to be ≥ 50% on subsequent repeat biopsy ([NCCN 2024 Mar from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_2)).
* The prevalence of atypical glands suspicious for cancer or atypical small acinar proliferation has been reported to be 5% in initial extended prostate biopsy ([Crit Rev Clin Lab Sci 2017 Aug;54(5):309](http://pubmed.ncbi.nlm.nih.gov/28828885)).
* Atypical glands suspicious for cancer or atypical small acinar proliferation may represent either benign mimics of prostate cancer, or possible malignancy that lacks the architectural or cytological atypia that can be considered as a definitive diagnosis of malignancy ([NCCN 2024 Mar from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_2)).
* Histological features of atypical glands:
  + Morphological features include acini with varying size, shape, and spacing, but no cellular atypia, and infiltrative growth that is similar to prostate cancer ([Crit Rev Clin Lab Sci 2017 Aug;54(5):309](http://pubmed.ncbi.nlm.nih.gov/28828885)).
  + Cytological features:
    - Common cytological features are as follows:
      * Enlarged nucleoli
      * Mild enlargement of nuclei
      * Intraluminal eosinophilic secretions
      * Possible presence of intraluminal basophilic mucin
    - Other features with limited diagnostic utility include the following:
      * Possible presence of crystalloids, which is not a specific feature
      * Nuclear hyperchromasia, which may also be a confounding finding due to staining
      * Usually the absence of mitotic figures, which is a rare finding
    - PubMed28828885Critical reviews in clinical laboratory sciencesCrit Rev Clin Lab Sci20170801545309-325309Reference - [Crit Rev Clin Lab Sci 2017 Aug;54(5):309](http://pubmed.ncbi.nlm.nih.gov/28828885)

Benign Lesions

Recommendations From Professional Organizations on Detection of Benign Lesions

* National Comprehensive Cancer Network (NCCN) recommendations on detection of benign lesions detected on initial prostate biopsy:
  + Testing for patients with no prior high-quality multiparametric magnetic resonance imaging (MRI)
    - Consider further testing with biomarkers and/or multiparametric MRI ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
    - Biomarkers that improve specificity of screening include percent free prostate-specific antigen (PSA), Prostate Health Index (PHI), ConfirmMDx, 4Kscore, ExoDx Prostate Test, prostate cancer antigen 3 (PCA3), MyProstateScore (MPS), and IsoPSA([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)). See [Prostate Cancer Screening](https://dpa-pde-oxford.shinyapps.io/prevention/prostate-cancer-screening) for additional information.
    - For patients with atypia, consider repeat biopsy in 12-24 months with relative increase in sampling of atypical sites ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
  + Testing for patients with prior high-quality multiparametric MRI
    - Consider repeat testing with PSA and digital rectal exam (DRE) at intervals of 12-24-months ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
    - Consider testing biomarkers that improve specificity of screening ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)), including percent free PSA, PHI, ConfirmMDx, 4Kscore, ExoDx Prostate Test, PCA3, MPS, and IsoPSA ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)). See [Prostate Cancer Screening](https://dpa-pde-oxford.shinyapps.io/prevention/prostate-cancer-screening) for additional information.
    - Consider repeat prostate biopsy with refined techniques ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)), such as imaging guidance from MRI/ultrasound fusion.
  + Reference - [NCCN 2024 Jan from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_2)

Atypical Adenomatous Hyperplasia (AAH)

* AAH is one of the most common benign lesions.
* It is not associated with increased risk of prostate cancer.
* The prevalence of AAH has been reported as follows:
  + < 1 % in needle core biopsy
  + About 20%-60% in radical prostatectomy specimen
  + About 2%-20% in transurethral resection of prostate specimen
* Histological features of AAH:
  + AAH is morphologically similar to low-grade transition zone carcinoma (Gleason pattern 3).
  + The most important features that distinguish AAH from adenocarcinoma include the following:
    - Circumscribed and noninfiltrative growth, which may appear as pseudoinfiltrative growth in limited needle biopsy cores
    - No enlarged nucleoli
    - Small, large, crowded glands with cytoplasmic and nuclear features similar to adjacent benign glands
    - Presence of fragmented and patchy basal cell layer
  + Other features of AAH include the following:
    - Corpora amylacea, which is not commonly found in carcinoma
    - Features that may also appear in carcinoma, such as focal luminal crystalloids, dense secretions, and blue mucin (rare)
* PubMed29297489Modern pathology : an official journal of the United States and Canadian Academy of Pathology, IncMod Pathol2018010131S1S22-46S22Reference - [Mod Pathol 2018 Jan;31(S1):S22](http://pubmed.ncbi.nlm.nih.gov/29297489)

Atrophy

* Simple atrophy:
  + Simple atrophy is the most common morphological type of atrophy.
  + There is insufficient evidence to determine if it is associated with increased risk of prostate cancer or other precancerous lesions.
  + It is most commonly identified in the peripheral zone, but it may also be found in the central and transitional zones.
  + Histological features of simple atrophy:
    - There are inflammatory infiltrates within and around foci of atrophy, which are uncommon in adenocarcinoma.
    - There is lobular and noninfiltrative growth.
    - There is basophilic appearance on hematoxylin and eosin staining.
  + Cytologic features are as follows:
    - Increased nucleus-to-cytoplasm ratio
    - Crowded, small and bland-appearing nuclei
    - Scant cytoplasm
    - No enlarged nucleoli
  + The gland appears as irregular or angulated shape and is the same size or smaller than adjacent nonatrophic glands.
  + Cystic dilation is commonly found adjacent to or in continuity with foci of atrophy, and may be present within areas of atrophy
  + PubMed29297489Modern pathology : an official journal of the United States and Canadian Academy of Pathology, IncMod Pathol2018010131S1S22-46S22Reference - [Mod Pathol 2018 Jan;31(S1):S22](http://pubmed.ncbi.nlm.nih.gov/29297489)
* Postatrophic hyperplasia:
  + Postatrophic hyperplasia is also called lobular atrophy.
  + Histological features of acini:
    - There are crowded, compact clusters of small, atrophic acini.
    - Acini are arranged around larger feeder duct.
    - Acini are lined by cuboidal secretory cells that lack apical and lateral cytoplasm.
    - There is an increased nucleus-to-cytoplasm ratio compared to adjacent benign epithelial cells, with small to mildly enlarged nuclei.
  + The lesion has a lobular appearance, where smaller glands in grape-like appearance cluster around the larger duct.
  + The stroma around the lesion may be sclerotic or elastotic.
  + There is a basophilic appearance.
  + PubMed29297489Modern pathology : an official journal of the United States and Canadian Academy of Pathology, IncMod Pathol2018010131S1S22-46S22Reference - [Mod Pathol 2018 Jan;31(S1):S22](http://pubmed.ncbi.nlm.nih.gov/29297489)
* Partial atrophy:
  + Partial atrophy may mimic low-grade carcinoma.
  + Histological features of partial atrophy:
    - There is usually lobular and noninfiltrative growth, but it may be more disorganized and irregular compared to simple atrophy and postatrophic hyperplasia.
    - Foci of atrophy may be adjacent to or admixed with foci of simple atrophy.
    - Histological features of acini:
      * The cytoplasmic appearance is pale and clear. There is scant apical cytoplasm and abundant lateral cytoplasm.
      * The nuclei are small and have cylindrical or elongated appearance.
      * There are usually no enlarged nucleoli.
    - There is no basophilic appearance.
    - Basel cells are not apparent or are patchy.
    - Luminal features include possible granular secretions, and there are usually no crystalloids or blue mucin.
  + PubMed29297489Modern pathology : an official journal of the United States and Canadian Academy of Pathology, IncMod Pathol2018010131S1S22-46S22Reference - [Mod Pathol 2018 Jan;31(S1):S22](http://pubmed.ncbi.nlm.nih.gov/29297489)

Management

Management

Management of Localized or Locally Advanced Prostate Cancer

Management of Very-Low-Risk Disease

* TOPIC\_QZY\_3S4\_41C\_\_LI\_SPM\_TWG\_CBCGSU04162404/16/2024 10:23:58 AMguidelineSummaryUpdatestandardOncologic\_Disease Urologic\_DisordersNational Comprehensive Cancer Network (NCCN) recommendations on management of prostate cancer (NCCN 2024 Mar) If life expectancy is ≥ 20 years, consider active surveillance only ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
* If life expectancy is < 10 years, consider watchful waiting only ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
* See [Management of Localized or Locally Advanced Prostate Cancer](https://dpa-pde-oxford.shinyapps.io/management/management-of-localized-or-locally-advanced-prostate-cancer) for details.

Management of Low-Risk Disease

* TOPIC\_AMZ\_3S4\_41C\_\_LI\_JMF\_SWG\_CBCGSU04162404/16/2024 10:23:22 AMguidelineSummaryUpdatestandardOncologic\_Disease Urologic\_DisordersEuropean Association of Urology recommendations on management of prostate cancer (EAU 2024 Apr)Management of patients with life expectancy ≥ 10 years:
  + Active surveillance is the preferred management option ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
  + Other options are as follows:
    - brachytherapy ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE))
    - external beam radiation therapy ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [AUA Strong or Conditional recommendation, Grade A-B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE))
    - radical prostatectomy ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)
* If life expectancy is ≤ 5-10 years, offer watchful waiting only, especially for patients with asymptomatic disease ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
* See [Management of Localized or Locally Advanced Prostate Cancer](https://dpa-pde-oxford.shinyapps.io/management/management-of-localized-or-locally-advanced-prostate-cancer) for details.

Management of Intermediate-Risk Disease

* Management of favorable-intermediate-risk disease:
  + Management of patients with life expectancy ≥ 10 years:
    - Primary management options are as follows:
      * Radical prostatectomy ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)) plus extended pelvic lymph node dissection if patients have high risk of lymph node metastasis ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE))
      * External beam radiation therapy (EBRT) ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE))
      * Brachytherapy ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE))
    - In select patients, consider active surveillance ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Weak recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
    - Only consider cryotherapy, high-intensity focused ultrasound, or focal ablative therapy in the setting of a clinical trial or well-designed cohort study ([EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Expert opinion](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
  + Management of patients with life expectancy ≤ 5-10 years:
    - Offer watchful waiting as the management preferred option, especially for patients with asymptomatic disease ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
    - Other management options include EBRT or brachytherapy monotherapy ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
* Management of unfavorable-intermediate-risk disease:
  + Management of patients with life expectancy ≥ 10 years:
    - Primary management options are as follows:
      * Radical prostatectomy ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)) with extended pelvic lymph node dissection if patients have high risk of lymph node metastasis ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE))
      * EBRT plus ADT for 4-6 months ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE))
      * EBRT plus brachytherapy with or without the addition of ADT for 4-6 months ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [AUA Strong recommendation, Grade A-B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE))
    - Only consider cryotherapy or high-intensity focused ultrasound in the setting of a clinical trial or well-designed cohort study ([EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Expert opinion](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
  + Management of patients with life expectancy is ≤ 5-10 years:
    - Offer watchful waiting as the preferred option, especially for patients with asymptomatic disease ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
    - Alternatively, consider EBRT and/or brachytherapy plus ADT for 4-6 months ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
* See [Management of Localized or Locally Advanced Prostate Cancer](https://dpa-pde-oxford.shinyapps.io/management/management-of-localized-or-locally-advanced-prostate-cancer) for details.

Management of High-Risk Disease

* If the disease is symptomatic or if life expectancy is > 5 years, the management options are as follows:
  + Radical prostatectomy plus extended pelvic lymph node dissection as a part of multimodal therapy ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Weak recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE))
  + External beam radiation therapy (EBRT) plus androgen-deprivation therapy (ADT) for 1-3 years ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE))
  + EBRT plus brachytherapy ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Weak recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A-B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)) with the addition of ADT for 1-3 years ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE))
* Management of disease that is asymptomatic and life expectancy is ≤ 5 years:
  + Offer watchful waiting ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
  + In select patients with complications such as hydronephrosis or if metastasis is expected within 5 years, consider monotherapy with either ADT or EBRT ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
* See [Management of Localized or Locally Advanced Prostate Cancer](https://dpa-pde-oxford.shinyapps.io/management/management-of-localized-or-locally-advanced-prostate-cancer) for details.

Management of Locally Advanced Disease (Including Very-High-Risk Disease)

* Management of patients with nodal negative disease (≥ cT3, cN0, cM0 disease):
  + Management of the disease that is symptomatic or if life expectancy is > 5 years:
    - Offer external beam radiation therapy (EBRT) plus androgen-deprivation therapy (ADT) for 1 to ≥ 2 years ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)), with the possible addition of abiraterone acetate for 2 years for patients with very high risk ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE)).
    - Consider EBRT plus brachytherapy ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Weak recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A-B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)) with the addition of ADT for 1-3 years ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
    - For highly selected patients, radical prostatectomy plus extended pelvic lymph node dissection as a part of multimodal therapy may be a management option ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Weak recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
  + Management of the disease that is asymptomatic and life expectancy is ≤ 5 years:
    - Offer watchful waiting ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
    - In select patients with complications such as hydronephrosis or if metastasis is expected within 5 years, consider monotherapy with either ADT or EBRT ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
* For patients with nodal positive disease (any T, cN1, cM0 disease):
  + Primary management for patients with symptomatic disease or life expectancy > 5 years:
    - Consider external beam radiation therapy (EBRT) plus long-term androgen-deprivation therapy (ADT) plus abiraterone acetate ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE)).
    - For highly selected patients, consider radical prostatectomy plus extended pelvic lymph node dissection as a part of multimodal therapy, with the addition of long-term ADT ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
  + Other management options for patients with symptomatic disease or life expectancy > 5 years are as follows:
    - EBRT plus ADT ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE))
    - ADT with or without the addition of abiraterone acetate ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE))
  + For asymptomatic patients whose life expectancy is ≤ 5 years, consider either watchful waiting or ADT ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
* See [Management of Localized or Locally Advanced Prostate Cancer](https://dpa-pde-oxford.shinyapps.io/management/management-of-localized-or-locally-advanced-prostate-cancer) for details.

Management of Biochemical Relapse of Localized Prostate Cancer

Management of Prostate-Specific Antigen Persistence or Recurrence After Radical Prostatectomy

* Consider enrollment into a clinical trial ([AUA Clinical principle](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
* Management of patients with no pelvic recurrence and no distant metastases, and life expectancy > 5 years:
  + Preferably consider salvage external beam radiation therapy ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE) ; [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Conditional or Moderate recommendation, Grade B-C](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)) with or without androgen deprivation therapy (ADT) ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Weak recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Moderate recommendation, Grade B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
  + Alternatively, consider monitoring only, especially for patients with low risk ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE) ; [EAU Weak recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE)).
* For patients with pelvic recurrence but no distant metastases, and life expectancy > 5 years, consider salvage external beam radiation therapy plus ADT with or without abiraterone acetate ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [AUA Expert opinion](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
  + The STAMPEDE trial ([28578639N Engl J Med 2017 Jul 27;377(4):338](http://pubmed.ncbi.nlm.nih.gov/28578639?dopt=Abstract)) that studied the use of abiraterone acetate only contained a small subgroup of patients with recurrence. Therefore, the evidence on the use of abiraterone acetate on patients with pelvic recurrence may not be very robust.
* For patients with no distant metastases, do not offer ADT routinely, especially for patients with low risk (PSA doubling time > 12 months) ([EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Expert opinion](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
* Management of patients with disease progression after salvage therapy who have exhausted maximal pelvic salvage therapy:
  + Preferably consider monitoring ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [AUA Clinical principle](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
  + Alternatively, consider ADT only, possibly as intermittent ADT to reduce toxicity ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [AUA Conditional recommendation, Grade C](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
  + For patients with PSA doubling time ≤ 9 months and PSA ≥ 1 ng/mL after primary radical prostatectomy, consider enzalutamide with or without leuprolide ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
* For patients with life expectancy ≤ 5 years, consider watchful waiting ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
* See [Management of Biochemical Relapse of Localized Prostate Cancer](https://dpa-pde-oxford.shinyapps.io/management/management-of-biochemical-relapse-of-localized-prostate-cancer) for details.

Management of Prostate-Specific Antigen Recurrence After Radiation Therapy

* Consider enrollment into a clinical trial ([AUA Clinical principle](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
* For patients with no local recurrence, no distant metastases, and life expectancy > 5 years, consider monitoring, or ADT (possibly as intermittent ADT to reduce toxicity) ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)). For patients with biopsy-proven local recurrence, alternatively consider salvage radical prostatectomy plus pelvic lymph node dissection, cryotherapy, reirradiation, or high-intensity focused ultrasound ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Moderate recommendation, Grade C](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)). Offer local therapy only in the setting of a clinical trial or a well-designed prospective cohort study ([EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE)).
* For patients with pelvic recurrence, and life expectancy > 5 years, management options include monitoring, ADT (possibly as intermittent ADT to reduce toxicity) ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)), pelvic lymph node irradiation or reirradiation with or without ADT ([NCCN Category 2A-2B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [AUA Expert opinion](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)), or pelvic lymph node dissection with or without ADT ([NCCN Category 2A-2B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [AUA Conditional recommendation, Grade C](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
* For patients with no distant metastases, do not offer ADT routinely, especially for patients with low risk (PSA doubling time > 12 months) ([EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Expert opinion](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
* Management of patients with disease progression after salvage therapy who have exhausted maximal pelvic salvage therapy:
  + Preferably consider monitoring ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [AUA Clinical principle](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
  + Alternatively, consider ADT only, possibly as intermittent ADT to reduce toxicity ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [AUA Conditional recommendation, Grade B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
  + For patients with PSA doubling time ≤ 9 months and PSA ≥ 2 ng/mL after primary radiation therapy, consider enzalutamide with or without leuprolide ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
* For patients with life expectancy ≤ 5 years, consider watchful waiting ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
* See [Management of Biochemical Relapse of Localized Prostate Cancer](https://dpa-pde-oxford.shinyapps.io/management/management-of-biochemical-relapse-of-localized-prostate-cancer) for details.

Management of Hormone-Sensitive Metastatic Prostate Cancer

* Management of patients with life expectancy > 5 years who can tolerate combination therapy:
  + As the preferred management option, offer androgen deprivation therapy (ADT) ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE) ; [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A-B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)) in combination with any one of the following options :
    - Abiraterone acetate and prednisone (regardless of disease volume) ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE) ; [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE))
    - Apalutamide (regardless of disease volume) ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE) ; [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE))
    - Enzalutamide (regardless of disease volume) ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE) ; [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE))
    - Docetaxel plus either abiraterone with prednisone, or darolutamide (for high-volume synchronous or metachronous metastases, or low-volume synchronous metastases only) ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE) ; [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A-B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE))
  + For patients with synchronous metastases with low metastatic burden, consider ADT in combination with external beam radiation therapy to the primary tumor plus abiraterone and prednisone, or docetaxel ([NCCN Category 2A-2B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE) ; [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Conditional recommendation, Grade C](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
* For patients with asymptomatic disease and life expectancy ≤ 5 years, consider either early ADT or observation ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
* Primary options for ADT include orchiectomy, luteinizing-hormone releasing hormone (LHRH) agonist, or LHRH antagonist ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [AUA Strong recommendation, Grade B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
* Considerations for ADT:
  + For patients with evidence of impending spinal cord compression or bladder outlet obstruction, offer orchiectomy or LHRH antagonist ([EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE)).
  + For patients initiating LHRH agonist, consider preceding with short-term first-generation antiandrogens to reduce the risk of testosterone flare ([EAU Weak recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE)).
  + For ADT monotherapy, intermittent ADT may be considered to reduce toxicity. However, a randomized trial suggested that intermittent ADT may not have noninferior overall survival compared to continuous ADT.
* See [Management of Hormone-Sensitive Metastatic Prostate Cancer](https://dpa-pde-oxford.shinyapps.io/management/management-of-hormone-sensitive-metastatic-prostate-cancer-1) for details.

Management of Castration-Resistant Prostate Cancer

Management of Nonmetastatic Castration-Resistant Prostate Cancer

* Continue androgen deprivation therapy to maintain castration level of testosterone, regardless of decisions on further therapies ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [AUA Strong recommendation, Grade A, Clinical principle](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
* Initial treatment depends on prostate-specific antigen (PSA) doubling time.
  + If PSA doubling time is > 10 months, consider observation as the preferred option ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [AUA Clinical principle](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
  + If PSA doubling time is ≤ 10 months, offer one of the following preferred options: apalutamide, darolutamide, and enzalutamide ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE) ; [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).

Management of Metastatic Castration-Resistant Prostate Cancer

Management of Adenocarcinoma

* Continue androgen deprivation therapy to maintain castration level of testosterone, regardless of decisions on further therapies ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [AUA Strong recommendation, Grade A-B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
* Preferred first-line therapy options include abiraterone acetate plus prednisone, enzalutamide, docetaxel, or radium-223 (for patients with symptomatic bone metastases but no visceral metastases) ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade A-B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
* If there is disease progression after first-line abiraterone acetate or enzalutamide, the preferred second-line therapy option include docetaxel, or olaparib or rucaparib for patients with germline and/or somatic *BRCA1* or *BRCA2* pathogenic variants ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)). Consider not sequencing second-generation antiandrogens (enzalutamide) and CYP17 inhibitor (abiraterone acetate) ([EAU Weak recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE)).
* If there is disease progression after first-line docetaxel, the preferred second-line therapy options include abiraterone acetate plus prednisone ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE)), enzalutamide ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE)), or cabazitaxel ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Conditional recommendation, Grade B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)).
* If there is disease progression after both docetaxel and hormonal therapy, the preferred third-line therapy options include cabazitaxel ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Strong recommendation, Grade B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)) or docetaxel rechallenge ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
* See [Management of Castration-Resistant Prostate Cancer](https://dpa-pde-oxford.shinyapps.io/management/management-of-castration-resistant-prostate-cancer-1) for details.

Management of Small Cell or Neuroendocrine Tumor

* First and subsequent lines of chemotherapy include cisplatin plus etoposide, carboplatin plus etoposide, docetaxel plus carboplatin, or cabazitaxel plus carboplatin plus growth factor support ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
* Consider systemic therapy options similar to small cell lung cancer. See Systemic Therapy for Extensive Stage Disease in [Management of Small Cell Lung Cancer](https://dpa-pde-oxford.shinyapps.io/management/management-of-small-cell-lung-cancer#CHEMOTHERAPY_FOR_EXTENSIVE_DISEASE) for additional information.
* See [Management of Castration-Resistant Prostate Cancer](https://dpa-pde-oxford.shinyapps.io/management/management-of-castration-resistant-prostate-cancer-1) for details.

Management of Bone Health

* Management of patients with bone metastases:
  + Offer denosumab (Xgeva) ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Moderate recommendation, Grade B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)) or consider zoledronic acid ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE); [AUA Moderate recommendation, Grade B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2020GRADE)) to prevent osseous complications. For patients receiving either bone protective agents, monitor serum calcium level and provide supplemental calcium and vitamin D ([EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE)).
  + Offer palliative radiation therapy and analgesics for painful disease ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE); [EAU Strong recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE)).

Management of Adverse Effects

* Disease-related or treatment-related adverse effects include the following:
  + Sexual dysfunction
  + Urinary complications
  + Radical prostatectomy-related complications, including pain, and blood loss
  + Radiation-induced proctitis or rectal bleeding
  + Androgen-deprivation therapy-related complications, including fractures, hot flashes, cardiovascular disease, diabetes, and gynecomastia
* See [Management of Localized or Locally Advanced Prostate Cancer](https://dpa-pde-oxford.shinyapps.io/management/management-of-localized-or-locally-advanced-prostate-cancer) for additional information on management of adverse effects.

