Technoleg Iechyd Cymru
Health Technology Wales

Topic Exploration Report

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

- Determine the quantity of evidence available for a technology of interest.
- Identify any gaps in the evidence.
- Inform decisions on topics that warrant fuller assessment by Health Technology Wales (HTW).

Topic exploration report number:	TER359
Topic:	Genetic testing for prostate cancer care
Summary of findings:	Health Technology Wales researchers searched for evidence on the clinical and cost effectiveness of genetic testing for prostate cancer care. This included genetic testing for people at risk of prostate cancer, for active surveillance of prostate cancer, and pharmacogenetic testing to inform treatment decisions. We did not identify any evidence in a clinical setting that reported on patient outcomes for pharmacogenomic testing in prostate cancer or genetic testing in people at risk of prostate cancer. We did however identify evidence reporting on genetic testing that may be used to estimate prostate disease outcome and progression. We identified one health technology assessment and three systematic reviews that reported on predictive genomic biomarker tests related to prostate cancer. We also found one relevant validation study, and an ongoing clinical trial that aims to determine the clinical impact of genetic testing in prostate cancer care. There was a lack of evidence found on pharmacogenomics for prostate cancer in a clinical setting. The evidence identified suggests that genomic biomarkers may be useful to estimate disease progression and predict response to clinical treatment which may guide treatment decision making. However, direct evidence on the use of pharmacogenomics for prostate cancer compared to standard care was not identified, so any improvements in clinical outcomes such as survival, tumour progression and quality life are uncertain. The ongoing randomised controlled trial may address some of the gaps in the evidence.

Introduction and aims

Pharmacogenomics involves using a patient's genomic information to tailor the selection of drugs used to manage their condition. In this way, pharmacogenomics aims to provide a more personalised approach to the use of available medication in treating patients. Pharmacogenomics may be useful for numerous disease areas; however, this report focussed on genetic testing for people at risk of prostate cancer, for active surveillance of prostate cancer, and pharmacogenetic testing to inform treatment decisions.

Prostate cancer is the second most common cancer in the UK. Prostate cancer often grows very slowly at first without even causing symptoms. Treatment may not be needed straightaway, but this depends on whether the cancer has spread within the prostate or to other parts of the body. This means decisions about treatment, what it should be and when it should start, are different for everyone.

People at risk of developing prostate cancer are currently monitored using regular prostate-specific antigen (PSA) tests. Standard treatment options for people diagnosed with prostate cancer is guided by best practice guidelines. This would typically involve surgery or radiotherapy in early-stage disease. Hormone therapy (androgen deprivation therapy), chemotherapy and immunotherapy may be used in later stages. The use of pharmacogenetic testing may allow for such treatments and therapies to be tailored to the individual to maximise benefit.

Health Technology Wales researchers searched for evidence on the clinical and cost effectiveness of genetic testing for prostate cancer care.

Evidence overview

We did not identify any evidence in a clinical setting that reported on patient outcomes for pharmacogenomics in prostate cancer or genetic testing in people at risk of prostate cancer. We did identify evidence reporting on commercially available gene panels that may be used to estimate prostate disease outcome and progression. For completion, we searched for additional evidence on these specific gene panels and have summarised the findings below.

We identified one guideline that details the treatment pathway for people with prostate cancer with reference to genomic bio-marker based treatment, one health technology assessment reporting on genomic testing and three systematic reviews reporting on predictive genomic biomarkers tests related to prostate cancer. We also identified a relevant validation study and one ongoing randomised controlled trial.

Guidelines

We identified a NICE guideline (NG131) for the diagnosis and management of prostate cancer published in 2019. The guideline references genomic biomarker-based treatment for metastatic hormone-relapsed prostate cancer; however, it states that the point at which to use genomic biomarker-based therapy in solid tumour treatment pathways is uncertain.

Secondary evidence

We identified an Ontario health technology assessment that sought to determine the clinical utility, economic impact, and patients' perceptions of the value of the Prolaris cell cycle progression (CCP) test in low- and intermediate-risk localised prostate cancer. Ontario (2017) included two before-and-after studies. In one study, the results of the CCP test appeared to change the treatment plan (from initial to final plan) in 64.9% of cases overall. In the other study, the CCP test changed the treatment received in nearly half of cases overall, compared with the initial plan. The authors found no evidence to demonstrate the impact of the Prolaris CCP test on patient-important clinical outcomes.

We identified a systematic review that reported on the available evidence supporting the clinical utility of the Decipher genomic classifier. Jairath et al. (2021) included 42 studies with a total of 407 patients. The authors found that in 32 studies, Decipher was independently prognostic for all study endpoints and in five studies Decipher changed the management in active surveillance and postprostatectomy. Jairath et al. (2021) concluded that the test helps identify which cancers are more or less aggressive, which in turn aids in personalised treatment decision-making.

We identified a systematic review that reported on genomic tests for prostate cancer and included 21 studies; eight studies on Prolaris, eight studies on Oncotype Dx, and five studies on Decipher (Fine et al. 2019). For each genomic test the authors extracted data regarding the risk of adverse pathology, biochemical recurrence, metastasis, and prostate cancer mortality. Fine et al. (2019) found that the results of genomic tests that use biomarkers derived from prostate biopsy can be used in conjunction with clinicopathologic variables to improve the ability to risk stratify patients with newly diagnosed prostate cancer. However, it was stated that additional data was needed on the impact of using these tests on long-term patient outcomes and their cost effectiveness.

