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PET Imaging with Prostate-Specific Membrane Antigen for Prostate Cancer: Clinical Utility

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Research Question

1. What is the clinical utility of positron emission tomography (PET) imaging using prostate-specific membrane antigen (PSMA) labelled with gallium-68 (Ga-68) or fluorine-18 (F-18) in patients with suspected or confirmed metastatic or biochemically recurrent prostate cancer?

Key Findings

Four systematic reviews (one with a meta-analysis)s, one randomized controlled trial, and 30 non-randomized studies were identified regarding the clinical utility of positron emission tomography imaging using prostate-specific membrane antigen labelled with gallium-68 or fluorine-18 in patients with suspected or confirmed metastatic or biochemically recurrent prostate cancer.

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were prostate specific membrane antigen and prostatic neoplasms. Search filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, or network meta-analyses, and any types of clinical trials or observational studies. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 01, 2015 and October 29, 2020. Internet links were provided, where available.

Selection Criteria and Summary Methods

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed. The Overall Summary of Findings was based on information available in the abstracts of selected publications.

Table 1: Selection Criteria

Population	Patients (any age) previously diagnosed with prostate cancer with suspected or confirmed metastatic or biochemically recurrent prostate cancer
Intervention	Positron emission tomography (PET) imaging using prostate-specific membrane antigen (PSMA) labelled with gallium-68 (Ga-68) or fluorine-18 (F-18)
Comparator	Prostate-specific antigen (PSA) blood testing, bone scan, computed tomography (CT), magnetic resonance imaging (MRI), biopsy, PET or PET-CT imaging using other prostate cancer-specific PET radiotracers (e.g., 18F-fluorodeoxyglucose [18F-FDG], 18F-sodium fluoride [18F-NaF], 11C-choline, 18F-choline, 18F-fluciclovine), active surveillance, watchful waiting, or no comparator

Outcomes	Clinical utility (e.g., effect on clinical decisions, health care utilization, timely treatment, health effects of false positive or negative test result, clinician/patient confidence in prognosis, health-related quality of life, anxiety, mortality, safety)
Study Designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies

CT = computed tomography; F-18 = fluorine-18; GA-68 = gallium-68; MRI = magnetic resonance imaging; PET = positron emission tomography; PET-CT = positron emission tomography-computed tomography; PSA = prostate specific antigen; PSMA = prostate specific membrane antigen

Results

Four systematic reviews[1-4] (one with a meta-analysis[1]), one randomized controlled trial,[5] and 30 non-randomized studies[6-35] were identified regarding the clinical utility of PET imaging using PSMA labelled with Ga-68 or F-18 in patients with suspected or confirmed metastatic or biochemically recurrent prostate cancer. No relevant health technology assessments were identified in the literature.

Additional references of potential interest that did not meet the inclusion criteria are provided in the appendix.

Overall Summary of Findings

Four systematic reviews[1-4] (one with a meta-analysis[1]), one randomized controlled trial,[5] and 30 non-randomized studies[6-35] were identified regarding the clinical utility of PET imaging using PSMA labelled with Ga-68 or F-18 in patients with suspected or confirmed metastatic or biochemically recurrent prostate cancer. The authors of all four systematic reviews,[1-4] including the one with a meta-analysis,[1] found that using PSMA imaging labelled with Ga-68 had an impact on management or treatment planning for prostate cancer patients with recurrent prostate cancer. The authors of the randomized controlled trial[5] found that use of PSMA imaging labelled with Ga-68 led to more management changes compared to conventional imaging for biopsy-proven prostate cancer patients with high risk features. The authors of 22 non-randomized studies[7-9,11-15,17,18,21-26,28-31,33,35] found that use of PSMA imaging labelled with Ga-68 led to changes in management or treatment plans for prostate cancer patients with metastatic or biochemical recurrence. The author of one non-randomized study found PSMA imaging labelled with Ga-68 did not change management for patients with metastatic prostate cancer.[14] The authors of three of the non-randomized studies[16,32,34] found PSMA imaging labelled with Ga-68 did not lead to adverse events. The authors of four of the non-randomized studies[6,10,19,27] found using PSMA imaging labelled with F-18 led to changes in management or treatment plans for prostate cancer patients with metastatic or biochemical recurrence. The author of one non-randomized study[19] found PSMA imaging labelled with F-18 led to some mild adverse events, while another non-randomized study[20] found no significant adverse events. A detailed summary of the identified studies can be found in Table 2.

