

**Pregnancy Screening Strategies
for Diagnostic
Nuclear Medicine Procedures**

Daphne J James

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STATEMENT OF ORIGINALITY

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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ACKNOWLEDGEMENT OF AUTHORSHIP

I hereby certify that this thesis is in the form of a series of published papers of which I am a joint author. I have included as part of the thesis a written statement from each co-author, endorsed by the Faculty Dean (research Training), attesting to my contribution to the joint publications.

Daphne James

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THESIS PUBLICATIONS AND PRESENTATIONS

Manuscripts published in peer reviewed journals

1. **James DJ**, Cardew P, Warren-Forward HM. Determining the pregnancy status of patients prior to diagnostic nuclear medicine procedures: The Australian Experience. JNMT 2011; 39(3):220-225
2. **James DJ**, Cardew P, Warren-Forward HM. Pregnancy screening strategies for diagnostic nuclear medicine: Survey results from Australia and New Zealand. JNMT 2013; 41(3):216-222
3. **James DJ**, Cardew P, Warren-Forward HM. Pregnancy screening strategies for potentially challenging patients prior to diagnostic nuclear medicine procedures: qualitative survey analysis. JNMT 2013; 41(4):292-298
4. **James, DJ.**, & Warren-Forward, HM. Research methods for formal consensus development in health. Nurse Researcher 2015; 22(3):35-40
5. **James, DJ.**, & Warren-Forward, HM. Development of consensus statements for pregnancy screening strategies in nuclear medicine. JNMT2015. Published January 22, 2015 as doi:10.2967/jnmt.114.148262

Manuscripts submitted to peer reviewed journals

1. **James, DJ.**, & Warren-Forward, HM. Diagnostic accuracy of pregnancy screening strategies in early pregnancy: a systematic review. *Submitted to the Medical Journal of Australia in February 2015.*

Peer reviewed systematic review protocol

1. **James, DJ.**, & Warren-Forward, HM. The diagnostic accuracy of strategies used to identify early pregnancy: a systematic review. JBI Library of Systematic Reviews 2012; 10(56 Suppl) ,S303 - S312.

Peer Reviewed Conference Publications

1. **James DJ**, Cardew P, Warren-Forward HM. Determining A Patient's Pregnancy Status Prior to Diagnostic Nuclear Medicine Imaging. 42nd Annual Scientific Meeting of A.N.Z.S.N.M., July 2011, Darwin, Australia. Internal Medicine Journal 2011; 41 (Suppl. 3): 1–48. (Oral Presentation).
2. **James DJ**, Cardew P, Warren-Forward HM. Pregnancy Screening Prior to Diagnostic Nuclear Medicine Procedures. 43rd Annual Scientific Meeting of A.N.Z.S.N.M., April 2012, Melbourne, Australia. Internal Medicine Journal 2012; 42 (suppl. 3): 51. (Poster presentation)
3. **James DJ**, Cardew P, Warren-Forward HM. Is a standardised practice guideline needed for pregnancy screening in diagnostic nuclear medicine? 60th Annual Meeting of S.N.M.M.I., June 2013, Vancouver, Canada. Journal of Nuclear Medicine. 2013; 54 (Supplement 2):2648. (Poster Presentation).
4. **James DJ**, Warren-Forward HM. Development of consensus statements for pregnancy screening in diagnostic nuclear medicine: A Delphi technique. 45th Annual Scientific Meeting of A.N.Z.S.N.M., April 2014, Adelaide, Australia. Internal Medicine Journal 2014; 44 (suppl. 1): 1-18. (Oral presentation)

