

# evidence | *note*

In response to an enquiry from SCIN PET-CT Working Group

Number 73 December 2017

## Is FDG PET/CT clinically and cost effective in the staging and/or re-staging of disease in patients with penile or testicular cancers?

### What is an evidence note?

Evidence notes are rapid reviews of published secondary clinical and cost-effectiveness evidence on health technologies under consideration by decision makers within NHSScotland. They are intended to provide information quickly to support time-sensitive decisions. Information is available to the topic referrer within a 6-month period and the process of peer review and final publication of the associated advice is usually complete within 6–12 months. Evidence notes are not comprehensive systematic reviews. They are based on the best evidence that Healthcare Improvement Scotland could identify and retrieve within the time available. The reports are subject to peer review. Evidence notes do not make recommendations for NHSScotland, however the Scottish Health Technologies Group (SHTG) produces an Advice Statement to accompany all evidence reviews.

### Key points

- There is insufficient evidence to recommend the routine use of FDG PET-CT imaging in the staging or re-staging of patients with penile or testicular cancer in NHSScotland.
- No evidence was identified which assessed the cost effectiveness of FDG PET-CT in patients with male genitourinary cancers. Therefore, no conclusions can be drawn about the cost effectiveness of FDG PET-CT in this patient group.
- The diagnostic accuracy of CT imaging as a comparator may be underestimated as reported CT imaging methods often differed from how CT imaging is performed in clinical practice in Scotland.
- Further research may be required to consider whether patient preferences could be considered alongside the risks involved in exposure to different imaging modalities.

### Definitions

**Staging:** the process of categorising patients by characteristics of their disease, for example severity, based on diagnostic findings.

**Re-staging:** the process of categorising the presence or absence of recurrence or spread of cancer following initial treatment. Restaging can also be used to monitor response to cancer treatment.

**Sensitivity:** the probability that a person having a disease will be correctly identified by a clinical test<sup>1</sup>, that is the number of true positive results divided by the total number with the disease.

**Specificity:** the probability that a person not having a disease will be correctly identified by a clinical test<sup>1</sup>, that is the number of true negative results divided by the total number of those without the disease.

## Literature search

A systematic search of the secondary literature was carried out between 8 and 16 May 2017 to identify systematic reviews, health technology assessments and other evidence-based reports. Medline, Medline in process, Medline ePub ahead of print, Embase, Cinahl and Web of Science databases were also searched for systematic reviews and meta-analyses.

Key websites were searched for guidelines, policy documents, clinical summaries and economic studies.

The primary literature was systematically searched between 22 and 23 May 2017 using the following databases: Medline, Medline in process, Medline ePub ahead of print, Embase, Cinahl and Web of Science. Results were limited to primary studies on the topics of penile cancer from 2012 onwards and testicular cancer from 2013 onwards.

The searches were conducted as part of a wider search strategy whereby concepts used in all searches included urological cancer/neoplasm, bladder, renal/kidney, urinary tract, ureter, urethra, renal pelvis, testicular, penile and positron emission tomography-computed tomography (PET/CT). A full list of resources searched and terms used are available on request.

## Introduction

Functional imaging with positron emission tomography (PET)/computed tomography (CT) (PET-CT) is widely used in the diagnosis and staging of a variety of cancer types. Imaging with PET-CT has primarily utilised <sup>18</sup>F-fluorodeoxyglucose (FDG) as a radiolabelled tracer for oncological indications (FDG PET-CT).

At present, although medical imaging forms an essential part of the staging and/or re-staging of penile<sup>2,3</sup> and testicular<sup>4-6</sup> cancers, and guidance allows for FDG PET-CT as an option at specified points within these patient pathways<sup>2-7</sup>, FDG PET-CT is not routinely indicated in the staging or re-staging for either penile or testicular cancer. The potential added diagnostic value identified from the use of FDG PET-CT imaging compared with current practice must be considered alongside its cost effectiveness. Initially, the focus of interest was to compare FDG PET-CT with imaging by either CT or magnetic resonance imaging (MRI) imaging alone. However, it was found that few studies provided any information directly comparing FDG PET-CT and CT as their main purpose because CT imaging alone is currently not used as the sole reference standard. This evidence note reviews the clinical and cost effectiveness of FDG PET-CT in the staging and/or restaging for patients with suspected penile or testicular cancer, using the reference standard(s) as described.