Table 2: Summary of Included Studies

First Author, Year	Study Characteristics and Population	Intervention and Comparator(s)	Relevant Outcome(s)	Authors' Conclusions
Systematic Reviews and Meta-analyses				
Diao, 2020[1]	**Study design:** Systematic review and meta-analysis **Population:** Prostate cancer patients with biochemical recurrence **N** = 20 included studies	**Intervention:** ^{68}GA-PSMA **Comparator(s):** NR	Management impact of ^{68}GA-PSMA	Management of prostate cancer was altered in more than half of prostate cancer patients with biochemical recurrence following the use of ^{68}GA-PSMA tracers
Luiting, 2020[2]	**Study design:** Systematic Review **Population:** Prostate cancer patients with biochemical recurrence **N** = 11 included studies	**Intervention:** ^{68}GA-PSMA PET **Comparator(s):** NR	Management impact of ^{68}GA-PSMA PET	^{68}GA-PSMA PET had a high impact on radiotherapy planning in patients with early biochemical recurrence after radical prostatectomy
Eissa, 2018[3]	**Study design:** Systematic review **Population:** Patients with recurrent prostate cancer **N** = 37 included studies	**Intervention:** ^{68}GA-PSMA PET **Comparator(s):** CT; MRI; choline-based PET scans	Management impact of ^{68}GA-PSMA PET scan	^{68}GA-PSMA PET was found to be effective in identifying recurrence localization which permitted to choosing the best therapeutic strategy as early as possible
Health Technology Wales, 2018[4]	**Study design:** Rapid systematic review and critical appraisal **Population:** Patients with recurrent prostate cancer **N** = 20 included studies	**Intervention:** Fluorine and gallium PSMA PET **Comparator(s):** Other tracers	Management impact of ^{68}GA-PSMA PET	^{68}GA-PSMA PET can influence subsequent patient management but the proportion of patients affected by management change varied between studies
Randomized Controlled Trial				
Hofman, 2020[5]	**Study design:** Multicentre, two-arm, randomized control trial **Population:** Patients with biopsy-proven prostate cancer and high-risk features with pelvic nodal or distant metastatic disease **N** = 302	**Intervention:** ^{68}GA-PSMA-11 PET-CT **Comparator(s):** Conventional imaging (CT and bone scanning)	Management impact of ^{68}GA-PSMA-11 PET-CT	Conventional imaging led to less management change compared to ^{68}GA-PSMA-11 PET-CT

First Author, Year	Study Characteristics and Population	Intervention and Comparator(s)	Relevant Outcome(s)	Authors' Conclusions
Non-Randomized Studies				
Anttinen, 2020[6]	**Study design:** Single arm prospective cohort study **Population:** Patients with newly diagnosed high risk prostate cancer undergoing primary metastasis staging **N** = 79	**Intervention:** ^{18}F-PSMA-1007 PET-CT **Comparator(s):** Bone scan, CT, SPECT-CT, WBMRI	Clinical decision making using ^{18}F-PSMA-1007 PET-CT	^{18}F-PSMA-1007 PET-CT led to an influence in clinical decision making in 14/79 prostate cancer patients
Counago, 2020[7]	**Study design:** Single arm prospective cohort study **Population:** Patients with primary or recurrent prostate cancer **N** = 27	**Intervention:** ^{68}GA-PSMA PET-CT **Comparator(s):** CT, MRI, bone scans	Management impact of ^{68}GA-PSMA PET-CT	^{68}GA-PSMA PET led to a modification of the therapeutic approach in a substantial proportion of prostate cancer patients
Deandreis, 2020[8]	**Study design:** Single arm prospective cohort study **Population:** Patients with diagnosed prostate cancer and proven biochemical recurrence or persistence **N** = 223	**Intervention:** ^{68}Ga-PSMA-11 PET-CT **Comparator(s):** No comparator	Management impact of ^{68}Ga-PSMA-11 PET-CT use	^{68}Ga-PSMA-11 PET-CT influenced the clinical management in 35.4% of patients
Fendler, 2020[9]	**Study design:** Single arm prospective cohort study **Population:** Men with prostate cancer biochemical recurrence **N** = 588	**Intervention:** ^{68}Ga-PSMA-11 PET **Comparator(s):** No comparator	Management impact of ^{68}Ga-PSMA-11 PET	^{68}Ga-PSMA-11 PET clarified site of cancer recurrence and disease localization which changed the management in more than half of patients
Liu, 2020[10]	**Study design:** Single arm prospective cohort study **Population:** Men with radio-recurrent prostate cancer **N** = 79	**Intervention:** ^{18}F-DCFPyL PSMA PET-CT **Comparator(s):** Diagnostic imaging	Management impact of ^{18}F-DCFPyL PSMA PET-CT	Proposed patient management was changed as a result of ^{18}F-DCFPyL PSMA PET-CT use

