

# The association between prostatitis and prostate cancer. Systematic review and meta-analysis

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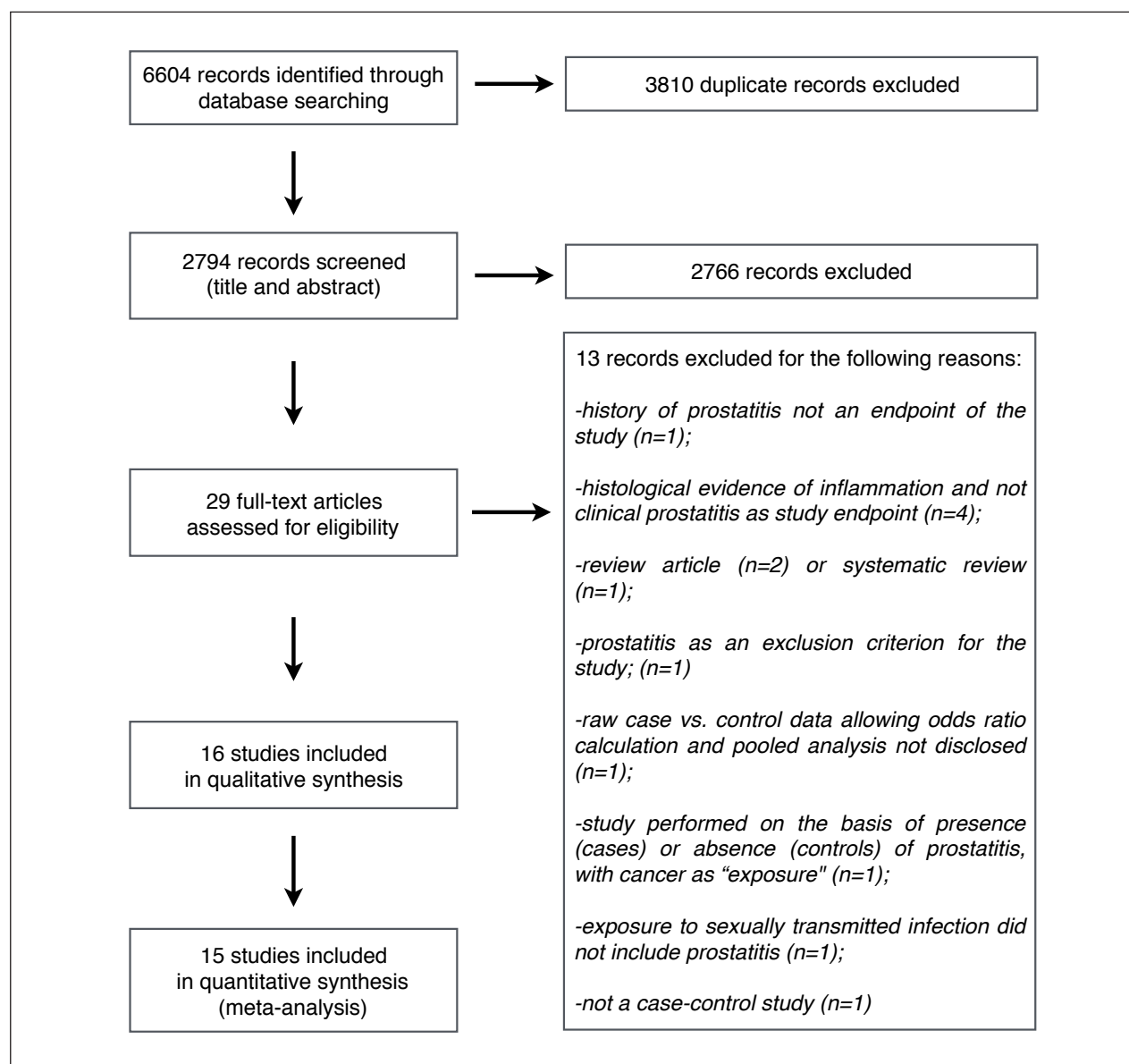
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**Figure 1.**