## Health technology description

PET-CT is a non-invasive imaging technique that combines information from two different imaging modalities: PET provides information about functional and metabolic cellular activity, while CT images give precise anatomical localisation<sup>8</sup>. The procedure usually involves injecting a radiolabelled tracer into the body, but the tracer can be ingested or inhaled. The radiolabelled tracer is taken up and accumulates in metabolically active cells (such as malignant cells), and emits gamma rays detected by the PET and CT technology to produce colour-coded images of the body demonstrating the cellular activity of both normal and malignant tissue. Images acquired from both PET and CT devices can be combined into a single superimposed image (PET-CT) and provide important diagnostic information as well as assessing the effectiveness of treatment in cancer. The radiolabelled tracers are then passed out of the body in the urine or bowel movement. . <sup>18</sup>F-fluorodeoxyglucose (FDG) is the most common radiolabelled tracer used with PET-CT imaging.

There are currently six PET-CT machines in operational use within the NHS in Scotland, although one is owned by the University of Edinburgh [Personal communication with National Services Scotland, 22 August 2017].

## Epidemiology

Penile cancer is uncommon in developed countries, although there are variations according to ethnicity and geographical location.<sup>3</sup> Risk factors include exposure to the human papilloma virus (HPV), smoking and deprivation. Circumcision, particularly from birth, appears to be protective against penile cancer.<sup>2</sup> In Scotland, 71 cases of penile cancer were diagnosed in 2015. In the last 25 years, the number of cases diagnosed annually has generally increased but it is not clear whether the increase is statistically significant.<sup>9</sup> Mortality from penile cancer has also increased in recent years, but owing to the low incidence, the number of people affected is low and there were 23 deaths from penile cancer registered in Scotland in 2015.<sup>9</sup> Whilst it can be cured in most cases if diagnosed early, it has been noted that life-saving treatment can still be mutilating and/or potentially devastating for the patient's psychological wellbeing.<sup>2</sup>

Testicular cancer is currently the 16<sup>th</sup> most common cancer in men in Scotland and approximately one in every 183 men will be diagnosed with testicular cancer before the age of 90.<sup>9,10</sup> Genetic markers may indicate elevated risk, as can familial history of testicular tumours and being Caucasian. Short stature may be protective against the disease but further research on this is required.<sup>5</sup> Scottish incidence data appear to show a trend of slight increase over recent years,<sup>9</sup> and such a trend has also been seen in other industrialised countries.<sup>5</sup> Nevertheless, testicular cancer has the highest 5-year survival rate of all cancers affecting men in Scotland, with 93.4% of men alive 5 years after diagnosis.<sup>10</sup> This is likely due to testicular cancer being particularly sensitive to chemotherapy.<sup>5</sup> However, the toxicity of these agents is significant: treatment-related deaths and long term effects have been documented, including impacts on outcomes such as employment and fertility,<sup>4</sup> which is pertinent owing to the fact that the disease typically affects men aged between 15 and 40 years old.<sup>6</sup>

## Current guidelines

At present, the staging and/or re-staging of penile cancer typically involves the use of routine imaging techniques including ultrasound and MRI.<sup>2,3</sup> CT imaging is recommended for exploration of the pelvic lymph nodes to check for metastatic disease as palpable lymph nodes in this area are highly suspicious. FDG PET-CT is noted as an imaging option for confirmation,<sup>2</sup> although its value at present is uncertain.<sup>3</sup> FDG PET-CT is also noted as an option for identifying distant metastases where there is confirmed positive lymph node involvement<sup>2</sup> where its use is described as 'encouraging'.<sup>3</sup>

