MSAC Application 1822

F-18 Fluorodeoxyglucose (FDG) positron emission tomography (PET) for evaluation of complex infection

PICO Set 2

F-18 FDG for complex infection

Population

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

FDG-PET for complex infection is intended primarily for patients in whom standard initial clinical evaluation (which may include conventional imaging) have not provided a definitive diagnosis of infection, are contraindicated, or where the infection is difficult to localize or characterize. It is a second-line investigative tool in challenging cases where treatment decisions depend on accurate and timely identification of sites of infection, which includes:

- Suspected spinal infections (vertebral osteomyelitis, discitis or epidural abscess)
- Suspected osteomyelitis in cases of a known soft tissue infection (including diabetic foot ulcers), fracture related osteomyelitis, and to assess for dissemination of infection to other skeletal sites or organs
- Suspected bone and joint infections in children, where FDG-PET can remove the necessity for general anaesthesia (as required for MRI) and enable better ability to distinguish between acute and chronic infections, or reparative bone tissue;
- Suspected prosthetic joint infection or other orthopaedic hardware infection, if more than 2 years post-surgery
- Suspected infective endocarditis, including following congenital heart disease, or due to prosthetic valve infection, cardiac implantable electronic device infection and septic emboli
- Extrapulmonary non-tuberculous mycobacterial (EPNTM) infection
- Bacteraemia (for example *Staphylococcus aureus* or other pathogens with a high risk of metastatic infection) where metastatic infection is suspected

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:

<u>Spinal Infection</u>

Patients with spinal infection most commonly present to their healthcare provider with back pain, which may be the sole presenting symptom. Fever is absent in up to half of cases, contributing to frequent delays in diagnosis. Many patients initially undergo plain radiography to exclude more common causes of back pain; however, X-rays are typically insensitive in the early stages of spinal infection. A thorough clinical history and physical examination are essential to raise suspicion, and wherever possible, the source and causative organism should be identified prior to initiation of antibiotic therapy.

Initial investigations for suspected spinal infection include:

- Laboratory testing—white blood cell count, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR)
- Contrast-enhanced Magnetic Resonance Imaging (MRI)[1]
  When first-line investigations are non-diagnostic or contraindicated, additional imaging is required. Computed tomography (CT) may demonstrate bony destruction but is less sensitive for early disease. Nuclear medicine studies, including gallium-67 SPECT, bone

scintigraphy, or labelled white blood cell scans, may also be used to identify inflammatory or infective activity[2].

In this second-line setting, when MRI fails to establish a diagnosis, FDG PET/CT is increasingly being proposed as the preferred imaging modality. Evidence suggests that FDG PET/CT has higher sensitivity for early-stage spinal infection than CT alone[3] and demonstrates similar or superior diagnostic performance compared with traditional nuclear medicine techniques. With increasing availability and advantages over older tracers such as gallium-67[4], FDG PET/CT is emerging as a valuable tool in the diagnostic pathway for spinal infection.

Osteomyelitis

In Australia, a patient with suspected osteomyelitis typically presents to a healthcare provider with fever, pain, swelling and inflammation. Initial assessment includes evaluation of local symptoms (bone pain, swelling, reduced function), systemic features, and risk factors such as diabetes, recent trauma, surgery, or immunosuppression.

First-line investigations include:

- FBC, ESR, CRP, EUC, LFT
- Plain X-ray of affected area (any periostitis, osteopenia)
- Microscopy and culture of any discharge or aspirate collected
- Blood cultures (in adults - two sets collected from separate sites)[5]

When first-line investigations fail to provide a diagnosis, patients are routinely referred for one of the following:

- Biopsy of infected site
- Nuclear Medicine imaging (bone scan, labelled WBC scan)
- Radiography (CT and/or MRI if advanced infection)

Guidelines from the EANM, EBJIS, ESR and ESCMID have suggested that both nuclear medicine or radiography technique are equivalent as second-line investigations, depending on availability and expertise, however have recommended the use of FDG PET-CT for bone infection for patients without metallic hardware, recent surgery or fracture, as well as for suspicion of dissemination, or if radiography investigations were equivocal[6].

Prosthesis

Patients with suspected prosthetic infections will consult their healthcare provider similarly to those with osteomyelitis, presenting with fever, pain, swelling and inflammation on the background of a prosthetic implant. Initial assessment includes evaluation of local symptoms (bone pain, swelling, reduced function), systemic features, and risk factors such as diabetes, recent trauma, surgery, or immunosuppression.

First-line investigations include:

- FBC, ESR, CRP, EUC, LFT
- Plain X-ray of affected area (any periostitis, osteopenia, loosening of prosthesis)
- Microscopy and culture of any discharge or aspirate collected
- Blood cultures (two sets collected from separate sites)

If the initial prosthesis surgery was less than 2 years prior, the patient will receive a referral to orthopaedic surgery to continue their care, otherwise will be treated by the infectious diseases specialists.

As with osteomyelitis, when first-line investigations fail to provide a diagnosis, patients are routinely referred for one of the following:

- Biopsy of infected site
- Nuclear Medicine imaging (bone scan, labelled WBC scan)
- Radiography (CT and/or MRI if advanced)

Guidelines from the EANM, EBJIS, ESR and ESCMID have suggested that either nuclear medicine or radiography technique is the preferred standard, depending on availability and expertise however, have recommended the use of FDG PET-CT prosthetic joint infection for patients whose prosthesis is greater than 2 years old, as the high sensitivity will exclude infection if negative[7].

Cardiac Infection

Infective endocarditis (IE) typically affects patients with underlying cardiac risk factors, including those with prosthetic heart valves, previous endocarditis, congenital heart disease, rheumatic heart disease, or implanted cardiac devices. Clinically, patients may present with non-specific symptoms such as fever, malaise, weight loss, and night sweats, or with more specific features including new or changing heart murmurs, and embolic or immunological phenomena, (petechiae, splinter haemorrhages, Osler nodes, or Janeway lesions)[8].

Investigation of suspected IE in Australia follows established guideline-based practice. Initial assessment includes thorough history and examination, and if suspicion is high, referral to emergency care.

First line investigations include:

- 3 blood cultures taken at 3 different time points:
- Full blood count
- C-Reactive protein or Erythrocyte sedimentation rate
- Urine MCS
- ECG: look monitoring for widening PR interval, p mitrale, T-wave inversion, dysrhythmia
- Transthoracic Echocardiogram[9,10]

Diagnosis is based on the modified Duke criteria, which integrate clinical features, microbiological evidence, and imaging findings to classify cases as “definite infective endocarditis,” “possible infective endocarditis,” or “rejected infective endocarditis.” A positive FDG PET/CT scan is recognised as one of the ten major criteria, and the presence of three major criteria is sufficient to establish a diagnosis of definite infective endocarditis[11].

In most cases, infective endocarditis is diagnosed using blood culture results in combination with transthoracic or transoesophageal echocardiography. However, in patients classified as having “possible” or “rejected” infective endocarditis despite a high degree of clinical suspicion, FDG PET/CT is strongly recommended to aid diagnostic clarification, particularly in those with prosthetic heart valves. This approach is supported by guidelines from the European Society of

Cardiology, the European Association for Cardio-Thoracic Surgery, and the European Association of Nuclear Medicine[12]

Bacteraemia

Patients with bacteraemia may present to their healthcare provider or emergency department with fever, rigors, hypotension, and systemic inflammatory response, or with more subtle features such as delirium, malaise, or unexplained deterioration. Metastatic infection should be suspected when there are focal symptoms or signs indicating secondary seeding, such as back pain, joint pain and swelling, focal neurological deficits, persistent fever despite antibiotics, or recurrent positive blood cultures[13].

Investigation within the Australian health care system prioritises early identification of the causative organism and potential secondary infection sites. Initial investigations include history and physical examination. First line investigations include:

- Blood cultures
- Blood test (full blood count, inflammatory markers, renal and liver function tests, and lactate)
- ECG to rule out endocarditis
- Targeted Imaging (depending on location suspicion)[14]

The role of FDG PET/CT is increasingly being proposed as a diagnostic test of choice for targeted imaging of bacteraemia, especially when metastatic infection is suspected. Unlike conventional imaging modalities that focus on a specific region, FDG PET/CT provides whole-body functional imaging, particularly useful in Staphylococcus aureus bacteremia, where metastatic complications are common and often clinically silent, and where early identification of infectious foci can meaningfully guide targeted therapy and interventions[15].

