# Data S1

## Appendix S1. Inclusion criteria.

| Item       | Included                                                                 | Excluded                                                                 |
|------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Population | • Men (aged ≥18 yrs) with known DDR status with:                          | • Pediatric or adolescent populations                                    |
|            |   o mCRPC                                                                | • Upregulated or downregulated wild-type DDR genes                       |
|            |   o mPC                                                                  |                                                                          |
|            |   o CRPC                                                                 |                                                                          |
|            |   o Any type of PC                                                       |                                                                          |
| Interventions | Not relevant                                                             | Not relevant                                                             |
| Comparator | Not relevant                                                             | Not relevant                                                             |
| Outcomes   | • Incidence/prevalence rates of DDR+ (germline or somatic mutations)      | • Incidence/prevalence of individual polymorphisms—unless proven to be    |
|            | • Incidence/prevalence of DDR (germline or somatic mutations) expressed as a percentage |                                                                          |
|            | • Incidence/prevalence of DDR (germline or somatic mutations) expressed as a proportion |                                                                          |
| Note:     | The 11 DDR genes of interest are listed below.                            |                                                                          |
| Note:     | These data may be based on archival and/or fresh tissue samples and/or liquid (eg, blood) samples. Both patient-level and sample-level data will be included, where relevant. |                                                                          |
| Study design | • Any observational study (retrospective, prospective, cross-sectional) | • Clinical trials, experimental studies, and interventional studies involving highly selected patient populations |
|            | • Database registry studies                                               | • Studies that analyze only cell lines rather than primary patient specimens |
|            | • Systematic reviews (these will be checked for primary studies)          | • Case reports                                                           |
| DDR        | • Any of the following individual genes: ATM, ATR, BRCA1, BRCA2, CHEK2, FANCA, MLH1, MRE11A, NBN, PALB2, and RAD51C. DDR defined as any combination of the listed genes. | • When the prevalence of multiple variants for a given gene were presented (or single nucleotide polymorphisms), only those described as pathogenic were extracted; others were excluded. |

ATM, ataxia telangiectasia mutated; ATR, ataxia telangiectasia and Rad3-related protein; BRCA, breast cancer susceptibility gene; CHEK2, checkpoint kinase 2; CRPC, castration-resistant PC; DDR, DNA damage repair; FANCA, Fanconi anemia complementation group A; m, metastatic; MLH1, mutL homolog 1; MRE11A, MRE11 homolog A, double-strand break repair nuclease; NBN, nibrin; PALB2, partner and localizer of BRCA2; PC, prostate cancer; RAD51C, RAD51 paralog C.

## Appendix S2. Literature searches.
Searches were carried out to identify studies in the treatment and epidemiology of DDR-positive prostate cancer. All search methods were conducted to follow best practice standards in systematic reviews (1,2).

Search strategies were developed specifically for each database and the key words adapted according to the configuration of each database. Only studies conducted in humans were sought. Searches were not limited by language or publication status (unpublished or published).

The following databases were searched from study inception to December 2017:

- MEDLINE (Ovid): 1946-2017/11/wk 4
- MEDLINE In-Process Citations, Medline Daily Update & Epub Ahead of Print (Ovid): up to 2017/12/05
- Embase (Ovid): 1974-2017/12/04
- Cochrane Database of Systematic Reviews (CDSR) (Wiley): Issue 12/Dec 2017
- Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley): Issue 11/Nov 2017
- Database of Abstracts of Reviews of Effects (DARE) (Wiley): Issue 4/April 2015
- Health Technology Assessment Database (HTA) (Wiley): Issue 4/Oct 2016
- NHS Economic Evaluation Database (NHS EED) (Wiley): Issue 4/April 2015
- PubMed (NLM) (Internet): up to 2017/12/11
- CINAHL (EBSCO): 1981-2017/12/06
- LILACS (BIRME): up to 2017/12/11

Supplementary searches were undertaken in the following trial registers:

- ClinicalTrials.gov (Internet): up to 2017/12/11 http://www.clinicaltrials.gov/
- WHO International Clinical Trials Registry Platform (ICTRP): up to 2017/12/12 http://www.who.int/ictrp/en/

Conference abstracts and proceedings were identified as part of a 3-stage approach:

- The main Ovid Embase search strategy was employed to include conference abstracts and proceedings;
- A second tailored search was conducted using the Northern Light Life Sciences Conference Abstracts database via Ovid (2016-2017/wk 47)
- Limited internet scanning was conducted for any unindexed conference proceedings, selected by Pfizer.

The named conference proceedings were checked against Embase and Northern Light to determine which proceedings were indexed within the databases. The following proceedings were indexed and included in the Embase and Northern Light database searches:

- American Society for Clinical Oncology (ASCO): 2016 & 2017
- ASCO Genitourinary Cancers Symposium: 2016 & 2017
• European Society for Medical Oncology (ESMO): 2016 only
• European CanCer Organisation (ECCO): 2017 only
• American Urological Association (AUA): 2016 & 2017
• European Association of Urology (EAU): 2016 & 2017
• American Association for Cancer Research (AACR): 2016 & 2017

Limited additional scanning of internet conference proceedings was carried for the following unindexed proceedings (2016-2017 only):
• European Society for Medical Oncology (ESMO): 2017 only
• National Comprehensive Cancer Network (NCCN): 2016 & 2017
• Society of Urologic Oncology (SUO): 2016 & 2017

Handling of citations
Identified references were downloaded into Endnote X8 software for further assessment and handling. Individual records within the Endnote reference library were tagged with searching information, such as searcher, date searched, database host, database searched, strategy name and iteration, theme or search question.

Quality assurance within the search process
The main Embase strategy was independently peer reviewed by a second Information specialist. Strategy peer review was informed by items based on the CADTH checklist (3,4).

Search Strategies
Embase (Ovid): 1974-2017/12/04
Searched 5.12.17
1 exp prostate cancer/ (183779)
2 exp prostate tumor/ (208063)
3 (prostat$ adj4 (cancer$ or neoplas$ or carcinoma$ or malignan$ or adenocarcinoma$ or tumo?r$ or adenoma$ or met or mets or metastas$)).ti,ab,ot. (184826)
4 (prostat$ adj3 (castrat$ resist$ or hormone refrac$ or androgen independ$ or androgen insensi$ or androgen in-sensit$ or androgen resist$)).ti,ab,ot. (14783)
5 (mpc or mcrpc or crpc).ti,ab,ot. (11297)
6 or/1-5 (235566)
7 exp DNA damage/ (128563)
8 exp DNA repair/ (82299)
9 (DNA adj2 damag$).ti,ab,ot. (93314)
10 (DNA adj2 repair$).ti,ab,ot. (60659)
11 (DNA adj2 injur$).ti,ab,ot. (753)
12 DDR$.ti,ab,ot. (6742)
13 (base excision repair$ or BER).ti,ab,ot. (7366)
14 (deoxyribonucleic acid adj3 (damag$ or injur$)).ti,ab,ot. (315)
15 (dna adj2 lesion$).ti,ab,ot. (9081)
16 ((photoinduced or photo induced) adj2 dna).ti,ab,ot. (208)
17 (genotoxic adj2 stress$).ti,ab,ot. (3467)
18 (Homologous recombination deficit$ or HRD).ti,ab,ot. (653)
19 (double strand break$ or DSB).ti,ab,ot. (21165)
20 (single strand break$ or SSB).ti,ab,ot. (9297)
21 (H2AX or pH2AX or phosphorylated H2AX or phosphorylated-H2AX or gamma-H2AX or gamma H2AX or yH2AX).ti,ab,ot. (6742)
22 comet assay/ (11267)
23 (comet adj2 assay$).ti,ab,ot. (11305)
24 BRCA1 protein/ (14056)
25 BRCA2 protein/ (10158)
26 (BRCAS or gBRCA or BRIP1 or BACH1).ti,ab,ot. (24734)
27 Rad51 protein/ (4150)
28 RAD51c$.ti,ab,ot. (506)
29 Fanconi anemia/ (5758)
30 Fanconi anemia protein/ or Fanconi anemia group A protein/ (956)
31 (FANCA or FA-H or FA1 or FAA or FACA or FAH or FANCH or "Fanconi anemia complementation group A" or Fam175a).ti,ab,ot. (3110)
32 ((familial or hereditary) adj3 hypoplastic$ adj3 an?emia).ti,ab,ot. (7)
33 ((familial or hereditary) adj3 aplastic$ adj3 an?emia).ti,ab,ot. (35)
34 (fanconi$ adj3 an?emia).ti,ab,ot. (5138)
35 ((fanconi$ or congenital) adj3 pancytop?enia).ti,ab,ot. (81)
36 mckusick 2276$.ti,ab,ot. (0)
37 checkpoint kinase 2/ (3796)
38 ((Checkpoint adj2 Kinase) or CHEK2 or CHK2 or HuCds or HCds1 or CDS1).ti,ab,ot. (4937)
39 cyclin dependent kinase/ (9776)
40 ((cyclin or cycle) adj3 kinase).ti,ab,ot. (19964)
41 (Cdc2 or CRKRS or CRK7 or KIAA0904 or HCDK12 or CRKR).ti,ab,ot. (5709)
(PALB2 or PNCA3).ti,ab,ot. (929)

(MRE11$ or Meiotic Recombination or AT-Like Disease$ or HNGS1).ti,ab,ot. or MRE11 protein/ (4761)

nibrin/ (1157)

(nibrin or NBN or NBS1 or Nijmegen breakage syndrome$).ti,ab,ot. (2271)

(KIAA1794 or Protein FACI).ti,ab,ot. (2)

ATM protein/ (8350)

(ATM or Ataxia Telangiectasia or A-T Mutated or Telomere Maintenance 1 or AT Mutated).ti,ab,ot. (20754)

ATR protein/ (3016)

(ATE or FRP1 or Mitosis Entry Checkpoint).ti,ab,ot. (10857)

(FACD$ or FA-D2 or FAD2 or FA4).ti,ab,ot. (315)

MutL protein homolog 1/ (567)

(MLH1 or MLH3 or COCA2 or HNPCC7 or (MutL adj3 homolog)).ti,ab,ot. (5322)

or/7-53 (304179)

exp nicotinamide adenine dinucleotide adenosine diphosphate ribosyltransferase inhibitor/ (8926)

((PARP$ or PARS$) adj3 inhibitor$).ti,ab,ot,rn. (5297)

talazoparib/ (292)

(talazoparib or BMN-673 or bmn673 or BMN-673ts or bmn673ts or 1207456-01-6 or 1373431-65-2).ti,ab,ot,rn. (348)

olaparib/ (2790)

(olaparib or Lynparza or AZD-2281 or AZD2281 or ku-0059436 or ku0059436 or ku-59436 or ku59436 or 763113-22-0).ti,ab,ot,rn. (2867)

veliparib/ (1334)

(Veliparib or ABT-888 or abt888 or 912444-00-9).ti,ab,ot,rn. (1490)

rucaparib/ (594)

(Rucaparib or rubraca or ag-014699 or ag014699 or ag-14447 or ag14447 or ag14699 or ag-14699 or co-338 or co338 or pf-01367338 or pf1367338 or pf01367338 or pf-1367338 or pf1367338bw or pf-1367338bw or 859053-21-6 or 283173-50-2 or 459868-92-9).ti,ab,ot,rn. (625)

niraparib/ (385)

(Niraparib or Zejula or MK-4827 or MK4827 or 038915-60-4).ti,ab,ot,rn. (403)

or/55-66 (9985)

54 or 67 (308401)
69 6 and 68 (6611)
70 animal/ or animal experiment/ (3989568)
71 (rat or rats or mouse or mice or murine or rodent or rodents or hamster or hamsters or pig or pigs or porcine or rabbit or rabbits or animal or animals or dogs or dog or cats or cow or bovine or sheep or ovine or monkey or monkeys).ti,ab,ot,hw. (6682078)
72 70 or 71 (6682078)
73 exp human/ or human experiment/ (19273429)
74 72 not (72 and 73) (5205450)
75 (letter or editorial or note).pt. (2256220)
76 69 not (74 or 75) (5987)
Appendix S3. A. Studies not included in the analysis of prevalence in the unselected population or in subgroup analysis.

| Author, year | Country | PC Group | Selected population | Germline or somatic mutation | Mutation Definition | Period of data collection | Gene | % prevalence | No. patients | References |
|--------------|---------|----------|---------------------|-----------------------------|---------------------|--------------------------|------|--------------|-------------|------------|
| Unselected population | | | | | | | | | | |
| Liu et al, 2016 | NR | PC | Unselected | Somatic | Undefined | NR | ATM | 5.6 | 36 | (5) |
| Sonpavde et al, 2017 | NR | mCRPC | Unselected | Somatic | Undefined | NR | BRCA1 | 5.0 | 514 | (6) |
| Tanaka et al, 2009 | Japan | PC | Unselected | Somatic | MLH1 T/A at codon 384 (genotype) | 1997 to 2003 | MLH1 | 3.4 | 177 | (7) |
| Dall'Era et al, 2017 | USA | Primary PC | Unselected | NR/unclear | 85 DDR genes associated with cancer predisposition syndromes (undefined) | NR | DDR | 20.1 | 936 | (8) |
| Dall'Era et al, 2017 | USA | mPC | Unselected | NR/unclear | 85 DDR genes associated with cancer predisposition syndromes (undefined) | NR | DDR | 18.8 | 936 | (8) |
| Daniel et al, 2017 | USA | mPC | Unselected | NR/unclear | ≥1 deleterious BRCA GA (BRCA1 or BRCA2) | NR | DDR | 11.3 | 1911 | (9) |
| Feldman et al, 2014 | USA | PC | Unselected | NR/unclear | ATM (undefined) | NR | ATM | 5 | >330 | (10) |
| Dawson et al, 2016 | USA | PC | Unselected | NR/unclear | Alterations in ≥1 DNA repair gene (tested using a 592 gene hybrid capture NGS) | NR | DDR | 84 | 31 | (11) |
| USA | PC | Unselected | NR/unclear | BRCA2 (undefined) | NR | BRCA2 | 6 | 437 | |
| Author, year | Country | PC Group | Selected population | Germline or somatic mutation | Mutation Definition | Period of data collection | Gene | % prevalence | No. patients | References |
|--------------|---------|----------|---------------------|----------------------------|---------------------|--------------------------|------|-------------|-------------|------------|
| Uchida et al, 1999 | Japan | Primary PC | Unselected | NR/ unclear | LOH at ≥1 loci on chr17q (D17S250, D17S1320, D17S855, D17S1322, D17S1323, D17S579, D17S588) | NR | BRCA1 | 16.7 | 24 | (12) |
| Angele et al, 2004 | UK | PC | Unselected | Germline | ATM 3161C>G | 1993 to 2002 | ATM | 7.4 | 226 | (13) |
| Browning et al, 2006 | USA | PC | Unselected | Germline | ATM heterozygous IVS62+60G/A polymorphism | 1997 | ATM | 30.61 | 98 | (14) |
| | | | | | ATM homozygous IVS62+60G/G | 1997 | ATM | 18.37 | 98 | |
| | | | | | ATM homozygous IVS62+60A/A | 1997 | ATM | 51.02 | 98 | |
| Nam et al, 2005 | Canada | PC | Unselected | Germline | All CHEK2 (1100delC) | Jun 1998 to Jan 2003 | CHEK2 | 0.2 | 996 | (15) |
| Naslund Koch et al, 2016 | Denmark | PC | Unselected | Germline | All CHEK2*1100delC | 2003-2010 | CHEK2 | 0.74 | 39014 | (16) |
| Gambhir et al, 2016 | USA | mCRPC | Unselected | Somatic | BRCA1, BRCA2, ATM, CDK12, MLH1 and/or MSH2 | NR | DDR | 54 | 13 | (17) |
| Xia et al, 2015 | USA | PC | Unselected | Somatic | All ATM (c.8012T>G (p.V2671G)) | NR | ATM | 5.0 | 20 | (18) |
| | | | | | All ATR (c.7762G>A (p.A2588T)) | | ATR | 5.0 | 20 | |
| | | | | | All (CHEK2 c.721G>A (p.V241I)) | | CHEK2 | 5.0 | 20 | |
| Author, year | Country | PC Group | Selected population | Germline or somatic mutation | Mutation Definition | Period of data collection | Gene | % prevalence | No. patients | References |
|--------------|---------|----------|---------------------|-----------------------------|---------------------|--------------------------|------|--------------|-------------|------------|
| Beltran et al, 2015 | USA | mPC | Unselected | Somatic | FANCA c.1626G>T (pE542D) | Feb 2013 to Sep 2014 | FANC A | 5.0 | 20 | (19) |
| | USA | mPC | Unselected | Somatic | FANCA c.4009delA (p.S1337fs) | | FANC A | 5.0 | 20 | |
| | USA | mPC | Unselected | Somatic | All FANCA (c.4009delA (p.S1337fs); c.1626G>T (pE542D)) | | FANC A | 10.0 | 20 | |
| | USA | mPC | Unselected | Somatic | All MLH1 (c.547T>A (p.Y183N)) | | MLH1 | 5.0 | 20 | |
| Palapattu et al, 2015 | USA | PC | Unselected | Somatic | All (K2524fs) | NR | BRCA2 | 11.1 | 9 | (20) |
| Robbins et al, 2011 | USA | mPC | Unselected | Somatic | All. 7840C>T likely damaging | NR | BRCA2 | 12.5 | 8 | (21) |
| Beltran et al, 2013 | USA | CRPC | Unselected | Somatic | DNA alterations in ATM in CRPC | NR | ATM | 8 | 25 | (22) |
| | USA | CRPC | Unselected | Somatic | DNA alterations in \(\text{BRCA2}\) in CRPC | NR | BRCA2 | 12 | 25 | |
| | USA | mPC | Unselected | Somatic | DNA alterations in ATM in metastatic hormone-naïve PC | NR | ATM | 0 | 4 | |
| | USA | mPC | Unselected | Somatic | DNA alterations in \(\text{BRCA2}\) in metastatic hormone-naïve PC | NR | BRCA2 | 25 | 4 | |
| Author, year | Country | PC Group | Selected population | Germline or somatic mutation | Mutation Definition | Period of data collection | Gene | % prevalence | No. patients | References |
|-------------|---------|----------|---------------------|-----------------------------|---------------------|------------------------|------|-------------|-------------|------------|
| Cheng et al., 2011 | Australia | PC | Familial | NR/unclear | Undefined | NR | BRCA2 | 26.5 | 147 | (23) |
| Nicolas et al., 2015 | USA | PC | Familial | Germline | One affected gene; high-value DDR or androgen signalling pathway gene variants that may contribute to familial prostate risk | NR | DDR | 91.7 | 12 | (24) |
| Meyer et al., 2007 | Germany | Primary PC | Treatment | Germline | ATM missense variant P1054R | Oct 2000 to Apr 2006 | ATM | 9.6 | 261 | (25) |
| Author, year | Country | PC Group | Selected population | Germline or somatic mutation | Mutation Definition | Period of data collection | Gene | % prevalence | No. patients | References |
|--------------|---------|----------|---------------------|-----------------------------|---------------------|---------------------------|-------|--------------|-------------|----------|
| Damaraju et al, 2006 | Canada | Primary PC | Treatment | Germline | MLH1 C>T, Val219Ile | Sept 1996 to Dec 2000 | MLH1 | 11 | 84 | (26) |
| | | | | | NBN G>C, Glu185Gln | | NBN | 83 | 84 | |
| | | | | | BRCA1 G>A, Met1652Ile | | BRCA1 | 6 | 83 | |
| | | | | | BRCA1 A>G, Arg356Gln | | BRCA1 | 11 | 83 | |
| | | | | | BRCA2 A>G, Lys1132Lys | | BRCA2 | 57 | 83 | |
| | | | | | ATM A>G, Asp1853Asn | | ATM | 69 | 84 | |
| Schweizer et al, 2016 | USA | Ductal PC | Ductal PC | Somatic | All (c.5946delT+likely LOH) | NR | BRCA2 | 11.1 | 9 | (27) [Linked: True 2017(28)] |
| | | | | | All (c.1100delC+LOH) | NR | CHEK 2 | 11.1 | 9 | |
| | | | | | All (exon 19+ 3’UTR homozygous deletion) | NR | MLH1 | 11.1 | 9 | |
| | | | | | CHEK2, BRCA2, MSH6, MSH2, MLH1 | NR | DDR | 66.7 | 9 | |
| Stephens et al, 2016 | NR | Neuroendocrine PC | Neuroendocrine PC | Somatic | Undefined | NR | DDR | 14 | 32 | (29) |

Red text indicates criteria that led to studies being deemed irrelevant to the analysis. ATM, ataxia telangiectasia mutated; ATR, ataxia telangiectasia and Rad3-related protein; BRCA, breast cancer susceptibility gene; CHEK2, checkpoint kinase 2; CRPC, castration-resistant PC; DDR, DNA damage repair; FANCA, Fanconi anemia complementation group A; LOH, loss of heterozygosity; m, metastatic; MLH1, mutL homolog 1; MRE11A, MRE11 homolog A, double-strand break repair nuclease; MSH, MutS homolog; NBN, nibrin; PALB2, partner and localizer of BRCA2; PC, prostate cancer; RAD51C, RAD51 paralog C.
### B. Excluded records at full paper screening.

| Reference | Reason for exclusion |
|-----------|----------------------|
| [1] Abida W, Brennan R, Armenia J, Curtis KR, Gopalan A, Arcila ME, et al. Genomic characterization of primary and metastatic prostate cancer (PC) using a targeted next-generation sequencing assay. In: American Society of Clinical Oncology Genitourinary Cancers Symposium 2016; 07-Jan-2016, 2016. Available from: American Society of Clinical Oncology (ASCO) https://discovery.northernlight.com/document.php?datasource=PHE&docid=PE2016020202001400&context=WK%40northernlight.com&doctype=abstract&docurl=http%3A%2F%2Fmeetinglibrary.asco.org%2Fcontent%2F158192-172&token=b3e6fad5b65095a7eeacccf610b2e1b http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=dscv6&AN=PE2016020202001400 | Duplicate |
| [2] A'Hern R, De Bono J, Sandhu S, Kalaitzaki E, Usdin M, Hall EE. Phase II investigation of a PARP inhibitor (olaparib) in castration resistant prostate cancer (CRPC) which incorporates the possibility that treatment effect may be restricted to biomarker defined subgroups. Trials 2011. | No relevant outcome |
| [3] A'Hern R, De Bono J, Sandhu S, Kalaitzaki E, Usdin M, Hall E. A two stage phase II design incorporating the possibility that the treatment effect may be restricted to a biomarker defined subgroup: Investigation of a PARP inhibitor (Olaparib) in Castration Resistant Prostate Cancer (CRPC). Clin Trials 2012;9(4):552-553. | No relevant outcome |
| [4] Allen-Brady K, Farnham JM, Camp NJ, Karlins E, Ostrander EA, Cannon-Albright LA. No evidence of BRCA2 mutations in chromosome 13q-linked Utah high-risk prostate cancer pedigrees. BMC Res Notes 2009;2:94. | Not a relevant population |
| [5] Annala M, Struss WJ, Warner EW, Beja K, Vandekerkhove G, Wong A, et al. Treatment outcomes and tumor loss of heterozygosity in germline DNA repair-deficient prostate cancer. Eur Urol 2017;72(1):34-42. | Not relevant study design |
| [6] Anonymous. Repair-Gene Mutations Uncovered in Metastatic Prostate Cancer. Cancer Discovery 2016;6(9):OF3. | Not primary research |
| [7] Evans JR. (S028) patient-level DNA damage and repair pathway profiles are prognostic after prostatectomy for high-risk prostate cancer. Oncology 2015;29(4 Suppl 1):21. | No DDR mutation/not relevant |
| [8] Armenia J, Mullane S, Gao J, Chakravarty D, Kundra R, Huang F, et al. The long tail of significantly mutated genes in prostate cancer. Cancer Res 2017. | No data (abstract) |
| [9] Armenia J, Mullane SA, Gao JJ, Chakravarty D, Kundra R, Huang FW, et al. The long tail of significantly mutated genes in prostate cancer. J Clin Oncol 2017. | No data (abstract) |
| [10] AstraZeneca. Open label study to assess efficacy and safety of olaparib in confirmed genetic BRCA1 or BRCA2 mutation pats. NCT01078662. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2012 [accessed 11.12.17]. Available from: https://ClinicalTrials.gov/show/NCT01078662. | No relevant outcome |
| No. | Source | Description | Relevant Outcome |
|-----|--------|-------------|------------------|
| [11] | AstraZeneca. Study of Olaparib (Lynparza™) Versus enzalutamide or abiraterone acetate in men with metastatic castration-resistant prostate cancer (PROfound Study). NCT02987543. In: WHO International Clinical Trials Registry Platform (ICTRP) [Internet]. Geneva: World Health Organization (WHO). 2016 [accessed 12.12.17]. Available from: https://clinicaltrials.gov/show/NCT02987543. | No relevant outcome |
| [12] | AstraZeneca. Study of Olaparib (Lynparza™) Versus enzalutamide or abiraterone acetate in men with metastatic castration-resistant prostate cancer (PROfound Study). EUCTR2016-000300-28-SE. In: WHO International Clinical Trials Registry Platform (ICTRP) [Internet]. Geneva: World Health Organization (WHO). 2017 [accessed 12.12.17]. Available from: https://www.clinicaltrialregister.eu/ctr-search/search?query=eudract_number:2016-000300-28. | No relevant outcome |
| [13] | AstraZeneca. Study of olaparib (Lynparza™) versus enzalutamide or abiraterone acetate in men with metastatic castration-resistant prostate cancer (PROfound Study). NCT02987543. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2020 [accessed 11.12.17]. Available from: https://ClinicalTrials.gov/show/NCT02987543. | Duplicate |
| [14] | Aurelius Omlin. Carboplatin in castration-resistant prostate cancer. NCT02311764. In: WHO International Clinical Trials Registry Platform (ICTRP) [Internet]. Geneva: World Health Organization (WHO). 2014 [accessed 12.12.17]. Available from: https://clinicaltrials.gov/show/NCT02311764. | No relevant outcome |
| [15] | Banks P, San Leong H, Ryland G, Beshay V, Tran B, Toner G, et al. DNA repair gene defects in Australian men with metastatic castration-resistant prostate cancer (mCRPC). BJU Int 2017. | No data (abstract) |
| [16] | Banks P, Leong HS, Ryland G, Beshay V, Tran B, Toner G, et al. DNA repair gene defects in Australian men with metastatic castration-resistant prostate cancer (MCRPC). Asia Pac J Clin Oncol 2017. | No data (abstract) |
| [17] | Barrett A, Schwartz LE. Morphologic and clinical comparison of BRCA+ and BRCA prostate carcinoma. In: United States & Canadian Academy of Pathology Annual Meeting 2017; 04-Mar-2017, 2017. Available from: United States & Canadian Academy of Pathology (USCAP). https://discovery.northernlight.com/document.php?datasource=PHE&docid=PE20170228000002090&context=WK%40northernlight.com http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=dscv6&AN=PE20170228000002090 | Duplicate |
| [18] | Barrett A, Schwartz LE. Morphologic and clinical comparison of BRCA+ and brca prostate carcinoma. Lab Invest 2017. | No relevant outcome |
| [19] | Basu S, Majumder S, Bhowal A, Ghosh A, Naskar S, Nandy S, et al. A study of molecular signals deregulating mismatch repair genes in prostate cancer compared to benign prostatic hyperplasia. PLoS One 2015;10(5):e0125560. | No relevant outcome |
| [20] | Bednarz N, Eltze E, Semjonow A, Rink M, Andreas A, Mulder L, et al. BRCA1 loss preexisting in small subpopulations of prostate cancer is associated with advanced disease and metastatic spread to lymph nodes and peripheral blood. Clin Cancer Res 2010;16(13):3340-3348. | No relevant outcome |
| No. | Reference                                                                                                                                   | Outcome |
|-----|----------------------------------------------------------------------------------------------------------------------------------------------|---------|
| 21  | Bednarz N, Semjonow A, Oster PJ, Brandt B. BRCA1 loss in prostate cancer is associated with metastatic spread: Novel predictor of parp-inhibitory therapy? Biochimica Clinica 2013;37:S160. | No relevant outcome |
| 22  | BeiGene Usa Inc, Myriad Genetics Inc, BeiGene. Study to assess safety, tolerability and clinical activity of BGB-290 in combination with temozolomide (TMZ) in subjects with locally advanced or metastatic solid tumors. NCT03150810. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2020 [accessed 11.12.17]. Available from: https://ClinicalTrials.gov/show/NCT03150810. | No relevant outcome |
| 23  | Beltran H, Stephens PJ, Mosquera JM, Cronin MT, Rubin MA, Yelensky R, et al. Massively parallel DNA-sequencing of aggressive prostate cancer reveals disease heterogeneity and identifies targetable mutations. Cancer Res 2012. | Not a relevant population |
| 24  | Beltran H, Yelensky R, Frampton G, Park K, Downing S, Macdonald T, et al. Targeted next-generation sequencing (NGS) of advanced prostate cancer (PCA) using formalin-fixed tissue. J Clin Oncol 2012. | Not a relevant population |
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| No. | Reference                                                                                                                                   | Summary                                                                                           | Notes                                                                                       |
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| Reference                                                                 | Country          |
|--------------------------------------------------------------------------|------------------|
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Appendix S4.

Table of Contents for Appendix S4.

| Location | Subgroup         | Description of Data                                                                 |
|----------|------------------|-------------------------------------------------------------------------------------|
| A1       | Familial PC      | Summary of *BRCA2* or DDR gene mutation prevalence in familial prostate cancer germline tissues |
| B1       | Familial PC      | Reported prevalence for familial *BRCA2* and DNA damage response mutations in germline prostate cancer populations |
| C1       | Familial PC      | Reported prevalence for familial *BRCA2* and DDR mutations in germline PC populations (definitions of familial and inclusion criteria) |
| A2       | Familial PC      | Familial germline mutations in patients with prostate cancer                         |
| B2       | Ashkenazi Jewish | DDR mutations in Ashkenazi Jewish patients with prostate cancer                      |
| C2       | Pre-specified treatment regimen | DDR mutations in patients receiving a pre-specified treatment regimen             |
| D2       | Young-onset PC   | DDR mutations in patients with young-onset PC                                       |
| E2       | African-American | DDR mutations in African-American patients                                           |
| F2       | Lethal PC        | DDR mutations in patients with lethal PC                                            |

A1. Summary of *BRCA2* and DDR gene mutation prevalence in familial prostate cancer germline tissues.

| % period prevalence, median (range) | Prostate cancer |
|------------------------------------|-----------------|
| Specific *BRCA2*                   | 0.5 (0.21, 2.63) |
|                                   | 3 studies (n=703) |
|                                   | 12 datasets (n=3248) |
| All *BRCA2*                        | 3.7 (1.3, 7.9) |
|                                   | 6 studies (n=945) |


### DDR

29.3 (7.3, 91.67)  
3 studies \((n=327)\)  
4 datasets \((n=339)\)

\[\text{DDR}=\text{multiple gene definitions for DNA damage response gene that includes at least one of our genes of interest.}\]

*BRCA*, breast cancer susceptibility gene; DDR, DNA damage repair; n, sample size.

### B1. Reported prevalence for familial *BRCA2* and DNA damage response mutations in germline prostate cancer populations.

| Gene                           | DDR definition                                      | % prevalence | N   | Variant described as pathogenic for PC? | Variant described as pathogenic for other cancers? | Variant shown to be associated with PC or risk to PC? | Country | Author, year       | References |
|-------------------------------|----------------------------------------------------|--------------|-----|----------------------------------------|---------------------------------------------------|-----------------------------------------------------|---------|-------------------|------------|
| **Specific BRCA2**           |                                                    |              |     |                                        |                                                   |                                                     |         |                   |            |
| *BRCA2* (5531delTT)          |                                                    | 2.63         | 38  | Yes                                    | Yes                                               | Yes                                                 | UK      | Gayther *et al*, 2000 | (50)       |
| *BRCA2* (6710delACAA)        |                                                    | 2.63         | 38  | Yes                                    | Yes                                               | Yes                                                 | UK      | Gayther *et al*, 2000 | (50)       |
| *BRCA2* (9078 G>T or K2950N) |                                                    | 2.63         | 38  | No                                     | Yes                                               | Yes                                                 | UK      | Gayther *et al*, 2000 | (50)       |
| *BRCA2* (c.1813_14._insA or I605fs) frameshift | 0.21                          | 474          | Yes | Yes                                    | Yes                                               | Yes                                                 | Germany | Maier *et al*, 2014 | (72)       |
| *BRCA2* (c.3847delGT or V128fs) frameshift | 0.21                          | 474          | Yes | Yes                                    | Yes                                               | Yes                                                 | Germany | Maier *et al*, 2014 | (72)       |
| *BRCA2* (c.4449delA or T1483fs) frameshift | 0.21                          | 474          | Yes | Yes                                    | Yes                                               | Yes                                                 | Germany | Maier *et al*, 2014 | (72)       |
| *BRCA2* (c.6037A>T or K2013X) nonsense | 0.21                          | 474          | Yes | Yes                                    | Yes                                               | Yes                                                 | Germany | Maier *et al*, 2014 | (72)       |
| *BRCA2* (c.7495C>T or Q2499X) nonsense | 0.21                          | 474          | Yes | Yes                                    | Yes                                               | Yes                                                 | Germany | Maier *et al*, 2014 | (72)       |
| *BRCA2* c.4876_4877del: p.(Asn1626Serfs*12) | 0.52                          | 191          | Yes | Unclear                                | Yes                                               | Yes                                                 | UK      | Leongamornlert *et al*, 2014 | (70)       |
| BRCA2 | c.4981del:p.(Tyr1661Ilefs*9) | 0.52 | 191 | Yes | Unclear | Yes | UK | Leongamornlert et al, 2014 (70) |
|-------|-----------------------------|------|-----|-----|---------|-----|----|---------------------------------|
| BRCA2 | c.5909C>A:p.(Ser1970*)      | 0.52 | 191 | Yes | Unclear | Yes | UK | Leongamornlert et al, 2014 (70) |
| BRCA2 | c.9382C>T:p.(Arg3128*)      | 0.52 | 191 | Yes | Unclear | Yes | UK | Leongamornlert et al, 2014 (70) |

**All BRCA2**

| BRCA2 | 3.23 | 124 | NA | NA | NA | USA | Leдет et al, 2017 (67) |
|-------|------|-----|----|----|----|-----|-----------------------|
| BRCA2 exon sequence variants | 1.3 | 382 | NA | NA | NA | Germany | Maier et al, 2014 (72) |
| Five BRCA2 variants (L61P, H1458R, G2508S, H3056Y, and R3384X) | 4.24 | 118 | NA | NA | NA | Japan | Hayano et al, 2016 (57) |
| Total undefined BRCA2 variants | 7.9 | 38 | NA | NA | NA | UK | Gayther et al, 2000 (50) |
| Undefined BRCA2 | 4.35 | 92 | NA | NA | NA | USA | Marshall et al, 2017 (74) |
| All BRCA2 (c.9382C>T:p.(Arg3128*); c.4876_4877del:p.(Asn1626Serfs*12); c.4981del:p.(Tyr1661Ilefs*9) | 2.09 | 191 | NA | NA | NA | UK | Leongamornlert et al, 2014 (70) |

**DDR**

| DDR (25-79 cancer-related genes) | 16.9 | 124 | NA | NA | NA | USA | Leдет et al, 2017 (67) |
|---------------------------------|------|-----|----|----|----|-----|-----------------------|
| Deleterious LoF mutations | 7.3 | 191 | NA | NA | NA | UK | Leongamornlert et al, 2014 (70) |
One affected gene; High value DDR or androgen signalling pathway gene variants that may contribute to familial prostate risk

Two or more affected genes: High value DDR or androgen signalling pathway gene variants that may contribute to familial prostate risk

BRCA, breast cancer susceptibility gene; DDR, DNA damage repair; LoF, loss of function; NA, not available; PC, prostate cancer.