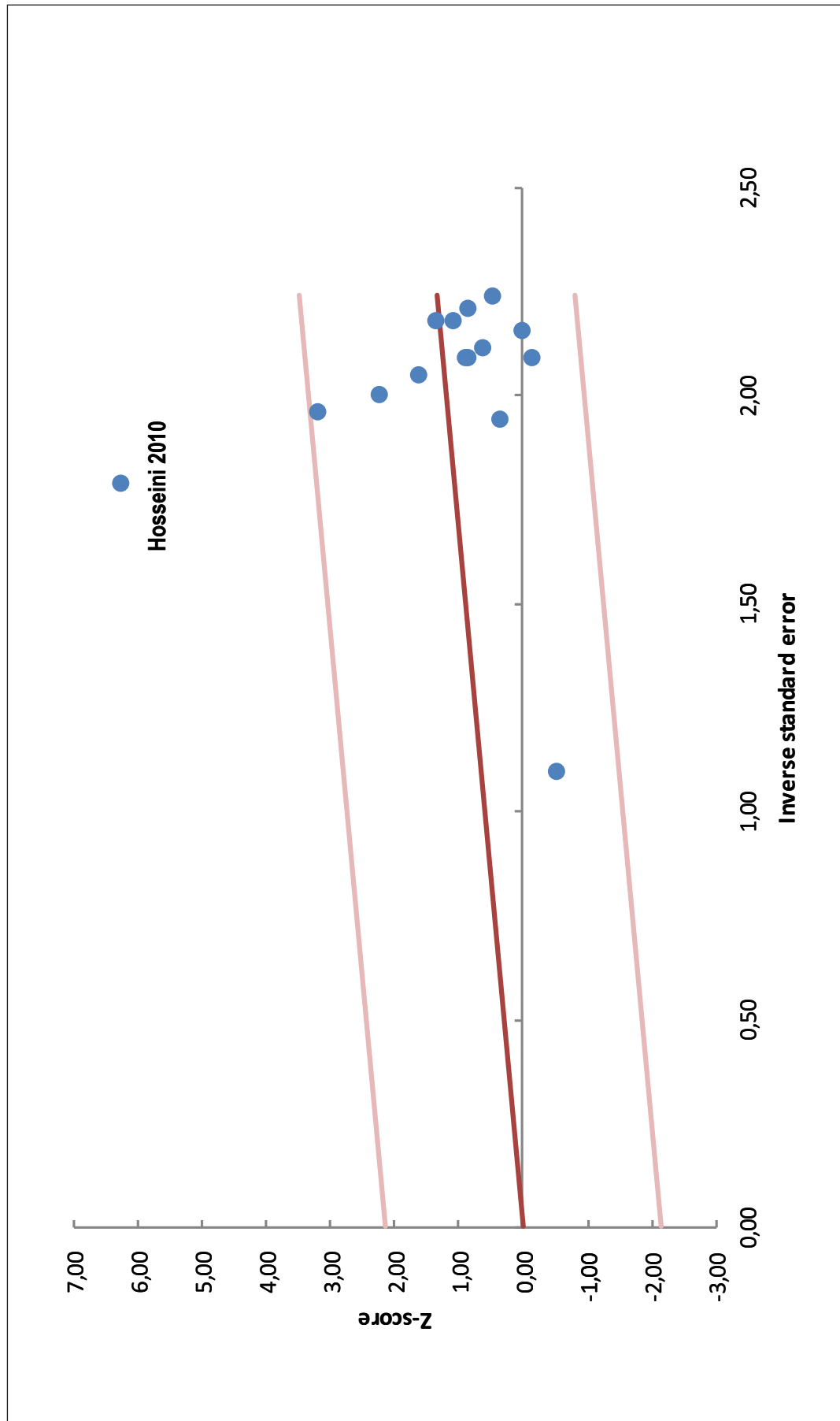


Figure 2.