Extrapulmonary Non-Tuberculous Mycobacterial (EPNTM) infection

Clinical presentations of NTM infections are highly variable and depend on both host and pathogen factors. Infections in both immunocompetent and immunocompromised may present acutely as febrile illnesses with haemodynamic compromise in those with disseminated infection or as subacute presentations with weight loss, night sweats, recurrent or relapsing skin and soft tissue lesions, persistent cough or pain in affected bones and joints. Therefore, care may be sought in primary care or tertiary subspeciality care within public and private health systems.

Clinical suspicion of the possibility of NTM infection in the differential diagnosis is key to initiation of appropriate first line investigations and may include:

- Mycobacterial blood cultures
- Tissue biopsies culture of affected areas (eg. skin, soft tissues, bone biopsy, joint washout fluid, sputum or deep respiratory specimen samples) specifically cultured for mycobacteria
- Histology of tissue biopsies to confirm presence/absence of granulomatous inflammation and/or acid-fast bacilli (AFB)
- Targeted imaging depending on the location of clinical symptoms/signs and may include CT and/or MRI[16]

There is an evolving body of published literature evaluating the potential role for FDG PET/CT for the management of NTM infections that is lagging behind real-world clinical application and utility of FDG PET/CT imaging. Due to its ability to provide whole-body functional imaging, FDG PET/CT has been utilised clinically with good clinical outcomes to both document the extent of dissemination of EPNTM infections at the outset to guide duration of induction phase of combination antimicrobial agents, delineate the extent of tissue involvement to facilitate optimal source control which is a cornerstone to achieving cure of infection and for confirmation of cure at completion of long courses of therapy (6-12 months minimum) or detecting early relapse of infection in a similar manner to its utility in monitoring treatment and relapse in cancer care[17,18].

Provide a rationale for the specifics of the eligible population:

Eligible patients are those who have already undergone standard baseline investigations for complex infection. Initial investigations identifies a cause in many cases using low-cost, high-yield methods. Performing FDG PET/CT only after this stage ensures it is used when true diagnostic uncertainty persists, avoiding unnecessary cost.

Scanning later than this window may increase healthcare costs from utilisation of lowered sensitivity scans, delay definitive intervention, and increase morbidity and hospital stay. Therefore, the optimal timing for FDG PET/CT is immediately after negative baseline investigations but before extended empirical management, when whole-body metabolic imaging is most likely to localize occult infection, inflammation, or malignancy and meaningfully alter clinical management.

The listed infectious diseases have been selected based on a substantial body of evidence demonstrating the clinical utility of FDG PET in these settings, with most studies reporting sensitivities exceeding 85% and/or high negative predictive values for excluding active disease[19].

Are there any prerequisite tests?

Yes

Are the prerequisite tests MBS funded?

Yes

Provide details to fund the prerequisite tests:

Provide a response if you answered 'No' to the question above

Intervention

Name of the proposed health technology:

^{18}F-FDG PET/CT

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

18F-FDG can be produced on-site in facilities equipped with a cyclotron and radiopharmacy or obtained from a commercial supplier. Patients are required to fast for 4–6 hours prior to administration. The FDG is administered intravenously approximately 60 minutes before imaging, during which patients remain resting quietly in a dimly lit room to minimize muscular and brown fat uptake. After this period, patients are transferred to the PET camera room and positioned on the scanning bed for image acquisition.

The administered activity of 18F-FDG depends on patient body mass and PET scanner specifications. For an average 75 kg individual, typical activity ranges from 180 to 260 MBq, and dosage is generally calculated at approximately 3-5 MBq per kilogram of body weight, with ARPANSA recommending 3.5MBq/kg. Estimated effective doses for patients receiving between 150 and 450MBq of FDG are 3-9mSv.[20]

PET imaging is performed according to a standardized protocol, which typically incorporates a low-dose CT scan for attenuation correction and anatomical localization. These CTs generally add 4-5mSv radiation dose depending on arm position and length of scan. When clinically indicated by the referring physician, a diagnostic-quality CT may be performed concurrently, often with oral and/or intravenous contrast, resulting in a PET/CT diagnostic study whereby the PET images can be directly fused to the diagnostic CT images for additional information. The PET field-of-view is generally determined by the clinical indication but most commonly spans from the base of the skull to the upper thighs or to the toes, offering an entire-body investigation, but can be localised to specific areas of clinical concern if deemed appropriate by referrer and reporting doctor. Acquisition times for modern PET scanners are usually under 30 minutes, although the exact duration depends on the scanner's performance characteristics, the extent of the field-of-view, and the administered FDG activity.

PET images are generally reconstructed using the manufacturer's recommended protocols and software, fusing the acquired PET images to the localisation CT or the diagnostic CT if performed.

Interpretation of the images, including any available correlated imaging, is performed by a nuclear medicine specialist, who prepares a clinical report for the referring clinician.

Identify how the proposed technology achieves the intended patient outcomes:

FDG PET/CT uses 18F-fluorodeoxyglucose (FDG), a radioactive glucose analogue, to detect infection by identifying areas of increased glucose metabolism. During infection, activated immune cells display heightened glycolytic activity, increased blood flow, and inflammatory cell recruitment. FDG accumulates in these metabolically active cells, appearing as "hot spots" on the scan. Due to the metabolic nature of FDG uptake, infection can be detected before structural changes become visible, and the whole-body uptake allows scanning of the entire body without additional radiation dose, allowing detection of unknown foci for patients with infections of unknown origins.

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

No

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):

No

Provide details and explain:

Patients should only require a single PET scan to establish or exclude diagnosis of infection. As infections can occur multiple times per lifetime, especially in the most vulnerable populations, placing any restrictions on the number of scans allowable can be highly detrimental.

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

PET services are provided by credentialled nuclear medicine specialists registered with general or specialist registration and have recognition by AHPRA as a specialist in nuclear medicine.

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

PET services are a specialised service that can only be provided by trained and registered Nuclear Medicine specialists, who consult on and obtain consent from the patient, tailor the scan dependent on medical indication, and prepare a report using the relevant clinical data. Equipment handling and radiopharmaceutical administration are performed by trained and registered Nuclear Medicine Technologists. Other staff may be involved, including clerical staff and nurses.

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

PET services are provided on request from a medical specialist

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:

18-F FDG PET scans for infection imaging will be performed by:

a) a nuclear medicine specialist or consultant physician credentialled under the Joint Nuclear Medicine Specialist Credentialling Program for the Recognition of the Credentials of Nuclear Medicine Specialists for Positron Emission Tomography overseen by the Joint Nuclear Medicine Credentialling and Accreditation Committee of the RACP and RANZCR;

or

b) a practitioner who is a Fellow of either RACP or RANZCR, and who, prior to 1 November 2011, reported 400 or more studies forming part of PET services for which a Medicare benefit was payable, and who holds a current licence from the relevant State radiation licensing body to prescribe and administer the intended PET radiopharmaceuticals to humans

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

Inpatient private hospital

Inpatient public hospital

Outpatient clinic

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

Yes

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:

For complex infection, including spinal infection, osteomyelitis, prosthetic infections, cardiac infection, bacteraemia and extrapulmonary NTM infection, imaging techniques may be included already within the first-line investigations. As such, these should not be seen as a comparator for this service, as the proposal of the use of FDG PET is when these investigations are equivocal or contraindicated.

Suitable comparators for complex infection would include localised MRI and CT, ^{67}Ga scintigraphy, labelled leukocyte scans and 3-phase bone scans.