Supportive Care

Activity

Exercise and Nutrition in General Cancer Management

* American Cancer Society guidelines on nutrition and physical activity during and after cancer treatment include cautions about exercise
  + if severe anemia, delay exercise until anemia improved
  + if immunocompromised, avoid exercise in public until white cell count returns to safe levels
  + if severe fatigue, approach exercise cautiously
  + if undergoing radiation, avoid chlorinated swimming pools
  + if catheter, avoid swimming
  + if peripheral neuropathy or dizziness, consider restricted balance and coordination in planning exercise
  + Reference - [22539238CA Cancer J Clin 2012 Jul;62(4):242](http://pubmed.ncbi.nlm.nih.gov/22539238?dopt=Abstract)[full-text](http://onlinelibrary.wiley.com/doi/10.3322/caac.21142/full)
* **exercise during active treatment may improve quality of life and physical functioning in adults with cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Cochrane Review[CD008465Cochrane Database Syst Rev 2012 Aug 15;(8):CD008465](http://www.ncbi.nlm.nih.gov/pubmed?term=22895974%5buid%5d%20AND%20CD008465%5bpg%5d)

studySummary2

* + based on Cochrane review limited by clinical heterogeneityCochrane Review
  + systematic review of 56 randomized or quasi-randomized trials evaluating exercise during active treatment phase in 4,826 adults with cancer
  + analyses were limited by heterogeneity in exercise interventions, control groups, and outcome measure assessment
  + comparing exercise to control
    - exercise associated with improvement at < 12 weeks in
      * overall quality of life in analysis of 11 trials with 806 adults
      * physical function in analysis of 8 trials with 540 adults
      * social function in analysis of 5 trials with 378 adults
      * role function in analysis of 7 trials with 439 patients
      * fatigue in analysis of 12 trials with 971 adults
    - all results limited by significant heterogeneity
  + greater improvement with moderate-to-vigorous exercise than mild exercise
  + CochraneCD008465The Cochrane database of systematic reviews20120815Cochrane Database Syst Rev8CD008465CD008465Reference - [CD008465Cochrane Database Syst Rev 2012 Aug 15;(8):CD008465](http://www.ncbi.nlm.nih.gov/pubmed?term=22895974%5buid%5d%20AND%20CD008465%5bpg%5d)
* **walking during cancer treatment may improve cardiorespiratory fitness and self-reported physical function (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Randomized Trial[19637345Cancer 2009 Oct 15;115(20):4874](http://pubmed.ncbi.nlm.nih.gov/19637345?dopt=Abstract)[Full Text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2761503/?tool=pubmed)

studySummary2

* + based on randomized trial without attention control and with high crossover rate Randomized Trial
  + 126 patients (mean age 60.2 years) with prostate (55.6%), breast (32.5%) or other cancers were randomized to home-based walking intervention vs. usual care (mean duration 12 weeks)
  + patients also received usual treatment including external beam radiation therapy (52.3%) and chemotherapy (34.9%)
  + adherence limited with 32% of exercisers who stopped walking, 22% of controls exercised
  + exercise associated with
    - maintenance or improvement of cardiorespiratory fitness and self-reported fitness function
    - improvement in peak oxygen uptake (VO2) maintenance in patients with prostate cancer compared to patients with other cancers
    - decreased Medical Outcomes Study pain at end of cancer treatment (p = 0.046)
    - greater Medical Outcomes Study physical function role limitations by end of cancer treatment (p = 0.037)
  + younger age was associated with improved Medical Outcomes Study physical function (p = 0.048)
  + no significant difference in change of pain scores between groups
  + PubMed19637345Cancer20091015Cancer1152048744874 Reference - [19637345Cancer 2009 Oct 15;115(20):4874](http://pubmed.ncbi.nlm.nih.gov/19637345?dopt=Abstract)[full-text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2761503/?tool=pubmed)
* **physical activity may be associated with multiple positive effects in cancer survivors (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Systematic Review[Cancer Epidemiol Biomarkers Prev 2005 Jul;14(7):1588](http://pubmed.ncbi.nlm.nih.gov/16030088-controlled-physical-activity-trials-in-cancer-survivors-a-systematic-review-and-meta-analysis/?dopt=Abstract)[Full Text](http://cebp.aacrjournals.org/content/14/7/1588.long)

studySummary

* + Systematic Review based on systematic review of mostly low-quality trials and limited by clinical heterogeneity
  + 22 studies considered high quality but problems with data adequacy reported
  + most interventions involved moderate-to-vigorous aerobic activity for 20-30 minutes 3-5 times/week for 5-12 weeks
  + benefits found for exercise intervention during cancer treatment (all small-to-moderate effect sizes) include improvements in
    - cardiorespiratory fitness
    - fatigue or tiredness
    - quality of life
    - depression
    - anxiety
  + benefits found for exercise intervention after cancer treatment include improvements in
    - cardiorespiratory fitness
    - fatigue or tiredness
    - vigor or vitality
    - quality of life
    - depression
    - anxiety
  + PubMed16030088Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive OncologyCancer Epidemiol Biomarkers Prev200507011471588-951588Reference - [Cancer Epidemiol Biomarkers Prev 2005 Jul;14(7):1588](http://pubmed.ncbi.nlm.nih.gov/16030088-controlled-physical-activity-trials-in-cancer-survivors-a-systematic-review-and-meta-analysis/?dopt=Abstract)[full-text](http://cebp.aacrjournals.org/content/14/7/1588.long)
  + systematic review of 33 controlled trials (25 randomized trials) found positive results for physical function and no increase in fatigue ([15801488Cancer Causes Control 2004 Dec;15(10):1035](http://pubmed.ncbi.nlm.nih.gov/15801488?dopt=Abstract))
  + systematic review of 34 trials found multiple positive benefits but had only 4 trials which met all 7 methodologic quality criteria ([15923576J Clin Oncol 2005 Jun 1;23(16):3830](http://pubmed.ncbi.nlm.nih.gov/15923576?dopt=Abstract))
* **resistance training ≥ 1 day/week associated with reduced all-cause mortality in adult cancer survivors (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Cohort Study[24958698Mayo Clin Proc 2014 Aug;89(8):1108](http://pubmed.ncbi.nlm.nih.gov/24958698?dopt=Abstract)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4126241/)

studySummary2

* + based on prospective cohort study Cohort Study
  + 2,863 adult cancer survivors without history of myocardial infarction or stroke and with body mass index > 18.5 kg/m2 were assessed for self-reported physical activity at baseline medical exam
  + 44% performed resistance training ≥ 1 day/week
  + 4% died during mean 7.3-year follow-up
  + compared to no resistance training, resistance training ≥ 1 day/week associated with decreased all-cause mortality (adjusted hazard ratio 0.67, 95% CI 0.45-0.99)
  + PubMed24958698Mayo Clinic proceedings20140801Mayo Clin Proc89811081108Reference - [24958698Mayo Clin Proc 2014 Aug;89(8):1108](http://pubmed.ncbi.nlm.nih.gov/24958698?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4126241/), commentary can be found in [25282433Mayo Clin Proc 2014 Oct;89(10):1465](http://pubmed.ncbi.nlm.nih.gov/25282433?dopt=Abstract)
* **home-based diet and exercise intervention associated with reduced rate of functional decline and might improve physical function in older patients with overweight and with prior breast, prostate, or colorectal cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Randomized Trial[19436015JAMA 2009 May 13;301(18):1883](http://pubmed.ncbi.nlm.nih.gov/19436015?dopt=Abstract)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2752421/)

studySummary2

* + based on randomized trial without attention control and with allocation concealment not statedRandomized Trial
  + 641 patients with overweight (body mass index [BMI] 25-40 kg/m2) aged 65-91 years who survived breast, prostate, or colorectal cancer for ≥ 5 years were randomized to immediate intervention vs. delayed intervention (wait-list control) for 12 months
    - breast cancer in 45.1%
    - prostate cancer in 40.7%
    - colorectal cancer in 14.2%
  + intervention was home-based tailored program of telephone counseling and mailed materials promoting exercise, improved diet quality, and modest weight loss
  + 50 patients dropped out of intervention vs. 33 from control (p = 0.04)
  + all outcomes based on self-report
  + diet and exercise intervention associated with
    - reduced decline in mean function scores (p = 0.03)
    - small improvement in mean basic lower extremity function score (vs. decreased function with wait-list, p = 0.005)
    - improvements in physical activity, dietary behaviors, and overall quality of life (p < 0.05)
    - greater weight loss (2.06 kg [4.5 lbs] vs. 0.92 kg [2 lbs] with wait-list, p < 0.001)
  + PubMed19436015JAMA20090513JAMA3011818831883Reference - RENEW trial ([19436015JAMA 2009 May 13;301(18):1883](http://pubmed.ncbi.nlm.nih.gov/19436015?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2752421/)), commentary can be found in [19706856JAMA 2009 Aug 26;302(8):845](http://pubmed.ncbi.nlm.nih.gov/19706856?dopt=Abstract)
  + **home-based diet-exercise intervention appears to have sustained physical function and weight loss benefits at 1 year postdiscontinuation**
    - based on follow-up study of RENEW trial
    - 558 patients (87.1%) crossed over to other trial arm at 1 year for 1 additional year
      * intervention initiated in 289 patients originally receiving wait-list control
      * intervention discontinued in 269 patients originally receiving intervention
    - 488 (76.1%) completed 2-year follow-up, including
      * breast cancer in 45.3%
      * prostate cancer in 39.5%
      * colorectal cancer in 15.2%
    - in patients discontinuing intervention, diet and exercise intervention associated with improvements from baseline at 2 years in physical activity and BMI (each p = 0.001)
    - diet and exercise intervention in delayed-intervention group associated with similar improvements at 2 years as reported in immediate-intervention group at 1 year
    - Reference - [22614994J Clin Oncol 2012 Jul 1;30(19):2354](http://pubmed.ncbi.nlm.nih.gov/22614994?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3675693/), editorial can be found in [22614991J Clin Oncol 2012 Jul 1;30(19):2294](http://pubmed.ncbi.nlm.nih.gov/22614991?dopt=Abstract)

Efficacy of Exercise in Prostate Cancer

* **exercise may improve cancer-specific fatigue and physical fitness, but may not improve cancer-specific quality of life in patients with stage I-IV prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Systematic Review[26632144Eur Urol 2016 Apr;69(4):693](http://pubmed.ncbi.nlm.nih.gov/26632144?dopt=Abstract)

studySummary2

* + based on systematic review of trials without blinding of patients or caregivers Systematic Review
  + systematic review of 16 randomized trials comparing exercise vs. usual care in 1,574 patients with stage I-IV prostate cancer
  + follow-up ranged from 8 weeks to 12 months
  + exercise associated with
    - improved cancer-specific fatigue (p = 0.03) in analysis of 10 trials with 1,031 patients, analysis limited by significant heterogeneity
    - improved physical fitness, including aerobic fitness (6 trials with 346 patients), upper body strength (4 trials with 277 patients), and lower body strength (6 trials with 345 patients) (p < 0.05 for each)
    - nonsignificant improvement in sexual activity (p = 0.05) in analysis of 2 trials with 119 patients
  + no significant differences in
    - cancer-specific quality of life in analysis of 7 trials with 912 patients, analysis limited by significant heterogeneity
    - disease progression in analysis of 5 trials with 388 patients
    - sexual function in analysis of 3 trials with 212 patients
  + PubMed26632144European urology20160401Eur Urol694693693 Reference - [26632144Eur Urol 2016 Apr;69(4):693](http://pubmed.ncbi.nlm.nih.gov/26632144?dopt=Abstract)
  + **resistance and aerobic exercise program may improve strength and physical function in patients receiving androgen suppression therapy for prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**
    - based on small randomized trial
    - 57 patients with prostate cancer receiving androgen suppression therapy randomized to resistance and aerobic exercise vs. usual care for 12 weeks
    - exercise associated with significantly improved muscle mass, strength, physical function, and balance
    - Reference - [mdc19949016pJ Clin Oncol 2010 Jan 10;28(2):340](http://pubmed.ncbi.nlm.nih.gov/19949016?dopt=Abstract)
  + **exercise program might improve cardiorespiratory fitness in prostate cancer survivors following androgen deprivation therapy plus radiation therapy (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**
    - based on randomized trial without blinding of outcome assessors
    - 100 patients with prostate cancer for > 5 years were randomized to supervised exercise for 6 months followed by home-based maintenance exercise program for 6 months vs. printed physical activity educational material (control)
    - all patients were previously treated with androgen deprivation therapy plus radiation therapy
    - 28% in exercise group and 16% in control group did not complete treatment, all patients included in analyses
    - comparing exercise vs. control at 12 months
      * mean reduction in 400-meter walk time 17.6 seconds vs. 2.3 seconds (p = 0.028)
      * mean reduction in chair rise time 1.1 second vs. 0.1 second (p = 0.001)
    - exercise program associated with significant improvement in muscle strength outcomes, lower body physical function, and self-reported physical function
    - Reference - [24113319Eur Urol 2014 May;65(5):856](http://pubmed.ncbi.nlm.nih.gov/24113319?dopt=Abstract), editorial can be found in [24315708Eur Urol 2014 May;65(5):873](http://pubmed.ncbi.nlm.nih.gov/24315708?dopt=Abstract)
* **clinician referral to supervised exercise program may increase physical activity intensity in patients who completed active treatment for prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Randomized Trial[25877784Cancer 2015 Aug 1;121(15):2646](http://pubmed.ncbi.nlm.nih.gov/25877784?dopt=Abstract)[Full Text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4654333/)

studySummary2

* + based on cluster-randomized trial without attention control Randomized Trial
  + 15 clinicians were randomized to refer patients who completed active treatment for prostate cancer in previous 3-12 months to 1 of 2 interventions for 12 weeks
    - supervised exercise program consisting of 2 weekly in-person sessions (50 minutes each) at local gym and 1 weekly home-based session plus therapist advice
    - usual care with clinicians providing minimal physical activity information
  + 147 patients (mean age 66 years) were included in trial
  + 85% in supervised program completed ≥ 18 of 24 gym-based sessions and 81% completed ≥ 9 of 12 home-based sessions
  + 12% did not complete trial and were excluded from analyses
  + comparing supervised exercise program vs. usual care at 12 weeks
    - moderate to vigorous physical activity ≥ 150 minutes/week in 69.6% vs. 43.4% (p = 0.002, NNT 4)
    - mean duration of vigorous physical activity 94 minutes/week vs. 42 minutes/week (p = 0.01)
    - mean duration of moderate physical activity 162 minutes vs. 111 minutes (not significant)
  + supervised exercise program associated with improved total anxiety score (p = 0.02)
  + no significant differences in accelerometer-measured physical activity intensity, quality of life, or depression symptoms
  + PubMed25877784Cancer20150801Cancer1211526462646 Reference - ENGAGE trial ([25877784Cancer 2015 Aug 1;121(15):2646](http://pubmed.ncbi.nlm.nih.gov/25877784?dopt=Abstract)[full-text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4654333/))

Counseling

* **psychosocial strategies associated with small short-term improvement in physical health-related and cancer-related quality of life in patients with prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Cochrane Review[chhCD008529Cochrane Database Syst Rev 2013 Dec 24;(12):CD008529](http://www.ncbi.nlm.nih.gov/pubmed?term=24368598%5buid%5d%20AND%20CD008529%5bpg%5d)

studySummary2

* + based on Cochrane review of trials with methodologic limitations and limited by clinical heterogeneity Cochrane Review
  + systematic review of 19 randomized trials comparing psychosocial strategies vs. usual care in 3,204 patients with prostate cancer
  + psychosocial strategies included cognitive behavioral, psychoeducational, supportive, and counseling interventions (alone or in combination)
  + all trials had unclear or no blinding or had unclear allocation concealment
  + psychosocial strategies associated with
    - improved physical component of general health-related quality of life at end of intervention in analysis of 6 trials with 1,414 patients, but effect size of questionable clinical relevance; no significant effect at later time points
    - improved cancer-related quality of life at end of intervention in analysis of 3 trials with 497 patients, but effect size of questionable clinical relevance; no significant effect at later time points
    - increased prostate cancer knowledge in analysis of 2 trials with 506 patients
  + for depression, no significant differences between groups in overall analysis of 3 trials with 434 patients, but results limited by significant heterogeneity
    - using individual-based intervention, psychosocial strategies significantly reduced depression in 1 trial with 72 patients
    - using group-based intervention, no significant differences in depression in analysis of 2 trials with 362 patients
  + no significant differences in mental component of general health-related quality of life, prostate-specific quality of life, and symptom-related quality of life
  + CochraneCD008529The Cochrane database of systematic reviews20131224Cochrane Database Syst Rev12CD008529CD008529 Reference - [chhCD008529Cochrane Database Syst Rev 2013 Dec 24;(12):CD008529](http://www.ncbi.nlm.nih.gov/pubmed?term=24368598%5buid%5d%20AND%20CD008529%5bpg%5d)
* **psychosocial strategies associated with reduction in anxiety and depression compared to routine care in patients with prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Systematic Review[cxh92600908pInt J Nurs Stud 2014 Jan;51(1):28](http://pubmed.ncbi.nlm.nih.gov/23398917?dopt=Abstract)

studySummary2

* + based on systematic review of trials with methodologic limitations Systematic Review
  + systematic review of 14 randomized trials evaluating the effect of psychosocial strategies in reducing anxiety and depression compared to usual or standard care in patients with prostate cancer
  + psychosocial strategies included cognitive behavioral interventions, informational and educational interventions, nonbehavioral counseling or therapy, and social support
  + outcomes assessed by Hospital Anxiety and Depression Scale, Spielberger State Anxiety Inventory, the Centre for Epidemiologic Studies Depression Scale, and other questionnaires
  + all trials lacked blinding or had unclear allocation concealment
  + compared to usual or routine care, psychosocial strategies associated with
    - reduction in anxiety 3 months after intervention (but not immediately after intervention)
    - reduction in depression immediately after and 3 months after intervention (but not 1, 6, or 12 months after intervention)
  + PubMed23398917International journal of nursing studies20140101Int J Nurs Stud5112828 Reference - [cxh92600908pInt J Nurs Stud 2014 Jan;51(1):28](http://pubmed.ncbi.nlm.nih.gov/23398917?dopt=Abstract)
* **psychoeducational interventions might improve sexual function after radical prostatectomy in adults with prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Systematic Review[23782275J Adv Nurs 2013 Dec;69(12):2602](http://pubmed.ncbi.nlm.nih.gov/23782275?dopt=Abstract)

studySummary2

* + based on systematic review of low- to moderate-quality trials with clinical heterogeneity Systematic Review
  + systematic review of 8 randomized trials evaluating psychoeducational interventions following radical prostatectomy in 915 adults ≥ 50 years old
    - psychoeducational interventions included coping skills training, counseling, group education sessions, cognitive behavioral stress management, and peer support
    - controls included standard care or wait-list control
  + no meta-analyses performed due to clinical heterogeneity in type of psychoeducational intervention and in outcomes reported
  + compared to controls, psychoeducational interventions associated with significantly improved
    - sexual function in 4 of 7 trials
    - sexual bother in 6 of 7 trials
  + no significant differences in
    - urinary incontinence in 5 of 6 trials
    - fecal incontinence in 3 of 3 trials
  + PubMed23782275Journal of advanced nursing20131201J Adv Nurs691226022602 Reference - [23782275J Adv Nurs 2013 Dec;69(12):2602](http://pubmed.ncbi.nlm.nih.gov/23782275?dopt=Abstract)
  + **family intervention may improve quality of life for spouses of patients with prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**
    - based on randomized trial without attention control
    - 263 patients with prostate cancer and their spouses were randomized to family intervention (5 sessions) vs. control
    - follow-up completed by 235 couples (90%) at 4 months and by 218 couples (83%) at 4, 8, and 12 months
    - intervention patients reported less uncertainty and better communication with spouses at 4 months, but no differences in quality of life
    - intervention spouses reported better mental and overall quality of life at 4 months, but not at 8 or 12 months
    - intervention spouses reported better physical quality of life at 8 and 12 months, but not at 4 months
    - Reference - [17999405Cancer 2007 Dec 15;110(12):2808](http://pubmed.ncbi.nlm.nih.gov/17999405?dopt=Abstract)[full-text](http://onlinelibrary.wiley.com/doi/10.1002/cncr.23114/full)
  + **brief presurgical stress management intervention may improve preoperative mood disturbances (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**
    - based on randomized trial with high dropout rate
    - 159 patients with early-stage prostate cancer and having radical prostatectomy were randomized to 2-session (plus two boosters) presurgical stress management intervention vs. 2-session (plus two boosters) supportive attention group vs. standard care group and followed for 12 months
    - 94% completed 1-week presurgical and 63.5% completed 1-year follow-up
    - stress management intervention had fewer preoperative mood disturbances (p = 0.006) and better 1-year postoperative mood scores (p = 0.0009) compared to standard care
    - no significant difference between stress management group and supportive attention group
    - Reference - [mdc19349551pJ Clin Oncol 2009 Jul 1;27(19):3169](http://pubmed.ncbi.nlm.nih.gov/19349551?dopt=Abstract)[full-text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2716938/?tool=pubmed)
* COUNSELING\_\_LI\_YBZ\_S2W\_CXBEU04122304/12/2023 04:41:09 PMevidenceUpdatestandardOncologic\_Disease Urologic\_Disorderstailored online sexual recovery intervention may not improve satisfaction with sex life in patients or their partners 6 months after prostate cancer treatment (Cancer 2022 Apr 1)

**tailored online sexual recovery intervention may not improve satisfaction with sex life in patients or their partners 6 months after prostate cancer treatment (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Randomized Trial[Cancer 2022 Apr 1;128(7):1513](https://pubmed.ncbi.nlm.nih.gov/34985771)

studySummary

* + Randomized Trial based on randomized trial with high dropout rate
  + 222 adults with localized prostate cancer treated with surgery, radiation, or combined radiation and androgen deprivation therapy and their partners of ≥ 6 months were randomized to online TrueNTH sexual recovery intervention vs. standard informational resources (control)
  + online sexual recovery intervention was tailored to treatment type and sexual orientation
    - intervention consisted of 6 modules accessible over 7 months, covering concepts including expectations for treatment-related sexual side effects and emotional impact, sexual aids for couples, and guidance on talking to healthcare providers about sexual concerns
    - each module included introductory video, content relevant to stage of recovery, and suggested activities for couples to maintain emotional and sexual connection
  + primary outcome was Patient-Reported Outcomes Measurements Information System (PROMIS) Global Satisfaction with Sex Life (GSSL) score at 6 months (higher score indicates greater satisfaction with sex life)
  + 142 couples (64% of randomized; median age 61 years for patients and 59 years for partners) who completed baseline surveys received intervention and were included in analysis
    - 85% of patients had surgery, 11% received radiation, and 4% received radiation plus androgen deprivation therapy
    - mean GSSL score at baseline comparing online sexual recovery intervention vs. control
      * 62 points vs. 60 points (not significant) in patients
      * 58 points vs. 60 points (not significant) in their partners
    - 105 patients (47% of randomized) and 87 partners (39% of randomized) completed 6-month follow-up
  + comparing online sexual recovery intervention vs. control
    - mean GSSL scores at 6 months
      * 53 points vs. 51 points (not significant) in patients
      * 53 points vs. 55 points (not significant) in their partners
    - increase in ≥ 1 nonpenetrative sexual activity at 3 months in
      * 68% vs. 53% (p = 0.07) of patients
      * 73% vs. 60% (p = 0.037, NNT 8) of their partners
  + online sexual recovery intervention associated with increased vaginal penetration at 3 months, but no significant differences at 6 months
  + no significant differences in sexual interest or increase in ≥ 1 nonpenetrative sexual activity at 6 months for both patients and their partners
  + PubMed34985771CancerCancer20220105Reference - [Cancer 2022 Apr 1;128(7):1513](https://pubmed.ncbi.nlm.nih.gov/34985771), commentary can be found in [Nat Rev Urol 2022 Jun;19(6):329](https://pubmed.ncbi.nlm.nih.gov/35277665)
* **self-guided online psychological intervention plus online forum might reduce psychological distress compared to online forum alone, but not online psychological intervention alone in patients with localized prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Randomized Trial[25454611Eur Urol 2015 Sep;68(3):471](http://pubmed.ncbi.nlm.nih.gov/25454611?dopt=Abstract)

studySummary2

* + based on randomized trial with low adherence Randomized Trial
  + 142 patients (mean age 61 years) previously treated or currently receiving treatment for localized prostate cancer (88% had radical prostatectomy) were randomized to 1 of 3 groups for 10 weeks
    - online psychological intervention consisting of 6 self-guided modules focusing on improved well-being in context of prostate cancer
    - online psychological intervention plus online moderated peer forum
    - online forum alone
  + psychological distress assessed on 21-item Depression, Anxiety, and Stress Scale (range 0-126, with higher score indicating greater psychological distress)
  + baseline psychological distress scores in all 3 groups were similar to general population, suggesting absence of high distress
  + mean 59% of self-guided module content was completed in online psychological intervention groups, with completion rate declining as patients progressed through modules (mean 87% of module 1 completed vs. mean 36% of module 6 completed)
  + 27% dropped out and were excluded from analysis
  + mean change in psychological distress score at 10 weeks
    - -0.2 with online psychological intervention alone (not significant vs. online forum alone)
    - -7.1 with online psychological intervention plus online forum (p = 0.02 vs. online forum alone) (not significant vs. psychological intervention alone)
    - +1.7 with online forum alone
  + PubMed25454611European urology20150901Eur Urol683471471 Reference - [25454611Eur Urol 2015 Sep;68(3):471](http://pubmed.ncbi.nlm.nih.gov/25454611?dopt=Abstract)
  + Absence of high distress in any group at baseline may have affected the ability to show significant improvement in outcomes.
* **group mindfulness-based cognitive therapy delivered by teleconference may not improve distress or quality of life in patients with advanced prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Randomized Trial[cxh120780376pmdc27870567pJ Clin Oncol 2017 Jan 20;35(3):291](http://pubmed.ncbi.nlm.nih.gov/27870567?dopt=Abstract)

studySummary2

* + based on randomized trial without attention control Randomized Trial
  + 189 patients (mean age 71 years) with advanced prostate cancer were randomized to mindfulness-based cognitive therapy delivered by teleconference in group setting 1 weekly session for 8 weeks vs. usual care (minimally enhanced by providing patient education materials) and followed for 9 months
  + 75% completed follow-up, all patients included in analyses
  + no significant differences between groups in psychological distress, cancer-specific distress, quality of life, prostate-specific antigen anxiety, or mindfulness skills
  + no adverse events associated with mindfulness-based intervention reported
  + PubMed27870567Journal of clinical oncology : official journal of the American Society of Clinical Oncology20170120J Clin Oncol353291291 Reference - [cxh120780376pmdc27870567pJ Clin Oncol 2017 Jan 20;35(3):291](http://pubmed.ncbi.nlm.nih.gov/27870567?dopt=Abstract)

Multidimensional Rehabilitation

* **multidimensional (physical plus psychosocial) rehabilitation programs may improve physical but not mental health scores in adult cancer survivors (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Cochrane Review[CD007730Cochrane Database Syst Rev 2013 Mar 28;(3):CD007730](http://www.ncbi.nlm.nih.gov/pubmed?term=23543556%5buid%5d%20AND%20CD007730%5bpg%5d)

studySummary2

* + based on Cochrane review of trials with methodologic limitationsCochrane Review
  + systematic review of 12 randomized trials evaluating multidimensional rehabilitation programs in 1,669 adult cancer (any type and any stage) survivors
  + most adults had prostate (52.5%) or breast (40.9%) cancer
  + multidimensional rehabilitation defined as program including both physical (exercise, dietary recommendations) and psychosocial (counseling, cognitive behavioral therapy, psychoeducational strategies) rehabilitation components
  + most trials had ≥ 1 limitation including unclear allocation concealment and lack of or unclear blinding
  + all trials compared multidimensional rehabilitation to control (standard care, less intensive rehabilitation program)
  + multidimensional rehabilitation associated with increased 36-Item Short Form Health Survey (SF-36) Physical Component score (mean difference 2.22 points, 95% CI 0.12-4.31 points) in analysis of 5 trials
  + no significant difference in SF-36 Mental Component Summary score in analysis of 3 trials, results limited by significant heterogeneity
  + CochraneCD007730The Cochrane database of systematic reviews20130328Cochrane Database Syst Rev3CD007730CD007730Reference - [CD007730Cochrane Database Syst Rev 2013 Mar 28;(3):CD007730](http://www.ncbi.nlm.nih.gov/pubmed?term=23543556%5buid%5d%20AND%20CD007730%5bpg%5d)

Complementary and Alternative Therapies

* **addition of electroacupuncture associated with reduced pain following radical prostatectomy in adults receiving postoperative analgesia with tramadol and ketamine (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Randomized Trial[24480836Acupunct Med 2014 Jun;32(3):215](http://pubmed.ncbi.nlm.nih.gov/24480836?dopt=Abstract)

studySummary2

* + based on single-blind randomized trial Randomized Trial
  + 75 adults aged 50-75 years having retropubic radical prostatectomy for prostate malignancy randomized to electroacupuncture as adjunct to postoperative analgesia vs. sham electroacupuncture performed during closure of abdominal walls and immediately after extubation
  + all patients received IV bolus of 1.5 mg/kg [tramadol](https://dpa-pde-oxford.shinyapps.io/drug-monograph/tramadol) and 10 mg ketamine 30 minutes before end of surgery, and continued IV infusion of 0.15 mg/kg/hour tramadol and ketamine via adjustable flow pump
  + electroacupuncture associated with
    - reduced pain at 45 minutes, and 2, 6, 12, and 24 hours postoperatively (p < 0.05 at all time points)
    - less rescue analgesia at 45 minutes, and in total amount of analgesia required (p < 0.001 for each)
  + sham acupuncture associated with more persons with absence of bowel movement at 45 minutes (p < 0.001) and 2 hours (p < 0.05) postoperatively
  + PubMed24480836Acupuncture in medicine : journal of the British Medical Acupuncture Society20140601Acupunct Med323215215 Reference - [24480836Acupunct Med 2014 Jun;32(3):215](http://pubmed.ncbi.nlm.nih.gov/24480836?dopt=Abstract), editorial can be found in [24777617Acupunct Med 2014 Jun;32(3):212](http://pubmed.ncbi.nlm.nih.gov/24777617?dopt=Abstract)
* **caffeine consumption 1 hour before exercise might improve exercise capacity, but not other functional performance measures in prostate cancer survivors (**[**level 3 [lacking direct] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Randomized Trial[24977700Med Sci Sports Exerc 2015 Mar;47(3):468](http://pubmed.ncbi.nlm.nih.gov/24977700?dopt=Abstract)

studySummary3

* + based on small randomized crossover trial without clinical outcomes Randomized Trial
  + 34 prostate cancer survivors (mean age 70 years) randomized to anhydrous caffeine 6 mg/kg orally vs. placebo once 1 hour before exercise, then crossed over to alternate group after 3- to 4-week washout period
  + 88% completed trial and were included in analyses
  + caffeine associated with improved exercise capacity, systolic blood pressure, and heart rate (p < 0.05 for each) and nonsignificant improvement in isometric grip strength (p ≤ 0.06)
  + no significant differences in other functional performance measures (mobility, leg strength, dynamic balance, or gait speed), fatigue, or perception of exertion
  + PubMed24977700Medicine and science in sports and exercise20150301Med Sci Sports Exerc473468468 Reference - [24977700Med Sci Sports Exerc 2015 Mar;47(3):468](http://pubmed.ncbi.nlm.nih.gov/24977700?dopt=Abstract)

Complications

* Complications from advanced prostate cancer include the following:
  + Urinary obstruction ([NCCN 2024 Jan from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_2))
  + Prostatic bleeding ([NCCN 2024 Jan from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_2))
  + PubMed32151466Critical reviews in oncology/hematologyCrit Rev Oncol Hematol20200401148102861102861Hematuria ([Crit Rev Oncol Hematol 2020 Apr;148:102861](http://pubmed.ncbi.nlm.nih.gov/32151466))
  + Hematospermia ([Crit Rev Oncol Hematol 2020 Apr;148:102861](http://pubmed.ncbi.nlm.nih.gov/32151466))
  + Bone metastases and associated complications, including vertebral collapse or deformity, pathological fractures, and spinal cord compression[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__NCCN),[2](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-B81C561F-B956-4055-8075-DFF184448856__EAU2023)
* See [Management of Localized or Locally Advanced Prostate Cancer](https://dpa-pde-oxford.shinyapps.io/management/management-of-localized-or-locally-advanced-prostate-cancer) for additional information on management-related complications.