**Table 1.**  
Patient characteristics and study data.

| STUDY ID (first author, year [reference]) | LOCATION  | STUDY DESIGN   | AGE  | MAIN COHORT      |               |                     |                  | TOTAL CASES | TOTAL CONTROLS | TOTAL POPULATION | NOTABLE STUDY FEATURES   | NOTE |
|---|-----------|--|--|------------------|---------------|---------------------|------------------|-------------|----------------|------------------|--|------|
|   |           |  |  | NONEXPOSED CASES | EXPOSED CASES | NONEXPOSED CONTROLS | EXPOSED CONTROLS |             |                |                  |  |      |
| Boehm 2016, [18]                          | Canada    | Case-control   | Cases, 64; controls, 65 (mean)   | 1661             | 223           | 1811                | 134              | 1965        | 3849           | #                | //   |      |
| Chao 2010, [21] Cheng 2010, [20]          | USA       | Case-control   | Cases, 61.5; controls, 58.1 (mean)   | 1420             | 139           | 70596               | 4788             | 75334       | 78543          | #                | Both reports describe data from a single study. General population data extracted from Chao 2010; African-American subgroup data extracted from Cheng 2010. Data were computed from percentages presented in published article               |      |
| Hoseini 2009, [20]                        | Iran      | Case-control   | Not disclosed  | 21               | 116           | 117                 | 20               | 137         | 274            | #                | Extreme outlier odds ratio   |      |
| Huang 2008, [23]                          | USA       | Patient history report from sexual-transmitted infection study | Not disclosed  | 790              | 78            | 1194                | 89               | 1283        | 2151           | #                | Data were computed from percentages presented in published article   |      |
| Nair-Shanker 2016, [16]                   | Australia | Case-control   | Cases, 65; controls, 59 (median)   | 1083             | 97            | 837                 | 25               | 862         | 2042           | #                | //   |      |
| Patel 2005, [27]                          | USA       | Case-control   | Same age range for cases and controls (50-74)  | 563              | 86            | 558                 | 38               | 596         | 1265           |                  | Cases diagnosed between 1997 and 1998; 47% of population was African-American  |      |
| Relucchi 2006, [26]                       | Italy     | Case-control   | Cases, 67; controls, 61 (median)   | 278              | 2             | 681                 | 8                | 689         | 969            |                  | //   |      |
| Roberts 2004, [29]                        | USA       | Case-control   | Same median age and age range for cases (70.2; 63.8-76.1) and controls (70.1; 63.6-76.8) | 384              | 25            | 761                 | 42               | 803         | 1212           |                  | Acute prostatitis cases were excluded; chronic bacterial or atypical prostatitis (single or multiple episodes) included in the present meta-analysis. It is unknown whether Old "multiple episodes" cohort included acute prostatitis cases. |      |
| Rosenblatt 2001, [30]                     | USA       | Case-control   | Same age range for cases and controls (40-64)  | 666              | 87            | 646                 | 57               | 703         | 1456           |                  | Patients diagnosed either before or after 3 years from reference date were included in computations  |      |
| Rothman 2004, [28]                        | USA       | Case-control   | Agematched; age range of cases and controls, 40-64                                       | 660              | 90            | 644                 | 58               | 702         | 1462           |                  | //   |      |

|                     |     |  |  |      |     |        |       |      |        |        |        |  |   |
|---------------------|-----|--|--|------|-----|--------|-------|------|--------|--------|--------|--|---|
| Rybocki 2016, [17]  | USA | Case-control   | Not disclosed                                      | 502  | 72  | 497    | 77    | 574  | 574    | 574    | 1148   | Cohorts contain matched numbers of acute prostatitis cases   | Acute prostatitis cases were excluded from the present meta-analysis  |
| Sarma 2006, [25]    | USA | Case-control   | Age distributions provided                         | 95   | 34  | 659    | 47    | 706  | 706    | 835    | 835    | Performed exclusively on African-American subjects   | Outlier odds ratio  |
| Sudillo 2006, [24]  | USA | Case-control   | Age range: 40 to 75 years                          | 1809 | 421 | 270480 | 51543 | 2230 | 322023 | 324253 | 324253 | Data collected between 1986 and 1992 (older definitions of prostatitis), and analyzed in 2006  | //  |
| Weinmann 2010, [19] | USA | Case-control   | Only age range at death of cases disclosed (45-84) | 649  | 119 | 784    | 145   | 768  | 929    | 1687   | 1687   | Only lethal prostate cancer cases included in the study; nonlethal cases might have been included in the control cohort  | //  |
| Wright 2012, [31]   | USA | Case-control study investigating the link between PCa and circumcision | Six different age strata provided                  | 1535 | 217 | 1513   | 132   | 1752 | 1645   | 3367   | 3367   | Data from two separate studies were merged together, including patients diagnosed with cancer between 1993 and 1996 (study 1), and between 2002 and 2005 (study 2) | A study investigating the association between PCa and circumcision. Data on history of prostatitis extracted from patient baseline clinical characteristics |

