

MSAC Application

**Genetic testing for the detection of
germline variants in cancer
predisposition genes in people with
prostate cancer and their relatives**

PICO Set 1

Population

Describe the population in which the proposed health technology is intended to be used:

The population proposed for this testing is patients with prostate cancer for whom clinical and family history criteria indicate greater than 10% risk of having a pathogenic or likely pathogenic (P/LP) germline variant in cancer predisposition genes.

Prostate cancer

The prostate is a small, walnut-shaped gland located below the bladder and in front of the rectum in males. This tiny gland secretes fluid that mixes with semen, keeping sperm healthy for conception.

Most patients who present with prostate cancer are asymptomatic. Patients with locally advanced prostate cancer may have urinary symptoms (obstructive or irritative) with blood in the urine or semen (Cancer Council Victoria, 2021). Other symptoms that may be caused by prostate cancer include frequent urination, weak urine flow or flow that starts and stops, dysuria, urinary or faecal incontinence, painful ejaculation and erectile dysfunction, blood in semen or urine, and pain in the low back, hip or chest (The Cleveland Clinic, 2026).

The most common type of prostate cancer is adenocarcinoma, accounting for over 96% of prostate cancers in Australia (AIHW, 2025; Cancer Australia). Prostate cancer grading using the Gleason score, which ranges from 6 to 10, is a marker of the aggressiveness of the cancer. A higher grade (grade 8-10) is associated with a poorer prognosis, higher risk of developing metastases and an increased likelihood of a germline P/LP variant in a cancer predisposition gene.

Prostate cancer incidence

Prostate cancer was estimated to be the most commonly diagnosed cancer for males and Australians overall in 2025 (AIHW, 2025). With an estimated 28,868 new cases diagnosed in 2025, prostate cancer is estimated to account for 30% of cancers diagnosed in males (AIHW, 2025). In Australia, the median age at diagnosis for prostate cancer is 69.6 years (AIHW).

The most common risk factors for prostate cancer include age, ancestry, family history, and germline P/LP variants in genes encoding components of the homologous recombination repair or mismatch repair pathways, which are associated with cancer risk. A high polygenic risk score based on single nucleotide polymorphisms is also associated with a higher risk of developing prostate cancer (McHugh et al., 2025; Nordström et al., 2014).

Prostate cancer mortality

In 2025, it is estimated that prostate cancer mortality rates will be 33 deaths per 100,000 males, just over a half of the peak mortality rate (Figure 1) (AIHW, 2025), and it is estimated there will be 3,975 deaths in 2025. The reducing mortality rate for prostate cancer over time may reflect the impact of treatments for prostate cancer. Population growth in combination with an ageing population exceeds reductions in age-standardised mortality rates to result in increasing numbers of deaths from prostate cancer (AIHW, 2025).

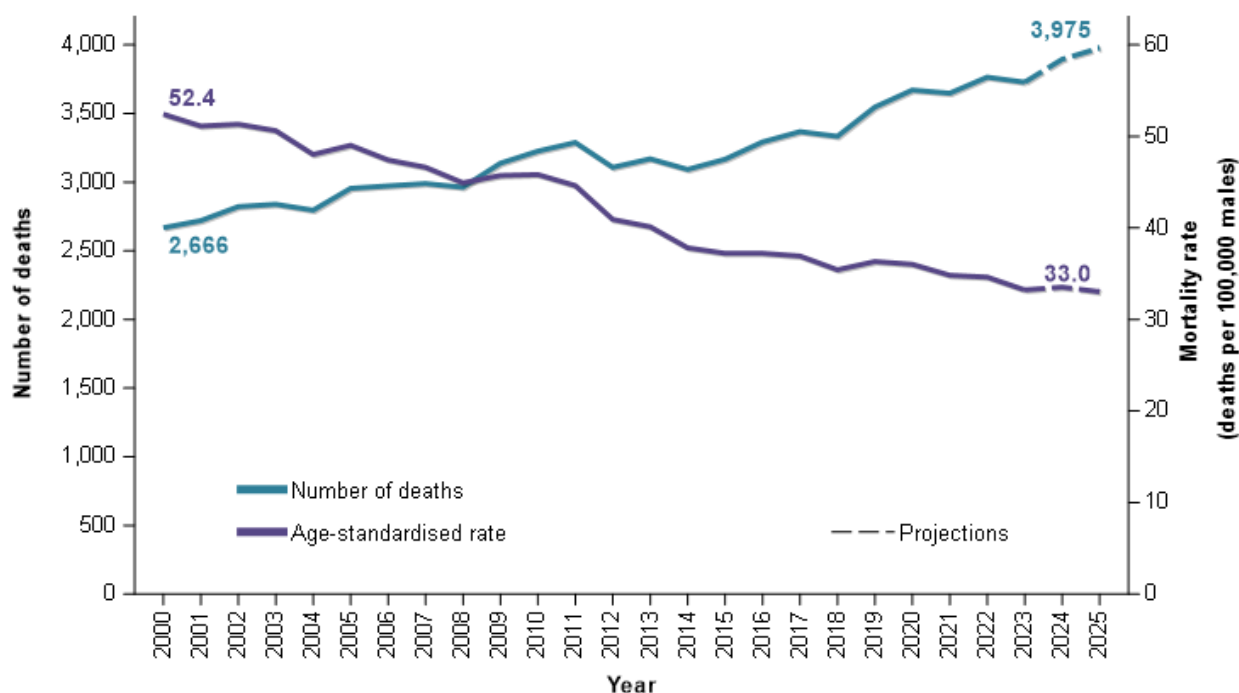


Figure 1: Prostate cancer deaths and age-standardised mortality rate, 2000-2025.

Source: (AIHW, 2025).

Prostate cancer genetics

Familial prostate cancer and hereditary prostate cancer are two sides of the same coin: familial prostate cancer is where there is a pattern of cancer seeming to run in a family (but no genetic cause for this has been identified), whereas hereditary (or genetic) cancer is when a specific variant is known to cause the cancer to run in the family (Peter MacCallum Cancer Centre, 2026). Prostate cancer has the highest degree of genetic transmission of any form of malignancy, with hereditary patterns often mimicking autosomal dominant inheritance in pedigrees (Lynch et al., 2016). A prospective study reported 57% heritability for prostate cancer, and substantially higher risk in monozygotic than dizygotic twins when the other twin is diagnosed with prostate cancer (Mucci et al., 2016).

Up to 15% of familial prostate cancer may be explained by the inheritance of a P/LP variant in one or more of the rare high- and moderate-risk genes. Alternatively, familial prostate cancer may be due to the presence of variants in lower risk alleles (often single nucleotide polymorphisms) that in combination may increase the risk of prostate cancer; this risk can be estimated using a polygenic risk score (McHugh et al., 2025).

Germline P/LP variants in *BRCA1/2* and possibly *ATM* have been linked with a younger age of cancer onset, increased cancer mortality and a more aggressive phenotype (Teppala et al., 2024; Tuffaha et al., 2024).

Prevalence of germline variants in prostate cancer patients

Due to the availability of MBS-funded somatic and germline genetic testing for access to poly (ADP-ribose) polymerase (PARP) inhibitors in those with metastatic disease, the prostate cancer patients proposed in this PICO set are more likely to have early-stage disease.