C1. Reported prevalence for familial BRCA2 and DDR mutations in germline PC populations (definitions of familial and inclusion criteria).

| Gene                      | DDR definition                  | % prevalence | N  | Definition of familial cancer | Inclusion criteria                                                                 | Author, year        | References |
|---------------------------|---------------------------------|--------------|----|--------------------------------|------------------------------------------------------------------------------------|---------------------|------------|
| Specific BRCA2            | BRCA2 (5531delTT)               | 2.63         | 38 | NR                             | Clusters with a relative risk of developing prostate cancer of ≥4; clusters of ≥3 prostate cancers at any age or in sibling pairs, preferably where one is <65 years at diagnosis | Gayther et al., 2000 | (50)       |
|                           | BRCA2 (6710delACAA)             | 2.63         | 38 |                                |                                                                                    |                     |            |
|                           | BRCA2 (9078 G>T or K2950N)      | 2.63         | 38 |                                |                                                                                    |                     |            |
| BRCA2                    | (c.1813_14_insA or l605fs) frameshift | 0.21     | 474 | NR                             | Patients with familial PC who are members of families with PC clustering; or patients with sporadic early onset PC who underwent radical                        | Maier et al, 2014   | (72)       |
| BRCA2                    | (c.3847delGT or V128fs) frameshift | 0.21     | 474 |                                |                                                                                    |                     |            |
| BRCA2 variants                                      | Frequency | Patients/PCs | Notes                                                                 |
|----------------------------------------------------|-----------|--------------|----------------------------------------------------------------------|
| BRCA2 (c.4449delA or T1483fs) frameshift          | 0.21      | 474          | prostatectomy and reported a negative family history for prostate cancer |
| BRCA2 (c.6037A>T or K2013X) nonsense              | 0.21      | 474          |                                                                     |
| BRCA2 (c.7495C>T or Q2499X) nonsense              | 0.21      | 474          |                                                                     |
| BRCA2 c.4876_4877del: p.(Asn1626Serfs*12)          | 0.52      | 191          | Two or more relatives affected by PC                                |
| BRCA2 c.4981del:p. (Tyr1661Ilefs*9)                | 0.52      | 191          | Men with PC who had two or more relatives affected by PC             |
| BRCA2 c.5909C>A: p.(Ser1970*)                       | 0.52      | 191          |                                                                     |
| BRCA2 c.9382C>T: p.(Arg3128*)                      | 0.52      | 191          |                                                                     |
| All BRCA2                                          | 3.23      | 124          | PC patients with a family history that met NCCN guidelines for genetic testing |
| BRCA2 exons sequence variants                      | 1.3       | 382          | Patients with prostate cancer who met NCCN guidelines for genetic testing |
| Five BRCA2 variants (L61P, H1458R, G2508S, H3056Y, and R3384X) | 4.24      | 118          | Patients in families with two or more prostate cancer patients       |
| Total undefined BRCA2 variants                     | 7.9       | 38           |                                                                      |
| BRCA2 | 4.35 | 92 | Personal history of PC and ≥1 close blood relative with breast, ovarian, pancreatic or prostate cancer; or a personal history of PC | Men with PC; personal history of PC and ≥1 close blood relative with breast, ovarian, pancreatic or prostate cancer; or a personal history of PC | Marshall et al, 2017 | (74) |
|---|---|---|---|---|---|---|
| All BRCA2 (c.9382C>T: p.(Arg3128*); c.4876_4877del: p.(Asn1626Serfs*12); c.4981del:p.(Tyr1661Ilefs*9); BRCA2 c.5909C>A: p.(Ser1970*)) | 2.09 | 191 | Two or more relatives affected by PC | Men with PC who had two or more relatives affected by PC | Leongamornlert et al, 2014 | (70) |
| DDR (25-79 cancer-related genes) | 16.9 | 124 | PC patients with a family history that met NCCN guidelines for genetic testing | Patients with prostate cancer who met NCCN guidelines for genetic testing | Ledet et al, 2017 | (67) |
| Deleterious LoF mutations | 7.3 | 191 | Two or more relatives affected by PC | Men with PC who had two or more relatives affected by PC | Leongamornlert et al, 2014 | (70) |
| One affected gene; High value DDR or androgen signalling pathway gene variants that may contribute to familial prostate risk | 91.67 | 12 | NR | Strong family cancer history with either multiple first-degree or second-degree relatives with prostate cancer or other cancers | Nicolas et al, 2015 | (24) |
| Two or more affected genes; High value DDR or androgen signalling pathway gene variants that may contribute to familial prostate risk | 41.67 | 12 | | | | |
**BRCA**, breast cancer susceptibility gene; DDR, DNA damage repair; LoF, loss of function; NCCN, National Comprehensive Cancer Network; NR, not reported; PC, prostate cancer.

### A2. Familial germline mutations in patients with prostate cancer.

| Country      | Gene     | DDR definition                                      | % prevalence | n   | Period of data collection | Author, year          | References |
|--------------|----------|-----------------------------------------------------|--------------|-----|---------------------------|------------------------|------------|
| Australia    | **BRCA1**| Undefined (unclear germline or somatic)             | 7.5          | 147 | NR                        | Cheng et al, 2011     | (23)       |
|              | **BRCA2**| Undefined (unclear germline or somatic)             | 26.5         | 147 | NR                        |                        |            |
| Germany      | **BRCA2**| *BRCA2* (c.1813_14_insA or l605fs) frameshift ^a   | 0.2 ^c        | 474 | 1998-2007                 | Maier et al, 2014     | (72) (107) |
|              |          | *BRCA2* (c.3847delGT or V128fs) frameshift ^a       | 0.2 ^c        | 474 | 1998-2007                 |                        |            |
|              |          | *BRCA2* (c.4449delA or T1483fs) frameshift ^a       | 0.2 ^c        | 474 | 1998-2007                 |                        |            |
|              |          | *BRCA2* (c.6037A>T or K2013X) nonsense ^a           | 0.2 ^c        | 474 | 1998-2007                 |                        |            |
|              |          | *BRCA2* (c.7495C>T or Q2499X) nonsense ^a           | 0.2 ^c        | 474 | 1998-2007                 |                        |            |
|              |          | *BRCA2* exon sequence variants                      | 1.3 ^e        | 382 | 1998-2007                 |                        |            |
|              | **NBN**  | NBN 657del5 ^a                                       | 0.0          | 299 | NR                        | Hebbring et al, 2006  | (58)       |
| Japan        | **BRCA2**| Five *BRCA2* variants                                | 4.2 ^b        | 118 | NR                        | Hayano et al, 2016    | (57)       |
| Multi-national| **NBN** | NBN 657del5 ^a                                       | 0.2          | 1819 | NR                       | Hebbring et al, 2006  | (58)       |
| UK           | **ATM**  | *ATM* c.7327C>T:p.(Arg2443*) ^a                      | 0.5          | 191 | NR                        | Leongamornlert et al, 2014 | (70) |
|              |          | *ATM* c.7777C>T:p.(Gln2593*) ^a                      | 0.5          | 191 | NR                        |                        |            |
|              |          | All *ATM* (c.7777C>T: p.(Gln2593*); c.7327C>T:p.(Arg2443*)) | 1.0 | 191 | NR                        |                        |            |
|              | **BRCA1**| Total undefined *BRCA1* variants                    | 0.0          | 38  | NR                        | Gayther et al, 2000   | (50)       |
| Gene |  | Variants (c.4065_4068del: p.(Asn1355Lysfsa10)) |  |  |  |  |
|------|---|---------------------------------|---|---|---|---|
| BRCA1 | All | (c.9382C>T: p.(Arg3128*); c.4876_4877del: p.(Asn1626Serfs*12); c.4981del:p.(Tyr1661Ilefs*9); BRCA2 c.5909C>A: p.(Ser1970*)) | 0.5 | 191 | NR | Leongamornlert et al, 2014 (70) |
| BRCA2 | BRCA2 | (5531delTT) | 2.6 | 38 | NR | Gayther et al, 2000 (50) |
| BRCA2 | BRCA2 | (6710delACAA) | 2.6 | 38 | NR | |
| BRCA2 | BRCA2 | (9078 G>T or K2950N) | 2.6 | 38 | NR | |
| BRCA2 | BRCA2 | c.4876_4877del: p.(Asn1626Serfs*12) | 0.5 | 191 | NR | Leongamornlert et al, 2014 (70) |
| BRCA2 | BRCA2 | c.4981del:p.(Tyr1661Ilefs*9) | 0.5 | 191 | NR | |
| BRCA2 | BRCA2 | c.5909C>A: p.(Ser1970*) | 0.5 | 191 | NR | |
| BRCA2 | BRCA2 | c.9382C>T: p.(Arg3128*) | 0.5 | 191 | NR | |
| BRCA2 | Total undefined | BRCA2 variants | 7.9 | 38 | NR | Gayther et al, 2000 (50) |

| Gene |  | Variants (c.9382C>T: p.(Arg3128*); c.4876_4877del: p.(Asn1626Serfs*12); c.4981del:p.(Tyr1661Ilefs*9); BRCA2 c.5909C>A: p.(Ser1970*)) | 2.1 | 191 | NR | Leongamornlert et al, 2014 (70) |

| Gene |  | Variants (c.1263del:p.(Ser422Valfs*15)) |  |  |  |  |
|------|---|--------------------------------|---|---|---|---|
| CHEK2 | CHEK2 | c.1263del:p.(Ser422Valfs*15) | 0.5 | 191 | NR | |
| CHEK2 | CHEK2 | c.869del:p.(Asn290Thrfs*14) | 0.5 | 191 | NR | |
| CHEK2 | All | (CHEK2 c.869del:p.(Asn290Thrfs*14); c.1263del:p.(Ser422Valfs*15)) | 1.0 | 191 | NR | |
| MLH1 | NA | (no mutations identified) | 0.0 | 191 | NR | |
| MRE11 | NA | (no mutations identified) | 0.0 | 191 | NR | |
| NBN | NA | (no mutations identified) | 0.0 | 191 | NR | |
| PALB2 | All | PALB2 (c.3507_3508del:p.(His1170Phefs*19)) | 0.5 | 191 | NR | |
| RAD51 | NA | (no mutations identified) | 0.0 | 191 | NR | |
| DDR | Deleterious LoF mutations | 7.3 | 191 | NR | |
|    | Gene | Description | Value | Frequency | Year  | Reference | IW Score | Notes |
|----|------|-------------|-------|-----------|-------|-----------|----------|-------|
| USA | ATM  | Undefined ATM | 1.6 | 124 | 2015 to 2016 | Ledet et al, 2017 (linked: Lin et al, 2017) | (67) (108) |
|    |      |             | 2.1 | NR | NR | LaDuca et al, 2017 | (65) |
|    |      |             | 3.3 | 92 | NR | Marshall et al, 2017 | (74) |
| BRCA1 | Undefined BRCA1 | 2.4 | 124 | 2015 to 2016 | Ledet et al, 2017 (linked: Lin et al, 2017) | (67) (108) |
|    |      |             | 1.1 | 92 | NR | Marshall et al, 2017 | (74) |
| BRCA2 | Undefined BRCA2 | 3.2 | 124 | 2015 to 2016 | Ledet et al, 2017 (linked: Lin et al, 2017) | (67) (108) |
|    |      |             | 4.3 | 92 | NR | Marshall et al, 2017 | (74) |
| CHEK2 | Undefined CHEK2 | 2.4 | 124 | 2015 to 2016 | Ledet et al, 2017 (linked: Lin et al, 2017) | (67) (108) |
|    |      |             | 2.2 | 92 | NR | Marshall et al, 2017 | (74) |
| NBN | NBN |             | 0.8 | 124 | 2015 to 2016 | Ledet et al, 2017 (linked: Lin et al, 2017) | (67) (108) |
|    | NBN 657del5 |             | 0.3 | 1520 | NR | Hebbrinck et al, 2006 | (58) |
|    | novel S706* G>C |             | 1.2 | 85 | NR | Zuhlke et al, 2012 | (102) |
|    | rs1805794 C>G E185Q |         | 54.1 | 85 | NR | | |
### B2. DDR mutations in Ashkenazi Jewish patients with prostate cancer.

| Country | Germline or somatic mutation | Prostate cancer group | Gene | DDR definition | % prevalence | n | Period of data collection | Author, year | References |
|---------|------------------------------|-----------------------|------|----------------|-------------|---|-------------------------|--------------|------------|
| Canada  | Germline                     | PC                    | BRCA1| BRCA1 (185delAG)*<sup>a</sup> | 0.0<sup>c</sup> | 146 | 1991 to 2002           | Hamel et al, 2003 | (55)       |
|         |                              |                       | BRCA2| BRCA1 (5382insC)*<sup>a</sup> | 0.0<sup>c</sup> | 146 | 1991 to 2002           |              |            |
|         |                              |                       |      | BRCA2 (6174delT)*<sup>a</sup> | 1.4<sup>c</sup> | 146 | 1991 to 2002           |              |            |
|         |                              |                       | CHEK2| CHEK2 exon 10 1180G>A E394F | 0.0<sup>c</sup> | 136 | NR                     | Tischkowitz et al, 2008 | (97)       |
|         |                              |                       |      | CHEK2 exon 11 1270T>C Y424H | 0.0<sup>c</sup> | 136 | NR                     |              |            |
|         |                              |                       |      | CHEK2 exon 11 1283C>T S428F | 2.8<sup>c</sup> | 141 | NR                     |              |            |
|         |                              |                       |      | CHEK2 exon 11 1312G>T D438Y | 0.7<sup>c</sup> | 143 | NR                     |              |            |
| Israel  | Germline                     | PC                    | BRCA1| BRCA1 (185delAG)<sup>a</sup> | 2.3<sup>c</sup> | 87  | Jan 1991 to Jul 1997   | Hubert et al, 1999 | (59)       |
|         |                              |                       |      | BRCA1 (5382insC)<sup>a</sup> | 3.3<sup>c</sup> | 60  | 1998                   | Vazina et al, 2000 | (98)       |

<sup>a</sup>Analysis for a specific mutation (not all mutations for a given gene), these studies were not highlighted in grey; <sup>b</sup>high risk of bias for country representation and statistical analysis; <sup>c</sup>high risk of bias for country representation.

Note all patients are designated ‘PC’ and all mutations are germline (except Cheng 2011 which has unclear germline or somatic designation). ATM, ataxia telangiectasia mutated; BRCA, breast cancer susceptibility gene; CHEK2, checkpoint kinase 2; DDR, DNA damage repair; LoF, loss of function; MLH1, mutL homolog 1; MRE11A, MRE11 homolog A, double-strand break repair nuclease; NA, not applicable; NBN, nibrin; NR, not reported; PALB2, partner and localizer of BRCA2; PC, prostate cancer; RAD, DNA repair protein.
| Somatic                               | USA Germline                                      | CRPC                      |
|--------------------------------------|---------------------------------------------------|---------------------------|
| **BRCA2**                            | **BRCA2 (6174delT)** a                             |                           |
| **DDR**                              | **BRCA1 (185delAG) or BRCA2 (6174delT)**          |                           |
| **BRCA1**                            | **BRCA1 (185delAG)** a                            |                           |
| **BRCA1 (5382insC)** a               | **BRCA1 (185delAG)** a                            |                           |
| Total **BRCA1** [185delAG or 5382insC] a | **BRCA2 (6174delT)** a                           |                           |
| **BRCA2**                            | **BRCA2 (6174delT)** a                            |                           |
|                                      | **BRCA2*185delAG and BRCA2*6174delIT** *          |                           |
| **BRCA1**                            | **BRCA1*185delAG** a                              |                           |
| **BRCA2**                            | **BRCA2*6174delT** a                              |                           |
|                                      | **185delAG** a                                     |                           |
|                                      | **185delAG *and 5382insC** a                      |                           |
|                                      | **5382insC** a                                     |                           |
|                                      | **6174delIT** a                                    |                           |
|                                      | **15delAG** a                                      |                           |
|                                      | **15delAG *and 5382insC** a                       |                           |
|                                      | **5382insC** a                                     |                           |
|                                      | **6174delIT** a                                    |                           |

| **Reference** | **Frequency** | **Year** | **Description** | **Comments** |
|---------------|---------------|----------|-----------------|--------------|
| Hubert et al, 1999 | 1.1c          | 1998     | Jan 1991 to Jul 1997 |              |
| Giusti et al, 2003 | 1.5           | 1994 to 1995 |                   |              |
| Lehrer et al, 1998 | 0.1           | 1998 to 2005 |                   |              |
| Agalliu et al, 2009 | 0.2           | 1994 to 1995 |                   |              |
| Nastiuk et al, 1999 | 1.1           | 1998 to 2005 |                   |              |
| Kirchoff et al, 2004 | 2.0c          | Apr 2000 to Sep 2002 |               |              |
| Gallagher et al, 2011 | 8.0           | Jun 1998 to Dec 2007 |            |              |
| Gallagher et al, 2010 | 3.4c          | Jun 1998 to Dec 2007 |            |              |
| Gallagher et al, 2010 | 4.5c          | Jun 1998 to Dec 2007 |            |              |
| Lehrer et al, 1998  | 0.0c          | 60       | NR              |              |
| Lehrer et al, 1998  | 1.1           | 965      | 1998 to 2005    |              |
| Lehrer et al, 1998  | 1.2b,c        | 83       | 1991 to 1996    |              |
| Lehrer et al, 1998  | 2.0c          | 251      | Apr 2000 to Sep 2002 |            |
| Lehrer et al, 1998  | 0.1           | 975      | 1998 to 2005    |              |
| Lehrer et al, 1998  | 0.0c          | 60       | NR              |              |
| Country | Germline or somatic mutation | Prostate cancer group | Gene     | DDR definition                        | % prevalence | n   | Period of data collection | Author, year | Reference(s) |
|---------|-----------------------------|-----------------------|----------|--------------------------------------|--------------|-----|--------------------------|--------------|--------------|
| Germany | Somatic                     | mCRPC                 | BRCA1    | Undefined                            | 0.0          | 53  | 1998 and 2016            | Nientiedt et al, 2017 | (82)         |
|         |                             |                       | BRCA2    | Deleterious, otherwise undefined     | 15.1         | 53  | 1998 and 2016            |              |              |
| USA     | Germline                    |                       | ATM      | All ATM mutations (c.C4106A; c.5707dupA; c.6227delT) | 1.7          | 172 | Oct 2011 to Dec 2015     | Antonarakis et al, 2018 | (34)         |

**C2. DDR mutations in patients receiving a pre-specified treatment regimen.**

*Analysis for a specific mutation (not all mutations for a given gene); *b*high risk of bias for country representation and statistical analysis; *c*high risk of bias for country representation. Note only Tischkowitz 2008(97) analyzed all mutations for a given gene. Agalliu 2009 (32) most representative of USA; Giusti 2003(51) most representative of Israel. All mutations were reported as founder mutations (except Tishkowitz 2008). BRCA, breast cancer susceptibility gene; CHEK2, checkpoint kinase 2; CRPC, castration-resistant PC; DDR, DNA damage repair; NR, not reported; PC, prostate cancer.
| Gene       | Description                                                                 | Frequency | Patients | Time Period               | Ref.                                                                 | Additional Info                        |
|------------|-----------------------------------------------------------------------------|-----------|----------|---------------------------|----------------------------------------------------------------------|----------------------------------------|
| ATM        | (c.5707dupA)                                                               | 0.6       | 172      | Oct 2011 to Dec 2015      |                                                                       |                                        |
| ATM        | (c.6227delT)                                                               | 0.6       | 172      | Oct 2011 to Dec 2015      |                                                                       |                                        |
| ATM        | (c.C4106A)                                                                  | 0.6       | 172      | Oct 2011 to Dec 2015      |                                                                       |                                        |
|            | All pathogenic (c.7271T>G; p.Val2424Gly missense; c.3245_3247delinsTGAT; p.His1082LeufsX14 framshift) | 2.9       | 69       | Jun 2013 to Aug 2014      | Hart et al, 2016 (Linked: NCT01953640)                               | (Linked: NCT01953640) (56) (109)       |
|            | c.3245_3247delinsTGAT; p.His1082LeufsX14 framshift                          | 1.4       | 69       | Jun 2013 to Aug 2014      |                                                                       |                                        |
|            | c.7271T>G; p.Val2424Gly missense                                            | 1.4       | 141      | Jun 2013 to Aug 2014      |                                                                       |                                        |
|            | All ATM c.A>8266>T; p.K>2756>X                                              | 0.7e      | 69       | 2001 to 2015              | Pomerantz et al, 2017                                                | (85)                                   |
| ATR        | All ATR c.4957C>T; p.Arg1653X Stop gained                                   | 1.4       | 141      | Jun 2013 to Aug 2014      | Hart et al, 2016 (Linked: NCT01953640)                               | (Linked: NCT01953640) (56) (109)       |
| ATR        | All ATR (c.2634-1G>A)                                                      | 0.6       | 69       | Oct 2011 to Dec 2015      | Antonarakis et al, 2018                                              | (34)                                   |
| BRCA1      | Undefined pathogenic                                                       | 0.0       | 172      | Jun 2013 to Aug 2014      | Hart et al, 2016 (Linked: NCT01953640)                               | (Linked: NCT01953640) (56) (109)       |
| BRCA2      | All BRCA2 mutations (c.5946delT; c.C9076T; c.5946delT; c.C9285T; c.5946delT) | 2.9       | 69       | Oct 2011 to Dec 2015      | Antonarakis et al, 2018                                              | (34)                                   |
| BRCA2 (c.5946delT) | 0.6 | 172 | Oct 2011 to Dec 2015 |
|-------------------|-----|-----|---------------------|
| BRCA2 (c.C9076T) | 0.6 | 172 | Oct 2011 to Dec 2015 |
| BRCA2 (c.C9285T) | 0.6 | 141 | Oct 2011 to Dec 2015 |
| All BRCA2 variants | 5.7 | 172 | 2001 to 2015 |

| c.1189_1190insTTAG; p.Q>397>fs | 0.7 | 172 | 2001 to 2015 |
|--------------------------------|-----|-----|----------------|
| c.2330dupA; p.D>777>fs | 0.7 | 172 | 2001 to 2015 |
| c.3545_3546del; p.F>1182>fs | 0.7 | 141 | 2001 to 2015 |
| c.5946delIT; p.S>1982>fs | 2.1 | 141 | 2001 to 2015 |
| c.6275_6276del; p.L>2092>fs | 0.7 | 141 | 2001 to 2015 |
| c.8537_8538del p.E>2846>fs | 0.7 | 69 | 2001 to 2015 |

| All pathogenic variants (c.469_470delAA; p.Lys157ValfsX25 (frameshift); c.6444dupT; p.Ile2149TyrfsX2 frameshift; c.9513_9516delACTT; p.Leu3172AlafsX44 frameshift) | 4.3 | 141 | Jun 2013 to Aug 2014 |
|----------------------------------------------------------------|-----|-----|---------------------|
| c.469_470delAA; p.Lys157ValfsX25 (frameshift) | 1.4 | 141 | Jun 2013 to Aug 2014 |

Pomerantz et al., 2017 (85)
| Gene | Mutation | NR/Frequency | Date Range | Reference |
|------|----------|--------------|------------|-----------|
| **c.6444dupT; p.Ile2149TyrfsX2 frameshift** † | | 1.4 | Jun 2013 to Aug 2014 | |
| **c.9513_9516delACTT; p.Leu3172AlafsX44 frameshift** a | | 1.4 | Jun 2013 to Aug 2014 | |
| **CHEK2** | All CHEK2 (c.A349G) | 0.6 | Oct 2011 to Dec 2015 | Antonarakis et al, 2018 (34) |
| **DDR** | 50 defined DDR genes, including: ATM, ATR, BRCA1, BRCA2, CHEK2, FANCA, FANCD2, MLH1, MRE11A, NBN, PALB2, RAD51C, BAP1, BRD1, BLM, BRAP, BRIP1, CDH1, CDK12, CENPQ, CHEK1, EPCAM1, ERCC1, ERCC2, ERCC3, ERCC4, ERCC6, FAM175A, FAM175B, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, GEN1, HDAC2, MLH3, MSH2, MSH6, MUTYH, PIF1, PMS2, RAD51, RAD51B, RAD51D, RAD54L, RDM1, TP53, and XRCC2. | 12.8 | Oct 2011 to Dec 2015 | |
| **FANCA** | NR | 0.0 | Oct 2011 to Dec 2015 | |
| All FANCA c.A>100>T; p.K>34>X | 0.7 | 172 | 2001 to 2015 | Pomerantz et al, 2017 (85) |
| **MLH1** | NR | 0.0 | Oct 2011 to Dec 2015 | Antonarakis et al, 2018 (34) |
| **MRE11A** | NR | 0.0 | Oct 2011 to Dec 2015 | |
| Gene   | NR  | Value | Year   | Reference                                                                 |
|--------|-----|-------|--------|---------------------------------------------------------------------------|
| NBN    | NR  | 0.0   | Oct 2011 to Dec 2015 | |
| PALB2  | NR  | 0.0   | Oct 2011 to Dec 2015 | |
| RAD51C | NR  | 0.0   | Oct 2011 to Dec 2015 | |
| PC     | 25 ATM genetic variants | 44.0<sup>c</sup> | Jun 1990 to Mar 2006 | Cesaretti <i>et al</i>, 2007 (Linked: Cesaretti <i>et al</i>, 2005) (41); (110) |
| ATM    | 5557G>A<sup>a</sup> | 9.0<sup>b</sup> | NR | Zhu et al, 2010 |

<sup>a</sup>Analysis for a specific mutation (not all mutations for a given gene), these studies were not highlighted in grey; <sup>b</sup>high risk of bias for country representation and statistical analysis; <sup>c</sup>high risk of bias for country representation.

Treatments were as follows: Nientiedt 2017 (docetaxel); Antonarakis 2018 (enzalutamide or abiraterone); Hart 2016 (androgen deprivation therapy); Pomerantz 2017 (carboplatin-based chemotherapy); Cesaretti 2007 (brachytherapy).

*ATM*, ataxia telangiectasia mutated; *ATR*, ataxia telangiectasia and Rad3-related protein; *BAP1*, *BRCA1*-associated protein 1; *BLM*, Bloom syndrome RecQ like helicase; *BRCA*, breast cancer susceptibility gene; *BRAP*, *BRCA1*-associated binding protein; *BRIP1*, *BRCA1* interacting protein C-terminal helicase 1; *CDH1*, cadherin 1; *CDK*, cyclin-dependent kinase; *CENPQ*, centromere protein Q; *CHEK2*, checkpoint kinase 2; *CRPC*, castration-resistant PC; *DDR*, DNA damage repair; *EPCAM*, epithelial cell adhesion molecule; *ERCC*, excision repair cross-complementation group; *FAM175*, family with sequence similarity 175,member; *FANC*, Fanconi anemia complementation group; *GEN1*, *GEN1*, Holliday junction 5’ flap endonuclease; *HDAC*, histone deacetylase; *m*, metastatic; *MLH1*, mutL homolog 1; *MRE11A*, *MRE11* homolog A, double-strand break repair nuclease; *MSH*, muS homolog; *MUTYH*, mutY DNA glycosylase; *NBN*, nibrin; *PALB2*, partner and localizer of *BRCA2*; *PC*, prostate cancer; *PIF1*, PIF1 5’-to-3’ DNA helicase; *PMS2*, *PMS1* homolog 2, mismatch repair system component; *RAD*, DNA repair protein; *RDM1*, *RAD52* motif containing 1XRCC, x-ray repair cross complementing.
D2. DDR mutations in patients with young-onset PC.

| Country | PC Group | Selected population | Germline or somatic mutation | Definition | Period of data collection | Gene | % prevalence | n  | Author, year | References |
|---------|----------|---------------------|-------------------------------|------------|---------------------------|------|--------------|----|--------------|------------|
| UK      | Young-onset PC (≤65 years) | Young-onset PC (≤65 years) | Germline | All *BRCA2* (protein-truncating mutations - 16 frameshift and 3 nonsense) | NR | *BRCA2* | 1.2 | 1589 | Kote-Jarai *et al.*, 2011 (Linked: Kote-Jarai *et al.*, 2011) |
|         | Young-onset PC (≤55 years) | Young-onset PC (≤55 years) | | All *BRCA2* (deleterious; 5 frameshift, 1 splice site) | 1992 to 1999 | | 2.3 | 263 | Edwards *et al.*, 2010 (Linked: Edwards *et al.*, 2003) |
| USA     | | | All protein truncating and SNPs in *BRCA2* | Jan 1993 to Dec 2005 | | | 0.69 | 290 | Agalliu *et al.*, 2007 (31) |

E2. DDR mutations in African-American patients.

| Country | PC Group | Selected population | Germline or somatic | Definition | Period of data collection | Gene | % prevalence | n  | Author, year | References |
|---------|----------|---------------------|----------------------------|------------|---------------------------|------|--------------|----|--------------|------------|
|         |          |                     |                           |            |                           |      |              |    |              |            |
| Country | PC Group | Selected population | Germline or somatic mutation | Definition | Period of data collection | Gene | % prevalence | n  | Author, yr | References |
|---------|----------|---------------------|----------------------------|------------|--------------------------|------|--------------|----|------------|------------|
| USA     | African American | African American | Somatic | Pathogenic and variant of unknown significance (VUS) mutations | NR | BRCA2 | 3.5 | 857 | Petrovics et al, 2016 | (84) |
| Germline | DDR (BRCA1 or BRCA2) | NR | DDR | 3.7 | 857 |

F. DDR mutations in patients with lethal PC.
## Appendix S5. Baseline characteristics.

| Abida et al, 2017 (30) |
|------------------------|
| **USA**                |
| **PC; mPC; mCRPC. Diagnosis: Histology** |
| Other details (Mixed population of locoregional (n=50); biochemically recurrent (n=53); metastatic (n=348)) |
| Population (further details): unselected (NR) |
| Treatment (further details): NR (NR) |
| **Total (n=451)** |
| Mean age (SD): NR (NR) |
| Median age (range): 61 (41, 84) |
| Ethnicity: White non-Hispanic (23.7); White Hispanic (0.7); White unknown (61.6); Black (5.3); Asian (1.6); Unknown (6.9); Other (0.2) |
| Gleason score: 6 (5.5); 7 (31.0); 8-10 (57.2); unknown (6.2) |
| AJCC stage: NR |
| TNM stage: M0 (75); M1 (24); Unknown MX (1) |
| ECOG score |
| 0: NR |
| 1: NR |
| 0-1: NR |
| ≥2: NR |
| Previous treatments: Surgery (57); ADT (23); Radiation +/- ADT (16); Other/Unknown (4) |
| Familial history of PC: NR |
Mean years since diagnosis (SD): NR (NR)
Median years since diagnosis (range): NR (NR)

Mean PSA ng/ml (SD): 9.1 (NR)
Median PSA ng/ml (range): NR) (0.9, 11330)

Comments: Age and PSA are mean levels at diagnosis; 451 patients were included for somatic mutation analysis; 221 patients were included for germline mutation analysis

ADT, androgen deprivation therapy; AJCC, American Joint Committee on Cancer; CRPC, castration-resistant PC; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Agalliu et al, 2007 (31)**

USA

Other. Diagnosis: Histology
Other details (early onset, <55 years)

Population (further details): unselected (NR)
Treatment (further details): NR (NR)

Total (n=290)

Mean age (SD): NR (NR)
Median age (range): NR (NR)

Ethnicity: Caucasian (86.8); African American (11.4); Jewish (1.7)

Gleason score: 2-4 (6.6); 5-6 (52.1); 3+4 (27.2); 4+3 (6.9); 8-10 (5.5); Missing (1.7)

AJCC stage: NR

TNM stage: NR
| ECOG score | 0: NR | 1: NR | 0-1: NR | ≥2: NR |
|------------|------|------|--------|-------|
| Previous treatments: | NR |
| Familial history of PC: | 108 (37.3) |
| Mean years since diagnosis (SD): | NR (NR) |
| Median years since diagnosis (range): | NR (NR) |
| Mean PSA ng/ml (SD): | NR (NR) |
| Median PSA ng/ml (range): | NR (NR) |
| Comments: | 35-49 years (33.4%); 50-54 years (66.6%). PSA ng/ml: 0-3.9 (19); 4.0-9.9 (48.3); 10-19.9 (12.4); ≥20 (10.3); missing (10) |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Agalliu et al, 2009 (32)**

USA

PC. Diagnosis: Reason for prostate cancer diagnosis: Abnormal PSA 741 (73.1), Abnormal DRE 123 (12.1), Symptoms 25 (2.5), TURP for BPH 15 (1.5), Other procedures 57 (5.6), Unknown 18 (1.8)

Other details (NR)

Population (further details): Ashkenazi (NR)

Treatment (further details): NR (NR)

Total (n=979)
| Attribute                                      | Value                                      |
|-----------------------------------------------|--------------------------------------------|
| Mean age (SD):                                | 69.4 (NR)                                  |
| Median age (range):                           | NR (NR)                                    |
| Ethnicity: Ashkenazi Jewish men                | (100)                                      |
| Gleason score:                                | 2-6 (63); 7 (25); 8-10 (12); unknown (8)   |
| AJCC stage:                                   | NR                                         |
| TNM stage:                                    | NR                                         |
| ECOG score                                    |                                            |
| 0: NR                                         |                                            |
| 1: NR                                         |                                            |
| 0-1: NR                                       |                                            |
| ≥2: NR                                        |                                            |
| Previous treatments:                          | NR                                         |
| Familial history of PC:                       | 276 (28.2)                                 |
| Mean years since diagnosis (SD):              | NR (NR)                                    |
| Median years since diagnosis (range):         | NR (NR)                                    |
| Mean PSA ng/ml (SD):                          | NR (NR)                                    |
| Median PSA ng/ml (range):                     | NR (NR)                                    |
| Comments: familial history in column AO is only data on first-degree family history |                                            |

**AJCC**, American Joint Committee on Cancer; **ECOG**, Eastern Cooperative Oncology Group; **m**, metastatic; **NR**, not reported; **PC**, prostate cancer; **PSA**, prostate-specific antigen; **SD**, standard deviation; **TNM**, Tumor Nodes Metastasis classification of malignant tumors.

**Angele et al, 2004 (13)**

UK
PC. Diagnosis: NR
Other details (NR)
Population (further details): unselected (NR)
Treatment (further details): NR (NR)
Total (n=637)
Mean age (SD): NR (NR)
Median age (range): NR (43, 86)
Ethnicity: Caucasian (100)
Gleason score: NR
AJCC stage: NR
TNM stage: NR
ECOG score
0: NR
1: NR
0-1: NR
≥2: NR
Previous treatments: NR
Familial history of PC: NR
Mean years since diagnosis (SD): NR (NR)
Median years since diagnosis (range): NR (NR)
Mean PSA ng/ml (SD): NR (NR)
Median PSA ng/ml (range): NR (NR)
AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Annala et al, 2017 (33)**

| Canada |
|----|
| PC. Diagnosis: NR |
| Other details (NR) |
| Population (further details): unselected (NR) |
| Treatment (further details): Mixed (AR-directed therapies, including prostatectomy 7 (32%); external beam radiation 5 (23%); androgen deprivation 8 (36%); brachytherapy 2 (9%); docetaxel/cabazitaxel 9 (41%); enzalutamide 5 (23%); abiraterone 8 (36%); Other 0 (0%)) |

| DDR+ (n=22) | DDR- (n=113) |
|----|----|
| Mean age (SD): 63 (NR) | Mean age (SD): 64 (NR) |
| Median age (range): NR (NR) | Median age (range): NR (NR) |
| Ethnicity: NR | Ethnicity: NR |
| Gleason score: 6 (9); 7 (23); 8-10 (59); unknown (9) | Gleason score: 6 (5); 7 (19); 8-10 (68); unknown (8) |
| AJCC stage: NR | AJCC stage: NR |
| TNM stage: NR | TNM stage: NR |
| ECOG score | ECOG score |
| 0: NR | 0: NR |
| 1: NR | 1: NR |
| 0-1: NR | 0-1: NR |
| ≥2: NR | ≥2: NR |
| Previous treatments: NR | Previous treatments: NR |
| Familial history of PC: NR | Familial history of PC: NR |
|---------------------------|---------------------------|
| Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): 10.3 (NR) | Mean PSA ng/ml (SD): 27.2 (NR) |
| Median PSA ng/ml (range): NR (NR) | Median PSA ng/ml (range): NR (NR) |

AJCC, American Joint Committee on Cancer; ECOG, AR, androgen receptor; Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Antonarakis et al, 2018 (34)**

**USA**

mCRPC. Diagnosis: Histologically confirmed prostate adenocarcinoma, progressive disease despite “castration levels” of serum testosterone (<50 ng/dl), and radiographic metastases on computed tomography (CT) or technetium-99 bone scans. Patients had to have three or more rising serum prostate-specific antigen (PSA) values measured ≥ 2 weeks apart.