Prognosis

Complications and Prognosis

Survival and Mortality Rates

* TOPIC\_Y45\_5QW\_BKB\_\_LI\_BML\_DHF\_Z1CEU04052404/05/2024 11:41:21 AMevidenceUpdatestandardOncologic\_Disease Urologic\_Disordersestimated global prostate cancer annual age-standardized mortality 7.3 per 100,000 persons per year in 2022 (Global Cancer Observatory: Cancer Today, accessed 2024 Apr 5)

**estimated global prostate cancer annual age-standardized mortality 7.3 per 100,000 persons per year in 2022**

[Global Cancer Observatory: Cancer Today, accessed 2024 Apr 5](https://gco.iarc.fr/today/en/dataviz/tables?mode=population&group_populations=0&multiple_populations=1&cancers=27&sexes=0&include_nmsc=1&types=1&age_end=17)

studySummary

* + based on population-based surveillancePopulation-based SurveillancePopulation-based Surveillance
  + global population-based surveillance information on prostate cancer during 2022 from 185 countries or territories in Global Cancer Observatory: Cancer Today database was evaluated
  + estimated global prostate cancer mortality 397,430
  + cumulative global lifetime risk of death until the age of 74 years was 0.61%
  + age-standardized rate (ASR) for prostate cancer mortality in 2022
    - overall ASR 7.3 per 100,000 persons per year

| Estimated Global Prostate Cancer Mortality by Global Region, 2022 | |
| --- | --- |
| **Region** | **ASRs per 100,000 Persons per Year** |
| Africa | 17.3 |
| Asia | 3.8 |
| Europe | 11.2 |
| Latin America and the Caribbean | 13.9 |
| Northern America | 8.3 |
| Oceania | 11.5 |
| Abbreviations: ASR, age-standardized rates. | |

* + CA: a cancer journal for clinicians20181101CA Cancer J Clin686394394 References - [Global Cancer Observatory: Cancer Today, accessed 2024 Apr 5](https://gco.iarc.fr/today/en/dataviz/tables?mode=population&group_populations=0&multiple_populations=1&cancers=27&sexes=0&include_nmsc=1&types=1&age_end=17)
* TOPIC\_Y45\_5QW\_BKB\_\_LI\_ABM\_CHF\_Z1CEU04052404/05/2024 11:41:07 AMevidenceUpdatestandardOncologic\_Disease Urologic\_Disordersannual age-adjusted prostate cancer mortality 18.8 per 100,000 persons per year in the United States in 2016-2020 (SEER Explorer, accessed 2024 Apr 5)

**annual age-adjusted prostate cancer mortality 18.8 per 100,000 persons per year in the United States in 2016-2020**

Population-based Surveillance[SEER Explorer, accessed 2024 Apr 5](https://seer.cancer.gov/statistics-network/explorer/application.html?site=66&data_type=2&graph_type=10&compareBy=race&chk_race_1=1&chk_race_6=6&chk_race_5=5&chk_race_4=4&chk_race_9=9&chk_race_8=8&series=9&hdn_sex=2&age_range=1&advopt_precision=1&advopt_show_ci=on&hdn_view=1&advopt_show_apc=on&advopt_display=2#resultsRegion1)

studySummary

* + Population-based Surveillance based on population-based surveillance
  + annual population-based surveillance information on prostate cancer during 2016-2020 in the United States from Surveillance, Epidemiology, and End Results (SEER) database was evaluated
  + 5-year age-adjusted prostate cancer mortality in 2016-2020

| 5-Year Age-Adjusted Prostate Cancer Mortality by Race/Ethnicity in 2016-2020 | |
| --- | --- |
| **Race/Ethnicity** | **Mortality (per 100,000 Persons per Year)** |
| All races | 18.8 |
| Hispanic | 15.3 |
| Non-Hispanic American Indian/Alaska Native | 19.5 |
| Non-Hispanic Asian/Pacific Islander | 8.6 |
| Non-Hispanic Black | 37.5 |
| Non-Hispanic White | 17.8 |

* + PubMed31912902CA: a cancer journal for cliniciansCA Cancer J Clin202001017017-307Reference - [SEER Explorer, accessed 2024 Apr 5](https://seer.cancer.gov/statistics-network/explorer/application.html?site=66&data_type=2&graph_type=10&compareBy=race&chk_race_1=1&chk_race_6=6&chk_race_5=5&chk_race_4=4&chk_race_9=9&chk_race_8=8&series=9&hdn_sex=2&age_range=1&advopt_precision=1&advopt_show_ci=on&hdn_view=1&advopt_show_apc=on&advopt_display=2#resultsRegion1)
* TOPIC\_Y45\_5QW\_BKB\_\_LI\_ABP\_BHF\_Z1CEU04052404/05/2024 11:40:46 AMevidenceUpdatestandardOncologic\_Disease Urologic\_Disorders5-year relative survival 97% in patients with prostate cancer during 2013-2019 in the United States (SEER Explorer, accessed 2024 Apr 5)

**5-year relative survival 97% in patients with prostate cancer during 2013-2019 in the United States**

Population-based Surveillance[SEER Explorer, accessed 2024 Apr 5](https://seer.cancer.gov/statistics-network/explorer/application.html?site=66&data_type=4&graph_type=5&compareBy=stage&chk_stage_101=101&chk_stage_104=104&chk_stage_105=105&chk_stage_106=106&series=9&hdn_sex=2&race=1&age_range=1&advopt_precision=1&advopt_show_ci=on&hdn_view=1&advopt_show_apc=on&advopt_display=2#resultsRegion1)

studySummary

* + Population-based Surveillance based on population-based surveillance
  + annual population-based surveillance information on prostate cancer during 2013-2019 in the United states from Surveillance, Epidemiology, and End Results (SEER) database was evaluated
  + 5-year relative survival
    - 97.1% for disease at all stages
    - 100% for localized disease
    - 100% for regional disease
    - 34.1% for distant stage disease
  + Reference - [SEER Explorer, accessed 2024 Apr 5](https://seer.cancer.gov/statistics-network/explorer/application.html?site=66&data_type=4&graph_type=5&compareBy=stage&chk_stage_101=101&chk_stage_104=104&chk_stage_105=105&chk_stage_106=106&series=9&hdn_sex=2&race=1&age_range=1&advopt_precision=1&advopt_show_ci=on&hdn_view=1&advopt_show_apc=on&advopt_display=2#resultsRegion1)
* Survival prediction:
  + Artificial Neural Networks (ANN) may provide accurate prognostic information.
    - Research on ANN for prostate cancer prognostication is underway, and the current information is based on data from over 5,000 patients who underwent radical prostatectomy and removal of pelvic lymph nodes as the primary treatment for clinically localized prostate cancer between 1982 and 1999 ([Prostate Calculator](http://www.prostatecalculator.org/introduction.html)).
    - NOC 1.0 is an ANN model to predict the risk of having cancer that has spread outside the prostate gland at the time of surgery for patients with clinically localized prostate cancer ([Prostate Calculator NOC](http://www.prostatecalculator.org/noc.html)).
    - LNS 2.0 is an ANN model to predict the risk of having cancer that has spread to the pelvic lymph nodes at the time of surgery for patients with clinically localized prostate cancer ([Prostate Calculator LNS](http://www.prostatecalculator.org/lns.html)).
    - PSA 2.0 calculator predicts risk for prostate-specific antigen (PSA) recurrence (biochemical failure) after radical prostatectomy as the primary treatment for clinically localized prostate cancer ([Prostate Calculator PSA](http://www.prostatecalculator.org/psa.html)).
  + TOPIC\_Y45\_5QW\_BKB\_\_LI\_YTR\_5QV\_4YBEU08262308/26/2023 11:41:39 AMevidenceUpdatestandardOncologic\_Disease Urologic\_Disordersnomogram based on 11 prognostic variables may help predict overall survival in patients with de novo metastatic castration-sensitive prostate cancer (Prostate Cancer Prostatic Dis 2023 Mar)

**nomogram based on 11 prognostic variables may help predict overall survival in patients with de novo metastatic castration-sensitive prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Prediction Rule[Prostate Cancer Prostatic Dis 2023 Mar;26(1):119](http://doi.org/10.1038/s41391-022-00560-3)

studySummary

* + - Prediction Rule based on prognostic cohort study without independent validation
    - 1,058 patients (median age 67 years) with de novo metastatic castration-sensitive prostate cancer in LATITUDE trial were randomly assigned to derivation cohort (743 patients) and validation cohort (315 patients)
    - 50.2% in derivation cohort and 49.5% in validation cohort received androgen deprivation therapy plus abiraterone
    - median overall survival was 44.9 months in derivation cohort and 44.7 months in validation cohort
    - nomogram was developed using 11 factors significantly associated with overall survival in derivation cohort (total score 0-350 points)
      * Eastern Cooperative Oncology Group (ECOG) performance status
      * Gleason score
      * albumin level
      * serum lactate dehydrogenase level
      * hemoglobin level
      * log-transformed serum prostate-specific antigen level
      * worst pain score using Brief Pain Inventory (Short Form)
      * number of skeletal metastases
      * presence of liver metastasis
      * nodal stage
      * treatment regimen
    - nomogram had moderate performance for predicting 2-year survival (c-statistic 0.74) and 3-year overall survival (c-statistic 0.72) in validation cohort
    - online calculator for predicting overall survival can be found at [shiny app](https://radoncdemo.shinyapps.io/OS_Calculator_mCSPC_PCa/)
    - PubMed35790787Prostate cancer and prostatic diseasesProstate Cancer Prostatic Dis20220705Reference - [Prostate Cancer Prostatic Dis 2023 Mar;26(1):119](http://doi.org/10.1038/s41391-022-00560-3)

Risk Prediction Tools to Guide Treatment

* Prostate cancer risk tools for patients contemplating various treatments for local, locally advanced, or biochemical recurrent prostate cancer include the following:
  + Pre-radical prostatectomy nomograms for predicting the risk of progression after radical prostatectomy ([Memorial Sloan Kettering Cancer Center (MSKCC) Pre-Radical Prostatectomy Nomogram](https://www.mskcc.org/nomograms/prostate/pre_op))
  + Nomogram predicting the risk of biochemical recurrence in patients who have had radical prostatectomy ([MSKCC Post-Radical Prostatectomy](https://www.mskcc.org/nomograms/prostate/post_op))
  + Nomogram predicting treatment success of salvage radiation therapy in patients having recurrence after radical prostatectomy ([MSKCC Salvage Radiation Therapy Nomogram](https://www.mskcc.org/nomograms/prostate/salvage_radiation_therapy))
  + Partin tables to predict the risk of extraprostatic extension, seminal vesicle involvement, and lymph node involvement ([Partin tables](https://www.hopkinsmedicine.org/brady-urology-institute/specialties/conditions-and-treatments/prostate-cancer/fighting-prostate-cancer/partin-table.html))
  + Briganti nomogram to predict pathologic lymph node involvement ([Eur Urol 2012 Mar;61(3):480](http://pubmed.ncbi.nlm.nih.gov/22078338)PubMed28412062European urologyEur Urol20171001724632-640632; updated in [Eur Urol 2017 Oct;72(4):632](http://pubmed.ncbi.nlm.nih.gov/28412062))
  + Pretreatment nomogram for predicting biochemical recurrence after radical prostatectomy or external beam radiation therapy ([mdc10458230pJ Clin Oncol 1999 Jan;17(1):168](http://pubmed.ncbi.nlm.nih.gov/10458230?dopt=Abstract))
  + Pretreatment nomogram for predicting the presence of small, moderately differentiated, confined tumors ([14532778J Urol 2003 Nov;170(5):1792](http://pubmed.ncbi.nlm.nih.gov/14532778?dopt=Abstract))
* TOPIC\_NTX\_2X1\_WNB\_\_LI\_CHF\_5MF\_VPBEU07181907/18/2019 06:04:48 PMevidenceUpdatestandardOncologic\_DiseasePredict Prostate Tool may help predict individualized 10- and 15-year overall survival associated with conservative or radical management in men diagnosed with nonmetastatic prostate cancer (PLoS Med 2019 Mar)

**Predict Prostate Tool may help predict individualized 10- and 15-year overall survival associated with conservative or radical management in patients diagnosed with nonmetastatic prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Prediction Rule[PLoS Med 2019 Mar;16(3):e1002758](http://pubmed.ncbi.nlm.nih.gov/30860997)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6413892/)

studySummary

* + Prediction Rule based on prognostic cohort study with independent derivation and validation cohorts and limited data to guide clinical use
  + derivation cohort included 7,063 patients diagnosed with nonmetastatic prostate cancer between 2000 and 2010 in United Kingdom and who had full data set
  + validation cohort included 2,546 patients diagnosed with nonmetastatic prostate cancer between 1990 and 2015 in Singapore and who had full data set
  + median follow-up 9.8 years for derivation cohort and 5.1 years for validation cohort
  + primary treatment in
    - derivation cohort was
      * radiation therapy in 34.8%
      * hormone monotherapy in 31.5%
      * conservative management (active surveillance and watchful waiting) in 19.6%
      * radical prostatectomy in 14.1%
    - validation cohort was
      * radiation therapy in 32.3%
      * hormone monotherapy in 6.4%
      * conservative management (active surveillance and watchful waiting) in 21.1%
      * radical prostatectomy in 39.7%
  + extended model developed using factors significantly associated with prostate-cancer-specific and nonprostate-cancer-specific mortality in derivation cohort included age, prostate-specific antigen (PSA), histological grade group, clinical tumor stage, percentage of positive cores, history of hospitalization, and primary treatment (conservative management, radical prostatectomy or radiation therapy, hormone monotherapy)
  + death events predicted by extended model and observed death events by risk quintile in validation cohort

| Death Events | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Risk Quintile** | **All-Cause Death** | | | | **Prostate-Cancer-Specific Death** | | | |
| **10-Year** | | **15-Year** | | **10-Year** | | **15-Year** | |
| **Predicted** | **Observed** | **Predicted** | **Observed** | **Predicted** | **Observed** | **Predicted** | **Observed** |
| First | 3 | 0 | 3 | 0 | 0 | 0 | 0 | 0 |
| Second | 13 | 5 | 13 | 5 | 2 | 1 | 2 | 1 |
| Third | 31 | 19 | 32 | 17 | 5 | 1 | 5 | 1 |
| Fourth | 71 | 84 | 81 | 102 | 12 | 15 | 15 | 13 |
| Fifth | 210 | 222 | 264 | 276 | 73 | 88 | 92 | 112 |

* + discrimination for overall survival was
    - good (c-statistic 0.73) for extended model including only patients treated with active surveillance, radical prostatectomy, or radiation therapy (p < 0.001 vs. each other model)
    - modest (c-statistic 0.61) for European Association of Urology (EAU) model
    - modest (c-statistic 0.61) for National Comprehensive Cancer Network (NCCN) model
    - modest (c-statistic 0.63) for Cancer of the Prostate Risk Assessment (CAPRA) model
  + online tool to predict individualized 10- and 15-year overall survival and risk of adverse events when choosing between conservative or radical treatment in patients without metastases can be found at [predict prostate](https://prostate.predict.nhs.uk/tool)
  + factors included in online tool
    - mandatory input includes age at diagnosis, PSA, histological grade, Gleason score, clinical tumor stage, and history of hospitalization within previous 2 years
    - optional input includes *BRCA* mutation status, number of biopsy cores, and number of biopsy cores with cancer
  + PubMed30860997PLoS medicinePLoS Med20190312163e1002758e1002758Reference - [PLoS Med 2019 Mar;16(3):e1002758](http://pubmed.ncbi.nlm.nih.gov/30860997)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6413892/)
  + The data in this summary is for the extended model, which is not the exact same model used in the online predict prostate tool.

Prognosis After Management or at Relapse

Prognosis After Radical Prostatectomy

Prediction Rules for Survival, Metastasis, and Recurrence After Prostatectomy

* **CAPRA-S score stratifies patients by 5-year risk of progression-free survival after radical prostatectomy but underpredicts absolute risk in low- to intermediate-risk patients (**[**level 1 [likely reliable] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Cohort Study[23587869Eur Urol 2014 Jun;65(6):1171](http://pubmed.ncbi.nlm.nih.gov/23587869?dopt=Abstract)

studySummary1

* + based on prognostic cohort study Cohort Study
  + 2,670 patients (mean age 62 years) who had radical prostatectomy and had full data available were followed for median 58 months
  + 34.3% had recurrence during follow-up

| CAPRA-S Score Calculated as Sum of Points for 6 Risk Factors (Range 0-12 Points) | | |
| --- | --- | --- |
| **Risk Factor** | **Level** | **Points** |
| Serum prostate-specific antigen | * + - 0-6     - 6.01-10     - 10.01-20     - > 20 | * + - 0     - 1     - 2     - 3 |
| Surgical margins | * + - Negative     - Positive | * + - 0     - 2 |
| Seminal vesicle invasion | * + - No     - Yes | * + - 0     - 2 |
| Gleason score | * + - 2 to 6     - 3+4     - 4+3     - 8-10 | * + - 0     - 1     - 2     - 3 |
| Extracapsular extension | * + - No     - Yes | * + - 0     - 1 |
| Lymph node involvement | * + - No     - Yes | * + - 0     - 1 |
| Abbreviation: CAPRA-S, Cancer of the Prostate Risk Assessment Postsurgical. | | |

* + estimated 5-year biochemical progression-free survival stratified by Cancer of the Prostate Risk Assessment Postsurgical (CAPRA-S) score categories
    - 72% for low risk (0-2 points)
    - 39% for intermediate risk (3-5 points)
    - 17% for high risk (6-12 points)
  + 5-year progression-free survival in validation cohort was lower than survival predicted by CAPRA-S score at all risk scores and significantly lower for each score from 0 to 4 points
  + CAPRA-S reported to be accurate for predicting 5-year risk of mortality (c-index 0.84) and metastasis (c-index 0.85)
  + PubMed23587869European urology20140601Eur Urol65611711171 Reference - [23587869Eur Urol 2014 Jun;65(6):1171](http://pubmed.ncbi.nlm.nih.gov/23587869?dopt=Abstract)
* **CAPRA-S and Eggener prediction rules help predict metastasis at 10 years after prostatectomy in patients with adverse histopathological features but not in patients who develop biochemical relapse (**[**level 1 [likely reliable] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Cohort Study[25922274Eur Urol 2016 Mar;69(3):496](http://pubmed.ncbi.nlm.nih.gov/25922274?dopt=Abstract)

studySummary1

* + based on prognostic cohort study Cohort Study
  + 3,089 patients (median age 60 years) with National Comprehensive Cancer Network intermediate- (91%) or high-risk localized prostate cancer having radical prostatectomy from 1992 to 2009 were assessed with [CAPRA-S Score](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_VQ2_XY1_WNB__ANC_68538889) and [Eggener prediction rule](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_VQ2_XY1_WNB__ANC_554316958)
  + after radical prostatectomy
    - all patients had initial undetectable PSA after surgery and did not receive therapy prior to metastasis
    - 43% had pT3 disease or positive surgical margins
    - 13% had biochemical relapse defined as PSA ≥ 0.2 ng/mL plus confirmation
  + 6% overall and 7.5% with pT3 disease or positive surgical margins had metastasis at 10 years
  + 38% with biochemical relapse had metastasis at 5 years

| Rates of Metastasis Stratified by Risk Score of CAPRA-S and Eggener Prediction Rules | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Prediction Rule** | **Score** | **All Patients** | | **Patients With pT3 Disease or Positive Surgical Margins** | | **Patients With Biochemical Relapse** | |
| **Number of Patients** | **10-Year Metastasis Rate** | **Number of Patients** | **10-Year Metastasis Rate** | **Number of Patients** | **5-Year Metastasis Rate After Relapse** |
| CAPRA-S | < 3 | 1,734 | 1.3% | 358 | 2.1% | 39 | 39.9% |
| 3-5 | 1,054 | 3.4% | 745 | 3.6% | 108 | 21.4% |
| > 5 | 300 | 35.8% | 224 | 27% | 143 | 55.8% |
| Eggener | < 2.5% | 2,078 | 0.9% | 606 | 0.7% | 54 | 24.1% |
| 2.5%-5% | 504 | 5.1% | 393 | 5% | 81 | 23.3% |
| 5%-15% | 360 | 12.8% | 227 | 12.4% | 73 | 41.4% |
| 15%-25% | 76 | 32.9% | 59 | 29.1% | 39 | 54.8% |
| > 25% | 70 | 63.4% | 42 | 49.6% | 43 | 79.3% |

* + discrimination for predicting metastasis was
    - strong for both prediction rules (c-statistic 0.87 for CAPRA-S and 0.83 for Eggener) in patients overall
    - strong with CAPRA-S (c-statistic 0.81) and good with Eggener (c-statistic 0.78) in patients with pT3 disease or positive surgical margins
    - poor with CAPRA-S (c-statistic 0.58) and moderate for Eggener (c-statistic 0.7) in patients with biochemical relapse
  + PubMed25922274European urology20160301Eur Urol693496496 Reference - [25922274Eur Urol 2016 Mar;69(3):496](http://pubmed.ncbi.nlm.nih.gov/25922274?dopt=Abstract)
  + factors necessary to use the nomogram for the Eggener prediction rule include preoperative PSA, age, presence of extracapsular extension, positive surgical margin, seminal vesicle invasion, and lymph node metastases, and primary and secondary Gleason scores; nomogram for Eggener prediction rule can be found in [21239008J Urol 2011 Mar;185(3):869](http://pubmed.ncbi.nlm.nih.gov/21239008?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4058776/)
* **Prostate Cancer-specific Comorbidity Index may predict risk of non-prostate cancer-related death over 10 years following radical prostatectomy (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Cohort Study[26558839Eur Urol 2016 May;69(5):764](http://pubmed.ncbi.nlm.nih.gov/26558839?dopt=Abstract)

studySummary2

* + based on retrospective validation cohort study with missing data and modifications to scoring system Cohort Study
  + 2,961 patients (median age 65 years) who had radical prostatectomy for prostate cancer were assessed with [age-adjusted Prostate Cancer-specific Comorbidity Index (PCCI)](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_ELS_NNB_WNB__ANC_411911871)
  + cohort lacked data for several factors used to calculate age-adjusted comorbidity index, including other neurological disease, mild renal disease, arrhythmia, valve disease, inflammatory bowel disease
  + modifications to scoring
    - no distinction made between mild and moderate-to-severe cases of COPD
    - mild angina or heart failure was excluded from scoring

| Predictive Performance for 10-Year Risk of Nonprostate Cancer-Related Death by PCCI Risk Score | | |
| --- | --- | --- |
| **Total Score** | **Proportion of Patients** | **10-Year Mortality** |
| 0 | 15.2% | 2% |
| 1-2 | 56.3% | 9% |
| 3-4 | 21.5% | 17% |
| 5-6 | 5.4% | 27% |
| 7-9 | 1.5% | 56% |
| ≥ 10 | 0.1% | 0% |
| Abbreviation: PCCI, Prostate Cancer-Specific Comorbidity Index. | | |

* + PubMed26558839European urology20160501Eur Urol695764764 Reference - [26558839Eur Urol 2016 May;69(5):764](http://pubmed.ncbi.nlm.nih.gov/26558839?dopt=Abstract)

Prognostic Factors for Survival, Metastasis, and Recurrence After Radical Prostatectomy

* **persistent PSA 6 weeks after radical prostatectomy associated with poorer overall and cancer-specific survival in adults with nonmetastatic prostate cancer**

