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Access, knowledge and experience with FDG-PET/CT in infection management: a survey of Australia and New Zealand infectious diseases physicians and microbiologists

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Declarations

This is an investigator-initiated study without a funding source. A.Douglas is undertaking a PhD through the University of Melbourne.

Authors contributions

AD, KT, LW, SH, MS were involved in the conception and design of the study.

AD collected all data. AD, KT, LW, SH, RH and MS were involved in the analysis and interpretation of data and writing of the manuscript.

Competing interests statement:

The authors declare no conflicts of interest.

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Abstract

Background: Despite FDG-PET/CT being funded only for staging and restaging of some malignancies in Australia, there is evidence of benefit of FDG-PET/CT for infection indications such as pyrexia of unknown origin (PUO), prolonged neutropenic fever (NF) and prosthetic device infection.

Aims: To evaluate the current knowledge, utilisation of and gaps in access to FDG-PET/CT for infectious indications by Australasian infectious diseases (ID) physicians and microbiologists.

Methods: An online survey was administered to ID and microbiology doctors practicing in adult medicine in Australia and New Zealand via two established email networks. Using targeted questions and case-based examples, multiple themes were explored, including: access to FDG-PET/CT, use and perceived benefit of FDG-PET/CT in diagnosis and monitoring of non-malignant conditions such as NF and PUO, and barriers to clinical use of FDG-PET/CT.

Results: A response was received from 120 participants across all states and territories. Onsite and offsite FDG-PET/CT access was 63% and 31%, respectively. Eighty-six per cent reported using FDG-PET/CT for one or more infection indications and all had found it clinically useful, with common indications being PUO, prosthetic device infections and use in the immunocompromised host for prolonged NF and IFI. Thirty-eight per cent reported barriers in accessing FDG-PET/CT for infection indications and 76% would utilise FDG-PET/CT more frequently if funding existed for infection indications.

Conclusions: Access to FDG-PET/CT in Australia and New Zealand is modest and is limited by lack of reimbursement for infection indications. There is discrepancy between recognised ID indications for FDG-PET/CT and funded indications.

Keywords: Positron emission tomography, infectious diseases, diagnosis, health funding, survey

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LIST OF ABBREVIATIONS

alloHSCT	Allogeneic haematopoietic stem cell transplant
autoHSCT	autologous haematopoietic stem cell transplant
CT	Computed tomography
FDG-PET/CT	Fluorodeoxyglucose positron emission tomography/ computed tomography
HSCT	Haematopoietic stem cell transplant
ID	Infectious Diseases
IFI	Invasive fungal infection
NF	Neutropenic fever
PET	Positron emission tomography
PUO	Pyrexia of unknown origin
TOE	Transoesophageal echocardiogram

INTRODUCTION

Fluorodeoxyglucose-positron emission tomography combined with X-ray computed tomography (FDG-PET/CT) imaging has been used for many years as an effective method to stage and restage malignancies(1). Several studies have demonstrated high sensitivity of FDG-PET/CT for diagnosis of infection of prosthetic devices, osteomyelitis and determining the aetiology of pyrexia of unknown origin (PUO)(2-4). Small studies have also demonstrated high clinical impact of FDG-PET/CT in patients with neutropenic fever (NF) of unclear cause, with benefits of de-escalating or rationalising antimicrobials, of directing further investigation such as bronchoscopy or tissue sampling and establishing an aetiological diagnosis of neutropenic fever(5, 6). There is emerging evidence that FDG-PET/CT is more sensitive for invasive fungal infection (IFI), its dissemination and response to therapy compared to traditional computed tomography (CT)(7, 8). Despite this, Medicare rebate for FDG-PET/CT scanning is still restricted to staging and restaging of some specific malignancies, with no rebate for any infection indication, significantly limiting access for Australian patients. As a consequence, PET scanner access is limited or non-existent in certain regions and health services in Australia. They are, thus, performed principally in tertiary haematology/oncology referral centres or patients are faced with significant out-of-pocket expenses in private facilities.