Other details (NR)

Population (further details): treatment (enzalutamide or abiraterone)

Treatment (further details): Enzalutamide was given at 160 mg daily, and abiraterone was given at 1000 mg daily (with prednisone 5 mg twice daily). (NR)

| DDR+ (n=22) | DDR- (n=150) |
|------------|-------------|
| Mean age (SD): NR (NR) | Mean age (SD): NR (NR) |
| Median age (range): 64 (NR) | Median age (range): 70 (NR) |
| Ethnicity: White (86.4); non-white (13.6) | Ethnicity: White (87.3); non-white (12.7) |
| Gleason score: ≥8 (68.2) | Gleason score: ≥8 (65.2) |
| AJCC stage: NR | AJCC stage: NR |
| TNM stage: T1/T2 (21.1); T3/T4 (78.9); M1 (19.0) | TNM stage: T1/T2 (55.8); T3/T4 (44.2); M1 (26.1) |
| ECOG score | Previous treatments: chemotherapy (22.7) |
|------------|----------------------------------------|
| 0: NR      |                                        |
| 1: NR      |                                        |
| 0-1: NR    |                                        |
| ≥2: NR     |                                        |

| Familial history of PC: NR |
|---------------------------|
| Familial history of PC: NR |

| Mean years since diagnosis (SD): 6.3 (NR) | Mean years since diagnosis (SD): 7.4 (NR) |
|------------------------------------------|------------------------------------------|
| Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): 22.9 (NR) | Median PSA ng/ml (range): 22.6 (NR) |

| Comments: ECOG ≥1 (5.3) | Comments: ECOG ≥1 (32.1) |
|--------------------------|--------------------------|

AJCC, American Joint Committee on Cancer; CRPC, castration-resistant PC; DDR, DNA damage repair; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Beltran et al, 2013 (22)**

USA

Primary PC; mPC; CRPC. Diagnosis: Histology

Other details (Localized PC, hormone-naïve mPC, and mCRPC)

Population (further details): unselected (NR)

Treatment (further details): NR (NR)

Total (n=45)
| Category                        | Value                        |
|--------------------------------|------------------------------|
| Mean age (SD)                  | 63 (NR)                      |
| Median age (range)             | NR (NR)                      |
| Ethnicity                      | NR                           |
| Gleason score                  | NR                           |
| AJCC stage                     | NR                           |
| TNM stage                      | NR                           |
| ECOG score                     |                              |
| 0: NR                          | NR                           |
| 1: NR                          | NR                           |
| 0-1: NR                        | NR                           |
| ≥2: NR                         | NR                           |
| Previous treatments            | NR                           |
| Familial history of PC         | NR                           |
| Mean years since diagnosis (SD)| NR (NR)                      |
| Median years since diagnosis (range)| NR (NR)               |
| Mean PSA ng/ml (SD)            | NR (NR)                      |
| Median PSA ng/ml (range)       | NR (NR)                      |
| Comments                       | Mean age calculated based on 20 out of 45 patients in supplementary table 3 |

AJCC, American Joint Committee on Cancer; CRPC, castration-resistant PC; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.
| **Beltran et al, 2015 (35)** |
|-----------------------------|
| **USA**                     |
| Primary PC; mPC. Diagnosis: Histology |
| Other details (Mixed population of localized PC (n=69) and advanced mPC (n=29)) |
| Population (further details): unselected (NR) |
| Treatment (further details): NR (NR) |
| **Total (n=97)**            |
| Mean age (SD): NR (NR)      |
| Median age (range): NR (NR) |
| Ethnicity: NR               |
| Gleason score: NR           |
| AJCC stage: NR              |
| TNM stage: NR               |
| ECOG score                  |
| 0: NR                       |
| 1: NR                       |
| 0-1: NR                     |
| ≥2: NR                      |
| Previous treatments: NR     |
| Familial history of PC: NR  |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): () |
| Mean PSA ng/ml (SD): NR (NR) |
|-----------------------------|
| Median PSA ng/ml (range): NR (NR) |
| Comments: For a full text study with a comprehensive supplementary appendix, there was very little information on population (age, cancer scores, previous treatments, etc) |
| AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors. |

**Boudadi et al, 2017 (36)**  

**USA**  

Other. Diagnosis: Histologically or cytologically confirmed adenocarcinoma of the prostate; Metastatic disease as defined by 2 or more bone metastases confirmed by bone scintigraphy or radiographic soft tissue metastasis; detectable circulating tumor cells (CTCs) with detectable AR-V7 splice-variant by reverse transcriptase (RT)-polymerase chain reaction (PCR).  

Other details (androgen receptor-variant-7 positive mCRPC)  

Population (further details): unselected (NR)  

Treatment (further details): Nivolumab and ipilimumab (Nivolumab 3 mg/kg IV over 60 minutes and ipilimumab 1 mg/kg IV over 90 minutes every 3 weeks for 12 weeks. Patients then receive maintenance nivolumab 3 mg/kg IV over 60 minutes every 2 weeks for 36 weeks in the absence of disease progression or unacceptable)  

Total (n=15)  

| Mean age (SD): NR (NR) |
|------------------------|
| Median age (range): 65 (NR) |
| Ethnicity: NR |
| Gleason score: NR |
| AJCC stage: NR |
| TNM stage: NR |
| ECOG score | 0: NR |
|-----------------|-------|
| 1: NR | |
| 0-1: NR | |
| ≥2: NR | |

Previous treatments: ≥4 prior treatment for mCRPC (60)

Familial history of PC: NR

Mean years since diagnosis (SD): NR (NR)
Median years since diagnosis (range): NR (NR)

Mean PSA ng/ml (SD): NR (NR)
Median PSA ng/ml (range): 115 (NR)

Comments: Median follow-up 8.4 months (range: 1.9, 10.5 months)

AJCC, American Joint Committee on Cancer; CRPC, castration-resistant PC; ECOG, Eastern Cooperative Oncology Group; m, metastatic; IV, intravenous; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Browning et al, 2006 (14)**

USA

PC. Diagnosis: Histology

Other details (NR)

Population (further details): unselected (NR)

Treatment (further details): NR (NR)

Total (n=98)
| Characteristic                                      | Value                              |
|----------------------------------------------------|------------------------------------|
| Mean age (SD):                                     | NR (NR)                            |
| Median age (range):                                | 63 (40, 81)                        |
| Ethnicity:                                        | White (100)                        |
| Gleason score:                                     | \(\leq 6 \) (63.3); >6 (36.7)     |
| AJCC stage:                                        | I (9.2); II (68.4); III (22.4)     |
| TNM stage:                                         | NR                                 |
| ECOG score                                         | 0: NR                              |
|                                                   | 1: NR                              |
|                                                   | 0-1: NR                            |
|                                                   | \(\geq 2\): NR                    |
| Previous treatments:                               | radical prostatectomy (100)        |
| Familial history of PC:                            | NR                                 |
| Mean years since diagnosis (SD):                   | NR (NR)                            |
| Median years since diagnosis (range):              | NR (NR)                            |
| Mean PSA ng/ml (SD):                               | \(\leq 4\) ng/ml (17.3%); 4-10 ng/ml (53.1); \(\geq 10\) ng/ml (29.6) (NR) |
| Median PSA ng/ml (range):                          | NR (NR)                            |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

The Cancer Genome Atlas, 2015 (37)
Multinational
| **PC. Diagnosis:** Histology |
|----------------------------|
| Other details (NR)         |
| Population (further details): unselected (NR) |
| Treatment (further details): radical prostatectomy (NR) |
| **Total (n=333)**         |
| Mean age (SD): NR (NR)    |
| Median age (range): 61 (43, 76) |
| Ethnicity: Caucasian (81.1); African descent (12.9); Asian (2.4); NR (3.6) |
| Gleason score: 3+3 (19.5); 3+4 (30.6); 4+3 (23.4); ≥8 (26.4) |
| AJCC stage: NR            |
| TNM stage: NR             |
| **ECOG score**            |
| 0: NR                     |
| 1: NR                     |
| 0-1: NR                   |
| ≥2: NR                    |
| Previous treatments: radical prostatectomy |
| Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): 7.4 (NR) |
| Median PSA ng/ml (range): NR) (1.6, 87) |
AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Castro et al, 2011 (38)**

|                  | Total (n=2181) | BRCA1+ (n=5) | BRCA2+ (n=34) | DDR- (n=2142) |
|------------------|----------------|--------------|---------------|---------------|
| UK               |                |              |               |               |
| PC. Diagnosis    | NR             |              |               |               |
| Other details    | NR             |              |               |               |
| Population       | unselected (NR)|              |               |               |
| Treatment        | NR (NR)        |              |               |               |
| Mean age (SD)    | NR (NR)        | Mean age (SD): NR (NR) | Mean age (SD): NR (NR) | Mean age (SD): NR (NR) |
| Median age (range): 57 (32, 89) | Mean age (range): NR (NR) | Mean age (range): NR (NR) | Mean age (range): NR (NR) |
| Ethnicity        | NR             | Ethnicity: NR |
| Gleason score    | NR             | Gleason score: ≥8 (20) |
| AJCC stage       | NR             | AJCC stage: NR |
| TNM stage        | NR             | TNM stage: N1 (50); M1 (20) |
| ECOG score       | NR             | ECOG score |
| Previous treatments | NR           | Previous treatments: NR |
| Familial history of PC | NR | Familial history of PC: NR |

Mean age (SD): NR (NR)  
Median age (range): 57 (32, 89)  
Ethnicity: NR  
Gleason score: NR  
AJCC stage: NR  
TNM stage: NR  
ECOG score  
0: NR  
1: NR  
0-1: NR  
≥2: NR  
Previous treatments: NR  
Familial history of PC: NR
| Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) |
|----------------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|
| Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR (NR) | Median PSA ng/ml (range): NR (NR) | Median PSA ng/ml (range): NR (NR) | Median PSA ng/ml (range): NR (NR) |
| Comments: details for BRCA1, BRCA2, and non-carriers | Comments: details for BRCA1, BRCA2, and non-carriers | Comments: details for BRCA1, BRCA2, and non-carriers | Comments: details for BRCA1, BRCA2, and non-carriers |

AJCC, American Joint Committee on Cancer; BRCA, breast cancer susceptibility gene; ECOG, Eastern Cooperative Oncology Group; IV, intravenous; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Castro et al, 2013 (39)**

| UK |
|----------------|
| PC. Diagnosis: Histology |
| Other details (NR) |
| Population (further details): unselected (NR) |

| Treatment (further details): Mixed treatment Primary radical treatment in non-metastatic disease: External-beam radiotherapy (35.4%), Radical prostatectomy (33.8%), Brachytherapy (3.1%), Any local radical treatment (72.3%). Primary hormone treatment indication for early disease: Neoadjuvant-adjuvant (35.9%), Single therapy (6.3%). Primary hormone treatment indication for advanced disease: Palliative (55.4%). Other treatments for metastatic disease: chemotherapy (17.1%). |
|----------------|

| DDR+ (n=79) | BRCA1+ (n=18) | BRCA2+ (n=61) | DDR- (n=1940) |
|                       | Mean age (SD): NR (NR) | Mean age (SD): NR (NR) | Mean age (SD): NR (NR) | Mean age (SD): NR (NR) |
|-----------------------|------------------------|------------------------|------------------------|------------------------|
| **Mean age**          |                        |                        |                        |                        |
| **Median age**        | 58.3 (41.7, 88)        | 60.8 (48.3, 73.5)      | 57.6 (41.7, 88)        | 57.2 (32.3, 88.9)      |
| **Ethnicity:**        | NR                     | NR                     | NR                     | NR                     |
| **Gleason score:**    | ≤6 (25.3); 7 (24.1); 8-10 (35.4); unknown=(15.2) | ≤6 (33.3); 7 (22.2); 8-10 (27.8); unknown=(16.7) | ≤6 (23.0); 7 (24.6); 8-10 (37.7); unknown=(14.8) | ≤6 (37.8); 7 (26.3); 8-10 (15.4); unknown=(20.5) |
| **AJCC stage:**       | I (10.1); IIa (11.4); IIb (16.5); III (16.5); IV (27.8); not assessed (17.7) | I (11.1); IIa (5.6); IIb (16.7); III (22.2); IV (16.7); not assessed (27.8) | I (9.8); IIa (13.1); IIb (16.4); III (18.1); IV (31.1); not assessed (11.5) | I (19.2); IIa (16.8); IIb (11.0); III (18.9); IV (12.8); not assessed (21.3) |
| **TNM stage:**        | NR                     | NR                     | NR                     | NR                     |
| **ECOG score:**       | 0: NR                  | 0: NR                  | 0: NR                  | 0: NR                  |
|                       | 1: NR                  | 1: NR                  | 1: NR                  | 1: NR                  |
|                       | 0-1: NR                | 0-1: NR                | 0-1: NR                | 0-1: NR                |
|                       | ≥2: NR                 | ≥2: NR                 | ≥2: NR                 | ≥2: NR                 |
| **Previous treatments:** | NR                     | NR                     | NR                     | NR                     |
| **Familial history of PC:** | NR                     | NR                     | NR                     | NR                     |
| **Mean years since diagnosis (SD):** | NR (NR) | NR (NR) | NR (NR) | NR (NR) |
|                       |                        |                        |                        |                        |
| **Median years since diagnosis (range):** | NR (NR) | NR (NR) | NR (NR) | NR (NR) |
|                       |                        |                        |                        |                        |
| **Mean PSA ng/ml (SD):** | NR (NR) | NR (NR) | NR (NR) | NR (NR) |
|                       |                        |                        |                        |                        |
| **Median PSA ng/ml (range):** | 11.5) (0.5, 3000) | 8.9) (0.7, 3000) | 15.1) (0.5, 761) | 11.3) (0.2, 7800) |
AJCC, American Joint Committee on Cancer; DDR, DNA damage repair; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Castro et al, 2015 (40)**

| **UK** | **UK** |
|--------|--------|
| Primary PC. Diagnosis: Histology | Population (further details): unselected (NR) |
| Other details (NR) | Treatment (further details): radical prostatectomy (NR) |
| | DDR+ (n=35) |
| | Mean age (SD): NR (NR) |
| | Median age (range): 58.7 (47.1, 65.3) |
| | Ethnicity: NR |
| | Gleason score: ≤6 (42.9); 7 (28.6); 8-10 (25.7); unknown=(2.9) |
| | AJCC stage: I (11.4); IIa (22.9); IIb (42.9); III (17.1); IV (5.7) |
| | TNM stage: NR |
| | DDR- (n=500) |
| | Mean age (SD): NR (NR) |
| | Median age (range): 56.9 (36.9, 85.8) |
| | Ethnicity: NR |
| | Gleason score: ≤6 (56.8); 7 (32.2); 8-10 (8.8); unknown (2.2) |
| | AJCC stage: I (34.2); IIa (35.4); IIb (12.6); III (15.8); IV (2.0) |
| | TNM stage: NR |
| ECOG score | ECOG score |
|------------|------------|
| 0: NR      | 0: NR      |
| 1: NR      | 1: NR      |
| 0-1: NR    | 0-1: NR    |
| ≥2: NR     | ≥2: NR     |

| Previous treatments: ADT (14.3) | Previous treatments: ADT (8.8) |
|---------------------------------|---------------------------------|

| Familial history of PC: NR     | Familial history of PC: NR     |
|--------------------------------|--------------------------------|

| Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) |
|-----------------------------------------|-----------------------------------------|
| Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) |

| Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) |
|-------------------------------|-------------------------------|
| Median PSA ng/ml (range): 6) (0.5, 29.1) | Median PSA ng/ml (range): 7.6) (0.7, 138.9) |

ADT, androgen deprivation therapy; AJCC, American Joint Committee on Cancer; DDR, DNA damage repair; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; UK, United Kingdom.

**Castro et al, 2015 (40)**

UK

Primary PC. Diagnosis: Histology

Other details (NR)

Population (further details): unselected (NR)

Treatment (further details): external-beam radiotherapy (NR)

| DDR+ (n=32) | DDR- (n=735) |
| \hline Mean age (SD): NR (NR) & Mean age (SD): NR (NR) \\
Median age (range): 59.3 (46.0, 77.5) & Median age (range): 57.3 (36.0, 79.0) \\
Ethnicity: NR & Ethnicity: NR \\
Gleason score: ≤6 (21.9); 7 (34.4); 8-10 (43.8); unknown (0) & Gleason score: ≤6 (44.1); 7 (35.1); 8-10 (18.5); unknown (2.3) \\
AJCC stage: I (12.5); IIa (6.3); IIb (18.8); III (37.5); IV (25.0) & AJCC stage: I (19.7); IIa (19.3); IIb (22.0); III (33.5); IV (5.4) \\
TNM stage: NR & TNM stage: NR \\
ECOG score & ECOG score \\
0: NR & 0: NR \\
1: NR & 1: NR \\
0-1: NR & 0-1: NR \\
≥2: NR & ≥2: NR \\
Previous treatments: ADT (84.4) & Previous treatments: ADT (77.7) \\
Familial history of PC: NR & Familial history of PC: NR \\
Mean years since diagnosis (SD): NR (NR) & Mean years since diagnosis (SD): NR (NR) \\
Median years since diagnosis (range): NR (NR) & Median years since diagnosis (range): NR (NR) \\
Mean PSA ng/ml (SD): NR (NR) & Mean PSA ng/ml (SD): NR (NR) \\
Median PSA ng/ml (range): 19.4 (2.1, 68.5) & Median PSA ng/ml (range): 13.9 (1.2, 143.0) \\
\hline
ADT, androgen deprivation therapy; AJCC, American Joint Committee on Cancer; DDR, DNA damage repair; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Cesaretti et al, 2007 (41)**

USA
| PC. Diagnosis: Biopsy and Histology |
|------------------------------------|
| Other details (Patients were staged according to the 1992 American Joint Committee on Cancer standard and had biopsy-proven prostatic adenocarcinoma) |

| Population (further details): treatment (Brachytherapy) |
|-------------------------------------------------------|
| Treatment (further details): Brachytherapy (125I implant, a 103Pd implant, or the combination of external beam radiotherapy with a 103Pd implant) |

| Total (n=108) |
|---------------|
| Mean age (SD): NR (NR) |
| Median age (range): 64 (46, 79) |

| Ethnicity: NR |
|---------------|
| Gleason score: 5 (5); 6 (81); 7 (12); 8-10 (3) |

| AJCC stage: NR |
|---------------|
| TNM stage: T1b (1); T1c (59); T2a (20); T2b (15); T2c (4); T recurrent after 70 Gy in 1996 (1) |

| ECOG score |
|------------|
| 0: NR |
| 1: NR |
| 0-1: NR |
| ≥2: NR |

| Previous treatments: NR |
|-------------------------|
| Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
Mean PSA ng/ml (SD): NR (NR)
Median PSA ng/ml (range): 6.1) (0.8, 41)

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Cheng et al, 2011 (23)**

Australia

PC. Diagnosis: Histology
Other details (NR)

Population (further details): familial (PC patients from familial breast cancer families)

Treatment (further details): NR (NR)

Total (n=147)

Mean age (SD): NR (NR)
Median age (range): NR (NR)

Ethnicity: NR

Gleason score: NR

AJCC stage: NR

TNM stage: NR

ECOG score
0: NR
1: NR
0-1: NR
≥2: NR
| Previous treatments: NR |
|-------------------------|
| Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR (NR) |
| Comments: Data apparently recorded but not presented in abstract |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

Chi et al, 2017 (42)

Canada

mCRPC. Diagnosis: Biopsy histology; PSA; bone or CT scan

Other details (NR)

Population (further details): unselected (NR)

Treatment (further details): Mixed (Abiraterone [Abi] acetate 1000 mg PO OD with prednisone 5 mg PO BID or 10 mg OD as per standard of care, or until PSA progression then cross-over to ENZ; enzalutamide 160 mg PO OD as per standard of care, or until PSA progression then cross-over to Abi)

Total (n=NR)

Mean age (SD): NR (NR)

Median age (range): 75 (49, 74)

Ethnicity: NR

Gleason score: NR
| **AJCC stage:** | NR |
| **TNM stage:** | NR |
| **ECOG score** |  
0: NR  
1: NR  
0-1: NR (83)  
≥2: NR |
| **Previous treatments:** | None |
| **Familial history of PC:** | NR |
| **Mean years since diagnosis (SD):** | NR (NR) |
| **Median years since diagnosis (range):** | NR (NR) |
| **Mean PSA ng/ml (SD):** | 36.1 (NR) |
| **Median PSA ng/ml (range):** | NR) (1.7, 2817) |

**AJCC**, American Joint Committee on Cancer; **BID**, twice daily; **CRPC**, castration-resistant PC; **CT**, computed tomography; **ECOG**, Eastern Cooperative Oncology Group; **NR**, not reported; **OD**, once daily; **PC**, prostate cancer; **PO**, per oral; **PSA**, prostate-specific antigen; **SD**, standard deviation; **TNM**, Tumor Nodes Metastasis classification of malignant tumors.

**Dall'Era et al, 2017 (8)**

**USA**

**Primary PC; mPC. Diagnosis:** NR

**Other details (NR)**

**Population (further details): treatment (NR)**

**Treatment (further details): NR (NR)**
| Total (n=936)                |
|-----------------------------|
| Mean age (SD): NR (NR)      |
| Median age (range): NR (NR) |
| Ethnicity: NR               |
| Gleason score: NR           |
| AJCC stage: NR              |
| TNM stage: NR               |
| ECOG score                  |
| 0: NR                       |
| 1: NR                       |
| 0-1: NR                     |
| ≥2: NR                      |
| Previous treatments: NR     |
| Familial history of PC: NR  |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR (NR) |
| Comments: Very limited patient characteristics provided |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.
**Damaraju et al, 2006 (26)**

| Country | Canada |
|---------|--------|

**Primary PC. Diagnosis:** Biopsy with T classification, staging bone scan and CT scan

**Other details (NR)**

**Population (further details): treatment (3-DCRT)**

**Treatment (further details):** 3-DCRT (The clinical target volume (prostatic tissue containing biopsy-proven adenocarcinoma or its suspected microscopic extensions) received a mean dose of 77.1 Gy (range, 68.3-82.1 Gy) in five daily fractions per week. The number of fractions ranged from 35 to 44, and in all patients, the planning target volume received a minimum dose per fraction of 1.8 to 2 Gy. Pelvic lymph nodes were not treated by intention in any patient).

**Total (n=83)**

- Mean age (SD): 67 (NR)
- Median age (range): NR (45, 78)
- Ethnicity: Caucasian (86%); Caucasian French-Canadian (7%); Aboriginal (4%); Pacific Asian (2%); Afro-Caribbean (1%)
- Gleason score: NR
- AJCC stage: NR
- TNM stage: T1 (22); T2 (53); T3 (24); Tx (1)
- ECOG score
  - 0: NR
  - 1: NR
  - 0-1: NR
  - ≥2: NR

**Previous treatments:** Abdominopelvic surgery (n=30; 36%); neoadjuvant hormone therapy (n=35; 42%); adjuvant hormone therapy (n=6; 7%).

**Familial history of PC:** NR
Mean years since diagnosis (SD): NR (NR)
Median years since diagnosis (range): NR (NR)
Mean PSA ng/ml (SD): 11.8 (NR)
Median PSA ng/ml (range): NR (0.2, 74.0)

AJCC, American Joint Committee on Cancer; CT, computed tomography; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; 3-DCRT, three dimensional conformational radiation therapy.

Daniel et al, 2017 (9)

USA
mCRPC. Diagnosis: NR
Other details (predominantly relapsed, refractory or metastatic prostate carcinoma (mPC + CRPC + mCRPC))
Population (further details): unselected (NR)
Treatment (further details): NR (NR)
Total (n=1911)
Mean age (SD): NR (NR)
Median age (range): NR (NR)
Ethnicity: NR
Gleason score: NR
AJCC stage: NR
TNM stage: NR
| ECOG score          | 0: NR |
|--------------------|------|
|                    | 1: NR |
| 0-1: NR            |      |
| ≥2: NR             |      |

| Previous treatments: | NR |
|----------------------|----|

| Familial history of PC: | NR |

| Mean years since diagnosis (SD): | NR (NR) |
|----------------------------------|---------|
| Median years since diagnosis (range): | NR (NR) |

| Mean PSA ng/ml (SD): | NR (NR) |
|----------------------|---------|
| Median PSA ng/ml (range): | NR (NR) |

| Comments: | no details |

AJCC, American Joint Committee on Cancer; CRPC, castration-resistant PC; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

**Dawson et al, 2016 (11)**

| USA |
|-----|

| PC. Diagnosis: | NR |
|----------------|----|

| Other details (NR): |
|---------------------|

| Population (further details): | unselected (NR) |

| Treatment (further details): | NR (NR) |

| Total (n=437): |
|----------------|

88
| **Mean age (SD): NR (NR)** |
|---------------------------|
| **Median age (range): 67 (NR)** |
| **Ethnicity: NR** |
| **Gleason score: NR** |
| **AJCC stage: NR** |
| **TNM stage: NR** |
| **ECOG score** |
| 0: NR |
| 1: NR |
| 0-1: NR |
| ≥2: NR |
| **Previous treatments: NR** |
| **Familial history of PC: NR** |
| **Mean years since diagnosis (SD): NR (NR)** |
| **Median years since diagnosis (range): NR (NR)** |
| **Mean PSA ng/ml (SD): NR (NR)** |
| **Median PSA ng/ml (range): NR (NR)** |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

**Decker et al, 2016 (43)**

Multinational
PC and mCRPC. Diagnosis: Histology
Other details (NR)

Population (further details): unselected (NR)

Treatment (further details): radical prostatectomy or NR (NR)

| PC USA (n=10) | PC Multinational (Australia; USA) (n=50) | mCRPC Multinational (USA, UK, Israel) (n=150) |
|---------------|------------------------------------------|-----------------------------------------------|
| Mean age (SD): 63.6 (NR) | Mean age (SD): NR (NR) | Mean age (SD): NR (NR) |
| Median age (range): NR (54, 77) | Median age (range): NR (NR) | Median age (range): NR (NR) |
| Ethnicity: European descent (100) | Ethnicity: NR | Ethnicity: NR |
| Gleason score: 7 (10); 8 (20); 9 (60); 10 (10) | Gleason score: <7 (70); 8-10 (22); NR (8) | Gleason score: NR |
| AJCC stage: NR | AJCC stage: NR | AJCC stage: NR |
| TNM stage: NR | TNM stage: NR | TNM stage: NR |
| ECOG score | ECOG score | ECOG score |
| 0: NR | 0: NR | 0: NR |
| 1: NR | 1: NR | 1: NR |
| 0-1: NR | 0-1: NR | 0-1: NR |
| ≥2: NR | ≥2: NR | ≥2: NR |
| Previous treatments: radical prostatectomy (100) | Previous treatments: treatment naïve (100) | Previous treatments: NR |
| Familial history of PC: 2 (20) | Familial history of PC: NR | Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): 11.6 (NR) | Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) |
|--------------------------------|--------------------------------|--------------------------------|
| Median PSA ng/ml (range): NR (4.4, 22.3) | Median PSA ng/ml (range): NR (NR) | Median PSA ng/ml (range): NR (NR) |

**Comments:** Original study cohort of ten patients from the Mayo clinic

**Comments:** Reference study of 50 patients from Baca et al

**Comments:** Second reference study of 150 patients from Robinson et al

**AJCC**, American Joint Committee on Cancer; **CRPC**, castration-resistant PC; **ECOG**, Eastern Cooperative Oncology Group; **m**, metastatic; **IV**, intravenous; **NR**, not reported; **PC**, prostate cancer; **PSA**, prostate-specific antigen; **SD**, standard deviation; **TNM**, Tumor Nodes Metastasis classification of malignant tumors; **UK**, United Kingdom; **USA**, United States of America.

**Edwards et al, 2003 (44)**

**UK**

Other. Diagnosis: <55, no further details

Other details (Young onset)

Population (further details): unselected (NR)

Treatment (further details): NR (NR)

Total (n=263)

Mean age (SD): 51 (NR)

Median age (range): NR (32, 55)

Ethnicity: White (96); Black African/Caribbean (4)

Gleason score: NR

AJCC stage: NR

TNM stage: NR
| ECOG score          | 0: NR          |
|--------------------|---------------|
|                    | 1: NR          |
|                    | 0-1: NR        |
|                    | ≥2: NR         |
| Previous treatments| NR            |
| Familial history of PC | NR    |
| Mean years since diagnosis | NR (NR) |
| Median years since diagnosis | NR (NR) |
| Mean PSA ng/ml (SD) | NR (NR) |
| Median PSA ng/ml (range) | NR (NR) |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; UK, United Kingdom.

**Evans et al, 2016 (45)**

USA

PC. Diagnosis: NR

Other details (high risk)

Population (further details): unselected (NR)

Treatment (further details): radical prostatectomy (NR)

| Mayo discovery (n=545) | Mayo validation (n=232) | Cleveland clinic (n=130) | Thomas Jefferson University (n=183) |
|------------------------|-------------------------|--------------------------|-------------------------------------|
| Mean age (SD): 65.3 (6.4) | Mean age (SD): 63.1 (7.4) | Mean age (SD): 61.6 (6.3) | Mean age (SD): 60 (7) |
|--------------------------|---------------------------|---------------------------|-----------------------|
| Median age (range): NR (NR) | Median age (range): NR (NR) | Median age (range): NR (NR) | Median age (range): NR (NR) |
| Ethnicity: NR | Ethnicity: NR | Ethnicity: NR | Ethnicity: NR |
| Gleason score: 6 (11); 7 (49); 8 (13); 9 (24); 10 (2); NA (1) | Gleason score: 6 (7); 7 (50); 8 (17); 9 (25); 10 (1); NA (1) | Gleason score: 6 (17); 7 (62); 8 (13); 9 (12); 10 (0); NA (0) | Gleason score: 6 (13); 7 (57); 8 (17); 9 (10); 10 (1.5); NA (1.5) |
| AJCC stage: I (0); II (40); III (46); IV (0); NA (13) | AJCC stage: I (0); II (42); III (44); IV (0); NA (14) | AJCC stage: NA (100) | AJCC stage: I (0); II (8); III (87); IV (5); NA (0) |
| TNM stage: NR | TNM stage: NR | TNM stage: NR | TNM stage: NR |
| ECOG score | ECOG score | ECOG score | ECOG score |
| 0: NR | 0: NR | 0: NR | 0: NR |
| 1: NR | 1: NR | 1: NR | 1: NR |
| 0-1: NR | 0-1: NR | 0-1: NR | 0-1: NR |
| ≥2: NR | ≥2: NR | ≥2: NR | ≥2: NR |
| Previous treatments: NR | Previous treatments: NR | Previous treatments: NR | Previous treatments: NR |
| Familial history of PC: NR | Familial history of PC: NR | Familial history of PC: NR | Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR (<10 (52); 10-20 (22); >20 (24); NA (3)) | Median PSA ng/ml (range): NR (<10 (54); 10-20 (27); >20 (19); NA (0)) | Median PSA ng/ml (range): NR (<10 (69); 10-20 (23); >20 (7); NA (1)) | Median PSA ng/ml (range): NR (<10 (64); 10-20 (19); >20 (11); NA (5)) |
AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NA, not available; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

| Fachal et al, 2012 (46) |
|-------------------------|
| Spain                   |
| PC. Diagnosis: NR       |
| Other details (NR)      |
| Population (further details): treatment (Three-dimensional conformational radiotherapy (3D-CRT)) |
| Treatment (further details): Three-dimensional conformational radiotherapy (3D-CRT) (1.8-2 Gy/fraction) |
| Total (n=698)           |
| Mean age (SD): 71 (NR)  |
| Median age (range): NR (47, 86) |
| Ethnicity: NR           |
| Gleason score: 2-4 (10.03); 5-6 (51.58); 7 (26.65); 8-10 (10.17); missing (1.58) |
| AJCC stage: NR          |
| TNM stage: ≤cT2a (33.1); cT2b (22.4); cT2c (15.5); cT3 (8.3); cT4 (1); recurrent (18.9); Missing (0.9) |
| ECOG score             |
| 0: NR                  |
| 1: NR                  |
| 0-1: NR                |
| ≥2: NR                 |
| Previous treatments: radiotherapy; prostatectomy (15.9%) |
Familial history of PC: NR

| Mean years since diagnosis (SD): NR (NR) |
|-----------------------------------------|
| Median years since diagnosis (range): NR (NR) |

| Mean PSA ng/ml (SD): 15.95 (NR) |
|---------------------------------|
| Median PSA ng/ml (range): NR (0.63, 236) |

Comments: patients with radical radiotherapy received a total dose for the PTV I that ranged from 70 to 76 Gy, as well as 56 Gy for the PTV II and 46 Gy for PTV III

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; PTV, planning target volume; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Feldman et al, 2014 (10)**

USA

PC. Diagnosis: Histology

Other details (NR)

Population (further details): unselected (NR)

Treatment (further details): NR (NR)

Total (n=330)

| Mean age (SD): NR (NR) |
|------------------------|
| Median age (range): NR (NR) |

Ethnicity: NR

Gleason score: NR

AJCC stage: NR
| TNM stage: NR |
|--------------|
| ECOG score  |
| 0: NR       |
| 1: NR       |
| 0-1: NR     |
| ≥2: NR      |
| Previous treatments: NR |
| Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR (NR) |
| Comments: no details |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Fontugne et al, 2015 (47)**

| Multinational |
|---------------|
| PC. Diagnosis: NR |
| Other details (Mixed population of patients with a spectrum of localized and advanced PC) |
| Population (further details): unselected (NR) |
| Treatment (further details): NR (NR) |
| Total (n=51) |
Mean age (SD): NR (NR)
Median age (range): NR (NR)
Ethnicity: NR
Gleason score: NR
AJCC stage: NR
TNM stage: NR
ECOG score
0: NR
1: NR
0-1: NR
≥2: NR
Previous treatments: NR
Familial history of PC: NR
Mean years since diagnosis (SD): NR (NR)
Median years since diagnosis (range): NR (NR)
Mean PSA ng/ml (SD): NR (NR)
Median PSA ng/ml (range): NR (NR)
Comments: 69 tumors from 51 patients analyzed

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Gallagher et al, 2012 (48)**
USA
| CRPC. Diagnosis: Pathology | Other details (NR) |
|---------------------------|-------------------|
| Population (further details): Ashkenazi (NR) | |
| Treatment (further details): Mixed treatment (For the total population, treatment was reported for 76 taxanes based therapies: single-agent docetaxel (n=33 patients), docetaxel + estramustine (17 patients), docetaxel + samarium (five patients), docetaxel + bevacizumab (four patients), docetaxel + 17AAG (two patients), docetaxel + DN-101 (two patients), docetaxel + carboplatin (one patient), docetaxel + traztusumab (one patient), docetaxel + cyclophosphamide (one patient), paclitaxel (three patients), paclitaxel + carboplatin + estramustine (six patients) and paclitaxel + estramustine (one patient).) | |

| DDR+ (n=7) | DDR- (n=81) |
|-----------|-----------|
| Mean age (SD): NR (NR) | Mean age (SD): NR (NR) |
| Median age (range): 72 (59, 82) | Median age (range): 72 (59, 82) |
| Ethnicity: Jewish (100) | Ethnicity: Jewish (100) |
| Gleason score: ≤ 6 (14); 7 (43); 8 (0); 9 (44); unknown (0) | Gleason score: ≤ 6 (16); 7 (35); 8 (23); 9 (23); unknown (2) |
| AJCC stage: NR | AJCC stage: NR |
| TNM stage: T1 (14); T2 (43); T3 (29); T4 (0); unknown (14) | TNM stage: T1 (14); T2 (26); T3 (27); T4 (4); unknown (30) |
| ECOG score | ECOG score |
| 0: NR | 0: NR |
| 1: NR | 1: NR |
| 0-1: NR | 0-1: NR |
| ≥2: NR | ≥2: NR |
| Previous treatments: Prostatectomy (43); Radiotherapy alone (14); Radiotherapy + ADT (29); Hormones alone (14); Watchful waiting (0); Chemotherapy (0) | Previous treatments: Prostatectomy (48); Radiotherapy alone (27); Radiotherapy + ADT (15); Hormones alone (9); Watchful waiting (4); Chemotherapy (1) |
| Familial history of PC: NR | Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) |
|----------------------------------------|----------------------------------------|
| Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): 199 (3, 811) | Median PSA ng/ml (range): 73 (18, 262) |

ADT, androgen deprivation therapy; AJCC, American Joint Committee on Cancer; CRPC, castration-resistant PC; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

**Gallagher et al, 2012 (49)**

**USA**

Primary PC. Diagnosis: Pathology
Other details (localized)

Population (further details): Ashkenazi (Ashkenazi Jewish background)

Treatment (further details): radical prostatectomy; radiation therapy; radiation therapy + hormones; Hormone therapy alone; Chemotherapy alone; Watchful waiting; (NR)

| BRCA1+ (n=6) | BRCA2+ (n=20) | DDR- (n=806) |
|--------------|---------------|--------------|
| Mean age (SD): NR (NR) | Mean age (SD): NR (NR) | Mean age (SD): NR (NR) |
| Median age (range): 67.1 (NR) | Median age (range): 62 (NR) | Median age (range): 68.2 (NR) |
| Ethnicity: Jewish (100) | Ethnicity: Jewish (100) | Ethnicity: Jewish (100) |
| Gleason score: <7 (50); ≥7 (50); NA (0) | Gleason score: <7 (10); ≥7 (85); NA (5) | Gleason score: <7 (40.2); ≥7 (54.2); NA (5.6) |
| AJCC stage: NR | AJCC stage: NR | AJCC stage: NR |
| TNM stage: NR | TNM stage: NR | TNM stage: NR |
| ECOG score | ECOG score | ECOG score |
|------------|------------|------------|
| 0: NR      | 0: NR      | 0: NR      |
| 1: NR      | 1: NR      | 1: NR      |
| 0-1: NR    | 0-1: NR    | 0-1: NR    |
| ≥2: NR     | ≥2: NR     | ≥2: NR     |

Previous treatments: Prostatectomy (0); Radiotherapy (17); Radiotherapy + Hormones (50); Hormones alone (34)

Previous treatments: Prostatectomy (50); Radiotherapy alone (20); Radiotherapy + Hormones alone (30)

Previous treatments: Prostatectomy (30); Radiotherapy alone (34); Radiotherapy + Hormones (27); Hormones alone (4); Watchful waiting (4); Chemotherapy (0.1)

Familial history of PC: NR

Familial history of PC: NR

Familial history of PC: NR

Mean years since diagnosis (SD): NR (NR)

Mean years since diagnosis (SD): NR (NR)

Mean years since diagnosis (SD): NR (NR)

Mean years since diagnosis (range): NR (NR)

Mean years since diagnosis (range): NR (NR)

Mean years since diagnosis (range): NR (NR)

Mean PSA ng/ml (SD): NR (NR)

Mean PSA ng/ml (SD): NR (NR)

Mean PSA ng/ml (SD): NR (NR)

Mean PSA ng/ml (range): 6.5 (5, 8)

Mean PSA ng/ml (range): 6.5 (5, 8)

Mean PSA ng/ml (range): 6.5 (5, 8)

Mean PSA ng/ml (range): 7 (6, 9)

Mean PSA ng/ml (range): 7 (6, 9)

Mean PSA ng/ml (range): 7 (6, 9)

Mean PSA ng/ml (range): 7 (2, 10)

Mean PSA ng/ml (range): 7 (2, 10)

Mean PSA ng/ml (range): 7 (2, 10)

AJCC, American Joint Committee on Cancer; BRCA, breast cancer susceptibility gene; CRPC, castration-resistant PC; DDR, DNA damage repair; ECOG, Eastern Cooperative Oncology Group; NA, not available; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

**Gambhira et al, 2016 (17)**

USA

mCRPC. Diagnosis:

Other details (NR)

Population (further details): unselected (NR)
|                          | Value            |
|--------------------------|------------------|
| Treatment (further details): | NR (NR)         |
| Total (n=13)             |                  |
| Mean age (SD):           | NR (NR)         |
| Median age (range):      | NR (NR)         |
| Ethnicity:               | NR              |
| Gleason score:           | NR              |
| AJCC stage:              | NR              |
| TNM stage:               | NR              |
| ECOG score              |                 |
| 0: NR                    |                  |
| 1: NR                    |                  |
| 0-1: NR                  |                  |
| ≥2: NR                   |                  |
| Previous treatments:     | NR              |
| Familial history of PC:  | NR              |
| Mean years since diagnosis (SD): | NR (NR) |
| Median years since diagnosis (range): | NR (NR) |
| Mean PSA ng/ml (SD):     | NR (NR)         |
| Median PSA ng/ml (range) | NR (NR)         |
| Comments:                | No patient characteristics provided |

AJCC, American Joint Committee on Cancer; CRPC, castration-resistant PC; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.
| Gayther et al, 2000 (50) |
|--------------------------|
| UK                      |
| PC. Diagnosis: NR        |
| Other details (NR)       |
| Population (further details): familial (NR) |
| Treatment (further details): NR (NR) |
| Total (n=38)             |
| Mean age (SD): 60.3 (NR) |
| Median age (range): NR (43, 76) |
| Ethnicity: NR            |
| Gleason score: NR        |
| AJCC stage: NR           |
| TNM stage: NR            |
| ECOG score               |
| 0: NR                    |
| 1: NR                    |
| 0-1: NR                  |
| ≥2: NR                   |
| Previous treatments: NR  |
| Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
### Mean PSA ng/ml (SD): NR (NR)
Median PSA ng/ml (range): NR (NR)

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; UK, United Kingdom.