Cohort Study[Eur Urol 2019 Jul;76(1):106](http://pubmed.ncbi.nlm.nih.gov/30772034)

studySummary

* + Cohort Study based on cohort study
  + 11,604 adults (median age 64-65 years) with nonmetastatic prostate cancer and persistent (8.8%) or undetectable (91.2%) PSA after 6 weeks from radical prostatectomy were evaluated
  + adults who were given neoadjuvant or adjuvant androgen deprivation therapies were excluded
  + persistent PSA defined as PSA ≥ 0.1 ng/mL
  + metastasis-free survival defined as time from prostatectomy to metastasis or last follow-up
  + median follow-up 46.4 months in adults with persistent PSA and 61.8 months in adults with undetectable PSA
  + comparing adults with persistent PSA vs. adults with undetectable PSA at 15 years
    - overall survival 64.7% vs. 81.2% (p < 0.001)
    - cancer-specific survival 75.5% vs. 96.2% (p < 0.001)
    - metastasis-free survival 53% vs. 93.2% (p < 0.001)
  + in multivariate analyses, persistent PSA associated with decreased
    - overall survival (hazard ratio [HR] for death 1.86, 95% CI 1.41-2.45)
    - cancer-specific survival (HR for death 3.15, 95% CI 1.92-5.18)
    - metastasis-free survival (HR for metastasis 3.59, 95% CI 2.83-4.57)
  + PubMed30772034European urologyEur Urol20190701761106-114106Reference - [Eur Urol 2019 Jul;76(1):106](http://pubmed.ncbi.nlm.nih.gov/30772034)
* **perineural invasion associated with increased risk for biochemical recurrence following radical prostatectomy**

Systematic Review[mnh29390991pcxh127744206t pmdc29390991pBMC Urol 2018 Feb 1;18(1):5](http://pubmed.ncbi.nlm.nih.gov/29390991?dopt=Abstract)[Full Text](https://bmcurol.biomedcentral.com/articles/10.1186/s12894-018-0319-6)

studySummary

* + based on systematic review limited by heterogeneity Systematic Review
  + systematic review of 19 retrospective cohort studies evaluating association between perineural invasion and biochemical recurrence following radical prostatectomy (13 studies) or radiation therapy (6 studies) in 13,412 patients treated for prostate cancer
  + biochemical recurrence after prostatectomy defined as detectable or rising PSA level ≥ 0.2 ng/mL
  + 31% had perineural invasion
  + perineural invasion associated with higher risk of biochemical recurrence after prostatectomy (hazard ratio 1.23, 95% CI 1.11-4.36) in analysis of 13 studies with 10,807 patients, results limited by significant heterogeneity
  + PubMed29390991BMC urology20180201BMC Urol18155 Reference - [mnh29390991pcxh127744206t pmdc29390991pBMC Urol 2018 Feb 1;18(1):5](http://pubmed.ncbi.nlm.nih.gov/29390991?dopt=Abstract)[full-text](https://bmcurol.biomedcentral.com/articles/10.1186/s12894-018-0319-6)
* **lymphatic vessel invasion associated with increased risk of biochemical recurrence after radical prostatectomy in patients without nodal metastases**

Cohort Study[29908878Eur Urol 2018 Sep;74(3):376](http://pubmed.ncbi.nlm.nih.gov/29908878?dopt=Abstract)

studySummarylymphatic vessel invasion associated with increased risk of biochemical recurrence after radical prostatectomy in men without nodal metastases (Eur Urol 2018 Sep)10/26/2018 01:02:00 PMGeriatricsOncologic\_DiseasePrimary\_CareSurgery\_and\_ProceduresUrologic\_DisordersGeriatrics Oncologic\_Disease Primary\_Care Surgery\_and\_Procedures Urologic\_Disorderslymphatic vessel invasion associated with increased risk of biochemical recurrence after radical prostatectomy in men without nodal metastases (Eur Urol 2018 Sep)10/26/2018 01:02:00 PM29908878

* + based on retrospective cohort study Cohort Study
  + 17,987 patients with prostate cancer who had radical prostatectomy in Germany were evaluated for lymphatic invasion and biochemical recurrence, including 14,528 who had analysis of immunohistochemical lymph vessel invasion
  + biochemical recurrence defined as postoperative PSA level ≥ 0.2 ng/mL confirmed by a second analysis with serum PSA ≥ 0.2 ng/mL
  + median follow-up 36 months
  + among 13,070 patients who had lymph node dissection
    - 12% had nodal metastases
    - presence of metastatic cells (even metastasis < 1 mm) associated with decreased probability of recurrence-free survival (p < 0.0001)
  + among 14,528 patients who had immunohistochemical lymph vessel invasion analysis
    - 14% had tumor cells present in intraprostatic lymphatic vessels (L1)
    - L1 status associated with unfavorable tumor type (including high pT stage and high Gleason score) and presence of lymph node metastases (p < 0.0001 for each)
    - L1 status was associated with decreased probability of recurrence-free survival in patients without nodal metastases (p < 0.0001) but not in patients with either small or large metastases
  + PubMed29908878European urology20180901Eur Urol743376376 Reference - [29908878Eur Urol 2018 Sep;74(3):376](http://pubmed.ncbi.nlm.nih.gov/29908878?dopt=Abstract)

Prognosis After Radiation Therapy

* **among patients with localized prostate cancer receiving definitive radiation therapy with or without ADT, Black patients appear to have lower risk of biochemical recurrence, distant metastasis, and prostate cancer-specific mortality compared to White patients**

individual patient data meta-analysis[JAMA Netw Open 2021 Dec 1;4(12):e2139769](https://pubmed.ncbi.nlm.nih.gov/34964855)

studySummary

* + individual patient data meta-analysisbased on meta-analysis of individual patient data from randomized trials
  + meta-analysis of individual patient data from 7 randomized trials conducted by NRG Oncology/Radiation Therapy Oncology Group in 1990-2010 evaluating outcomes in patients with localized prostate cancer receiving definitive radiation therapy with or without ADT
  + 8,814 patients (mean age 69 years) who self-identified as White (81.5%) or Black (18.5%) were included in analysis
  + compared to White patients, Black patients were younger (median age 68 years vs. 71 years) and were more likely to have high-risk disease (38% vs. 30%)
  + median follow-up was 10.6 years for surviving patients
  + estimated 10-year cumulative incidence of outcomes comparing Black vs. White patients
    - biochemical recurrence 40.5% vs. 44.6% (adjusted subdistribution hazard ratio [sHR] 0.79, 95% CI 0.72-0.88)
    - distant metastasis 8.4% vs. 11.6% (adjusted sHR 0.69, 95% CI 0.55-0.87)
    - prostate cancer-specific mortality 4.5% vs. 6.4% (adjusted sHR 0.68, 95% CI 0.5-0.93)
    - all-cause mortality 39.8% vs. 41.2% (no sHR reported)
  + PubMed34964855JAMA network openJAMA Netw Open20211201412e2139769e2139769Reference - [JAMA Netw Open 2021 Dec 1;4(12):e2139769](https://pubmed.ncbi.nlm.nih.gov/34964855), editorial can be found in [JAMA Netw Open 2021 Dec 1;4(12):e2140692](https://pubmed.ncbi.nlm.nih.gov/34964857)
* **distant metastases after salvage radiation therapy associated with increased mortality in patients with prostate cancer**

Cohort Study[29306514Eur Urol 2018 Oct;74(4):413](http://pubmed.ncbi.nlm.nih.gov/29306514?dopt=Abstract)

studySummarydistant metastases after postprostatectomy radiation therapy associated with increased mortality in men with prostate cancer (Eur Urol 2018 Oct)07/17/2018 04:36:00 PMOncologic\_DiseaseUrologic\_DisordersOncologic\_Disease Urologic\_Disordersdistant metastases after postprostatectomy radiation therapy associated with increased mortality in men with prostate cancer (Eur Urol 2018 Oct)07/17/2018 04:36:00 PM

* + based on retrospective cohort study Cohort Study
  + 566 patients (median age 63 years) who had radiation therapy following prostatectomy were followed for median 8.2 years
  + overall survival was
    - 98% at 1 year
    - 95% at 3 years
    - 90% at 5 years
    - 82% at 7 years
  + increased mortality after salvage radiation therapy associated with
    - distant metastases (hazard ratio [HR] 6.52, 95% CI 4.2-10.1)
    - castration-resistant prostate cancer (HR 2.47, 95% CI 1.56-3.92)
    - biochemical failure (HR 2.32, 95% CI 1.45-3.71)
  + distant metastases at 5 years had good discrimination for predicting overall survival in adjusted analysis (c-statistic 0.784)
  + PubMed29306514European urology20181001Eur Urol744413413 Reference - [29306514Eur Urol 2018 Oct;74(4):413](http://pubmed.ncbi.nlm.nih.gov/29306514?dopt=Abstract)
* **positive biopsy 2 years after starting radiation therapy associated with reduced biochemical progression-free survival but not overall survival in patients with nonmetastatic prostate cancer**

Randomized Trial[29307509Eur Urol 2018 Jun;73(6):968](http://pubmed.ncbi.nlm.nih.gov/29307509?dopt=Abstract)[Full Text](https://www.sciencedirect.com/science/article/pii/S0302283817310631?via%3Dihub)

studySummarypositive biopsy 2 years after starting radiation therapy associated with reduced biochemical progression-free survival but not overall survival in men with nonmetastatic prostate cancer (Eur Urol 2018 Jun)08/20/2018 05:32:00 PMGeriatricsOncologic\_DiseaseSurgery\_and\_ProceduresUrologic\_DisordersGeriatrics Oncologic\_Disease Surgery\_and\_Procedures Urologic\_Disorderspositive biopsy 2 years after starting radiation therapy associated with reduced biochemical progression-free survival but not overall survival in men with nonmetastatic prostate cancer (Eur Urol 2018 Jun)08/20/2018 05:32:00 PM29307509

* + based on cohort analysis of data from randomized trial Randomized Trial
  + 177 patients with T1b-T3a, N0, M0 prostate cancer who had prostate biopsy 18-36 months after radiation therapy were evaluated
    - all patients had PSA < 50 ng/mL prior to start of radiation therapy
    - median time from start of radiation therapy to biopsy 2.1 years
  + biopsy outcomes classified as positive (residual malignancy in any cells), negative (no malignant cells), or suspicious (inability to distinguish cancerous cells from radiation atypia)
  + biochemical progression defined as PSA > 2 ng/mL ≥ 6 months after start of radiation therapy and PSA increase from nadir by ≥ 50%
  + biochemical progression-free survival defined as freedom from biochemical progression, death from prostate cancer, or development of local, nodal, or metastatic disease
  + median follow-up 7.8 years after biopsy
  + compared to negative or suspicious biopsy, positive biopsy associated with increased risk for biochemical progression
  + biochemical progression-free survival
    - 14% in patients with positive biopsy (hazard ratio for progression 4.81, 95% CI 2.5-9.26 vs. suspicious and negative biopsy)
    - 67% in patients with suspicious biopsy
    - 68% in patients with negative biopsy
  + no significant differences among biopsy groups in overall survival or metastasis-free survival
  + other factors significantly associated with reduced biochemical progression-free survival included higher prostate-specific antigen level at 2-year follow-up and stage ≥ T3 disease
  + PubMed29307509European urology20180601Eur Urol736968968 Reference - [29307509Eur Urol 2018 Jun;73(6):968](http://pubmed.ncbi.nlm.nih.gov/29307509?dopt=Abstract)[full-text](https://www.sciencedirect.com/science/article/pii/S0302283817310631?via%3Dihub)
* **in patients with T1b-T2b prostate cancer treated with definitive radiation therapy, positive biopsy after radiation therapy associated with slightly decreased disease-specific survival**

Cohort Study[26104939Int J Radiat Oncol Biol Phys 2015 Jul 15;92(4):863](http://pubmed.ncbi.nlm.nih.gov/26104939?dopt=Abstract)

studySummary

* + based on cohort study Cohort Study
  + 831 patients (median age 70 years) with stage T1b-T2b prostate cancer treated with definitive radiation therapy (with or without complete androgen blockade) had postradiation biopsy 24 months after treatment and were followed for median 9 years
  + factors associated with higher risk of positive postradiation biopsy included
    - stage T2 (p = 0.001)
    - Gleason score ≥ 7 (p = 0.04)
    - radiation therapy alone (p = 0.0001)
  + comparing positive postradiation biopsy vs. negative biopsy
    - 10-year disease-specific survival 92% vs. 98% (p = 0.0001)
    - 10-year biochemical relapse rate 49% vs. 34% (p < 0.0001)
    - 10-year distant metastases rate 8% vs. 4% (p = 0.003)
  + PubMed26104939International journal of radiation oncology, biology, physics20150715Int J Radiat Oncol Biol Phys924863863 Reference - [26104939Int J Radiat Oncol Biol Phys 2015 Jul 15;92(4):863](http://pubmed.ncbi.nlm.nih.gov/26104939?dopt=Abstract)
* **perineural invasion associated with increased risk for biochemical recurrence following definitive radiation therapy**

Systematic Review[mnh29390991pcxh127744206t pmdc29390991pBMC Urol 2018 Feb 1;18(1):5](http://pubmed.ncbi.nlm.nih.gov/29390991?dopt=Abstract)[Full Text](https://bmcurol.biomedcentral.com/articles/10.1186/s12894-018-0319-6)

studySummary

* + based on systematic review limited by heterogeneity Systematic Review
  + systematic review of 19 retrospective cohort studies evaluating association between perineural invasion and biochemical recurrence following radical prostatectomy (13 studies) or radiation therapy (6 studies) in 13,412 patients treated for prostate cancer
  + biochemical recurrence after radiation therapy defined as PSA level ≥ 2 ng/mL above nadir
  + 31% had perineural invasion
  + perineural invasion associated with higher risk of biochemical recurrence after radiation therapy in analysis of 6 studies with 2,605 patients (pooled hazard ratio 1.22, 95% CI 1.12-1.34), results limited by significant heterogeneity
  + PubMed29390991BMC urology20180201BMC Urol18155 Reference - [mnh29390991pcxh127744206t pmdc29390991pBMC Urol 2018 Feb 1;18(1):5](http://pubmed.ncbi.nlm.nih.gov/29390991?dopt=Abstract)[full-text](https://bmcurol.biomedcentral.com/articles/10.1186/s12894-018-0319-6)
* **nadir PSA < 0.4 ng/mL after radiation therapy associated with increased biochemical disease-free survival in patients with intermediate-risk prostate cancer**

Cohort Study[25770875Radiother Oncol 2015 Apr;115(1):84](http://pubmed.ncbi.nlm.nih.gov/25770875?dopt=Abstract)

studySummary

* + based on cohort study Cohort Study
  + 183 patients (median age 67 years) with National Comprehensive Cancer Network (NCCN) intermediate-risk prostate cancer without metastases who were treated with high-dose-rate (HDR) brachytherapy boost prior to external beam radiation therapy (EBRT) in 2 uncontrolled trials
    - 59% had stage T1c prostate cancer
    - 41% had stage T2 prostate cancer
  + median follow-up 74 months
  + nadir PSA (defined as lowest PSA after treatment and before salvage therapy) measured in 180 patients
    - median nadir PSA was 0.08 ng/mL
    - 29 (16%) had nadir PSA < 0.4 ng/mL
    - 151 (84%) had nadir PSA ≥ 0.4 ng/mL
  + 6.6% had biochemical relapse defined as ≥ 2 ng/mL increase from PSA nadir
  + 5-year biochemical disease-free survival was 100% in patients who had nadir PSA < 0.4 ng/mL vs. 72% in patients with nadir PSA ≥ 0.4 ng/mL (p < 0.0001)
  + PubMed25770875Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology20150401Radiother Oncol11518484 Reference - [25770875Radiother Oncol 2015 Apr;115(1):84](http://pubmed.ncbi.nlm.nih.gov/25770875?dopt=Abstract)

Prognosis After Biochemical Recurrence

* EAU risk stratification of overall and cancer-specific mortality and distant metastases for patients with biochemical recurrence:
  + Risk stratification for biochemical recurrence after radical prostatectomy:
    - Patients are stratified as low risk if both of the following criteria are fulfilled:
      * Prostate-specific antigen (PSA)-doubling time (PSADT) > 1 year
      * Pathological International Society of Urological Pathology (ISUP) grade group < 4 (Gleason score < 8)
    - Patients are stratified as high risk if either of the following criteria is fulfilled:
      * PSADT < 1 year
      * Pathological ISUP grade group 4-5 (Gleason score 8-10)
  + Risk stratification for biochemical recurrence after radiation therapy:
    - Patients are stratified as low risk if both of the following are fulfilled:
      * Interval to biochemical failure > 18 months
      * Biopsy ISUP grade group < 4 (Gleason score < 8)
    - Patients are stratified as high risk if either of the following is fulfilled:
      * Interval to biochemical failure < 18 months
      * Biopsy ISUP grade group 4-5 (Gleason score 8-10)
  + Reference - [EAU 2024 Apr](https://uroweb.org/guidelines/prostate-cancer)[PDF](https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-EANM-ESTRO-ESUR-ISUP-SIOG-Guidelines-on-Prostate-Cancer-2024.pdf)
* **EAU stratification helps predict cancer-specific and metastatic progression-free survival in patients with biochemical recurrence after radical prostatectomy for prostate cancer (**[**level 1 [likely reliable] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Prediction Rule[Eur Urol 2019 Jun;75(6):896](http://pubmed.ncbi.nlm.nih.gov/30955970)

studySummary

* + Prediction Rule based on prognostic cohort study
  + 1,040 patients (median age 63 years) with biochemical recurrence (rising PSA level of ≥ 0.2 ng/mL on 2 consecutive measurements) after radical prostatectomy of prostate cancer were evaluated
  + patients were excluded if after prostatectomy
    - they received any neoadjuvant or adjuvant therapies
    - they developed PSA persistence
  + [EAU stratification](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_VQJ_RWQ_RNB__LI_J23_4RN_QYB) classified 510 patients as low risk of mortality and 530 patients as high risk of mortality
  + median follow-up for surviving patients 65 months from biochemical recurrence
  + comparing patients at low vs. high-risk
    - 5-year prostate cancer-specific survival 99.7% vs. 93.8% (p < 0.001)
    - 5-year metastatic progression-free survival 97.5% vs. 86.7% (p < 0.001)
  + PubMed30955970European urologyEur Urol20190601756896-900896Reference - [Eur Urol 2019 Jun;75(6):896](http://pubmed.ncbi.nlm.nih.gov/30955970)
* **4 risk factors may help stratify risk of distant metastases and prostate cancer-specific mortality in patients with biochemical relapse following external beam radiation therapy (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Prediction Rule[25308970Eur Urol 2015 Jun;67(6):1009](http://pubmed.ncbi.nlm.nih.gov/25308970?dopt=Abstract)

studySummary2

* + based on prognostic cohort study without validation Prediction Rule
  + 609 patients (median age 68 years) with localized prostate cancer treated with external beam radiation therapy and having biochemical recurrence in 1991-2008 were followed for median 122 months
  + from date of biochemical failure, median time to distant metastases 5.4 years, and median time to prostate cancer-specific mortality 10.5 years
  + factors significantly associated with decreased time to clinical progression (distant metastases, prostate cancer-specific mortality, and any death) in multivariate analysis
    - pretreatment Gleason score 8-10 (p < 0.0001)
    - pretreatment clinical tumor stage T3b-T4 (p = 0.0001)
    - posttreatment prostate-specific antigen (PSA) doubling time < 3 months (p = 0.0008)
    - posttreatment interval to biochemical failure < 3 years (p = 0.01)
  + patients were stratified into 3 risk categories for clinical progression for
    - 0 risk factors
    - 1 risk factor
    - ≥ 2 risk factors
  + incidence of distant metastases at 4 years after biochemical recurrence by risk category (extrapolated from graph)
    - 20% for 0 risk factors (p < 0.0001 vs. other groups in pairwise comparisons)
    - 38% for 1 risk factor
    - 75% for ≥ 2 risk factors
  + incidence of prostate cancer-specific mortality at 4 years after biochemical recurrence by risk category (extrapolated from graph)
    - 5% for 0 risk factors (p = 0.02 vs. 1 risk factor, p < 0.001 vs. 2 risk factors)
    - 15% for 1 risk factor (p = 0.02 compared to 0 risk factors)
    - 20% for ≥ 2 risk factors (p < 0.001 compared to 0 risk factors)
  + PubMed25308970European urology20150601Eur Urol67610091009 Reference - [25308970Eur Urol 2015 Jun;67(6):1009](http://pubmed.ncbi.nlm.nih.gov/25308970?dopt=Abstract)

Prognosis After Management of Metastatic Castration-Resistant Disease

* **prognostic model helps predict overall survival in patients who have received first-line chemotherapy or first-line enzalutamide and/or abiraterone acetate for metastatic castration-resistant prostate cancer (**[**level 1 [likely reliable] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Prediction Rule[24449231J Clin Oncol 2014 Mar 1;32(7):671](http://pubmed.ncbi.nlm.nih.gov/24449231?dopt=Abstract)Prediction Rule[37040594J Clin Oncol 2023 May 20;41(15):2736](http://pubmed.ncbi.nlm.nih.gov/37040594?dopt=Abstract)

studySummary1

* + based on prognostic cohort study with independent derivation and validation cohorts Prediction RulePrediction Rule
  + original prognostic cohort study
    - 1,050 patients with metastatic castration-resistant prostate cancer receiving first-line docetaxel with follow-up at 17- and 30-months were allocated to derivation cohort (705 patients) or internal validation cohort (345 patients)
    - external validation cohort included 942 similar patients receiving first-line docetaxel with follow-up at 14- and 26-months
    - median overall survival was 22.2 months in derivation cohort, 21.9 months in internal validation cohort, and 19.2 months in external validation cohort
    - model to predict overall survival derived using 8 factors
      * Eastern Cooperative Oncology Group performance status
      * disease site
      * opioid analgesic use
      * lactate dehydrogenase level
      * albumin level
      * hemoglobin level
      * prostate-specific antigen (PSA) level
      * alkaline phosphatase level
    - model classifies patients into low and high-risk categories (or low, intermediate, or high-risk categories in alternate version)
    - median survival by risk category
      * for high-risk, 17 months in derivation cohort and 14 months in external validation cohort
      * for low-risk, 31 months in derivation cohort and 26 months in external validation cohort
    - prognostic model had modest discrimination in both derivation cohort (c-statistic 0.66) and validation cohort (c-statistic 0.69)
    - online calculator at [first-line metastatic castrate-resistant prostate cancer patients](https://www.cancer.duke.edu/Nomogram/firstlinechemotherapy.html)
    - PubMed24449231Journal of clinical oncology : official journal of the American Society of Clinical Oncology20140301J Clin Oncol327671671 Reference - [24449231J Clin Oncol 2014 Mar 1;32(7):671](http://pubmed.ncbi.nlm.nih.gov/24449231?dopt=Abstract)
  + TOPIC\_UGW\_PXQ\_RNB\_\_LI\_RQ4\_Q3L\_B1CEU01112404/05/2024 11:40:00 AMevidenceUpdatestandardOncologic\_Disease Urologic\_Disordersprognostic model helps predict overall survival in patients who have received first-line chemotherapy or first-line enzalutamide and/or abiraterone acetate for metastatic castration-resistant prostate cancer (J Clin Oncol 2023 May 20)external validation cohort included 8,083 patients (median age 70 years) with metastatic castration-resistant prostate cancer who received first-line therapy from 7 randomized trials (ENTHUSE-33, MAINSAIL, READY, SYNGERGY, TASQ, A031201, and ACIS trials)
    - 4,545 patients from 4 trials received first-line docetaxel
    - 3,538 patients from 3 trials did not receive first-line docetaxel, including
      * 1,245 patients from 1 trial who received first-line tasquinimod or placebo
      * 1,311 patients from 1 trial who received first-line enzalutamide with or without abiraterone acetate
      * 982 patients from 1 trial who received first-line abiraterone acetate with or without apalutamide
    - median follow-up 31.9 months
    - median overall survival range 18.3-34.7 months
    - median overall survival when stratified into 2 risk categories in external validation cohort
      * for patients who have not received first-line enzalutamide and/or abiraterone acetate
        + 27.6 months in 3,218 patients with low risk
        + 13.8 months in 2,274 patients with high risk
      * for patients who have received first-line enzalutamide and/or abiraterone acetate
        + 41.1 months in 1,597 patients with low risk
        + 20 months in 597 patients with high risk
    - median overall survival when stratified into 3 risk categories
      * for patients who have not received first-line enzalutamide and/or abiraterone acetate
        + 29.7 months in 2,378 patients with low risk
        + 19 months in 1,607 patients with intermediate risk
        + 12.1 months in 1,507 patients with high risk
      * for patients who have received first-line enzalutamide and/or abiraterone acetate
        + 45.9 months in 1,176 patients with low risk
        + 29.8 months in 703 patients with intermediate risk
        + 16.8 months in 315 patients with high risk
    - prognostic model had good discrimination for predicting overall survival (c-statistic 0.75 adjusted for the use of enzalutamide and/or abiraterone acetate)
    - Reference - [37040594J Clin Oncol 2023 May 20;41(15):2736](http://pubmed.ncbi.nlm.nih.gov/37040594?dopt=Abstract), editorial can be found in [37040577J Clin Oncol 2023 May 20;41(15):2695](http://pubmed.ncbi.nlm.nih.gov/37040577?dopt=Abstract)
* TOPIC\_UGW\_PXQ\_RNB\_\_LI\_MHF\_XGF\_Z1CEU04052404/05/2024 11:39:33 AMevidenceUpdatelowOncologic\_Disease Urologic\_Disordersprognostic risk stratification and nomogram help predict overall survival in patients with metastatic castration-resistant prostate cancer who received or did not receive first-line enzalutamide or abiraterone acetate (Eur Urol 2021 Nov)

**prognostic risk stratification and nomogram help predict overall survival in patients with metastatic castration-resistant prostate cancer who received or did not receive first-line enzalutamide or abiraterone acetate (**[**level 1 [likely reliable] evidence**](https://www.ebsco.com/clinical-decisions/dynamed-solutions/about/evidence-based-process/editorial-process)**)**