**Table 2.** Newcastle-Ottawa scale and risk of bias assessment.

|                       |   |  |   |   |   |                                       |       |   |          |  |
|-----------------------|---|--|---|---|---|---------------------------------------|-------|---|----------|--|
| Patel 2005, [27]      | Cancer registry, no independent validation  | * Randomized selection of cases  | * Community controls  | Not provided; 6.7% of controls had a history of prostate cancer | *: Age and ethnicity matched; adjusted for age, ethnicity, family history of PCa in 1st degree relatives, education level           | Patient self-report (interview)       | * Yes | 20% cases, 27.3% controls   | 5*: poor | High (higher rates of sexually-transmitted diseases (STD) in the case cohort might imply more intensive medical uro-genital follow-up and higher incident PCa detection rates)       |
| Pelucchi 2006, [26]   | *: Histologically confirmed PCa within the preceding year   | Cases with short survival times (advanced metastatic spread) may be underrepresented | Hospital controls   | Not provided  | *: Multiple logistic regression adjustments included age, study center  | - Patient self-report (questionnaire) | * Yes | *: Fewer than 3% of patients and controls refused to be interviewed | 4*: poor | Unknown (higher percentages of control subjects had STD of any kind)   |
| Roberts 2004, [29]    | Record linkage; data extracted from cancer registry, with no independent validation   | Random sampling  | *: Non-hospitalized controls constituted of former patients registered in Mayo Clinic databases | Not provided  | *: Year of birth, duration of medical record and county residency matched; adjusted for age and number of episodes of prostatitis   | *: Medical records                    | * Yes | Unclear   | 5*: poor | Low (potential influence of PCa detection bias minimized by analyzing strata of cancer and prostatitis diagnoses performed before and after initiation of PSA screening [year 1987]) |
| Rosenblatt 2001, [30] | Data extracted from cancer registry, with no independent validation   | Cases with short survival times (advanced metastatic spread) may be underrepresented | *: Community controls   | Not provided  | *: Age-matched; adjusted for age, ethnicity, family history of PCa and number of PSA tests within 5 years before the reference date | Patient self-report (interview)       | * Yes | *: Cases, 17.9; controls, 24.2                                      | 4*: poor | High (compared to controls, higher proportions of cases were African-American, had family history of PCa, a history of BPH, more frequent DRE and PSA tests)                         |
| Rothman 2004, [28]    | *: Ascertained on city cancer registry, in the frame of NCI surveillance program, histologically confirmed and staged cases | Cases with short survival times (advanced metastatic spread) may be underrepresented | *: Randomly selected community controls   | Not provided  | *: Age and location matched; adjusted for age, ethnicity, family history of PCa in 1st degree relatives, education level            | Patient self-report (interview)       | * Yes | *: Cases, 17.9; controls, 24.2                                      | 5*: fair | High (DRE examination significantly more prevalent in exposed population; might have increased PCa detection rate)   |
| Rybicki 2016, [17]    | Unclear   | Unclear  | Both cases and controls were selected from a cohort of men with benign prostate specimen        | *: No evidence of malignancy                                    | *: Matched for age, race and type of specimen   | *: Medical records                    | * Yes | *: Same rate for both groups  | 6*: poor | High (more intensive prostatitis follow-up might increase incident PCa detection rate in cases)  |