The estimates reported below for prevalence of P/LP germline variants in unselected localised prostate cancer patients are lower than estimates from any-stage prostate cancer patients (reported further below), although they may be underestimates for the proposed population,

which due to the >10% risk criterion, will be enriched with high-risk tumour characteristics and/or a family history indicating a potential familial predisposition.

- In patients with high-risk localised prostate cancer, a 34-gene panel detected germline variants in 19/201 (**9.5%**) patients (Berchuck et al., 2021).
- A study using various prostate cancer gene panels reported that **11.2%** of localised prostate cancer patients (n=241) have a germline P/LP variant (Abusamra et al., 2025).

Prevalence of germline P/LP variants in genetic testing of all-stage prostate cancer patients:

- A meta-analysis reported that germline P/LP *BRCA1/2* variants were identified in 4.47% of any-stage prostate cancer patients (k=29, n=33,784) (Valsecchi et al., 2023). This figure likely underestimates the diagnostic yield for the testing proposed in this application as it was for *BRCA1/2* genes only, which other studies have reported comprise only 30.7% of germline variants in prostate cancer patients (Nicolosi et al., 2019). If a diagnostic yield of 4.47% for *BRCA* variants represents 30.7% of the variants among cancer predisposition genes commonly included on gene panels, then this implies a diagnostic yield of **14.6%** across commonly tested genes.
- Australian any-stage prostate cancer patients in families with at least 2 prostate cancer cases were tested using an 84-gene panel, yielding a clinically notifiable P/LP variant in 16/94 (**17.0%**) of cases (Mondschein et al., 2022). The authors also reported that 7/22 (31.8%) of variants (including non-clinically notifiable P/LP variants) were in *BRCA1/2*.
- In prostate cancer patients unselected for family history of cancer and disease stage (n=3,607), germline testing for commonly tested genes (panel composition varied at clinician discretion but 62% of cases used the 14-gene Invitae prostate cancer gene panel), 620 patients were found to have a germline variant, equating to a diagnostic yield of **17.2%** (Nicolosi et al., 2019). Only 30.7% of these variants were in *BRCA1/2*. This diagnostic yield may be an underestimate for the population proposed in this application, as prostate cancer patients irrespective of family history would likely have a lower rate of germline variants than prostate cancer patients with a family history of prostate cancer. The authors noted that 37% of patients found to have a germline variant would not have been eligible for testing under National Comprehensive Cancer Network (NCCN) guidelines, which rely heavily on family history.

Assessment of >10% risk of having a germline P/LP variant

The population of prostate cancer patients proposed for testing is those who have >10% risk of having a germline P/LP variant. In January 2026, the CanRisk model was extended to include risk estimates for prostate cancer, allowing assessment of the probability of a P/LP variant based on the family history including prostate, breast, ovarian and pancreatic cancer.

In addition to patients with metastatic prostate cancer, eviQ clinical guidelines (eviQ) recommend germline genetic testing in the following populations, where a gene panel test may be most appropriate:

- Individuals with prostate cancer and $\geq 10\%$ probability of detecting a *BRCA1* or *BRCA2* P/LP variant using a validated P/LP variant prediction tool (e.g. CanRisk).
- Individuals with prostate cancer with intraductal/ductal histology.
- Individuals with prostate cancer from a population where a founder P/LP variant of high prevalence exists (e.g. Ashkenazi Jewish, Swedish/Nordic).

An Australian Delphi study found consensus for considering germline genetic testing in four groups of prostate cancer patients: those with a family history of prostate cancer, a family history of hereditary breast and ovarian cancer (HBOC) syndrome, a family history of Lynch Syndrome, and those with localised prostate cancer and Ashkenazi Jewish ancestry (Edmunds et al., 2026).

NCCN guidelines recommend germline genetic testing in patients with localised prostate cancer with high/very high risk disease classification (i.e., spread of the cancer to the prostate capsule or beyond, Gleason grade group ≥ 4 or prostate specific antigen $>20\text{ng/mL}$), family history of prostate cancer, family history of breast or ovarian cancer, or Ashkenazi Jewish ancestry (Cheng et al., 2026).

Specify any characteristics of patients with, or suspected of having, the medical condition, who are proposed to be eligible for the proposed health technology, describing how a patient would be investigated, managed and referred within the Australian healthcare system in the lead up to being considered eligible for the technology:

Before receiving genetic testing for germline variants, patients diagnosed with early prostate cancer on a biopsy would be assessed for the factors outlined in the eviQ guidelines, incorporating their family history, ethnicity and any high-risk features such as Gleason score (grade ≥ 8 , <60 years of age). There are no specific additional prerequisite tests required to be eligible for germline genetic testing.

Provide a rationale for the specifics of the eligible population:

The eligible population are defined based on having prostate cancer, and a $>10\%$ likelihood of having a germline P/LP variant in a cancer predisposition gene.

Existing MBS-funded testing for the identification of germline variants in cancer predisposition genes in people with breast, ovarian, fallopian tube or primary peritoneal cancer (MBS item 73296) includes the requirement that clinical and family history criteria place the patient at greater than 10% risk of having a P/LP variant. Retaining the 10% risk criterion will ensure that this testing remains targeted to patients who have a high risk of carrying a relevant variant. The proposed amendment will therefore enable equity of access for prostate cancer patients to equivalent testing to that already provided for patients with breast, ovarian, fallopian tube and primary peritoneal cancer who are at the same level of risk of having a germline variant.

Are there any prerequisite tests?

No

Are the prerequisite tests MBS funded?

Not applicable

Provide details to fund the prerequisite tests:

Not applicable

Intervention

Name of the proposed health technology:

Genetic testing for germline variants in *BRCA1*, *BRCA2* and other cancer predisposition genes.

Describe the key components and clinical steps involved in delivering the proposed health technology:

Steps involved in delivering germline genetic testing

Patients with prostate cancer will undergo standard clinical investigations, including biopsy and relevant imaging. Those with metastatic disease may proceed directly to somatic testing whereas those with earlier stage disease may be referred to a familial cancer service where a detailed family history would be taken (usually incorporating a CanRisk assessment or Manchester risk score, depending on the family history).. Germline gene panel testing would then follow the same process as is currently used for patients with breast, ovarian, fallopian tube and primary peritoneal cancer. In brief, a sample is collected from the patient, with informed consent and genetic counselling as appropriate. The sample is sent to a suitably accredited laboratory for sequencing and analysis, and the results reported to the clinician to discuss with the patient.

Genes included in germline gene panel testing

Beyond *BRCA1* and *BRCA2*, other cancer predisposition genes may also be included in germline testing for patients with prostate cancer: *ATM*, *CHEK2*, *EPCAM*, *HOXB13*, *MLH1*, *MSH2*, *MSH6*, *PALB2*, *PMS2* and *TP53*. These genes constitute the green genes on the PanelApp Australia prostate cancer predisposition panel (PanelApp Australia, 2026). The only prostate cancer-specific gene is *HOXB13*; the other genes are common to next-generation sequencing (NGS) panels offered to patients with hereditary breast-ovarian cancer. This therefore represents the addition of a single additional gene for most gene panel tests. Non-MBS-funded testing has been available for some time in this population and this gene is already included in most multigene panels. A subset of these genes is also included in eviQ prostate cancer gene panel testing guidance (eviQ) and risk management as well as other international guidelines such as the National Comprehensive Cancer Network (NCCN) Guidelines (Cheng et al., 2026).