We identified a systematic review that reported on the use of genomic biomarkers in the prognosis of prostate cancer and prediction of therapeutic response. Boström et al. (2015) included genetic prostate cancer outcome studies that had clinical outcome end points including biochemical progression, clinical progression, and disease-specific survival. In total, 82 articles were included in the review. The majority of these studies were early-stage research or 'discovery' studies; five studies were external validation studies for commercially available gene panels (Prolaris, Oncotype DX Genomic Prostate Score, and Decipher). The authors reported that the most studied commercially available gene panels, may be used to estimate disease outcome in addition to clinical parameters or clinical nomograms. Boström et al. (2015) concluded that in addition to improved biopsy techniques and imaging, genomic tests may be used to estimate the potential of tumour progression. The Oncotype DX Genomic Prostate Score was investigated in this setting and found to provide additional information to clinical parameters and nomograms.

Individual studies

We identified a study on the validation of the Decipher test for predicting adverse pathology in candidates for prostate cancer active surveillance (Kim et al. 2019). Decipher was initially assessed in a prospective cohort of prostatectomies to explore the correlation with clinically meaningful biologic characteristics and then assessed in diagnostic biopsies from a retrospective multicentre cohort of 266 men with very low/low and favourable-intermediate risk prostate cancer. Kim et al. (2019) concluded that Decipher can be applied to prostate biopsies from very-low/low and favourable-intermediate risk patients to predict absence of adverse pathologic features and that these patients are predicted to be good candidates for active surveillance.

Economic evidence

The Health Quality Ontario (2017) HTA concluded that there was not sufficient data to undertake a primary economic evaluation for Polaris.

We identified a more recent economic study that aimed to determine the cost effectiveness of using the Oncotype DX Genomic Prostate Score (GPS), a 17-gene expression assay that can be used to inform decisions regarding active surveillance versus immediate treatment (Chang et al. 2019). The US study used a Markov model simulating 20-year outcomes for 65-year-old men with very low-, low-, or favourable intermediate-risk prostate cancer undergoing active surveillance versus immediate treatment using GPS versus no testing. Chang et al. (2019) concluded the use of the Oncotype DX was cost effective in guiding treatment decisions regarding active surveillance vs immediate treatment. The cost effectiveness was sensitive to small differences in the utilities of the active surveillance and no evidence of disease post-treatment states.

Ongoing trials

We identified one ongoing randomised clinical trial with a cluster-crossover design that aims to determine the clinical impact of Gene Expression Classifier (GEC) testing in prostate cancer care while also developing a pragmatic approach for improved GEC clinical use and future study. The study aims to recruit 900 participants in total and participants will be randomised to either standard care with genetic testing or standard care alone. The primary outcome of the trial is the binomial proportion of men on active surveillance without treatment at two years. The estimated primary study completion date is November 2023.

Areas of uncertainty

There was a lack of evidence found on use of genetic testing for prostate cancer in a clinical setting and reporting patient outcomes. Therefore, any improvements in clinical outcomes such as survival, tumour progression and quality of life are uncertain. Also, due to the lack of relevant economic evidence for pharmacogenomics in prostate cancer care, it is unclear if genetic testing would be cost effective compared to standard care.

Literature search results

Health technology assessments and guidance

NICE. (Last updated: December 2021). NICE guideline [NG131] Prostate cancer: diagnosis and management. Available at: https://www.nice.org.uk/guidance/ng131 [Accessed July 2022].

Evidence reviews and economic evaluations

Fine ND, LaPolla F, Epstein M, et al. (2019). Genomic Classifiers for Treatment Selection in Newly Diagnosed Prostate Cancer. BJU Int. doi: 10.1111/bju.14799

Health Quality O. (2017). Prolaris Cell Cycle Progression Test for Localized Prostate Cancer: A Health Technology Assessment. Ontario health technology assessment series. 17(6): 1-75.

Jairath NK, Dal Pra A, Vince R, Jr., et al. (2021). A Systematic Review of the Evidence for the Decipher Genomic Classifier in Prostate Cancer. Eur Urol. 79(3): 374-83. doi: 10.1016/j.eururo.2020.11.021

Chang EM, Punglia RS, Steinberg ML, et al. (2019). Cost Effectiveness of the Oncotype DX Genomic Prostate Score for Guiding Treatment Decisions in Patients With Early Stage Prostate Cancer. Urology. 126: 89-95. doi: https://doi.org/10.1016/j.urology.2018.12.016

Individual studies

Kim HL, Li P, Huang H-C, et al. (2019). Validation of the Decipher Test for predicting adverse pathology in candidates for prostate cancer active surveillance. Prostate Cancer and Prostatic Diseases. 22(3): 399-405. doi: 10.1038/s41391-018-0101-6

Ongoing research

NCT04396808
Genomics in Michigan to adjust outcomes in prostate cancer (G-MAJOR) for men with newly diagnosed favorable risk prostate cancer

https://clinicaltrials.gov/ct2/show/study/NCT04396808

Date of search:	May 2022
Concepts used:	Pharmacogenomics, pharmacogenetics, personalised medicine, genetic testing, prostate cancer, Decipher, Prolaris, Oncotype DX