A randomised trial of FDG-PET/CT versus conventional CT imaging for localising infection in high-risk NF is underway, with the ultimate aim of establishing a new diagnostic pathway for NF patients (Clinicaltrials.gov identifier: NCT03429387). In light of this, we aimed to survey the gaps in access to FDG-PET/CT, assess the current knowledge, attitudes towards and current utilisation of FDG-PET/CT for infectious indications by Australasian Infectious Diseases (ID) physicians, many of whom are involved in the care of haematology patients with suspected infection. This information will be important to establish the unmet need for FDG-PET/CT scanning as a part of ID practice and for investigation of high-risk NF nationally should the study support their use in preference to CT scanning.

METHODS

Survey development

A team of ID physicians and haematologists developed the survey tool, which was pre-tested among a sample of ID physicians in different settings to ensure interpretability and relevance to clinical practice. The survey contained directed questions relating to clinical setting (public versus private, metropolitan versus regional), overall clinician experience and experience in caring for oncology, haematology and haematopoietic stem cell transplant (HSCT) patients. Facility-level access to PET/CT scanning (onsite, offsite but within 1 hour transfer, or not available), clinician experience in use of FDG-PET/CT for infection indications,

and timeliness and limitations to access in the setting of perceived clinical need were captured. The use in monitoring infection outcomes and response to treatment, knowledge of radiation exposure relative to standard CT and the potential increase in utilization if Medicare rebate existed were explored. A case-based scenario was used to evaluate utility of FDG-PET/CT in potential infective endocarditis: a patient with intravascular prosthetic material (Bentall procedure) with methicillin-sensitive *Staphylococcus aureus* bacteraemia and persistent fever despite negative transoesophageal echocardiogram (TOE) and appropriate antibiotic therapy (Appendix).

Study population

In November 2017, the survey was distributed to ID Physicians and Microbiologists practicing in adult medicine across Australia and New Zealand who treat adults via the clinical/research networks of Ozbug (email group of the Australasian Society of Infectious Diseases) and CyberMIDG (email group of the Melbourne Infectious Diseases Group- with subscribers from Victoria and Tasmania), which covers the significant majority of clinicians across Australia and New Zealand. Surveys were administered electronically via REDCap(9). Clinicians were given 42 days to respond and 2 reminders were sent before termination of data collection. There were no financial incentives provided for completion of the survey.

Data analysis

Results were collated and descriptive statistics utilised to explore the responses to questions related to key themes. Partial responses were included if there was completion of over fifty per cent of questions.

Ethics review

The survey was approved by the Human Research Ethics Committee of the Peter MacCallum Cancer Centre (LNR/17/PMCC/187).

RESULTS

Participants

Of a possible 860 medical practitioners subscribing to the target email groups, 120 responses were received (14% response rate). There were 107 complete responses and 13 partially complete. Table 1 summarises the demographics of the respondent group including geography, clinical role and level of clinical experience, and health service provision of various haematology and oncology services.

Access to PET/CT

Figure 1 illustrates the distribution of PET scanners between states in Australia. There are no PET scanners in the Northern Territory. Most scanners are in the capital cities, with high density in Hobart, Melbourne, Perth and Sydney. There is

an uneven spread of scanners, for example, several sites have more than one scanner, and there are three PET scanners within 500 metres of each other in Hobart with no others in the state of Tasmania.

There were 112 complete responses in relation to access to PET. Onsite access to a FDG-PET/CT scanner was available to 71 (63%) of respondents, with 35 (31%) respondents having offsite access, and 6 respondents having no access. In centres other than tertiary metropolitan or metropolitan private hospitals, access to FDG-PET/CT was more often offsite (7/15 respondents- 47%) than onsite (6/15- 40%), with 2/15 without access.