There are multiple commercially available gene panels for hereditary prostate cancer testing (Marino et al., 2023), which largely include all 12 of the 'green genes' from the PanelApp Prostate Cancer Panel (Version 1.1). However, the expanded panel from Sonic Genetics omits the *HOXB13* and *EPCAM* genes (Table 1). Panel selection is informed by the patient's family history.

Table 1: Summary of genes included in prostate cancer testing panels.

Test name, Company	Genes
Hereditary Prostate Cancer Panel (Primary Panel) , Invitae	<i>ATM</i> , <i>BRCA1</i> , <i>BRCA2</i> , <i>CHEK2</i> , <i>EPCAM</i> , <i>HOXB13</i> , <i>MLH1</i> , <i>MSH2</i> , <i>MSH6</i> , <i>PALB2</i> , <i>PMS2</i> , <i>TP53</i>
Prostate Cancer Comprehensive Panel , Fulgent	<i>ABRAXAS1</i> , <i>ATM</i> , <i>ATR</i> , <i>BRCA1</i> , <i>BRCA2</i> , <i>BRIP1</i> , <i>CHEK2</i> , <i>EPCAM</i> , <i>GEN1</i> , <i>HOXB13</i> , <i>MLH1</i> , <i>MRE11</i> , <i>MSH2</i> , <i>MSH6</i> , <i>NBN</i> , <i>PALB2</i> , <i>PMS2</i> , <i>RAD51C</i> , <i>RAD51D</i> , <i>TP53</i>
CancerNext , Ambry Genetics	<i>APC</i> , <i>BARD1</i> , <i>BRIP1</i> , <i>EPCAM</i> , <i>HOXB13</i> , <i>MSH2</i> , <i>NF1</i> , <i>POLD1</i> , <i>RAD51D</i> , <i>TP53</i> , <i>ATM</i> , <i>BMPR1A</i> , <i>CDH1</i> , <i>FH</i> , <i>MBD4</i> , <i>MSH3</i> , <i>NTHL1</i> , <i>POLE</i> , <i>RPS20</i> , <i>TSC1</i> , <i>AXIN2</i> , <i>BRCA1</i> , <i>CDKN2A</i> , <i>FLCN</i> , <i>MET</i> , <i>MSH6</i> , <i>PALB2</i> , <i>PTEN</i> , <i>SMAD4</i> , <i>TSC2</i> , <i>BAP1</i> , <i>BRCA2</i> , <i>CHEK2</i> , <i>GREM1</i> , <i>MLH1</i> , <i>MUTYH</i> , <i>PMS2</i> , <i>RAD51C</i> , <i>STK11</i> , <i>VHL</i>
Prostate Cancer Panel , Prevention Genetics	<i>ATM</i> , <i>BRCA1</i> , <i>BRCA2</i> , <i>BRIP1</i> , <i>CHEK2</i> , <i>EPCAM</i> , <i>HOXB13</i> , <i>MLH1</i> , <i>MSH2</i> , <i>MSH6</i> , <i>NBN</i> , <i>PALB2</i> , <i>PMS2</i> , <i>RAD51C</i> , <i>RAD51D</i> , <i>TP53</i>

myRisk , Myriad Genetics	<i>APC, ATM, AXIN2, BAP1, BARD1, BLM, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A (p14ARF), CDKN2A (p16INK4a), CHEK2, CHEK2 Biallelic, CTNNA1, DICER1, EGFR, EPCAM, FH, FLCN, GALNT12, GREM1, HOXB13, KIT, MAX, MBD4 Biallelic, MBD4 Monoallelic, MEN1, MET, MTF, MLH1, MLH3 Biallelic, MLH3 Monoallelic, MSH2, MSH3 Biallelic, MSH3 Monoallelic, MSH6, MUTYH Biallelic, MUTYH Monoallelic, NF1, NTHL1 Biallelic, NTHL1 Monoallelic, PALB2, PDGFRA, PMS2, POLE, POLD1, POLE, PTEN, RAD51C, RAD51D, RB1, RET, RNF43, RPS20, SDHA, SDHAF2, SDHB, SDHC, SDHD, SMAD4, SMARCA4, STK11, TERT, TMEM127, TP53, TSC1, TSC2, VHL</i>
Familial cancer panel (germline) - expanded panel , Sonic Genetics	<i>ATM, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, MLH1, MSH2, MSH6, PALB2, PMS2, PTEN, RAD51C, RAD51D, STK11, and TP53.</i>
BRAoVO™ Plus Gene Panel , Genomic Diagnostics	<i>ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CDKN2A, CHEK2, EPCAM, HOXB13, MLH1, MSH2, MSH6, NF1, PALB2, PMS2, PTEN, RAD51C, RAD51D, STK11, TP53</i>
Prostate Panel, Peter MacCallum Cancer Centre	<i>ATM, BRCA1, BRCA2, CHEK2, EPCAM, HOXB13, MLH1, MSH2, MSH6, PALB2, PMS2, TP53</i>
Breast, Ovarian, Pancreas and Prostate Panel, Peter MacCallum Cancer Centre	<i>ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CDKN2A, CHEK2, EPCAM, HOXB13, MLH1, MSH2, MSH6, PALB2, PMS2, PTEN, RAD51C, RAD51D, STK11, TP53</i>

Sources: (Marino et al., 2023) and (Doan et al., 2021), with further investigation of Australian providers. Green font indicates 'green genes' from the PanelApp Prostate Cancer Panel (Version 1.1).

Identify how the proposed technology achieves the intended patient outcomes:

Germline genetic testing in individuals with prostate cancer enables the identification of heritable prostate cancer through the detection of P/LP variants in cancer predisposition genes. Identification of a P/LP germline variant can inform prognosis and guide clinical decision-making by influencing treatment selection, the frequency and intensity of monitoring, and the need for surveillance for second malignancies in the affected individual, as well as cascade testing for biological relatives (Shore et al., 2024; Xu et al., 2025). While there are currently no PBS-listed targeted treatments for non-metastatic prostate cancer, germline genetic testing remains clinically relevant as test results can still lead to meaningful changes in clinical management and follow-up strategies for the affected individual and familial risk assessment.

Positive germline genetic test results can alter clinical recommendations for patients with prostate cancer, with the nature and extent of change dependent on the specific gene variant identified. In current practice, germline findings are used to inform treatment selection, follow-up intensity, and thresholds for further investigation where disease progression is suspected or considered more likely. In the PROCLAIM study, patients with positive germline results were significantly more likely to receive recommendations for prostate treatment changes (18% vs 1.4%), follow-up changes (64% vs 11%), and cascade testing (71% vs 5.4%) compared with those with negative results (Shore et al., 2024). Multivariable analysis further showed that a positive germline result was strongly associated with changes to clinical management (treatment changes OR 69.7, $p < 0.001$; follow-up changes OR 80.6, $p < 0.001$) (Shore et al., 2024). These changes may include

closer clinical surveillance, altered imaging strategies, and a lower threshold for further investigation where disease progression is suspected or considered more likely.