First Author, Year	Study Characteristics and Population	Intervention and Comparator(s)	Relevant Outcome(s)	Authors' Conclusions
Barbaud, 2019[11]	**Study design:** Single arm retrospective cohort study **Population:** Prostate cancer patients presenting biochemical recurrence **N** = 42	**Intervention**: ^{68}Ga-PSMA-11 PET-CT **Comparator(s):** No comparator	Management impact of ^{68}Ga-PSMA-11 PET-CT	^{68}Ga-PSMA-11 PET-CT resulted in a major clinical impact with treatment change found in 70% of patients and a decrease in PSA levels among patients
Bashir, 2019[12]	**Study design:** Single arm retrospective cohort study **Population:** Prostate cancer patients with early biochemical relapse **N** = 28	**Intervention:** ^{68}Ga-PSMA PET-CT **Comparator(s):** No comparator	Management impact of ^{68}Ga-PSMA PET-CT in	^{68}Ga-PSMA PET-CT resulted in management change for 12 patients and may impact the choice of curative treatments
Bianchi, 2019[13]	**Study design:** Single arm prospective cohort study **Population:** Prostate cancer patients with biochemical recurrence **N** = 276	**Intervention:** ^{68}Ga-PSMA PET-CT **Comparator(s):** No comparator	Management impact of ^{68}Ga-PSMA PET-CT	^{68}Ga-PSMA PET-CT allowed radical change to intended treatment approach before imaging evaluations in most individuals
Davidson, 2019[14]	**Study design:** Single arm retrospective cohort study **Population:** Patients with prostate cancers undergoing imaging for biochemical failure of metastatic disease **N** = 95	**Intervention:** ^{68}Ga-PSMA PET-CT **Comparator(s):** No comparator	Management impact of ^{68}Ga-PSMA PET-CT	^{68}Ga-PSMA PET-CT may have an impact on clinical management in prostate cancer patients at the time of initial staging, however it does not appear useful in the management of patients with known metastatic disease
Farolfi, 2019[15]	**Study design:** Retrospective cohort study **Population:** Prostate cancer patients with biochemical recurrence **N** =	**Intervention:** ^{68}Ga-PSMA-11 PET-CT **Comparator(s):** No comparators	Management impact of ^{68}Ga-PSMA-11 PET-CT	^{68}Ga-PSMA-11 PET-CT led to a change in intended treatment in 30.2% of patients

First Author, Year	Study Characteristics and Population	Intervention and Comparator(s)	Relevant Outcome(s)	Authors' Conclusions
Fendler, 2019[16]	**Study design:** Single arm prospective cohort study **Population:** Patients with biochemically recurrent prostate cancer **N** = 635	**Intervention:** ^{68}Ga-PSMA-11 PET **Comparator(s):** No comparator	Safety of ^{68}Ga-PSMA-11 PET	No serious adverse events were associated with ^{68}Ga-PSMA-11 PET administration
Muller, 2019[17]	**Study design:** Single arm retrospective cohort study **Population:** Patients referred for recurrent prostate cancer **N** = 223	**Intervention:** ^{68}Ga-PSMA-11 PET **Comparator(s):** No comparator	Management impact of ^{68}Ga-PSMA-11 PET	^{68}Ga-PSMA-11 PET led to a change in management in 60% of the patients
Rousseau, 2019[18]	**Study design:** Single arm prospective cohort study **Population:** Prostate cancer patients presenting a recurrence **N** = 52	**Intervention:** ^{68}Ga-PSMA-11 PET-CT **Comparator(s):** No comparator	Management impact of ^{68}Ga-PSMA-11 PET-CT	Preliminary results showed ^{68}Ga-PSMA-11 PET-CT had a major clinical impact and resulted in treatment change in more than half of the patients
Rousseau, 2019[19]	**Study design:** Single arm prospective cohort study **Population:** Patients with prostate cancer and biochemical recurrence **N** = 130	**Intervention:** ^{18}F-DCFPyL PSMA PET-CT **Comparator(s):** No comparator	Management impact and safety of ^{18}F-DCFPyL PSMA PET-CT	A change was found in treatment intent, disease stage, and management plans following ^{18}F-DCFPyL PSMA PET-CT. Additionally, 22 subjects report mild adverse events after the scan.
Saga, 2019[20]	**Study design:** Single arm prospective cohort study **Population:** Prostate cancer patients with known metastatic lesions **N** = 6	**Intervention:** ^{18}F-FSU-880 **Comparator(s):** No comparator	Safety of ^{18}F-FSU-880	^{18}F-FSU-880 could be used without significant adverse effects
Afag, 2018[21]	**Study design:** Single arm retrospective cohort study	**Intervention:** ^{68}Ga-PSMA PET-CT	Management impact of ^{68}Ga-PSMA PET-CT	^{68}Ga-PSMA PET-CT altered the