Prediction Rule[30202945Ann Oncol 2018 Nov 1;29(11):2200](http://pubmed.ncbi.nlm.nih.gov/30202945?dopt=Abstract)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6888025/)Prediction Rule[Eur Urol 2020 Sep;78(3):347](http://doi.org/10.1016/j.eururo.2020.04.061)Prediction Rule[Eur Urol 2021 Nov;80(5):641](http://doi.org/10.1016/j.eururo.2021.07.014)

studySummary

* + Prediction RulePrediction RulePrediction Rule based on independent derivation and validation cohort studies
  + initial prognostic cohort study without external validation
    - 1,709 patients with metastatic castration-resistant prostate cancer who received first-line enzalutamide or placebo from the PREVAIL trial were randomized to derivation cohort (1,159 patients, median age 71 years), and validation cohort (550 patients, median age 71-72 years)
    - 51% in each derivation cohort and validation cohort received enzalutamide
    - median overall survival was 32.7 months in derivation and validation cohorts
    - risk stratification was developed using 11 risk factors significantly associated with decreased overall survival in derivation cohort, including
      * serum albumin level < 4 g/dL
      * serum alkaline phosphatase level ≥ upper limit of normal
      * serum hemoglobin level < 12.5 g/dL
      * serum lactate dehydrogenase level ≥ upper limit of normal
      * neutrophil-to-lymphocyte ratio ≥ 2.5
      * ≥ 10 bone metastases
      * pain score ≥ 2
      * presence of liver metastases (vs. bone metastases only, or lymph node metastases only)
      * serum prostate-specific antigen (PSA) level > 50 ng/mL
      * < 60 months since diagnosis
      * no use of enzalutamide
    - patients were stratified by number of risk factors
      * low risk if patients had 0-3 risk factors
      * intermediate risk if patients had 4-6 risk factors
      * high risk if patients had 7-10 risk factors
    - 2-year overall survival (estimated from graph) in validation cohort by risk stratification using the number of risk factors
      * 80% in 244 patients with low risk
      * 65% in 233 patients with intermediate risk
      * 25% in 73 patients with high risk
    - nomogram and risk score were also developed using the same 11 factors
    - nomogram stratified the patients by tertiles of the risk score into low, intermediate, and high risk
    - 3-year overall survival (estimated from graph) in validation cohort by nomogram risk stratification
      * 80% in 184 patients with low risk
      * 48% in 182 patients with intermediate risk
      * 20% in 184 patients with high risk
    - see articles for details of nomogram
    - Reference - [30202945Ann Oncol 2018 Nov 1;29(11):2200](http://pubmed.ncbi.nlm.nih.gov/30202945?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6888025/)
  + initial prognostic cohort study without external validation at median follow-up of 69 months
    - 1,709 patients from PREVAIL trial were included in analysis
    - 5-year overall survival 26% in patients who received enzalutamide and 21% in patients who received placebo
    - overall survival by risk stratification
      * 5-year overall survival in all 1,709 patients by risk stratification using the number of risk factors
        + 37% in 857 patients with low risk
        + 11% in 778 patients with intermediate risk
        + 1% in 74 patients with high risk
      * 5-year overall survival in all 1,709 patients by nomogram risk stratification
        + 42% in 570 patients with low risk
        + 24% in 569 patients with intermediate risk
        + 5% in 570 patients with high risk
    - Reference - [Eur Urol 2020 Sep;78(3):347](http://doi.org/10.1016/j.eururo.2020.04.061)
  + external validation cohort study
    - 1,088 patients with asymptomatic or mildly symptomatic metastatic castration-resistant prostate cancer who received first-line abiraterone acetate or placebo from COU-AA-302 trial were included as external validation cohort
    - median follow-up 47.9 months
    - median overall survival 33 months
    - no use of abiraterone acetate was substituted for no use of enzalutamide as the risk factor from the original prediction rule
    - 3-year overall survival (estimated from graph) in external validation cohort by risk stratification using the number of risk factors
      * 60% in 536 patients with low risk
      * 31% in 443 patients with intermediate risk
      * 13% in 109 patients with high risk
    - 3-year overall survival (estimated from graph) in external validation cohort by nomogram risk stratification
      * 65% in 363 patients with low risk
      * 40% in 363 patients with intermediate risk
      * 23% in 362 patients with high risk
    - Reference - [Eur Urol 2021 Nov;80(5):641](http://doi.org/10.1016/j.eururo.2021.07.014)
* **prognostic score predicts overall survival in patients with metastatic castration-resistant prostate cancer after first-line chemotherapy (**[**level 1 [likely reliable] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Prediction Rule[24136890J Natl Cancer Inst 2013 Nov 20;105(22):1729](http://pubmed.ncbi.nlm.nih.gov/24136890?dopt=Abstract)

studySummary1

* + based on prognostic cohort study with independent derivation and validation cohorts Prediction Rule
  + derivation and internal validation cohort included 755 patients (median age 67 years) from TROPIC trial with metastatic castration-resistant prostate cancer with progressive disease after first-line docetaxel-based chemotherapy
  + external validation cohort included 488 patients (median age 70 years) from SPARC trial with metastatic castration-resistant prostate cancer previously treated with docetaxel
  + prognostic score derived based on factors associated with overall survival in derivation cohort (online calculator can be found at [prediction tool for Metastatic Castrate Resistant Prostate Cancer Patients](https://www.cancer.duke.edu/Nomogram/secondlinechemotherapy.html))
  + score used to categorize patients into
    - 2 groups with low risk (< 188 points) or high risk (≥ 188 points)
    - 3 groups with low risk (< 175 points), intermediate risk (175-198.8 points), or high risk (> 198.8 points)
  + median survival 16.1 months in validation cohort
  + median overall survival in validation cohort by risk category using 3-group classification
    - 9.7 months (95% CI 8.8-10.8 months) in 112 high-risk patients
    - 15.9 months (95% CI12.6-19.2 months) in 118 intermediate-risk patients
    - 21.7 months (95% CI 20-23.9 months) in 189 low-risk patients
  + PubMed24136890Journal of the National Cancer Institute20131120J Natl Cancer Inst1052217291729 Reference - [24136890J Natl Cancer Inst 2013 Nov 20;105(22):1729](http://pubmed.ncbi.nlm.nih.gov/24136890?dopt=Abstract)
* **6-factor prognostic model predicts overall survival in metastatic castration-resistant prostate cancer treated with abiraterone or prednisone after first-line docetaxel (**[**level 1 [likely reliable] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Prediction Rule[26685010Ann Oncol 2016 Mar;27(3):454](http://pubmed.ncbi.nlm.nih.gov/26685010?dopt=Abstract)[Full Text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4769990/)

studySummary1

* + based on prognostic cohort study with independent derivation and validation cohorts Prediction Rule
  + derivation cohort included 762 patients with metastatic castration-resistant prostate cancer treated with abiraterone plus prednisone after progressing with first-line docetaxel
  + external validation cohort included 286 similar patients with same treatment
  + internal validation cohort included 398 similar patients treated with prednisone alone after progressing with first-line docetaxel
  + prognostic model derived using six factors significantly associated with reduced overall survival in derivation cohort
    - lactate dehydrogenase > 250 IU/L (upper limit of normal)
    - Eastern Cooperative Oncology Group (ECOG) Performance Status ≥ 2
    - presence of liver metastases
    - albumin ≤ 4 g/dL
    - alkaline phosphatase > 160 IU/L (upper limit of normal)
    - time from start of androgen-deprivation therapy to start of treatment with abiraterone plus prednisone ≤ 36 months
  + 3 categories to predict prognosis were defined by number of factors present

| Median Overall Survival by Prognostic Category | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Prognosis** | **Derivation Cohort** | | **External Validation Cohort** | | **Internal Validation Cohort** | |
| **Median Survival** | **Number of Patients** | **Median Survival** | **Number of Patients** | **Median Survival** | **Number of Patients** |
| Good (0-1 risk factors) | 21.3 months | 369 | 23.9 months | 63 | 19.7 months | 193 |
| Intermediate (2-3 risk factors) | 13.9 months | 321 | 16.2 months | 146 | 8.7 months | 149 |
| Poor (≥ 4 risk factors) | 6.1 months | 107 | 8.2 months | 77 | 5.3 months | 56 |

* + PubMed26685010Annals of oncology : official journal of the European Society for Medical Oncology20160301Ann Oncol273454454 Reference - [26685010Ann Oncol 2016 Mar;27(3):454](http://pubmed.ncbi.nlm.nih.gov/26685010?dopt=Abstract)[full-text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4769990/)
* **specific metastasis site associated with differential overall survival, with liver metastases associated with lowest survival in patients treated for metastatic castration-resistant prostate cancer**

Systematic Review[cxh115250208pmdc26951312pJ Clin Oncol 2016 May 10;34(14):1652](http://pubmed.ncbi.nlm.nih.gov/26951312?dopt=Abstract)

studySummary

* + based on systematic review of individual patient data without assessment of trial quality Systematic Review
  + systematic review of individual patient data from 9 randomized trials evaluating association between metastasis site and survival in 8,820 patients treated for metastatic castration-resistant prostate cancer
  + most common metastasis sites included
    - bone in 72.8% (29.8% also had lymph node involvement)
    - visceral sites in 20.8% (9.1% had lung metastases and 8.6% had liver metastases)
    - lymph nodes only in 6.4%
  + 62% died during median follow-up 21.8 months
  + median overall survival by metastasis site
    - 31.6 months (95% CI 27.9-35.5 months) in patients with lymph node-only metastasis (p < 0.05 vs. each of other sites)
    - 21.3 months (95% CI 20.5-21.9 months) in patients with bone metastases (p < 0.05 vs. each of lung and liver metastases)
    - 19.4 months (95% CI 17.8-20.7 months) in patients with lung metastases (p < 0.05 vs. liver metastasis)
    - 13.5 months (95% CI 12.7-14.4 months) in patients with liver metastases
  + PubMed26951312Journal of clinical oncology : official journal of the American Society of Clinical Oncology20160510J Clin Oncol341416521652 Reference - [cxh115250208pmdc26951312pJ Clin Oncol 2016 May 10;34(14):1652](http://pubmed.ncbi.nlm.nih.gov/26951312?dopt=Abstract)

Lifestyle Factors for Prognostication

* Smoking:
  + **current smoking associated with increased risk of cancer-specific mortality, metastasis, and biochemical recurrence in patients who were treated with definitive therapy for localized prostate cancer**

Systematic Review[JAMA Oncol 2018 Jul 1;4(7):953](http://pubmed.ncbi.nlm.nih.gov/29800115/)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6145736/)

studySummary

* + - Systematic Review based on systematic review of observational studies
    - systematic review of 16 observational studies (11 retrospective cohort studies, 4 prospective cohort studies, and 1 case-control study) evaluating association of smoking with prognosis in patients who were treated with definitive radical prostatectomy or radiation therapy for localized prostate cancer
    - 11 studies with 22,549 patients were included in meta-analysis
    - 4,202 patients (18.6%) were current smokers
    - median follow-up 72 months
    - compared to never or former smoking, current smoking status associated with increased risk of
      * cancer-specific mortality (hazard ratio [HR] 1.89, 95% CI 1.37-2.6) in analysis of 5 studies
      * metastasis (HR 2.51, 95% CI 1.8-3.51) in analysis of 3 studies
      * biochemical recurrence (HR 1.4, 95% CI 1.18-1.66) in analysis of 10 studies, results limited by significant heterogeneity
    - comparing former smoking to never smoking
      * former smoking associated with increased risk of biochemical recurrence (HR 1.19, 95% CI 1.09-1.3) in analysis of 7 studies
      * no significant differences in risk of
        + cancer-specific mortality in analysis of 4 studies
        + metastasis in analysis of 2 studies, results limited by significant heterogeneity
    - PubMed29800115JAMA oncologyJAMA Oncol2018070147953-961953Reference - [JAMA Oncol 2018 Jul 1;4(7):953](http://pubmed.ncbi.nlm.nih.gov/29800115/)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6145736/)

Medical Factors for Prognostication

Tumor and Microenvironment Characteristics

* **in patients with intermediate- or high-risk prostate cancer treated with radiation therapy, intraductal carcinoma may be associated with increased risk of early biochemical relapse and clinical progression**

Cohort Study[22405699Eur J Cancer 2012 Jun;48(9):1318](http://pubmed.ncbi.nlm.nih.gov/22405699?dopt=Abstract)

studySummary

* + based on retrospective cohort study Cohort Study
  + diagnostic specimens (prostate biopsy or transurethral resections) from 2 cohorts of patients with prostate cancer were assessed for intraductal carcinoma
    - 118 patients with intermediate-risk prostate cancer treated with radiation therapy were followed for median 6.5 years
    - 132 patients with high-risk prostate cancer who were allocated to radiation therapy plus long-term androgen deprivation vs. radiation therapy alone were followed for median 9.1 years
  + in analysis of all intermediate-risk patients
    - intraductal carcinoma identified in 19%
    - biochemical relapse in 23%
    - intraductal carcinoma associated with increased risk of biochemical relapse within 36 months of treatment initiation (hazard ratio [HR] 7.3, 95% CI 1.7-30.4)
  + in analysis of 130 high-risk patients with assessable data
    - intraductal carcinoma identified in 22%
    - intraductal carcinoma associated with increased risk of clinical progression
      * HR 2.83 (95% CI 1.16-6.92) for patients treated with radiation therapy plus long-term androgen deprivation
      * HR 3.54 (95% CI 1.88-6.69) for patients treated with radiation therapy alone
  + PubMed22405699European journal of cancer20120601Eur J Cancer48913181318 Reference - [22405699Eur J Cancer 2012 Jun;48(9):1318](http://pubmed.ncbi.nlm.nih.gov/22405699?dopt=Abstract)

Medication Use

* There is inconsistent evidence for the effect of aspirin on prostate cancer-related mortality.
  + **in patients with localized adenocarcinoma treated with radical prostatectomy or radiation therapy, aspirin use may be associated with decreased prostate cancer-related mortality**

Cohort Study[cxh82203241pmdc22927523pJ Clin Oncol 2012 Oct 1;30(28):3540](http://pubmed.ncbi.nlm.nih.gov/22927523?dopt=Abstract)[Full Text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3454771/)

studySummary

* + - based on retrospective cohort study Cohort Study
    - 5,955 patients (median age 64 years) with localized adenocarcinoma of prostate and treated with radical prostatectomy or radiation therapy followed for median 70 months
    - 37% received anticoagulants (84% with aspirin, 21% with warfarin, 14% with clopidogrel hydrogen sulfate, and 1% with enoxaparin)
    - 3.2% prostate cancer-related mortality during follow-up
    - aspirin use independently associated with reduced risk of prostate cancer-related mortality in multivariate analysis (adjusted hazard ratio 0.43, 95% CI 0.21-0.87)
    - comparing anticoagulant use vs. no anticoagulant use at 10 years (unadjusted analyses)
      * prostate cancer-related mortality 3% vs. 8% (p < 0.01)
      * prostate cancer recurrence in 28% vs. 36% (p < 0.01)
      * bone metastasis in 3% vs. 6% (p < 0.01)
    - PubMed22927523Journal of clinical oncology : official journal of the American Society of Clinical Oncology20121001J Clin Oncol302835403540 Reference - [cxh82203241pmdc22927523pJ Clin Oncol 2012 Oct 1;30(28):3540](http://pubmed.ncbi.nlm.nih.gov/22927523?dopt=Abstract)[full-text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3454771/)
  + **in most patients with nonmetastatic prostate cancer, daily aspirin use may not be associated with decreased prostate cancer-specific mortality**

Cohort Study[cxh99361241pmdc25332245pJ Clin Oncol 2014 Nov 20;32(33):3716](http://pubmed.ncbi.nlm.nih.gov/25332245?dopt=Abstract)

studySummary

* + - based on cohort study Cohort Study
    - 8,427 patients with nonmetastatic prostate cancer with data on daily aspirin use prior to diagnosis (based on questionnaire completed at mean 1.6 years before diagnosis) were evaluated
      * daily aspirin use in 36% and no use in 43%
      * mean follow-up 9.3 years
      * no significant difference in prostate cancer-specific mortality comparing daily aspirin use vs. no use in adjusted analysis
    - 7,118 patients with nonmetastatic prostate cancer with data on daily aspirin use after diagnosis (based on questionnaire completed at mean 1.4 years after diagnosis) were evaluated
      * daily aspirin use in 42% and no use in 42%
      * mean follow-up 6.4 years
      * no significant difference in prostate cancer-specific mortality in overall analysis comparing daily aspirin use vs. no use in adjusted analysis
      * in subgroup of patients with high-risk cancer (Gleason score ≥ 8 and/or stage T3), aspirin use after diagnosis associated with reduced risk of prostate cancer-specific death (hazard ratio 0.73, 95% CI 0.37-0.97)
    - PubMed25332245Journal of clinical oncology : official journal of the American Society of Clinical Oncology20141120J Clin Oncol323337163716 Reference - [cxh99361241pmdc25332245pJ Clin Oncol 2014 Nov 20;32(33):3716](http://pubmed.ncbi.nlm.nih.gov/25332245?dopt=Abstract)

Medical Comorbidities

* Body mass index (BMI):
  + **BMI > 25 kg/m2 at age 20 years but not at age 50 years associated with increased risk of fatal prostate cancer**

Randomized Trial[27754927 J Natl Cancer Inst 2017 Mar;109(3):djw225](http://pubmed.ncbi.nlm.nih.gov/27754927?dopt=Abstract)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5074530/)

studySummary

* + - based on cohort analysis of data from randomized trial Randomized Trial
    - 69,873 adults aged 55-74 years from PLCO Cancer Screening trial were assessed according to body mass index (BMI) and followed for median 11.5 years
    - at baseline, patients reported current height and body weight and recalled weight at 20 and 50 years of age
    - incident prostate cancer in 7,822 adults (aggressive in 58.6% and fatal in 3.3%)
    - compared to never having BMI > 25 kg/m2,
      * BMI > 25 kg/m2 at age 20 years associated with increased risk of fatal prostate cancer (adjusted hazard ratio [HR] 1.53, 95% CI 1.05-2.24)
      * no significant difference in risk of fatal prostate cancer associated with BMI > 25 kg/m2 at age 50 years (adjusted HR 1.14, 95% CI 0.8-1.61)
    - PubMed27754927Journal of the National Cancer Institute20170301J Natl Cancer Inst1093djw225djw225 Reference - [27754927 J Natl Cancer Inst 2017 Mar;109(3):djw225](http://pubmed.ncbi.nlm.nih.gov/27754927?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5074530/)
  + **higher BMI may be associated with improved overall and progression-free survival in hormone-sensitive metastatic prostate cancer, but not castration-resistant prostate cancer**

Cohort Study[17868721J Urol 2007 Nov;178(5):1946](http://pubmed.ncbi.nlm.nih.gov/17868721?dopt=Abstract)

studySummary

* + - based on pooled cohort analysis with 2 cohorts studies Cohort Study
    - 1,671 patients with either hormone-sensitive or castration-resistant metastatic prostate cancer treated with androgen deprivation or chemotherapy
    - in patients with hormone-sensitive prostate cancer, higher BMI associated with longer overall survival (p < 0.001) and progression-free survival (p = 0.009)
    - in patients with castration-resistant prostate cancer, no clear association between BMI and overall survival or progression-free survival
    - PubMed17868721The Journal of urology20071101J Urol178519461946 Reference - [17868721J Urol 2007 Nov;178(5):1946](http://pubmed.ncbi.nlm.nih.gov/17868721?dopt=Abstract), editorial can be found in [17868740J Urol 2007 Nov;178(5):1842](http://pubmed.ncbi.nlm.nih.gov/17868740?dopt=Abstract)
    - **in patients with metastatic castration-resistant prostate cancer, higher subcutaneous adipose tissue index associated with increase in overall survival**
      * based on cohort analysis of data from 2 randomized trials
      * 127 patients with metastatic castration-resistant prostate cancer who were randomized to abiraterone acetate or enzalutamide (in COU-AA-301 and AFFIRM trials) were assessed
      * median follow-up 45 months
      * 95% were stratified according to subcutaneous adipose tissue (SAT) index
        + median overall survival was 15 months with SAT index < 51.7 cm2/m2 vs. 18 months with SAT index ≥ 51.7 cm2/m2 (p = 0.008)
        + compared to median SAT index < 51.7 cm2/m2, SAT index ≥ 51.7 cm2/m2 associated with increase in overall survival (p = 0.036)
      * improvement in overall survival also associated with absence of visceral metastasis (p = 0.004) and pain (p = 0.015)
      * Reference - [26278649Eur J Cancer 2015 Nov;51(17):2570](http://pubmed.ncbi.nlm.nih.gov/26278649?dopt=Abstract)
* **Prostate Cancer-specific Comorbidity Index may predict risk of nonprostate cancer-related death over 10 years in patients with prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Prediction Rule[25623745J Urol 2015 Jul;194(1):73](http://pubmed.ncbi.nlm.nih.gov/25623745?dopt=Abstract)

studySummary2

* + based on prognostic cohort study without independent validation Prediction Rule
  + 1,598 veterans with prostate cancer were randomized to derivation and internal validation cohorts
  + final version of index was developed using combined cohorts based on factors associated with nonprostate cancer-related mortality
  + age-adjusted Prostate Cancer-specific Comorbidity Index (PCCI) (total score 0-22 points)
    - 1 point for age 60-65.9 years
    - 2 points for age 66-71.9 years
    - 3 points for age 72-77.9 years
    - 4 points for age 78-83.9 years
    - 1 point for presence of cerebrovascular disease, any nonprostate tumor, or diabetes with end-organ damage
    - 2 points for any of mild liver disease, peripheral vascular disease, other neurological disease, mild renal disease, angina, mild chronic obstructive pulmonary disease, arrhythmia, valve disease, connective tissue disease, gastrointestinal bleeding, inflammatory bowel disease, or peptic ulcer disease
    - 3 points for any of moderate-to-severe chronic obstructive pulmonary disease, moderate-to-severe renal disease, hemiplegia, dementia, or heart failure
    - 6 points for any of metastatic solid tumor, lymphoma, leukemia, or moderate-to-severe liver disease
  + primary treatment included radical prostatectomy (31%), watchful waiting (21%), ADT only (18%), radiation therapy (14%), radiation therapy plus ADT (12%), and brachytherapy (3%)

| Predictive Performance for Risk of 10-Year Nonprostate Cancer-Related Death by PCCI Risk Score | | |
| --- | --- | --- |
| **Total Score** | **Proportion of Patients** | **10-Year Mortality** |
| 0 | 25.8% | 10% |
| 1-2 | 30.2% | 19% |
| 3-4 | 20.4% | 35% |
| 5-6 | 12.3% | 60% |
| 7-9 | 7.4% | 79% |
| ≥ 10 | 3.8% | 99% |

* + PubMed25623745The Journal of urology20150701J Urol19417373 Reference - [25623745J Urol 2015 Jul;194(1):73](http://pubmed.ncbi.nlm.nih.gov/25623745?dopt=Abstract)
* **diabetic fasting glucose levels may be associated with increased risk of prostate cancer death among patients with prostate cancer**

Cohort Study[Prostate Cancer Prostatic Dis 2019 Sep;22(3):453](http://pubmed.ncbi.nlm.nih.gov/30679762)

studySummarydiabetic fasting glucose levels may be associated with increased risk of prostate cancer death among men with prostate cancer (Prostate Cancer Prostatic Dis 2019 Sep)05/09/2019 09:06:23 AMFamily\_MedicinePrimary\_CareUrologic\_DisordersFamily\_Medicine Primary\_Care Urologic\_Disordersdiabetic fasting glucose levels may be associated with increased risk of prostate cancer death among men with prostate cancer (Prostate Cancer Prostatic Dis 2019 Sep)05/09/2019 09:06:23 AM

* + based on cohort analysis of data from Finnish component of European Randomized Study of Screening for Prostate Cancer (FinRSPC trial)Cohort Study
  + 1,770 patients diagnosed with prostate cancer during FinRSPC trial who had ≥ 1 fasting serum glucose measurement before or after diagnosis were categorized based on yearly mean fasting glucose and followed for median 9.9 years
    - diabetic glucose level (≥ 7 mmol/L)
    - impaired glucose tolerance (6.1-6.9 mmol/L)
    - normoglycemic level (≤ 6 mmol/L)
  + compared to normoglycemic patients, patients with diabetic blood glucose levels had increased use of antidiabetic and antihypertensive medications (both p < 0.001), higher median prostate-specific antigen (PSA) (p = 0.003), and nonsignificantly higher rate of metastatic prostate cancer at diagnosis (p = 0.064)
  + risk of prostate cancer death assessed in multivariable analysis adjusted for age at diagnosis, tumor stage, Gleason grade, PSA level at diagnosis, and study arm
  + prostate cancer death in 10.3% overall
  + compared to normoglycemic level in multivariable analysis
    - diabetic fasting glucose level before diagnosis associated with increased risk of prostate cancer death (adjusted hazard ratio [HR] 1.69, 95% CI 1.05-2.72)
    - diabetic fasting glucose level after diagnosis associated with increased risk of prostate cancer-related mortality
      * in analysis of all patients (adjusted HR 1.67, 95% CI 1.18-2.36)
      * in analysis of patients with localized prostate cancer (adjusted HR 2.39, 95% CI 1.45-3.93)
  + impaired glucose tolerance level before or after diagnosis not associated with increased risk of prostate cancer death compared to normoglycemic level
  + PubMed30679762Prostate cancer and prostatic diseasesProstate Cancer Prostatic Dis20190901223453-460453 Reference - [Prostate Cancer Prostatic Dis 2019 Sep;22(3):453](http://pubmed.ncbi.nlm.nih.gov/30679762)