Ninety-six respondents (86%) reported using FDG-PET/CT for a non-malignant diagnosis. In those with experience in utilising FDG-PET/CT for infection indications, 38% (36 respondents) reported difficulty obtaining a FDG-PET/CT when thought to be clinically appropriate. Reasons for this included lack of reimbursement or institutional approval due to cost (28/36), lack of support from the institution's imaging department (12/36) and a long wait time rendering the scan not clinically helpful (12/36). The majority of respondents could obtain desired FDG-PET/CT within 1 week (Figure 2). Of the respondents who practice within an allogeneic haematopoietic stem cell transplant (alloHSCT) centre who have had experience with FDG-PET/CT (48 respondents),

35% could obtain a FDG-PET/CT within 3 days of request and 77% within one week.

In those who had not utilised FDG-PET/CT for infection indications (16 respondents), the most common responses were lack of reimbursement or imaging support (6 respondents), logistical issues (4 respondents) and the lack of perceived need (4 respondents). Seventy-six per cent of respondents (85/112) would utilise FDG-PET/CT more often if there was a Medicare rebate for infection indications.

Infection and FDG-PET/CT utilisation

Figure 3 displays the frequency of use of FDG-PET/CT amongst the 96 respondents with experience with FDG-PET/CT in infection. All respondents who had used FDG-PET/CT had experienced clinical benefit, including utility in localising and defining extent of infectious or inflammatory conditions, or ruling such conditions out. Figure 4 displays categories in which FDG-PET/CT was found useful and Figure 5 displays the specific indications for which FDG-PET/CT had been utilised. PUO was the most common infectious indication for FDG-PET/CT followed by prosthetic device infections (incorporating metal-ware infections and prosthetic valve endocarditis). Thirty-eight respondents had utilised FDG-PET/CT for fever in the immunocompromised host (40% of those

with any FDG-PET/CT in infection experience), and 19 (20%) had used FDG-PET/CT specifically to assess for the presence of IFI.

Twenty-six of 112 respondents had utilised FDG-PET/CT to assess response to therapy, most often in relation to bacterial collections, prosthetic device/graft infections, bone and joint infections (including prosthetic) and invasive fungal infections. Most of these respondents (20/26) had utilised FDG-PET/CT to guide treatment duration.

In the case study of persistent fever in the setting of MSSA bacteraemia in a patient with a history of Bentall procedure without evidence of infective endocarditis on TOE, there were 107 responses. The preferred next imaging investigation was FDG-PET/CT in 43 (40%), CT in 36 (34%), white cell scan in 10 (9%) and bone scan in 6 (6%).

Perceived radiation exposure in a standard FDG-PET/CT compared to an HRCT chest, included the spectrum of 'significantly less than HRCT' (16%) to 'significantly more' (6%), with 38% unsure of the degree of radiation exposure. Only 10% cent of respondents provided the appropriate response to this question - viz, that 'PET/CT has slightly more radiation exposure than a standard HRCT chest'.

DISCUSSION

Responses to this survey highlight both an interest and clinical experience in the use of FDG-PET/CT for infection management. There was broad representation of seniority levels among surveyed practitioners, including registrars, fellows and consultants, and also a representation across Australia and New Zealand. The vast majority of respondents were in metropolitan settings, likely reflecting the distribution of infectious diseases and/or microbiology specialists in large referral centres.

Access

A high proportion of respondents (94%) had reported some level of access to a PET/CT scanner. Access to a PET/CT scanner was also good for non-tertiary metropolitan centres, with 87% of respondents in secondary/regional centres reporting on or offsite access. It is important to note, however that only 63% and 47% of all respondents and non-metropolitan centres respectively had onsite access to PET/CT, and in the setting of an ill patient with fever, onsite access to a scanner is likely to be the only safe option, rendering PET/CT not practical in those with offsite access. Furthermore, a significant proportion of clinicians did report an issue with accessing PET/CT specifically for infection indications, largely due to lack of reimbursement and therefore lack of imaging department support for the scan, and it is possible that some clinicians may not have considered the PET scanner “accessible” to them despite there being a PET

scanner on site utilised for malignant indications. Others commented on the delay in scan access as a barrier, with other scans available in a more timely fashion. Certainly, those respondents who had not utilised FDG-PET/CT for infection indications generally had the same reasons as to why they scan had not been employed (lack of reimbursement/imaging department support or long wait times). Importantly, a majority of clinicians (76%) would use FDG-PET/CT more often for infection indications if there were Medicare reimbursement.