#### Giusti et al, 2003 (51)

**Israel**

**PC. Diagnosis:** Histology

**Other details (NR)**

**Population (further details):** Ashkenazi (Newly diagnosed Ashkenazi Israelis)

**Treatment (further details):** NR (NR)

| Total (n=940) | BRCA1+ (n=15) | BRCA2+ (n=14) | DDR- (n=145) |
|--------------|---------------|---------------|--------------|
| Mean age (SD): NR (NR) | Mean age (SD): 74.2 (NR) | Mean age (SD): 71.6 (NR) | Mean age (SD): 73.6 (NR) |
| Median age (range): NR (NR) | Median age (range): NR (NR) | Median age (range): NR (NR) | Median age (range): NR (NR) |
| Ethnicity: NR | Ethnicity: NR | Ethnicity: NR | Ethnicity: NR |
| Gleason score: NR | Gleason score: NR | Gleason score: NR | Gleason score: NR |
| AJCC stage: NR | AJCC stage: NR | AJCC stage: NR | AJCC stage: NR |
| TNM stage: NR | TNM stage: NR | TNM stage: NR | TNM stage: NR |
| ECOG score | ECOG score | ECOG score | ECOG score |
| 0: NR | 0: NR | 0: NR | 0: NR |
| 1: NR | 1: NR | 1: NR | 1: NR |
| 0-1: NR | 0-1: NR | 0-1: NR | 0-1: NR |
| ≥2: NR | ≥2: NR | ≥2: NR | ≥2: NR |
| Previous treatments: NR | Previous treatments: NR | Previous treatments: NR | Previous treatments: NR |
|------------------------|------------------------|------------------------|------------------------|
| Familial history of PC: NR | Familial history of PC: NR | Familial history of PC: NR | Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR (NR) | Median PSA ng/ml (range): NR (NR) | Median PSA ng/ml (range): NR (NR) | Median PSA ng/ml (range): NR (NR) |

AJCC, American Joint Committee on Cancer; BRCA, breast cancer susceptibility gene; DDR, DNA damage repair; ECOG, Eastern Cooperative Oncology Group; m, metastatic; IV, intravenous; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Gourdin et al, 2016 (52)**

USA

mPC. Diagnosis: 82% had CRPC

Other details (NR)

Population (further details): unselected (NR)

Treatment (further details): NR (NR)

Total (n=55)

Mean age (SD): NR (NR)

Median age (range): NR (NR)

Ethnicity: Caucasian (49%); African-American (49%); Asian (2%)
| Parameter                                    | Value   |
|----------------------------------------------|---------|
| Gleason score                                | NR      |
| AJCC stage                                   | NR      |
| TNM stage                                    | NR      |
| ECOG score                                   | 0: NR   |
|                                              | 1: NR   |
|                                              | 0-1: NR |
|                                              | ≥2: NR  |
| Previous treatments                          | NR      |
| Familial history of PC                       | NR      |
| Mean years since diagnosis (SD)              | NR (NR) |
| Median years since diagnosis (range)         | NR (NR) |
| Mean PSA ng/ml (SD)                          | NR (NR) |
| Median PSA ng/ml (range)                     | NR (NR) |
| Comments                                     | No patient characteristics provided other than ethnicity |

AJCC, American Joint Committee on Cancer; CRPC, castration-resistant PC; DDR, DNA damage repair; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

**Grasso et al, 2012 (53)**

USA

mCRPC and primary PC. Diagnosis: NR

Other details (NR)
| Population (further details): unselected (NR) |
| Treatment (further details): NR (NR) |
| mCRPC (n=50) | Primary PC (n=11) |
| Mean age (SD): 71 (7.5) | Mean age (SD): 60.9 (5.8) |
| Median age (range): 71 (52, 85) | Median age (range): 60 (54, 71) |
| Ethnicity: NR | Ethnicity: NR |
| Gleason score: NR | Gleason score: 7 (18.2); 8 (36.4); 9 (45.4) |
| AJCC stage: NR | AJCC stage: NR |
| TNM stage: NR | TNM stage: NR |
| Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): 1142 (1818) | Mean PSA ng/ml (SD): 10.9 (7.6) |
| Median PSA ng/ml (range): 324) (0, 8083) | Median PSA ng/ml (range): 6.5) (4.2, 27.1) |

AJCC, American Joint Committee on Cancer; CRPC, castration-resistant PC; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.
| **Hall et al, 1998 (54)** |
|--------------------------|
| USA                      |
| PC. Diagnosis: NR        |
| Other details (NR)       |
| Population (further details): treatment (External-beam conformal radiotherapy) |
| Treatment (further details): External-beam conformal radiotherapy (High-dose external-beam conformal radiotherapy) |
| Total (n=17)             |
| Mean age (SD): NR (NR)   |
| Median age (range): NR (NR) |
| Ethnicity: NR            |
| Gleason score: NR        |
| AJCC stage: NR           |
| TNM stage: NR            |
| ECOG score               |
| 0: NR                    |
| 1: NR                    |
| 0-1: NR                  |
| ≥2: NR                   |
| Previous treatments: NR  |
| Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
Mean PSA ng/ml (SD): NR (NR)
Median PSA ng/ml (range): NR (NR)

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

| Hamel et al, 2003 (55) |
|------------------------|
| Canada |
| PC. Diagnosis: Pathology reports from patients' medical charts |
| Other details (NR) |
| Population (further details): Ashkenazi (Both parents were reported as Ashkenazi Jewish, with no Sephardic heritage.) |
| Treatment (further details): NR (NR) |
| Total (n=146) |
| Mean age (SD): NR (NR) |
| Median age (range): 67.9 (48.6, 84.2) |
| Ethnicity: NR |
| Gleason score: ≤5 (36.35%); ≥6 (51.4%) |
| AJCC stage: NR |
| TNM stage: NR |
| ECOG score                      | 0: NR     |
|---------------------------------|----------|
|                                 | 1: NR     |
|                                 | 0-1: NR   |
|                                 | ≥2: NR    |

Previous treatments: NR

Familial history of PC: 13 (8.9%)

Mean years since diagnosis (SD): NR (NR)
Median years since diagnosis (range): 5.7 (0.3, 23.7)

Mean PSA ng/ml (SD): NR (NR)
Median PSA ng/ml (range): NR (NR)

Comments: 5 cases had missing information for the median time since diagnosis

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Hart et al, 2016 (56)**

USA

mCRPC. Diagnosis: Histology
Other details (NR)

Population (further details): treatment (Adenocarcinoma, Poorly differentiated, carcinoma NOS, Small-cell carcinoma, and Unknown)

Treatment (further details): androgen deprivation therapy (NR)

| DDR+ (n=13) | DDR- (n=56) |
| Mean age (SD): NR (NR) | Mean age (SD): NR (NR) |
|-----------------------|-----------------------|
| Median age (range): NR (NR) | Median age (range): NR (NR) |
| Ethnicity: NR | Ethnicity: NR |
| Gleason score: 7 (0); 8 (0); 9 (15); 10 (31); no data (54) | Gleason score: 7 (4); 8 (27); 9 (11); 10 (23); no data (38) |
| AJCC stage: NR | AJCC stage: NR |
| TNM stage: NR | TNM stage: NR |
| ECOG score | ECOG score |
| 0: NR | 0: NR |
| 1: NR | 1: NR |
| 0-1: NR | 0-1: NR |
| ≥2: NR | ≥2: NR |
| Previous treatments: NR | Previous treatments: NR |
| Familial history of PC: 10 (77) | Familial history of PC: 45 (80) |
| Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR (NR) | Median PSA ng/ml (range): NR (NR) |

AJCC, American Joint Committee on Cancer; CRPC, castration-resistant PC; DDR, DNA damage repair; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NOS, not otherwise specified; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

**Hayano et al, 2016 (57)**
Japan
| **PC. Diagnosis:** Histology |  |
|-------------------------------|--|
| **Other details (NR)**        |--|
| **Population (further details): familial** (Large PC families (with 3 or 4 patients with PC; n=22) or small PC families (2 patients with PC; n=118)) |  |
| **Treatment (further details): NR (NR)** |  |
| **Total (n=140)**             |--|
| **Mean age (SD): 69 (NR)**    |--|
| **Median age (range): NR (40, 88)** |  |
| **Ethnicity: NR**             |--|
| **Gleason score: <7 (30); ≥7 (69); unknown (1)** |  |
| **AJCC stage: NR**            |--|
| **TNM stage: NR**             |--|
| **ECOG score**                |--|
| 0: NR                         |--|
| 1: NR                         |--|
| 0-1: NR                       |--|
| ≥2: NR                        |--|
| **Previous treatments: NR**   |--|
| **Familial history of PC: NR**|--|
| **Mean years since diagnosis (SD): NR (NR)** |  |
| **Median years since diagnosis (range): NR (NR)** |  |
| **Mean PSA ng/ml (SD): NR (NR)** |  |
| **Median PSA ng/ml (range): NR (NR)** |  |
AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

Hebbring et al, 2006 (58)

|                  | Multinational (n=1819) | USA (Mayo Clinic) (n=428) | Germany (Ulm) (n=299) |
|------------------|------------------------|----------------------------|-----------------------|
| PC. Diagnosis    | NR                     |                            |                       |
| Other details    | (NR)                   |                            |                       |
| Population       | familial (NR)          |                            |                       |
| Treatment        | NR (NR)                |                            |                       |
| Multinational    |                         | USA (Mayo Clinic) (n=428)  | Germany (Ulm) (n=299) |
| Mean age (SD)    | NR (NR)                | Mean age (SD): 66 (NR)     | Mean age (SD): 64.6 (NR) |
| Median age (range)| NR (NR)                | Median age (range): 45, 84 | Median age (range): 47, 89 |
| Ethnicity        | NR                     | Ethnicity: NR              | Ethnicity: NR          |
| Gleason score    | NR                     | Gleason score: NR          | Gleason score: NR      |
| AJCC stage       | NR                     | AJCC stage: NR             | AJCC stage: NR         |
| TNM stage        | NR                     | TNM stage: NR              | TNM stage: NR          |
| ECOG score       |                         | ECOG score                 | ECOG score             |
| 0: NR            |                         | 0: NR                      | 0: NR                  |
| 1: NR            |                         | 1: NR                      | 1: NR                  |
| 0-1: NR          |                         | 0-1: NR                    | 0-1: NR                |
| ≥2: NR           |                         | ≥2: NR                     | ≥2: NR                 |
| Previous treatments | NR                  | Previous treatments: NR   | Previous treatments: NR |
| Familial history of PC: 1819 (100) | Familial history of PC: 428 (100) | Familial history of PC: 299 (100) |
|-----------------------------------|-----------------------------------|-----------------------------------|
| Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR (NR) | Median PSA ng/ml (range): NR (NR) | Median PSA ng/ml (range): NR (NR) |
| Comments: Limited population data presented | Comments: Mean age at diagnosis extracted | Comments: Mean age at diagnosis extracted |

**Hebbring et al, 2006 (58)**

| Multinational | USA (Mayo Clinic) (n=492) | Germany (Ulm) (n=338) |
|---------------|---------------------------|-----------------------|
| PC. Diagnosis: NR | Mean age (SD): 64 (NR) | Mean age (SD): 63.7 (NR) |
| Other details (NR) | Median age (range): 46, 79 | Median age (range): 42, 84 |
| Population (further details): unselected (NR) | Ethnicity: NR | Ethnicity: NR |
| Treatment (further details): NR (NR) | Gleason score: NR | Gleason score: NR |
| Multinational (n=1218) | AJCC stage: NR | AJCC stage: NR |
| Mean age (SD): NR (NR) | TNM stage: NR | TNM stage: NR |
| Median age (range): NR (NR) | | |
| ECOG score | ECOG score | ECOG score |
|------------|------------|------------|
| 0: NR      | 0: NR      | 0: NR      |
| 1: NR      | 1: NR      | 1: NR      |
| 0-1: NR    | 0-1: NR    | 0-1: NR    |
| ≥2: NR     | ≥2: NR     | ≥2: NR     |
| **Previous treatments:** NR | **Previous treatments:** NR | **Previous treatments:** NR |
| **Familial history of PC:** 0 (0) | **Familial history of PC:** 0 (0) | **Familial history of PC:** 0 (0) |
| **Mean years since diagnosis (SD):** NR (NR) | **Mean years since diagnosis (SD):** NR (NR) | **Mean years since diagnosis (SD):** NR (NR) |
| **Median years since diagnosis (range):** NR (NR) | **Median years since diagnosis (range):** NR (NR) | **Median years since diagnosis (range):** NR (NR) |
| **Mean PSA ng/ml (SD):** NR (NR) | **Mean PSA ng/ml (SD):** NR (NR) | **Mean PSA ng/ml (SD):** NR (NR) |
| **Median PSA ng/ml (range):** NR (NR) | **Median PSA ng/ml (range):** NR (NR) | **Median PSA ng/ml (range):** NR (NR) |
| **Comments:** Limited population data presented | **Comments:** Mean age at diagnosis extracted | **Comments:** Mean age at diagnosis extracted |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

**Hubert et al, 1999 (59)**

Israel

PC. Diagnosis: Histology and PSA

Other details (NR)

Population (further details): Ashkenazi (NR)
| Treatment (further details): NR (NR) | Total (n=87) | DDR+ (n=3) | DDR- (n=84) |
|-----------------------------------|-------------|------------|-------------|
| Mean age (SD): NR (NR) | Mean age (SD): 64 (NR) | Mean age (SD): NR (NR) |
| Median age (range): 71 (NR) | Median age (range): NR (57, 73) | Median age (range): NR (NR) |
| Ethnicity: NR | Ethnicity: NR | Ethnicity: NR |
| Gleason score: NR | Gleason score: 7 (33.3); ≥8 (66.6) | Gleason score: Average: 5.9 |
| AJCC stage: NR | AJCC stage: NR | AJCC stage: NR |
| TNM stage: NR | TNM stage: NR | TNM stage: NR |
| ECOG score | ECOG score | ECOG score |
| 0: NR | 0: NR | 0: NR |
| 1: NR | 1: NR | 1: NR |
| 0-1: NR | 0-1: NR | 0-1: NR |
| ≥2: NR | ≥2: NR | ≥2: NR |
| Previous treatments: NR | Previous treatments: NR | Previous treatments: NR |
| Familial history of PC: 5 (5.7) | Familial history of PC: NR | Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): 55.8 (NR) | Mean PSA ng/ml (SD): 23.6 (NR) |
| Median PSA ng/ml (range): NR (NR) | Median PSA ng/ml (range): NR (47, 60) | Median PSA ng/ml (range): NR (NR) |
| Comments: 71 years at diagnosis | | |

AJCC, American Joint Committee on Cancer; DDR, DNA damage repair; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.
| Hussain et al, 2017 (60) |
|-------------------------|
| USA                     |
| mCRPC. Diagnosis: Histology or cytology |
| Other details (NR) |
| Population (further details): unselected (NR) |
| Treatment (further details): Abiraterone (1000 mg per day plus prednisone 5 mg twice per day (arm A) or AAP plus veliparib 300 mg twice per day (arm B), for days 1 to 28. Treatment was continued until radiographic/clinical disease progression, inter-current illness, unacceptable adverse events (A). Abiraterone + veliparib (AAP plus veliparib 300 mg twice per day (arm B), for days 1 to 28. Arm B patients underwent lead-in treatment with AAP, followed on day 8 by veliparib, in cycle 1 only. Treatment was continued until radiographic/clinical disease progression, inter-current) |

| A (n=72) | A+V (n=76) |
|----------|------------|
| Mean age (SD): NR (NR) | Mean age (SD): NR (NR) |
| Median age (range): 69 (50, 90) | Median age (range): 68 (47, 85) |
| Ethnicity: Caucasian (83); African American (12); other (3) | Ethnicity: Caucasian (94); African American (4); other (3) |
| Gleason score: NR | Gleason score: NR |
| AJCC stage: NR | AJCC stage: NR |
| TNM stage: NR | TNM stage: NR |
| ECOG score | ECOG score |
| 0: 46 (62) | 0: 50 (63) |
| 1: 28 (38) | 1: 28 (35) |
| 0-1: NR | 0-1: NR |
| ≥2: 0 | ≥2: 1 (1) |
**Previous treatments:** Docetaxel/cabazitaxel (15); other chemotherapy (7); Enzalutamide (3); Sipuleucel-T (30); Experimental agent (26)

**Previous treatments:** Docetaxel/cabazitaxel (22); other chemotherapy (8); Enzalutamide (3); Sipuleucel-T (17); Experimental agent (19)

| Familial history of PC | NR |
|------------------------|----|
| Mean years since diagnosis (SD) | NR (NR) |
| Median years since diagnosis (range) | NR (NR) |
| Mean PSA ng/ml (SD) | NR (NR) |
| Median PSA ng/ml (range) | 32.7 (0.8, 1557.6) |
| Mean PSA ng/ml (range) | 36.4 (0.04, 1074.4) |

AJCC, American Joint Committee on Cancer; CRPC, castration-resistant PC; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

**Jefferies et al, 2017 (61)**

**UK**

Primary PC. Diagnosis: Histology

Other details (NR)

Population (further details): unselected (NR)

Treatment (further details): NR (NR)

Total (n=61)

| Mean age (SD) | NR (NR) |
|---------------|---------|
| Median age (range) | NR (NR) |
| Ethnicity | NR |
| Gleason score | NR |
| AJCC stage | NR |
TNM stage: NR

| ECOG score | NR |
|------------|----|
| 0          | NR |
| 1          | NR |
| 0-1        | NR |
| ≥2         | NR |

| Previous treatments: | NR |
|----------------------|----|
| Familial history of PC: | NR |

| Mean years since diagnosis (SD): | NR (NR) |
| Median years since diagnosis (range): | NR (NR) |
| Mean PSA ng/ml (SD): | NR (NR) |
| Median PSA ng/ml (range): | NR (NR) |

| Comments: | no details |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; UK, United Kingdom.

**Kaufman et al, 2015 (62)**

| Multi-national |
|----------------|
| mCRPC. Diagnosis: | NR |
| Other details (NR): |

| Population (further details): | unselected (NR) |
| Treatment (further details): | Olaparib (400 mg capsule twice daily) |
| Total (n=8): |

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### Demographic and Clinical Characteristics

| Parameter                        | Value                        |
|----------------------------------|------------------------------|
| Mean age (SD)                    | 66.6 (9.86)                  |
| Median age (range)               | 71 (51, 77)                  |
| Ethnicity                        | Caucasian (100)              |
| Gleason score                    | NR                           |
| AJCC stage                       | NR                           |
| TNM stage                        | NR                           |
| ECOG score                       |                              |
| 0: 1 (12.5)                      |                              |
| 1: 4 (50)                        |                              |
| 0-1: NR                          |                              |
| ≥2: 3 (37.5)                     |                              |
| Previous treatments              | Docetaxel (75); platinum carboplatin or cisplatin (50) |
| Familial history of PC           | NR                           |
| Mean years since diagnosis (SD)  | NR (NR)                      |
| Median years since diagnosis     | NR (NR)                      |
| Mean PSA ng/ml (SD)              | NR (NR)                      |
| Median PSA ng/ml (range)         | NR (NR)                      |
| Comments                         | No PSA details were presented|

**AJCC, American Joint Committee on Cancer; CRPC, castration-resistant PC; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.**

**Kirchoff et al, 2004 (63)**
| USA               |
|-------------------|
| PC. Diagnosis: NR |
| Other details (NR)|
| Population (further details): Ashkenazi (NR) |
| Treatment (further details): NR (NR) |
| Total (n=251)     |
| Mean age (SD): 65.7 (NR)  |
| Median age (range): NR (NR) |
| Ethnicity: Ashkenazi Jewish men (100) |
| Gleason score: NR |
| AJCC stage: NR    |
| TNM stage: NR     |
| ECOG score        |
| 0: NR             |
| 1: NR             |
| 0-1: NR           |
| ≥2: NR            |
| Previous treatments: NR |
| Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR) (NR) |
Comments: mean age for DDR+ PC cases, for controls (still DDR+ but no PC) mean age was 51.0, calculations age adjusted, see table 2

AJCC, American Joint Committee on Cancer; DDR, DNA damage repair; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

| **Kote-Jarai et al, 2011 (64)** |  |
|---|---|
| **UK** |  |
| Other. Diagnosis: <65 years; NR |  |
| Other details (Young-onset PC (onset \(\leq\) 65 years)) |  |
| Population (further details): unselected (NR) |  |
| Treatment (further details): NR (NR) |  |
| Total (n=1589) |  |
| Mean age (SD): NR (NR) |  |
| Median age (range): NR (36, 65) |  |
| Ethnicity: NR |  |
| Gleason score: NR |  |
| AJCC stage: NR |  |
| TNM stage: NR |  |
| ECOG score |  |
| 0: NR |  |
| 1: NR |  |
| 0-1: NR |  |
| \(\geq\)2: NR |  |
| Previous treatments: NR |
|------------------------|
| Familial history of PC: 85.1 |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR (NR) |
| AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; UK, United Kingdom. |

**LaDuca et al, 2017 (65)**

| USA |
|----------------|
| PC. Diagnosis: NR |
| Other details (NR) |
| Population (further details): familial (Patients referred for hereditary cancer multi-gene panel testing) |
| Treatment (further details): NR (NR) |
| Total (n=NR) |
| Mean age (SD): NR (NR) |
| Median age (range): NR (NR) |
| Ethnicity: NR |
| Gleason score: NR |
| AJCC stage: NR |
| TNM stage: NR |
| ECOG score          | 0: NR | 1: NR | 0-1: NR | ≥2: NR |
|---------------------|-------|-------|---------|--------|
| Previous treatments | NR    |       |         |        |
| Familial history of PC | NR    |       |         |        |
| Mean years since diagnosis (SD) | NR (NR) |       |         |        |
| Median years since diagnosis (range) | NR (NR) |       |         |        |
| Mean PSA ng/ml (SD) | NR (NR) |       |         |        |
| Median PSA ng/ml (range) | NR (NR) |       |         |        |
| Comments | No details provided regarding patient characteristics (nor even the number of patients) |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

**Lara et al, 2017 (66)**

USA

PC. Diagnosis: NR

Other details (NR)

Population (further details): unselected (NR)

Treatment (further details): NR (NR)

Total (n=207; 936)
| Attribute                                      | Value        |
|-----------------------------------------------|--------------|
| Mean age (SD):                                | NR (NR)      |
| Median age (range):                           | NR (NR)      |
| Ethnicity:                                    | NR           |
| Gleason score:                                | NR           |
| AJCC stage:                                   | NR           |
| TNM stage:                                    | NR           |
| ECOG score                                    |              |
| 0: NR                                         |              |
| 1: NR                                         |              |
| 0-1: NR                                       |              |
| ≥2: NR                                        |              |
| Previous treatments:                          | NR           |
| Familial history of PC:                       | NR           |
| Mean years since diagnosis (SD):              | NR (NR)      |
| Median years since diagnosis (range):         | NR (NR)      |
| Mean PSA ng/ml (SD):                          | NR (NR)      |
| Median PSA ng/ml (range):                     | NR (NR)      |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

_Ledet et al, 2017 (67)_

USA
| PC. Diagnosis: NR |
|--------------------|
| Other details (NR) |
| Population (further details): familial (PC patients with a family history that met NCCN guidelines for genetic testing) |
| Treatment (further details): NR (NR) |
| Total (n=124) |
| Mean age (SD): NR (NR) |
| Median age (range): NR (NR) |
| Ethnicity: NR |
| Gleason score: NR |
| AJCC stage: NR |
| TNM stage: NR |
| ECOG score |
| 0: NR |
| 1: NR |
| 0-1: NR |
| ≥2: NR |
| Previous treatments: NR |
| Familial history of PC: 124 (100) |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR) (NR) |
Comments: Limited description of population characteristics provided. Ethnicity described for the larger cohort of n=535 patients, but not for the finally selected study cohort of n=124

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NCCN, National Comprehensive Cancer Network; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

Lehrer et al, 1998 (68)

USA

PC. Diagnosis: Histology
Other details (NR)

Population (further details): Ashkenazi (Ethnic background was confirmed for all subjects by self-report or interview.)

Treatment (further details): NR (NR)

Total (n=60)

Mean age (SD): 70 (5.25)
Median age (range): NR (55, 80)

Ethnicity: Ashkenazi Jewish men (100)

Gleason score: NR
AJCC stage: NR
TNM stage: NR
ECOG score
0: NR
1: NR
0-1: NR
≥2: NR
Previous treatments: NR
Familial history of PC: 6 (10)
Mean years since diagnosis (SD): NR (NR)
Median years since diagnosis (range): NR (NR)
Mean PSA ng/ml (SD): NR (NR)
Median PSA ng/ml (range): NR (NR)
Comments: Only looking at PC, no controls but using two earlier papers for control cohort: "Following the finding of a 185delAG frameshift mutation of BRCA1 in several Ashkenazi Jewish breast/ovarian cancer families, the frequency of this mutation was found to be 0"

AJCC, American Joint Committee on Cancer; BRCA, breast cancer susceptibility gene; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

Leongamornlert et al, 2012 (69)

UK
PC. Diagnosis: NR
Other details (NR)
Population (further details): unselected (NR)
Treatment (further details): NR (NR)
Total (n=886)
Mean age (SD): NR (NR)
Median age (range): NR (36, 88)
Ethnicity: NR
Gleason score: NR
| AJCC stage: NR |
|----------------|
| TNM stage: NR |
| ECOG score    |
| 0: NR         |
| 1: NR         |
| 0-1: NR       |
| ≥2: NR        |
| Previous treatments: NR |
| Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR (NR) |
| Comments: Has data on BRCA1 prevalence stratified by age (36-55, 56-65, 66-88) |

**AJCC, American Joint Committee on Cancer; BRCA, breast cancer susceptibility gene; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; UK, United Kingdom.**

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**Leongamornlert et al, 2014 (70)**

**UK**

PC. Diagnosis: Clinical detection or PSA screening

Other details (NR)

Population (further details): familial (Two or more relatives affected by PC)
| Treatment (further details): NR (NR) |
|-----------------------------------|
| Total (n=191) | DDR+ (n=14) | DDR- (n=140) |
| Mean age (SD): NR (NR) | Mean age (SD): NR (NR) | Mean age (SD): NR (NR) |
| Median age (range): NR (NR) | Median age (range): 58.5 (41, 71) | Median age (range): 59 (47, 82) |
| Ethnicity: White (68.6); Black African/Caribbean (2.6); Ashkenazi Jew (0.5); unknown (28.3) | Ethnicity: NR | Ethnicity: NR |
| Gleason score: NR | Gleason score: ≤6 (35.71); 7 (14.29); ≥8 (21.43); unknown (28.57) | Gleason score: ≤6 (44.29); 7 (19.29); ≥8 (10.71); unknown (25.71) |
| AJCC stage: NR | AJCC stage: I-III (21.43); IV (35.71); unknown (42.86) | AJCC stage: I-III (48.57); IV (5.00); unknown (46.43) |
| TNM stage: NR | TNM stage: T1 (21.43); T2 (28.57); T3 (14.29); T4 (7.14); TX (28.57); N0 (28.57); N1 (21.43); NX (50.00); M0 (50.00) M1 (21.43); MX (28.57) | TNM stage: T1 (27.14); T2 (32.14); T3 (17.14); T4 (1.43); TX (22.14); N0 (54.29); N1 (0.71); NX (45.00); M0 (52.86) M1 (3.57); MX (43.57) |
| ECOG score | ECOG score | ECOG score |
| 0: NR | 0: NR | 0: NR |
| 1: NR | 1: NR | 1: NR |
| 0-1: NR | 0-1: NR | 0-1: NR |
| ≥2: NR | ≥2: NR | ≥2: NR |
| Previous treatments: NR | Previous treatments: NR | Previous treatments: NR |
| Familial history of PC: NR | Familial history of PC: NR | Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) |
|-------------------------------|-------------------------------|-------------------------------|
| Median PSA ng/ml (range): NR) (NR) | Median PSA ng/ml (range): 11.1) (3.09, 91.12) | Median PSA ng/ml (range): 8.25) (0.04, 259) |
| Comments: PSA given at diagnosis | Comments: PSA given at diagnosis | |

AJCC, American Joint Committee on Cancer; CRPC, castration-resistant PC; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; UK, United Kingdom.

**Liu et al, 2016 (5)**

| NR |
|----|
| PC. Diagnosis: Histology |
| Other details (NR) |
| Population (further details): unselected (NR) |
| Treatment (further details): NR (NR) |
| Total (n=36) |
| Mean age (SD): NR (NR) |
| Median age (range): NR (NR) |
| Ethnicity: NR |
| Gleason score: 7 (100) |
| AJCC stage: NR |
| TNM stage: NR |
| ECOG score | 0: NR  |
|-----------|-------|
|           | 1: NR  |
|           | 0-1: NR|
|           | ≥2: NR |

Previous treatments: NR

Familial history of PC: NR

Mean years since diagnosis (SD): NR (NR)
Median years since diagnosis (range): NR (NR)

Mean PSA ng/ml (SD): NR (NR)
Median PSA ng/ml (range): NR (NR)

AJCC, American Joint Committee on Cancer; DDR, DNA damage repair; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Lu et al, 2015 (71)**

Multi-national

PC. Diagnosis: NR
Other details (NR)

Population (further details): unselected (NR)

Treatment (further details): NR (NR)

Total (n=178)

Mean age (SD): 60.4 (6.9)
Median age (range): NR (NR)
| Ethnicity: Caucasian (73.03); Asian (1.12); African American (3.37); NR (5.62) |
|---|
| Gleason score: NR |
| AJCC stage: NR |
| TNM stage: NR |
| ECOG score |
| 0: NR |
| 1: NR |
| 0-1: NR |
| ≥2: NR |
| Previous treatments: NR |
| Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR (NR) |
| Comments: Very limited PC data available |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Maier et al, 2014 (72)**

Germany

PC. Diagnosis: NR

Other details (NR)
| Population (further details): familial and unselected (NR) |
|----------------------------------------------------------|
| Treatment (further details): NR (NR)                      |
| Familial (n=382)                                         | Unselected (n=92) |
| Mean age (SD): 61.1 (NR)                                 | Mean age (SD): 55.8 (NR) |
| Median age (range): NR (42, 80)                           | Median age (range): NR (29, 60) |
| Ethnicity: NR                                             | Ethnicity: NR |
| Gleason score: Gleason \( \leq 7 \) and <GIII (71.5); Gleason >7 or GIII (18.3); unknown Gleason and grading (10.2) | Gleason score: Gleason \( \leq 7 \) and <GIII (82.6); Gleason >7 or GIII (15.2); unknown Gleason and grading (2.2) |
| AJCC stage: NR                                            | AJCC stage: NR |
| TNM stage: T1 (2.1); T2 (55.2); T3 (27.2); T4 (5.2); Tx or not recorded (10.2) | TNM stage: T1 (1.1); T2 (56.5); T3 (35.9); T4 (4.3); Tx or not recorded (2.2) |
| ECOG score                                                | ECOG score |
| 0: NR                                                     | 0: NR |
| 1: NR                                                     | 1: NR |
| 0-1: NR                                                   | 0-1: NR |
| \( \geq 2 \): NR                                         | \( \geq 2 \): NR |
| Previous treatments: NR                                   | Previous treatments: Radical prostatectomy |
| Familial history of PC: 382 (100)                         | Familial history of PC: 0 (0) |
| Mean years since diagnosis (SD): NR (NR)                  | Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR)             | Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR)                              | Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): 9.6 (0.2, 1300)                 | Median PSA ng/ml (range): 8.2 (0.5, 94) |
| Comments: Lymph node involvement also reported (pN0, pN1, Nx); PSA level unknown in n=84 | Comments: Lymph node involvement also reported (pN0, pN1, Nx); PSA level unknown in n=6 |
AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

Manson-Bahr et al, 2015 (73)

| UK |  
|---|---|
| PC. Diagnosis: Histology |  
| Other details (NR) |  
| Population (further details): unselected (NR) |  
| Treatment (further details): NR (NR) |  
| Total (n=63) |  
| Mean age (SD): NR (NR) |  
| Median age (range): NR (56, 85) |  
| Ethnicity: NR |  
| Gleason score: 6 (13); 7 (60); 8 (13); 9 (14) |  
| AJCC stage: NR |  
| TNM stage: NR |  
| ECOG score |  
| 0: NR |  
| 1: NR |  
| 0-1: NR |  
| ≥2: NR |  
| Previous treatments: Hormone Therapy (27); Active Surveillance (8); Radiotherapy (40); Brachytherapy (6); Surgery (19) |  
| Familial history of PC: NR |  

134
Mean years since diagnosis (SD): NR (NR)
Median years since diagnosis (range): NR (NR)

Mean PSA ng/ml (SD): NR (NR)
Median PSA ng/ml (range): NR (5.5, 136)

Comments: Baseline details per individual data.