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

Radiography

56223 - Computed tomography—scan of spine, lumbosacral region, without intravenous contrast medium

56807 - Computed tomography—scan of chest, abdomen and pelvis with or without scans of soft tissues of neck with intravenous contrast medium and with any scans of chest, abdomen and pelvis with or without scans of soft tissue of neck before intravenous contrast injection, when performed

56007 - Computed tomography—scan of brain with intravenous contrast medium and with any scans of the brain before intravenous contrast injection, when performed

56030 - Computed tomography—scan of facial bones, para nasal sinuses or both, with scan of brain, without intravenous contrast medium

57712, 56620, 56622, 55867 - Computed Tomography - imaging of hip, knee, lower extremity, shoulder/upper arm without contrast

63304 - MRI—scan of musculoskeletal system for infection arising in bone or musculoskeletal system

Nuclear Medicine

61429 – Whole-body Ga 67 study (planar)

61430 – Whole-body Ga 67 study with SPECT

61442 - Whole-body Ga 67 study with SPECT (two or more body regions separately)

61450 - Localised study using gallium

61453 - Localised study using gallium, with SPECT

61477 - Supplementary item for Ga 67 scans

61462 - Repeat planar and SPECT imaging, or repeat planar imaging or single photon emission tomography imaging on an occasion subsequent to the performance of item , 61429, 61430, 61442, 61450, 61453, if there is no additional administration of radiopharmaceutical and if the previous radionuclide scan was abnormal or equivocal

61433 – Whole-body study using cells labelled with technetium

61434 - Whole-body labelled-cell study + SPECT

61454 - Localised study using cells labelled with technetium

61457 - Localised study using cells labelled with technetium, with SPECT

61446 - Regional scintigraphic study, using an approved bone scanning agent, including when undertaken, blood flow imaging, blood pool imaging and repeat imaging on a separate occasion

61449 - Regional scintigraphic study, using an approved bone scanning agent and SPECT, including when undertaken, blood flow imaging, blood pool imaging and repeat imaging on a separate occasion

Provide a rationale for why this is a comparator:

These modalities are regarded as comparators to FDG PET/CT because they reflect the conventional advanced imaging strategies used to evaluate patients with complex infection when initial evaluations fail to yield a diagnosis.

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?

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

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

FDG PET demonstrates high sensitivity for infection and a high negative predictive value in complex infection.[19] A negative scan may justify discontinuation of further diagnostic investigations and support conservative management, whereas a positive scan can identify a focal source, enabling targeted therapy.

The anatomical comparator imaging may be preferred by some referrers prior to referring for PET scan initially as it may be quicker, more available and, in some cases, similar sensitivity for detection. In some cases of complex infection, recommendations do not specify whether anatomical or metabolic imaging (excluding PET) is the preferred first choice after initial investigations as they yield similar diagnostic usefulness, so the addition of PET to the diagnostic pathway may mean utilization in place of other metabolic imaging but following equivocal anatomical imaging.

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

Diagnostic Accuracy
- Higher proportion of patients in whom a definitive diagnosis is established.
- Higher sensitivity and specificity
- Better positive predictive value (PPV) and negative predictive value (NPV).

Time to Diagnosis
- Smaller interval from initial presentation to definitive diagnosis.

Modification of antimicrobial therapy
- Initiation, escalation, de-escalation, or cessation of antimicrobial treatment
- Transition from empirical to targeted therapy based on improved localisation of infection

Health harms

Invasive Procedures Avoided
- Number of unnecessary biopsies, bronchoscopies, exploratory surgeries, or repeat imaging procedures avoided due to PET/CT findings.
- Lowered risk of procedural morbidity and patient discomfort
- Potential for avoidance of sedation in paediatric patients

Safety and Radiation Exposure
- Lowered cumulative radiation dose
- Less likely adverse events related to contrast agents or radiotracers
- No blood-handling (compared to labelled WBC scanning)

Resources

Health Resource Utilization and Cost-effectiveness

- Lowered total healthcare costs including imaging, hospitalisation, procedures, follow- up due to faster diagnosis and less investigative tests.

Value of knowing

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

A change in prognosis may occur through earlier diagnosis and timely initiation of appropriate therapy, more complete source control in deep-seated or disseminated infection, reduction in relapse risk through confirmation of treatment response, and prevention of morbidity associated with delayed diagnosis. FDG PET/CT is particularly beneficial in scenarios where MRI or CT are limited by metal artefact (such as prosthetic joints or vascular grafts), post-operative or post-treatment structural changes that obscure active infection, or the inability of conventional imaging to provide whole-body assessment for disseminated disease.

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):

Self-funded

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)	
Category number	Category 5
Category description	DIAGNOSTIC IMAGING SERVICES
Proposed item descriptor	Positron emission tomography study using 18F-fluorodeoxyglucose for the evaluation of suspected deep-seated or complex infection in whom first-line investigations were equivocal, including one or more of: i. Suspected spinal infection (vertebral osteomyelitis, discitis or epidural abscess); or ii. Suspected osteomyelitis in cases of a known soft tissue infection (including diabetic foot ulcers), fracture related osteomyelitis, and to assess for dissemination of infection to other skeletal sites or organs iii. Suspected prosthetic joint infection or other orthopaedic hardware infection, if more than 2 years post surgery iv. Suspected bone and joint infections in children, where FDG-PET can remove the necessity for general anaethesia (as required for MRI) and enable better ability to distinguish between acute and chronic infections, or reparative bone tissue; v. Suspected infective endocarditis, including following congenital heart disease, or due to prosthetic valve infection, cardiac implantable electronic device infection and septic emboli vi. High-risk bacteraemia (for example *Staphylococcus aureus* or other pathogens with a high risk of metastatic infection) where metastatic infection is suspected

	vii. Extrapulmonary non-tuberculous mycobacterial (EPNTM) infection with suspected disseminated infection
Proposed MBS fee	$953.00
Indicate the overall cost per patient of providing the proposed health technology	$953.00
Please specify any anticipated out of pocket expenses	N/A
Provide any further details and explain	

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:

Spinal Infection

First-line investigations for suspected spinal infection include:

- Laboratory testing—white blood cell count, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR)
- Contrast-enhanced Magnetic Resonance Imaging (MRI)[21]

Osteomyelitis

First-line investigations include:

- FBC, ESR, CRP, EUC, LFT
- Plain X-ray of affected area (any periostitis, osteopenia)
- Microscopy and culture of any discharge or aspirate collected
- Probe-to-bone (if applicable)
- Blood cultures (two sets collected from separate sites in adults)[22]

Prosthetic Infection

First-line investigations include:

- FBC, ESR, CRP, EUC, LFT
- Plain X-ray of affected area (any periostitis, osteopenia, loosening of prosthesis)
- Microscopy and culture of any discharge or aspirate collected
- Blood cultures (two sets collected from separate sites)

Infective Endocarditis

First line investigations include:

- 3 blood cultures taken at 3 different time points:
  - Full blood count
  - C-Reactive protein or Erythrocyte sedimentation rate
- Urine MCS
- ECG: look monitoring for widening PR interval, p mitrale, T-wave inversion, dysrhythmia
- Transthoracic Echocardiogram[23,24]

Bacteraemia

First line investigations include:

- Blood cultures
- Blood test (full blood count, inflammatory markers, renal and liver function tests, and lactate)
- ECG to rule out endocarditis
- Targeted Imaging (depending on location suspicion)[25]

Extrapulmonary non-tuberculous mycobacterial infection

First line investigations and may include:

- Mycobacterial blood cultures
- Tissue culture of affected areas (eg. skin, soft tissues, bone, joint fluid, sputum or deep respiratory specimens) specifically cultured for mycobacteria
- Histology of tissue biopsies to confirm presence/absence of granulomatous inflammation and/or acid-fast bacilli (AFB)
- Targeted imaging depending on the location of clinical symptoms/signs and may include CT and/or MRI[26]

If these investigations fail to yield a diagnosis, or are contraindicated (especially in relation to initial imaging tests), patients will then be referred to infectious diseases services.

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:

Please provide a response if you answered 'Yes' to the question above

USE OF THE HEALTH TECHNOLOGY

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

18F-FDG PET/CT is being proposed as a stand-alone service

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

Comparator imaging is used as a stand-alone service

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

Both use nil other health resources

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:

When initial investigations (which can include conventional imaging) fail to yield a diagnosis, further advanced imaging is engaged in the clinical management pathway in most complex infections. It is proposed that FDG PET can be utilized in this instance, or after other advanced imaging has been engaged, per regional availability and expertise. A positive scan will negate any further investigation, allowing targeted therapy, surgery or tailored care. Equivocal results can be managed by cascading down the current management algorithm (further anatomical or metabolic imaging, biopsy, then broad-spectrum treatment and monitoring), though this should be less likely with the inclusion of PET. Negative scans can allow cessation of investigation and movement into a more conservative treatment.