In testicular cancer, current Scottish guidance for the staging of testicular cancer requires contrast-enhanced CT imaging.<sup>4</sup> MRI is indicated as helpful in situations where CT results are inconclusive<sup>4</sup> but involvement of PET imaging does not contribute to initial staging.<sup>6</sup> For recurrent disease, re-staging requirements may depend on the tumour type. For example, FDG PET-CT is noted as an option within the European Urology Association (EAU) and European Society for Medical Oncology (ESMO) recommendations for the follow-up of seminoma patients post-chemotherapy<sup>5, 6</sup>, although not as part of routine follow-up investigations.<sup>4</sup> Timing of imaging may influence diagnostic results,<sup>4-6</sup> therefore a recommended wait upon completion of chemotherapy of at least 6 weeks is recommended,<sup>5, 6</sup> and certainly not less than 2 weeks.<sup>4</sup> The size of the residual mass is also a factor in the decision to utilise FDG PET-CT as it is indicated for larger (>3cm) tumours, although it is still optional for smaller lesions of this type.<sup>5</sup> For other types of tumour, in non-seminomatous disease, there is currently insufficient evidence to recommend FDG PET-CT<sup>5</sup>. For teratoma, SIGN guidelines note specificity concerns as “differentiated teratoma may not show uptake on FDG-PET scanning” owing to the use of FDG as a tracer.<sup>7</sup>

## Clinical effectiveness

Three Health Technology Assessment (HTA) agency reports were identified as having explored PET and/or PET-CT, including FDG PET-CT.<sup>11-13</sup> However, with the exception of one systematic review by Treglia and colleagues<sup>14</sup> included in the HTA report by Paone and colleagues,<sup>11</sup> the studies identified in these reports for testicular and penile cancers relate specifically to the use of standalone PET images rather than PET/CT hybrid images and so do not inform the evidence base.

Although all studies used a combination of either/both histopathology findings and regular follow-up imaging as the reference standard, studies varied in how recurrence and response were defined. This has implications for pooling the results.

## Penile cancer

One systematic review which met the inclusion criteria was identified.<sup>15</sup> The review is of reasonably high quality in terms of its reproducibility and the methods described, although search dates were not stated and the inclusion criteria were very broad (no date or language restrictions and meeting abstracts were included). It compared FDG PET-CT as the index test for staging penile squamous cell carcinoma against either inguinal lymph node dissection (or sentinel node biopsy) and/or follow-up of the patients as the gold standard. Only studies enabling 2x2 sensitivity and specificity were included and the quality of included studies was assessed using the Oxford Centre for Evidence-Based Medicine checklist<sup>16</sup> for diagnostic studies. Data on sensitivity and specificity are reported and pooled at the sample specimen level (for example groin imaging or biopsy of each individual lesion) and not the individual patient level.

Of note is that the systematic review inclusion criteria were broad. Two included studies were conference abstracts and a third was identified in our own search but excluded as it is a study of only three patients. In addition to the remaining four studies in this review,<sup>17-20</sup> our own search identified a further two primary studies comparing FDG PET-CT with the reference standard, both likely published after the original review concluded its searches.<sup>21 22</sup>

Details of the identified studies from the systematic review are provided in Table 1. Pooled sensitivity for the detection of inguinal lymph node involvement was 0.81 (95% confidence interval (CI) 0.7 to 0.89). Sensitivity in the more recent study by Souillac and colleagues (0.91) exceeded the confidence intervals for the pooled sensitivity in this review and had a larger sample size (60 inguinal lymph node areas) than all but one<sup>20</sup> of the review included studies. Pooled specificity in the review was 0.92 (95% CI 0.87 to 0.96). Of note is that for one study by Graaftland and colleagues,<sup>18</sup> specificity is dependent on how stable disease is defined. The authors of

this study defined stable disease via “a multidisciplinary tumour board after [patients had] two cycles of chemotherapy” as being indicative of response, but it is possible that a different group of clinicians could define it differently.

The systematic review concluded that FDG PET-CT imaging has relatively low sensitivity for the detection of inguinal lymph node involvement in penile cancer patients and, therefore, its routine use is not justified.<sup>15</sup>

Two studies had published sufficient evidence to compare CT alone, with the reference standard.<sup>18, 21</sup> In these studies, sensitivity results were identical to the FDG PET-CT results, but specificity results were poorer in one study,<sup>21</sup> and specificity in the other study was dependent on how stable disease was defined.<sup>18</sup> It must also be noted that CT was not always performed as contrast enhanced CT, which may have implications for the results depending on how CT is performed in clinical practice among these patients.