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; UK, United Kingdom.

| Marshall et al, 2017 (74) |
|--------------------------|
| USA                      |
| PC. Diagnosis: NR        |
| Other details (≥≥7 Gleason score) |
| Population (further details): familial (personal history of PC and ≥1 close blood relative with breast, ovarian, pancreatic or prostate cancer; or a personal history of PC) |
| Treatment (further details): NR (NR) |
| Total (n=92)             |
| Mean age (SD): NR (NR)   |
| Median age (range): NR (NR) |
| Ethnicity: NR            |
| Gleason score: NR        |
| AJCC stage: NR           |
| TNM stage: NR            |
| ECOG score          | 0: NR             | 1: NR             | 0-1: NR           | ≥2: NR            |
|---------------------|-------------------|-------------------|-------------------|------------------|
| Previous treatments | NR                |                   |                   |                  |
| Familial history of PC | 2 (1.4)         |                   |                   |                  |
| Mean years since diagnosis (SD): NR (NR) |                   |                   |                   |                  |
| Median years since diagnosis (range): NR (NR) |                   |                   |                   |                  |
| Mean PSA ng/ml (SD): NR (NR) |                   |                   |                   |                  |
| Median PSA ng/ml (range): NR (NR) |                   |                   |                   |                  |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

**Mateo et al, 2015 (75)**

| UK                  |                   |                   |                   |                  |
|---------------------|-------------------|-------------------|-------------------|------------------|
| mCRPC. Diagnosis: Histology |                   |                   |                   |                  |
| Other details (NR)  |                   |                   |                   |                  |
| Population (further details): unselected (NR) |                   |                   |                   |                  |
| Treatment (further details): Olaparib (400 mg tablet twice daily) |                   |                   |                   |                  |
| Total (n=50)        |                   |                   |                   |                  |
|                                |               |
|--------------------------------|---------------|
| Mean age (SD): NR (NR)          |               |
| Median age (range): 67.5 (40.8, 79.3) |           |
| Ethnicity: NR                  |               |
| Gleason score: NR              |               |
| AJCC stage: NR                 |               |
| TNM stage: NR                  |               |
| ECOG score                     |               |
| 0: 9 (18)                      |               |
| 1: 35 (70)                     |               |
| 0-1: NR                        |               |
| ≥2: 6 (12)                     |               |
| Previous treatments:           | Docetaxel (100); abiraterone acetate (96); cabazitaxel (58); radical prostatectomy or radiotherapy (50); castration (chemical or surgical) (100); enzalutamide (28); radium-223 (2). |
| Familial history of PC: NR     |               |
| Mean years since diagnosis (SD): NR (NR) |        |
| Median years since diagnosis (range): 5 (NR) |       |
| Mean PSA ng/ml (SD): NR (NR)   |               |
| Median PSA ng/ml (range): 349.5 (NR) |             |
| Comments: Circulating tumor-cell count (cells/7.5ml blood) was median 37 (IQR 14-110) |        |

AJCC, American Joint Committee on Cancer; CRPC, castration-resistant PC; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; UK, United Kingdom.

Meyer *et al*, 2007 (25)
Germany

| Primary PC. Diagnosis: Histology |
|----------------------------------|
| Other details (Clinically localized low risk early PC) |

| Population (further details): treatment (Brachytherapy I 125) |
|----------------------------------------------------------------|

| Treatment (further details): Brachytherapy I 125 (160 Gy) |
|-----------------------------------------------------------|

| DDR+ (n=25) | DDR- (n=236) |
|-------------|--------------|
| Mean age (SD): 63.8 (NR) | Mean age (SD): 65.5 (NR) |
| Median age (range): NR (NR) | Median age (range): NR (NR) |
| Ethnicity: NR | Ethnicity: NR |
| Gleason score: 3 (0); 4 (12); 5 (8); 6 (605); 7 (20); 8 (0) | Gleason score: 3 (1.5); 4 (5.9); 5 (19.9); 6 (69.5); 7 (2.5); 8 (0.3) |
| AJCC stage: NR | AJCC stage: NR |
| TNM stage: cT1c (0); cT2a (80); cT2b (12); cT2c (8); unknown (0) | TNM stage: cT1c (2); cT2a (73.7); cT2b (19); cT2c (1.7); unknown (3.4) |

| ECOG score |
|------------|
| 0: NR |
| 1: NR |
| 0-1: NR |
| ≥2: NR |

| Previous treatments: neoadjuvant hormone therapy (7) |
|-----------------------------------------------------|

| Familial history of PC: NR |
|----------------------------|

| Mean years since diagnosis (SD): NR (NR) |
|-----------------------------------------|
| Median years since diagnosis (range): NR (NR) |
Mean PSA ng/ml (SD): 6.6 (NR)  
Median PSA ng/ml (range): NR (NR)  
Mean PSA ng/ml (SD): 7 (NR)  
Median PSA ng/ml (range): NR (NR)

Comments: Mean PSA, Gleason and age are for carriers of P1054R variant

AJCC, American Joint Committee on Cancer; DDR, DNA damage repair; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

| Myers et al, 2016 (76) |
|------------------------|
| USA                    |
| PC. Diagnosis: NR      |
| Other details (NR)     |
| Population (further details): unselected (NR) |
| Treatment (further details): NR (NR) |
| DDR+ (n=12)            | DDR- (n=73)            |
| Mean age (SD): 58 (NR) | Mean age (SD): 62 (NR) |
| Median age (range): NR (NR) | Median age (range): NR (NR) |
| Ethnicity: NR          | Ethnicity: NR          |
| Gleason score: NR      | Gleason score: NR      |
| AJCC stage: NR         | AJCC stage: NR         |
| TNM stage: NR          | TNM stage: NR          |
| ECOG score       | ECOG score       |
|------------------|------------------|
| 0: NR            | 0: NR            |
| 1: NR            | 1: NR            |
| 0-1: NR          | 0-1: NR          |
| ≥2: NR           | ≥2: NR           |

| Previous treatments: NR | Previous treatments: NR |
|-------------------------|-------------------------|

| Familial history of PC: NR | Familial history of PC: NR |
|----------------------------|----------------------------|

| Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) |
|----------------------------------------|----------------------------------------|
| Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR (NR) | Median PSA ng/ml (range): NR (NR) |

**AJCC**, American Joint Committee on Cancer; DDR, DNA damage repair; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

**Na et al, 2017 (77)**

- Multi-national
- Other and Primary PC. Diagnosis: NR
- Other details (Lethal PC)
- Population (further details): unselected (NR)
- Treatment (further details): NR (NR)
- Lethal (n=313) | Primary PC (n=486)
| Mean age (SD): NR (NR) | Mean age (SD): NR (NR) |
|-----------------------|-----------------------|
| Median age (range): 62 (NR) | Median age (range): 65 (NR) |
| Ethnicity: European American (83.4); African American (9.6); Chinese (7.0) | Ethnicity: European American (72.4); African American (18.3); Chinese (9.3) |
| Gleason score: NR | Gleason score: NR |
| AJCC stage: NR | AJCC stage: NR |
| TNM stage: NR | TNM stage: NR |
| ECOG score | ECOG score |
| 0: NR | 0: NR |
| 1: NR | 1: NR |
| 0-1: NR | 0-1: NR |
| ≥2: NR | ≥2: NR |
| Previous treatments: NR | Previous treatments: NR |
| Familial history of PC: NR | Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): 13.1 (NR) | Median PSA ng/ml (range): 5.3 (NR) |
| Comments: Outcomes based on ethnicity in lethal vs localized PC are also available but not extracted (European American, African American, Chinese) | Comments: Outcomes based on ethnicity in lethal vs localized PC are also available but not extracted (European American, African American, Chinese) |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.
| **Nam et al, 2005 (15)** |
|-------------------------|
| Canada |
| PC. Diagnosis: Histology |
| Other details (NR) |
| Population (further details): unselected (NR) |
| Treatment (further details): NR (NR) |
| Total (n=996) |
| Mean age (SD): 66.2 (NR) |
| Median age (range): NR (NR) |
| Ethnicity: White (84.1); Black (11.0); Asian (2.9); Other (1.8) |
| Gleason score: NR |
| AJCC stage: NR |
| TNM stage: NR |
| ECOG score |
| 0: NR |
| 1: NR |
| 0-1: NR |
| ≥2: NR |
| Previous treatments: NR |
| Familial history of PC: 163 (16.3) |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
Mean PSA ng/ml (SD): NR (NR)
Median PSA ng/ml (range): NR (NR)
Comments: PSA levels (ng/ml) ≤ 4.0 (5.7%); 4.1-10.0 (56.8%); 10.1-20.0 (26.2%); >20.0 (11.2%)

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Naslund Koch et al, 2016 (16)**

Denmark

PC. Diagnosis: NR
Other details (NR)

Population (further details): unselected (NR)

Treatment (further details): NR (NR)

Total (n=39014)

Mean age (SD): NR (NR)
Median age (range): NR (NR)

Ethnicity: NR

Gleason score: NR

AJCC stage: NR

TNM stage: NR
| ECOG score               | 0: NR       |
|-------------------------|-------------|
|                         | 1: NR       |
|                         | 0-1: NR     |
|                         | ≥2: NR      |

| Previous treatments     | NR          |
|-------------------------|-------------|
| Familial history of PC  | NR          |
| Mean years since diagnosis (SD): | NR (NR)     |
| Median years since diagnosis (range): | NR (NR)     |
| Mean PSA ng/ml (SD):    | NR (NR)     |
| Median PSA ng/ml (range): | NR (NR)     |

**Comments:** Although age and family history were specified, this was only presented for the full cohort of 86,922 subjects (no details were provided regarding the male cohort).

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

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**Nastiuk et al, 1999 (78)**

| USA                     |
|-------------------------|
| PC. Diagnosis: NR       |
| Other details (Archival records from New York University and Columbia Presbyterian medical centers for stage B PC) |
| Population (further details): Ashkenazi (NR) |
| Treatment (further details): NR (NR) |
| Total (n=83)             |
| Mean age (SD): NR (NR) |
|------------------------|
| Median age (range): NR (NR) |
| Ethnicity: Ashkenazi Jewish men (100) |
| Gleason score: NR |
| AJCC stage: NR |
| TNM stage: NR |
| ECOG score |
| 0: NR |
| 1: NR |
| 0-1: NR |
| ≥2: NR |
| Previous treatments: NR |
| Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR (NR) |
| Comments: Only looking at PC, no controls, using earlier paper for cohort control (Roa BB, Boyd AA, Volcik K, Richards CS. Ashkenazi Jewish population frequencies for common mutations in BRCA1 and BRCA2. Nat. Genet. 1996; 14:185-187. [PubMed: 8841191].) |
| AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America. |

Nelson et al, 2016 (79)
Multi-national

mPC. Diagnosis: NR
Other details (NR)

Population (further details): unselected (NR)
Treatment (further details): NR (NR)

Total (n=569)
Mean age (SD): NR (NR)
Median age (range): NR (NR)

Ethnicity: NR
Gleason score: NR
AJCC stage: NR
TNM stage: NR

ECOG score
0: NR
1: NR
0-1: NR
≥2: NR

Previous treatments: NR
Familial history of PC: NR

Mean years since diagnosis (SD): NR (NR)
Median years since diagnosis (range): NR (NR)
Mean PSA ng/ml (SD): NR (NR)
Median PSA ng/ml (range): NR (NR)
Comments: No patient characteristics provided

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

| Nguyen et al, 2011 (80) |
|-------------------------|
| USA                     |
| Primary PC. Diagnosis: NR |
| Other details (NR)      |
| Population (further details): treatment (external radiation or brachytherapy) |
| Treatment (further details): external radiation or brachytherapy (NR) |
| Total (n=612)           |
| Mean age (SD): NR (NR)  |
| Median age (range): NR (NR) |
| Ethnicity: NR           |
| Gleason score: NR       |
| AJCC stage: NR          |
| TNM stage: NR           |
| ECOG score             |
| 0: NR                   |
| 1: NR                   |
| 0-1: NR                 |
| ≥2: NR                  |
| Previous treatments: NR |
| Familial history of PC: NR |
|---------------------------|
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR (NR) |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.
### Nicolas et al, 2015 (24)

**USA**

PC. Diagnosis: Histology

Other details (NR)

Population (further details): familial (NR)

Treatment (further details): NR (NR)

| Total (n=12) |
|--------------|
| Mean age (SD): 57.8 (NR) |
| Median age (range): NR (41, 68) |

**Ethnicity:** Caucasian (100), Hispanic (0)

Gleason score: 6 (41.7); 7 (50); 8 (8.3)

AJCC stage: NR

| TNM stage: |
|------------|
| T2cN0MX (41.7); T2aN0MX (8.3); T3bN0MX (8.3); T2cN0MX (8.3); T3aN0MX (8.3); T1c (8.3); T3bN1M0 (8.3); T2cNO (8.3) |

**ECOG score**

- 0: NR
- 1: NR
- 0-1: NR
- ≥2: NR

**Previous treatments:** NR

**Familial history of PC:** 12 (100)

Mean years since diagnosis (SD): NR (NR)

Median years since diagnosis (range): NR (NR)
Mean PSA ng/ml (SD): NR (NR)
Median PSA ng/ml (range): NR (NR)
AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

| **Nicolosi et al, 2017 (81)** |
|-------------------------------|
| USA                          |
| PC. Diagnosis: NR            |
| Other details (NR)           |
| Population (further details): unselected (NR) |
| Treatment (further details): NR (NR) |
| Total (n=1158)               |
| Mean age (SD): NR (NR)       |
| Median age (range): NR (NR)  |
| Ethnicity: NR                |
| Gleason score: NR            |
| AJCC stage: NR               |
| TNM stage: NR                |
| ECOG score | NR |
|------------|----|
| 0          | NR |
| 1          | NR |
| 0-1        | NR |
| ≥2         | NR |

| Previous treatments | NR |

| Familial history of PC | NR |

| Mean years since diagnosis (SD) | NR (NR) |
| Median years since diagnosis (range) | NR (NR) |

| Mean PSA ng/ml (SD) | NR (NR) |
| Median PSA ng/ml (range) | NR (NR) |

**Comments:** No patient characteristics provided

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

**Nientiedt et al, 2017 (82)**

Germany

mCRPC. Diagnosis: Histology

Other details (NR)

Population (further details): treatment (docetaxel)

Treatment (further details): docetaxel (NR)

Total (n=53)
| **Mean age (SD): NR (NR)**  |
|---------------------------|
| **Median age (range): 63 (40, 78)** |
| **Ethnicity: NR** |
| **Gleason score: 3+4 (9.4); 4+3 (9.4); 8 (9.4); 9-10 (69.8); unknown (1.9)** |
| **AJCC stage: NR** |
| **TNM stage: T2 (7.5); T3 (69.8); T4 (13.2); Tx (9.4); N0 (35.8); N1 (52.8); NxD (11.3); M0 (54.7); M1 (41.5); MxD (3.8)** |
| **ECOG score** |
| 0: 30 (56.6) |
| 1: 21 (39.6) |
| 0-1: 2 (3.8) |
| ≥2: 0 |
| **Previous treatments:** Radical prostatectomy (77.4) Primary radiotherapy (1.9) Androgen deprivation therapy (100) Adjuvant radiotherapy (24.5) Salvage radiotherapy (13.2) Enzalutamide and/or Abiraterone (15.1) |
| **Familial history of PC: NR** |
| **Mean years since diagnosis (SD): NR (NR)**  |
| **Median years since diagnosis (range): NR (NR)**  |
| **Mean PSA ng/ml (SD): NR (NR)**  |
| **Median PSA ng/ml (range): 30 (0.6, 6782)** |
| **Comments:** Population also included primary metastatic PC; Treatment prior to docetaxel is reported |

AJCC, American Joint Committee on Cancer; CRPC, castration-resistant PC; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Palapattu et al, 2015 (20)**
| USA |
|---|
| PC. Diagnosis: NR |
| Other details (NR) |
| Population (further details): unselected (NR) |
| Treatment (further details): NR (NR) |
| Total (n=9) |
| Mean age (SD): NR (NR) |
| Median age (range): NR (NR) |
| Ethnicity: NR |
| Gleason score: 7 (56) |
| AJCC stage: NR |
| TNM stage: NR |
| ECOG score |
| 0: NR |
| 1: NR |
| 0-1: NR |
| ≥2: NR |
| Previous treatments: NR |
| Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR) (NR) |
Comments: Gleason score all start at 6, after 1 year 5 of 9 are at GS7

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

### Patel et al, 2016 (83)

|               |               |
|---------------|---------------|
| USA           |               |
| PC. Diagnosis: | NR            |
| Other details (NR) |               |
| Population (further details): | unselected (NR) |
| Treatment (further details): | NR (NR)       |
| Total (n=327) |               |
| Mean age (SD): | NR (NR)       |
| Median age (range): | NR (NR)       |
| Ethnicity:    | NR            |
| Gleason score: | NR            |
| AJCC stage:   | NR            |
| TNM stage:    | NR            |
| ECOG score    |               |
| 0: NR         |               |
| 1: NR         |               |
| 0-1: NR       |               |
| ≥2: NR        |               |
| Previous treatments: NR |
|-------------------------|
| Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR (NR) |

AJCC, American Joint Committee on Cancer; DDR, DNA damage repair; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

**Petrovics et al, 2016 (84)**

USA

PC. Diagnosis: NR

Other details (NR)

Population (further details): unselected (NR)

Treatment (further details): NR (NR)

Total (n=857)

Mean age (SD): NR (NR)

Median age (range): NR (NR)

Ethnicity: African American (NR); Caucasian American (NR)

Gleason score:

AJCC stage: NR

TNM stage: NR
| ECOG score       |          |          |
|------------------|----------|----------|
| 0: NR            |          |          |
| 1: NR            |          |          |
| 0-1: NR          |          |          |
| ≥2: NR           |          |          |

| Previous treatments | NR     |
|---------------------|--------|

| Familial history of PC | NR |
|------------------------|----|

| Mean years since diagnosis (SD) | NR (NR) |
|---------------------------------|---------|
| Median years since diagnosis (range) | NR (NR) |

| Mean PSA ng/ml (SD) | NR (NR) |
|---------------------|---------|
| Median PSA ng/ml (range) | NR (NR) |

- **AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.**

**Pomerantz et al, 2017 (85)**

| USA |
|-----|

| mCRPC. Diagnosis | NR |
|------------------|----|

| Other details | NR |
|---------------|----|

| Population (further details): treatment (Carboplatin-based chemotherapy) |
|--------------------------------------------------------------------------|

| Treatment (further details): Carboplatin/docetaxel-based chemotherapy (At least two doses of carboplatin and docetaxel) |
|------------------------------------------------------------------------------------------------------------------|

| Total (n=141) | DDR+ (n=8) | DDR- (n=133) |
|---------------|------------|--------------|
| Mean age (SD): NR (NR) | Mean age (SD): NR (NR) | Mean age (SD): NR (NR) |
|------------------------|------------------------|------------------------|
| Median age (range): 59 (40, 80) | Median age (range): 53 (40, 62) | Median age (range): 60 (40, 80) |
| Ethnicity: European American (87.2); African American (2.8); Hispanic (1.4); Unknown (8.5) | Ethnicity: European American (100); African American (0); Hispanic (0); Unknown (0) | Ethnicity: European American (86.5); African American (3); Hispanic (1.5); Unknown (9) |
| Gleason score: 6 (6.4); 7 (22); 8-10 (62.4); unknown (9.2) | Gleason score: 6 (0); 7 (12.5); 8-10 (75); unknown (12.5) | Gleason score: 6 (6.8); 7 (22.6); 8-10 (61.7); unknown (9) |
| AJCC stage: NR | AJCC stage: NR | AJCC stage: NR |
| TNM stage: NR | TNM stage: NR | TNM stage: NR |
| ECOG score | ECOG score | ECOG score |
| 0: NR | 0: NR | 0: NR |
| 1: NR | 1: NR | 1: NR |
| 0-1: NR | 0-1: NR | 0-1: NR |
| ≥2: NR | ≥2: NR | ≥2: NR |
| Previous treatments: NR | Previous treatments: NR | Previous treatments: NR |
| Familial history of PC: 26 (18.4) | Familial history of PC: 2 (25) | Familial history of PC: 24 (18) |
| Mean years since diagnosis (SD): 6.3 (NR) | Mean years since diagnosis (SD): 4.5 (NR) | Mean years since diagnosis (SD): 6.3 (NR) |
| Median years since diagnosis (range): NR (0.5, 20.7) | Median years since diagnosis (range): NR (1.1, 13.7) | Median years since diagnosis (range): NR (0.5, 20.7) |
| Mean PSA ng/ml (SD): 170 (NR) | Mean PSA ng/ml (SD): 49 (NR) | Mean PSA ng/ml (SD): 204 (NR) |
| Median PSA ng/ml (range): NR) (0, 9145) | Median PSA ng/ml (range): NR) (1, 515) | Median PSA ng/ml (range): NR) (0, 9145) |
| Comments: PSA at diagnosis also available; PSA presented here is at start of chemo | Comments: PSA at diagnosis also available; PSA presented here is at start of chemo | Comments: PSA at diagnosis also available; PSA presented here is at start of chemo |
Pritchard et al, 2014 (86)

USA

mPC. Diagnosis: autopsy

Other details (primary and metastatic prostate cancer)

Population (further details): unselected (NR)

Treatment (further details): NR (NR)

Total (n=60)

Mean age (SD): NR (NR)

Median age (range): NR (NR)

Ethnicity: NR

Gleason score: NR

AJCC stage: NR

TNM stage: NR

ECOG score

0: NR
1: NR
0-1: NR
≥2: NR

Previous treatments: NR
### Familial history of PC: NR

| Metric                              | Value         |
|-------------------------------------|---------------|
| Mean years since diagnosis (SD)     | NR (NR)       |
| Median years since diagnosis (range)| NR (NR)       |
| Mean PSA ng/ml (SD)                 | NR (NR)       |
| Median PSA ng/ml (range)            | NR (NR)       |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

### Pritchard et al, 2016 (87)

#### Multi-national

mPC and Primary PC. Diagnosis: Histology

Other details (mPC cohort)

| Population (further details):         | Value         |
|---------------------------------------|---------------|
| Treatment (further details):          | NR (NR)       |

#### mPC (n=692) vs. Primary PC (n=499)

| Metric                              | Value         |
|-------------------------------------|---------------|
| Mean age (SD): <50 (7.2); 50-59 (31.7); 60-69 (43.5); 70-79 (13.6); ≥80 (1.9); unknown (2.2) (NR) | Mean age (SD): <50 (5.4); 50-59 (35.4); 60-69 (48.7); 70-79 (10.4); ≥80 (0); unknown (0) (NR) |
| Median age (range): NR (NR)          | Median age (range): NR (NR) |
| Ethnicity: Non-Hispanic white (83.2); Hispanic (1.6); non-Hispanic black (5.8); Asian or Pacific Islander (1.7); other or unknown (7.7) | Ethnicity: Non-Hispanic white (81.4); Hispanic (1.4); non-Hispanic black (11.6); Asian or Pacific Islander (2.4); other or unknown (3.2) |
| Gleason score: ≤6 (6.07); 3+4 (9.4); 4+3 (13.3); 8-10 (55.2); unknown (16.0) | Gleason score: ≤6 (9.0); 3+4 (29.7); 4+3 (20.2); 8-10 (41.1); unknown (0) |
| AJCC stage: NR | AJCC stage: NR |
|----------------|----------------|
| TNM stage: NR  | TNM stage: NR  |
| ECOG score     | ECOG score     |
| 0: NR          | 0: NR          |
| 1: NR          | 1: NR          |
| 0-1: NR        | 0-1: NR        |
| ≥2: NR         | ≥2: NR         |
| Previous treatments: NR | Previous treatments: NR |
| Familial history of PC: 133 (19.2) | Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR) (NR) | Median PSA ng/ml (range): NR) (NR) |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.
| **Pugh et al, 2009 (88)** |
|--------------------------|
| **Canada**               |
| **PC. Diagnosis: Histology and PSA** |
| Other details (NR)       |
| **Population (further details): treatment (Brachytherapy)** |
| **Treatment (further details): Brachytherapy** (Near-ideal rectal and prostate post-implant dosimetry: prostate D90 <175 Gy (dose covering 90% of the prostate <175 Gy), prostate V100 >85% (volume of the prostate covered by >85% of the radiation dose), and rectal VR100 <1.0 cm³ (volume of the rectum rec)) |
| **Total (n=41)**         |
| Mean age (SD): NR (NR)   |
| Median age (range): NR (NR) |
| **Ethnicity: NR**        |
| **Gleason score: NR**    |
| **AJCC stage: 1C (58); 2A (32); 2B (10)** |
| **TNM stage: NR**        |
| **ECOG score**           |
| 0: NR                    |
| 1: NR                    |
| 0-1: NR                  |
| ≥2: NR                   |
| **Previous treatments: NR** |
| **Familial history of PC: NR** |
### Robbins et al, 2011 (21)

| Information          | Details                  |
|----------------------|--------------------------|
| **USA**              |                          |
| mPC. Diagnosis:     | Histology                |
| Other details:      | NR                       |
| Population (further | unselected (NR)          |
| details):           |                          |
| Treatment (further  | NR (NR)                  |
| details):           |                          |
| Total (n=8)         |                          |
| Mean age (SD):      | NR (NR)                  |
| Median age (range): | NR (NR)                  |
| Ethnicity:          | NR                       |
| Gleason score:      | NR                       |
| AJCC stage:         | NR                       |
| TNM stage:          | NR                       |
| ECOG score          | 0: NR               |
|---------------------|---------------------|
|                     | 1: NR               |
|                     | 0-1: NR             |
|                     | ≥2: NR              |

| Previous treatments: | NR        |
|----------------------|-----------|

| Familial history of PC: | NR       |
|-------------------------|----------|

| Mean years since diagnosis (SD): | NR (NR) |
|----------------------------------|---------|
| Median years since diagnosis (range): | NR (NR) |

| Mean PSA ng/ml (SD): | NR (NR) |
|----------------------|---------|
| Median PSA ng/ml (range): | NR (NR) |

| Comments: | Extremely limited patient characteristics presented |

| AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America. |

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| Robinson et al, 2015 (89) |
|----------------------------|

| Multi-national |
|----------------|

| mCRPC. Diagnosis: Histology |
|-----------------------------|

| Other details (NR) |
|--------------------|

| Population (further details): unselected (NR) |
|-----------------------------------------------|

| Treatment (further details): NR (NR) |
|-------------------------------------|

| Total (n=150) |
|---------------|

---
| Parameter                                      | Value                      |
|-----------------------------------------------|----------------------------|
| Mean age (SD):                                | NR (NR)                    |
| Median age (range):                           | 68 (43, 84)                |
| Ethnicity:                                    | NR                         |
| Gleason score:                                | NR                         |
| AJCC stage:                                   | NR                         |
| TNM stage:                                    | NR                         |
| ECOG score                                    |                            |
| 0: NR                                         |                            |
| 1: NR                                         |                            |
| 0-1: NR                                       |                            |
| ≥2: NR                                        |                            |
| Previous treatments:                          | Abiraterone acetate or enzalutamide (48); taxane chemotherapy (41) |
| Familial history of PC:                       | NR                         |
| Mean years since diagnosis (SD):              | NR (NR)                    |
| Median years since diagnosis (range):         | NR (NR)                    |
| Mean PSA ng/ml (SD):                          | 55.78 ()                   |
| Median PSA ng/ml (range):                     | NR (0.04, 4654.92)         |

AJCC, American Joint Committee on Cancer; CRPC, castration-resistant prostate cancer; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.
**Romero et al, 2017 (90)**

Spain

mCRPC. Diagnosis: Histology

Other details (NR)

Population (further details): unselected (NR)

Treatment (further details): NR (NR)

Total (n=419)

Mean age (SD): NR (NR)

Median age (range): 73 (43, 94)

Ethnicity: NR

Gleason score: NR

AJCC stage: NR

TNM stage: NR

ECOG score

0: NR

1: NR

0-1: NR (91)

$\geq$2: NR (9)

Previous treatments: NR

Familial history of PC: NR

Mean years since diagnosis (SD): NR (NR)

Median years since diagnosis (range): NR (NR)
Mean PSA ng/ml (SD): NR (NR)
Median PSA ng/ml (range): 26.95 (<0.02, 5198)
Comments: Population data included for 'at diagnosis of mCRPC' rather than diagnosis of PC (more relevant to the study)
AJCC, American Joint Committee on Cancer; CRPC, castration-resistant prostate cancer; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

Sanchez et al, 2016 (91)
USA
Primary PC. Diagnosis: Initially through self-reporting that was confirmed by medical records and pathology reports
Other details (NR)
Population (further details): treatment (Radiotherapy or radical prostatectomy)
Treatment (further details): Radiotherapy (NR) Radical prostatectomy (NR)

| Radiotherapy (n=802) | Radical prostatectomy (n=1111) |
|---------------------|-------------------------------|
| Mean age (SD): 72.1 (5.9) | Mean age (SD): 65.6 (6.1) |
| Median age (range): NR (NR) | Median age (range): NR (NR) |
| Ethnicity: European descent | Ethnicity: European descent |
| Gleason score: ≤6 (64); 7 (25); ≥8 (11) | Gleason score: ≤6 (43); 7 (45); ≥8 (11) |
| AJCC stage: NR | AJCC stage: NR |
| TNM stage: T1/T2 (95); T3 (5) | TNM stage: T1/T2 (98); T3 (2) |
| ECOG score  | Previous treatments: Neoadjuvant/adjuvant ADT (33) | Previous treatments: Neoadjuvant/adjuvant ADT (9) |
|------------|---------------------------------------------------|---------------------------------------------------|
| 0: NR      | Familial history of PC: NR                        | Familial history of PC: NR                        |
| 1: NR      | Mean years since diagnosis (SD): NR (NR)         | Mean years since diagnosis (SD): NR (NR)         |
| 0-1: NR    | Median years since diagnosis (range): NR (NR)    | Median years since diagnosis (range): NR (NR)    |
| ≥2: NR     | Mean PSA ng/ml (SD): NR (NR)                      | Mean PSA ng/ml (SD): NR (NR)                      |
|            | Median PSA ng/ml (range): NR (NR)                | Median PSA ng/ml (range): NR (NR)                |

ADT, androgen deprivation therapy; AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

**Sandhu et al, 2013 (92)**

UK and Multi-national

mCRPC (UK) CRPC (Multi-national). Diagnosis: NR

Other details (NR)

Population (further details): unselected (NR)

Treatment (further details): Mixed treatment (Olaparib 200 mg (50%); Olaparib 300 mg (25%); Niraparib (MK-4827) (25%))

mCRPC (n=4) CRPC (n=23)
| Parameter                                      | Value                                                                 |
|------------------------------------------------|----------------------------------------------------------------------|
| Mean age (SD)                                  | 55.4 (6.4)                                                           |
| Median age (range)                             | NR (54.6, 58)                                                        |
| Ethnicity                                      | NR                                                                  |
| Gleason score                                  | 6 (25); 7 (25); 8 (25); NR (25)                                     |
| AJCC stage                                     | NR                                                                  |
| TNM stage                                      | T3N0M1 (50); T1cN1M0 (25); TxNXM1 (25)                               |
| ECOG score                                     | 0: NR; 1: NR; 0-1: NR; ≥2: NR                                        |
| Previous treatments                            | Androgen blockade (bicalutamide) (100); carboplatin AUC6 (25); docetaxel (50); docetaxel + figitumub (25); abiraterone (25); radical radiotherapy (25), radiotherapy to inguinal lymph nodes (25) |
| Familial history of PC                         | NR                                                                  |
| Mean years since diagnosis (SD)                | NR (NR)                                                             |
| Median years since diagnosis (range)           | NR (NR)                                                             |
| Mean PSA ng/ml (SD)                            | NR (NR)                                                             |
| Median PSA ng/ml (range)                       | NR (NR)                                                             |
| Comments                                       | Sandhu 2013(92)                                                      |

AJCC, American Joint Committee on Cancer; AUC, area under the curve; CRPC, castration-resistant prostate cancer; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; UK, United Kingdom.
| **Schweizer et al, 2016 (27)** |
|--------------------------------|
| **USA**                       |
| Ductal PC. Diagnosis: NR      |
| Other details (NR)            |
| Population (further details): unselected (NR) |
| Treatment (further details): NR (NR) |
| **Total (n=10)**              |
| Mean age (SD): 59 (NR)        |
| Median age (range): NR (40, 73) |
| Ethnicity: NR                 |
| Gleason score: 7 (20); 8 (20); 9 (60) |
| AJCC stage: NR                |
| TNM stage: NR                 |
| ECOG score                    |
| 0: NR                         |
| 1: NR                         |
| 0-1: NR                       |
| ≥2: NR                        |
| Previous treatments: NR       |
| Familial history of PC: NR    |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) |
|---------------------------|
| Median PSA ng/ml (range): NR (NR) |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

### Shapiro et al, 2017 (93)

| Multi-national |
|----------------|

mCRPC. Diagnosis: Histologically or cytologically confirmed adenocarcinoma or poorly differentiated carcinoma of the prostate; and has undergone surgical or medical castration with serum testosterone levels of $\leq 50$ ng/dL (1.73 nM)

Other details (NR)

| Population (further details): unselected (NR) |
|----------------------------------------------|

| Treatment (further details): Rucaparib (600 mg oral rucaparib administered twice daily) |
|--------------------------------------------------------------------------------------|

| DDR+ (n=NR) |
|-------------|

| Mean age (SD): NR (NR) |
|-----------------------|
| Median age (range): NR (NR) |
| Ethnicity: NR |
| Gleason score: NR |
| AJCC stage: NR |
| TNM stage: NR |

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| ECOG score | 0: NR | 1: NR | 0-1: NR | ≥2: NR |
|-----------|------|------|--------|-------|
| Previous treatments: | NR |
| Familial history of PC: | NR |
| Mean years since diagnosis (SD): | NR (NR) |
| Median years since diagnosis (range): | NR (NR) |
| Mean PSA ng/ml (SD): | NR (NR) |
| Median PSA ng/ml (range): | NR (NR) |
| Comments: | Ongoing trial with no reported details. |

AJCC, American Joint Committee on Cancer; CRPC, castration-resistant prostate cancer; DDR, DNA damage repair; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

| Sofronescu et al, 2012 (94) |
|-----------------------------|
| USA |
| PC. Diagnosis: | NR |
| Other details (NR) |
| Population (further details): treatment (radiotherapy) |
| Treatment (further details): radiotherapy (NR) |
| Total (n=87) |
| Parameter                        | Value          |
|---------------------------------|----------------|
| Mean age (SD):                  | NR (NR)        |
| Median age (range):             | NR (NR)        |
| Ethnicity:                      | NR             |
| Gleason score:                  | NR             |
| AJCC stage:                     | NR             |
| TNM stage:                      | NR             |
| ECOG score                      |                |
| 0: NR                           |                |
| 1: NR                           | NR             |
| 0-1: NR                         | NR             |
| ≥2: NR                          | NR             |
| Previous treatments:            | NR             |
| Familial history of PC:         | NR             |
| Mean years since diagnosis (SD):| NR (NR)        |
| Median years since diagnosis (range): | NR (NR)  |
| Mean PSA ng/ml (SD):            | NR (NR)        |
| Median PSA ng/ml (range):       | NR (NR)        |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; UK, United Kingdom.
| **Sonpavde et al, 2017 (6)** |
|-----------------------------|
| NR                          |
| mCRPC. Diagnosis: NR        |
| Other details (NR)          |
| Population (further details): unselected (NR) |
| Treatment (further details): NR (NR) |
| Total (n=514)               |
| Mean age (SD): NR (NR)      |
| Median age (range): 70 (39, 91) |
| Ethnicity: NR               |
| Gleason score: NR           |
| AJCC stage: NR              |
| TNM stage: NR               |
| ECOG score                  |
| 0: NR                       |
| 1: NR                       |
| 0-1: NR                     |
| ≥2: NR                      |
| Previous treatments: NR     |
| Familial history of PC: NR  |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): | NR (NR) |
|----------------------|---------|
| Median PSA ng/ml (range): | NR (NR) |