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

When initial investigations (which can include conventional imaging) fail to yield a diagnosis, further advanced imaging is engaged in the clinical management pathway in most complex infections. This differs between each indication, often initially utilizing anatomical imaging (CT, MRI, Ultrasound), then engaging a metabolic/physiological imaging technique (Labelled WBC, Ga-67) if still equivocal. If results are still equivocal, repeat imaging after close monitoring, invasive biopsies, or empirical or broad-spectrum therapy may be engaged if clinical suspicion persists. Positive results at any stage within the clinical management algorithm allow for targeted therapy, surgery or tailored care.

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

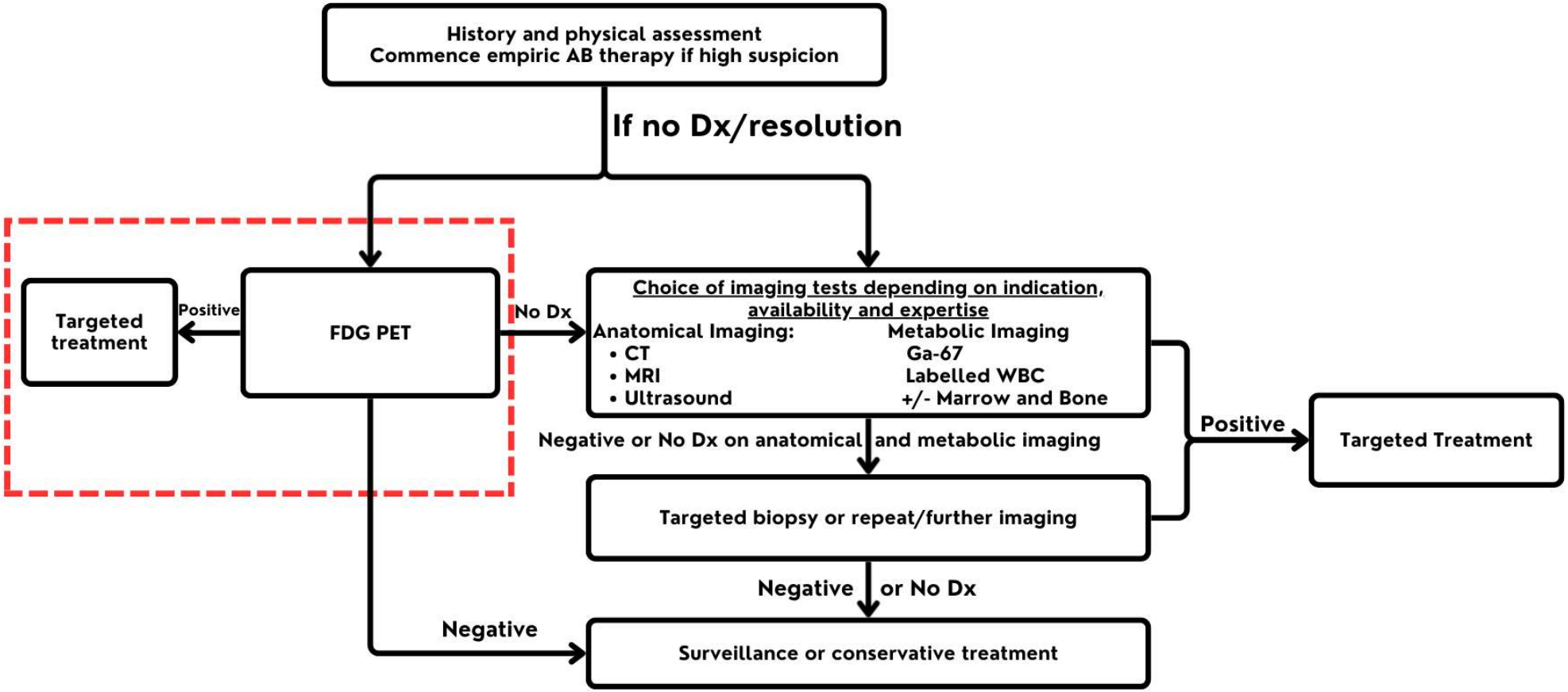
The addition of FDG PET within the management algorithm after initial investigations fail to yield a diagnosis is likely to have a 4-fold effect for patients with complex infection. In some conditions, including spinal infection and infective endocarditis, FDG PET displays a significantly higher sensitivity than the comparator imaging[27,28,29], allowing quicker diagnosis and treatment with lowered likelihood of repeat/further imaging. For other indications, including osteomyelitis and prosthetic infections, FDG PET displays matched sensitivity with other metabolic imaging, but has

a much shorter time to diagnosis due to the simplified imaging mechanism (1 time stamp, single day scans vs multiple day scanning for Ga-67 Scintigraphy and Labelled WBC + Bone Scintigraphy). In these same conditions, utilising an FDG PET scan in place of the alternative metabolic imaging may be cheaper overall in terms of healthcare resources, as Ga-67 fluctuates in cost and availability and has an overall higher price if claimed alongside the supplemental medicare payment and Labelled WBC scanning often requires bone marrow scan and/or Bone scan to achieve a higher sensitivity[1]. Lastly, utilising FDG PET within the management algorithm provides wholebody imaging, which can remove the need for scanning multiple different localised areas of suspicion through various imaging modalities (for example – using Echo for exclusion of IE whilst additionally using CT CAP to search for metastatic infection for patients with high-risk bacteraemia, when FDG PET could exclude/diagnose both[2]). Additionally, FDG PET has been shown to have a high negative predictive rate across complex infections[30,31,32,33,34,35,36], allowing cessation of investigation and movement into a more conservative treatment when clinical suspicion is low.

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

See next page

Complex Infection diagnosis Pathway



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

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

The clinical claim is that 18F-FDG PET imaging is superior to other second-line advanced imaging techniques for patients with complex infection, resulting in a quicker, more accurate diagnosis, and lowered healthcare burden. This can be broken into radiographical techniques and nuclear imaging techniques.

Radiography Techniques

FDG PET/CT provides standardised whole-body imaging and can be performed as a hybrid study with CT or MRI, integrating functional and anatomical information in a single examination. In the early stages of infectious disease, anatomical imaging alone is frequently limited, as structural changes may only become apparent once significant tissue involvement has occurred, leading to lower sensitivity than FDG PET scan. Reliance on lower-sensitivity anatomical imaging is unlikely to alter clinical management and may instead contribute to diagnostic delay, cumulative radiation exposure, and prolonged inpatient hospitalisation.

Nuclear Imaging Techniques

FDG PET/CT demonstrates diagnostic sensitivity comparable to labelled white blood cell scanning and gallium scintigraphy, with all modalities providing whole-body functional imaging for the detection of infection. Compared with Gallium-67 studies, FDG PET/CT offers important practical advantages, including greater tracer availability, lower overall cost, reduced need for close contact restrictions, shorter interruption to breastfeeding, and substantially faster acquisition. In contrast to labelled white blood cell imaging, PET/CT avoids blood handling, enabling safer and more efficient delivery, and tracer availability is less volatile. Image quality is superior, and increasing scanner availability further supports its role as the preferred functional imaging modality in this setting.

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

FDG PET provides whole-body, high-resolution metabolic imaging that can detect active infection before structural changes are visible. Unlike anatomical imaging modalities, which identify anatomical abnormalities, FDG PET highlights metabolically active lesions, allowing earlier detection of infection and guiding targeted interventions such as biopsy or drainage, often with higher sensitivity. The high negative predictive value of PET gives clinicians greater confidence when a diagnosis is not achieved, allowing conservative treatment without repeat scans or treatment delays, which is particularly important for high-risk, vulnerable or paediatric patients. Additionally, provision of a whole-body scan in certain indications (suspicion of metastatic infection, septic emboli or unknown cause) allows for thorough investigation without reliance on clinical suspicion alone, or risk of over-scanning.

Compared with WBC or Ga-67 scans, FDG PET is faster, offers superior image resolution, and detects a broader spectrum of infectious and inflammatory processes. Where PET is available, scans are performed sooner and with less discomfort for vulnerable patients (only 1 timestamp scanning, less close contact restrictions, nil blood-handling).