The identification of a P/LP germline variant is also associated with a shift toward more personalised and, in some cases, more intensive management strategies, particularly for carriers of variants associated with aggressive disease biology, such as *BRCA2* (Reiter & Hassler, 2024). In localised disease, *BRCA2* germline findings may influence shared decision-making by discouraging prolonged active surveillance in higher-risk carriers and supporting earlier escalation to definitive local therapy. Active surveillance is defined as monitoring of low-risk prostate cancer that is not causing problems or symptoms, avoiding unnecessary treatment while actively monitoring for changes that would trigger immediate action (Papa et al., 2022).

This approach is supported by empirical evidence demonstrating higher rates of tumour upgrading among *BRCA2* and *ATM* variant carriers undergoing active surveillance (HR 2.74, 95% CI = 1.26–5.96, $p = 0.01$), indicating an increased likelihood of disease progression compared with non-carriers (Carter et al., 2019).

Germline results may inform the use of genomically targeted systemic therapies, including PARP inhibitors or immune checkpoint inhibitors, in the event of disease progression, although the availability of such therapies varies by disease stage and funding arrangements (Reiter & Hassler, 2024). Adjuvant PARP inhibitor studies in BRCA-mutated breast cancer demonstrated an improvement in disease-free and overall survival (Geyer et al., 2022) and clinical trials in BRCA-mutated early prostate cancer are underway (McKay et al., 2026). Genetic testing to determine access to codependent therapies at later stages of disease is not the subject of this application, although some of that genetic testing may be replaced by the germline testing proposed in this application.

Beyond the management of the index cancer, germline genetic testing has important implications for the identification and management of additional cancer risks associated with specific hereditary cancer syndromes. Patients with positive results may require tailored surveillance for other malignancies, depending on the gene involved, and should be offered referral to a familial cancer service or genetic counsellor to support interpretation of results and facilitate cascade testing for at-risk relatives (Reiter & Hassler, 2024; Shore et al., 2024).

Germline genetic testing supports reproductive decision-making by providing information about the probability of transmitting a P/LP variant to future children. Evidence from qualitative and quantitative studies consistently demonstrates that patients value germline testing for the insight it provides into inheritance patterns and future family risk, with families commonly motivated by 'a desire for inheritance/causation information' and the opportunity to make proactive health and reproductive decisions (Hunter et al., 2024).

Health economic evidence

Although there is a modest health outcome improvement for prostate cancer patients themselves, the benefit of germline testing of prostate cancer patients is proposed to arise primarily through improved health outcomes for their biological relatives.

Reflecting this structure of anticipated health outcome benefits across the two populations, health economic studies have reported that adding cascade testing greatly improves cost-effectiveness compared to germline testing for only localised prostate cancer patients. An Australian study of germline *BRCA* testing for localised prostate cancer in three different populations reported a quality-adjusted life year (QALY) gain of 0.029 and an incremental cost-effectiveness ratio (ICER) of \$47,294/QALY for patients with a family history of prostate cancer plus cascade testing of their relatives (Teppala et al., 2025) (Table 2).

Genetic testing for the detection of germline variants in cancer predisposition genes in people with prostate cancer and their relatives – PICO Set 1

Table 2: Cost-utility of germline BRCA testing in prostate cancer: prostate cancer patients alone, and when cascade testing is added.

Population	Affected individuals only		Affected individuals + cascade	
	Incremental QALYs	ICER (\$/QALY)	Incremental QALYs	ICER (\$/QALY)
Risk classification: high / very high	0.003	\$591,408	0.087	\$18,872
Family history of prostate cancer	0.0003	\$3.9 million	0.029	\$47,294
Ashkenazi Jewish ancestry	0.002	\$650,098	0.112	\$14,637

Source: (Teppala et al., 2025)

Does the proposed health technology include a registered trademark component with characteristics that distinguishes it from other similar health components?

No

Explain whether it is essential to have this trademark component or whether there would be other components that would be suitable:

Not applicable

Are there any proposed limitations on the provision of the proposed health technology delivered to the patient (For example: accessibility, dosage, quantity, duration or frequency):

Yes

Provide details and explain:

It is unlikely that a patient will require more than one test per cancer diagnosis, however this may depend on the specific genes that are included.

If applicable, advise which health professionals will be needed to provide the proposed health technology:

This application does not propose changing requestors for these existing MBS items. As per the current descriptor for item 73296, a specialist or consultant physician is required to request this service. Appropriate pre- and post-test genetic counselling should be provided to the patient by the specialist treating practitioner (e.g. the treating oncologist), a genetic counselling service or a clinical geneticist on referral as per the existing practice note (PN.0.23).

If applicable, advise whether delivery of the proposed health technology can be delegated to another health professional:

Not applicable

If applicable, advise if there are any limitations on which health professionals might provide a referral for the proposed health technology:

A referral may be provided by a specialist or consultant physician.

Is there specific training or qualifications required to provide or deliver the proposed service, and/or any accreditation requirements to support delivery of the health technology?

Yes

Provide details and explain:

Testing would be delivered by approved practising pathologists with appropriate scope of practice in pathology laboratories with the relevant National Association of Testing Authorities (NATA) accreditation for this service.

Indicate the proposed setting(s) in which the proposed health technology will be delivered:

- ☒ Consulting rooms
- ☐ Day surgery centre
- ☐ Emergency Department
- ☐ Inpatient private hospital
- ☐ Inpatient public hospital
- ☒ Laboratory
- ☒ Outpatient clinic
- ☐ Patient's home
- ☐ Point of care testing
- ☐ Residential aged care facility
- ☐ Other (please specify)

Genetic testing is provided through public and private clinical genetics services and familial cancer centres.

Some services operate mainstream genetic testing models, in which cancer specialists directly request genetic testing for their patients, with support from a familial cancer centre for those with a positive or uncertain finding. Mainstream genetic testing has the benefit of being faster, enabling genetic testing discussions to occur at the point of cancer care rather than requiring separate genetics appointments, and is often associated with greater uptake of testing (Jennings et al., 2026).

Is the proposed health technology intended to be entirely rendered inside Australia?

Yes

Provide additional details on the proposed health technology to be rendered outside of Australia:

Not applicable.

Comparator

Nominate the appropriate comparator(s) for the proposed medical service (i.e., how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian healthcare system). This includes identifying healthcare resources that are needed to be delivered at the same time as the comparator service:

No germline genetic testing.

List any existing MBS item numbers that are relevant for the nominated comparators:

Not applicable.

Provide a rationale for why this is a comparator:

Currently germline genetic testing is not funded by the MBS for patients with early prostate cancer. Therefore 'no germline genetic testing' is the appropriate comparator.

Pattern of substitution – Will the proposed health technology wholly replace the proposed comparator, partially replace the proposed comparator, displace the proposed comparator or be used in combination with the proposed comparator?

