



## 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:

1. Inform discussions on new topics received by HTW.
2. Determine the quantity and type of evidence available on a topic.
3. Assess the topic against HTW selection criteria.

Topic:	PET scanning with $^{18}\text{F}$ -Choline or $^{68}\text{Ga}$ -PSMA ligand positron emission tomography/computed topography (PET/CT) for screening and diagnosis of prostate cancer
Topic exploration report number	TER004
Referrer:	Chris Marshall, Wales Research and Diagnostic Positron Emission Tomography Imaging Centre
Topic exploration undertaken by:	Cedar Researchers on behalf of Health Technology Wales

### Aim of Search

On behalf of Health Technology Wales, Cedar researchers searched for evidence on the clinical and cost effectiveness of PET scanning with  $^{18}\text{F}$ -choline or  $^{68}\text{Ga}$ -PSMA ligand PET/CT in the staging and diagnosis of metastatic and/or recurrent prostate cancer.

### Summary of Findings

A number of systematic reviews were identified, though there was variation in terms of the interventions, comparisons and populations included. None directly compare the interventions of interest for this topic. The topic proposal included details of a comparative study (Morigi et al, 2015) and a brief review of the literature suggests that a number of comparative studies may be available, although a full and comprehensive search of the available literature would be required to confirm this to be the case.

#### *Technology assessments*

The Scottish Health Technologies Group undertook an assessment on non-FDG PET tracers in 2016. This includes evidence on  $^{18}\text{F}$ -choline or  $^{68}\text{Ga}$ -PSMA ligand PET, but only in the context of recurrent prostate cancer.

#### *Guidelines*

One set of evidence based guidelines published in the Republic of Ireland in 2016, states that the evidence for  $^{18}\text{F}$ -choline PET/CT is not sufficiently robust to be able to recommend its use. These

guidelines also highlight the emerging evidence for  $^{68}\text{Ga}$ -PSMA PET/CT but again make no recommendations on its use.

#### *Systematic Reviews*

Several systematic reviews were identified, though these varied in terms of the intervention and comparisons. No review compared  $^{18}\text{F}$ -choline PET or PET/CT with  $^{68}\text{Ga}$ -PSMA PET/CT

#### *Economic Evaluations*

No economic evaluations of either intervention were identified.

#### *Ongoing studies*

Two studies were identified on clinicaltrials.gov, however both studies are in the early stages (recruiting or not yet recruiting). Both studies are investigating the interventions in highly specific populations (high risk prostate cancer patients and bone metastases), which may limit the generalisability of the results when they publish.

## Conclusions

Evidence exists about the clinical effectiveness of both  $^{18}\text{F}$ -choline PET or PET/CT and  $^{68}\text{Ga}$ -PSMA PET/CT, although this evidence may be limited in both applicability and quality. The applicability of the evidence will largely depend on the specific research question and scope. The quality of the evidence will be impacted by factors such as study design, patient numbers, settings, comparisons and reported outcomes.

There is reported variation in the sensitivity and specificity of both  $^{18}\text{F}$ -choline PET and  $^{68}\text{Ga}$ -PSMA PET. The extent to which this variation is impacted by study design, study size, population included, comparison and/or target condition cannot be assessed without full review of the published evidence.

No literature was found relating to the cost effectiveness of either  $^{18}\text{F}$ -choline or  $^{68}\text{Ga}$ -PSMA PET/CT.

## Areas of Uncertainty

There appears to be uncertainty around the cost effectiveness of the interventions, but we did not identify any evidence that could address this uncertainty.

It is unclear whether a fuller assessment would cover the use of these tests in primary prostate cancer, or whether the focus would be solely on recurrent/metastatic disease. This requires clarification when the scope of the appraisal is determined.

## Feasibility of Technology Assessment

HTW's Assessment Group concluded to progress this topic to Evidence Appraisal, using the scope of SHTG Evidence Note 67 as the basis for the subsequent appraisal. HTW's appraisal will be published as EAR005 - please refer to this for the final agreed inclusion criteria for evidence.