Identify how the proposed technology achieves the intended patient outcomes:

FDG PET/CT uses 18F-fluorodeoxyglucose (FDG), a radioactive glucose analogue, to detect infection by identifying areas of increased glucose metabolism. During infection, activated immune cells display heightened glycolytic activity, increased blood flow, and inflammatory cell recruitment. FDG accumulates in these metabolically active cells, appearing as "hot spots" on the scan. Due to the metabolic nature of FDG uptake, infection can be detected before structural changes become visible, and the whole-body uptake allows scanning of the entire body without additional radiation dose, allowing detection of unknown foci for patients with infections of unknown origins.

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:

<u>Change in Clinical Management</u>

- Detection of infection sooner, prompting earlier targeted therapy.
- Identification of the most metabolically active site for biopsy, increasing diagnostic yield.
- Supports de-escalation or discontinuation of empiric therapy when negative
- Reduction of the need for further imaging studies

<u>Change in Health Outcomes</u>

- Reduced time to diagnosis
- Higher likelihood of diagnosis (increased sensitivity, less negative/equivocal results)
- Earlier treatment, reducing morbidity and mortality in vulnerable patients
- Lower risk of complications
- Shorter duration of broad-spectrum antimicrobial exposure
- Potential reduction in length of hospital stay or avoidance altogether

<u>Other Benefits</u>

- Whole body assessment avoiding multiple regional scans, reducing overall radiation exposure
- Quicker scanning, more reliable tracer availability, higher resolution than other metabolic imaging techniques
- Potential long-term cost-effectiveness

- Can shift care from prolonged empiric treatment and repeated testing to directed therapy based on identified pathology.

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

Less costly

Provide a brief rationale for the claim:

Compared to anatomical imaging techniques, PET is more costly. PET involves radiotracer production, handling and freight, longer scan time, specialized equipment including camera, injection supplies and shielding, and nuclear medicine staff, all of which increase per-scan cost compared with a standard CT, Ultrasound or MRI. They typically only require the scanner, radiographer/sonographer time, and contrast (if used), making it less expensive on a per-test basis.

Compared to other metabolic imaging techniques, FDG PET could be higher or lower cost, depending on the way the comparator scan is performed. Both PET and comparator imaging requires specialised equipment including radiopharmaceutical production and freight, so are more costly overall than anatomical imaging. A simple whole-body or localised Ga-67 or Labelled WBC scan has medicare rebates as low as $421.3 and $303, though these scans are often performed with SPECT and attenuation correction CT and delayed imaging, and additional bone and bone marrow scans to improve diagnostic accuracy. This can bring the rebates to $1034 plus the additional $1019.55 supplemental rebate for Ga-67 scans due to availability issues, and $1691 for Labelled WBC + Bone + Bone marrow. A whole-body FDG-PET has an average rebate of $1099 ($999 for PET code + $100 CT attenuation correction code)

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.

This application relates to the use of 18F-FDG for a new clinical indication. 18F-FDG is already TGA-approved and MBS-rebatable for multiple other indications. The clinical claim presented in this submission is based directly on the published evidence evaluating 18F-FDG PET/CT in Fever of unknown origin and neutropenic fever. The diagnostic performance, clinical utility, and management impact data cited are specific to 18F-FDG and are not extrapolated from other radiopharmaceutical products.

Summary of Evidence

Provide one or more recent (published) high quality clinical studies that support use of the proposed health service/technology. At 'Application Form lodgement',

	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
1.	Systematic review Bivariate meta-analysis	Diagnostic performance of 18F-FDG PET/CT in patients with spinal infection	Analysis of 26 articles, totaling 833 patients. 12 studies with 396 patients were included in the analysis Pooled sensitivity: 94.8% (95% CI: 88.9–97.6%), pooled specificity: 91.4% (95% CI: 78.2–96.9%); pooled diagnostic odds ratio (DOR) 63.4 (95% CI: 28.9–139)	https:// doi.org/10.1007/s00259-019-04571-6	2019
2.	Prospective diagnostic accuracy study	Prospective comparison of whole-body (18)F-FDG PET/CT and MRI of the spine in the diagnosis of haematogenous spondylodiscitis	26 patients with clinically suspected haematogenous spondylodiscitis included in study. PET/CT sensitivity 83%, specificity 88%, PPV 94%, NPV 70%; MRI in same cohort: sensitivity 94%, specificity 38%, PPV 77%, NPV 75%. Overall accuracy was found to be PET/CT - 84%, MRI - 81%	https:// doi.org/10.1007/s00259-019-04571-6	2020
3.	Clinical Trial Prospective diagnostic accuracy study	The diagnostic value of ^{18}F-FDG-PET/CT and MRI in suspected vertebral osteomyelitis - a prospective study	Clinical study including 32 patients with suspected vertebral osteomyelitis; PET/CT + MRI performed with blinding of image readers For PET/CT: sensitivity 100%, specificity 83.3%, PPV 90.9%, NPV 100%. For MRI: sensitivity 100%, specificity 91.7%, PPV 95.2%, NPV 100%. PET/CT showed advantages in detection of metastatic infection. MRI was more sensitive for small epidural/spinal abscesses.	https:// doi.org/10.1007/s00259-017-3912-0	2018

	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
4	Prospective diagnostic accuracy study	18F-fluorodeoxyglucose uptake pattern in patients with suspected spondylodiscitis	Clinical study of 42 patients with suspected spondylodiscitis. PET correctly identified spondylodiscitis in 95% of patients and absence in 86%; reported sensitivity 86%, specificity 95%, 3 false-negatives, 1 false-positive. Authors noted PET helpful also for differentiating inflammatory/infectious vs degenerative vertebral changes.	https://doi.org/10.1097/MNM.0b013e328365abec	2013
5	Comparative retrospective study	A comparison of the diagnostic value of MRI and ^{18}F-FDG-PET/CT in suspected spondylodiscitis	Study included 68 patients who underwent both MRI and PET/CT for suspected spondylodiscitis. PET/CT: sensitivity 96%, specificity 95%, PPV 98%, NPV 90%, overall accuracy 96%. MRI in same patients: sensitivity 67%, specificity 84%, PPV 92%, NPV 50%, overall accuracy 72%	https://doi.org/10.1007/s15010-016-0914-y	2017
6	Meta-analysis	Diagnostic accuracy of fluorine-18 fluorodeoxyglucose positron emission tomography for suspected primary and postoperative pyogenic spondylitis	Systematic review/meta-analysis pooling multiple PET or PET/CT series for pyogenic spinal infection. Included 18 studies, and 660 patients. For PET/CT: pooled sensitivity 86% (95% CI 0.78–0.91), specificity 91% (95% CI 0.76–0.97); pooled PLR 9.6, NLR 0.16, diagnostic odds ratio 62, accuracy of 92%	https://doi.org/10.1186/s13018-023-03507-z	2023
7	Retrospective study	A Combined Scoring Method Based on ^{18}F-FDG PET/CT for Distinguishing Spinal Infection From Malignancy	Study exploring the additional value of FDG PET for patients with equivocal MRI findings. 71 patients included. FDG showed sensitivity of 100%, with moderate-to-excellent agreement with MRI	https://doi.org/10.1097/BRS.0000000000004528	2023