Most clinicians had access to a PET/CT for an inpatient at between 3 days and 1 week post request, which would likely lead to delays in diagnosis and prolonged hospital length of stay. When attempting to diagnose IFI in the immunocompromised, a shorter waiting time is strongly desired, hence with PET/CT wait times as they currently are, alternative imaging such as CT is likely to be utilised. The issue of delays in PET/CT access are likely due to competing interests with imaging for staging and restaging of malignancy. A Medicare reimbursement for selected infection indications would offer a financial incentive for the purchasing of more PET scanners, with improved access overall and reduced wait times. Ultimately, this would lead to a more viable service being available to those with sick inpatients who may benefit most from the scan.

Experience with FDG-PET/CT and awareness of its role in infection

Experience in using FDG-PET/CT for infection indications was relatively high (86%) and most were using a FDG-PET/CT every three to six months, suggesting frequent utilisation despite lack of funding (in addition to the abovementioned desire that clinicians showed to use it more often if funding was available). As clinicians recognise the benefit of FDG-PET/CT over other available tests, this increases strain on hospital unit budgets to pay for these unfunded scans or on patients to self-fund. Most clinicians were aware of the most well-recognised, general ID indications for FDG-PET/CT including PUO, prosthetic infections and endocarditis, and certainly the case study demonstrated the majority of clinicians would deem FDG-PET/CT the next most appropriate step beyond TOE in the common clinical scenario of *S. aureus* bacteraemia and poor source control. Further, this result may reflect a conservative estimate of the preference for PET/CT as the question was posed based on the clinician's current daily practice. With reduced barriers to availability combined with the demonstrated desire clinicians have to use PET/CT more, it is likely that even more clinicians would use PET/CT as a first choice with ready access. There are data to show cost-effectiveness of PET/CT in high risk patients with gram positive bacteraemia(10). Therefore, not only is it useful diagnostically in this scenario, but there is also a cost-benefit argument for improved access to PET/CT for this indication.

Knowledge and experience with FDG-PET/CT in the immunocompromised host was modest among ID clinicians, likely reflecting the sub-specialist nature of this practice and limited publication of benefits of FDG-PET/CT in immunocompromised hosts within the general ID literature(6, 7).

It is clear that knowledge of radiation exposure in FDG-PET/CT among ID physicians and microbiologists is poor, however this is not entirely surprising and likely reflects an overall lack of education in this field(11).

Limitations

As in any voluntary survey, there may have been inherent biases in response rates for clinicians with more interest and experience with FDG-PET/CT for infection indications. Response rate was low-modest (14%), but comparable to many previous voluntary surveys of clinical practice in Australia, which have achieved response rates in the order of 5-30%(12, 13). Factors possibly contributing to the low response rates to surveys in Australia include the inactivity of many subscribers on mailing lists (e.g. clinicians who have retired, or expired email addresses) and email and survey fatigue, in the setting of an abundance of correspondence through these mailing list channels.

This survey may not have accurately surveyed all types of health facilities in Australia given the likely skewed distribution of ID physicians to tertiary centres.

However, given FDG-PET/CT is usually indicated in contexts that require specialist care, this is unlikely to be a significant issue.

CONCLUSIONS

Access to PET/CT in Australia and New Zealand is modest and is limited for infection indications due to lack of reimbursement. There is a clear mismatch between recognised infectious diseases indications for FDG-PET/CT and funding provision, with most clinicians expressing a need to use FDG-PET/CT more frequently, and often relying upon hospital budgets to pay for unfunded scans given the recognised clinical benefits.

We recommended a formal review of Medicare reimbursement criteria for FDG-PET/CT in order to keep pace with the current medical literature and best practice, to ultimately improve access and outcomes for our patients.