AJCC, American Joint Committee on Cancer; CRPC, castration-resistant prostate cancer; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Stephens et al, 2016 (29)**

| NR |
|----|
| Other. Diagnosis: Histology |
| Other details (Relapsed/metastatic neuroendocrine carcinoma of the prostate (NCAP)) |
| Population (further details): unselected (NR) |
| Treatment (further details): NR (NR) |
| Total (n=37) |
| Mean age (SD): 65.1 (NR) |
| Median age (range): NR (43, 83) |
| Ethnicity: NR |
| Gleason score: NR |
| AJCC stage: IV (100) |
| TNM stage: NR |
### ECOG score
- 0: NR
- 1: NR
- 0-1: NR
- ≥2: NR

### Previous treatments: NR
### Familial history of PC: NR

### Mean years since diagnosis (SD): NR (NR)
### Median years since diagnosis (range): NR (NR)

### Mean PSA ng/ml (SD): NR (NR)
### Median PSA ng/ml (range): NR (NR)

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

### Struss et al, 2017 (95)

#### Canada

mCRPC. Diagnosis: NR
Other details (NR)

Population (further details): unselected (NR)

Treatment (further details): chemotherapy; androgen deprivation therapy (NR)

Total (n=319)

Mean age (SD): NR (NR)
Median age (range): NR (NR)
| Ethnicity: NR |
|-----------------------------|
| Gleason score: NR |
| AJCC stage: NR |
| TNM stage: NR |
| ECOG score |
| 0: NR |
| 1: NR |
| 0-1: NR |
| ≥2: NR |
| Previous treatments: NR |
| Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR (NR) |

AJCC, American Joint Committee on Cancer; CRPC, castration-resistant prostate cancer; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Tanaka et al, 2009 (7)**

| Japan |
| PC. Diagnosis: Pathology (TNM and Grade) |
| Other details (NR) |
| Population (further details): | unselected (NR) |
|-------------------------------|-----------------|
| Treatment (further details):  | NR (NR)         |
| Total (n=177)                 |
| Mean age (SD): 68.6 (0.4)     |
| Median age (range): NR (NR)   |
| Ethnicity: NR                 |
| Gleason score: NR             |
| AJCC stage: NR                |
| TNM stage: NR                 |
| ECOG score                    |
| 0: NR                         |
| 1: NR                         |
| 0-1: NR                       |
| ≥2: NR                        |
| Previous treatments: NR       |
| Familial history of PC: NR    |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): 11.6 (0.8) |
| Median PSA ng/ml (range): NR (NR) |
| Comments: Age and PSA levels in BPH patients also available |

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AJCC, American Joint Committee on Cancer; BPH, benign prostatic hyperplasia; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Timms et al, 2016 (96)**

|                        | Biobank (n=39)                                                                 | Transatlantic Prostate Group Cohort (n=45)                                                                 |
|------------------------|--------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------|
| PC. Diagnosis: Histology|                                                                                  |                                                                                                          |
| Other details (NR)     |                                                                                  |                                                                                                          |
| Population (further details): | unselected (commercial biobank), unselected (Transatlantic Prostate Group Cohort) |                                                                                                          |
| Treatment (further details): | NR (NR)                                                                 |                                                                                                          |
| Mean age (SD): NR (NR) |                                                                                  | Mean age (SD): NR (NR)                                                                                  |
| Median age (range): NR (NR) |                                                                                  | Median age (range): NR (NR)                                                                            |
| Ethnicity: NR          |                                                                                  | Ethnicity: NR                                                                                            |
| Gleason score: <7 (21); 3+4 (64); 4+3 (15); >7 (0) |                                                                                                          | Gleason score: <7 (2); 3+4 and 4+3 (82); >7 (18)                                                       |
| AJCC stage: NR         |                                                                                  | AJCC stage: NR                                                                                           |
| TNM stage: NR          |                                                                                  | TNM stage: NR                                                                                            |
| ECOG score             |                                                                                  | ECOG score                                                                                              |
| 0: NR                  |                                                                                  | 0: NR                                                                                                   |
| 1: NR                  |                                                                                  | 1: NR                                                                                                   |
| 0-1: NR                |                                                                                  | 0-1: NR                                                                                                 |
| ≥2: NR                 |                                                                                  | ≥2: NR                                                                                                  |
| Previous treatments: NR|                                                                                  | Previous treatments: NR                                                                                  |
| Familial history of PC: NR | Familial history of PC: NR |
|--------------------------|--------------------------|
| Mean years since diagnosis (SD): NR (NR) | Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) | Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) | Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR (NR) | Median PSA ng/ml (range): NR (NR) |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Tischkowitz et al, 2008 (97)**

Canada

PC. Diagnosis: NR

Other details (NR)

Population (further details): Ashkenazi (chosen based on the presence of a family history and/or a high Gleason score)

Treatment (further details): NR (NR)

| family history and/or a high Gleason score (n=25) | Total (n=125) |
|-------------------------------------------------|---------------|
| Mean age (SD): NR (NR) | Mean age (SD): NR (NR) |
| Median age (range): NR (NR) | Median age (range): NR (NR) |
| Ethnicity: NR | Ethnicity: NR |
| Gleason score: mean Gleason score: 7.4 | Gleason score: mean Gleason score: 5.6 |
| AJCC stage: NR | AJCC stage: NR |
| TNM stage: NR | TNM stage: NR |
| ECOG score       | Previous treatments: NR |
|------------------|-------------------------|
| 0: NR            |                         |
| 1: NR            |                         |
| 0-1: NR          |                         |
| ≥2: NR           |                         |

| Familial history of PC: NR | Mean years since diagnosis (SD): NR (NR) |
|----------------------------|-----------------------------------------|
|                             | Median years since diagnosis (range): NR (NR) |
|                             | Mean PSA ng/ml (SD): NR (NR)               |
|                             | Median PSA ng/ml (range): NR (NR)         |
| Comments: mean age at diagnosis: 67.5 years | Comments: mean age at diagnosis: 68.2 years |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

**Uchida et al, 1999 (12)**

| Japan |
|-------|
| Primary PC. Diagnosis: Pathology (Stage and Grade) |
| Other details (NR) |
| Population (further details): unselected (NR) |
| Treatment (further details): NR (NR) |
| Total (n=24) |
| Description                                                                 | Value                                                                 |
|----------------------------------------------------------------------------|----------------------------------------------------------------------|
| Mean age (SD): NR (NR)                                                      |                                                                        |
| Median age (range): NR (NR)                                                 |                                                                        |
| Ethnicity: NR                                                              |                                                                        |
| Gleason score: NR                                                          |                                                                        |
| AJCC stage: NR                                                             |                                                                        |
| TNM stage: NR                                                              |                                                                        |
| ECOG score                                                                 | 0: NR                                                                |
|                                                                            | 1: NR                                                                |
|                                                                            | 0-1: NR                                                              |
|                                                                            | ≥2: NR                                                               |
| Previous treatments: NR                                                    |                                                                        |
| Familial history of PC: NR                                                 |                                                                        |
| Mean years since diagnosis (SD): NR (NR)                                   |                                                                        |
| Median years since diagnosis (range): NR (NR)                              |                                                                        |
| Mean PSA ng/ml (SD): NR (NR)                                                |                                                                        |
| Median PSA ng/ml (range): NR (NR)                                          |                                                                        |
| Comments: Staged as A2 in 1 patient, B in 3, C in 5, and D in 15 patients. | 4 patients had well-differentiated, 9 had moderately differentiated,   |
|                                                                       | 11 had poorly differentiated tumors.                                  |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.
| Vazina et al, 2000 (98) |
|------------------------|
| **Israel** |
| **PC. Diagnosis: Clinical and histopathological diagnosis** |
| Other details (NR) |
| **Population (further details): Unselected or Ashkenazi (Unselected prostate cancer patients (95 out of 174 of Ashkenazi origin))** |
| **Treatment (further details): NR (NR)** |
| **Total (n=174)** |
| **Mean age (SD): NR (NR)** |
| **Median age (range): 66 (45, 81)** |
| **Ethnicity: Ashkenazi (54.6); non-Ashkenazis (45.4)** |
| **Gleason score: 5-7 (48.3); 8-10 (6.9)** |
| **AJCC stage: NR** |
| **TNM stage: T2 (60%); T3 (26.4%)** |
| **ECOG score** |
| 0: NR |
| 1: NR |
| 0-1: NR |
| ≥2: NR |
| **Previous treatments: NR** |
| **Familial history of PC: 19 (10.9)** |
| **Mean years since diagnosis (SD): NR (NR)** |
| **Median years since diagnosis (range): NR (NR)** |
Mean PSA ng/ml (SD): NR (NR)
Median PSA ng/ml (range): NR (NR)

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors.

| Williams et al, 1996 (99) |
|---------------------------|
| USA                       |
| Primary PC. Diagnosis: NR |
| Other details (stage B)   |
| Population (further details): unselected (NR) |
| Treatment (further details): radical prostatectomy (NR) |
| Total (n=23)              |
| Mean age (SD): NR (NR)    |
| Median age (range): NR (NR) |
| Ethnicity: NR             |
| Gleason score: NR         |
| AJCC stage: NR            |
| TNM stage: NR             |
| ECOG score                |
| 0: NR                     |
| 1: NR                     |
| 0-1: NR                   |
| ≥2: NR                    |
| Previous treatments: radical prostatectomy (100) |
|------------------------------------------------|
| Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): NR (NR) |
| Median PSA ng/ml (range): NR (NR) |
| Comments: Very limited patient characteristics presented |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

**Wu et al, 2006 (100)**

USA

Primary PC. Diagnosis: NR

Other details (NR)

Population (further details): unselected (NR)

Treatment (further details): NR (NR)

Total (n=84)

Mean age (SD): NR (NR)

Median age (range): NR (48, 75)

Ethnicity: NR

Gleason score: NR

AJCC stage: NR
| Table 1: Patient Characteristics in the Study of Xia et al., 2015 (18) |
|---------------------------------------------------------------|
| **TNM stage**: NR |
| **ECOG score** |
| 0: NR |
| 1: NR |
| 0-1: NR |
| ≥2: NR |
| **Previous treatments**: NR |
| **Familial history of PC**: NR |
| **Mean years since diagnosis (SD)**: NR (NR) |
| **Median years since diagnosis (range)**: NR (NR) |
| **Mean PSA ng/ml (SD)**: NR (NR) |
| **Median PSA ng/ml (range)**: NR (NR) |
| **Comments**: Very limited baseline characteristics presented |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.

**Xia et al., 2015 (18)**

USA

**PC. Diagnosis**: NR

**Other details**: NR

**Population (further details)**: unselected (NR)

**Treatment (further details)**: NR (NR)
| Total (n=20) |
|-------------|
| Mean age (SD): 65.5 (NR) |
| Median age (range): NR (49, 81) |
| Ethnicity: NR |
| Gleason score: 5 (5); 6 (5); 7 (35); 8 (10); 9 (45) |
| AJCC stage: NR |
| TNM stage: T1 (0); T2 (451); T3 (45); T4 (5); TX (5); N0 (20); N1 (35); N2(5); Nsx(40); M0(65); M1 (35). |
| ECOG score |
| 0: NR |
| 1: NR |
| 0-1: NR |
| ≥2: NR |
| Previous treatments: NR |
| Familial history of PC: NR |
| Mean years since diagnosis (SD): NR (NR) |
| Median years since diagnosis (range): NR (NR) |
| Mean PSA ng/ml (SD): 18.9 (NR) |
| Median PSA ng/ml (range): NR (0.33, 126) |
| Comments: PSA levels reported at the time of the first sample collection |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.
**Zhu et al, 2010 (101)**

| Country                  | USA |
|--------------------------|-----|
| PC. Diagnosis            | NR  |
| Other details            | NR  |
| Population (further details): treatment | External beam radiotherapy |
| Treatment (further details): | External beam radiotherapy (NR) |
| Total (n=31)             |     |
| Mean age (SD)            | NR  |
| Median age (range)       | NR  |
| Ethnicity                | NR  |
| Gleason score            | NR  |
| AJCC stage               | NR  |
| TNM stage                | NR  |
| ECOG score               |     |
| 0: NR                    |     |
| 1: NR                    |     |
| 0-1: NR                  |     |
| ≥2: NR                   |     |
| Previous treatments      | NR  |
| Familial history of PC   | NR  |
| Mean years since diagnosis (SD) | NR  |
| Median years since diagnosis (range) | NR  |
### Zuhlke et al, 2012 (102)

| Description                                      | Details                                                                 |
|--------------------------------------------------|-------------------------------------------------------------------------|
| Country (USA)                                     | USA                                                                     |
| Diagnosis: medical record review whenever possible|                                                                         |
| Other details (NR)                                |                                                                         |
| Population (further details): familial (hereditary prostate cancer) |                                                               |
| Treatment (further details): NR (NR)              |                                                                         |
| Total (n=94)                                      |                                                                         |
| Mean age (SD): NR (NR)                            |                                                                         |
| Median age (range): NR (NR)                       |                                                                         |
| Ethnicity: Seven families were of African descent, 2 were of Asian descent, and the remaining 85 were of European descent |                                                                 |
| Gleason score: NR                                 |                                                                         |
| AJCC stage: NR                                    |                                                                         |
| TNM stage: NR                                     |                                                                         |
| ECOG score | Previous treatments: radical prostatectomy |
|------------|-------------------------------------------|
| 0: NR      |                                           |
| 1: NR      |                                           |
| 0-1: NR    |                                           |
| ≥2: NR     |                                           |

| Familial history of PC: NR |
|---------------------------|

| Mean years since diagnosis (SD): NR (NR) |
|-----------------------------------------|
| Median years since diagnosis (range): NR (NR) |

| Mean PSA ng/ml (SD): NR (NR) |
|-----------------------------|
| Median PSA ng/ml (range): NR (NR) |

AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; NR, not reported; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation; TNM, Tumor Nodes Metastasis classification of malignant tumors; USA, United States of America.
### Appendix S6. Methods for DDR gene mutational analysis.

| Germline or somatic mutation | Source of DNA | Methods | Details of methods | DDR definition | Author, year | References |
|-----------------------------|---------------|---------|-------------------|----------------|--------------|------------|
| **Australia**               |               |         |                   |                |              |            |
| NR/unclear                  | NR            | NR      | NR                | BRCA1 and BRCA2 (undefined) | Cheng et al, 2011 | (23)       |
| **Canada**                  |               |         |                   |                |              |            |
| Germline                    | Blood sample  | other   | Sequencing using an ABI 3730XL DNA Sequencer. Sequences were analysed using Chromas 2.3. Long-range PCR to confirm all variants were located within functional copy of CHEK2 (chromosome 22q12) | CHEK2 variants (exon 11 1270T>CY424H; exon 11 1283C>T S428F; exon 11 1312G>T D438Y; exon 13 1525C>T P509S) | Tischkowitz et al, 2008 | (97)       |
| PCR                         | PCR and pyrosequencing |         |                   | ATM; BCL2; BRCA1; BRCA2; CYP1A1; CYP2C9; CYP2C19; CYP3A5; CYP2D6; CYP11B2; CYP17A1; ERCC2; ESR1; LIG4; MSH6; NBN; NR3C1; RAD51; RAD52; TGFB1; XPF; XRCC1, XRCC2, XRCC3 | Damaraju et al, 2006 | (26)       |
| Multiplex sizing assay. Samples demonstrating a band shift were run again for confirmation |         |         |                   | BRCA1 (185delAG); BRCA1 (5382insC); BRCA2 (6174delT) | Hamel et al, 2003 | (55)       |
| RFLP                        |               |         | CHK2 (1100delC)    |                | Nam et al, 2005 | (15)       |
| Country | Method | Target | Description | Samples | Reference |
|---------|--------|--------|-------------|---------|-----------|
| Denmark | Sanger sequencing | Sanger sequencing method for all 26 coding exons of BRCA2 (NM_000059.3) | Undefined BRCA2 mutations | 22 undefined DDR genes (including BRCA2, PALB2, and CDK12) | Akbari et al., 2014 |
|         | plasma ctDNA PCR | Targeted germline sequencing | Struss et al., 2017 |

**Denmark**

- **Germline Blood sample PCR**
  - Presence of CHEK2*1100delC was determined by Taqman PCR and sequencing
  - CHEK2*1100delC
  - Naslund Koch et al., 2016

**Germany**

- **Germline Blood sample PCR**
  - Allele frequencies assessed using RFLP analysis with AlwI after PCR amplification of a genomic DNA fragment spanning the exons 23 and 24
  - ATM missense variant P1054R
  - Meyer et al., 2007

- Sanger sequencing
  - 25 target regions spanning all 26 coding exons of the BRCA2 gene were amplified by PCR and sequenced by Sanger sequencing. Sequence variants with no codon change and alleles with observed frequencies of >2% were omitted
  - BRCA2 exon sequence variants
  - Maier et al., 2014

- **Somatic Tumor biopsy PCR**
  - Limited details. Ion Torrent AmpliSeq™ technology
  - BRCA1 or BRCA2
  - Nientiedt et al., 2017

**Israel**

- **Germline Blood sample NR/unclear NR**
  - BRCA1 (185delAG, 5382insC); BRCA2 (6174delT)
  - Hubert et al., 1999
| Sample Type                  | Tumor Source                  | PCR Method | PCR Products                                                                 | Founder Mutations in BRCA1 and BRCA2 | Reference                  | Page |
|------------------------------|-------------------------------|------------|------------------------------------------------------------------------------|-------------------------------------|-----------------------------|------|
| Peripheral blood and matched paraffin embedded tumor | PCR                            | PCR with chr17 markers (D17S250, D17S579, D17S855, D17S1322, D17S1325, D17S1323, D17S1327) (all internal to the BRCA1 locus) and D17S1327 (both telomeric to the BRCA1 locus) to measure allelic loss; PCR and restriction enzyme digest to identify three predominant mutations across BRCA1 and BRCA2 | Founder mutations in BRCA1 [185delAG; 5382insC] and BRCA2 [6174delT] | Vazina et al, 2000          | (98) |
| Somatic Tumor sample from paraffin fixed sections | PCR                            | Multiplex PCR | Founder mutations in BRCA1 [185delAG; 5382insC] and BRCA2 [6174delT]     | Giusti et al, 2003                | (51) |
| Japan |
|---|
| **Germline Blood sample** | NGS | Looked for any germline variants in PC, reported for five *BRCA2* variants (L61P, H1458R, G2508S, H3056Y, and R3384X) |
| | | Hayano *et al*, 2016 |
| | | (57) |
| NR/unclear | Tumor sample | NGS | DNA was amplified by PCR using primers for the four polymorphic sites. PCR products were subjected to direct DNA sequencing. Sequence analysis of purified products was determined using the same primers with ABI 377 sequencer and dye terminator cycle sequencing kit | *MLH1* polymorphisms that lead to amino acid changes at codons 132, 219, 384, and 723 | Tanaka *et al.*, 2009 | (7) |
|---|---|---|---|---|---|---|
| Tumor and matched peripheral blood | PCR | DNA was amplified by PCR. LOH was determined using 7 highly polymorphic tandem repeat markers: D17S250, D17S1320, D17S855, D17S1322, D17S1323, D17S579 and D17S588. All coding regions from exons 1 to 24 of the *BRCA1* gene were analyzed | Mutations in *BRCA1* coding regions or LOH on chromosome 17q21 | Uchida *et al.*, 1999 | (12) |
**Spain**

| Germline | Blood sample | Sanger sequencing | Validation of pathogenic mutations by Sanger, MLPA or additional NGS performed for 24 genes on the BROCA panel | Aberrations in 24 undefined DNA-repair genes (reported primarily BRCA1, BRCA2, ATM, and PALB2 genes) | Romero *et al.*, 2017 | (90) |
|----------|--------------|------------------|-------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|------------------|--------|

**UK**

| Germline | Blood sample | Other | UKGPCS: The coding region of the BRCA1 and BRCA2 genes were screened using multiplex fluorescent heteroduplex detection, Sanger sequencing, and multiplex ligation-dependent probe amplification | Undefined BRCA1 and BRCA2 | Castro *et al.*, 2011 | (38) |
|----------|--------------|-------|-------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|------------------|--------|

| PCR      | PCR followed by high-performance liquid chromatography or RFLP | Five ATM single-nucleotide polymorphisms: 5557G>A, 5558A>T, 3161C>G, ivs38-8t>c, ivs38-15g>c | | | | |
|----------|----------------------------------------------------------------|-------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|------------------|--------|

| PCR      | High-throughput multiplex fluorescent heteroduplex analysis method. Multiplexed, dye-tagged PCR fragments were run on an ABI3130xl Genetic Analyzer. Genetic alterations were confirmed by sequencing | germline mutations in BRCA2 | | | | |
|----------|----------------------------------------------------------------|-------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|------------------|--------|

| | | | | Angele *et al.*, 2004 | (13) |
|----------|----------------------------------------------------------------|-------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|------------------|--------|

| | | | | Kote-Jarai *et al.*, 2011 | (104) |
| Germline | Capture sequencing | Mutations detected by multiplex PCR, sequenced to identify variants, and deleterious mutations were confirmed by Sanger sequencing | BRCA1 (4 variants: c.68_69delAG; c.212+1G>T; c.1954dupA; c.2475delC) | Leongamo-rnlert et al, 2012 | (69) |
|---|---|---|---|---|---|
| Germline | Peripheral blood and tumor tissue | PCR | BRCA1 and BRCA2 were both screened for germline mutations using a combination of the protein truncation test (PTT) and a non-radioactive heteroduplex analysis (HA) to identify variants in the sample set. PTT was used to analyse exon 11 of BRCA1 (representing approximately 60% of the coding sequence), and exons 10 and 11 BRCA2 (60% of the coding sequence). Direct sequence analysis was used for confirmation | Undefined BRCA1 and BRCA2 | Gayther et al, 2000 | (50) |
| Somatic | Tumor biopsy | NGS  | The Sanger CGP Cancer Genes V3 panel of 365 genes was screened. Eight samples were sequenced to a median depth of 962 reads (IQR, 896-983X) in the target regions, with a median of 93% (IQR, 92.5%-93%) of the target regions being covered at a depth >100×  | 365 target genes, which included all our genes of interest (except \textit{RAD51C}) and \textit{CDK12} | Manson-Bahr \textit{et al}, 2015 (73) |
|----------|-------------|------|--------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|----------------------------------------|
| Formalin-fixed paraffin embedded (FFPE) | NGS | Targeted-NGS was performed using the Life Technologies Ion Torrent: Ion AmpliSeq Cancer Hotspot Panel v2 and the Ion Personal Genome Machine sequencer. The hotspot panel covers ~2800 COSMIC mutations of 50 oncogenes and tumor suppressor genes | DNA repair genes such as \textit{ATM} (no further definition) | Jefferies \textit{et al}, 2017 (61) |
| USA | Germline | Blood sample | NGS | Next-generation targeted sequencing using the Illumina TruSight Cancer Sequencing panel that includes 94 genes (35 have been identified as being involved in human DNA repair) | 35 undefined DDR genes. Results were presented for \textit{BRCA2}, \textit{ATM}, \textit{BLM}, \textit{FANCA}, \textit{MSH2} only | Pomerantz \textit{et al}, 2017 (85) |
| Other | TaqMan SNP genotyping assay | 5557G>A | Zhu \textit{et al}, 2010 (101) |
| Germline | Blood sample | PCR | PCR was used to amplify each of the 62 exons, and short intronic regions flanking each exon, that constitute the coding region of the *ATM* gene | Fifty-nine *ATM* genetic alterations, representing 25 different variants, were found in the expressed portions (exons) of the *ATM* gene, or within 10 nucleotides of each exon encompassing potential splice sites. | Cesaretti *et al*, 2007 (41) |
| --- | --- | --- | --- | --- | --- |
| Genotype | Sample type | PCR | The TaqMan (fluorogenic 5′ nuclease) assay was used for SNP genotyping | *BRCA1*185delAG and *BRCA2*6174delT | Gallagher *et al*, 2012 (48) |
| --- | --- | PCR | PCR products were analysed by RFLP, using modified sites (ACRES) for restriction enzymes TaqI (185delAG), DdeI (538insC), and BstXI [6174delT (15)]. Carriers were recognized by the comparison of test digest with digests of PCR analyses of previously verified *BRCA1/2* carriers | *BRCA1* (185delAG, 5382insC) and *BRCA2* (6174delT) | Kirchoff *et al*, 2004 (63) |
| | | PCR | Aliquots of amplified DNA were transferred to membranes (Hybond) using a standard protocol (Sambrook *et al*, 1989) | *BRCA1* (185delAG) and *BRCA2* (6174delT) | Lehrer *et al*, 1998 (68) |
| | | PCR | Genomic DNA was purified and amplified using 47 primer pairs and sequenced using BigDye Terminator v3.1 sequencing kit | Protein truncating or SNP *BRCA2* mutations. (4625_4629delACATT and 4074_4075delGT; both in exon 11). | Agalliu *et al*, 2007 (31) |
| WES | Variants were restricted to a subset of 157 target genes associated with hereditary cancer risk | 157 target genes associated with hereditary cancer risk (ST1). Results reported for \textit{ATM}, \textit{ATR}, \textit{BRCA2}, \textit{FANCL}, \textit{MSR1}, \textit{MUTYH}, \textit{RB1}, \textit{TSHR}, and \textit{WRN}. | Hart \textit{et al}, 2016 | (56) |
| Exome sequencing of germline DNA was performed at 30x coverage using a VCRome kit for library preparation, and 100bp paired end processing using the HiSeq platform. Human hg19 reference-guided alignment and variant calling were performed using Illumina CASAVA | High value DDR or androgen signalling pathway gene variants that may contribute to familial prostate risk. 826 genes analysed including all DDR genes of interest. | Nicolas \textit{et al}, 2015 | (24) |
| Germline | NR | NR/unclear | WES focused on the exonic regions of 50 known DDR genes. The final exome library was sequenced using an Illumina HiSeq 3000 for 75 bp paired-end sequencing with a target sequencing coverage of 30x. Only protein-truncating alterations (nonsense/stop-gains, frameshift insertions and deletions, and donor and acceptor splice-site mutations) were coded as pathogenic or likely pathogenic for the current analysis, while missense and other variants of undetermined significance or alterations with lower levels of evidence were excluded, unless specifically designated as pathogenic in ClinVar | 50 defined DDR genes including *ATM, ATR, BRCA1, BRCA2, CDK12, CHEK2, FANCA, MLH1, MRE11A, NBN, PALB2, RAD51C* | Antonarakis et al, 2018 | (34) |
| Germline | NR | NR/unclear | Hereditary cancer multi-gene panel test (MGPT) was used to identify pathogenic or likely pathogenic variant frequencies for 34 genes known to predispose to at least one of the six included cancers | Undefined 34-gene hereditary cancer multi-gene panel test (MGPT). Included *ATM, BRCA1, BRCA2, CHEK2, FANCA, and PALB2*; unclear for others. | LaDuca et al, 2017 | (65) |
| Germline | NR | NR/unclear | Genetic testing using a commercially available panel (Invitae) consisting of 25-79 cancer-related genes to identify mutations and selected exonic deletions/duplications | Undefined 25-79 cancer-related genes. Included *ATM, BRCA1, BRCA2, CHEK2*, and *NBN*; unclear for others. | Ledet et al, 2017 | (67) |
| Method                                           | PCR                                      | DNA sequencing and exon-level copy number analysis | DDR (included 14 undefined genes on a hereditary PCa panel, most of which were DNA repair genes, results reported for BRCA and BRCA2) | Marshall et al, 2017 (74) |
|--------------------------------------------------|------------------------------------------|---------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|---------------------------|
| Buccal cells and/or a blood sample              | Genomic DNA from blood /buccal swabs using Puregene DNA Isolation kit (Gentra Systems). DNA content quantified using PicoGreen dsDNA quantitation kit using a Perkin-Elmer HTS7000 BioAssay Reader | BRCA1 (185delAG, 5382insC) and BRCA2 (6174delT) | Agalliu et al, 2009 (32)                                          |                           |
| Archived blood DNA specimens                    | Ion AmpliSeq targeted sequencing         | BRCA1, BRCA2 (undefined)                           | Petrovics et al, 2016 (84)                                          |                           |
| Tumor sample                                    | ABI Prism 7900 HT sequence detection system using Taqman probes | ATM (homozygous IVS62+60G/G, heterozygous IVS62+60G/A, and homozygous IVS62+60A/A) | Browning et al, 2006 (14)                                          |                           |
| Germline | Tumor sample | Microarray | Microarray Description | DNA Analysis | Ref. |
|----------|--------------|------------|------------------------|--------------|------|
| Germline | Tumor sample | Microarray | Purified total RNA was whole-transcriptome amplified using the WT-Ovation FFPE system, fragmented and labelled using the Encore Biotin Module, and hybridized to Affymetrix Human Exon 1.0 ST GeneChips. Profiling of 9 DDR pathways using 17 gene sets for GSEA (Gene Set Enrichment Analysis) of high-density microarray gene expression data | 17 gene sets involving 9 DDR gene pathways (over 200 genes analysed including all DDR genes of interest). | Evans et al, 2016 (45) |
| Germline and somatic (mixed) | Tumor and matched blood | NGS | MSK-IMPACT sequencing assay. Germline variants were identified in matched blood samples and filtered out in the somatic analysis process. Mutation clonality was estimated as a cancer cell fraction, and implemented in the FACETS algorithm. Germline analysis of 76 known cancer predisposing genes was performed as previously described (ref 16a - Schrader 2016 (not in library)) | Memorial Sloan Kettering-Integrated Mutation Profiling of Actionable Cancer Targets (MSK-IMPACT) gene oncpanel that targets 410 cancer-associated genes plus germline analysis of 76 known cancer-predisposing genes (germline). This included ATM, BRCA1, BRCA2, CHEK2, FANCA, MLH1, and NBN, but was unclear for others | Abida et al, 2017 (30) |
| Tumor sample | Method | Description | Probe/Ref | References |
|-------------|--------|-------------|--------|------------|
| Tumor with matched adjacent normal tissue biopsy or peripheral blood or buccal swab | IHC/ISH/FISH | *FANCA* gene specific probe (BAC clone RP11-79A1) and a reference probe located at 16p12 (BAC clone RP11-450G5) were used for this approach. Five-µm thick tissue sections were used for FISH analysis. Deletion was defined as presence of only copy of *FANCA* specific probe in the presence of two reference signals, per nucleus. At least 100 nuclei were evaluated per tissue section or 50 nuclei per tissue core in tissue microarrays (TMAs), using a fluorescence microscope (Olympus BX51; Olympus Optical, Tokyo, Japan). | *FANCA* deletions | Beltran et al, 2015 (19) |
| Tumor sample | PCR | DNA isolated from tumor tissues was paired with primers targeting exons 10-14. Products were subject to direct sequencing | *CHEK2* | Wu et al, 2006 (100) |
| NR/unclear | Genomic DNA | NGS | Targeted sequencing | *NBN* | Zuhlke et al, 2012 (102) |
| NR | Other | sequencing (NGS, Sanger, pyrosequencing) | *ATM* | Feldman et al, 2014 (10) |
| Sample Type                  | Method | Sample Preparation | DNA Isolation | Genes Identified                                                                 | Reference/Year               | Notes |
|-----------------------------|--------|--------------------|---------------|----------------------------------------------------------------------------------|-----------------------------|-------|
| Non-tumor tissue (principally lymph Nodes), formalin fixed and embedded in paraffin | PCR    | Genomic DNA from sections from paraffin blocks then processing using a tissue DNA isolation kit (Qiagen). Mutant alleles detected by heteroduplex analysis (HDA) of the PCR products. Amplification products of primer pair A sequenced from nested primer for each on an ABI 373A sequencer at the Columbia University Cancer Center |  | BRCA1 (185delAG) and BRCA2 (6174delT) | Nastiuk et al, 1999 | (78) |
| Tumor tissue or blood sample | NGS    | NR                 |               | BRCA1, BRCA2                                                                     | Daniel et al, 2017          | (9)   |
| Tumor biopsy                | Other  | DNA underwent hybrid capture for all coding exons of 395 cancer-related genes. Utilized two described lists of genes involved in DNA repair: our own in-house list of 74 (UCD) and a list of 20 DNA repair genes associated with cancer predisposition syndromes utilized in a recent publication by Pritchard et al | Genes involved in DNA repair, associated with cancer predisposition syndromes. Undefined but included ATM, ATR, BRCA1, BRCA2, and MLH1 | Dall'Era et al, 2017 | (8)   |
| Somatic | NR | Other | Tests included gene sequencing (Sanger or NGS), protein expression (IHC), and/or gene amplification (C/FISH) | BRCA1, BRCA2 (undefined) | Myers et al, 2016 | (76) |
|---------|----|-------|--------------------------------------------------------------------------------------------------|------------------------|------------------|------|
| Tumor and needle biopsy | NGS | NGS | UW-OncoPlex was performed. Microsatellite instability (MSI) testing was performed directly on NGS data using the mSINGS method. Total mutation burden was estimated from targeted NGS data as previously described, with hyper-mutation defined as >12 mutations/megabase | Undefined mismatch repair genes (including MLH1) and homologous repair (including BRCA2, CHEK2) | Schweizer et al, 2016 | (27) |
| **Somatic** | **Cell-free DNA (cfDNA) present in the plasma** | **PCR** | cfDNA was isolated from patient plasma samples using the Qiagen circulating nucleic acid kit. 100ng of cfDNA was utilized for library construction; and the libraries were paired-end sequenced on the Illumina HiSeq 2000. Focused analysis on copy number variations related to AR associated and DNA repair genes |
| **NGS** | DNA repair genes partial/full amplifications (BRCA1, BRCA2, ATM, CDK12, MLH1, and/or MSH2) | **Gambhir et al, 2016** |

| **Cell-free DNA (cfDNA) present in the plasma and matched blood lymphocyte DNA** | **NGS** | Plasma DNA was used to prepare DNA libraries using a NEXTflex DNA-Seq kit. The Comprehensive Cancer Panel (Roche NimbleGen, Madison, WI) was used for NGS. The panel covers 4Mb genomic sequences and targets 578 cancer-related genes. Gene mutations were detected by comparing cfDNA to lymphocyte gDNA in the same patient with 2% variant alleles as the cut-off for mutation calls. Allele-specific PCR was used to validate mutations detected by sequencing |
| **Comprehensive Cancer Panel (578 cancer-related genes). Results reported for ATM, ATR, CHEK2, FANCA, MLH1, and NBN (unclear for other genes of interest)** | **Xia et al, 2015** |

| **Circulating tumor DNA** | **PCR** | A publicly-accessible assay (Guardant Health) was used to analyse 68 known cancer genes for anomalies (missense mutations, amplifications) by a digital PCR technique |
| **DNA repair genes (BRCA1, BRCA2, or ATM)** | **Gourdin et al, 2016** |
| Circulating tumor DNA; tumor tissue | NGS | Foundation ACT NGS assay; Foundation One NGS assay | BRCA1 and BRCA2 alterations | Lara et al, 2017 | (66) |
|-----------------------------------|-----|--------------------------------------------------|----------------------------|------------------|-----|
| Tumor biopsy and matched normal tissue | Capture sequencing | Sequenced exome to identify mutations using exome libraries of matched pairs of tumor /normal genomic DNAs. All captured DNA libraries were sequences with the Illumina GAII Genome Analyser or the Illumina HiSeq. Considered only mutations called at covered annotated targeted positions. Sanger sequencing used to validate | ATM, BRCA2 | Grasso et al, 2012 | (53) |
| Tumor sample | NGS | PCR-based NGS | BRCA2 (K2524fs) | Palapattu et al, 2015 | (20) |
| Somatic | Tumor sample | NGS | Targeted NGS using the OncoPanel platform (includes point mutations, insertions, and deletions within exons and select introns/enhancers of 300 candidate genes with a role in oncogenesis). The CIMBA database of published germline BRCA2 mutations was used to determine whether BRCA2 mutations found in the prostate tumors studied here have also been reported in the germline | 300 genes in the OncoPanel platform. Results reported for ATM, BRCA1, BRCA2, and PALB2 (unclear for other DDR genes of interest). | Patel et al, 2016 | (83) |
| Tumor sample | NGS | Fresh-frozen metastatic prostate lesions. DNA fragment libraries for each of the RainDance-amplified PCR samples were constructed for sequence analysis on the SOLiD next-generation sequencing platform. After PCR, massively parallel sequencing was conducted for 577 candidate genes. | Somatic copy number alterations in 577 undefined cancer related genes, result reported for *BRCA2* (unclear if other included in definition) | Robbins *et al*, 2011 | (21) |
|---|---|---|---|---|---|
| PCR | Paired end sequencing (49x49 cycles) was performed using the HiSeq 2000 (based on libraries that were hybrid captured with custom biotinylated RNA oligo pools) and mapped to the reference human genome (hg19). All copy number alterations involving *BRCA2* that were identified by NGS were confirmed by FISH. | 182 cancer-related genes (3230 exons) and 14 commonly rearranged genes (37 introns). Included all DDR genes of interest (except *MRE11A*, *NBN*, and *PALB2*). | Beltran *et al*, 2013 | (22) |
| | Autopsy samples; formalin-fixed paraffin-embedded tissue or from fresh-frozen tissue Microsatellite instability PCR, Exome sequencing, targeted deep sequencing | MMR hyper-mutation (>300 somatic protein altering mutations based on the distribution of total mutation burden in metastatic tumors, which had matched normal tissue available); Undefined list which included *MSH2*, *MSH6*, and *MLH1* | Pritchard *et al*, 2014 | (86) |
| Single cell suspensions and touch preparations | FISH | P1 phage FISH probes were prepared, LOH experiments were carried out 'as previously described' | BRCA1, 3 flanking sites on 17q12-21 | Williams et al, 1996 | (99) |