First Author, Year	Study Characteristics and Population	Intervention and Comparator(s)	Relevant Outcome(s)	Authors' Conclusions
	Population: Prostate cancer patients with biochemical recurrence **N** = 100	**Comparator(s):** No comparator		management plans in 39% of patients
De Bari, 2018[22]	**Study design:** Single arm retrospective cohort study **Population:** Patients with prostate cancer presenting a biochemical relapse **N** = 40	**Intervention:** ^{68}Ga-PSMA-11 PET-CT **Comparator(s):** No comparator	Management impact of ^{68}Ga-PSMA-11 PET-CT	^{68}Ga-PSMA-11 PET-CT led to a change in therapeutic approach in 70% of patients
Frenzel, 2018[23]	**Study design:** Single arm retrospective cohort study **Population:** Prostate cancer patients with biochemical relapse and localized metastases **N** = 106	**Intervention:** ^{68}Ga-PSMA PET-CT **Comparator(s):** CT	Management impact of ^{68}Ga-PSMA PET-CT	^{68}Ga-PSMA PET-CT was shown to be superior to CT alone and led to a change in the radiotherapy regime for 46% of patients
Grubmuller, 2018[24]	**Study design:** Retrospective cohort study **Population:** Prostate patients with biochemical recurrence **N** = 117	**Intervention:** ^{68}Ga-PSMA-11 PET-CT **Comparator(s):** CT, MRI	Management impact of ^{68}Ga-PSMA-11 PET-CT	^{68}Ga-PSMA-11 PET-CT led to a change in therapeutic decision making in 67 patients
Koerber, 2018[25]	**Study design:** Single arm prospective cohort study **Population:** Men with prostate cancer with primary or recurrent disease **N** = 121	**Intervention:** ^{68}Ga-PSMA-11 PET-CT **Comparator(s):** Conventional imaging	Management impact of ^{68}Ga-PSMA-11 PET-CT	^{68}Ga-PSMA-11 PET-CT led to a change in tumor classification in 49 patients and radiotherapeutic management in 62 patients
Mattiolli, 2018[26]	**Study design:** Single arm retrospective cohort study	**Intervention:** ^{68}Ga-PSMA PET-CT **Comparator(s):** No comparator	Management impact of ^{68}Ga-PSMA PET-CT	^{68}Ga-PSMA PET-CT led to a treatment change in 63.4% of patients and showed