REFERENCES

1. Gambhir SS, Czernin J, Schwimmer J, Silverman DH, Coleman RE, Phelps ME. A tabulated summary of the FDG PET literature. *J Nucl Med.* 2001;42(5 Suppl):1S-93S.
2. Takeuchi M, Dahabreh IJ, Nihashi T, Iwata M, Varghese GM, Terasawa T. Nuclear Imaging for Classic Fever of Unknown Origin: Meta-Analysis. *J Nucl Med.* 2016;57(12):1913-9.
3. Granados U, Fuster D, Pericas JM, Llopis JL, Ninot S, Quintana E, et al. Diagnostic accuracy of 18F-FDG PET/CT in infective endocarditis and implantable cardiac electronic device infection: A cross-sectional study. *J Nucl Med.* 2016;57(11):1726-32.
4. Smids C, Kouijzer IJ, Vos FJ, Sprong T, Hosman AJ, de Rooy JW, et al. A comparison of the diagnostic value of MRI and (18)F-FDG-PET/CT in suspected spondylodiscitis. *Infection.* 2017;45(1):41-9.
5. Guy SD, Tramontana AR, Worth LJ, Lau E, Hicks RJ, Seymour JF, et al. Use of FDG PET/CT for investigation of febrile neutropenia: Evaluation in high-risk cancer patients. *Eur J Nucl Med Mol Imaging.* 2012;39(8):1348-55.
6. Koh KC, Slavin MA, Thursky KA, Lau E, Hicks RJ, Drummond E, et al. Impact of fluorine-18 fluorodeoxyglucose positron emission tomography on diagnosis and antimicrobial utilization in patients with high-risk febrile neutropenia. *Leuk Lymphoma.* 2012;53(10):1889-95.
7. Chamilos G, Macapinlac HA, Kontoyiannis DP. The use of 18F-fluorodeoxyglucose positron emission tomography for the diagnosis and management of invasive mould infections. *Med Mycol.* 2008;46(1):23-9.
8. Douglas AP, Thursky KA, Worth LJ, Drummond E, Hogg A, Hicks RJ, et al. FDG PET/CT imaging in detecting and guiding management of invasive fungal infections: a retrospective comparison to conventional CT imaging. *Eur J Nucl Med Mol Imaging.* 2018.
9. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform.* 2009;42(2):377-81.
10. Vos FJ, Bleeker-Rovers CP, Kullberg BJ, Adang EM, Oyen WJ. Cost-effectiveness of routine (18)F-FDG PET/CT in high-risk patients with gram-positive bacteremia. *J Nucl Med.* 2011;52(11):1673-8.
11. Keijzers GB, Britton CJ. Doctors' knowledge of patient radiation exposure from diagnostic imaging requested in the emergency department. *Med J Aust.* 2010;193(8):450-3.
12. Lingaratnam S, Slavin MA, Mileschkin L, Solomon B, Burbury K, Seymour JF, et al. An Australian survey of clinical practices in management of neutropenic fever in adult cancer patients 2009. *Intern Med J.* 2011;41(1b):110-20.

13. van Hal SJ, Gilroy NM, Morrissey CO, Worth LJ, Szer J, Tam CS, et al. Survey of antifungal prophylaxis and fungal diagnostic tests employed in malignant haematology and haemopoietic stem cell transplantation (HSCT) in Australia and New Zealand. *Intern Med J.* 2014;44(12b):1277-82.

FIGURE LEGENDS

Figure 1- Distribution of PET centres within Australia. Total number of PET centres Australia-wide= 72.

NSW- New South Wales, QLD- Queensland, VIC- Victoria, WA- Western Australia, SA- South Australia, Tas- Tasmania, ACT- Australian Capital Territory, NT- Northern Territory.