### Multi-national

| Germline Blood sample | WES | WES performed on germline DNA using an Illumina HiSeq 2500 system. The mean sequencing depth of coverage was 71x. In addition, a customized next-generation sequencing panel targeting 222 cancer related genes was used to sequence the germline DNA of the remaining lethal PCa patients and all the indolent PCa patients. The mean sequencing depth of coverage was 135 overall and was 180, 208, and 219 for ATM, BRCA1, and BRCA2, respectively. All the targeted bases in these three genes were successfully sequenced (> 20) in >99% samples. Sanger sequencing was used for confirmation | ATM, BRCA1, BRCA2 | Na et al, 2017 | (106) |
| Blood lymphocyte, saliva, or tissue uninvolved with cancer | Other | Multiplex sequencing assays | Undefined 20 DRGs associated with autosomal dominant cancer predisposition syndromes. Included all DDR genes of interest except FANCA and MLH1 | Nelson et al, 2016 | (79) |
| Sample Type | Tumor Type | Methodology | Genes | Reference |
|-------------|------------|-------------|--------|-----------|
| Buccal swabs, buffy coats, whole blood, non-tumor tissue | Other | Case series 1,2,6: whole exome sequencing of germline and tumor DNA; case series 3: libraries for targeted sequencing constructed using customized GeneRead Dnaseq Panel covering 53 genes and run on the Illumina MiSeq Sequencer; case series 4: Targeted deep sequencing performed using BROCA panel of 53 DNA repair pathway genes; case series 5: exome sequencing; case series 7: genomic sequencing performed using MSK-IMPACT hybrid capture-based next-generation sequencing assay | ATM, ATR, BAP1, BARD1, BRCA1, BRCA2, BRIP1, CHEK2, FAM175A, GEN1, MLH1, MRE11A, MSH2, MSH6, NBN, PALB2, PMS2, RAD51C, RAD51D, XRCC2 | Pritchard et al, 2016 (87) |
| Germline and somatic (mixed) | Other | Searched for candidate germline cancer predisposition variants in the exome sequence data (Cancer Genome Atlas). Sequencing data were aligned to GRCh37-lite version of the human reference using BWA v0.5.9 and de-duplicated using Picard 1.29 | Undefined candidate cancer-associated genes (including ATM, ATR, BRCA1, BRCA2, FANCA, and PALB2) | Lu et al, 2015 (71) |
| Germline and somatic (mixed) | Tumor sample | Whole-exome capture libraries constructed using DNA from normal and tumor tissue subjected to hybrid capture using SureSelect Exome v4 baits (Agilent) and aligned to the hg19 human genome build | Somatic mutations, copy number laterations, and oncogenic structural DNA rearrangements. Included ATM, BRCA1, BRCA2, CHEK2, MLH1, and PALB2 | Robinson et al, 2015 (89) |
DNA sequenced with the Illumina HiSeq 2000 Genome Analyzer. Reads were aligned to the NCBI GRCh37 human reference genome. The authors performed SNV and indel discovery, genotyping and variant quality score recalibration in all tumor and germline samples simultaneously, according to the GATK HaplotypeCaller v.3.2 best practices recommendations.

| NR/unclear | NR | PCR | Samples genotyped for 657del5 alteration using either ABI3100 and fluorescently labelled PCR (Mayo Clinic, University of Michigan and Universität'sklinikum Ulm), direct sequencing using an Amersham Megabase (Johns Hopkins), or by DNA sequencing (Tampere University Hospital). E185Q and D95N genotyped were obtained using minisequencing (Tampere University Hospital). R215W genotypes were determined using ddNTP-primer extension (Universitätsklinikum Ulm) | *BRCA2*. Germline and somatic variants, including single nucleotide variants, indels and structural variants | Decker et al, 2016 (43) |

| NR/unclear | NR | PCR | Samples genotyped for 657del5 alteration using either ABI3100 and fluorescently labelled PCR (Mayo Clinic, University of Michigan and Universität'sklinikum Ulm), direct sequencing using an Amersham Megabase (Johns Hopkins), or by DNA sequencing (Tampere University Hospital). E185Q and D95N genotyped were obtained using minisequencing (Tampere University Hospital). R215W genotypes were determined using ddNTP-primer extension (Universitätsklinikum Ulm) | *NBN* 657del5 mutation | Hebbring et al, 2006 (58) |
| Somatic Tumor sample | NGS |
|---------------------|-----|
| After hybridisation capture, sequencing was performed (Illumina HiSeq 2500). Raw sequences were aligned to the human genome reference sequence. An in-house tool identified the somatic single nucleotide variants (SNVs) by comparing the tumor to its matched normal. | DDR gene alterations that may be related to prostate cancer progression, including undefined genes related to DDR pathways (n=112), recurrently mutated genes in PC (n=334), and other cancer-related genes (n=77). Reported BRCA2 and NBN; unclear for other genes of interest |
| NGS extracted from FFPE tumor tissue. Included sequencing of 45 DDR genes | Fontugne et al, 2015 (47) |

| Somatic Tumor sample | WES |
|---------------------|-----|
| Whole-exome capture was performed using the Agilent SureSelect Human All Exon protocol containing 188,260 exons from ≈18,560 genes. Sequencing was performed on the Illumina HiSeq 2000 platform | DDR included ATM, BRCA1, BRCA2, FANCD2, MLH1, and RAD51C0. Unclear for other DDR genes of interest. |
| | Cancer Genome Atlas 2015 (37) |
| Germline and somatic (mixed) | Whole-genome sequencing | DNA sequenced with the Illumina HiSeq 2000 Genome Analyser. Reads were aligned to the NCBI GRCh37 human reference genome. The authors performed SNV and indel discovery, genotyping and variant quality score recalibration in all tumor and germline samples simultaneously, according to the GATK HaplotypeCaller v.3.2 best practices recommendations | BRCA2. Germline and somatic variants, including single nucleotide variants, indels and structural variants | No details provided | DDR (undefined); BRCA2, BRCA1 reported. Germline and somatic variants, including single nucleotide variants, indels and structural variants | Decker et al, 2016 | (43) |
|---|---|---|---|---|---|---|---|
| Country not reported | Somatic | Tumor biopsy | NGS | 70-gene cfDNA next generation sequencing panel from a CLIA-licensed, CAP-accredited laboratory (Guardant Health, Inc.) | 70 genes including BRCA1, BRCA2 | Sonpavde et al, 2017 | (6) |
| Formalin-fixed and paraffin embedded tumor | Capture sequencing | Comprehensive genomic profiling was performed on hybridization captured, adaptor ligation-based libraries to a mean coverage depth of 583X for up to 315 cancer related genes plus 37 introns from 14 genes frequently rearranged in cancer. Clinically relevant GA (CRGA) were defined as genomic alterations linked to drugs on the market or under evaluation in mechanism driven clinical trials | Undefined BRCA2 | Stephens et al, 2016 | (29) |
| NGS | NGS using the commercially available Ion Torrent Hotspot Cancer Panel. This test is for gene mutation, not for copy number changes or translocations | ATM, MLH1 | Liu et al, 2016 | (5) |

*ATM*, ataxia telangiectasia mutated; *ATR*, ataxia telangiectasia and Rad3-related protein; *BAP1*, *BRCA1*-associated protein 1; *BARD1*, *BRCA1*-associated RING domain 1; *BLM*, Bloom syndrome RecQ like helicase; *BRCA*, breast cancer susceptibility gene; *BRIP1*, *BRCA1*-interacting protein C-terminal helicase 1; *CDK*, cyclin-dependent kinase; *ctDNA*, cell-free DNA; *CHEK2*, checkpoint kinase 2; *cTNA*, circulating tumor DNA; *CYP*, cytochrome P450; *DDR*, DNA damage repair; *dsDNA*, double-stranded DNA; *ERCC2*, excision repair cross-complementation group 2; *ESR*, estrogen receptor 1; *FAM175A*, family with sequence similarity 175, member A; *FANCA*, Fanconi anemia complementation group A; *FFPE*, formalin-fixed paraffin-embedded; *FISH*, fluorescent in situ hybridization; *gDNA*, genomic DNA; *GEN1*, GEN1, Holliday junction 5' flap endonuclease; *IHC*, immunohistochemistry; *LIG4*, DNA ligase 4; *LOH*, loss of heterozygosity; *MGPT*, multi-gene panel test; *MLH1*, mutL homolog 1; *MLPA*, multiplex ligation-dependent probe amplification; *MMR*, mismatch repair; *MRE11A*, *MRE11* homolog A, double-strand break repair nuclease; *MSH*, muS homolog; *MUTYH*, mut*Y* DNA glycosylase; *NBN*, nibrin; *NCBI*, National Center for Biotechnology Information; *NGS*, next-generation sequencing; *NR*, not reported; *NR3C1*, nuclear receptor subfamily 3 group C member 1; *PALB2*, partner and localizer of *BRCA2*; *PC*, prostate cancer; *PCR*, polymerase chain reaction; *PMS2*, *PMS1* homolog 2, mismatch repair system component; *PPP2R2A*, protein phosphatase 2 regulatory subunit B alpha; *RAD*, DNA repair protein; *RB1*, RB transcriptional corepressor 1; *RFLP*, restriction fragment length polymorphism; *RING*, really interesting new gene; *SNP*, single nucleotide polymorphism; *TGFB1*, transforming growth factor beta 1; *TSHR*, thyroid stimulating hormone receptor; *UKGPCS*, UK genetic prostate cancer study; *WES*, whole-exome sequencing; *WRN*, Werner syndrome RecQ like helicase; *XPF*, xeroderma pigmentosum complementation group F; *XRCC*, x-ray repair cross complementing
## Appendix S7. Summary of risk of bias (Joanna Briggs Institute [JBI] Critical Appraisal Checklist).

| Author, year       | Publication type | Was the sample representative of the target population? | Were the study participants recruited in an appropriate way? | Was the sample size adequate? | Were the study subjects and setting described in detail? | Is the data analysis conducted with sufficient coverage? | Were objective, standard criteria used for measurement of PC$^a$? | Was the condition measured reliably? | Was there appropriate statistical analysis? | Are all important confounding factors accounted for? | Were subpopulations identified using objective criteria? | References |
|--------------------|-----------------|--------------------------------------------------------|------------------------------------------------------------|-------------------------------|--------------------------------------------------------|----------------------------------------------------------|------------------------------------------------|-------------------------------|-----------------------------------|-----------------------------------------------|------------------------------------------------|-----------|
| Abida et al, 2017 | Full paper      | No                                                     | Unclear                                                    | Yes                           | Yes                                                    | Yes                                                      | Yes                                                         | Yes                           | Yes                               | Yes                                            | NA                                            | (30)       |
| Agalliu et al, 2007 | Full paper      | Unclear                                                | Unclear                                                   | Yes                           | Yes                                                    | Yes                                                      | Unclear                                                      | Yes                           | Unclear                           | NA                                            | NA                                            | (31)       |
| Agalliu et al, 2009 | Full paper      | Yes                                                    | Yes                                                       | Yes                           | Yes                                                    | Unclear                                                  | Unclear                                                      | Yes                           | Yes                               | Unclear                                                       | (32)                                           |
| Akbari et al, 2014 | Full paper      | No                                                     | Yes                                                       | Yes                           | No                                                     | Yes                                                      | Unclear                                                      | Unclear                       | Yes                               | Unclear                                                        | NA                                            | (103)      |
| Angele et al, 2004 | Full paper      | No                                                     | Yes                                                       | No                            | Yes                                                    | Unclear                                                  | Unclear                                                      | Yes                           | Unclear                           | NA                                            | NA                                            | (13)       |
| Antonarakis et al, 2018 | Full paper | Unclear                                                | Unclear                                                  | Yes                           | Unclear                                               | Yes                                                      | Unclear                                                      | Yes                           | Yes                               | Yes                                            | (34)                                           |
| Beltran et al, 2013 | Full paper      | No                                                     | Unclear                                                  | No                            | No                                                    | Yes                                                      | Unclear                                                      | Yes                           | Yes                               | No                                             | Yes                                            | NA (22)    |
| Beltran et al, 2015 | Full paper      | No                                                     | Unclear                                                  | Yes                           | No                                                    | Yes                                                      | Unclear                                                      | Yes                           | Yes                               | Unclear                                                        | NA                                            | (19)       |
| Browning et al, 2006 | Full paper      | No                                                     | Unclear                                                  | Yes                           | Yes                                                    | Yes                                                      | Yes                                                         | Yes                           | Yes                               | Yes                                            | NA                                            | (14)       |
| Reference                        | Type         | Available | Mitochondria | BRCA | p53 | p16 | Myc | Lamin A | Lamin B | Lamin C | Lamin D | APOBEC | NA |
|---------------------------------|--------------|-----------|--------------|------|-----|-----|-----|---------|---------|---------|---------|---------|-----|
| Cancer Genome Atlas 2015        | Full paper   | Yes       | Yes          | Yes  | Yes | Yes | Yes | Unclear | Yes     | Unclear | NA      | (37)   |
| Castro et al., 2011             | Abstract     | Yes       | Yes          | Yes  | No  | Yes | Unclear | Unclear | Yes     | Unclear | NA      | (38)   |
| Cesaretti et al., 2007          | Full paper   | No        | Unclear      | Yes  | Yes | Yes | Yes | Yes     | Yes     | Yes     | Unclear | Yes    | (41)   |
| Cheng et al., 2011              | Abstract     | Unclear   | Yes          | Yes  | No  | Yes | Unclear | Unclear | Yes     | Unclear | Unclear | Yes    | (23)   |
| Dall'Era et al., 2017           | Abstract     | Unclear   | Yes          | No   | Yes | Yes | Yes | Yes     | Yes     | Yes     | Yes     | Yes    | (8)    |
| Damaraju et al., 2006           | Full paper   | No        | Unclear      | Yes  | Yes | Yes | Yes | Yes     | Yes     | Yes     | Yes     | Yes    | (26)   |
| Daniel et al., 2017             | Abstract     | Unclear   | Yes          | No   | Yes | Unclear | Yes | Unclear | NA      | NA      | (9)     |
| Dawson et al., 2016             | Abstract     | Unclear   | Yes          | No   | Yes | Unclear | Unclear | Yes     | Unclear | NA      | (11)   |
| Decker et al., 2016             | Full paper   | Yes       | Unclear      | Yes  | No  | Unclear | Yes | Unclear | Yes     | Unclear | NA      | (43)   |
| Edwards et al., 2003            | Full paper   | Yes       | Yes          | Yes  | No  | Yes | Unclear | Unclear | Yes     | Yes     | NA      | (105)  |
| Evans et al., 2016              | Full paper   | Yes       | Unclear      | Yes  | No  | Yes | Yes | Unclear | NA      | NA      | (45)   |
| Feldman et al., 2014            | Abstract     | Unclear   | Yes          | No   | Unclear | Yes | Unclear | No     | Unclear | NA      | (10)   |
| Fontugne et al., 2015           | Abstract     | Unclear   | Yes          | No   | Yes | Unclear | Unclear | No     | Unclear | NA      | (47)   |
| Study                        | Document Type | Complete? | Evidence? | Description? | Timeframe? | Replication? | Unclear? | Address? | Study? |
|-----------------------------|---------------|-----------|-----------|---------------|------------|--------------|----------|----------|--------|
| Gallagher et al, 2012       | Full paper    | No        | Yes       | Yes           | Yes        | Yes          | Unclear  | Yes      | Unclear (48) |
| Gambhira et al, 2016        | Abstract      | Unclear   | Unclear   | No            | No         | Yes          | Unclear  | Yes      | Unclear NA (17) |
| Gayther et al, 2000         | Full paper    | Unclear   | Unclear   | No            | No         | No           | Unclear  | Yes      | Yes    (50) |
| Giusti et al, 2003          | Full paper    | Yes       | Yes       | Yes           | No         | Yes          | Unclear  | Yes      | Unclear Yes (51) |
| Gourdin et al, 2016         | Abstract      | Unclear   | Unclear   | Yes           | No         | Yes          | Unclear  | Unclear  | NA     (52) |
| Grasso et al, 2012          | Full paper    | Unclear   | Unclear   | No            | Yes        | Yes          | Unclear  | Yes      | Unclear NA (53) |
| Hamel et al, 2003           | Full paper    | No        | No        | Yes           | No         | Yes          | Unclear  | Yes      | Unclear Yes (55) |
| Hart et al, 2016            | Full paper    | Yes       | Unclear   | Yes           | Yes        | Yes          | Unclear  | Yes      | Yes    (56) |
| Hayano et al, 2016          | Full paper    | Unclear   | Unclear   | Yes           | No         | Yes          | Unclear  | Yes      | Yes    (57) |
| Hebrbing et al, 2006        | Full paper    | Yes       | Unclear   | Yes           | No         | Yes          | Unclear  | No       | Unclear Yes (58) |
| Hubert et al, 1999          | Letter        | No        | Unclear   | Yes           | No         | Yes          | Unclear  | Yes      | No     (59) |
| Jefferies et al, 2017       | Abstract      | No        | Unclear   | Yes           | No         | Unclear      | Unclear  | Yes      | Unclear NA |
| Kirchoff et al, 2004        | Full paper    | No        | Unclear   | Yes           | No         | No           | Unclear  | Yes      | Unclear (63) |
| Kote-Jarai                  | Full paper    | Yes       | Yes       | Yes           | No         | Yes          | Unclear  | Yes      | NA     (104) |
| Authors, Year | Type    | Unclear | Unclear | No  | Unclear | Unclear | Unclear | No  | Unclear | No  |
|--------------|---------|---------|---------|-----|---------|---------|---------|-----|---------|-----|
| et al, 2011  | Abstract| Unclear | Unclear | No  | Unclear | Unclear | Unclear | No  | Unclear | No  |
| LaDuca et al, 2017 | Abstract | Unclear | Unclear | Yes | No      | Yes     | Unclear | Yes | Unclear | NA  |
| Lara et al, 2017 | Abstract | No      | Yes     | Yes | No      | Yes     | Unclear | Yes | Yes     | Unclear |
| Ledet et al, 2017 | Abstract | No      | Yes     | Yes | No      | Yes     | Unclear | Yes | Yes     | Unclear |
| Lehrer et al, 1998 | Full paper | No      | Unclear | Yes | No      | Yes     | Unclear | Yes | Yes     | Unclear |
| Leongamornlert et al, 2012 | Full paper | Yes     | Unclear | Yes | No      | Unclear | Unclear | Yes | Yes     | Yes  |
| Leongamornlert et al, 2014 | Full paper | Yes     | Unclear | Yes | Yes     | Yes     | Yes     | Unclear | Yes | Yes     |
| Liu et al, 2016 | Abstract | Unclear | Unclear | No  | No      | Yes     | Unclear | Unclear | Unclear | NA  |
| Lu et al, 2015  | Full paper | Yes     | Unclear | Yes | No      | Yes     | Unclear | No  | Unclear | NA  |
| Maier et al, 2014 | Full paper | No      | Unclear | Yes | Yes     | Yes     | Yes     | Unclear | Yes | Yes     | Unclear |
| Manson-Bahr et al, 2015 | Full paper | Unclear | Unclear | Yes | Yes     | Yes     | Unclear | Unclear | Unclear | NA  |
| Marshall et al, 2017 | Abstract | Unclear | Unclear | Yes | No      | Unclear | Yes     | Unclear | Yes | Yes     | Yes  |
| Meyer et al, 2017 | Full paper | No      | Yes     | Yes | Yes     | Yes     | Yes     | Yes | Yes     | Yes  |
| Year     | Type         | Unclear | Unclear | Yes | No | Yes | Unclear | Unclear | Yes | Unclear | NA |
|----------|--------------|---------|---------|-----|----|-----|---------|---------|-----|---------|----|
| 2007     | Abstract     | Unclear | Unclear | Yes | No | Yes | Unclear | Unclear | Yes | Unclear | NA |
| Myers et al, 2016 | Full paper | Unclear | Unclear | Yes | No | Yes | Unclear | Unclear | Yes | Yes | NA (76) |
| Na et al, 2017 | Full paper | No | Yes | Yes | Yes | Unclear | Unclear | Yes | Yes | NA (106) |
| Nam et al, 2005 | Full paper | No | Yes | Yes | Yes | Unclear | Unclear | Yes | Yes | NA (15) |
| Naslund Koch et al, 2016 | Full paper | No | Yes | Yes | No | Yes | Unclear | Unclear | Yes | Unclear | NA (16) |
| Nastiuk et al, 1999 | Full paper | No | Unclear | Yes | No | Unclear | Unclear | Unclear | No | Unclear | Unclear | NA (78) |
| Nelson et al, 2016 | Abstract | Yes | Unclear | Yes | No | Yes | Unclear | Unclear | Yes | Unclear | NA (79) |
| Nicolas et al, 2015 | Full paper | No | Unclear | No | No | Yes | Yes | Unclear | Yes | Unclear | Yes | NA (24) |
| Nicolosi et al, 2017 | Abstract | Unclear | Unclear | Yes | No | Unclear | Unclear | Unclear | Unclear | Unclear | NA (81) |
| Nientiedt et al, 2017 | Full paper | No | Unclear | Unclear | Yes | Unclear | Yes | Unclear | Yes | Unclear | Unclear | NA (82) |
| Palapattu et al, 2015 | Abstract | Unclear | Unclear | No | No | Yes | Unclear | Unclear | Yes | Unclear | NA (20) |
| Patel et al, 2016 | Abstract | No | Unclear | Yes | No | Yes | Unclear | Unclear | Yes | Unclear | NA (83) |
| Petrovics et al, 2016 | Abstract | Unclear | Unclear | Yes | Unclear | Yes | Unclear | Unclear | Yes | Unclear | NA (84) |
| Pomerantz | Full paper | No | Yes | Yes | Yes | Unclear | Unclear | Yes | Yes | Yes | 2017 |
| Reference                        | Type      | Study Design | Case Report | NRI | TAA | SSA | AAR | Carcass Testing | NCT | NTA | Notes     |
|---------------------------------|-----------|--------------|-------------|-----|-----|-----|-----|-----------------|-----|-----|-----------|
| et al, 2017                     |           |              |             |     |     |     |     |                 |     |     |           |
| Pritchard et al, 2014           | Full paper| Unclear      | Yes          | No  | Yes | Unclear | Unclear | Yes             | NA  | NA  | (85)      |
| Pritchard et al, 2016           | Full paper| Yes          | Unclear      | Yes | Yes | Yes   | Yes   | Unclear         | Yes | Yes | NA (86)  |
| Robbins et al, 2011             | Full paper| Unclear      | No           | No  | Yes | Unclear | Unclear | Yes             | NA  | (21) |
| Robinson et al, 2015            | Full paper| Yes          | Unclear      | Yes | No  | Yes   | Unclear | Unclear         | Unclear | NA (89) |
| Romero et al, 2017              | Abstract  | Yes          | Unclear      | No  | Yes | Unclear | Unclear | Yes             | Unclear | NA (90) |
| Schweizer et al, 2016           | Full paper| No           | Yes          | No  | No  | Yes   | Yes   | Yes             | Yes | Unclear | NA (27) |
| Sonpavde et al, 2017            | Abstract  | Unclear      | Yes          | No  | Yes | Unclear | Unclear | Yes             | Unclear | NA (6) |
| Stephens et al, 2016            | Abstract  | Unclear      | No           | No  | Yes | Unclear | Unclear | No              | Unclear | NA (29) |
| Struss et al, 2017              | Abstract  | Unclear      | Yes          | No  | Unclear | Unclear | Unclear | Yes             | Unclear | NA (95) |
| Tanaka et al, 2009              | Full paper| No           | Unclear      | Yes | No  | No    | Yes   | Unclear         | Yes | Unclear | NA (7) |
| Timms et al, 2016               | Poster    | Unclear      | Yes          | No  | Unclear | Unclear | Unclear | Unclear         | Unclear | NA (96) |
| Tischkowitz et al, 2008         | Full paper| No           | Unclear      | Yes | No  | Yes   | Unclear | Yes             | Unclear | No (97) |
| Uchida et al, 1999              | Full paper| Unclear      | No           | No  | Yes | Yes   | Unclear | Yes             | Unclear | NA (12) |
| Authors            | Type       | Diagnostic Criterion CLC | Sample Identification CLC | Data Reliability CLC | Study Quality CLC | Publication Status | Paper No. |
|--------------------|------------|---------------------------|----------------------------|----------------------|-------------------|-------------------|------------|
| Vazina *et al.*, 2000 | Full paper | No                        | Yes                        | No                   | Yes               | Unclear          | Yes        | Unclear    | No         | (98)      |
| Williams *et al.*, 1996 | Full paper | Unclear                   | Unclear                    | No                   | No                | Yes               | Unclear    | Unclear    | NA         | (99)      |
| Wu *et al.*, 2006    | Full paper | No                        | Yes                        | Yes                  | No                | Yes               | Unclear    | Unclear    | NA         | (100)     |
| Xia *et al.*, 2015   | Full paper | Unclear                   | Yes                        | No                   | Yes               | Yes               | Unclear    | No         | Yes        | NA        | (18)      |
| Zhu *et al.*, 2010   | Abstract   | Unclear                   | Unclear                    | No                   | Yes               | Unclear          | Unclear    | No         | Unclear    | NA        | (101)     |
| Zuhlke *et al.*, 2012 | Full paper | Unclear                   | Yes                        | No                   | Yes               | Unclear          | Unclear    | Yes        | Unclear    | Yes       | (102)     |

NA, not applicable. *a*Was the diagnostic criterion clearly reported? *b*Who performed the diagnosis and were all samples diagnosed in the same way?
Appendix S8. Summary of DDR gene mutation prevalence in germline tissue.

| % period prevalence, median (range) | General prostate cancer (PC) | Metastatic prostate cancer (mPC) | Metastatic castration-resistant prostate cancer (mCRPC) | Castration-resistant prostate cancer (CRPC) |
|--------------------------------------|-----------------------------|---------------------------------|--------------------------------------------------------|------------------------------------------|
| ATM                                  | 1.5 (0.41, 3.4)             | 1.7 (1.59, 1.8)                 | 1.91 (NA)                                              | NR                                       |
|                                      | 4 studies (n=1384)          | 2 studies (n=1261)              | 1 study (n=419)                                        |                                          |
| ATR                                  | 0 (NA)                     | 0.3 (0.3, 0.3)                  | NR                                                    | NR                                       |
|                                      | 1 study (n=499)             | 2 studies (n=1261)              |                                                        |                                          |
| BRCA1                                | 0.6 (0.2, 1.0)              | 0.9 (0.9, 0.9)                  | 0.8 (0.7, 1.0)                                        | NR                                       |
|                                      | 7 studies (n=4784)          | 2 studies (n=1261)              | 2 studies (n=569)                                      |                                          |
| BRCA2                                | 1.1 (0.0, 0.9)              | 5.2 (5.1, 5.4)                  | 5.0 (3.3, 5.3)                                        | NR                                       |
|                                      | 8 studies (n=5894)          | 2 studies (n=1261)              | 3 studies (n=888)                                      |                                          |
| CHEK2                                | 1.8 (0.4, 10.7)             | 1.5 (1.2, 1.9)                  | 1.0 (NA)                                              | NR                                       |
|                                      | 5 studies (n=1769)          | 2 studies (n=1103)              | 1 study (n=419)                                       |                                          |
| FANCA                                | 0.56 (NA)                  | NR                              | NR                                                    | NR                                       |
|                                      | 1 study (n=178)             |                                  |                                                        |                                          |
| MLH1                                 | 0.0 (NA)                   | 0.0 (NA)                        | NR                                                    | NR                                       |
|                                      | 1 study (n=499)             | 1 study (n=692)                 |                                                        |                                          |
| MRE11A                                | 0.2 (NA)                   | 0.2 (0.1, 0.2)                  | NR                                                    | NR                                       |
|                                      | 1 study (n=499)             | 2 studies (n=1261)              |                                                        |                                          |
| NBN                                  | 0.3 (0.2, 0.5)              | 0.2 (0.2, 0.3)                  | NR                                                    | NR                                       |
|                                      | 2 studies (n=720)           | 2 studies (n=1261)              |                                                        |                                          |
| PALB2                                | 0.5 (0.4, 0.6)              | 0.5 (0.4, 0.5)                  | 0.6 (NA)                                              | NR                                       |
|                                      | 3 studies (n=898)           | 2 studies (n=1261)              | 1 study (n=319)                                       |                                          |
| RAD51C                                | 0.5 (0.4, 0.6)              | 0.2 (0.1, 0.2)                  | NR                                                    | NR                                       |
|                                      | 2 studies (n=677)           | 2 studies (n=1261)              |                                                        |                                          |
| DDRa                                  | 18.6 (17.2, 19)             | 11.6 (11.4, 11.8)               | 8.3 (7.5, 9.1)                                        | NR                                       |

Note: NR indicates not reported in the studies.
aDDR=multiple gene definitions for DNA damage response gene that includes at least one of our genes of interest. ATM, ataxia telangiectasia mutated; ATR, ataxia telangiectasia and Rad3-related protein; BRCA, breast cancer susceptibility gene; CHEK2, checkpoint kinase 2; DDR, DNA damage repair; FANCA, Fanconi anemia complementation group A; MLH1, MutL homolog 1; MRE11A, MRE11 homolog A, double-strand break repair nuclease; n, sample size; NA, not applicable; NBN, nibrin; NR, not reported; PALB2, partner and localizer of BRCA2; RAD51C, RAD51 paralog C. Original study data can be found in “Mutations in ATM gene” in Appendix S7.

### Summary of DDR gene mutation prevalence in somatic tissue

| % period prevalence, median (range) | General prostate cancer (PC) | Metastatic prostate cancer (mPC) | Metastatic castration-resistant prostate cancer (mCRPC) | Castration-resistant prostate cancer (CRPC) |
|------------------------------------|------------------------------|---------------------------------|--------------------------------------------------------|--------------------------------------------|
| ATM                                | 3.9 (2.4, 8.0) 7 studies (n=2066) | 4 (NA) 1 study (n=70) | 6 (0.0, 12.0) 2 studies (n=203) | NR |
| ATR                                | 0.6 (0.0, 1.2) 2 studies (n=714) | NR | NR | NR |
| BRCA1                              | 1.1 (0.6, 2.4) 5 studies (n=2487); 6 datasets a | NR | 2.8 (0.7, 5.0) 2 studies (n=664) | NR |
| BRCA2                              | 4.9 (0, 11.8) 9 studies (n=3266); 10 datasets a | NR | 5.0 (2.0, 6.0) 3 studies (n=714) | NR |
| CHEK2                              | 1.2 (0.8, 2.4) 3 studies (n=798) | NR | NR | NR |
| FANCA                              | 2.1 (0.5, 16.0) 4 studies (n=1234) | NR | NR | NR |
| Gene        | Odds Ratio (95% CI) | Sample Size | Studies | Odds Ratio (95% CI) | Sample Size | Studies | Odds Ratio (95% CI) | Sample Size | Studies |
|-------------|---------------------|-------------|---------|---------------------|-------------|---------|---------------------|-------------|---------|
| MLH1        | 0.6 (0.2, 1.0)      | 2 studies (n=1081) | 3.3 (NA) | 1 study (n=60)      | NR          | NR |
| MRE11A      | 0.0 (NA)            | 1 study (n=630) | NR      | NR |
| NBN         | 1.2 (0.3, 65)       | 3 studies (n=783) | NR      | NR |
| PALB2       | 1.3 (0.6, 2.0)      | 2 studies (n=1081) | 0.0 (NA) | 1 study (n=70)      | 4.0 (NA)    | 1 study (n=153) |
| RAD51C      | 1.5 (0.0, 3.0)      | 2 studies (n=963) | NR      | NR |
| DDR         | 10.7 (4.9, 22)      | 3 studies (n=680); 4 datasets | 13.2 (10, 16.4) | 2 studies (n=105) |

*One study provided 2 data sets, and both were included; DDR=multiple gene definitions for DNA damage response gene that includes at least 1 of our genes of interest; one study provided two definitions, and both were included. ATM, ataxia telangiectasia mutated; ATR, ataxia telangiectasia and Rad3-related protein; BRCA, breast cancer susceptibility gene; CHEK2, checkpoint kinase 2; DDR, DNA damage repair; FANCA, Fanconi anemia complementation group A; MLH1, MutL homolog 1; MRE11A, MRE11 homolog A, double-strand break repair nuclease; n, sample size; NA, not applicable; NBN, nibrin; NR, not reported; PALB2, partner and localizer of BRCA2; RAD51C, RAD51 paralog C. Original study data can be found in Mutations in ATM gene in Appendix S7.
Summary of DDR gene mutation prevalence in unselected populations.