	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
8	Comparative clinical study	18F-FDG-PET/CT better localizes active spinal infection than MRI for successful minimally invasive surgery	Comparison of FDG PET with MRI for 9 patients with spinal infection. PET identified fewer but more precise areas of active infection compared with MRI, with 100% sensitivity and 79% specificity. MRI had 76% sensitivity and 42% specificity	https://doi.org/10.1177/0284185114541983	2015
9	Prospective observational clinical study	^{18}F-FDG hybrid PET in patients with suspected spondylitis	Study involving 16 patients who underwent combination of FDG PET, MRI, Ga-67 and MDP bone scan for spinal infection. PET was superior to MRI in patients with a history of surgery and high-grade infection, paravertebral abscess formation, low-grade spondylitis or discitis. PET outperformed MDP and Ga-67	https://doi.org/10.1007/s00259-001-0719-8	2002
10	Retrospective study	The diagnostic value of [(18)F]FDG PET for the detection of osteomyelitis and implant-associated infections	Study including 215 patients who underwent PET or PET/CT for osteomyelitis / implant-associated infections. Showed for PET/CT a sensitivity of 88%, specificity of 76%, PPV 76%, NPV 89% and accuracy of 82%. PET/CT outperformed stand-alone PET	https://doi.org/10.1007/s00259-015-3221-4	2016
11	Retrospective study	Diagnostic value of hybrid FDG-PET/MR imaging of chronic osteomyelitis	Study including 36 patients with suspected chronic osteomyelitis. PET/MRI showed sensitivity of 78%, specificity of 100% and an accuracy of 86% Though this is PET/MRI (not PET/CT), authors note accuracy in line with literature for PET/CT	https://doi.org/10.1186/s41824-022-00125-6	2022
12	Retrospective study	Assessing diagnostic accuracy: 18F-FDG PET-CT scans in post-traumatic long bone non-unions	Analysis of 12 studies including 676 patients, of whom 408 underwent FDG PET/CT for suspected chronic infection in fracture non-union Reported sensitivity and specificity of 67%, PPV of 79% and NPV of 52%. Authors suggest PET/CT may be better in complicated post-trauma bone infections	https://doi.org/10.1016/j.injury.2024.111712	2024

	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
13	Retrospective study	Diagnostic performance of 18F-FDG PET/CT in diagnosing fracture-related infections	Analysis of 135 patients who underwent PET/CT for fracture-related infection. Showed sensitivity of 89%, specificity of 80%, PPV of 74%, NPV of 91% and accuracy of 83%. Noted greater false results when scans performed within 1 month of surgery	https://doi.org/10.1007/s00259-018-4218-6	2019
14	Retrospective study	Evaluation of the Accuracy of the Fluorodeoxyglucose-PET CT in the Diagnosis of Chronic Osteomyelitis	Study involving 18 patients with lower extremity chronic osteomyelitis. PET/CT showed sensitivity of 100%, specificity of 66.7%, PPV of 93.75, NPV of 100% and accuracy of 94.44%	https://doi.org/10.21608/bmfj.2021.44908.1321	2021
15	Retrospective study	Diagnostic value of 18F-FDG PET/CT in trauma patients with suspected chronic osteomyelitis	Analysis of 33 patients undergoing PET/CT for chronic osteomyelitis. Showed sensitivity of 94% (88% for axial skeleton, 100% for appendicular), specificity of 87% (100% for axial, 85% for appendicular) and accuracy of 91% (90% for axial, 91% for appendicular)	https://doi.org/10.1007/s00259-006-0290-4	2007
16	Prospective Study	The Role of 18F-FDG PET/CT in Diabetic Foot Osteomyelitis	Analysis of 39 patients with known diabetic soft tissue infection with suspected osteomyelitis. PET/CT showed 100% sensitivity, 92% specificity and 95% accuracy. Outperformed MRI in separating soft-tissue vs bone involvement	https://doi.org/10.1007/s00259-012-2183-z	2012
17	Meta-Analysis	A meta-analysis of fluorodeoxyglucose-positron emission tomography versus scintigraphy in the evaluation of suspected osteomyelitis	Analysis of 23 studies including 851 patients. FDG PET showed sensitivity 92.3% and specificity 92%, with AUC 0.9666, superior to labelled leukocytes (sensitivity 74.2%, specificity 70.5%, AUC 0.9139), Bone Scan (sensitivity 82.7%, specificity 92%, AUC 0.6514) and MAB (sensitivity 88.3%, specificity 70.5%, AUC 0.8897)	https://doi.org/10.1097/MNM.0b013e32834b455c	2011

	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
18	Meta-analysis	Diagnostic performance of Fluorine-18-Fluorodeoxyglucose positron emission tomography for the diagnosis of osteomyelitis related to diabetic foot: a systematic review and a meta-analysis	Analysis of 9 studies including 299 patients with diabetic foot ulcers suspecting osteomyelitis. Showed sensitivity of 74%, specificity of 91%, AUC of 0.874. Highlighted the usefulness of PET/CT, especially when combined with MRI	https://doi.org/10.1016/j.foot.2013.07.002	2013
19	Systematic review	Imaging tests for the detection of osteomyelitis: a systematic review	Review of 81 studies comparing MRI, PET, BS, WBC, CT and Xray. PET showed 85.1% sensitivity and 92.8% specificity. Concluded that osteomyelitis is reliably diagnosed by MRI, PET and SPECT, with no clear reason to prefer one test over the other in terms of diagnostic accuracy.	https://doi.org/10.3310/hta23610	2019
20	Systematic review	Accuracy of diagnostic imaging modalities for peripheral post-traumatic osteomyelitis - a systematic review of the recent literature.	Review of 16 studies/71 patients for post-traumatic osteomyelitis. FDG PET had sensitivity between 86 and 94% and specificity between 76 and 100%. Both FDG PET and WBC PET had diagnostically suitable accuracy.	https://doi.org/10.1007/s00259-017-3683-7	2017
21	Systematic review and meta-analysis	Comparative diagnostic accuracy of respective nuclear imaging for suspected fracture-related infection: a systematic review and Bayesian network meta-analysis.	Review including 22 eligible studies with 1,565 patients comparing nuclear imaging techniques. FDG PET and labelled WBC outperformed Bone scanning, FDG PET/CT had greatest diagnostic accuracy of the 3 tests.	https://doi.org/10.1007/s00402-020-03506-3	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
22	Systematic review and meta-analysis	Detection of Osteomyelitis in the Diabetic Foot by Imaging Techniques: A Systematic Review and Meta-analysis Comparing MRI, White Blood Cell Scintigraphy, and FDG-PET	Review of 27 articles comparing MRI, BS, PET, and WBC. PET had sensitivity 89%; specificity 92%; DOR- 95, positive likelihood ratio- 11; and negative LR- 0.11. FDG and labelled WBC had best sensitivity and specificity.	https://doi.org/10.2337/dc17-0532	2017
23	Systematic review and meta-analysis	Imaging for detection of osteomyelitis in people with diabetic foot ulcers: A systematic review and meta-analysis	Review of 36 studies comparing PET, MRI and other nuclear SPECT studies. PET had 84.3% sensitivity and 92.8% specificity. Both PET and MRI were comparable in accuracy, however favoured MRI due to availability and lack of radiation.	https://doi.org/10.1016/j.ejrad.2020.109215	2020
24	Retrospective study	Diagnostic Role of FDG PET/CT in Pediatric Patients With Chronic Recurrent Multifocal Osteomyelitis	21 **Paediatric** patients included in study evaluating FDG PET for CRMO. Compared with CT scans, FDG PET exhibits superior sensitivity in detecting lesions associated with CRMO.	https://doi.org/10.1097/RLU.0000000000005216	2024
25	Prospective diagnostic accuracy study	FDG PET for diagnosing infection in hip and knee prostheses: prospective study in 221 prostheses and comparison with WBC imaging	Study including 134 hip and 87 knee prosthesis, scanning both PET/CT and labelled WBC FDG PET showed sensitivity 81.8%, specificity 93.1%, PPV 79.4 and NPV 94%. WBC showed sensitivity of 38.5%, specificity of 95.7%, PPV of 25% and NPV of 92%	https://doi.org/10.1097/RLU.0000000000000464	2014
26	Systematic Review and meta-analysis	The accuracy of imaging techniques in the assessment of periprosthetic hip infection: a systematic review and meta-analysis.	Analysis of 31 studies, including 1753 hip prosthesis. FDG PET had sensitivity 86% and specificity 93%, labelled WBC had sensitivity 88% and specificity 92% and bone scan had sensitivity 80% and specificity 69% Found both labelled WBC scans and FDG PET scans to have satisfactory accuracy.	https://doi.org/10.2106/JBJS.15.00898	2016