Figure 2- Duration of time between requesting a FDG-PET/CT for potential infection and performance of desired scan

Figure 3- Frequency of FDG-PET/CT use for infection indications

Figure 4- Percentage of respondents who utilised FDG-PET/CT for non-malignant indications by broad clinical category

Figure 5- Percentage of respondents who utilised FDG-PET/CT for specific infectious indications

PUO- pyrexia of unknown origin, ICH- immunocompromised host, LAD- lymphadenopathy, IFI- invasive fungal infection, Ix- investigation.

TABLES

Table 1- Characteristics of surveyed clinicians

Characteristic	N (%) (total n=120)
Specialties	
• ID and/or microbiology	112 (93%)
• General medicine with ID interest	7 (6%)
• Respiratory medicine	1 (1%)
Clinical role	
• Consultant	82 (68%)
• Fellow	2 (2%)
• Registrar	36 (30%)
State/country of practice	
• ACT	3 (3%)
• NSW	21 (18%)
• NZ	6 (5%)
• NT	4 (3%)
• QLD	20 (17%)
• SA	7 (6%)
• TAS	4 (3%)
• VIC	42 (35%)
• WA	13 (11%)
Type of institution (primary practice)	
• Tertiary metropolitan	99 (83%)
• Metropolitan private	4 (3%)
• Secondary metropolitan	2 (2%)
• Large regional centre	13 (11%)
• Small regional centre	1 (1%)
• Specialist cancer centre	1 (1%)
Institution performs alloHSCt	
• Yes	64 (53%)
• No	53 (44%)
• Unsure	3 (3%)
Institution performs autoHSCt (119 resp)	
• Yes	88 (74%)
• No	31 (26%)
• Unsure	0
Institution treats acute leukaemia with curative chemotx	
• Yes	96 (80%)
• No	20 (17%)
• Unsure	4 (3%)
Institution has an oncology unit (119 resp)	
• Yes	113 (94%)
• No	6 (5%)
• Unsure	0

Clinician experience consulting on patients post HSCT	
• Frequent	46 (38%)
• Occasional	67 (56%)
• None	7 (6%)

ID- infectious diseases, alloHSCT- allogeneic haematopoietic stem cell transplant, autoHSCT- autologous haematopoietic stem cell transplant, chemotx- chemotherapy

APPENDICES

APPENDIX 1- Letter of invitation

Dear Colleagues,

You are warmly invited to participate in a 10-15 minute online survey to explore your access to and experience with using PET/CT scanning in assessing patients with potential infection, with a focus on infections in cancer. This survey is designed for registrars, fellows and consultants in infectious diseases and/or microbiology who care for adult patients. The survey uses a combination of multiple-choice questions and case scenarios.

We suspect there is a large variation in clinicians' access to PET/CT scanning for infectious indications and therefore a large variation in the use and experience with this investigation for indications such as fever of unknown origin and neutropenic fever. *Even if you have had minimal experience with PET/CT and infection, it is still certainly valuable that you respond.* With your help, we hope to demonstrate the gaps in access and experience with PET/CT in some settings, and alternatively the experience of benefit in other settings. This survey will help to set the scene prior to a multicentre study we will undertake to assess the clinical utility and cost-effectiveness of PET/CT scanning in prolonged neutropenic fever.

This study is led by the XXXXXXXXXXXXXXX and will form part of Dr XXXXXXXXXX's PhD.

The survey can be found here:

<https://redcap.healthinformatics.unimelb.edu.au/surveys/?s=YCRCT3MKCW>

(closing date: 31st December 2017).

If the link does not launch, please paste link into your web browser window.

Thank you in advance for your involvement,

Dr XXXXXXXXXXXX
Infectious Diseases Physician and PhD candidate
XXXXXXXXXXXXXX

APPENDIX 2- Survey

Access, attitudes and experience with FDG-PET in infection Survey

INFECTIOUS DISEASES FORM

Unless stated otherwise, please select the *single most appropriate* response for the following questions. If affiliated with more than one healthcare facility, please answer for location at which you primarily practice (greatest EFT allocation).

Note: this survey is related to ADULT patients only.