Unless the study population specifically referred to staging or re-staging, studies did not always separate results by this issue. However, where this was done, sensitivity was 0.2 for staging<sup>19</sup> and 0.91 for restaging<sup>17</sup>, and specificity was 0.92 for staging<sup>19</sup> and 1 for re-staging.<sup>17</sup>

Table 1: Characteristics of included studies (penile cancer)

| Source       | Author Year     | Setting (Country)                    | Duration (months) | Study purpose   | Reference standard   | Tools used to quantify disease on FDG PET-CT               | Data collection | Sample size (images) | Median age (range)        | Median follow-up (months) | Was CT performed as contrast enhanced? |
|--------------|-----------------|--------------------------------------|-------------------|---|--|--|-----------------|----------------------|---------------------------|---------------------------|--|
| Sadeghi 2012 | Leijte 2009     | Single hospital centre (Netherlands) | 14                | Staging clinically node negative patients   | Histopathology (Dynamic Sentinel Node Biopsy)  | Lesions categorised by clinicians but SUVmax not mentioned | Prospective     | 24 (42)              | 61 (46-82)                | 15.4 (11-28 months)       | No                                     |
| Sadeghi 2012 | Graaftland 2009 | Single hospital centre (Netherlands) | 40                | Re-staging for pelvic node involvement in patients with lymph node involvement                            | Histopathology of surgical specimens/ images for metastases beyond loco-regional lymph nodes | Lesions categorised by clinicians but SUVmax not mentioned | Retrospective   | 21 (28)              | 62 (46-73)                | 7 (1-31 months)           | Not in all cases                       |
| Sadeghi 2012 | Graaftland 2010 | Single hospital centre (Netherlands) | 46                | Monitoring treatment response in patients with inoperable advanced disease but without distant metastases | Multi-disciplinary board defined response or non-response                                    | SUVmax used to inform results                              | Retrospective   | 8 (8)                | 66 (52-79)                | N/R                       | No                                     |
| Sadeghi 2012 | Schlenker 2012  | Single hospital centre (Germany)     | 55                | Assess lymph node involvement   | Histopathology (diagnosis had been confirmed at baseline).                                   | Imaging lesions categorised by clinician but SUVmax        | Prospective     | 35 (70)              | 60.6 <sup>†</sup> (36-80) | 31 (31-68 months)         | Yes                                    |

| Source        | Author Year   | Setting (Country)               | Duration (months) | Study purpose  | Reference standard                                  | Tools used to quantify disease on FDG PET-CT   | Data collection | Sample size (images) | Median age (range) | Median follow-up (months) | Was CT performed as contrast enhanced? |
|---------------|---------------|---------------------------------|-------------------|--|---|--|-----------------|----------------------|--------------------|---------------------------|--|
|               |               |                                 |                   |  |   | not mentioned  |                 |                      |                    |                           |  |
| Primary Study | Souillac 2012 | Single hospital centre (France) | 58                | Assess lymph node involvement in "invasive" disease  | Biopsy or follow-up imaging                         | Imaging lesions categorised by clinician but SUVmax not mentioned                          | Prospective     | 30 (60)              | 69 (41-94)         | N/R                       | Not reported                           |
| Primary Study | Zhang 2016    | Single hospital centre (China)  | 44                | Staging/re-staging among those with suspected disease/ follow-up after treatment for disease | Histopathology from biopsy or surgery for treatment | SUVmax is mentioned but it is unclear whether it informed clinicians' assessment of images | Prospective     | 48 (42)              | 56.6 (29-77)       | N/R                       | Not reported                           |

† Data reported as mean rather than median

One study<sup>22</sup> reported additional outcomes on a survey of clinicians about the effect of FDG PET-CT imaging on patient management. Results indicate disease management was influenced in 25 of 44 patients (56.8%). Accounting for the fact that other types of imaging could have also influenced management in the absence of FDG PET-CT, this was 40.9% of patients (18/44). Treatment was commenced and/or altered in at least eight patients and additional tests (biopsy and/or additional imaging) were avoided in at least seven patients.