|                       |   |  |   |   |   |                                       |       |   |          |  |
|-----------------------|---|--|---|---|---|---------------------------------------|-------|---|----------|--|
| Patel 2005, [27]      | Cancer registry, no independent validation  | * Randomized selection of cases  | * Community controls  | Not provided; 6.7% of controls had a history of prostate cancer | ** Age and ethnicity matched; adjusted for age, ethnicity, family history of PCa in 1st degree relatives, education level           | Patent self-report (interview)        | * Yes | 20% cases; 27.3% controls   | 5%; poor | High (higher rates of sexually-transmitted diseases (STD) in the case cohort might imply more intensive medical uro-genital follow-up and higher indolent PCa detection rates)       |
| Pe lucchi 2006, [26]  | ** Histologically confirmed PCa within the preceding year   | Cases with short survival times (advanced metastatic spread) may be underrepresented | Hospital controls   | Not provided  | ** Multiple logistic regression adjustments included age, study center  | - Patient self-report (questionnaire) | * Yes | ** Fewer than 3% of patients and controls refused to be interviewed | 4%; poor | Unknown (higher percentages of control subjects had STD of any kind)   |
| Roberts 2004, [29]    | Record linkage; data extracted from cancer registry, with no independent validation   | Random sampling  | ** Non-hospitalized controls constituted of former patients registered in Mayo Clinic databases | Not provided  | ** Year of birth, duration of medical record and county residency matched; adjusted for age and number of episodes of prostatitis   | * Medical records                     | * Yes | Unclear   | 5%; poor | Low (potential influence of PCa detection bias minimized by analyzing strata of cancer and prostatitis diagnoses performed before and after initiation of PSA screening (year 1987)) |
| Rosenblatt 2001, [30] | Data extracted from cancer registry, with no independent validation   | Cases with short survival times (advanced metastatic spread) may be underrepresented | * Community controls  | Not provided  | ** Age-matched; adjusted for age, ethnicity, family history of PCa and number of PSA tests within 5 years before the reference date | Patent self-report (interview)        | * Yes | ** Cases, 17.9; controls, 24.2                                      | 4%; poor | High (compared to controls, higher proportions of cases were African-American, had family history of PCa, a history of BPH, more frequent DRE and PSA tests)                         |
| Rollman 2004, [28]    | ** Ascertained on city cancer registry, in the frame of NCI surveillance program, histologically confirmed and staged cases | Cases with short survival times (advanced metastatic spread) may be underrepresented | * Randomly selected community controls  | Not provided  | ** Age and location matched; adjusted for age, ethnicity, family history of PCa in 1st degree relatives, education level            | Patent self-report (interview)        | * Yes | ** Cases, 17.9; controls, 24.2                                      | 5%; fair | High (DRE examination significantly more prevalent in exposed population; might have increased PCa detection rate)   |
| Rybicki 2016, [17]    | Unclear   | Unclear  | Both cases and controls were selected from a cohort of men with benign prostate specimen        | ** No evidence of malignancy                                    | ** Matched for age, race and type of specimen   | * Medical records                     | * Yes | ** Same rate for both groups  | 6%; poor | High (more intensive prostatitis follow-up might increase indolent PCa detection rate in cases)  |

|                      |  |  |                      |  |   |  |        |   |          |   |
|----------------------|--|--|----------------------|--|---|--|--------|---|----------|---|
| Sarma 2006, [25]     | Independent validation for 27/129; cancer registry for remaining cases                                     | Doubtful due to high non-response rate in cases; moreover, authors state that cases with short survival times (advanced metastatic spread) may be underrepresented | * Community controls | * No history of PCa, confirmed by clinical tests (PSA, DRE, ultrasound)                                    | ** Adjusted for age, income, history of PSA and DRE examination, smoking habit, family history of PCa, alcohol consumption, income,   | Patent self-report (interview); interview not blinded to case/control status | ** Yes | 48.6 % in cases; ~13.75 % in controls                   | 4*; poor | High (*A significantly greater proportion of cases reported having undergone DRE (p 0.0005) or PSA testing (p 0.0008) in the previous 5 years*) |
| Sutcliffe 2006, [24] | Patent self-report (questionnaire), confirmed in about 90% of cases by medical records or pathology report | Cases with short survival times (advanced metastatic spread) may be underrepresented   | * Community controls | No reported history of PCa   | ** Adjusted for age, ethnicity, family history of PCa, body mass index, energy intake, tomato sauced/ meat/fish/ fructose/calcium/ vitamin E/zinc intake, vasectomy, diabetes | Patent self-report (questionnaire)   | ** Yes | * Minor (6%) non-response rate to follow-up assessments | 4*; poor | High (more intensive prostatitis follow-up might increase indolent PCa detection rate in cases)   |
| Weinmann 2010, [19]  | * Medical records  | Only lethal PCa cases included   | * Community controls | Controls might have been patients diagnosed with non-lethal prostate cancer or any other history of cancer | ** Age-matched, health plan-matched, ethnicity-matched; adjusted for age, ethnicity, health plan, history of PCa screening  | * Health care plan medical records   | ** Yes | Unknown   | 6*; fair | High (a higher percentage of cases had confounding prostatic comorbidities/ treatments, e.g. BPH, transurethral resection)                      |
| Wright 2012, [31]    | Cancer registry  | Cases with short survival times (advanced metastatic spread) may be underrepresented, as 66% of cases had less aggressive disease                                  | * Community controls | * No history of PCa  | ** Age-matched by 5-year age groups   | Patent self-report (interview)   | ** Yes | Unknown   | 5*; poor | High (a greater proportion of cases had PSA testing)  |