	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
27	Meta-analysis	Diagnostic performance of FDG PET or PET/CT in prosthetic infection after arthroplasty: a meta-analysis	Analysis of 14 studies including 838 prothesis. Calculated sensitivity of 86%, specificity of 86% and AUC of 0.93	https://pubmed.ncbi.nlm.nih.gov/24469570/	2014
28	Meta-analysis	A Systematic Review and Meta-Analysis on the Accuracy of Fluorodeoxyglucose Positron Emission Tomography/ Computerized Tomography for Diagnosing Periprosthetic Joint Infections	Analysis of 23 studies including 1437 prosthesis. Calculated sensitivity as 85%, specificity as 86% and AUC of 0.92	https://doi.org/10.3389/fsurg.2022.698781	2022
29	Meta-analysis and systematic review	FDG-PET for diagnosing prosthetic joint infection: systematic review and metaanalysis	Analysis of 11 studies including 635 prosthesis of hip and knee. Sensitivity calculated as 82.1%, specificity as 86.6%. Found better diagnostic performance using iterative reconstruction	https://doi.org/10.1007/s00259-008-0887-x	2008
30	Prospective Study	Potential clinical implication of (18) F-FDG PET/CT in diagnosis of periprosthetic infection and its comparison with (18) F-Fluoride PET/CT	Prospective evaluation of 42 hip prosthesis prior to revision arthroplasty. Calculated sensitivity of 93.7%, specificity of 92.3%, PPV of 88.2%, NPV of 96% and accuracy of 92.8% for FDG PET/CT	https://doi.org/10.1111/1754-9485.12444	2016
31	Meta-analysis	What is the Accuracy of Nuclear Imaging in the Assessment of Periprosthetic Knee Infection? A Meta-analysis	A review of 23 studies including 1027 scans for infected knee replacements. PET had sensitivity of 70% and specificity of 84%. Found Labelled WBC better scan for Knee prosthesis evaluation	https://doi.org/10.1007/s11999-016-5218-0	2017

	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
32	Meta-analysis and systematic review	Diagnostic role of PET or PET/CT for prosthetic joint infection: A systematic review and Meta-analysis	Review of 19 studies (826 patients), sensitivity for PET/CT was 88% and specificity of 89% with DOR of 57.	Https://doi.org/10.1967/s002449912309.	2021
33	Meta-Analysis	Prosthetic vascular graft infection: A systematic review and meta-analysis on diagnostic accuracy of 18FDG PET/CT	Analysis of 10 studies including 320 patients with vascular graft infections undergoing FDG PET/CT Calculated sensitivity of 92%, specificity of 76% and Diagnostic Odds ratio of 37.12 Used SUV analysis	https://doi.org/10.1007/s11748-021-01682-6	2021
34	Comparative Study	Accuracy of FDG-PET-CT in the diagnostic work-up of vascular prosthetic graft infection	25 patients with clinically suspected vascular prosthetic infection underwent FDG PET and CT scanning, with images assessed individually by 2 physicians. FDG PET had sensitivity 93%, specificity 70%, PPV 82% and NPV 88%, with inter-observer agreement kappa of 1.00, superior to CT	https://doi.org/10.1016/j.ejvs.2010.05.016	2010
35	Meta-analysis	Meta-analysis assessing the sensitivity and specificity of ^{18}F-FDG PET/CT for the diagnosis of prosthetic valve endocarditis (PVE) using individual patient data (IPD)	Analysis of 17 studies including 537 patients, who were assessed as “definite, possible or rejected PVE” using preliminary Duke classification. Sensitivity and specificity were 85% and 86.5%. Best diagnostic utility was found to be greatest in patients with preliminary DUKE classification of “Possible PVE”	https://doi.org/10.1016/j.ahj.2023.03.004	2023
36	Meta-analysis	Diagnosis of Infective Endocarditis by Subtype Using ^{18}F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography: A Contemporary Meta-Analysis	26 studies including 1358 patients. Overall sensitivity and specificity were 74% and 88%. Native valve IE sensitivity and specificity- 31% and 98%. Prosthetic valve IE sensitivity and specificity- 86% and 84% Authors noted improvement of performance over time with technology advancements. CIED-IE sensitivity- 72% and specificity was 83%	https://doi.org/10.1161/CIRCIMAGING.120.010600	2020

	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
37	Retrospective Study	18F-FDG PET/CT in the diagnosis of prosthetic valve endocarditis	Small cohort study (8 patients with final diagnoses of definite PVE) compared to negative control group. Sensitivity calculated as 75%, specificity as 84%, AUC of 0.9	https://doi.org/10.1007/s10554-015-0814-8	2015
38	Retrospective observational study	Diagnostic Utility of 18F-FDG PET/CT in Infective Endocarditis	Study involving 70 patients with suspected IE, with FDG-PET after clinical, microbiological and echocardiographic assessment. PET/CT-sensitivity 83.3% (94.1% excluding native valve IE), specificity 93.7%, PPV 83.3% and NPV 93.7%. PET confirmed PVE in 13 patients classified as 'possible' under Duke criteria. PET also detected septic emboli in 5 and malignancies in 3	https://doi.org/10.3390/microorganisms13061299	2025
39	Meta-analysis	Role of ^{18}F-FDG PET/CT in the diagnosis of cardiovascular implantable electronic device infections: A meta-analysis	Analysis of 14 studies including 492 patients with suspected infection of cardiac implantable electronic device. PET sensitivity- 83%, specificity- 89%. For diagnosis of pocket infections, sensitivity- 96% and specificity- 97%. For lead infections or Cardiac Implantable Electronic Device – Infective Endocarditis, sensitivity- 76% and specificity- 83%	https://doi.org/https://doi.org/10.1007/S12350-017-1063-0	2019
40	Retrospective Study	The Role of the 18F-FDG PET/CT in the Management of Patients Suspected of Cardiac Implantable Electronic Devices' Infection	Retrospective analysis of 48 patients, who underwent18F-FDG PET/CT for the clinical suspicion of Cardiac Implantable Electronic Device infection. Sensitivity was 96.2%, Specificity was 81.8%, PPV was 86.2%, NPV was 94.7% and Diagnostic Accuracy was 89.6%.	https://doi.org/10.3390/jpm14010065	2024

	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
41	Prospective study and Cross-Sectional Study	Diagnostic Accuracy of 18F-FDG PET/CT in Infective Endocarditis and Implantable Cardiac Electronic Device Infection: A Cross-Sectional Study	Study including 80 patients with suspected IE and ICED infection Sensitivity- 82%, specificity- 96%, PPV- 94% and NPV- 87%. 90% initially classified as possible by Duke criteria were reclassified after PET/CT (18 to definite and 45 to rejected). Additionally, identified 8 cases of septic embolism and 3 of CRC	https://doi.org/10.2967/jnumed.116.173690	2016
42	Prospective Single Centre Analysis	Accuracy of ^{18}F-FDG PET/CT in patients with the suspicion of cardiac implantable electronic device infections	Study of 63 patients with suspected CIED undergoing PET/CT as part of workup. For lead infection, sensitivity was 38.5% and specificity was 98.0%, For Pocket Infection, sensitivity was 72.2% and specificity was 95.6%	https://doi.org/10.1007/s12350-020-02285-z	2022
43	Case report	Utility of 18F-FDG PET/CT Imaging in Diagnosing Pulmonary Prosthetic Valve Endocarditis in a Pediatric Patient	**Paediatric** patient with a history of complex congenital heart disease and prior pulmonary valve replacement. 18F-FDG PET performed after inconclusive findings from CT angiography, transthoracic echocardiography, and transesophageal echocardiography. PET/CT detected increased 18F-FDG uptake in the region of the pulmonary valve prosthesis, typical for infection, and confirmed diagnosis of bacterial infective endocarditis	https://doi.org/10.1097/RLU.0000000000003656	2021
44	Systematic Review	The role of [18F]FDG-PET/CT in gram-positive and gram-negative bacteraemia: A systematic review	Analysis of 10 studies including 1,902 patients, (553 did not receive PET/CT) with blood culture-confirmed bacteraemia. FDG-PET/CT was the first to identify an infectious site in 35.5% to 67.2% of overall foci identified	https://doi.org/10.3389/fnume.2022.1066246	2022