### Testicular cancer

One systematic review was identified<sup>14</sup> containing a meta-analysis of the diagnostic accuracy of FDG-PET or FDG PET/CT in post-chemotherapy management of patients. Two of the included nine studies specifically looked at FDG PET/CT,<sup>23, 24</sup> with the other seven looking at FDG PET without CT. The diagnostic accuracy of FDG PET-CT is likely to be superior to the diagnostic accuracy of FDG PET, potentially underestimating the diagnostic accuracy of FDG PET-CT. However, by pooling a mixture of FDG PET and FDG PET-CT studies, the meta-analysis is not consistently considering the additive effect of the PET component of FDG PET-CT compared with CT alone. Nevertheless, both the FDG PET-CT studies had large sample sizes (third and fourth largest of the nine studies), so the overall effect is unclear. The details included in the review from the study by Ambrosini and colleagues are actually a sub-sample of the patients included in the primary study, due to the review inclusion criteria. The review only includes the seminoma patients at restaging, follow-up after treatment or at suspected relapse. Additional diagnostic accuracy details from other testicular cancer patient groups (seminoma patients undergoing staging after primary surgery and non-seminoma patients at each of the aforementioned stages) are available from the primary study.<sup>23</sup>

There are some deficiencies in the review methods, but they are adequate. Reproducibility is reasonable, although the authors followed guidance relating to the reporting of systematic reviews in general (the PRISMA statement) when more specific guidance is available for diagnostic accuracy studies (the STARD statement) and there is a lack of detail about any comparator tests and/or the reference standard in the inclusion criteria. Quality assessment using the Oxford Centre for Evidence-Based Medicine checklist has been undertaken, and consideration has been given to publication bias using statistical methods to characterise this. Five additional primary studies were identified from our search<sup>25-29</sup> and all except one<sup>29</sup> were published more recently than the review. Of note, the study by Sterbis and colleagues is assumed to have performed FDG PET-CT but the radiolabelled tracer described in the methods is unspecified.<sup>29</sup> Details of the included studies can be found in Table 2.

Pooled sensitivity from the review was 0.78 (95% CI 0.67 to 0.87). This was exceeded in three out of the five primary studies identified.<sup>26, 28, 29</sup> It reached 0.89 in the study by Kassem and colleagues, 0.93 in the study by Sterbis and colleagues and 0.94 in the study by Sharma and colleagues.

Pooled specificity from the review was 0.86 (95% CI 0.81 to 0.89). Compared with data from the identified primary studies, the confidence intervals for this pooled specificity were exceeded by the results of two of the studies; by Nikoletic and colleagues where it was 0.9, and in the study by Sterbis and colleagues where it was 0.97. However, in the study by Sharma and colleagues specificity was poorer than the confidence intervals for the pooled review result, at 0.75.<sup>27-29</sup> Review authors concluded FDG PET-CT was demonstrated to be accurate in the post-chemotherapy management of patients with seminoma, although they noted the literature focusing on the use of FDG PET and PET-CT in this setting remains limited.

Unless the study population specifically referred to staging or re-staging, studies did not always separate results by this issue. However, where this was done, sensitivity for staging disease ranged from 0.6 to

0.93 and specificity ranged from 0.88 to 1.<sup>23, 25, 26, 29</sup> For re-staging, sensitivity ranged from 0.77 to 0.94, and specificity ranged from 0 to 0.95.<sup>23, 25, 28</sup> However, the poor specificity is due to one study<sup>25</sup> reporting imaging results for patients who were re-staged due to rising tumour markers whereby no true negative results or false positive results were found and so specificity is actually incalculable. When this result is removed, specificity ranged from 0.75 to 0.95.

Table 2: Characteristics of included studies (testicular cancer)

| Source        | Author Year    | Setting (Country)               | Duration (months) | Study purpose   | Reference standard  | Tools used to quantify disease on FDG PET-CT            | Data collection | Sample size (images)                   | Median age (range) | Median follow-up (range)       | Was CT performed as contrast enhanced? |
|---------------|----------------|---------------------------------|-------------------|---|---|---|-----------------|--|--------------------|--------------------------------|--|
| Treglia 2014  | Ambrosini 2014 | Single hospital centre (Italy)  | 106               | Staging and/or re-staging upon follow up after treatment or suspicion of recurrence           | “Clinical, imaging and follow-up data” (not further described). | Uptake used to define images, but SUVmax not mentioned. | Retrospective   | 56 (45 in review subgroup/ 121 images) | 37.7‡ (16-66)      | 2.9‡ years (0.01 to 8.8 years) | Yes                                    |
| Treglia 2014  | Siekiera 2012  | Single hospital centre (Poland) | 60                | Follow up of patients with seminoma after chemotherapy/ radiotherapy                          | Histopathology (from RPLND dissection) or follow-up images      | SUVmax not mentioned.                                   | Retrospective   | 60 (37)                                | N/R                | 40 months (NR)                 | Not reported                           |
| Primary study | Cook 2015      | Unclear (England)               | 82                | Staging and/or re-staging upon follow up after treatment                                      | Histopathology, follow-up images or tumour marker assessment    | SUVmax used to inform results.                          | Retrospective   | 62 (75)                                | 34.8‡              | 36 months (3-77)               | Not reported                           |
| Primary study | Kassem 2016    | Single hospital centre (Egypt)  | N/R               | Pre-operative staging after diagnosis   | Histopathology (surgery or biopsy) and tumour serum markers     | SUVmax used to inform results.                          | Prospective     | 34 (34)                                | 33‡ (22-56)        | N/R                            | No                                     |
| Primary study | Nikoletic 2015 | Single hospital centre (Serbia) | N/R               | Patients with testicular carcinoma being referred for PET-CT imaging for various reasons (for | Histopathology, follow-up images or tumour serum markers        | SUVmax not mentioned.                                   | Retrospective   | 23 (25)                                | 35.5‡ (20-54)      | N/R                            | No                                     |