First Author, Year	Study Characteristics and Population	Intervention and Comparator(s)	Relevant Outcome(s)	Authors' Conclusions
	Population: Prostate cancer patients with biochemical recurrence **N** = 125			an impact on patient management
Mena, 2018[27]	**Study design:** Single arm prospective cohort study **Population:** Prostate cancer patients with biochemical recurrence **N** = 68	**Intervention:** ^{18}F-DCFBC PET-CT **Comparator(s):** MRI	Management impact of ^{18}F-DCFBC PET-CT	^{18}F-DCFBC PET-CT imaging led clinicians to change treatment strategy in 51.2% of patients
Roach, 2018[28]	**Study design:** Prospective cohort study **Population:** Prostate cancer patients with primary or recurrent prostate cancer **N** = 431	**Intervention:** ^{68}Ga-PSMA PET-CT **Comparator(s):** No comparator	Management impact of ^{68}Ga-PSMA PET-CT	^{68}Ga-PSMA PET-CT led to a change in planned management in 51% of patients
Zacho, 2018[29]	**Study design:** Single arm prospective cohort study **Population:** Prostate cancer patients with biochemical recurrence **N** = 70	**Intervention:** ^{68}Ga-PSMA PET-CT **Comparator(s):** No comparator	Management impact of ^{68}Ga-PSMA PET-CT	^{68}Ga-PSMA PET-CT resulted in a change in patient management in 22% of patients and guided the choice of treatment in another 22% of patients
Albisinni, 2017[30]	**Study design:** Single arm prospective cohort study **Population:** Patients with recurring prostate cancer **N** = 131	**Intervention:** ^{68}Ga-PSMA PET-CT **Comparator(s):** No comparator	Management impact of ^{68}Ga-PSMA PET-CT	Performing ^{68}Ga-PSMA PET-CT can be clinically useful in changing the treatment strategy in a significant proportion of patients
Hope, 2017[31]	**Study design:** Cross-sectional prospective study **Population:** Prostate cancer patients with biochemical recurrence **N** = 126	**Intervention:** ^{68}Ga-PSMA-11 PET-CT **Comparator(s):** No comparator	Management impact of ^{68}Ga-PSMA PET-CT	^{68}Ga-PSMA PET-CT resulted in a major change of management in 53% of patients

First Author, Year	Study Characteristics and Population	Intervention and Comparator(s)	Relevant Outcome(s)	Authors' Conclusions
Nielsen, 2017[32]	**Study design:** Single arm prospective cohort study **Population:** Patients with newly diagnosed or recurrent prostate cancer **N** = 88	**Intervention:** ^{68}Ga-PSMA-11 PET-CT **Comparator(s):** No comparator	Safety of ^{68}Ga-PSMA PET-CT	^{68}Ga-PSMA PET-CT was well tolerated and no adverse events were reported
Bluemel, 2016[33]	**Study design:** Single arm prospective cohort study **Population:** Prostate cancer patients with PSA persistence or biochemical recurrence **N** = 45	**Intervention:** ^{68}Ga-PSMA PET-CT **Comparator(s):** No comparator	Management impact of ^{68}Ga-PSMA PET-CT	^{68}Ga-PSMA PET-CT impacted the treatment planning in more than 40% of patients scheduled to undergo salvage radiotherapy
Hankenberens, 2016[34]	**Study design:** Single arm prospective cohort study **Population:** Prostate cancer patients with biochemical recurrence **N** = 29	**Intervention:** ^{68}Ga-PSMA PET-CT **Comparator(s):** No comparator	Management impact of ^{68}Ga-PSMA PET-CT	Radiotherapy based on ^{68}Ga-PSMA PET-CT showed effective local control and treatment response without clinically important side effects
Sterzing, 2016[35]	**Study design:** Retrospective cohort study **Population:** Prostate cancer patients with biochemical recurrence **N** = 57	**Intervention:** ^{68}Ga-PSMA-11 PET-CT **Comparator(s):** Conventional imaging (bone scintigraphy, CT or MRI)	Management impact of ^{68}Ga-PSMA PET-CT	^{68}Ga-PSMA PET-CT led to a change in therapy for 50.8% of cases and could be important for the individualized radiotherapy management in prostate cancer

^{18}F-DCFBC PET-CT = N-[N-[(S)-1,3-dicarboxypropyl]carbamoyl]-4-F-fluorobenzyl-L-cysteine positron emission tomography - computed tomography; ^{18}F-DCFPyL PSMA PET-CT = ^{18}Fluoro-pyridine-3-carbonyl prostate-specific membrane antigen positron emission tomography - computed tomography; ^{18}F-PSMA-1007 PET-CT = ^{18}Fluorine prostate-specific membrane antigen positron emission tomography; ^{68}GA-PSMA = ^{68}Gallium prostate-specific membrane antigen; ^{68}GA-PSMA PET = ^{68}Gallium prostate-specific membrane antigen positron emission tomography; CT = computed tomography; MRI = magnetic resonance imaging; NR = not reported; PET = positron emission tomography; PSA = prostate specific antigen; SPECT-CT = single-photon emission computed tomography; WBMRI = whole-body magnetic resonance imaging

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Health Technology Assessments

No literature identified.

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Appendix — Further Information

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