1. Please indicate the nature of your specialty:
 - Infectious Diseases
 - General medicine with infectious diseases interest
 - General medicine
 - Other medical specialty, specify _____
2. What is your clinical role?
 - Registrar
 - Fellow
 - Consultant
 - Approximately how many years have you been a consultant for? _____
3. In which jurisdiction do you practice? *This pertains to the practice you have the most EFT with.*
 - VIC
 - NSW
 - ACT
 - QLD
 - NT
 - WA
 - SA
 - TAS
4. Which of the following best indicates the nature of the institution where you are primarily employed?
 - Tertiary metropolitan hospital
 - Metropolitan private hospital

- Large regional hospital
 - Small regional hospital
 - Regional private hospital
 - Specialist cancer centre
 - Other _____
5. Does your hospital perform allogeneic haematopoietic stem cell transplants?
- Yes
 - No
 - Unsure
6. Does your hospital treat acute leukaemia with induction chemotherapy with curative intent?
- Yes
 - No
 - Unsure
7. Does your hospital perform autologous haematopoietic stem cell transplants?
- Yes
 - No
 - Unsure
8. Does your hospital have an oncology unit?
- Yes
 - No
 - Unsure
9. What is your experience with consulting on haematology and haematopoietic stem cell patients?
- None
 - Occasional
 - Frequent
10. You have decided that you would like to order a FDG-PET/CT for one of your patients.. At your institution, the availability of FDG-PET/CT scanning for routine clinical care is:
- Available on-site
 - Available off-site
 - Not available

11. When a patient has neutropenic fever on broad-spectrum antibiotics, at what time point would you consider ordering further imaging (apart from plain X-ray) to find a source?
- Immediately
 - At 48-72 hours of persistent fever
 - At 72-96 hours of persistent fever
 - At 5 days- 1 week of persistent fever
 - Greater than a week of persistent fever
 - Never
12. In the setting of prolonged neutropenic fever (>5 days), which imaging modality would you use to assess source of fever? [Assume no localising signs or symptoms and that first-line investigations (blood cultures, urine cultures, plain X-Rays) have been non-diagnostic.]
- CT sinuses and chest
 - CT sinuses, chest, abdo, pelvis
 - CT chest, abdo, pelvis
 - HRCT Chest
 - Standard resolution CT chest
 - FDG-PET/CT
 - Other _____
 - None
13. If a conventional CT scan was negative for a cause of neutropenic fever and there was no clinically obvious source, would you go on to perform a FDG-PET/CT scan if it was available?
- Yes
 - No
 - Unsure
14. Have you ever used FDG PET/CT to assess for a *non-malignant* diagnosis?
- Yes
 - No
- 14a. For those who said YES to Q14: At approximately what frequency would you have used FDG-PET/CT to diagnose a *non-malignant* condition (i.e. infective or inflammatory condition)?
- Less frequent than once a year
 - Once a year
 - Once every six months
 - Once every three months
 - Once a month

- Once a fortnight
- Once a week
- More than once a week
- Other _____

14b. For those who said YES to Q14: In the context of other available investigations to diagnose *non-malignant* conditions, did you find PET useful? (*can circle more than one response*)

- No
- Yes- for finding a focus of infection
- Yes- for finding extent of infection (including dissemination)
- Yes- for ruling out infection
- Yes- for finding inflammatory conditions
- Yes- for ruling out inflammatory conditions

14c. For those who said YES to Q14: For diagnostic purposes, what of the below indications have you used PET/CT for? (*can circle more than one response*)

- Pyrexia of unknown origin (fever >3 weeks, cause not determined on first line investigations)
- Prosthetic device infections (including prosthetic valve endocarditis)
- Fever in the immunocompromised host (including neutropenic fever)
- Septic thrombophlebitis
- Investigation of generalised lymphadenopathy
- Tuberculosis
- Investigation of potential invasive fungal infection
- Investigation of known abscesses/collections
- Pneumonitis
- Investigation of autoimmune disorder (e.g vasculitis)
- Other _____

14d. For those who said YES to Q14: Have you had difficulties in getting a FDG-PET/CT scan for a *non-malignant* indication?