| Source        | Author Year  | Setting (Country)                     | Duration (months) | Study purpose  | Reference standard  | Tools used to quantify disease on FDG PET-CT | Data collection | Sample size (images) | Median age (range)        | Median follow-up (range) | Was CT performed as contrast enhanced? |
|---------------|--------------|---------------------------------------|-------------------|--|---|--|-----------------|----------------------|---------------------------|--------------------------|--|
|               |              |                                       |                   | example abnormal CT)   |   |  |                 |                      |                           |                          |  |
| Primary study | Sterbis 2010 | Single veterans hospital centre (USA) | 39                | Staging/evaluation of patients with testicular cancer  | Histopathology (from RPLND) or follow-up images or tumour serum markers | SUVmax used to inform results                | Prospective     | 49 (49)              | 27 (19-57)                | 39 months (4-85)         | No                                     |
| Primary study | Sharma 2014  | Single hospital centre (India)        | 13                | Re-staging of primary malignant germ cell tumours upon suspicion of recurrence or post-chemotherapy evaluation | Histopathology and/or follow-up images or tumour serum markers          | SUVmax used to inform results                | Retrospective   | 92 <sup>†</sup> (92) | 31.94 <sup>‡</sup> (3-66) | 13 months (6-26)         | Yes                                    |

<sup>†</sup>Includes six female participants with germ cell tumours.

<sup>‡</sup>Reported mean rather than median

Ambrosini and colleagues reported the change in clinical management as a result of the addition of FDG PET-CT, in 106 of the 121 images (82.1%). In most of these cases (77 images), the result was surveillance rather than a commencement, change or continuation of treatment (29 images). Nevertheless, the number of CT images that may have changed clinical practice in the absence of hybrid FDG PET-CT imaging is not clear.<sup>23</sup>

### Patient experience

Patients may have preferences for how they are managed. In testicular cancer this has to be considered alongside guidance on the risks of management involving radiation-emitting imaging technologies, given the average age of disease onset in this population is younger.<sup>5,6</sup> In addition, patients may elect to receive treatment where imaging results are equivocal (on CT) or negative (FDG PET-CT), and the study by Cook and colleagues reports this occurring in NHS clinical practice in England.<sup>25</sup>

In penile cancer, the population is older and invasive procedures required to assess the extent of disease, let alone treat the disease, may concern patients. Zhang and colleagues noted that biopsy is not always possible because of the risk with lesions deep in the pelvis near vascular structures, or patient refusal, and in such cases they argue that PET-CT could prove useful.<sup>22</sup> Whether this is relevant to existing clinical practice in Scotland, or would be useful to consider for future practice, is unclear.

### Safety

None of the included studies quantified radiation exposure for either hybrid PET-CT or CT alone, even though the guidance, particularly for testicular cancer, stipulates concern about routine use of imaging tests that expose patients to radiation.<sup>2,3,5,6</sup>

One study noted the potential value of using FDG PET-CT in patients who were allergic to intravenous contrast used in CT images.<sup>29</sup> However, it is not clear if intravenous contrast is typically used in CT images for these indications, or if the prevalence of such an allergy is sufficient to warrant an amendment to existing clinical practice.