☐ Full

☐ None (used with the comparator)

☐ Displaced (comparator will likely be used following the proposed technology in some patients)

☐ Partial (in some cases, the proposed technology will replace the use of the comparator, but not all)

☒ Full (subjects who receive the proposed intervention will not receive the comparator)

Outline and explain the extent to which the current comparator is expected to be substituted:

Where germline genetic testing is conducted, it will fully substitute the comparator of no germline testing.

Outcomes

List the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be measured in assessing the clinical claim for the proposed medical service/technology (versus the comparator):

☒ Health benefits

Outcome description – include information about whether a change in patient management, or prognosis, occurs as a result of the test information:

Test-related outcomes

- Test accuracy (sensitivity, specificity, positive/negative predictive value) - these are already established for the NGS gene panels likely to be used for this test purpose.
- Diagnostic yield
- **Allows biological relatives to receive cascade testing**

Health benefits

- Diagnosis of germline variant and subclassification of the type of prostate cancer
- Prognostic information regarding the likelihood of disease progression or a different primary cancer which may inform the approach taken to surveillance (including modality of imaging, threshold for biopsy where progression or a new cancer diagnosis suspected)
- Change in management/treatment
- Change in patient health outcomes (including mortality, morbidity, quality of life)
- Disease-specific patient-reported outcomes
- In the future, should the patient experience disease progression, this test will have established eligibility for access to PARP inhibitor therapy
- Other benefits

List the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be measured in assessing the clinical claim for the proposed medical service/technology (versus the comparator):

☒ Health harms

Outcome description – include information about whether a change in patient management, or prognosis, occurs as a result of the test information:

Health harms

- Test-related adverse events
- Genetic testing pathways are well-established with appropriate pre- and post-test counselling offered and informed consent being sought prior to undertaking germline testing. Where mainstreaming is undertaken, the patient would be referred to provide counselling regarding the test result and follow up of familial implications.
- Consequences of false positive/negative results
- Consequences of identifying VUS

List the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be measured in assessing the clinical claim for the proposed medical service/technology (versus the comparator):

☒ Resources

Outcome description – include information about whether a change in patient management, or prognosis, occurs as a result of the test information:

Resources

- Cost of germline genetic testing
 - Offset: reduction in germline testing no longer provided to a proportion of patients who subsequently develop metastatic castration-resistant prostate cancer
- Cost of the intervention (change in cost of treatments undertaken)
- Cost-effectiveness (cost per diagnosis, cost per QALY)
- Total Australian Government healthcare costs

List the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be measured in assessing the clinical claim for the proposed medical service/technology (versus the comparator):

☒ Value of knowing

Outcome description – include information about whether a change in patient management, or prognosis, occurs as a result of the test information:

Other relevant considerations

- Value of knowing (emotional benefits and harms to family, family planning, social benefits and harms to family). Relevant non-health outcomes may include:
 - Explanation of why cancer diagnosis is likely to have occurred (especially for those diagnosed at a young age)
 - For those who test positive, reproductive interventions to reduce the risk of passing on the variant to any future children.
 - For those who test negative, reduction in anxiety.
- Ethical considerations (equity of access, considerations regarding informed consent, considerations regarding cascade testing, including notification of carrier status).

Proposed MBS items

How is the technology/service funded at present? (e.g., research funding; State-based funding; self-funded by patients; no funding or payments):

State-based funding or self-funded by patients or referral/testing not offered.

Provide at least one proposed item with their descriptor and associated costs, for each Population/Intervention:

MBS item number (where used as a template for the proposed item)	73296
Category number	6
Category description	Pathology Services
Proposed item descriptor	Characterisation of germline gene variants, including copy number variation where appropriate, requested by a specialist or consultant physician: (a) in predisposition genes for breast, ovarian, fallopian tube, primary peritoneal or prostate cancer, which must include at least: i. BRCA1 and BRCA2 genes; and ii. one or more other relevant genes; and (b) in a patient: i. with breast, ovarian, fallopian tube, primary peritoneal or prostate cancer; and ii. for whom clinical and family history criteria place the patient at greater than 10% risk of having a pathogenic or likely pathogenic variant associated with breast, ovarian, fallopian tube, primary peritoneal or prostate cancer. Once per cancer diagnosis
Proposed MBS fee	Same as current MBS fee for item 73296 (As of March 2026; Fee: \$1,200.00 Benefit: 75% = \$900.00 85% = \$1,095.50).
Indicate the overall cost per patient of providing the proposed health technology	\$1,200.00
Please specify any anticipated out of pocket expenses	\$0.00
Provide any further details and explain	Gap fee is unlikely to be charged.

Algorithms

PREPARATION FOR USING THE HEALTH TECHNOLOGY

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, before patients would be eligible for the proposed health technology:

Individuals typically enter the prostate cancer diagnostic pathway through the investigation of urinary symptoms or following an abnormal screening result. Initial assessment is completed by a General Practitioner, and this is followed by a prostate-specific antigen (PSA) blood test and midstream urine test.

Individuals with elevated PSA and/or high-risk clinical features will be referred to a urologist for further evaluation. Patients will also have a multiparametric MRI and prostate biopsy before the diagnosis of prostate cancer is made.

Is there any expectation that the clinical management algorithm before the health technology is used will change due to the introduction of the proposed health technology?

No

Describe and explain any differences in the clinical management algorithm prior to the use of the proposed health technology vs. the comparator health technology:

Not applicable

USE OF THE HEALTH TECHNOLOGY

Explain what other healthcare resources are used in conjunction with delivering the proposed health technology:

Prior to the sample being collected, information regarding the family history is collected, genetic counselling provided and informed consent obtained in conjunction with germline genetic testing.

A tissue sample (blood or buccal) would need to be collected. This process could involve phlebotomists, nurses, pathology collection staff, and/or practice staff.

The sample would be tested at an accredited laboratory, which would involve a multidisciplinary team of pathologists, scientists, laboratory technicians and clinical genetics specialists.

Explain what other healthcare resources are used in conjunction with the comparator health technology:

No other healthcare resources are used in conjunction with the comparator health technology (no germline genetic testing; Figure 2). When germline genetic testing does not take place, a tissue sample is not collected, and genetic counselling is not required.

Describe and explain any differences in the healthcare resources used in conjunction with the proposed health technology vs. the comparator health technology:

The proposed health technology requires pre- and post-test genetic counselling, data collection, sample collection and analysis whereas none of these are required where no genetic testing is undertaken (comparator).

The staff, facilities, and equipment required to deliver the proposed health technology are already established and funded through existing public and private healthcare arrangements. Implementation is therefore expected to result in only a modest increase in healthcare resources proportionate to the additional population becoming eligible.

CLINICAL MANAGEMENT AFTER THE USE OF HEALTH TECHNOLOGY

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, after the use of the proposed health technology:

After completing genetic testing, individuals will attend a post-test counselling appointment to discuss their results with the specialist or consultant physician. Appropriate pre- and post-test genetic counselling should be provided to the patient by the specialist treating practitioner, a genetic counselling service or a clinical geneticist on referral.

The results of the testing will shift the clinical care pathway towards becoming more personalised and risk-adapted, influencing both treatment selection and ongoing testing and surveillance (Figure 3).