- No
- Yes
 - If yes, Why?
 - Lack of reimbursement/lack of institutional approval due to cost
 - Lack of support from imaging department
 - Long wait time

14e. At your institution, FDG-PET/CT scans for inpatients for *non-malignant* purposes (ie not staging malignancy) are generally performed:

- Within 24 hours
- Within 3 days
- Within 1 week
- Within 2 weeks
- Not accessible/greater than 2 weeks

14f. For those who answered NO to Q14: Why have you not used FDG-PET/CT for a *non-malignant* cause? (tick all that apply)

- Too logistically difficult – e.g. not available, too far away
- Waiting too long for the scan
- No perceived need – other diagnostic tests provide all necessary information
- Data do not currently support its use
- Lack of reimbursement/lack of institutional approval due to cost
- Lack of support from imaging department
- Other _____

15. Do you use FDG-PET/CT to monitor the progress of an infection during or following treatment?

- Yes
- No

15a. For those who said YES, what types of infection did you use FDG-PET/CT for follow-up progress of? *Tick all that apply*

- Fungal infections
- Abscesses/bacterial collections
- Tuberculosis
- Septic thrombophlebitis
- Bone and joint infections (including prostheses)
- Other _____

15b. For those who said YES, did you use the FDG-PET/CT scan to guide duration of antimicrobial therapy?

- Yes
- No

16. FDG-PET/CT is currently not medicare-rebatable for infection indications, and is only rebatable for staging or restaging malignancy. If FDG-PET/CT

was medicare-rebatable for infection indications, would you utilise it more often?

- Yes
- No

17. The radiation exposure from a FDG-PET/low dose CT scan:

- Is significantly less than a HRCT scan
- Is less than a HRCT scan
- Is the same as a HRCT scan
- Is slightly more than a HRCT scan
- Is significantly more than a HRCT scan
- Uncertain of radiation exposure

18. Case study 1

Please read the following case study and respond based on how you would treat this patient in current daily practice:

A 35yo man has had an aortic valve and aortic root replacement (Bentall procedure) 1 year ago. He presents with a febrile illness without clear focus. Methicillin-sensitive *Staphylococcus aureus* grows on blood cultures drawn on admission. You suspect endocarditis and order a transoesophageal echocardiogram (TOE). There is no evidence of infective endocarditis or valve failure on TOE, however despite adequate antibiotic therapy, the patient is persistently febrile. What is your next imaging investigation?

- CT
- PET/CT
- White cell scan
- Other _____
- No further imaging at this time

19. Case study 2

Please read the following case study and respond based on how you would treat this patient in current daily practice:

A 28yo woman has stage IV diffuse large B cell lymphoma with pulmonary lesions, treated with chemotherapy and is now 6 months post an allogeneic haematopoietic stem cell transplant. This has been complicated by pulmonary and cutaneous chronic graft versus host disease requiring ongoing immunosuppression with prednisolone and cyclosporine. She is on posaconazole solution for antifungal prophylaxis, Bactrim and valaciclovir and is compliant with these. The patient develops a fever and a worsening dry cough. HRCT is difficult to interpret, with background graft versus host disease

and previous lymphoma involvement. Your major differential diagnosis in invasive fungal infection. What would you do next?

- Treat empirically for a breakthrough fungal infection without further investigation
- Treat empirically for breakthrough fungal infection, no further imaging, arrange a bronchoscopy for a BAL
- Treat empirically for breakthrough fungal infection whilst awaiting PET/CT
- Get a PET/CT, hold off on antifungal therapy
- Not sure, I have little experience with this patient group
- Other _____

Thank you for your time and participation.

All responses remain anonymous. Pooled results of questionnaires will be published in a peer-reviewed journal. All questions may be directed to Dr XXXX

XXXXX

E: XXXXXXXXXXXXXXXXXXXXX

T: XXXXXXXXXXXX