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LIST OF ABBREVIATED TERMS

^{18}F -FDG	^{18}F Fluorine-fluorodeoxyglucose
$^{99\text{m}}\text{Tc}$	$^{99\text{m}}$ Technetium
ACR	American College of Radiology
ACT	Australian Capital Territory
ALARA	As Low As Reasonably Achievable
ANZSNM	Australian and New Zealand Society of Nuclear Medicine
ARPANSA	Australian Radiation Protection and Nuclear Safety Agency
ARSAC	Administration of Radioactive Substances Advisory Committee
BMI	Body mass index
BNMS	British Nuclear Medicine Society
CT	Computed Tomography
hCG	Human Chorionic Gonadotrophin
IAEA	International Atomic Energy Agency
ICRP	International Commission on Radiation Protection
IVF	In vitro fertilisation
LMP	Last menstrual period
mGy	milliGray
mSv	milliSievert
MBq	megabecquerel
NCRP	National Council on Radiation Protection and Measurements
NMS	Nuclear Medicine Scientist
NMT	Nuclear Medicine Technologist
NSW	New South Wales
OSCC	Oxford Study of Childhood Cancers
PET	Positron Emission Tomography
QLD	Queensland
SNMMI	Society of Nuclear Medicine and Molecular Imaging
SPECT	Single Photon Emission Computed Tomography
UNSCEAR	United Nations Scientific Committee on the Effects of Atomic Radiation
VIC	Victoria

ABSTRACT

Nuclear medicine involves the use of ionising radiation to image the physiological functions of the body and to treat certain diseases. Ionising radiation has the potential to cause biological harm and foetal tissue is particularly sensitive especially in the early stages of pregnancy. Although diagnostic nuclear medicine procedures use relatively low levels of radiation, there is still a risk to a foetus if inadvertently exposed during maternal examinations. National and international radiation protection documents recommend that all women of childbearing age be questioned about their pregnancy status prior to any procedure that uses ionising radiation. However, they do not provide any clear guidelines on what constitutes childbearing age, or how to question the patient prior to diagnostic nuclear medicine procedures.

This thesis reports on four interconnected research phases: two literature reviews (systematic and narrative), an interview study, a cross-sectional survey, and a Delphi study. The systematic review on the accuracy of pregnancy screening strategies to identify early pregnancy revealed that serum and urine HCG pregnancy tests are highly sensitive. However, urine tests have a high false-negative rate when used in the early stages of pregnancy. The review also revealed that self-assessment of pregnancy is reliable, particularly in the absence of pregnancy. A narrative review of formal methods of consensus development identified the Delphi Technique as the best method for development of consensus statements for identifying/assessing early pregnancy in women patients prior to diagnostic NM scans.

Phase two of the research involved a series of semi-structured interviews to investigate current practice and identify any associated problems or difficult to question groups, such as teenagers. The interview findings were used to develop a questionnaire for a National online cross-sectional survey of nuclear medicine personnel in Australia and New Zealand (Phase three). Both studies revealed wide variations in current practice which may lead to inadvertent foetal irradiation. The studies highlighted the need for a consistent approach and the development of consensus guidelines.

Finally, a three-round Delphi study was conducted to develop consensus statements regarding questioning patients prior to diagnostic nuclear medicine procedures. The age range for questioning was defined by consensus as 12-55 years. A method for questioning patients was developed which included advice regarding previously identified difficult to question groups. A flowchart was created as a visual aid.

Identification of pregnant and potentially pregnant women prior to diagnostic nuclear medicine procedures is imperative to avoid foetal exposure to ionising radiation. This research identified the lack of a consistent approach and developed consensus guidelines for questioning patients about their pregnancy status. The implementation of these consensus guidelines into nuclear medicine practice will help accurately identify pregnancy and minimise any unnecessary foetal irradiation.

CHAPTER ONE

INTRODUCTION

1.1 THESIS OVERVIEW

The thesis is presented in publication style. The thesis describes the development of a set of consensus statements which will assist the Nuclear Medicine Scientists (NMS) to determine the pregnancy status of their female patients prior to **diagnostic nuclear medicine imaging procedures**. There are four main phases of research (Figure 1.1).

Phase one involved a standard literature review and a systematic review of literature. The literature review assesses the potential foetal effects from irradiation by ionizing radiation and the current national and international legislation and recommendations for the use of ionizing radiation in pregnant, or potentially, pregnant patients. The systematic review was conducted to evaluate the available evidence regarding pregnancy screening strategies used in the health care setting. A review of research methods for developing consensus was conducted to guide the selection of method used in Phase 4.