Individuals who have a variant of uncertain significance (VUS) identified by germline genetic testing would have no change in clinical management based on this result, as identification of a VUS is a clinically uninformative result. Re-curation of VUS may occur later, but this is not publicly funded nor proposed for public funding within this application.

In individuals with localised prostate cancer, the identification of a germline P/LP variant in a cancer predisposition gene prompts more cautious active surveillance and may support later consideration of changing systemic therapy (e.g. platinum chemotherapy for advanced disease, and timing of treatment intensification (Shore et al., 2024)), reflective of evidence that germline variants are associated with more aggressive tumour biology and poorer prognosis (Castro et al., 2013).

A health economic assessment of germline genetic testing in prostate cancer patients included treatment probabilities that differed depending on *BRCA* variant status (Teppala et al., 2025) (Table 3). These illustrate that even within a prostate cancer risk grouping, *BRCA* positive patients are less likely to undergo active surveillance and external beam radiotherapy, and more likely to undergo radical prostatectomy.

Table 3: Probabilities of treatments for patients with prostate cancer, by *BRCA* variant status.

Treatment	Prostate cancer risk group	Treatment probability	
		<i>BRCA</i> positive	<i>BRCA</i> negative
Active surveillance	Low	0.75	0.80
	Intermediate	0.00	0.15
Radical prostatectomy	Low	0.25	0.15
	Intermediate	0.82	0.59
	High / very high	0.89	0.49
External beam radiotherapy	Low	0.00	0.05
	Intermediate	0.18	0.26
	High / very high	0.11	0.51

Source: (Teppala et al., 2025).

Affected individuals who are found not to have a germline P/LP variant would have no genetic reason for escalation of treatment interventions. These individuals would receive treatment recommendations as per standard of care (informed by their other risk factors), and cascade testing would not be indicated for their biological relatives.

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, after the use of the comparator health technology:

All newly diagnosed prostate cancer cases will have their treatment discussed at a multidisciplinary team meeting prior to treatment initiation.

For individuals with localised disease, standard of care management options include active surveillance, with regular PSA testing, imaging and repeat biopsies to monitor for disease progression; or definitive treatment with radical prostatectomy or radiotherapy where appropriate. PSA testing is offered based on age, and risk due to family history (RACGP). Some individuals may have androgen deprivation therapy.

Individuals with locally advanced disease or metastatic prostate cancer are likely to require systemic therapy. This typically includes androgen deprivation therapy, chemotherapy, or radiotherapy.

Supportive care, including the management of treatment-related side effects, psychosocial support, are integral components of care at all stages of disease.

Describe and explain any differences in the healthcare resources used after the proposed health technology vs. the comparator health technology:

In the absence of genetic testing (comparator), individuals do not have access to targeted therapies or genetic-informed disease management. There is also limited awareness of other potential cancer risks, meaning that risk-based surveillance and preventive interventions are not recommended or undertaken unless informed by family history. Furthermore, without identification of P/LP variants, cascade testing cannot be offered to at-risk family members.

When a germline variant is identified through genetic testing of patients with prostate cancer, there is typically a shift toward more intensive management, with increased use of diagnostic imaging, repeat biopsies, multidisciplinary review, and definitive treatments, as well as greater demand for genetic counselling and follow-up services. Despite this upfront increase in surveillance and treatment intensity for variant-positive individuals, downstream healthcare costs are partially offset through earlier definitive management in higher-risk individuals having the potential to reduce later disease progression, prolonged systemic therapy, repeated hospitalisations, and the cumulative resource use associated with advanced or recurrent disease.

Targeted systemic treatments represent a more efficient use of healthcare resources because they are directed to patients most likely to benefit, reducing exposure to ineffective therapies and avoiding the costs associated with trial-and-error treatment, unnecessary toxicity, and repeated treatment changes. These approaches can also delay progression, reduce complications and hospitalisations, and limit prolonged use of high-intensity therapies.

While input from mental health professionals, specialist nurses, primary care and supportive care services is still required, the earlier escalation to definitive treatment and targeted treatments can mitigate psychosocial burden by reducing treatment uncertainty.

Currently, MBS item 73303 provides germline genetic testing for *BRCA* status in patients with metastatic castration-resistant prostate cancer, to enable access to a PBS-listed therapy. The introduction of the proposed health technology to provide germline genetic testing to patients

with a greater than 10% risk of having a germline variant is expected to reduce uptake of testing under MBS item 73303, as some patients will have received the testing earlier through the proposed pathway.

Insert diagrams demonstrating the clinical management algorithm with and without the proposed health technology:

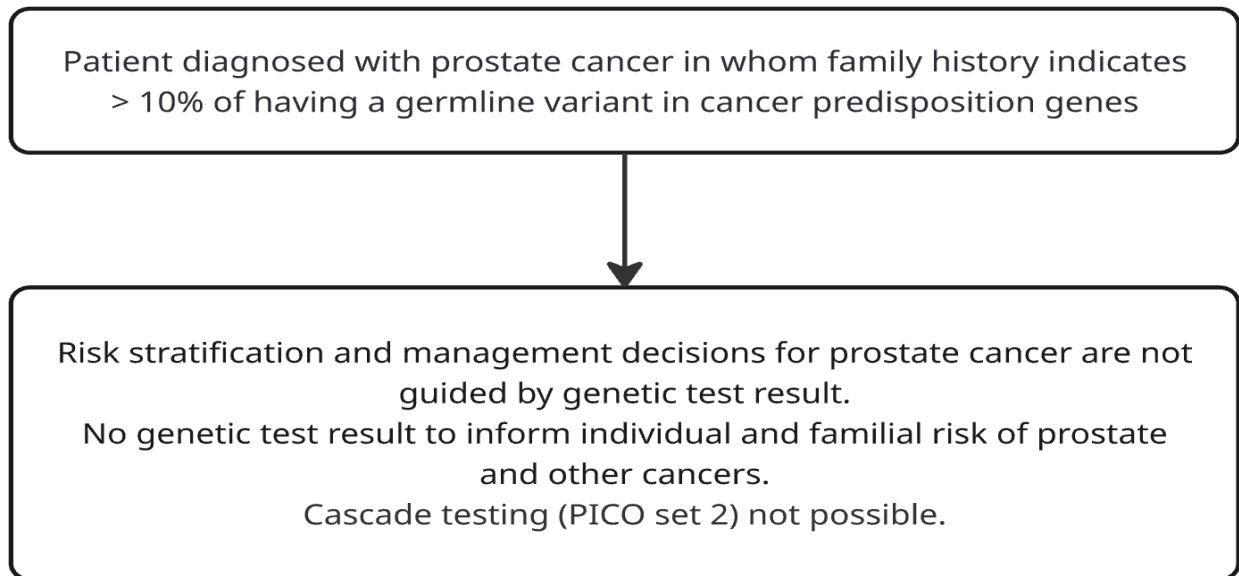


Figure 2: Current clinical management pathway for affected individuals

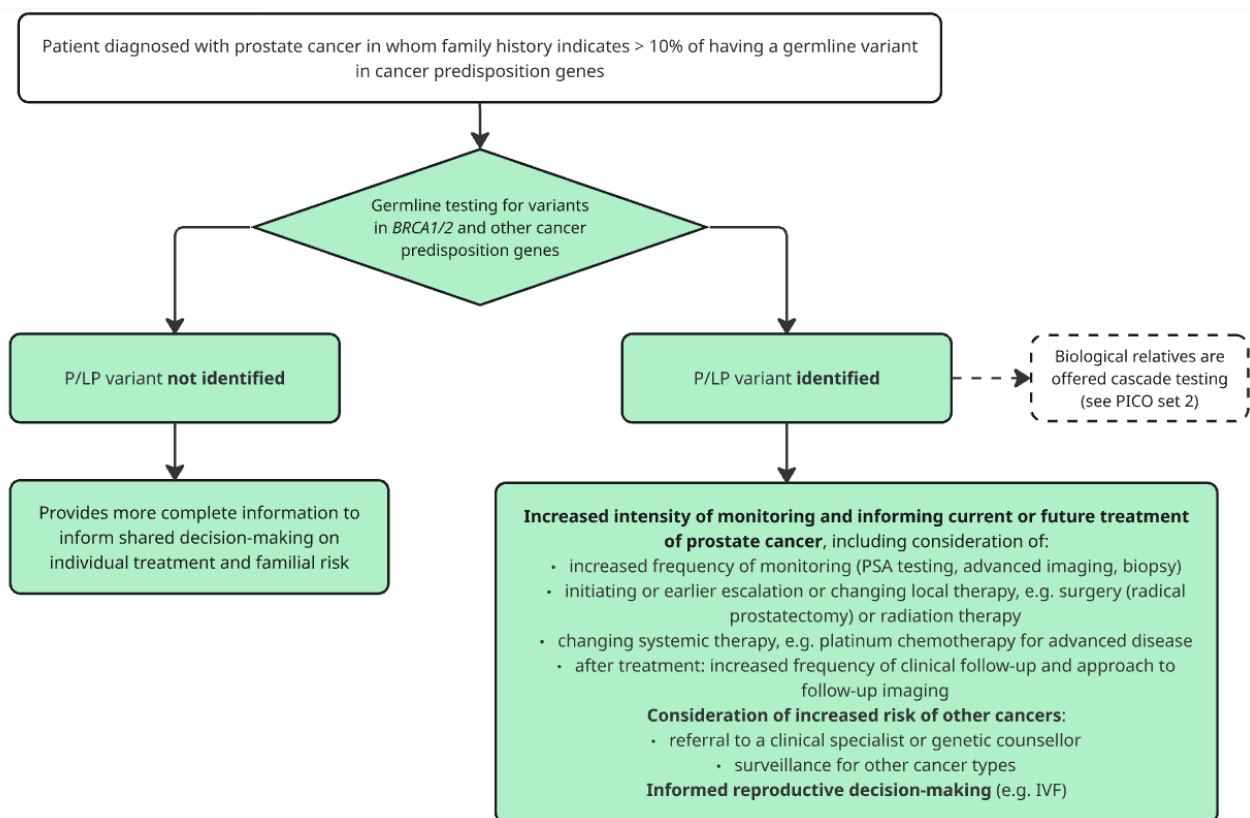


Figure 3: Proposed clinical management algorithm for affected individuals

Parts that differ between the comparator and intervention are shown in green.

IVF = in-vitro fertilisation; P/LP = pathogenic or likely pathogenic; PSA = Prostate-Specific Antigen; VUS = variant(s) of uncertain significance.

Claims

In terms of health outcomes (comparative benefits and harms), is the proposed technology claimed to be superior, non-inferior or inferior to the comparator(s)?

- ☒ Superior
☐ Non-inferior
☐ Inferior

Please state what the overall claim is, and provide a rationale:

The proposed germline genetic testing of cancer predisposition genes is likely to have non-inferior safety and superior effectiveness in patients with prostate cancer, compared to no germline genetic testing of cancer predisposition genes.

Safety is likely to be non-inferior because extension of the current MBS items to include offering testing to patients with prostate cancer raises no new safety concerns. The testing process itself does not alter or delay standard prostate cancer diagnostic pathways. Potential non-physical risks, such as psychological distress, anxiety, or concerns about genetic discrimination, are well recognised in genetic testing programs. However, these risks are mitigated through existing clinical safeguards, including pre-test and post-test genetic counselling, informed consent processes, and privacy protections. Such measures are routinely embedded in clinical genetics services and are considered part of standard best practice.

Effectiveness in prostate cancer patients is likely to be superior. For patients with prostate cancer, germline testing results may influence their follow-up intensity, treatment decisions, and/or later eligibility for targeted therapies. In the PROCLAIM study, patients with a pathogenic germline variant were more likely than patients without a pathogenic germline variant to receive recommended changes to follow-up (64% vs 11%, $P < 0.001$), treatment (18% vs 1.4%, $P < 0.001$), and cascade testing (71% vs 5.4%, $P < 0.001$) (Shore et al., 2024). Patients who did not have a germline variant were more likely to be reassured of their disease prognosis and have interventional treatments de-escalated (Shore et al., 2024). A prospective cohort study showed that patients with germline *BRCA1/2* or *ATM* pathogenic variants undergoing active surveillance were significantly more likely to experience tumour grade reclassification on follow-up biopsies than those with no pathogenic variant (Carter et al., 2019), supporting that testing identifies a higher risk population.

A key utility of this testing arises from improved health outcomes in biological relatives, who receive cascade testing as a consequence of patients with prostate cancer having received germline testing. Relatives who test positive can receive earlier, increased and targeted surveillance, and where appropriate, risk-reducing interventions. For example, 30% of female relatives found to carry a P/LP variant in *BRCA1/2* take up risk-reducing bilateral mastectomy and 53% take up risk-reducing salpingo-oophorectomy (Teppala et al., 2025). Relatives who test negative for the familial P/LP variant have their cancer risk downgraded to an average population risk and do not require the additional surveillance or intervention recommended for those testing positive and those with a family history without knowledge of their mutation status.

Why would the requestor seek to use the proposed investigative technology rather than the comparator(s)?

Knowing whether a patient carries a germline P/LP variant, and the variant's associations with prognosis and treatment response, is informative to an individual's cancer management and risk

of other cancers, and for their family. The risk assessment models for familial risk such CanRisk include genetic test results.

- Management of the patient's prostate cancer may change upon identification of a germline P/LP variant, resulting in a modest improvement in health outcomes and shared decision-making.
- Additional surveillance or early investigation of symptoms would occur if the P/LP variant found is associated with a more aggressive phenotype and higher likelihood of recurrence, or an increased risk of developing other cancers (e.g. chest wall surveillance in men, eligibility for Australian pancreatic cancer screening with a P/LP variant in *BRCA2*, *BRCA1*, *ATM*, *PALB2*, *MLH1*, *MSH2*, *MSH6*, *PMS2* or *EPCAM*, eligibility for colonoscopies and gastroscopy for any of the Lynch syndrome genes and immune checkpoint inhibitors for advanced disease).
- The presence of a P/LP variant in *BRCA2* and/or *ATM* would support shared decision-making about the extent of initial treatment versus willingness to have active surveillance.
- A positive finding also allows provision of an explanation for why their cancer developed and from identifying that their prostate cancer is hereditary, allowing referral of family members for cascade testing and accurate estimation of their risk and appropriate risk management.