Biomarkers for Prognostication

Prediction Rules

* **high score on 22-gene genomic classifier may help predict 10-year prostate cancer-specific mortality in patients with adverse pathologic features after radical prostatectomy (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Cohort Study[28400167Eur Urol 2018 Feb;73(2):168](http://pubmed.ncbi.nlm.nih.gov/28400167?dopt=Abstract)

studySummary2

* + based on prognostic study combining data from case-control and cohort studies Cohort Study
  + 561 patients with adverse pathologic features after radical prostatectomy were evaluated using 22-gene Decipher [genomic classifier (GC)](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_AMC_HSQ_RNB__ANC_1751437698)
  + adverse pathologic features defined as stages pT3 or pN1, positive margins, or Gleason score > 7
  + GC derived from tumor expression of 22 genes associated with increased risk of metastasis (range 0-1, with higher values indicating worse outcomes)
  + high risk defined as PSA level > 20 ng/mL, Gleason score 8-10 at prostatectomy, or stage pT3b or pN1
  + overall, 20% died of prostate cancer-specific causes within 10 years of prostatectomy
  + compared to GC score ≤ 0.6 (low-intermediate), GC score > 0.6 (high) associated with increased likelihood of prostate cancer-specific mortality within 10 years of prostatectomy in
    - all patients (adjusted odds ratio [OR] 3.91, 95% CI 2.43-6.29)
    - high-risk patients (adjusted OR 3.96, 95% CI 2.35-6.69)
    - patients with biochemical recurrence within 2 years (adjusted OR 3.06, 95% CI 1.62-5.76)
    - patients with metastasis (adjusted OR 1.95, 95% CI 1.12-3.39)
    - patients without postoperative treatment (adjusted OR 3.29, 95% CI 1.9-5.67)
  + GC model comparing scores > 0.6 vs. ≤ 0.6 and adjusted for [CAPRA-S](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_VQ2_XY1_WNB__ANC_1606884959) score had good discrimination for predicting prostate cancer-specific mortality within 10 years of prostatectomy in all patients (c-statistic 0.77)
  + PubMed28400167European urology20180201Eur Urol732168168 Reference - [28400167Eur Urol 2018 Feb;73(2):168](http://pubmed.ncbi.nlm.nih.gov/28400167?dopt=Abstract)
* **genomic classifier score predicts risk of 5-year metastasis in patients having salvage radiation therapy for recurrent prostate cancer after radical prostatectomy (**[**level 1 [likely reliable] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Cohort Study[26806658Eur Urol 2016 Oct;70(4):588](http://pubmed.ncbi.nlm.nih.gov/26806658?dopt=Abstract)[Full Text](http://www.sciencedirect.com/science/article/pii/S0302283816000592)

studySummary1

* + based on prognostic cohort study Cohort Study
  + 170 patients (median age 61 years) having salvage radiation therapy for recurrent prostate cancer after radical prostatectomy were assessed with genomic classifier (GC), [CAPRA-S](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_VQ2_XY1_WNB__ANC_1606884959), and Briganti scores
  + GC previously derived from tumor expression of 22 genes associated with increased risk of metastasis (range 0-1)
  + GC risk categories were low risk (score < 0.45), intermediate risk (score 0.45-0.6), and high risk (score > 0.6)
  + 12% developed metastatic disease in median follow-up 5.7 years
  + 5-year cumulative incidence of metastasis by risk category

| 5-Year Cumulative Incidence of Metastasis by Risk Category | | | |
| --- | --- | --- | --- |
| **Risk Score** | **Risk Category** | **Proportion of Patients** | **Incidence of Metastasis** |
| Genomic classifier | Low | 50.6% | 2.7% |
| Intermediate | 30% | 8.4% |
| High | 19.4% | 33.1% |
| CAPRA-S score | Low | 9.2% | 17% |
| Intermediate | 54.6% | 2% |
| High | 36.1% | 18% |
| Briganti score | Low | 26.8% | 8% |
| Intermediate | 42.8% | 6% |
| High | 30.3% | 18% |

* + prognostic performance of GC to predict metastasis at 5 years
    - at cutoff 0.45, sensitivity 94% and specificity 54%
    - at cutoff 0.6, sensitivity 67% and specificity 86%
  + PubMed26806658European urology20161001Eur Urol704588588 Reference - [26806658Eur Urol 2016 Oct;70(4):588](http://pubmed.ncbi.nlm.nih.gov/26806658?dopt=Abstract)[full-text](http://www.sciencedirect.com/science/article/pii/S0302283816000592)
  + derivation and validation study of genomic classifier can be found in [aph88909763pa9h88909763pafh88909763pcxh88909763pmdc23826159pPLoS One 2013;8(6):e66855](http://pubmed.ncbi.nlm.nih.gov/23826159?dopt=Abstract)[full-text](http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0066855)
* Prediction rules for castration-resistant prostate cancer:
  + **derived neutrophil to lymphocyte ratio < 2 predicts increased survival in patients with metastatic castration-resistant prostate cancer receiving first-line chemotherapy (**[**level 1 [likely reliable] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Prediction Rule[25515657Ann Oncol 2015 Apr;26(4):743](http://pubmed.ncbi.nlm.nih.gov/25515657?dopt=Abstract)

studySummary1

* + - based on prognostic cohort study with independent derivation and validation cohorts Prediction Rule
    - derivation cohort included 1,224 patients (median age 68 years) with metastatic castration-resistant prostate cancer receiving docetaxel plus prednisone with or without aflibercept
    - validation cohort included 1,006 patients (median age 68 years) with metastatic castration-resistant prostate cancer receiving prednisone plus either docetaxel or mitoxantrone
    - median overall survival was 21.1 months in derivation cohort and 19.2 months in validation cohort
    - derived neutrophil to lymphocyte ratio (dNLR) calculated as absolute count of neutrophils divided by the difference of leukocytes and neutrophils in peripheral blood
    - patients stratified to 2 groups with dNLR 2 as cutoff derived in derivation cohort

| Median Overall Survival | | |
| --- | --- | --- |
| **dNLR** | **Derivation** | **Validation** |
| < 2 | 26 months | 19.8 months |
| ≥ 2 | 19.1 months | 15.7 months |
| Abbreviation: dNLR, derived neutrophil to lymphocyte ratio. | | |
| Rate of ≥ 50% Reduction in PSA | | |
| **dNLR** | **Derivation** | **Validation** |
| < 2 | 76% | 70% |
| ≥ 2 | 67% | 53% |
| Abbreviations: dNLR, derived neutrophil to lymphocyte ratio; PSA, prostate-specific antigen. | | |

* + - in both derivation and validation cohorts, median overall survival and rate of ≥ 50% reduction in prostate-specific antigen (PSA) in dNLR < 2 group each significantly different from dNLR ≥ 2 group (p < 0.001 for all)
    - PubMed25515657Annals of oncology : official journal of the European Society for Medical Oncology20150401Ann Oncol264743743 Reference - [25515657Ann Oncol 2015 Apr;26(4):743](http://pubmed.ncbi.nlm.nih.gov/25515657?dopt=Abstract), editorial can be found in [25646369Ann Oncol 2015 Apr;26(4):622](http://pubmed.ncbi.nlm.nih.gov/25646369?dopt=Abstract)
  + **6-gene prognostic model stratifies mortality risk in adults with castration-resistant prostate cancer (**[**level 1 [likely reliable] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Prediction Rule[23059047Lancet Oncol 2012 Nov;13(11):1105](http://pubmed.ncbi.nlm.nih.gov/23059047?dopt=Abstract)

studySummary1

* + - based on prognostic cohort study with independent derivation and validation cohorts Prediction Rule
    - derivation cohort included 62 adults aged 49-86 years with castration-resistant prostate cancer who had whole blood tested with panel of 168 inflammation-related and prostate cancer-related genes
    - prognostic model to stratify patients to low- and high-mortality risk was derived using regression coefficients for 6 genes from panel
    - low mortality risk by 6 gene model associated with increased survival compared to high mortality risk group (hazard ratio 9.7, 95% CI 2.9-33.1)
    - validation cohort included 140 adults aged 48-93 years with castration-resistant prostate cancer
    - median survival in validation cohort by risk category
      * 18.5 months in low mortality risk patients (p < 0.0001 vs. high mortality risk)
      * 9.2 months in high mortality risk patients
    - performance of 6-gene model was significantly greater than clinicopathological model based on Eastern Cooperative Oncology Group (ECOG) performance status and hemoglobin in receiver operating curve analysis
    - PubMed23059047The Lancet. Oncology20121101Lancet Oncol131111051105 Reference - [23059047Lancet Oncol 2012 Nov;13(11):1105](http://pubmed.ncbi.nlm.nih.gov/23059047?dopt=Abstract), editorial can be found in [23059048Lancet Oncol 2012 Nov;13(11):1067](http://pubmed.ncbi.nlm.nih.gov/23059048?dopt=Abstract), commentary can be found in [23147923Nat Rev Urol 2012 Dec;9(12):666](http://pubmed.ncbi.nlm.nih.gov/23147923?dopt=Abstract)

Biomarkers for Survival

Prostate-Specific Antigen (PSA)

* **in patients with localized prostate cancer, higher posttreatment PSA nadir associated with increased estimated mortality at 7 years**

Randomized Trial[22498212J Urol 2012 Jun;187(6):2068](http://pubmed.ncbi.nlm.nih.gov/22498212?dopt=Abstract)

studySummary

* + based on secondary analysis of randomized trial Randomized Trial
  + 206 patients (mean age 72 years) with clinically localized prostate cancer (T1b-T2b, N0, M0) were randomized to radiation therapy plus androgen deprivation therapy vs. radiation therapy alone for 6 months with regular PSA measurements during median 6.9-year follow-up
  + 36% mortality at median 6.9-year follow-up
  + median PSA nadir 0.1 ng/mL for radiation plus androgen deprivation therapy vs. 0.7 ng/mL for radiation alone
  + comparing PSA nadir at ≤ median value vs. > median value
    - estimated prostate cancer-specific mortality at 7 years in 3.7% vs. 18.3% (p = 0.0005, NNT 7)
    - estimated all-cause mortality at 7 years in 31.5% vs. 55% (p = 0.002, NNT 5)
  + higher PSA nadir associated with increased
    - prostate cancer mortality (adjusted hazard ratio 1.18 per 1 ng/mL PSA increase, 95% CI 1.07-1.31)
    - all-cause mortality (adjusted hazard ratio 1.10 per 1 ng/mL PSA increase, 95% CI 1.04-1.17)
  + PubMed22498212The Journal of urology20120601J Urol187620682068 Reference - [22498212J Urol 2012 Jun;187(6):2068](http://pubmed.ncbi.nlm.nih.gov/22498212?dopt=Abstract)
* **early reduction in PSA at 4 weeks after start of abiraterone treatment may be associated with increased overall survival in patients with metastatic castration-resistant prostate cancer**

Cohort Study[26965561Eur Urol 2016 Nov;70(5):724](http://pubmed.ncbi.nlm.nih.gov/26965561?dopt=Abstract)[Full Text](http://www.sciencedirect.com/science/article/pii/S0302283816002451)

studySummary

* + based on retrospective cohort Cohort Studystudy
  + 274 patients with metastatic castration-resistant prostate cancer treated with abiraterone before (117 patients) or after (157 patients) docetaxel were evaluated for prostate-specific antigen (PSA) levels at 4 and 12 weeks after start of abiraterone
  + median follow-up was 14.6 months
  + 46% had early response defined as ≥ 30% reduction in PSA at 4 weeks
  + 37.2% had early increase defined as ≥ 25% increase in PSA at 4 weeks
  + all-cause mortality 66.1% overall
  + median survival
    - 25.8 months in patients with early response vs.15.1 months in patients without early response (p < 0.001)
    - 15.1 months in patients with early increase vs. 23.8 months in patients without early increase (p = 0.001)
  + change in PSA levels at 4 weeks and 12 weeks were significantly correlated (r = 0.82)
  + PubMed26965561European urology20161101Eur Urol705724724 Reference - [26965561Eur Urol 2016 Nov;70(5):724](http://pubmed.ncbi.nlm.nih.gov/26965561?dopt=Abstract)[full-text](http://www.sciencedirect.com/science/article/pii/S0302283816002451)
* TOPIC\_W1C\_3SB\_WNB\_\_LI\_O2C\_KRN\_JVBEU11012211/01/2022 03:08:36 PMevidenceUpdatestandardOncologic\_Disease Urologic\_Disorderselevated PSA (> 0.2 ng/mL) after 6 months of ADT associated with increased all-cause mortality and prostate-cancer-specific mortality in patients with hormone-sensitive prostate cancer (J Urol 2022 Aug)

**elevated PSA (> 0.2 ng/mL) after 6 months of ADT associated with increased all-cause mortality and prostate-cancer-specific mortality in patients with hormone-sensitive prostate cancer**

Cohort Study[J Urol 2022 Aug;208(2):317](https://pubmed.ncbi.nlm.nih.gov/35343252)

studySummary

* + Cohort Study based on retrospective cohort study
  + 9,170 patients with hormone-sensitive prostate cancer who received androgen deprivation therapy (ADT) for ≥ 6 months in 2000-2019 and were followed for ≥ 6 months after ADT were assessed
  + after 6 months of ADT
    - 38.3% had low PSA (≤ 0.2 ng/mL)
    - 37.3% had intermediate PSA (0.2-4 ng/mL)
    - 24.4% had high PSA (> 4 ng/mL)
  + median follow-up after 6 months of ADT was 37.8 months
  + propensity score for likelihood of having low, intermediate, or high PSA was calculated for each patient based on demographic and clinical factors; outcomes were assessed in analyses adjusted using inverse propensity score weighting
  + comparing low vs. intermediate vs. high PSA
    - estimated 2-year overall survival 93.9% vs. 88.6% vs. 63.6%
    - estimated 5-year overall survival 85.2% vs. 71.2% vs. 38.6%
  + compared to low PSA after 6 months of ADT
    - increased all-cause mortality associated with
      * intermediate PSA (adjusted hazard ratio [HR] 1.68, 95% CI 1.54-1.82)
      * high PSA (adjusted HR 4.71, 95% CI 4.32-5.13)
    - increased prostate-cancer-specific mortality associated with
      * intermediate PSA (adjusted HR 3.03, 95% CI 2.56-3.58)
      * high PSA (adjusted HR 15.36, 95% CI 13.08-18.03)
  + comparing 510 patients with undetectable PSA (< 0.01 ng/mL) to 2,574 patients with low PSA (0.01-0.2 ng/mL) after 6 months of ADT, no significant differences in all-cause mortality or prostate-cancer-specific mortality in adjusted analyses
  + PubMed35343252The Journal of urologyJ Urol20220328101097JU0000000000002676101097JU0000000000002676Reference - [J Urol 2022 Aug;208(2):317](https://pubmed.ncbi.nlm.nih.gov/35343252)

*BRCA2* Mutation

* ***BRCA2mut* associated with increased all-cause mortality and metastatic disease in patients with prostate cancer**

Systematic Review[cxh117169326pmdc27225637pProstate 2016 Sep;76(13):1135](http://pubmed.ncbi.nlm.nih.gov/27225637?dopt=Abstract)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5470321/)

studySummary

* + based on systematic review of observational studies Systematic Review
  + systematic review of 12 studies (11 cohort and 1 case series) comparing 261 patients (median age 62 years) with prostate cancer carrying germline *BRCA2mut* gene mutations vs. 7,109 patients (median age 65 years) with prostate cancer who are not carriers
  + comparing *BRCA2mut* to no *BRCA2mut*, *BRCA2mut* associated with
    - increased all-cause mortality (hazard ratio 3.29, 95% CI 1.56-6.95) in analysis of 3 studies, results limited by significant heterogeneity
    - increased cause-specific mortality (hazard ratio 3, 95% CI 2.2-4) in analysis of 4 studies
  + comparing *BRCA2mut* vs. no *BRCA2mut* at diagnosis in pooled analyses of individual data (p < 0.006 for all)
    - metastatic disease in 26% vs. 8%
    - Gleason score ≥ 7 in 71% vs. 54%
    - stage T3 or T4 in 47% vs. 35%
    - median prostate specific antigen 15.1 ng/dL vs. 11 ng/dL
  + PubMed27225637The Prostate20160901Prostate761311351135 Reference - [cxh117169326pmdc27225637pProstate 2016 Sep;76(13):1135](http://pubmed.ncbi.nlm.nih.gov/27225637?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5470321/)
* ***BRCA2* mutation, but not *BRCA1* mutation, associated with increased cancer-specific mortality in patients with prostate cancer**

Cohort Study[Eur Urol 2020 Jan;77(1):24](http://pubmed.ncbi.nlm.nih.gov/31495749)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6926480/)

Oncologic\_Disease Urologic\_DisordersBRCA2 mutation, but not BRCA1 mutation, associated with increased cancer-specific mortality in men with prostate cancer (Eur Urol 2020 Jan)12/22/2020 04:20:50 PMstudySummary

* + Cohort Study based on prospective cohort study
  + 823 patients (median age 51-54 years) with either *BRCA1* or *BRCA2* mutation from United Kingdom and Ireland were evaluated for incidence and prognosis of prostate cancer
    - 376 patients had *BRCA1* mutation
    - 447 patients had *BRCA2* mutation
  + median follow-up 5.9 years for patients with *BRCA1* mutation and 5.3 years for patients with *BRCA2* mutation
  + 16 patients (4.3%) with *BRCA1* mutation and 26 patients (5.8%) with *BRCA2* mutation developed incident prostate cancer
  + compared to general population, patients with *BRCA2* mutation had increased prostate cancer-specific mortality (standardized mortality ratio 3.85, 95% CI 1.44-10.3)
  + no significant difference in prostate cancer-specific mortality comparing patients with *BRCA1* mutation to general population
  + PubMed31495749European urologyEur Urol2020010177124-3524Reference - [Eur Urol 2020 Jan;77(1):24](http://pubmed.ncbi.nlm.nih.gov/31495749)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6926480/)

Other Serum Biomarkers

* **abnormal alkaline phosphatase level is associated with decreased overall survival in patients with metastatic hormone-sensitive prostate cancer**

Cohort Study[25277272Eur Urol 2015 Aug;68(2):196](http://pubmed.ncbi.nlm.nih.gov/25277272?dopt=Abstract)

studySummary

* + based on prognostic cohort study Cohort Study
  + 385 patients (median age 63 years) with metastatic hormone-sensitive prostate cancer treated with androgen deprivation therapy (ADT) plus docetaxel or ADT alone were followed for median 58.3 months
  + abnormal alkaline phosphatase (ALP) defined as above upper limit of normal or below lower limit of normal
  + median overall survival 33.5 months with abnormal ALP vs. 75 months with normal ALP levels (p < 0.001)
  + PubMed25277272European urology20150801Eur Urol682196196 Reference - [25277272Eur Urol 2015 Aug;68(2):196](http://pubmed.ncbi.nlm.nih.gov/25277272?dopt=Abstract), editorial can be found in [25457495Eur Urol 2015 Aug;68(2):205](http://pubmed.ncbi.nlm.nih.gov/25457495?dopt=Abstract)

Biomarkers for Recurrence

* **in patients with prostate cancer having radical prostatectomy, increasing score on cell-cycle progression gene panel may be associated with increased risk of recurrence**

Cohort Study[cxh86636564pmdc23460710pJ Clin Oncol 2013 Apr 10;31(11):1428](http://pubmed.ncbi.nlm.nih.gov/23460710?dopt=Abstract)

studySummary

* + based on cohort study Cohort Study
  + 413 patients who had radical prostatectomy were assessed with cell-cycle progression gene panel
  + cell-cycle progression gene panel is calculated as average expression of 31 cell-cycle progression genes normalized to 15 housekeeper genes
  + 19.9% of patients experienced recurrence (defined as 2 prostate-specific antigen levels ≥ 0.2 ng/mL or salvage treatment) at median 34 months
  + increased cell-cycle progression gene panel score associated with increased risk of recurrence (hazard ratio 2.1, 95% CI 1.6-2.9 per unit increase in score)
  + PubMed23460710Journal of clinical oncology : official journal of the American Society of Clinical Oncology20130410J Clin Oncol311114281428 Reference - [cxh86636564pmdc23460710pJ Clin Oncol 2013 Apr 10;31(11):1428](http://pubmed.ncbi.nlm.nih.gov/23460710?dopt=Abstract)

Prevention and Screening

Prevention and Screening

Prevention

Chemoprevention Strategies in Prostate Cancer

5-Alpha Reductase Inhibitors (5-ARIs)

* The use of 5-ARIs may reduce risk of prostate cancer. However, benefits of chemoprevention should be weighed against potential harms, including possible increase in risk of high-grade prostate cancer and treatment-related adverse effects.
  + American Society of Clinical Oncology/American Urological Association (ASCO/AUA) recommendations on the use of 5-ARIs for prostate cancer chemoprevention:
    - Discussion of benefits and risks associated with 5-ARIs recommended for the following patients:
      * Asymptomatic patients with prostate-specific antigen (PSA) ≤ 3 ng/mL who are regularly screened with PSA or anticipating having annual PSA screening for early detection of prostate cancer
      * Patients taking 5-ARIs for benign conditions (for example, benign prostatic hyperplasia)
    - Potential benefits of 5-ARIs may include reduction in overall risk of prostate cancer, lower rates of urinary tract obstructive symptoms, and lower rates of male pattern baldness.
    - Potential harms of 5-ARIs may include the following:
      * Increased risk of high-grade prostate cancer
      * Sexual dysfunction (although it may not be clinically significant), such as decreased libido, decreased ejaculate volume, and erectile dysfunction
      * Gynecomastia
      * Dizziness
      * Postural hypertension
    - References - [19249063J Urol 2009 Apr;181(4):1642](http://pubmed.ncbi.nlm.nih.gov/19249063?dopt=Abstract), [mdc19252137pJ Clin Oncol 2009 Mar 20;27(9):1502](http://pubmed.ncbi.nlm.nih.gov/19252137?dopt=Abstract)[PDF](http://jco.ascopubs.org/content/27/9/1502.full.pdf)
  + **5-ARIs may reduce risk of prostate cancer in persons who have regular prostate cancer screening, but might increase risk for high-grade prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Cochrane Review[chhCD007091Cochrane Database Syst Rev 2008 Apr 16;(2):CD007091](http://www.ncbi.nlm.nih.gov/pubmed?term=18425978%5buid%5d%20AND%20CD007091%5bpg%5d)

studySummary2

* + - based on Cochrane review of trials with methodologic limitations Cochrane Review
    - systematic review of 9 randomized trials evaluating 5-ARIs for prevention of prostate cancer in 34,410 persons
    - 8 trials evaluating finasteride, 1 trial evaluated dutasteride
    - 3 trials evaluating finasteride with 24,969 persons lasted ≥ 4 years but only 1 trial (Prostate Cancer Prevention Trial [PCPT]) was specifically designed to assess impact of 5-ARIs on prostate cancer period-prevalence
    - methodologic limitations included
      * unclear allocation concealment in 6 trials
      * absent blinding of outcome assessors in 6 trials
    - "for-cause" prostate cancer defined as prostate cancer clinically detected based on symptoms, abnormal digital rectal exam, or detected as result of abnormal PSA value
    - in largest trial ([PCPT](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_TFJ_JZK_CKB__LI_PVG_22L_XNB)) primary intention-to-treat analysis included prostate cancer "for cause" or based on end-of-study biopsy
    - compared to placebo, 5-ARIs associated with
      * decreased risk for "for-cause" prostate cancer in analysis of 6 trials with 28,505 patients
        + risk ratio (RR) 0.74 (95% CI 0.67-0.83)
        + NNT 66-81 with 4.9% incidence in placebo group
      * decreased risk for prostate cancer overall detected in analysis of 7 trials with 28,557 patients
        + RR 0.74 (95% CI 0.56-0.98)
        + NNT 27-47 with 9.2% rate in placebo group
      * increased risk of impotence or erectile dysfunction in analysis of 7 trials with 25,446 patients, results limited by significant heterogeneity
        + RR 1.71 (95% CI 1.11-2.65)
        + NNH 23-55 with 47.2% rate in placebo group
      * increased risk of gynecomastia in analysis of 2 trials with 23,205 patients, results limited by significant heterogeneity
        + RR 2.13 (95% CI 1.15-3.95)
        + NNH 32-108 with 2.4% rate in placebo group
      * no significant differences in overall mortality or prostate cancer-specific mortality
    - greater number of high Gleason score tumors (7 or 8) occurred in persons on finasteride in [PCPT trial](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_TFJ_JZK_CKB__LI_PVG_22L_XNB) described below
    - CochraneCD007091The Cochrane database of systematic reviews20080416Cochrane Database Syst Rev2CD007091CD007091 Reference - [chhCD007091Cochrane Database Syst Rev 2008 Apr 16;(2):CD007091](http://www.ncbi.nlm.nih.gov/pubmed?term=18425978%5buid%5d%20AND%20CD007091%5bpg%5d), also published in [mnh20977593paph54623626pa9h54623626pbyh54623626pcxh54623626pmdc20977593pBJU Int 2010 Nov;106(10):1444](http://pubmed.ncbi.nlm.nih.gov/20977593?dopt=Abstract)
    - **finasteride may reduce risk of prostate cancer, but may increase risk for high-grade prostate cancer in adults > 55 years old with no history of prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**
      * based on randomized trial with detection bias
      * 18,882 adults > 55 years old with no history of prostate cancer, normal digital rectal exam (DRE), and PSA < 3 ng/mL were randomized to finasteride 5 mg vs. placebo orally once daily for 7 years
      * PSA and digital rectal done yearly, prostate biopsy done if abnormal and at end of study
      * study stopped early due to statistically significant planned interim analysis
      * current report based on 86.3% of adults who have completed 7 years of the study
      * diagnosis of prostate cancer at end-of-study biopsy in 59.6% with finasteride vs. 63% with placebo (p < 0.001)
      * 865 adults excluded since end-of-study biopsy performed after 7.25 years and 64 adults excluded with data still in process, so results based on 9,060 adults (48%)
      * comparing finasteride vs. placebo over 7-year period
        + prostate cancer occurred in 18.4% vs. 24.4% (p < 0.001, NNT 17)
        + prostate cancer of Gleason grades 7-10 occurred in 6.4% vs. 5.1% (p < 0.001, NNH 77)
        + biopsy due to abnormal PSA level or DRE occurred in 22.5% vs. 24.8% (p < 0.001) (finasteride reduces PSA levels so PSA level in finasteride group reported as 2-2.3 times its value to clinicians to maintain blinding)
      * side effects more common with finasteride included
        + erectile dysfunction (p < 0.001, NNH 17)
        + loss of libido (p < 0.001, NNH 17)
        + gynecomastia (p < 0.001, NNH 59)
        + reduced ejaculate volume (p < 0.001, NNH 7)
      * side effects more common with placebo included
        + urinary urgency or urinary frequency (p < 0.001, NNT 37)
        + prostatitis (p < 0.001, NNT 59)
        + urinary tract infections (p < 0.001, NNT 333)
        + urinary retention (p < 0.001, NNT 48)
      * Reference - PCPT trial ([12824459N Engl J Med 2003 Jul 17;349(3):215](http://pubmed.ncbi.nlm.nih.gov/12824459?dopt=Abstract)[full-text](http://www.nejm.org/doi/full/10.1056/NEJMoa030660#t=article)), editorial can be found in [12824458N Engl J Med 2003 Jul 17;349(3):297](http://pubmed.ncbi.nlm.nih.gov/12824458?dopt=Abstract)
      * commentary can be found in [14562808N Engl J Med 2003 Oct 16;349(16):1569](http://pubmed.ncbi.nlm.nih.gov/14562808?dopt=Abstract), [Bandolier 2003 Aug;114:5](http://www.medicine.ox.ac.uk/bandolier/band114/b114-5.html), [mnh14599370paph11354798pa9h11354798pbyh11354798pafh11354798phch11354798pnyh11354798ppbh11354798pcxh11354798pmdc14599370pJ Fam Pract 2003 Nov;52(11):833](http://pubmed.ncbi.nlm.nih.gov/14599370?dopt=Abstract), [Am Fam Physician 2004 Feb 1;69(3):647](http://www.aafp.org/afp/2004/0201/p647.html), [15616218N Engl J Med 2004 Dec 23;351(26):2773](http://pubmed.ncbi.nlm.nih.gov/15616218?dopt=Abstract)
      * The 24.4% rate of prostate cancer in the placebo group raises possibility that many of these cancers are not clinically significant.
      * critiques of PCPT suggest that observed, unadjusted increased risk of high-grade disease with finasteride may have been due to facilitated diagnosis resulting from increased biopsy sensitivity with finasteride
        + detection bias

reanalysis of PCPT included more patients (3 more months of data) and adjusted for detection bias

observed results comparing finasteride vs. placebo in 10,182 patients

prostate cancer occurred in 16.6% vs. 22.9% (p = 0.0001, NNT 16)

high-grade prostate cancer (Gleason score ≥ 7) occurred in 5.8% vs. 4.8% (p = 0.02, NNH 100)

bias-adjusted analysis (adding assumptions for missing data) comparing finasteride vs. placebo in 15,990 patients

prostate cancer estimated to occur in 14.7% vs. 21.1% (p = 0.0001, NNT 16)

high-grade prostate cancer (Gleason score ≥ 7) estimated to occur in 4.8% vs. 4.2% (not significant)