	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
45	Observational Study	The diagnostic value of [^{18}F]FDG-PET/CT in detecting septic thrombosis in patients with central venous catheter-related Staphylococcus aureus bacteremia	Study including 93 patients with a catheter-related Staphylococcus aureus bacteremia. Correlation was noted between higher SUV values of clinically confirmed cases, and PET/CT uptake was a deciding factor in diagnosis in 85% of the positive cases.	https://doi.org/10.1016/j.biopha.2021.112296	2021
46	Prospective cohort study with a matched historical control group.	18F-FDG PET/CT for detection of metastatic infection in gram-positive bacteremia	Study including 115 patients, compared with a matched historical control group More diagnosed with metastatic foci in the PET/CT group (67.8% vs. 35.7%) Sensitivity was 100%, specificity was 87%, PPV was 89% and NPV was 100% . Relapse rates and mortality rates were lower in the PET/CT cohort	https://doi.org/10.2967/jnumed.109.072371	2010
47	Retrospective Observational Cohort Study	Mortality in patients with high risk Staphylococcus aureus bacteremia undergoing or not PET-CT: A single center experience	Study including 102 patients (48 undergoing PET/CT, 54 not) Metastatic foci identified in 45.8% of cases. The mortality rate (at 1 year) was 16.6% for patients that underwent PET/CT and 44.4% for those who did not.	https://doi.org/10.1016/j.jiac.2019.04.016	2019
48	Prospective Interventional Matched-cohort Study	Integration of FDG-PET/CT in the Diagnostic Workup for Staphylococcus aureus Bacteremia: A Prospective Interventional Matched-cohort Study	Study including 299 patients with Staphylococcus aureus bacteremia. 149 patients underwent PET/CT to determine treatment, 150 were treated without. Patients in the PET/CT group had lower mortality than the control group -13.9% vs 28.5%	https://doi.org/10.1093/cid/ciaa929	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
49	Retrospective Observational Cohort Study	^{18}F-FDG PET/CT Optimizes Treatment in *Staphylococcus Aureus* Bacteremia and Is Associated with Reduced Mortality	Study including 105 patients undergoing PET and matched control PET/CT detected metastatic infectious foci in 73.7% of high-risk patients, and led to a total of 104 treatment modifications Three-month mortality was 32.7% for control vs. 12.4% for PET group. PET/CT was only factor independently associated with reduced mortality	https://doi.org/10.2967/jnumed.117.191981	2017
50	Retrospective Diagnostic Accuracy	FDG-PET/CT for Detecting an Infection Focus in Patients With Bloodstream Infection: Factors Affecting Diagnostic Yield	185 consecutive patients with a BSI who underwent an FDG-PET/CT scan for the detection of an infection focus FDG-PET/CT sensitivity- 80.2%, specificity- 79.6%, PPV- 90.8%, and NPV- 61.4% for detecting an infection focus	https://doi.org/10.1097/RLU.0000000000002381	2019
51	Retrospective observational study	The additional value of ^{18}F-FDG PET-CT imaging in guiding the treatment strategy of non-tuberculous mycobacterial patients	Analysis of 23 NTM patients who had FDG-PET/CT and compared clinical data with metabolic parameters of ^{18}F-FDG and found that the ROC curves showed that SUVTop, SURLiver, SURBlood, SUVI—lung, and SUVMarrow had a high sensitivity and specificity for the identification of immune status, lesion extent, and severity of disease in NTM patients.	https://doi.org/10.1186/s12931-024-02757-7	2024
52	Prospective observational study	Usefulness of ^{18}F-fluorodeoxyglucose positron emission tomography for diagnosing disease activity and monitoring therapeutic response in patients with pulmonary mycobacteriosis	Study of 47 consecutive patients with culture confirmed pulmonary tuberculosis (n=25) or mycobacterium avium complex MAC, n=22) Correlation was noted between SUV values and HRCT findings of severity with and found a change in SUV following treatment in 14 patients with follow up scans confirming positive response to treatment.	https:// DOI 10.1007/s00259-008-1009-5	2009

	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
53	Secondary analysis of a prospective observational cohort study	18-fluorodeoxyglucose positron emission tomography (FDG-PET) in patients with non-tuberculous mycobacterial infections	Analysis of 20 NTM lung disease patients undergoing FDG-PET/CT, 15% with concurrent HIV or malignancy. Study found that FDG PET/CT aided diagnosis, dictated commencement of treatment. Authors suggested 3 potential roles for FDG PET/CT in differential diagnosis, determining disease activity and need for treatment and for evaluating treatment response	https://doi.org/10.1016/j.jinf.2023.03.013	2023
54	Retrospective observational study	Lung and nodal involvement in nontuberculous mycobacterial disease: PET/CT role	Study of 26 patients with pulmonary NTM 6 of whom had PET/CT and 486 pulmonary TB patients 6 of whom had PET/CT correlated with clinical data. Study found differential SUV between parenchyma and nodal disease and between TB and NTM infection suggesting a potential role for PET/CT in defining extent of disease and severity.	http://dx.doi.org/10.1155/2015/353202	2015
55	Case report	Disseminated non-tuberculous mycobacterial infection mimic metastases on PET/CT	Case report of role of FDG PET/CT in patient presumed to have TB and treated empirically with poor clinical response with FGD avid lesions resulting in second biopsy to confirm NTM infection with subsequent targeted treatment and confirmed response with resolution of activity on subsequent FDG PET/CT	https://doi.org/10.1097/RLU.0b013e3181662fb2	2008
56	Case report	Disseminated nontuberculous mycobacterial infection mimicking lymphoma in an adult without diagnosed immunodeficiency: A case report	Case report of a 70 yr old male presenting with urinary symptoms and CT imaging suggestive of lymphoma where FDG PET/CT assisted in facilitating biopsy that subsequently confirmed disseminated mycobacterium kansasii infection	https://doi.org/10.1016/j.heliyon.2024.e39503	2024

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

	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
1.	Non-randomised trial	Evaluation of F18 FDG PET/CT in infection of the extremities. **ACTRN12612000479808**	Compares labelled white cell scintigraphy to FDG PET-CT in suspected osteomyelitis of the extremities to evaluate the feasibility of FDG PET-CT for infection imaging and to gain preliminary data on the agreement between FDG PET-CT and labelled white cell imaging/bone scan in peripheral infection imaging • 30 enrolled • Completed • Not yet published	https://anzctr.org.au/Trial/Registration/TrialReview.aspx?ACTRN=12612000479808?utm_source=chatgpt.com	Registered 2012
2.	Observational Retrospective cohort study	Spondylodiscitis: a Retrospective Observational Study **NCT07164235**	This study evaluates diagnostic approaches such as MRI and 18F-FDG PET/CT, as well as microbiological testing (blood cultures or biopsy), to better characterize infection sources and treatment outcomes for spondylodiscitis • 137 enrolled • Active	https://clinicaltrials.gov/study/NCT07164235	Registered 2022

	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
3.	Observational Prospective multicenter cohort study	A Prospective Multicenter Study to Determine the Usefulness of Systematic 18F-FDG PET-CT for the Management of Invasive Fungal Infection (PETIFI Project) **NCT05688592**	Evaluates whether systematic 18F-FDG PET-CT improves the diagnosis, staging, and treatment monitoring of invasive fungal infections (IFI) compared with conventional imaging • 224 enrolled • Currently recruiting	https://clinicaltrials.gov/study/NCT05688592	Registered 2023
4	Interventional Randomized controlled trial	18-fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in Staphylococcus aureus Bacteraemia (PET-SAB) **NCT05361135**	Evaluates whether early FDG PET/CT can detect hidden infectious foci in patients with S. aureus bloodstream infection (SAB). • 820 enrolled • Currently recruiting	https://clinicaltrials.gov/study/NCT05361135	Registered 2023
5	Interventional Open-label randomized controlled trial	Impact of 18 FDG PET/CT on the Management of Patients With Staphylococcus Aureus Bloodstream Infection: An Open Comparative Randomized Trial (TEPSTAR) **NCT03419221**	Assesses whether whole-body PET/CT performed within 14 days of SAB diagnosis increases detection of deep infection foci compared with routine imaging strategies. • 291 enrolled. • Completed • Not yet published	https://clinicaltrials.gov/study/NCT03419221	Registered 2018
6	Interventional Prospective single-arm impact study	Effect of 18-FDG PET/CT Imaging on Clinical Decision Making During the Acute Phase of Infective Endocarditis: A Multicenter Prospective Impact Study (TEPvENDO) **NCT02287792**	Evaluates how whole-body FDG PET/CT affects clinical decision-making in patients with suspected or confirmed infective endocarditis. • 150 enrolled • Completed • Not yet published	https://clinicaltrials.gov/study/NCT02287792	Study completed 2017