A key benefit of testing prostate cancer patients arises from the opportunity to have family referred for cascade testing, which may rule out a cancer predisposition in those relatives who test negative, and allow surveillance and risk management strategies in those who test positive (see PICO set 2). The potential for early detection and/or prevention and associated improved health outcomes may ease some of the anxieties of learning there is a hereditary explanation for their cancer.

Identify how the proposed technology achieves the intended patient outcomes:

The testing establishes the presence or absence of a P/LP variant, which then supports evidence-based guideline-derived changes in healthcare, depending on the gene. Finding a P/LP variant means their biological relatives can receive cascade testing if indicated and follow guidelines regarding cancer risk and cancer risk management. The absence of a P/LP variant rules out the involvement of any of the genes tested as best possible, and those individuals receive management of their cancer risk based on family history and other personal risk factors.

For some people, compared with the comparator(s), does the test information result in:

A change in clinical management? Yes

A change in health outcome? Yes

Other benefits? Yes

Please provide a rationale, and information on other benefits if relevant:

Health outcomes for affected individuals improve modestly upon germline genetic testing. These individuals will also gain some value from knowing whether their prostate cancer is hereditary. Biological relatives who receive cascade testing are expected to have greater health outcome improvement.

In terms of the immediate costs of the proposed technology (and immediate cost consequences, such as procedural costs, testing costs etc.), is the proposed technology claimed to be more costly, the same cost or less costly than the comparator?

- ☒ More costly
☐ Same cost
☐ Less costly

Provide a brief rationale for the claim:

Germline genetic testing is more costly than the comparator of no germline genetic testing.

If your application is in relation to a specific radiopharmaceutical(s) or a set of radiopharmaceuticals, identify whether your clinical claim is dependent on the evidence base of the radiopharmaceutical(s) for which MBS funding is being requested. If your clinical claim is dependent on the evidence base of another radiopharmaceutical product(s), a claim of clinical noninferiority between the radiopharmaceutical products is also required.

Not applicable.

Summary of Evidence

Provide one or more recent (published) high quality clinical studies that support use of the proposed health service/technology.

Type of study design	Title of journal article or research project	Short description of research	Website link to journal article or research	Date of publication
Real-world evidence study	Geographic Variability in Germline Genetic Testing for Prostate Cancer: A Nationwide Medicare Claims Study With Evidence of Low Uptake	This US study used national Medicare claims data to identify newly diagnosed prostate cancer patients who underwent germline genetic testing. This testing was only performed in 2.38% (17,821/749,202) of men with prostate cancer, despite 36.5% of the patients meeting clinicopathologic criteria for testing based on SEER data.	Korn et al. (2025) - https://doi.org/10.6004/jnccn.2025.7074	December 2025
Cohort study	Germline Mutations in <i>ATM</i> and <i>BRCA1/2</i> Are Associated with Grade Reclassification in Men on Active Surveillance for Prostate Cancer	Germline testing of <i>BRCA1</i> , <i>BRCA2</i> and <i>ATM</i> was undertaken in 2 cohorts of patients with early prostate cancer in active surveillance program with regular biopsies. Those with pathogenic variants identified were significantly more likely to have their tumour upgraded on subsequent biopsies, indicating a more aggressive phenotype.	Carter et al. (2019) - https://pubmed.ncbi.nlm.nih.gov/30309687/	May 2019
Cost-utility analysis	The cost-utility of targeted germline <i>BRCA</i> testing in localised prostate cancer followed by cascade testing first-degree relatives with pathogenic variants	This Australian study evaluated the cost-utility of germline <i>BRCA</i> testing in prostate cancer patients and their relatives. Testing patients with family history of prostate cancer yielded an ICER of \$3.9million/QALY, however adding cascade testing of first-degree relatives reduced the ICER to \$47,294/QALY.	Teppala et al. (2025) - https://doi.org/10.1016/j.jgim.2025.101463	May 2025

Type of study design	Title of journal article or research project	Short description of research	Website link to journal article or research	Date of publication
Consensus guidelines for germline prostate cancer implementation (Delphi model)	Implementation of Germline Testing for Prostate Cancer: Philadelphia Prostate Cancer Consensus Conference 2019	Recommend change in management where <i>BRCA2</i> and possibly <i>ATM</i> pathogenic variants due to more aggressive phenotype (discuss active surveillance versus more definitive local treatment)	Giri et al. (2020) - https://pmc.ncbi.nlm.nih.gov/articles/PMC7430215/pdf/JCO.20.00046.pdf	June 2020
Observational study	Clinician-Reported Management Recommendations in Response to Universal Germline Genetic Testing in Patients With Prostate Cancer	Prostate cancer patients (n=982) received germline testing through the PROCLAIM study. Those with identified pathogenic variant(s) (100/982, 10%), were more likely to receive recommended clinical management changes than those without, including for follow-up (64% vs 11%, $P<0.001$), treatment (18% vs 1.4%, $P<0.001$), and cascade testing (71% vs 5.4%, $P<0.001$).	Shore et al. (2024) - https://doi.org/10.1097/JU.0000000000004190	December 2024
Pooled analysis of 5 randomised, multicentre clinical trials	Impact of Pathogenic Germline DNA Damage Repair alterations on Response to Intense Neoadjuvant Androgen Deprivation Therapy in High-risk Localized Prostate Cancer	This study evaluated the response to neoadjuvant androgen deprivation in those with and without pathogenic germline variants in DNA damage repair genes in men with high-risk localised prostate cancer. Using a 34-gene panel, pathogenic germline variants were identified in 9.5% (19/201) of patients, with <i>BRCA2</i> and <i>ATM</i> as the most frequently altered genes.	Berchuck et al. (2021) - https://doi.org/10.1016/j.eururo.2021.03.031	September 2021

Type of study design	Title of journal article or research project	Short description of research	Website link to journal article or research	Date of publication
Cross-sectional cohort study	Prevalence of Germline Variants in Prostate Cancer and Implications for Current Genetic Testing Guidelines	From an unselected cohort of men diagnosed with prostate cancer who underwent germline genetic testing, 17.2% (620/3607) had a positive result and 30.7% of these were <i>BRCA1/2</i> variants. 37% (229/620) of those who tested positive would not have been approved for testing using the NCCN guidelines.	Nicolosi et al. (2019) - https://doi.org/10.1001/jamaoncol.2018.6760	February 2019
Retrospective case study	Germline Mutations in <i>ATM</i> and <i>BRCA1/2</i> Distinguish Risk for Lethal and Indolent Prostate Cancer and are Associated with Early Age at Death	Presence of pathogenic germline variants in <i>BRCA1/2</i> and <i>ATM</i> was significantly higher in 313 patients who died of prostate cancer (6.07%) compared with 486 patients with localised prostate cancer (1.44%), $p = 0.0007$, and was an independent predictor of a shorter survival time after initial diagnosis, and earlier age at death.	Na et al. (2017) https://doi.org/10.1016/j.eururo.2016.11.033	May 2018

Identify yet-to-be-published research that may have results available in the near future (that could be relevant to your application).

None identified.

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