Phase two consisted of a series of semi-structured interviews with NMS to investigate current practice in determining pregnancy status in nuclear medicine departments in Australia and New Zealand, and any issues that NMS identified as being problematic. These interviews revealed the lack of a consistent approach and the method of questioning female patients varied between, and within departments. The interviews identified a number of key problem areas: lack of awareness of national and departmental policy, no clear definition of age range, questioning of young teenage patients, use of pregnancy testing, and lack of knowledge of the effects of ionising radiation.

Phase three was an online National survey developed following analysis of the interview transcripts. This survey was distributed to nuclear medicine personnel in Australia and New Zealand to provide a nationwide perspective. It provided quantitative and qualitative data that reinforced the findings from the interview study and revealed the need for a consensus approach to determining the pregnancy status of female patients prior to diagnostic nuclear medicine procedures.

Due to the limited evidence available in the literature, **Phase four** utilised a Delphi technique to gather consensus opinion on how to determine the pregnancy status of patients prior to diagnostic nuclear medicine procedures and formulate a set of consensus statements.

The series of publications that form the body of this thesis are associated with one of the four phases of research (Table 1.1)

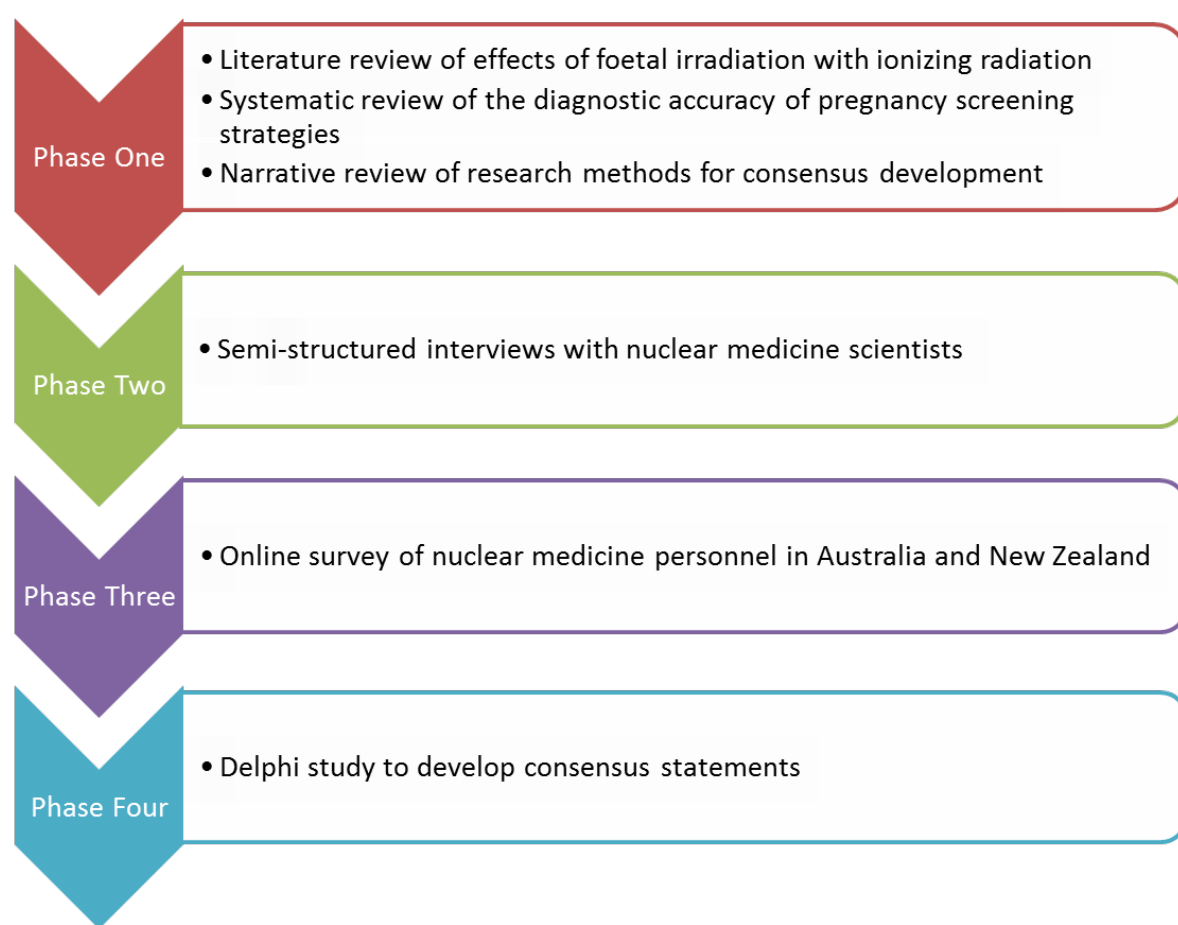


Figure 1.1: Four phases of research

Table 1.1: Research phases and associated publications

Research phase	Associated Peer Reviewed Publications
Literature Review	James DJ , Warren-Forward HM. Diagnostic accuracy of pregnancy screening strategies: A systematic review. Submitted to BJOG: An International Journal of Obstetrics and Gynaecology in July 2014
	James DJ , Warren-Forward HM. Research methods for formal consensus development. Nurse Researcher 2014 (in press)
Interview study	James DJ , Cardew P, Warren-Forward HM. Determining the pregnancy status of patients prior to diagnostic nuclear medicine procedures: The Australian Experience. JNMT 2011; 39(3):220-225
Survey analysis	James DJ , Cardew P, Warren-Forward HM. Pregnancy screening strategies for diagnostic nuclear medicine: Survey results from Australia and New Zealand. JNMT 2013; 41(3):216-222
	James DJ , Cardew P, Warren-Forward HM. Pregnancy screening strategies for potentially challenging patients prior to diagnostic nuclear medicine procedures: qualitative survey analysis. JNMT 2013; 41(4):292-298