## Brief literature search results

Resource	Results
<a href="#">Healthcare Improvement Scotland:</a>	SHTG. (2017). Non-FDG tracers for use in PET-CT for suspected recurrent prostate cancer. Evidence note 67. Scottish Healthcare Technologies Group. Available at: <a href="http://www.healthcareimprovementscotland.org/our_work/technologies_and_medicines/shtg_-_evidence_notes/evidence_note_67.aspx">http://www.healthcareimprovementscotland.org/our_work/technologies_and_medicines/shtg_-_evidence_notes/evidence_note_67.aspx</a>
<a href="#">NICE</a> (guidelines, technology appraisals, diagnostics guidance, interventional procedures, medical technologies)	No results
<a href="#">CRD database</a>	<i>Search Terms</i> Prostate Cancer, PSMA, Prostate Specific Membrane Antigen, Choline <i>Results</i> Nothing new to add to any of the reviews identified in other databases
<a href="http://evidence.nhs.uk/">evidence.nhs.uk/</a>	<i>Guidelines</i> Fendler WP (2017) 68Ga-PSMA PET/CT: Joint EANM and SNMMI procedure guideline for prostate cancer imaging: version 1.0 <i>Eur J Nucl Med Mol Imaging</i> 44:1014-1024 Department of Health (Ireland). Diagnosis, staging and treatment of patients with prostate cancer. National Clinical Guideline No. 8. June 2015. Updated March 2016. <i>Systematic Reviews</i> Corfield J (2018) 68Ga-prostate specific membrane antigen (PSMA) positron emission tomography (PET) for primary staging of high-risk prostate cancer: a systematic review. <i>World J Urol.</i> 36(4):519-527 Von Eyben FE (2016) 68Ga-Labeled Prostate-specific Membrane Antigen Ligand Positron Emission Tomography/Computed Tomography for Prostate Cancer: A Systematic Review and Meta-analysis. <i>Eur Urol Focus.</i> S2405-4569(16)30160-2
<a href="#">Cochrane library</a> (Cochrane Reviews, Other Reviews, Technology Assessments, Economic Evaluations)	<i>Cochrane Reviews</i> No Results <i>Other Reviews</i> Evangelista L , Guttilla A , Zattoni F , Muzzio PC and Zattoni F Utility of choline positron emission tomography/computed tomography for lymph node involvement identification in intermediate- to high-risk prostate cancer: a systematic literature review and meta-analysis <i>European Urology</i> , 2013, 63(6), 1040-1048 Evangelista L , Cervino AR , Burei M , Gregianin M , Saladini G , Marzola MC , Chondrogianis S and Rubello D. Comparative studies of radiolabeled choline positron emission tomography, histology of primary tumor and other imaging modalities in prostate cancer: a systematic review and meta-analysis <i>Clinical and Translational Imaging</i> , 2013, 1(2), 99-109 <i>Technology Assessments</i> HAYES and Inc (2014) Choline PET and PET-CT for suspected recurrent prostate cancer (Structured abstract) Atienza Merino G (2012) Role of PET/CT with choline analogue radiotracers in the diagnosis and staging of prostate cancer (Structured abstract) <i>Economic Evaluations</i> No Results
Medline	Perera M; Papa N; Christidis D; Wetherell D; Hofman MS; Murphy DG; Bolton D; Lawrentschuk N. Sensitivity, Specificity, and Predictors of Positive 68Ga-Prostate-specific Membrane Antigen Positron Emission Tomography in Advanced Prostate Cancer: A Systematic Review and Meta-analysis. [Review] <i>European Urology</i> . 70(6):926-937, 2016 12. Barrio M; Fendler WP; Czernin J; Herrmann K. Prostate specific membrane antigen (PSMA) ligands for diagnosis and therapy of prostate cancer. [Review]

	<i>Expert Review of Molecular Diagnostics. 16(11):1177-1188, 2016 11.</i>
Ongoing studies	<p>Study 1:  <b>Title:</b> Place of 68Ga-PSMA-11 PET-CT in the Therapeutic Decision at the End of the Initial Staging for High Risk Prostate Cancer Patients  <b>Recruitment:</b> Not yet recruiting  <b>Study Results:</b> No Results Available  <b>Conditions:</b> Prostate Cancer  <b>Interventions:</b> Diagnostic Test: 68Ga-PSMA-11   Diagnostic Test: 18F-Choline PET-CT  <b>Locations:</b> Central hospital Nancy, Nancy, France  <b>URL:</b> <a href="https://ClinicalTrials.gov/show/NCT03344822">https://ClinicalTrials.gov/show/NCT03344822</a></p> <p>Study 2:  <b>Title:</b> Diagnostic Imaging of Bone Metastases in Prostate Cancer Patients  <b>Recruitment:</b> Recruiting  <b>Study Results:</b> No Results Available  <b>Conditions:</b> Prostate Cancer Metastatic to Bone  <b>Interventions:</b> Diagnostic Test: WB-MRI   Diagnostic Test: SPECT-CT   Diagnostic Test: Cholin-PET-CT   Diagnostic Test: PSMA-PET-CT  <b>Locations:</b> Department of Radiology/Department of Nuclear Medicine, Herlev, Denmark  <b>URL:</b> <a href="https://ClinicalTrials.gov/show/NCT03134261">https://ClinicalTrials.gov/show/NCT03134261</a></p>
Evidence identified by topic proposer	<p>Kumaraswamy G Kallur et al, Clinical Utility of Gallium-68 PSMA PETCT Scan for Prostate Cancer, Indian J Nucl Med (2017) 32(2) 110-117  Morigi JJ et al, Prospective Comparison of 18FFluoromethylcholine Versus 68Ga-PSMA PET/CT in Prostate Cancer Patients Who Have Rising PSA After Curative Treatment and Are Being Considered for Targeted Therapy. J Nucl Med (2015) 56(8) 1185-90  Witkowska-Patena E et al, 68Ga-PSMA PETCT Imaging in Recurrent Prostate Cancer: Where are we Now? Cent European J Urol (2017) 37-43  Ceci F, New aspects of Molecular Imaging in Prostate Cancer, Methods (2910&amp;) 36-41  Ceci F, Current Application and Future Perspectives of PSMA PET Imaging in Prostate Cancer, QJ Nucl Med Mol Imaging (2018) Mar 8  Alves, F Cyclotron Production of Ga-68 for Human Use from Liquid Targets : From Theory to Practice, AIP Conference Proceedings Vol 1845 Issue 1. May 2017</p>

Date of search:	April 2018
Concepts used:	Choline, PSMA, Prostate Specific Membrane Antigen, Positron Emission Tomography, PET, Prostate Cancer