### Cost effectiveness

No evidence was identified which assessed the cost effectiveness of FDG PET-CT in patients with male genitourinary cancers.

The HTA report by Paone and colleagues<sup>11</sup> contains a chapter on cost effectiveness. However, the evidence identified in two studies related specifically to lung and pancreatic cancer and the report authors note the medium/poor methodological quality of the two studies.

### Conclusion

There is insufficient evidence that FDG PET-CT is clinically useful when compared with the current reference standard incorporating histopathology and/or regular follow-up imaging in the staging and re-staging of penile cancer or testicular cancer patients. As CT imaging is not the current reference standard in the staging and/or re-staging of these patients, and as the research studies in most cases avoided contrast enhancement on CT imaging, it was not possible to directly compare FDG PET-CT and CT imaging alone in order to quantify any additional benefit that FDG PET-CT might have over CT in clinical practice.

As no evidence was identified which assessed the cost effectiveness of FDG PET-CT in patients with male genitourinary cancers, no conclusions can be drawn about the cost effectiveness of FDG PET-CT in this patient group.

In addition, although there is some evidence to indicate that the results of an FDG PET-CT image can influence clinical management, and that for specific individual patient circumstances it may be a useful tool in addition to methods used in current practice, the evidence base at present cannot justify a change to the routine use of PET-CT for the staging and/or re-staging of penile or testicular cancer patients in the NHS in Scotland.

### Identified research gaps

Direct comparisons between FDG PET-CT and CT alone were not possible as neither imaging technique is the current reference standard on its own. It is possible that a larger review could consider each imaging modality compared to the reference standard, but in many cases the reference standard involved the use of follow-up imaging and so a considerable degree in heterogeneity owing to the methods is expected.

No studies routinely utilised MRI imaging as an imaging modality among these study populations and no studies considered the comparative radiation exposure of FDG PET-CT compared with CT imaging alone and so any important trade-offs in terms of the benefits and harms of imaging alternatives for patients wishing to spare particularly invasive procedures for surveillance of cancer, are unclear at this point.

### Equality and diversity

Healthcare Improvement Scotland is committed to equality and diversity in respect of the nine equality groups defined by age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion, sex, and sexual orientation.

The process for producing evidence notes has been assessed and no adverse impact across any of these groups is expected. The completed equality and diversity checklist is available on [www.healthcareimprovementscotland.org](http://www.healthcareimprovementscotland.org)

### About evidence notes

Evidence Notes are produced to inform a decision at a particular point in time and are therefore not routinely updated. They will however be considered for review if requested by stakeholders, based upon the availability of new published evidence which is likely to materially change the advice given.

For further information about the evidence note process see:

[www.healthcareimprovementscotland.org/our\\_work/clinical\\_cost\\_effectiveness/shtg/standard\\_operating\\_procedures.aspx](http://www.healthcareimprovementscotland.org/our_work/clinical_cost_effectiveness/shtg/standard_operating_procedures.aspx)

To propose a topic for an evidence note, email [shtg.hcis@nhs.net](mailto:shtg.hcis@nhs.net)

References can be accessed via the internet (where addresses are provided), via the NHS Knowledge Network [www.knowledge.scot.nhs.uk](http://www.knowledge.scot.nhs.uk), or by contacting your local library and information service.

A glossary of commonly used terms in Health Technology Assessment is available from [htaglossary.net](http://htaglossary.net).

## Acknowledgements

Healthcare Improvement Scotland and SHTG invited the following individuals and organisations to peer review the draft evidence note:

- Dr John Brush, Consultant Radiologist & Lead Clinician for Radiology, NHS Lothian
- Dr Ross Clark, Consultant Urologist, NHS Ayrshire & Arran

Declarations of interest were sought from all peer reviewers. All contributions from peer reviewers were considered by the group. However the peer reviewers had no role in authorship or editorial control and the views expressed are those of Healthcare Improvement Scotland. The DOI Code of Practice is available from the Healthcare Improvement Scotland website.

## Healthcare Improvement Scotland development team

- Jenni Hislop, Lead Author/Health Economist
- Paul Herbert, Information Scientist
- Karen McGeary, Communications and Publications Co-ordinator
- Shonagh Ramsey, Project Officer
- Members of the SHTG evidence review committee (membership details can be found on the Healthcare Improvement Scotland website)

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