Delphi study	James DJ , Warren-Forward HM. Development of consensus statements for pregnancy screening strategies in nuclear medicine. Submitted to the Journal of Nuclear Medicine Technology in September 2014.

1.2 THESIS OUTLINE

This thesis is presented as a series of published and submitted research papers. The background, methods, results and discussion for each individual research study is embedded within the research papers. A more thorough discussion of the research design and methodology is available in the Appendices with additional data pertaining to the design and methodology of the studies, such as questionnaires. The final chapter (Chapter 6) provides an overall discussion and summary of the findings and implications of the research. An outline of the thesis is provided below.

1.2.1 CHAPTER 1

This chapter introduces the background and rationale for the research. Aims, objectives and participants of the research are discussed. The author outlines the significance and

scope of the research, including any limitations, assumptions or bias. Ethics approvals for the research will be detailed.

1.2.2 CHAPTER 2

This chapter consists of a literature review discussing nuclear medicine, the use of ionising radiation in nuclear medicine, the biological effects of ionising radiation, and international regulations and recommendations regarding the determination of pregnancy prior to procedures using ionising radiation and concludes with a discussion on developing clinical guidelines. This chapter includes two embedded published papers including systematic review on the diagnostic accuracy of pregnancy screening strategies used in health care, and a review of research methods for developing consensus.

1.2.3 CHAPTER 3

This chapter details the findings from the initial interview study examining current practice in Australia and New Zealand and the problems nuclear medicine scientists associate with determining pregnancy status in female patients. This is in the form of a published research article.

1.2.4 CHAPTER 4

This chapter describes the design, and quantitative and qualitative results of a nationwide survey investigating current practice for determining the pregnancy status of female patients prior to diagnostic nuclear medicine imaging procedures in Australia and New Zealand. This is in the form of 2 published research articles.

1.2.5 CHAPTER 5

This chapter details the design and outcomes of a Delphi study conducted to illicit expert opinion in the development of consensus statements for determining pregnancy status in nuclear medicine. This is in the form of a published research article.

1.2.6 CHAPTER 6

This chapter provides discussion and summary of the findings of the research, its significance, implications for practice, implications for future research, and final conclusions of the thesis.