Reference - [19138953Cancer Prev Res (Phila) 2008 Aug;1(3):174](http://pubmed.ncbi.nlm.nih.gov/19138953?dopt=Abstract)[full-text](http://cancerpreventionresearch.aacrjournals.org/content/1/3/174.full), editorial can be found in [19138948Cancer Prev Res (Phila) 2008 Aug;1(3):151](http://pubmed.ncbi.nlm.nih.gov/19138948?dopt=Abstract)

detection bias may be due to effect of finasteride on prostate volume ([17848668J Natl Cancer Inst 2007 Sep 19;99(18):1366](http://pubmed.ncbi.nlm.nih.gov/17848668?dopt=Abstract)[full-text](http://jnci.oxfordjournals.org/content/99/18/1366.full)), editorial can be found in [17848666J Natl Cancer Inst 2007 Sep 19;99(18):1355](http://pubmed.ncbi.nlm.nih.gov/17848666?dopt=Abstract)

* + - * + different misclassification rates in finasteride and placebo groups

reanalysis of PCPT used statistical model to extrapolate radical prostatectomy Gleason results to all adults using a missing-at-random assumption

estimated rates of true high-grade (Gleason 7-10) and true low-grade disease, where true Gleason grade is what is (or would have been) found on radical prostatectomy

comparing finasteride vs. placebo

estimated misclassification rate of true high-grade disease 34.6% vs. 52.6% (p < 0.05)

estimated misclassification rate of true low-grade disease 15.2% vs. 8.8% (p = 0.05)

estimated rate of true high-grade disease 3.9% vs. 4.6% (not significant)

estimated rate of true low-grade disease 4.9% vs. 8% (p < 0.05)

Reference - [19138954Cancer Prev Res (Phila) 2008 Aug;1(3):182](http://pubmed.ncbi.nlm.nih.gov/19138954?dopt=Abstract)[full-text](http://cancerpreventionresearch.aacrjournals.org/content/1/3/182.full), editorial can be found in [19138948Cancer Prev Res (Phila) 2008 Aug;1(3):151](http://pubmed.ncbi.nlm.nih.gov/19138948?dopt=Abstract)

* + **dutasteride may reduce risk of prostate cancer in high-risk adults, but might increase risk for high-grade prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Randomized Trial[20357281N Engl J Med 2010 Apr 1;362(13):1192](http://pubmed.ncbi.nlm.nih.gov/20357281?dopt=Abstract)[Full Text](http://www.nejm.org/doi/full/10.1056/NEJMoa0908127#t=article)

studySummary2

* + - based on randomized trial without intention-to-treat analysis Randomized Trial
    - 8,231 adults aged 50-75 years with 1 negative prostate biopsy (6-12 cores) within 6 months and PSA level 2.5-10 ng/mL randomized to dutasteride 0.5 mg/day vs. placebo for 4 years
    - 82% completed ≥ 1 transrectal ultrasound-guided biopsy
    - comparing dutasteride vs. placebo in adults with ≥ 1 biopsy
      * cancer on biopsy in 19.9% vs. 25.1% (p < 0.001, NNT 20)
      * tumors with Gleason score 7-10 during years 1-4 were 220 vs. 233 (not significant)
      * tumors with Gleason score 8-10 during years 3-4 were 12 (0.49%) vs. 1 (0.04%) (p = 0.003, NNH 222)
      * acute urinary retention in 1.6% vs. 6.7% (p < 0.001, NNH 20)
      * benign prostatic hyperplasia-related surgery in 1.4% vs. 5.1% (p < 0.001, NNT 27)
      * urinary tract infection in 5.3% vs. 8.8% (p < 0.001, NNH 29)
    - compared with placebo, dutasteride associated with
      * increased risk for composite cardiac failure (defined as heart failure, cardiac failure, acute cardiac failure, ventricular failure, cardiopulmonary failure, and congestive cardiomyopathy) (relative risk 1.91, 95% CI 1.04-3.5)
      * no significant difference observed in cardiovascular events or cardiovascular-related deaths
    - PubMed20357281The New England journal of medicine20100401N Engl J Med3621311921192 Reference - REDUCE trial ([20357281N Engl J Med 2010 Apr 1;362(13):1192](http://pubmed.ncbi.nlm.nih.gov/20357281?dopt=Abstract)[full-text](http://www.nejm.org/doi/full/10.1056/NEJMoa0908127#t=article)), editorial can be found in [20357287N Engl J Med 2010 Apr 1;362(13):1237](http://pubmed.ncbi.nlm.nih.gov/20357287?dopt=Abstract)
  + **5-ARIs not associated with increased risk of high grade or lethal prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Cohort Study[mdc24887392pJAMA Intern Med 2014 Aug 1;174(8):1301](http://pubmed.ncbi.nlm.nih.gov/24887392?dopt=Abstract)

studySummary

* + - based on prospective cohort study Cohort Study
    - 38,058 adults from Health Professionals Follow-up Study (HPFS) aged 40-75 years at baseline in 1986 followed for 14 years
    - 3,681 incident cases prostate cancer reported (289 lethal [metastatic or fatal], 456 high grade [Gleason sum (GS) 8-10], 1,238 GS 7, and 1,600 low grade [GS 2-6])
    - 7.6% reported use of 5-ARIs
    - no association noted between use of 5-ARIs and high grade or lethal prostate cancer
    - any use of 5-ARIs during study period associated with reduced risk of prostate cancer
      * overall (adjusted hazard ratio [HR] 0.77, 95% CI 0.65-0.91)
      * GS 7 (adjusted HR 0.67, 95% CI 0.49-0.91)
      * low grade (adjusted HR 0.74, 95% CI 0.57-0.95)
    - PubMed24887392JAMA internal medicine20140801JAMA Intern Med174813011301 Reference - [mdc24887392pJAMA Intern Med 2014 Aug 1;174(8):1301](http://pubmed.ncbi.nlm.nih.gov/24887392?dopt=Abstract)

Aspirin

* **aspirin associated with decreased risk of prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Systematic Review[20091856Int J Cancer 2010 Oct 1;127(7):1680](http://pubmed.ncbi.nlm.nih.gov/20091856?dopt=Abstract)

studySummary

* + based on systematic review of observational studies Systematic Review
  + systematic review and meta-analysis of 10 case-control and 14 cohort studies evaluating effect of NSAIDs on prostate cancer risk and mortality in 24,320 patients
  + aspirin use associated with reduced risk of
    - total prostate cancer (pooled odds ratio [OR] 0.83, 95% CI 0.77-0.89)
    - advanced prostate cancer (OR 0.81, 95% CI 0.72-0.92)
  + evaluation of effect of nonaspirin NSAIDs or all NSAIDs limited by heterogeneity
  + PubMed20091856International journal of cancer20101001Int J Cancer127716801680 Reference - [20091856Int J Cancer 2010 Oct 1;127(7):1680](http://pubmed.ncbi.nlm.nih.gov/20091856?dopt=Abstract)
* **aspirin but not NSAID use associated with decreased risk of prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Cohort Study[25520389Clin Cancer Res 2015 Feb 15;21(4):756](http://pubmed.ncbi.nlm.nih.gov/25520389?dopt=Abstract)

studySummary

* + based on cohort analysis of data from [REDUCE trial](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_TFJ_JZK_CKB__LI_Z1B_DYC_SNB)Cohort Study
  + 6,390 adults aged 50-75 years with prior negative prostate biopsy and prostate-specific antigen level 2.5-10 ng/mL were analyzed
  + 50% used no anti-inflammatory drugs, 21% used aspirin, 18% used NSAIDs, and 11% used both
  + prostate cancer detected in 22% (7% had high-grade disease and 16% had low-grade disease)
  + compared to no anti-inflammatory drug use, aspirin use associated with
    - decreased risk of overall prostate cancer (adjusted odds ratio [OR] 0.81, 95% CI 0.68-0.96)
    - nonsignificant decrease in risk of high-grade prostate cancer (adjusted OR 0.77, 95% CI 0.58-1.02)
    - nonsignificant decrease in risk of low-grade prostate cancer (adjusted OR 0.83, 95% CI 0.68-1.01)
  + no significant differences in risk of overall, high-grade, or low-grade prostate cancer with each of NSAID use alone or NSAID plus aspirin use
  + PubMed25520389Clinical cancer research : an official journal of the American Association for Cancer Research20150215Clin Cancer Res214756756 Reference - [25520389Clin Cancer Res 2015 Feb 15;21(4):756](http://pubmed.ncbi.nlm.nih.gov/25520389?dopt=Abstract)
* **aspirin but not ibuprofen use associated with decreased risk of prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Cohort Study[mnh22722313paph77351157pa9h77351157pbyh77351157pafh77351157pcxh77351157pmdc22722313pBr J Cancer 2012 Jun 26;107(1):207](http://pubmed.ncbi.nlm.nih.gov/22722313?dopt=Abstract)[Full Text](http://www.nature.com/bjc/journal/v107/n1/full/bjc2012227a.html)

studySummary

* + based on prospective cohort study Cohort Study
  + 29,450 adults aged 55-74 years were screened for prostate cancer and followed for median 11.7 years
  + at baseline, self-reported use within past year of aspirin in 54% and ibuprofen in 25%
  + 12.1% developed prostate cancer during follow-up
  + compared with no aspirin use, ≥ 1 aspirin/day associated with decreased risk of prostate cancer (adjusted hazard ratio 0.92, 95% CI 0.85-0.99)
  + no significant association found between ibuprofen use and prostate cancer
  + PubMed22722313British journal of cancer20120626Br J Cancer1071207207 Reference - [mnh22722313paph77351157pa9h77351157pbyh77351157pafh77351157pcxh77351157pmdc22722313pBr J Cancer 2012 Jun 26;107(1):207](http://pubmed.ncbi.nlm.nih.gov/22722313?dopt=Abstract)[full-text](http://www.nature.com/bjc/journal/v107/n1/full/bjc2012227a.html)

Metformin

* There is inconsistent evidence on whether metformin decreases the risk of prostate cancer.
  + **metformin may not be associated with reduced risk of prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Systematic Review[Medicine (Baltimore) 2019 Mar;98(12):e14955](http://pubmed.ncbi.nlm.nih.gov/30896668)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6709307/)

studySummary

* + - Systematic Review based on systematic review of observational studies
    - systematic review of 18 observational studies (15 cohort and 3 nested case-control studies) evaluating effect of metformin on risk of prostate cancer in 1,217,368 persons
      * 16 studies included persons with diabetes
      * 52,328 persons (4.3%) had prostate cancer
    - comparing metformin use to no use, use of other antidiabetic drugs, or persons with diet control, no significant difference in risk of prostate cancer in analysis of all studies, results limited by significant heterogeneity
    - PubMed30896668MedicineMedicine (Baltimore)201903019812e14955e14955Reference - [Medicine (Baltimore) 2019 Mar;98(12):e14955](http://pubmed.ncbi.nlm.nih.gov/30896668)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6709307/)
    - **metformin may not be associated with reduced risk of prostate cancer in adults with diabetes (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**
      * based on cohort analysis of [REDUCE trial](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_TFJ_JZK_CKB__LI_Z1B_DYC_SNB)
      * 540 adults 50-75 years old with diabetes were evaluated for association of metformin with risk of prostate cancer
      * 194 adults (36%) reported metformin use, 141 adults (26%) reported use of ≥ 1 non-metformin antidiabetic drugs, and 205 adults (38%) reported no use of any antidiabetic drugs
      * follow-up 4 years
      * 122 adults (23%) developed prostate cancer during follow-up
      * comparing metformin use to no antidiabetic drug use, no significant differences in
        + any prostate cancer
        + [International Society of Urological Pathology (ISUP) grade group](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_RVM_VBD_XLB) 1 prostate cancer
        + [ISUP grade group](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_RVM_VBD_XLB) ≥ 2 prostate cancer
      * PubMed26353947Cancer prevention research (Philadelphia, Pa.)Cancer Prev Res (Phila)201511018111055-601055Reference - [Cancer Prev Res (Phila) 2015 Nov;8(11):1055](http://pubmed.ncbi.nlm.nih.gov/26353947)[full-text](https://cancerpreventionresearch.aacrjournals.org/content/8/11/1055.long)
  + **metformin associated with decreased risk of prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Systematic Review[aph100187931pa9h100187931pafh100187931pcxh100187931pmdc25545701pPLoS One 2014;9(12):e116327](http://pubmed.ncbi.nlm.nih.gov/25545701?dopt=Abstract)[Full Text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4278883/)

studySummary2

* + - based on systematic review of observational studies Systematic Review
    - systematic review of 21 retrospective cohort or case-control studies evaluating effect of metformin on risk of prostate cancer, or biochemical recurrence and all-cause mortality in persons with prostate cancer
    - study duration ranged from 2 to 22 years
    - compared to other hypoglycemic agents or no metformin use, metformin use associated with reduced risk of prostate cancer (odds ratio 0.91, 95% CI 0.85-0.97) in analysis of 12 studies with 963,991 persons, results limited by significant heterogeneity
    - PubMed25545701PloS one201401PLoS One912e116327e116327 Reference - [aph100187931pa9h100187931pafh100187931pcxh100187931pmdc25545701pPLoS One 2014;9(12):e116327](http://pubmed.ncbi.nlm.nih.gov/25545701?dopt=Abstract)[full-text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4278883/)

Statins

* **statins do not affect risk of prostate cancer (**[**level 1 [likely reliable] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Systematic Review[mdc16391219pJAMA 2006 Jan 4;295(1):74](http://pubmed.ncbi.nlm.nih.gov/16391219?dopt=Abstract)[Full Text](http://jama.jamanetwork.com/article.aspx?articleid=202141)

studySummary1

* + based on systematic review Systematic Review
  + systematic review and meta-analysis of 26 randomized trials with 86,936 persons
  + trial durations ranged from 1.9 years to 10.4 years
  + no significant effect on incidence of prostate cancer in meta-analysis of 3 trials with 20,063 patients
  + PubMed16391219JAMA20060104JAMA29517474 Reference - [mdc16391219pJAMA 2006 Jan 4;295(1):74](http://pubmed.ncbi.nlm.nih.gov/16391219?dopt=Abstract)[full-text](http://jama.jamanetwork.com/article.aspx?articleid=202141), commentary can be found in [mdc16788123pJAMA 2006 Jun 21;295(23):2720](http://pubmed.ncbi.nlm.nih.gov/16788123?dopt=Abstract)
  + similar findings in 2 other meta-analyses ([mnh16214597paph18482936pa9h18482936pbyh18482936pafh18482936pbeh18482936phch18482936pnyh18482936pnxh18482936pbth18482936ppbh18482936pcxh18482936pmdc16214597pLancet 2005 Oct 8;366(9493):1267](http://pubmed.ncbi.nlm.nih.gov/16214597?dopt=Abstract), [17131313Int J Cancer 2007 Feb 15;120(4):833](http://pubmed.ncbi.nlm.nih.gov/17131313?dopt=Abstract))
* **statins do not appear to reduce overall risk of prostate cancer but might reduce risk of advanced prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Systematic Review[18491405Int J Cancer 2008 Aug 15;123(4):899](http://pubmed.ncbi.nlm.nih.gov/18491405?dopt=Abstract)

studySummary2

* + based on systematic review with heterogeneity Systematic Review
  + systematic review of 6 randomized trials with 40,178 patients and 13 observational studies (6 cohort studies and 7 case-control studies with total 840,000 patients) evaluating effect of statins on risk of prostate cancer
  + no evidence of association between statins and total prostate cancer in meta-analysis of randomized trials or observational studies separately or in combination
  + compared with no statin use, statin use associated with reduced incidence of advanced prostate cancer (relative risk 0.77, 95% CI 0.64-0.93)
  + PubMed18491405International journal of cancer20080815Int J Cancer1234899899 Reference - [18491405Int J Cancer 2008 Aug 15;123(4):899](http://pubmed.ncbi.nlm.nih.gov/18491405?dopt=Abstract)
* **statins may not be associated with reduced risk of prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Cohort Study[24518774J Urol 2014 Aug;192(2):379](http://pubmed.ncbi.nlm.nih.gov/24518774?dopt=Abstract)[Full Text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4104140/)

studySummary2

* + based on cohort analysis of data from [PCPT trial](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_TFJ_JZK_CKB__LI_PVG_22L_XNB)Cohort Study
  + 9,457 adults ≥ 55 years old who were randomized to placebo were assessed
  + 23.8% used statins during 7-year follow-up
  + no significant differences in risk of total, lower-grade, or higher-grade prostate cancer comparing statin use to no statin use
  + PubMed24518774The Journal of urology20140801J Urol1922379379 Reference - [24518774J Urol 2014 Aug;192(2):379](http://pubmed.ncbi.nlm.nih.gov/24518774?dopt=Abstract)[full-text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4104140/)

Diet and Lifestyle

Recommendations From Professional Organizations

* American Cancer Society (ACS) recommendations for lifestyle factors which may reduce risk for prostate cancer:
  + Eat ≥ 2.5 cups of a variety of vegetables and fruits daily.
  + Engage in regular [physical activity](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_SKN_HYK_CKB__LI_SZY_KYK_CKB).
  + Maintain [healthy weight](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_OJ3_121_WNB__LI_WZT_C21_WNB).
  + Consider limiting [calcium](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_DDL_TLV_BKB__LI_F55_3B1_WNB) supplementation and not exceeding recommended dietary intake.
  + PubMed22237782CA: a cancer journal for cliniciansCA Cancer J Clin2012010162130-6730Reference - [CA Cancer J Clin 2012 Jan;62(1):30](http://pubmed.ncbi.nlm.nih.gov/22237782)[full-text](https://acsjournals.onlinelibrary.wiley.com/doi/full/10.3322/caac.20140)

Dietary Considerations

Fatty Acid

* **omega-3 fatty acid supplementation does not reduce risk of prostate cancer in adults without history of cancer or cardiovascular disease (**[**level 1 [likely reliable] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Randomized Trial[N Engl J Med 2019 Jan 3;380(1):33](http://pubmed.ncbi.nlm.nih.gov/30415629)[Full Text](https://www.nejm.org/doi/10.1056/NEJMoa1809944?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dwww.ncbi.nlm.nih.gov)

studySummary1omega-3 fatty acid supplementation does not reduce risk of prostate cancer in adults without history of cancer or cardiovascular disease (N Engl J Med 2019 Jan 3)11/26/2018 03:22:00 PMFamily\_MedicineGeriatricsOncologic\_DiseasePrevention\_and\_ScreeningPrimary\_CareUrologic\_DisordersFamily\_Medicine Geriatrics Oncologic\_Disease Prevention\_and\_Screening Primary\_Care Urologic\_Disordersomega-3 fatty acid supplementation does not reduce risk of prostate cancer in adults without history of cancer or cardiovascular disease (N Engl J Med 2019 Jan 3)11/26/2018 03:22:00 PM30415629

* + based on randomized trial Randomized Trial
  + 25,871 adults (male adults ≥ 50 years old and female adults ≥ 55 years old) without history of cancer or cardiovascular disease were randomized in 2-by-2 factorial design to
    - omega-3 fatty acids (marine n-3 fatty acids) 1 g orally once daily vs. placebo
    - vitamin D3 (cholecalciferol) 2,000 units orally once daily vs. placebo
  + median follow-up 5.3 years
  + 82% took ≥ 66% of omega-3 or placebo capsules, 100% included in analysis
  + comparing omega-3 vs. placebo
    - prostate cancer in 1.7% vs. 1.5% (not significant)
    - invasive cancer of any type in 6.3% vs. 6.2% (not significant)
    - cancer-related mortality 1.3% vs. 1.4% (hazard ratio 0.97, 95% CI 0.79-1.2), not significant, but CI includes possibility of benefit or harm
    - all-cause mortality 3.8% vs. 3.7% (not significant)
  + no significant differences in
    - risk of major cardiovascular events (composite of myocardial infarction, stroke, and cardiovascular mortality)
    - monitored safety conditions including gastrointestinal bleeding, blood in urine, easy bruising, frequent nosebleeds, or kidney failure or dialysis
    - adverse events including stomach upset or pain, nausea, constipation, and diarrhea
  + no significant association between vitamin D supplementation and risk of invasive cancer of any type (for details, see VITAL trial [vitamin D arm] in [Vitamin D Intake and Supplementation](https://dpa-pde-oxford.shinyapps.io/drug-review/vitamin-d-intake-and-supplementation))
  + no significant interaction between omega-3 and vitamin D supplementation
  + PubMed30415629The New England journal of medicineN Engl J Med20190103380133-4433 Reference - VITAL trial (omega-3 arm) ([N Engl J Med 2019 Jan 3;380(1):33](http://pubmed.ncbi.nlm.nih.gov/30415629)[full-text](https://www.nejm.org/doi/10.1056/NEJMoa1809944?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dwww.ncbi.nlm.nih.gov)), editorial can be found in [N Engl J Med 2019 Jan 3;380(1):91](http://pubmed.ncbi.nlm.nih.gov/30415594)

Selenium

* Selenium supplementation may not reduce risk of prostate cancer, even though high selenium level may be associated with reduced prostate cancer risk.
  + Selenium supplementation:
    - **neither selenium nor vitamin E supplementation appears to reduce risk of prostate cancer or other cancers (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Randomized Trial[mdc19066370pJAMA 2009 Jan 7;301(1):39](http://pubmed.ncbi.nlm.nih.gov/19066370?dopt=Abstract)[Full Text](http://jama.jamanetwork.com/article.aspx?articleid=183163)

studySummary2

* + - * based on randomized trial with unclear allocation concealment Randomized Trial
      * 35,533 adults ≥ 55 years old (or > 50 years old if African American) with serum PSA ≤ 4 ng/mL without prostate cancer randomized to 1 of 4 groups and followed for median 5.5 years (range 4.2-7.3 years)
        + selenium 200 mcg/day from L-selenomethionine plus placebo
        + vitamin E 400 units/day (from racemic alpha-tocopheryl acetate) plus placebo
        + selenium plus vitamin E
        + double placebo
      * planned follow-up 7-12 years
      * trial terminated at 7 years at planned interim analysis due to no evidence of benefit
      * adherence to ≥ 1 agent 87% at year 1 and 72% at year 5
      * no significant differences in incidence of clinically diagnosed prostate cancer
        + 4.56% with selenium
        + 4.93% vitamin E
        + 4.56% with selenium plus vitamin E
        + 4.43% with placebo
      * no significant differences in
        + lung, colorectal, or any other primary cancers
        + cardiovascular events or mortality
      * PubMed19066370JAMA20090107JAMA30113939 Reference - SELECT trial ([mdc19066370pJAMA 2009 Jan 7;301(1):39](http://pubmed.ncbi.nlm.nih.gov/19066370?dopt=Abstract)[full-text](http://jama.jamanetwork.com/article.aspx?articleid=183163)), editorial can be found in [mdc19066369pJAMA 2009 Jan 7;301(1):102](http://pubmed.ncbi.nlm.nih.gov/19066369?dopt=Abstract), commentaries can be found in [mdc19436009pJAMA 2009 May 13;301(18):1876](http://pubmed.ncbi.nlm.nih.gov/19436009?dopt=Abstract), [mnh19306492tmdc19306492tAnn Intern Med 2009 Mar 17;150(6):JC3](http://pubmed.ncbi.nlm.nih.gov/19306492?dopt=Abstract)
    - **selenium supplementation does not appear to reduce risk for prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Cohort Study[mnh17943452pmdc17943452pCancer Causes Control 2008 Feb;19(1):75](http://pubmed.ncbi.nlm.nih.gov/17943452?dopt=Abstract)

studySummary

* + - * based on prospective cohort study Cohort Study
      * 35,242 persons from western Washington state, United States 2000-2002 completed questionnaire including detailed questions about vitamin E and selenium supplement intake during previous 10 years
      * 830 new cases of prostate cancer documented from western Washington Surveillance, Epidemiology and End Results (SEER) cancer registry from baseline through 2004, incidence 2.4%
      * no significance between no supplementation and mean selenium supplement intake > 50 mcg/day over 10 years for risk of prostate cancer
      * PubMed17943452Cancer causes & control : CCC20080201Cancer Causes Control1917575 Reference - VITAL study cohort ([mnh17943452pmdc17943452pCancer Causes Control 2008 Feb;19(1):75](http://pubmed.ncbi.nlm.nih.gov/17943452?dopt=Abstract))
  + Serum selenium level:
    - **increasing toenail selenium concentration, but not blood selenium concentration, associated with reduced risk of prostate cancer**

Systematic Review[J Natl Cancer Inst 2016 Nov;108(11):doi:10.1093/jnci/djw153](http://pubmed.ncbi.nlm.nih.gov/27385803)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/27385803/)

studySummary

* + - * Systematic Review based on individual patient data analysis from systematic review of observational studies
      * systematic review of 15 studies (8 nested case-control studies and 7 cohort analyses of randomized trials) evaluating association of selenium levels in toenail and blood with risk of prostate cancer in 14,604 persons (mean age range 55-69.1 years)
      * 6,497 persons (44.5%) had prostate cancer
      * every 80th percentile increase in toenail selenium concentration associated with reduced risk of prostate cancer (adjusted odds ratio 0.29, 95% CI 0.22-0.4) in analysis of 4 studies with 4,065 persons, results limited by significant heterogeneity
      * no significant difference in risk of prostate cancer for every 80th percentile increase in blood selenium concentration in analysis of 11 studies with 10,548 persons
      * PubMed27385803Journal of the National Cancer InstituteJ Natl Cancer Inst2016070610811Reference - [J Natl Cancer Inst 2016 Nov;108(11):doi:10.1093/jnci/djw153](http://pubmed.ncbi.nlm.nih.gov/27385803)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/27385803/)

Other Dietary Considerations

* Dietary factors associated with decreased risk of prostate cancer from mostly observational studies with limited evidence from randomized trials include the following:
  + [Phytoestrogen intake](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_PJR_MLK_CKB__LI_ZDC_TVK_CKB)
  + [Lycopene, carotene, or tomato intake](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_PJR_MLK_CKB__LI_IKV_TVK_CKB)
  + [Vegetable intake](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_PJR_MLK_CKB__LI_L2B_YBX_3NB)
  + [Coffee consumption](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_PJR_MLK_CKB__LI_BMH_TVK_CKB)

Lifestyle Considerations

* Physical activity:
  + **greater total physical activity associated with decreased risk of prostate cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Systematic Review[21802197Eur Urol 2011 Nov;60(5):1029](http://pubmed.ncbi.nlm.nih.gov/21802197?dopt=Abstract)

studySummary

* + - based on systematic review of observational studies Systematic Review
    - systematic review of 19 cohort studies and 24 case-control studies evaluating effect of physical activity on prostate cancer in 88,294 patients
    - greater total physical activity (TPA) associated with decreased risk of prostate cancer (pooled relative risk [RR] 0.9, 95% CI 0.84-0.95)
    - PubMed21802197European urology20111101Eur Urol60510291029 Reference - [21802197Eur Urol 2011 Nov;60(5):1029](http://pubmed.ncbi.nlm.nih.gov/21802197?dopt=Abstract)
  + **physical activity, in particular vigorous physical activity, may decrease risk of prostate cancer, especially advanced prostate cancer, in adults ≥ 65 years old (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Cohort Study[mdc15883238pArch Intern Med 2005 May 9;165(9):1005](http://pubmed.ncbi.nlm.nih.gov/15883238?dopt=Abstract)

studySummary

* + - based on prospective cohort study Cohort Study
    - 47,620 US male health professionals evaluated for incident, advanced (defined as seminal vesicle invasion, metastasis, or fatal), fatal, or high-grade prostate cancer during 14 years follow-up
    - 2,892 new cases of prostate cancer identified (482 were advanced, 280 of which were fatal)
    - compared to adults ≥ 65 years old who had 0 metabolic equivalents of physical activity per week, adults ≥ 65 years old with > 29 hours of vigorous activity per week had
      * decreased risk of advanced prostate cancer (relative risk [RR] 0.33, 95% CI 0.17-0.62)
      * decreased risk of fatal prostate cancer (RR 0.26, 95% CI 0.11-0.66)
    - in persons < 65 years old, no significant differences in prostate cancer for different levels of physical activity
    - PubMed15883238Archives of internal medicine20050509Arch Intern Med165910051005 Reference - [mdc15883238pArch Intern Med 2005 May 9;165(9):1005](http://pubmed.ncbi.nlm.nih.gov/15883238?dopt=Abstract)
* [Lower body mass index](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#TOPIC_OJ3_121_WNB__LI_WZT_C21_WNB) may be associated with reduced incidence of prostate cancer.