(A) Mutations in the *ATM* gene.

| PC group | Germline or somatic | % prevalence | N    | DDR definition         | Country | Study level inclusion criteria\(^a\)                                                                                                                                                                                                                                                                                                                                 | Baseline Gleason score (% of population) | Author, year | References |
|----------|---------------------|--------------|------|------------------------|---------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|--------------|------------|
| mCRPC    | Germline            | 1.91         | 419  | Undefined              | Spain   | Patients ≥18 years of age; histologically confirmed prostate cancer; presence of metastatic disease according to bone, CT, and/or MRI scan; confirmed castration-resistant prostate cancer; due to start or have started first-line treatment with any approved survival-prolonging therapy for mCRPC within a period of 6 months from study entry; ECOG performance status ≤21 | NR                                       | Romero et al, 2017 | (90)        |
|          | Somatic             | 0            | 50   | *ATM* non-synonymous point mutation | USA     | Lethal heavily pre-treated CRPCs obtained at rapid autopsy; or high-grade localized prostate cancers                                                                                                                                                                                                                                                                                                                                 | NR                                       | Grasso et al, 2012 | (53)        |
|          |                     | 12           | 153  | *ATM* mut/del          | USA     | PC patients consenting to genomic analysis of their tumor and germline DNA                                                                                                                                                                                                                                                                                                                                                       | NR                                       | Abida et al, 2017 | (30)        |
| mPC      | Germline            | 1.59         | 692  | *ATM*                  | Multi-national | Diagnosis of metastatic prostate cancer, as determined by histologic evaluation of a tumor biopsy specimen or surgical resection specimen                                                                                                                                                                                                                                                                                           | ≤6 (6.07); 3+4 (9.4); 4+3 (13.3); 8-10 (55.2); unknown (16.0) | Pritchard et al, 2016 | (87)        |
|          |                     | 1.8          | 569  | *ATM* (undefined)      | Multi-national | Men had to have mPC based on a biopsy of a metastatic site                                                                                                                                                                                                                                                                                                                                                                       | NR                                       | Nelson et al, 2016 | (79)        |
|          | Somatic             | 4            | 70   | *ATM* mut/del          | USA     | PC patients consenting to genomic analysis of their tumor and germline DNA                                                                                                                                                                                                                                                                                                                                                       | NR                                       | Abida et al, 2017 | (30)        |
| PC       | Germline            | 2            | 221  | *ATM* undefined        | USA     |                                                                                                                                                                                                                                                                                                                                                                     | NR                                       | Abida et al, 2017 | (30)        |
| PC | Somatic | 2.38 | 84 | Defective \( AT^M \) genes (one affected allele) | Multi-national | Selection of PC patients from a commercial biobank and the Transatlantic Prostate Group Cohort | NR | Timms et al, 2016 (96) |
|---|---|---|---|---|---|---|---|---|
| 3 | 630 | Mutation frequency from DNA_REPAIR gene set | USA | Tumor samples were from 4 published retrospective prostatectomy patient cohorts at the Mayo Clinic (MCI and MCII), Cleveland Clinic (CC), and Thomas Jefferson University (TJU) | NR | Evans et al, 2016 (45) |
| 3.17 | 63 | Undefined | UK | Patients diagnosed with PC, whose biopsy contained >5% of cancer | 6 (13); 7 (60); 8 (13); 9 (14) | Manson-Bahr et al, 2019 (73) |
| 3.90 | 333 | Truncating and missense mutations | Multi-national | Patients diagnosed with prostate adenocarcinoma, and had not received prior treatment for their disease (chemotherapy, radiotherapy, or hormonal ablation therapy) | 3+3 (19.5); 3+4 (30.6); 4+3 (23.4); ≥8 (26.4) | Cancer Genome Atlas 2015 (37) |
| 5 | 451 | \( AT^M \) undefined | USA | PC patients consenting to genomic analysis of their tumor and germline DNA | 6 (5.5); 7 (31.0); 8-10 (57.2); unknown (6.2) | Abida et al, 2017 (30) |
| 5.62 | 178 | \( AT^M \) somatic mutation | Multi-national | Patients with prostate adenocarcinoma and sequence data from germline and tumor | NR | Lu et al, 2015 (71) |
DNA; 50% coverage of the targeted exome having at least 20x coverage in both germline and tumor samples

| PC group | Germline or somatic | % prevalence | N | DDR definition | Country | Study level inclusion criteria | Baseline Gleason score (% of population) | Author, yr | Reference |
|----------|---------------------|--------------|---|----------------|---------|-------------------------------|----------------------------------------|-----------|-----------|
| mPC      | Germline            | 0.29         | 692| ATR            | Multi-national | Diagnosis of metastatic prostate cancer, as determined by histologic evaluation of a tumor biopsy specimen or surgical resection specimen | ≤6 (6.07); 3+4 (9.4); 4+3 (13.3); 8-10 (55.2); unknown (16.0) | Pritchard et al, 2016 | (87)      |
|          |                     | 0.3          | 569| ATR (undefined) | Multi-national | Men had to have mPC based on a biopsy of a metastatic site | NR | Nelson et al, 2016 | (79)      |
| PC       | Somatic             | 0            | 630| Gene frequency from DNA_REPAIR gene set | USA | Tumor samples were from 4 published retrospective prostatectomy patient cohorts at the Mayo Clinic (MCI and MCII), Cleveland Clinic (CC), and Thomas Jefferson University (TJU) | NR | Evans et al, 2016 | (45)      |
|          |                     | 1.19         | 84 | Defective ATR genes (both alleles affected) | Multi-national | Selection of PC patients from a commercial biobank and the Transatlantic Prostate Group Cohort | NR | Timms et al 2016 | (96)      |
| PC       | Germline            | 0            | 499| ATR            | Multi-national | Diagnosis of metastatic prostate cancer, as determined by histologic evaluation of a tumor biopsy specimen or surgical resection specimen | ≤6 (9.0); 3+4 (29.7); 4+3 (20.2) | Pritchard et al, 2016 | (87)      |

*B Study level inclusion criteria may not reflect prostate subgroups because multiple groups are included. ATM, ataxia telangiectasia mutated; CRPC, castration-resistant PC; CT, computed tomography; DDR, DNA damage repair; ECOG, Eastern Cooperative Oncology Group; m, metastatic; MRI, magnetic resonance imaging; NR, not reported; PC, prostate cancer. More baseline details can be found in Appendix S5.

(B) Mutations in the ATR gene.
| PC group | Germline or somatic | % prevalence | N | DDR definition | Country | Study level inclusion criteriaa | Baseline Gleason score (% of population) | Author, year | References |
|----------|---------------------|--------------|---|----------------|---------|--------------------------------|------------------------------------------|-------------|------------|
| mCRPC    | Germline            | 0.66         | 150 | Biallelic loss | Multi-national | Discovery set PC patients were selected based on high Gleason score and availability of both peripheral blood DNA and fresh frozen prostatectomy samples. 150 samples from Robinson 2015 (89) | 7 (10); 8 (20); 9 (60); 10 (10) | Decker et al, 2016 | (43)      |
|          |                     | 0.95         | 419 | Undefined      | Spain    | Patients ≥18 years of age; histologically confirmed prostate cancer; presence of metastatic disease according to bone, CT, and/or MRI scan; confirmed castration-resistant prostate cancer; due to start or have started first-line treatment with any approved survival-prolonging therapy for mCRPC within a period of 6 months from study entry; ECOG performance status ≤21 | NR | Romero et al, 2017 | (90)      |
| mCRPC    | Somatic             | 0.66         | 150 | Biallelic loss | Multi-national | Discovery set PC patients were selected based on high Gleason score and availability of both peripheral blood DNA and fresh frozen prostatectomy samples. 150 samples from Robinson 2015 (89) | 7 (10); 8 (20); 9 (60); 10 (10) | Decker et al, 2016 | (43)      |

*CStudy level inclusion criteria may not reflect prostate subgroups because multiple groups are included. ATR, ataxia telangectasia and Rad3-related protein; DDR, DNA damage repair; m, metastatic; NR, not reported; PC, prostate cancer. More baseline details can be found in Appendix S5.*

(C) Mutations in the *BRCA1* gene.
| Group | Status | Gene | Country | Description | NR | Reference |
|-------|--------|------|---------|-------------|----|-----------|
| mPC   | Germline | BRCA1 | Multi- | Diagnosis of metastatic prostate cancer, as | NR | Sonpavde <i>et al</i>, 2017 | (6) |
|       |         |      | national| determined by histologic evaluation of a |    |           |
|       |         |      |         | tumor biopsy specimen or surgical resection |    |           |
|       |         |      |         | specimen |    |           |
| PC    | Germline | BRCA1 | Multi- | Men had to have mPC based on a biopsy of | NR | Nelson <i>et al</i>, 2016 | (79) |
|       |         |      | national| a metastatic site |    |           |
|       |         | (undefined) |         | | | | |
|       |         |      |         | | | | |
| PC    | Germline | BRCA1 | UK     | Patients enrolled in the UKGPCS between1990-2005 with available genomic DNA and clinical and survival data in our prospectively maintained UKGPCS database | NR | Castro <i>et al</i>, 2011 | (38) |
|       |         |      |         | | | | |
|       |         | Total BRCA1 (4 variants: c.68_69delAG; c.212+1G>T; c.1954dupA; c.2475delC) | UK | Patients enrolled in the UKGPCS. Age at diagnosis of ≤65 years (821 cases; age range 36-65 years); and aged >65 years (92 cases; age range 66-88 years) with a family history of one or more first-degree relatives with PC | NR | Leongamo <i>rnlert et al</i>, 2012 | (69) |
|       |         |      |         | | | | |
|       |         | BRCA1 truncation variant | Multi- | Patients with prostate adenocarcinoma and sequence data from germline and tumor DNA; 50% coverage of the targeted exome having at least 20x coverage in both germline and tumor samples | NR | Lu <i>et al</i>, 2015 | (71) |
|       |         |      | national| | | | |
|       |         | BRCA1 undefined | USA    | PC patients consenting to genomic analysis of their tumor and germline DNA | NR | Abida <i>et al</i>, 2017 | (30) |
|   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|
|   |   |   |   |   |   |   |
|   |   |   |   |   |   |   |
| 1.00 | 333 | All $BRCA1$ mutation | Multi-national | Patients diagnosed with prostate adenocarcinoma, and had not received prior treatment for their disease (chemotherapy, radiotherapy, or hormonal ablation therapy) | 3+3 (19.5); 3+4 (30.6); 4+3 (23.4); $\geq$8 (26.4) | Cancer Genome Atlas 2015 (37) |
| 0.41 | 486 | $BRCA1$ | Multi-national | NR | NR | Na et al, 2017 (106) |
| 0.60 | 499 | $BRCA1$ | Multi-national | Diagnosis of metastatic prostate cancer, as determined by histologic evaluation of a tumor biopsy specimen or surgical resection specimen | $\leq$6 (9.0); 3+4 (29.7); 4+3 (20.2); 8-10 (41.1); unknown (0) | Pritchard et al, 2016 (87) |
|   |   |   |   |   |   |   |
|   |   |   |   |   |   |   |
|   |   |   |   |   |   |   |
|   |   |   |   |   |   |   |
| PC | Somatic | 0.56 | 178 | $BRCA1$ somatic mutation | Multi-national | Patients with prostate adenocarcinoma and sequence data from germline and tumor DNA; 50% coverage of the targeted exome having at least 20x coverage in both germline and tumor samples. | NR | Lu et al, 2015 (71) |
|   |   |   |   |   |   |   |
|   |   |   |   |   |   |   |
|   |   |   |   |   |   |   |
|   |   |   |   |   |   |   |
| 0.60 | 630 | Gene frequency from DNA_REPA IR gene set | USA | Tumor samples were from 4 published retrospective prostatectomy patient cohorts at the Mayo Clinic (MCI and MCII), Cleveland Clinic (CC), and Thomas Jefferson University (TJU) | NR | Evans et al, 2016 (45) |
|   |   |   |   |   |   |   |
|   |   |   |   |   |   |   |
|   |   |   |   |   |   |   |
| 1.00 | 451 | $BRCA1$ undefined | USA | PC patients consenting to genomic analysis of their tumor and germline DNA | 6 (5.5); 7 (31.0); 8-10 (57.2); unknown (6.2) | Abida et al, 2017 (30) |
| 1.18 | 936 | Known or likely deleterious mutations in $BRCA1$ | USA | Men with PC; No other details | NR | Lara et al, 2017 (66) |
(D) Mutations in the *BRCA2* gene.

| PC group | Germline or somatic | % prevalence | N  | DDR definition | Country | Study level inclusion criteria<sup>a</sup>                                                                 | Baseline Gleason score (% of population) | Author, year | References |
|----------|---------------------|--------------|----|----------------|---------|----------------------------------------------------------------------------------------------------------------|------------------------------------------|--------------|------------|
| mCRPC    | Germline            | 3.34         | 419| Undefined      | Spain   | Patients ≥18 years of age; histologically confirmed prostate cancer; presence of metastatic disease according to bone, CT, and/or MRI scan; confirmed castration resistant prostate cancer; due to start or have started first-line treatment with any approved survival-prolonging therapy for mCRPC within a period of 6 months from study entry; ECOG performance status ≤21 | NR                                       | Romero et al, 2017 | (90)       |
|          |                     | 5.02         | 319| Undefined deleterious mutation | Canada | Patients with mCRPC                                                                                   | NR                                       | Struss et al, 2017 | (95)       |

<sup>a</sup>Study level inclusion criteria may not reflect prostate subgroups, because multiple groups are included. *BRCA*, breast cancer susceptibility gene; CRPC, castration-resistant PC; DDR, DNA damage repair; ECOG, Eastern Cooperative Oncology Group; m, metastatic; NR, not reported; PC, prostate cancer; UKGPCS, UK Genetic Prostate Cancer Study. More baseline details can be found in Appendix S5.
| mCRPC | Somatic | 2.00 | 50 | BRCA2 non-synonymous point mutation | USA | Lethal heavily pre-treated CRPCs obtained at rapid autopsy; or high-grade localized prostate cancers | NR | Grasso et al, 2012 (53) |
|-------|---------|------|----|-----------------------------------|-----|-------------------------------------------------------------------------------------------------|----|------------------------|
|       |         | 5.00 | 514 | Undefined                         | USA | Patients with mCRPC that underwent baseline ctDNA analysis for potentially actionable alterations using Guardant360 before new systemic therapy were identified | NR | Sonpavde et al, 2017 (6) |
|       |         | 6.00 | 150 | Biallelic mutation                | Multi-national | Discovery set PC patients were selected based on high Gleason score and availability of both peripheral blood DNA and fresh frozen prostatectomy samples. 150 samples from Robinson 2015 (89) | NR | Decker et al, 2016 (43) |
| mPC | Germline | 5.10 | 569 | BRCA2 (undefined)                | Multi-national | Men had to have mPC based on a biopsy of a metastatic site | NR | Nelson et al, 2016 (79) |
|       |         | 5.35 | 692 | BRCA2                            | Multi-national | Diagnosis of metastatic prostate cancer, as determined by histologic evaluation of a tumor biopsy specimen or surgical resection specimen | ≤6 (6.07); 3+4 (9.4); 4+3 (13.3); 8-10 (55.2); unknown (16.0) | Pritchard et al, 2016 (87) |
| PC   | Germline | 0.00 | 92  | BRCA2 exon sequence variants     | Germany | Patients with familial PC who are members of families with PC clustering; or patients with sporadic early onset PC who underwent radical prostatectomy and reported a negative family history for prostate cancer | Gleason ≤7 and <GIII (82.6); Gleason >7 or GIII (15.2); unknown (2.2) | Maier et al, 2014 (72) |
| p-value | Count | Study Design | Study Details | BRCA2 variant | Reference | Study ID |
|---------|-------|--------------|---------------|---------------|-----------|----------|
| 0.00    | 178   | Multi-national | Patients with prostate adenocarcinoma and sequence data from germline and tumor DNA; 50% coverage of the targeted exome having at least 20x coverage in both germline and tumor samples. | BRCA2 truncation variant | Lu et al, 2015 | (71) |
| 1.40    | 1904  | Canada        | Men diagnosed with prostate cancer at biopsy in a cohort of men who underwent a prostate biopsy because of an elevated prostate-specific antigen (PSA) blood test (>4.0 ng/ml) or an abnormal digital rectal examination | Undefined | Akbari et al, 2014 | (103) |
| 1.56    | 2181  | UK            | Patients enrolled in the UKGPCS between 1990-2005 with available genomic DNA and clinical and survival data in our prospectively maintained UKGPCS database. | Undefined BRCA2 | Castro et al, 2011 | (38) |
| 1.80    | 333   | Multi-national | Patients diagnosed with prostate adenocarcinoma and had not received prior treatment for their disease (chemotherapy, radiotherapy, or hormonal ablation therapy) | BRCA2 | Cancer Genome Atlas 2015 | (37) |
| 9.00    | 221   | USA           | PC patients consenting to genomic analysis of their tumor and germline DNA | BRCA2 undefined | Abida et al, 2017 | (30) |
| 0.20    | 499   | Multi-national | Diagnosis of metastatic prostate cancer, as determined by histologic evaluation of a tumor biopsy specimen or surgical resection specimen | BRCA2 | Pritchard et al, 2016 | (87) |
| 0.82    | 486   | Multi-national | NR | BRCA2 | Na et al, 2017 | (106) |
| Gene | Somatic | Frequency | Tumor Type | Tissue Type | Study Details | Frequency Details | Study Reference |
|------|---------|-----------|------------|-------------|---------------|-------------------|-----------------|
| PC   | Somatic | 0.00      | NR         | Multi-national | Discovery set PC patients were selected based on high Gleason score and availability of both peripheral blood DNA and fresh frozen prostatectomy samples. 150 samples from Robinson 2015 (89) | <7 (70); 8-10 (22); NR (8) | Decker et al, 2016 (43) |
|      |         | 1.60      | Gene frequency from DNA_REPAIR gene set | USA | Tumor samples were from 4 published retrospective prostatectomy patient cohorts at the Mayo Clinic (MCI and MCII), Cleveland Clinic (CC), and Thomas Jefferson University (TJU) | NR | Evans et al, 2016 (45) |
|      |         | 1.69      | BRCA2 somatic mutation | Multi-national | Patients with prostate adenocarcinoma and sequence data from germline and tumor DNA; 50% coverage of the targeted exome having at least 20x coverage in both germline and tumor samples | NR | Lu et al, 2015 (71) |
|      |         | 3.00      | Undefined BRCA2 mutation | Multi-national | Patients diagnosed with prostate adenocarcinoma, and had not received prior treatment for their disease (chemotherapy, radiotherapy, or hormonal ablation therapy) | 3+3 (19.5); 3+4 (30.6); 4+3 (23.4); ≥8 (26.4) | Cancer Genome Atlas 2015 (37) |
|      |         | 4.00      | BRCA2 | USA | Men with prostate cancer who had undergone treatment at the Dana Farber Cancer Institute; consented to targeted next generation sequencing | NR | Patel et al, 2016 (83) |
|      |         | 5.80      | Known or likely deleterious mutations in BRCA2 | USA | Men with PC; no other details | NR | Lara et al, 2017 (66) |
|      |         | 6.00      | BRCA2 SNVs and indels | Multi-national | | NR | Fontugne et al, 2015 (47) |
| N   | N   | Country  | Study level inclusion criteria | Baseline Gleason score (% of population) | Author, year | Reference |
|-----|-----|----------|--------------------------------|----------------------------------------|-------------|-----------|
| 7.00| 451 | USA      | PC patients consenting to genomic analysis of their tumor and germline DNA | 6 (5.5); 7 (31.0); 8-10 (57.2); unknown (6.2) | Abida et al, 2017 | (30) |
| 11.43| 936 | USA      | Men with PC; no other details | NR | Lara et al, 2017 | (66) |
| 11.76| 85  | USA      | Advanced prostate cancer patients | NR | Myers et al, 2016 | (76) |

*Study level inclusion criteria may not reflect prostate subgroups, because multiple groups are included. BRCA, breast cancer susceptibility gene; CRPC, castration-resistant PC; CT, computed tomography; DDR, DNA damage repair; ECOG, Eastern Cooperative Oncology Group; m, metastatic; MRI, magnetic resonance imaging; NR, not reported; PC, prostate cancer; SNVs, single nucleotide variations; UKGPCS, UK Genetic Prostate Cancer Study. More baseline details can be found in Appendix S5.

(E) Mutations in the CHEK2 gene.

| PC group | Germline or somatic | % prevalence | N   | DDR definition | Country | Study level inclusion criteria | Baseline Gleason score (% of population) | Author, year | Reference |
|----------|---------------------|--------------|-----|----------------|---------|-------------------------------|------------------------------------------|-------------|-----------|
| mCRPC    | Germline            | 0.95         | 419 | Undefined      | Spain   | Patients ≥18 years of age; histologically confirmed prostate cancer; presence of metastatic disease according to bone, CT, and/or MRI scan; confirmed castration resistant prostate cancer; due to start or have started first-line treatment with any approved survival-prolonging therapy for mCRPC within a period of 6 months from study entry; ECOG performance status ≤21 | NR | Romero et al, 017 | (90) |
| mPC      | Germline            | 1.20         | 569 | CHEK2 (undefined) | Multi-national | Men had to have mPC based on a biopsy of a metastatic site | NR | Nelson et al, 2016 | (79) |
| Chek2 Status | Gene | Multinational | NR | Research Details | Publication Details |
|-------------|------|---------------|----|------------------|---------------------|
| PC Germline | CHEK2 | 1.79 613 | NR | CHEK2 germline pathogenic mutations | Pritchard et al, 2016 (87) |
| PC Somatic  | CHEK2 | 0.80 630 | NR | Gene frequency from DNA_DAM AGE_CHEC KPOINT gene set | Evans et al, 2016 (45) |
| PC Somatic  | CHEK2 | 1.19 84 | NR | Defective CHEK2 genes (both alleles affected) | Timms et al, 2016 (96) |
| PC group | Germline or somatic | % prevalence | N  | DDR definition                                                                 | Country | Study level inclusion criteria<sup>a</sup>                                                                 | Baseline Gleason score (% of population) | Author, year | References |
|----------|---------------------|--------------|----|--------------------------------------------------------------------------------|---------|----------------------------------------------------------------------------------------------------------------|----------------------------------------|--------------|------------|
| mCRPC    | Germline            | 7.50         | 319| Undefined deleterious germline DDR mutations (22 genes including BRCA2, PALB2, CDK2) | Canada  | Patients with mCRPC                                                                                           | NR                                     | Struss et al, 2017 | (95)       |
|          |                     | 9.10         | 419| Aberrations in 24 DNA repair genes                                               | Spain   | Patients ≥18 years of age; histologically confirmed prostate cancer; presence of metastatic disease according to bone, CT, and/or MRI scan; confirmed castration resistant prostate cancer; due to start or have started first-line treatment with any approved survival-prolonging therapy for mCRPC within a period of 6 months from study entry; ECOG performance status ≤21 | NR                                     | Romero et al, 2017 | (90)       |

<sup>a</sup>Study level inclusion criteria may not reflect prostate subgroups, because multiple groups are included. CHEK2, checkpoint kinase 2; CRPC, castration-resistant PC; CT, computed tomography; ECOG, Eastern Cooperative Oncology Group; m, metastatic; MRI, magnetic resonance imaging; NR, not reported; PC, prostate cancer. More baseline details can be found in Appendix S5.

(F) Mutations in DDR genes
| mPC    | Germline | 11.40   | 569   | 20 DNA repair genes associated with autosomal dominant cancer predisposition syndromes (included BRCA2, ATM, CHEK2, BRCA1, PALB2, RAD51D, ATR, FAM175A, GEN1, MRE11A, MSH2, MSH6, RAD51C, NBN). | Multi-national | Men had to have mPC based on a biopsy of a metastatic site | NR | Nelson et al, 2016 (79) |
|--------|----------|---------|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|----------------------------------------------------------------------------------|----|------------------------|
|        |          | 11.80   | 692   | DDR (20-gene panel: ATM, ATR, BAP1, BARD1, BRCA1, BRCA2, BRIP1, CHEK2, FAM175A, GEN1, MLH1, MRE11A, MSH2, MSH6, NBN, PALB2, PMS2, RAD51C, RAD51D, XRCC2) | Multi-national | Diagnosis of metastatic prostate cancer, as determined by histologic evaluation of a tumor biopsy specimen or surgical resection specimen | ≤6 (6.07); 3+4 (9.4); 4+3 (13.3); 8-10 (55.2); unknown (16.0) | Pritchard et al, 2016 (79) |
| mPC    | Somatic  | 10.00   | 50    | MMR (mismatch repair) genes                                                                                                                                    | USA           | Human primary and metastatic prostate cancer tissues were obtained as part of the University of Washington Prostate Cancer Donor Rapid Autopsy Program | NR | Pritchard et al, 2014 (86) |
|        |          | 16.40   | 55    | BRCA1, BRCA2, ATM | USA | Patients with metastatic prostate cancer | NR | Gourdin et al, 2016 (52) |
| PC     | Germline | 18.62   | 333   | ATM, BRCA1, BRCA2, CDK12, FANCD2, RAD51C                                                                                                                   | Multi-national | Patients diagnosed with prostate adenocarcinoma, and had not received prior treatment for their disease (chemotherapy, radiotherapy, or hormonal ablation therapy) | 3+3 (19.5); 3+4 (30.6); 4+3 (23.4); ≥8 (26.4) | Cancer Genome Atlas 2015 (37) |
|        |          | 19.00   | 221   | DDR (including BRIP1, NBN, PALB2, PMS2, MITF, RECQL, ATM, CHEK2, BRCA1, BRCA2, FH) |
|        |          |         |       | USA | PC patients consenting to genomic analysis of their tumor and germline DNA | NR | Abida et al, 2017 (30) |
DDR (included 14 genes on a hereditary PC panel, most of which were DNA repair genes, including BRCA and \(BRCA2\))

USA

Men with PC

NR

Nicolosi et al, 2017 (81)

Defective DDR genes (one allele affected); \(RAD50\), \(ATM\), \(NBN\), \(ATR\), \(PPP2R2A\), \(CHEK2\), \(FANCA\), \(RAD52\)

Multi-national

Selection of PC patients from a commercial biobank and the Transatlantic Prostate Group Cohort

NR

Timms et al, 2016 (96)

DDR (including \(BRCA2\), \(BRCA1\), \(ATM\), \(FANCA\), \(RAD50\), \(PALB2\), and \(CDK12\))

USA

PC patients consenting to genomic analysis of their tumor and germline DNA

6 (5.5); 7 (31.0); 8-10 (57.2); unknown (6.2)

Abida et al, 2017 (30)

DNA repair genes such as \(ATM\)

UK

Primary prostate cancer samples for the Welsh Cancer Bank

NR

Jefferies et al, 2017 (61)

*Study level inclusion criteria may not reflect prostate subgroups, because multiple groups are included. \(ATM\), ataxia telangiectasia mutated; \(ATR\), ataxia telangiectasia and Rad3-related protein; \(BAP1\), \(BRCA1\)-associated protein 1; \(BARD1\), \(BRCA1\)-associated RING domain 1; \(BRCA\), breast cancer susceptibility gene; \(BRIP1\), \(BRCA1\) interacting protein C-terminal helicase 1; \(CHEK2\), checkpoint kinase 2; CRPC, castration-resistant PC; CT, computed tomography; DDR, DNA damage repair; ECOG, Eastern Cooperative Oncology Group; \(FAM175A\), family with sequence similarity 175,member A; \(FANC\), Fanconi anemia complementation group; \(FH\), fumarate hydratase; \(GEN1\), \(GEN1\), Holliday junction 5’ flap endonuclease; \(m\), metastatic; \(MITF\), melanogenesis-associated transcription factor; \(MLH1\), mutL homolog 1; MMR, mismatch repair; \(MRE11A\), \(MRE11\) homolog A, double-strand break repair nuclease; MRI, magnetic resonance imaging; \(MSH\), muS homolog; \(NBN\), nibrin; \(PALB2\), partner and localizer of \(BRCA2\); \(NR\), not reported; PC, prostate cancer; \(PMS\), \(PMS1\) homolog 2, mismatch repair system component; \(PPP2R2A\), protein phosphatase 2 regulatory subunit B alpha; RAD, DNA repair protein; \(RECQL\), RecQ like helicase; RING, really interesting new gene; \(XRCC\), x-ray repair cross complementing.

More baseline details can be found in Appendix S4.

### (G) Mutations in \(FANCA\) gene.

| PC group | Germline or somatic | \% prevalence | N | DDR definition | Country | Study level inclusion criteria* | Baseline Gleason score (% of population) | Author, year | References |
|----------|---------------------|----------------|---|----------------|---------|---------------------------------|----------------------------------------|-----------|-----------|

240
| PC group | Germline or somatic | % prevalence | N  | DDR definition | Country | Study level inclusion criteria | Baseline Gleason score (% of population) | Author, year | References |
|----------|---------------------|--------------|----|----------------|---------|-------------------------------|--------------------------------------------|-------------|------------|
| mPC      | Germline            | 0.00         | 692| MLH1           | Multi-national | Diagnosis of metastatic prostate cancer, as determined by histologic evaluation of a tumor biopsy specimen or surgical resection specimen | ≤6 (6.07); 3 + 4 (9.4); 4 + 3 (13.3); 8-10 (55.2); unknown (16.0) | Pritchard et al, 2016 | (87)       |
### Mutations in the MRE11A gene.

| PC group | Germline or somatic | % prevalence | N   | DDR definition | Country | Study level inclusion criteria<sup>a</sup> | Baseline Gleason score (% of population) | Author, year | References |
|----------|---------------------|--------------|-----|----------------|---------|--------------------------------------------|------------------------------------------|-------------|------------|
| mPC      | Germline            | 0.14         | 692 | MRE11A         | Multi-national | Diagnosis of metastatic prostate cancer, as determined by histologic evaluation of a tumor biopsy specimen or surgical resection specimen | ≤6 (6.0); 3+4 (9.4); 4+3 (13.3); 8-10 (55.2); unknown (16.0) | Pritchard et al, 2016 | (87)       |
|          |                     | 0.18         | 569 | MRE11A (undefined) | Multi-national | Men had to have mPC based on a biopsy of a metastatic site | NR | Nelson et al, 2016 | (79)       |

<sup>a</sup>Study level inclusion criteria may not reflect prostate subgroups, because multiple groups are included. DDR, DNA damage repair; m, metastatic; MLH1, mutL homolog 1; NR, not reported; PC, prostate cancer. More baseline details can be found in Appendix S5.
| PC group | Germline or somatic | % prevalence | N  | DDR definition | Country | Study level inclusion criteria<sup>a</sup> | Baseline Gleason score (% of population) | Author, year | References |
|----------|---------------------|--------------|----|----------------|---------|----------------------------------------|----------------------------------------|-------------|------------|
| mPC      | Germline            | 0.18         | 569| NBN (undefined) | Multinational | Men had to have mPC based on a biopsy of a metastatic site | NR                      | Nelson et al, 2016 | (79)       |
| mPC      | Germline            | 0.29         | 692| NBN            | Multinational | Diagnosis of metastatic prostate cancer, as determined by histologic evaluation of a tumor biopsy specimen or surgical resection specimen | ≤6 (6.07); 3+4 (9.4); 4+3 (13.3); 8-10 (55.2); unknown (16.0) | Pritchard et al, 2016 | (87)       |
| PC       | Germline            | 0.45         | 221| NBN undefined  | USA        | PC patients consenting to genomic analysis of their tumor and germline DNA | NR                      | Abida et al, 2017 | (30)       |
| PC       | Germline            | 0.20         | 499| NBN            | Multinational | Diagnosis of metastatic prostate cancer, as determined by histologic evaluation of a tumor biopsy specimen or surgical resection specimen | ≤6 (9.0); 3+4 (29.7); 4+3 (20.2); 8-10 (41.1); unknown (0) | Pritchard et al, 2016 | (87)       |

<sup>a</sup>Study level inclusion criteria may not reflect prostate subgroups, because multiple groups are included. DDR, DNA damage repair; m, metastatic; MRE11A, MRE11 homolog A, double-strand break repair nuclease; NR, not reported; PC, prostate cancer. More baseline details can be found in Appendix S5.

(J) Mutations in the NBN gene.
Gene frequency from DNA_REPAIR gene set

Tumor samples were from 4 published retrospective prostatectomy patient cohorts at the Mayo Clinic (MCI and MCII), Cleveland Clinic (CC), and Thomas Jefferson University (TJU).

Evans et al, 2016 (45)

Defective NBN genes (both alleles affected)

Selection of PC patients from a commercial biobank and the Transatlantic Prostate Group Cohort

Timms et al, 2016 (96)

NBN amplifications

NR

Fontugne et al, 2015 (47)

Study level inclusion criteria may not reflect prostate subgroups, because multiple groups are included. DDR, DNA damage repair; m, metastatic; NBN, nibrin; NR, not reported; PC, prostate cancer. More baseline details can be found in Appendix S5.

(K) Mutations in the PALB2 gene.

| PC group | Germline or somatic | % prevalence | N   | DDR definition                                      | Country       | Study level inclusion criteriaa | Baseline Gleason score (% of population) | Author, year | References |
|----------|---------------------|--------------|-----|----------------------------------------------------|---------------|---------------------------------|------------------------------------------|-------------|------------|
| mCRPC    | Germline            | 0.63         | 319 | Undefined deleterious mutation                     | Canada        | Patients with mCRPC             | NR                                       | Struss et al, 2017                        | (95)        |
| mCRPC    | Somatic             | 4.00         | 153 | PALB2 mut/del in metastatic tumor samples          | USA           | PC patients consenting to genomic analysis of their tumor and germline DNA | NR                                       | Abida et al, 2017                         | (30)        |
| mPC      | Germline            | 0.43         | 692 | PALB2                                             | Multi-national| Diagnosis of metastatic prostate cancer, as determined by histologic evaluation of a tumor biopsy specimen or surgical resection specimen | ≤6 (6.07); 3+4 (9.4); 4+3 (13.3); 8-10 (55.2); unknown (16.0) | Pritchard et al, 2016                     | (87)        |
|          |                     | 0.50         | 569 | PALB2 (undefined)                                  | Multi-national| Men had to have mPC based on a biopsy of a metastatic site | NR                                       | Nelson et al, 2016                        | (79)        |
| mPC      | Somatic             | 0.00         | 70  | PALB2 mut/del in metastatic tumor samples          | USA           | PC patients consenting to genomic analysis of their tumor and germline DNA | NR                                       | Abida et al, 2017                         | (30)        |
| PC group | Germline or somatic | % prevalence | N | DDR definition | Country | Study level inclusion criteria<sup>a</sup> | Baseline Gleason score (% of population) | Author, year | References |
|----------|---------------------|--------------|---|----------------|---------|--------------------------------------------|------------------------------------------|-------------|-----------|
| PC       | Germline            | 0.45         | 221 | PALB2 undefined | USA     | NR                                        | Abida <i>et al</i>, 2017                  | (30)        |
|          |                     | 0.56         | 178 | PALB2 truncations | Multi-national | Patients with prostate adenocarcinoma and sequence data from germline and tumor DNA; 50% coverage of the targeted exome having at least 20x coverage in both germline and tumor samples | NR | Lu <i>et al</i>, 2015 | (71) |
|          |                     | 0.40         | 499 | PALB2          | Multi-national | Diagnosis of metastatic prostate cancer, as determined by histologic evaluation of a tumor biopsy specimen or surgical resection specimen | ≤6 (9.0); 3+4 (29.7); 4+3 (20.2); 8-10 (41.1); unknown (0) | Pritchard <i>et al</i>, 2016 | (87) |
| PC       | Somatic             | 0.60         | 630 | gene frequency from REACTOME_DNA_REPAIR gene set | USA | Tumor samples were from 4 published retrospective prostatectomy patient cohorts at the Mayo Clinic (MCI and MCII), Cleveland Clinic (CC), and Thomas Jefferson University (TJU). | NR | Evans <i>et al</i>, 2016 | (45) |
|          |                     | 2.00         | 451 | PALB2 undefined | USA     | PC patients consenting to genomic analysis of their tumor and germline DNA | 6 (5.5); 7 (31.0); 8-10 (57.2); unknown (6.2) | Abida <i>et al</i>, 2017 | (30) |

<sup>a</sup>Study level inclusion criteria may not reflect prostate subgroups, because multiple groups are included. CRPC, castration-resistant PC; m, metastatic; NR, not reported; PALB2, partner and localizer of BRCA2; PC, prostate cancer. More baseline details can be found in Appendix S5.

**L) Mutations in the RAD51C gene.**
| mPC | Germline | 0.14 | 692 | RAD51C | Multi-national | Diagnosis of metastatic prostate cancer, as determined by histologic evaluation of a tumor biopsy specimen or surgical resection specimen | ≤6 (6.07); 3+4 (9.4); 4+3 (13.3); 8-10 (55.2); unknown (16.0) | Pritchard et al, 2016 (87) |
|-----|---------|------|-----|--------|----------------|---------------------------------------------------------------------------------|---------------------------------------------------------------------|----------------------|
|     |         | 0.18 | 569 | RAD51C | Multi-national | Men had to have mPC based on a biopsy of a metastatic site | NR | Nelson et al, 2016 (79) |
| PC  | Germline | 0.56 | 178 | RAD51C | Multi-national | Patients with prostate adenocarcinoma and sequence data from germline and tumor DNA; 50% coverage of the targeted exome having at least 20x coverage in both germline and tumor samples. | NR | Lu et al, 2015 (71) |
|     |         | 0.40 | 499 | RAD51C | Multi-national | Diagnosis of metastatic prostate cancer, as determined by histologic evaluation of a tumor biopsy specimen or surgical resection specimen | ≤6 (9.0); 3+4 (29.7); 4+3 (20.2); 8-10 (41.1); unknown (0) | Pritchard et al, 2016 (87) |
| PC  | Somatic | 0.00 | 630 | any RAD51C | USA | Tumor samples were from 4 published retrospective prostatectomy patient cohorts at the Mayo Clinic (MCI and MCII), Cleveland Clinic (CC), and Thomas Jefferson University (TJU) | NR | Evans et al, 2016 (45) |
|     |         | 3.00 | 333 | any RAD51C | Multi-national | Patients diagnosed with prostate adenocarcinoma, and had not received prior treatment for their disease (chemotherapy, radiotherapy, or hormonal ablation therapy) | 3+3 (19.5); 3+4 (30.6); 4+3 (23.4); ≥8 (26.4) | Cancer Genome Atlas 2015 (37) |

*Study level inclusion criteria may not reflect prostate subgroups, because multiple groups are included. DDR, DNA damage repair; m, metastatic; NR, not reported; PC, prostate cancer; RAD, DNA repair protein. More baseline details can be found in Appendix S5.*
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Figure S1. Percentage of studies meeting JBI prevalence quality criteria by question. JBI, Joanna Briggs Institute; NA, not applicable.