Screening

* Major guidelines recommend some level of shared decision making for prostate-specific antigen (PSA) screening for prostate cancer:
  + Oncology guidelines:
    - National Comprehensive Cancer Network (NCCN) recommends discussing benefits and risk of baseline PSA testing ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__NCCNGRADE)).
    - American Society of Clinical Oncology (ASCO) recommends discussing benefits and harms associated with PSA testing before screening ([ASCO Informal consensus, Strong recommendation, Indeterminate quality evidence](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__ASCOGRADES)).
    - American Cancer Society (ACS) recommends that asymptomatic patients with life expectancy ≥ 10 years should have the opportunity to make informed decision with their health care provider about whether to be screened for prostate cancer.
  + Urology guidelines:
    - American Urological Association (AUA) recommends shared decision making for screening in adults aged 55-69 years, with screening decision based on patient values and preferences ([AUA Standard, Grade B Evidence](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__AUA2018GRADE)).
    - European Association of Urology (EAU) recommends individualized risk-adapted strategy for early detection in well-informed patients with good performance status and life expectancy of ≥ 10-15 years ([EAU Weak recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__EAU2018GRADE)).
  + Public health guidelines:
    - United States Preventive Services Task Force (USPSTF) recommendations:
      * In adults aged 55-69 years, decision to undergo periodic PSA screening should be made on individual basis and should involve shared decision-making between patients and clinicians with the discussion of potential benefits and harms based on family history, race/ethnicity, comorbidities, patient values, and other health needs ([USPSTF Grade C recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__USPSTFGRADE)).
      * In adults ≥ 70 years old, periodic PSA screening is not recommended ([USPSTF Grade D recommendation](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__USPSTFGRADE)).
    - Canadian Task Force on Preventive Health Care (CTFPHC) recommends against screening for prostate cancer for patients < 55 years old or ≥ 70 year old ([CTFPHC Strong recommendation, Low-quality evidence](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__WCRFGRADE)) and for adults aged 55-69 years ([CTFPHC Weak recommendation, Moderate-quality evidence](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_0074d589/#GUID-3A1D5D8B-DAAD-4473-999A-C724D77F926D__WCRFGRADE))
  + Primary care guidelines
    - American College of Physicians (ACP) recommends that clinicians inform adults aged 50-69 years about the limited potential benefits and substantial harms of screening for prostate cancer, and recommends against PSA screening in patients who do not express a clear preference for screening.
* Shared decision-making:
  + Potential benefits include early detection and associated survival benefit, and peace of mind.
  + Potential harms of screening include unnecessary anxiety, detection of clinically unimportant cancer, false results, and potential for subsequent harms of treatment, such as effects on urinary function, bowel function, or sexual function.
  + Decision aids for patients are available from the following sources:
    - [National Cancer Institute](http://www.cancer.gov/cancertopics/factsheet/detection/PSA/print) or in [Spanish](http://www.cancer.gov/espanol/recursos/hojas-informativas/deteccion-diagnostico/antigeno-prostatico-especifico/print)
    - [Centers for Disease Control and Prevention (CDC)](https://www.cdc.gov/cancer/prostate/index.htm)
    - [American Cancer Society (ACS) PDF](http://www.cancer.org/acs/groups/content/@editorial/documents/document/acspc-024618.pdf)
    - [Mayo Clinic](http://www.mayoclinic.org/diseases-conditions/prostate-cancer/in-depth/prostate-cancer/art-20048087)
    - [Patient UK](https://medical.azureedge.net/pdf/12689.pdf?v=636939494289621149)
  + PubMed23567643Annals of internal medicineAnn Intern Med2013052115810761-769761 American College of Physicians "Talking Points With Patients" provides specific guidance on key information to include in a discussion with patients ([Ann Intern Med 2013 May 21;158(10):761](http://pubmed.ncbi.nlm.nih.gov/23567643)).
  + Several different decision aids may be associated with increased prostate cancer knowledge and/or reduced decisional conflict ([level 3 [lacking direct] evidence](https://www.dynamed.com/home/editorial/editorial-process)), but they have inconsistent results for effects on screening rates for prostate cancer.
  + Prostate cancer screening decision aids may be associated with reduced interest in prostate-specific antigen testing in patients seeking routine care ([level 3 [lacking direct] evidence](https://www.dynamed.com/home/editorial/editorial-process)).
* see [Prostate Cancer Screening](https://dpa-pde-oxford.shinyapps.io/prevention/prostate-cancer-screening#OTHER_SCREENING_METHODS) for more details

Guidelines and Resources

Guidelines

International Guidelines

* PubMed26492179The American journal of surgical pathologyAm J Surg Pathol20160201402244-52244International Society of Urological Pathology (ISUP) Consensus Conference on:
  + Gleason grading of prostatic carcinoma can be found in [Am J Surg Pathol 2016 Feb;40(2):244](http://pubmed.ncbi.nlm.nih.gov/26492179).
  + Handling and staging of radical prostatectomy specimens can be found in [21654361Adv Anat Pathol 2011 Jul;18(4):301](http://pubmed.ncbi.nlm.nih.gov/21654361?dopt=Abstract).
* PubMed31195356European journal of cancer (Oxford, England : 1990)Eur J Cancer20190701116116-136116 International Society of Geriatric Oncology (SIOG) updated recommendations on prostate cancer management in older adults can be found in [Eur J Cancer 2019 Jul;116:116](http://pubmed.ncbi.nlm.nih.gov/31195356?dopt=Abstract).
* PubMed32532513European urologyEur Urol20200901783371-378371International Multidisciplinary Consensus (IMC) guideline on standardized nomenclature and surveillance methodologies after focal therapy and partial gland ablation for localized prostate cancer can be found in [Eur Urol 2020 Sep;78(3):371](http://pubmed.ncbi.nlm.nih.gov/32532513).
* World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) recommendations on diet, nutrition, physical activity and prostate cancer can be found at [WCRF/AICR 2018 PDF](https://www.wcrf.org/sites/default/files/Prostate-cancer-report.pdf).
* American Society of Clinical Oncology/Cancer Care Ontario (ASCO/CCO):
  + ASCO/CCO joint guideline update on brachytherapy for patients with prostate cancer can be found at [CCO 2017 Mar](https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/37776) or in [cxh123998413pmdc28346805pJ Clin Oncol 2017 May 20;35(15):1737](http://pubmed.ncbi.nlm.nih.gov/28346805?dopt=Abstract), [a9h124004313pcxh124004313pmdc28350514pJ Oncol Pract 2017 Jun;13(6):392](http://pubmed.ncbi.nlm.nih.gov/28350514?dopt=Abstract).
  + ASCO/CCO clinical practice guideline on systemic therapy in patients with metastatic castration-resistant prostate cancer can be found in [cxh98905456pmdc25199761pJ Clin Oncol 2014 Oct 20;32(30):3436](http://pubmed.ncbi.nlm.nih.gov/25199761?dopt=Abstract) update can be found in [36112960J Clin Oncol 2022 Nov 1;40(31):3664](http://pubmed.ncbi.nlm.nih.gov/36112960?dopt=Abstract).

United States Guidelines

* National Comprehensive Cancer Network (NCCN) practice guidelines on:
  + UNITED\_STATES\_GUIDELINES\_\_LI\_GKL\_2CB\_QYBGNU08302304/05/2024 11:37:00 AMguidelineNotationUpdatelowOncologic\_Disease Urologic\_DisordersNational Comprehensive Cancer Network (NCCN) practice guidelines on prostate cancer (NCCN 2024 Mar)Prostate cancer can be found at [NCCN 2024 Mar from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_1).
  + UNITED\_STATES\_GUIDELINES\_\_LI\_ISV\_FCB\_QYBGNU08302304/05/2024 11:38:00 AMguidelineNotationUpdatelowOncologic\_Disease Urologic\_DisordersNational Comprehensive Cancer Network (NCCN) practice guidelines on prostate cancer early detection can be found at (NCCN 2024 Mar) Prostate cancer early detection can be found at [NCCN 2024 Mar from NCCN website (free registration required)](https://www.nccn.org/guidelines/category_2).
* UNITED\_STATES\_GUIDELINES\_\_LI\_K4C\_PDD\_5XBGNU061323\_106/13/2023 10:23:57 AMguidelineNotationUpdatelowOncologic\_DiseaseNational Comprehensive Cancer Network (NCCN) statement on mitigating the impacts of anticancer drug shortages (NCCN 2023 Jun 7)National Comprehensive Cancer Network (NCCN) statement on mitigating the impacts of anticancer drug shortages can be found at [NCCN 2023 Jun 7 PDF](https://www.nccn.org/docs/default-source/oncology-policy-program/NCCN-Statement-on-Anti-Cancer-Drug-Shortages.pdf).
* American Urological Association/Society of Urologic Oncology (AUA/SUO):
  + UNITED\_STATES\_GUIDELINES\_\_LI\_SD5\_MXC\_PXBGNU05262305/26/2023 12:35:19 PMguidelineNotationUpdatelowOncologic\_DiseaseAmerican Urological Association/Society of Urologic Oncology (AUA/SUO) guideline on early detection of prostate cancer (AUA/SUO 2023 Apr)AUA/SUO guideline on early detection of prostate cancer part I: prostate cancer screening can be found in [37096582J Urol 2023 Jul;210(1):46](http://pubmed.ncbi.nlm.nih.gov/37096582?dopt=Abstract).
  + AUA/SUO guideline on early detection of prostate cancer part II: considerations for a prostate biopsy can be found in [37096575J Urol 2023 Jul;210(1):54](http://pubmed.ncbi.nlm.nih.gov/37096575?dopt=Abstract).
  + AUA/SUO guideline on advanced prostate cancer can be found in [37096583J Urol 2023 Jun;209(6):1082](http://pubmed.ncbi.nlm.nih.gov/37096583?dopt=Abstract).
* AUA/American Society for Radiation Oncology (AUA/ASTRO):
  + AUA/ASTRO guideline on clinically localized prostate cancer can be found at [35536144J Urol 2022 Jul;208(1):10](http://pubmed.ncbi.nlm.nih.gov/35536144?dopt=Abstract), [35536148J Urol 2022 Jul;208(1):19](http://pubmed.ncbi.nlm.nih.gov/35536148?dopt=Abstract), [35536141J Urol 2022 Jul;208(1):26](http://pubmed.ncbi.nlm.nih.gov/35536141?dopt=Abstract).
  + AUA/ASTRO guideline on adjuvant and salvage radiotherapy after prostatectomy can be found in [38421253J Urol 2024 Apr;211(4):509](http://pubmed.ncbi.nlm.nih.gov/38421253?dopt=Abstract), [38421243J Urol 2024 Apr;211(4):518](http://pubmed.ncbi.nlm.nih.gov/38421243?dopt=Abstract), [38421252J Urol 2024 Apr;211(4):526](http://pubmed.ncbi.nlm.nih.gov/38421252?dopt=Abstract).
* AUA/ASTRO/SUO guideline on hypofractionated radiation therapy for localized prostate cancer can be found in [J Urol 2019 Mar;201(3):528](http://pubmed.ncbi.nlm.nih.gov/30759696?dopt=Abstract) or in [J Clin Oncol 2018 Oct 11:JCO1801097](http://pubmed.ncbi.nlm.nih.gov/30307776)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6269129/).
* AUA/Society of Abdominal Radiology (AUA/SAR) consensus statement on prostate magnetic resonance imaging (MRI) and MRI-targeted biopsy in patients with a prior negative biopsy can be found in [27320841J Urol 2016 Dec;196(6):1613](http://www.ncbi.nlm.nih.gov/pubmed/27320841?dopt=Abstract).
* AUA/Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (AUA/SUFU) guidelines on incontinence after prostate treatment can be found in [J Urol 2019 Aug;202(2):369](http://pubmed.ncbi.nlm.nih.gov/31059663?dopt=Abstract).
* UNITED\_STATES\_GUIDELINES\_\_LI\_D1K\_12D\_5XBGNU061323\_106/13/2023 10:27:54 AMguidelineNotationUpdatelowOncologic\_DiseaseASCO position on prioritization of antineoplastic agents in limited supply for first intervention (ASCO 2023 Jun 13)American Society of Clinical Oncology (ASCO) position on prioritization of antineoplastic agents in limited supply for first intervention can be found at [ASCO](https://old-prod.asco.org/practice-patients/practice-support/drug-shortages/clinical-guidance), accessed 2023 Jun 13.
* American Society of Clinical Oncology (ASCO):
  + Clinical practice guidelines on:
    - UNITED\_STATES\_GUIDELINES\_\_LI\_NJK\_WTL\_GXBGNU04252304/25/2023 01:32:39 PMguidelineNotationUpdatelowOncologic\_DiseaseAmerican Society of Clinical Oncology clinical practice guideline on initial management of noncastrate advanced, recurrent, or metastatic prostate cancer (J Clin Oncol 2023 Jul 10)PubMed37011338Journal of clinical oncology : official journal of the American Society of Clinical OncologyJ Clin Oncol20230403JCO2300155JCO2300155Initial management of noncastrate advanced, recurrent, or metastatic prostate cancer can be found in [J Clin Oncol 2023 Jul 10;41(20):3652](https://pubmed.ncbi.nlm.nih.gov/37011338).
    - UNITED\_STATES\_GUIDELINES\_\_LI\_ULC\_XQD\_BZBGNU10092310/09/2023 11:47:53 AMguidelineNotationUpdatelowOncologic\_Disease Urologic\_DisordersAmerican Society of Clinical Oncology guideline on systemic therapy for tumor control in metastatic well-differentiated gastroenteropancreatic neuroendocrine tumors (J Clin Oncol 2023 Nov 6)Systemic therapy in patients with metastatic castration-resistant prostate cancer can be found at [25199761J Clin Oncol 2014 Oct 20;32(30):3436](http://pubmed.ncbi.nlm.nih.gov/25199761?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4876355/), and rapid updates can be found in [36112960J Clin Oncol 2022 Nov 1;40(31):3664](http://pubmed.ncbi.nlm.nih.gov/36112960?dopt=Abstract), and [37931186J Clin Oncol 2023 Nov 6;JCO2302128](http://pubmed.ncbi.nlm.nih.gov/37931186?dopt=Abstract).
    - PubMed33939491Journal of clinical oncology : official journal of the American Society of Clinical OncologyJ Clin Oncol2021062039182037-20482037Appropriate systemic therapy dosing for obese adult patients with cancer can be found in [J Clin Oncol 2021 Jun 20;39(18):2037](http://pubmed.ncbi.nlm.nih.gov/33939491).
    - PubMed33497248Journal of clinical oncology : official journal of the American Society of Clinical OncologyJ Clin Oncol2021041039111274-13051274Initial management of noncastrate advanced, recurrent, or metastatic prostate cancer can be found in [J Clin Oncol 2021 Apr 10;39(11):1274](https://pubmed.ncbi.nlm.nih.gov/33497248).
    - PubMed31940221Journal of clinical oncology : official journal of the American Society of Clinical OncologyJ Clin Oncol2020061038171963-19961963Optimum imaging strategies for advanced prostate cancer can be found in [J Clin Oncol 2020 Jun 10;38(17):1963](http://pubmed.ncbi.nlm.nih.gov/31940221).
    - PubMed31829902Journal of clinical oncology : official journal of the American Society of Clinical OncologyJ Clin Oncol2020050138131474-14941474Molecular biomarkers in localized prostate cancer can be found in [J Clin Oncol 2020 May 1;38(13):1474](http://pubmed.ncbi.nlm.nih.gov/31829902).
    - Initial hormonal management of androgen-sensitive metastatic, recurrent or progressive prostate cancer can be found in [mdc17404365pJ Clin Oncol 2007 Apr 20;25(12):1596](http://pubmed.ncbi.nlm.nih.gov/17404365?dopt=Abstract).
    - Optimizing anticancer therapy in metastatic non-castrate prostrate cancer can be found in [J Clin Oncol 2018 May 20;36(15):1521](http://pubmed.ncbi.nlm.nih.gov/29608397?dopt=Abstract).
    - PubMed28441112Journal of clinical oncology : official journal of the American Society of Clinical OncologyJ Clin Oncol2017061035171952-19641952Provisional clinical opinion on second-line hormonal therapy for patients with chemotherapy-naive, castration-resistant prostate cancer can be found in [J Clin Oncol 2017 Jun 10;35(17):1952](http://pubmed.ncbi.nlm.nih.gov/28441112).
    - PubMed31990618Journal of clinical oncology : official journal of the American Society of Clinical OncologyJ Clin Oncol2020052038151736-17431736Endorsement of Cancer Care Ontario guidelines on bone health and bone-targeted therapies for prostate cancer can be found in [J Clin Oncol 2020 May 20;38(15):1736](http://pubmed.ncbi.nlm.nih.gov/31990618).
  + Endorsement of Cancer Care Ontario guidelines on bone health and bone-targeted therapies for prostate cancer can be found in [J Clin Oncol 2020 May 20;38(15):1736](http://pubmed.ncbi.nlm.nih.gov/31990618).
* UNITED\_STATES\_GUIDELINES\_\_LI\_YK1\_DXD\_XWBGNU03232303/23/2023 07:15:50 AMguidelineNotationUpdatelowOncologic\_Disease​American Cancer Society (ACS) recommendations on prostate cancer early detection (ACS 2023)​American Cancer Society (ACS) recommendations on prostate cancer early detection can be found at [ACS 2023](https://www.cancer.org/cancer/prostate-cancer/detection-diagnosis-staging/acs-recommendations.html).
* American Cancer Society (ACS) guideline on early detection of prostate cancer (2010 update) can be found in [mnh20200110pcxh62549006pmdc20200110pCA Cancer J Clin 2010 Mar-Apr;60(2):70](http://pubmed.ncbi.nlm.nih.gov/20200110?dopt=Abstract)[full-text](http://onlinelibrary.wiley.com/doi/10.3322/caac.20066/full).
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  + Darolutamide with androgen deprivation therapy and docetaxel for treating hormone-sensitive metastatic prostate cancer can be found at [NICE 2023 Jun 21:TA903](https://www.nice.org.uk/guidance/ta903)[PDF](https://www.nice.org.uk/guidance/ta903/resources/darolutamide-with-androgen-deprivation-therapy-and-docetaxel-for-treating-hormonesensitive-metastatic-prostate-cancer-pdf-82615424991685).
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  + National Institute for Health and Care Excellence (NICE) guideline on denosumab for prevention of skeletal-related events in adults with bone metastases from solid tumors can be found at [NICE 2012 Oct:TA265](http://www.nice.org.uk/guidance/TA265)[PDF](http://www.nice.org.uk/guidance/ta265/resources/denosumab-for-the-prevention-of-skeletalrelated-events-in-adults-with-bone-metastases-from-solid-tumours-82600553671621).
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Canadian Guidelines

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  + PubMed32374715Canadian Urological Association journal = Journal de l'Association des urologues du CanadaCan Urol Assoc J20200601146163-168163CUA/CUOG guidelines on management of prostate cancer during COVID-19 pandemic can be found at [CUA 2020 Jun PDF](https://cuaj.ca/index.php/journal/article/view/6667/4420) or in [Can Urol Assoc J 2020 Jun;14(6):163](http://pubmed.ncbi.nlm.nih.gov/32374715).
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  + CUA algorithm on erectile rehabilitation following prostate cancer treatment can be found at [CUA 2019 Aug PDF](https://cuaj.ca/index.php/journal/article/view/5653/4157) or in [Can Urol Assoc J 2019 Aug;13(8):239](http://pubmed.ncbi.nlm.nih.gov/30526799)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6737730/).
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* Alberta Health Services (AHS):
  + AHS clinical practice guidelines on local prostate cancer can be found at [AHS 2022 Dec PDF](https://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-gu012-local-prostate.pdf).
  + AHS clinical practice guidelines on advanced/metastatic prostate cancer can be found at [AHS 2023 May PDF](https://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-gu010-met-prostate.pdf).
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  + CCO guidelines on hereditary cancer testing eligibility criteria can be found at [CCO 2022 Oct](https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/70161).
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  + CCO guidelines on risk reduction of prostate cancer with drugs or nutritional supplements can be found at [CCO 2012 May](https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/426).
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European Guidelines

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* PubMed32593798Annals of oncology : official journal of the European Society for Medical OncologyAnn Oncol202009013191119-11341119European Society for Medical Oncology (ESMO) clinical practice guideline on diagnosis, treatment, and follow-up of cancer of the prostate can be found in [Ann Oncol 2020 Sep;31(9):1119](http://pubmed.ncbi.nlm.nih.gov/32593798).
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* European Association of Urology Nurses (EAUN) guideline on transrectal ultrasound guided biopsy of prostate can be found at [EAUN 2011 PDF](http://uroweb.org/wp-content/uploads/1607-Prostate-Cancer_LRV3.pdf).
* S3 Bisphosphonat-assoziierte Kiefernekrose (BP-ONJ) und andere Medikamenten-assoziierte Kiefernekrosen finden Sie unter [AWMF 2012 PDF](https://www.bzaek.de/fileadmin/PDFs/za/007-091l_S3_Bisphosphonat-assoziierte_Kiefernekrose_2012-04.pdf) [Deutsch].
* Italian Association of Medical Oncologists (Associazione Italiana Oncologi Medici) (AIOM) guideline on tumors of the elderly can be found at Sistema Nazionale Linee Guida dell’Istituto Superiore di Sanità [(SNLG-ISS) Sep 2020 PDF](https://snlg.iss.it/wp-content/uploads/2020/09/LG-283-Tumori-Anziano.pdf) [Italian].
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  + AFU expert guideline on treatment of prostate cancer in older adults can be found in [19945664Prog Urol 2009 Dec;19(11):810](http://pubmed.ncbi.nlm.nih.gov/19945664?dopt=Abstract), commentary can be found in [19945665Prog Urol 2009 Dec;19(11):818](http://pubmed.ncbi.nlm.nih.gov/19945665?dopt=Abstract) [French].
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* ​Finnish Medical Society Duodecim (FMSD) guideline on prostate cancer can be found at [FMSD 2023 May 29](https://www.kaypahoito.fi/khp00006) [Finnish].
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Asian Guidelines

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Australian and New Zealand Guidelines

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Middle Eastern Guidelines

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Review Articles

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  + [Lancet 2021 Sep 18;398(10305):1075](https://pubmed.ncbi.nlm.nih.gov/34370973)PubMed32151466Critical reviews in oncology/hematologyCrit Rev Oncol Hematol20200401148102861102861
  + [Crit Rev Oncol Hematol 2020 Apr;148:102861](http://pubmed.ncbi.nlm.nih.gov/32151466)
  + [26074382Lancet 2016 Jan 2;387(10013):70](http://pubmed.ncbi.nlm.nih.gov/26074382?dopt=Abstract)
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* To search MEDLINE for (Prostate Cancer) with targeted search (Clinical Queries), click [therapy](https://pubmed.ncbi.nlm.nih.gov/?term=(Prostate%20Cancer)%20AND%20(randomized%20controlled%20trial%5bPublication%20Type%5d%20OR%20(randomized%5bTitle/Abstract%5d%20AND%20controlled%5bTitle/Abstract%5d%20AND%20trial%5bTitle/Abstract%5d))), [diagnosis](https://pubmed.ncbi.nlm.nih.gov/?term=(Prostate%20Cancer)%20AND%20(specificity%5bTitle/Abstract%5d)), or [prognosis](https://pubmed.ncbi.nlm.nih.gov/?term=(Prostate%20Cancer)%20AND%20(prognos*%5bTitle/Abstract%5d%20OR%20(first%5bTitle/Abstract%5d%20AND%20episode%5bTitle/Abstract%5d)%20OR%20cohort%5bTitle/Abstract%5d)).