1.2.7 APPENDICES

The appendices contain more thorough discussion on the research methodology for each of the four phases of research and other additional information including:

- systematic review protocol
- participant information sheets
- consent forms
- questionnaires
- conference presentations.

1.3 BACKGROUND

1.3.1 INTRODUCTION TO NUCLEAR MEDICINE

Nuclear medicine utilises radioactive materials to obtain images and information about the anatomy and physiological pathways of the human body, and to perform therapeutic applications (1). The radioactive material is chemically bonded to a physiological compound which allows the combined “radiopharmaceutical” to localise in a specific organ or system of the body. For diagnostic imaging procedures the radiopharmaceutical is usually administered intravenously, but may also be given orally or by inhalation (1). The radiopharmaceutical circulates throughout the body and ionising radiation, in the form of gamma rays, is emitted from the body. The gamma rays can be visualised using a gamma or PET camera and images of the distribution of the radiopharmaceutical can be acquired and analysed (1). For therapeutic applications the radiopharmaceutical is designed to localise in a specific organ or tumour type and the ionising radiation emissions are used to destroy the diseased cells.

In Australia, the number of nuclear medicine procedures performed each year has continued to increase, with the number of services increasing from 329319 services in

2005 to 629519 services in 2013, a 47.7% increase (Figure 1.2) (2). There has also been rapid development and proliferation of hybrid imaging systems in nuclear medicine over the past 10 years (3). These systems combine nuclear medicine imaging and computed tomography (CT) into a single imaging system. The main advantages of this technology are its ability to fuse physiological (NM) and anatomic (CT) imaging to provide diagnostic information and perform attenuation corrections (4). However the use of these systems, such as SPECT/CT, has the potential to considerably increase the radiation exposure to the patient due to the addition of the dose from the CT component (5).

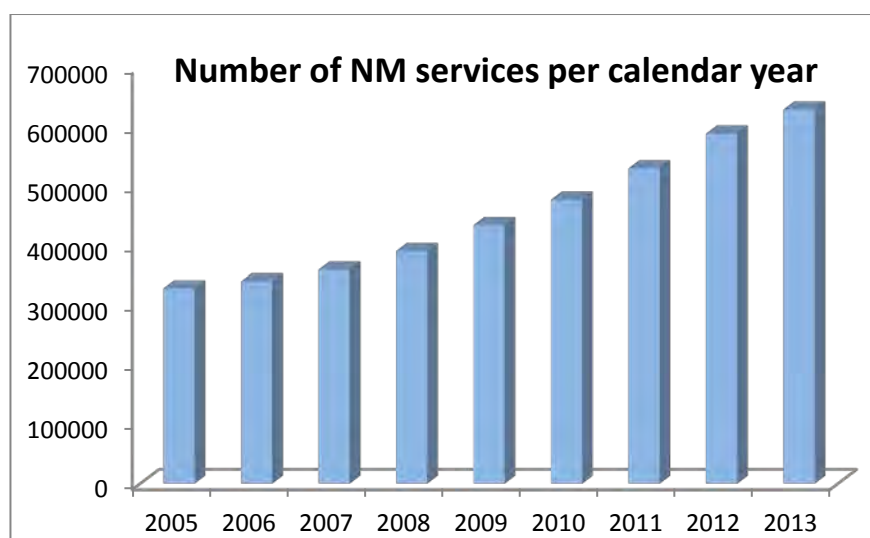


Figure 1.2: Number of nuclear medicine services per calendar year (2)

1.3.2 DIAGNOSTIC NUCLEAR MEDICINE DOSES

Nuclear medicine diagnostic imaging procedures are generally considered low dose procedures (1, 5, 6) because they use short-lived radionuclides such as ^{99m}Tc , which has a physical half-life of 6.02 hours, and the administered activity is relatively small. As such, the effective dose to an adult patient usually remains less than 20 mSv (Table 1.2) (5). The amount of radioactive material administered for a therapeutic application is generally much larger than for diagnostic procedures (7-9) (Figure 1.3). For therapeutic applications, the patient often receives multiple doses over a period of time and the activities in Figure 1.3 are an indication of the minimum activities administered for several therapy radiopharmaceuticals.

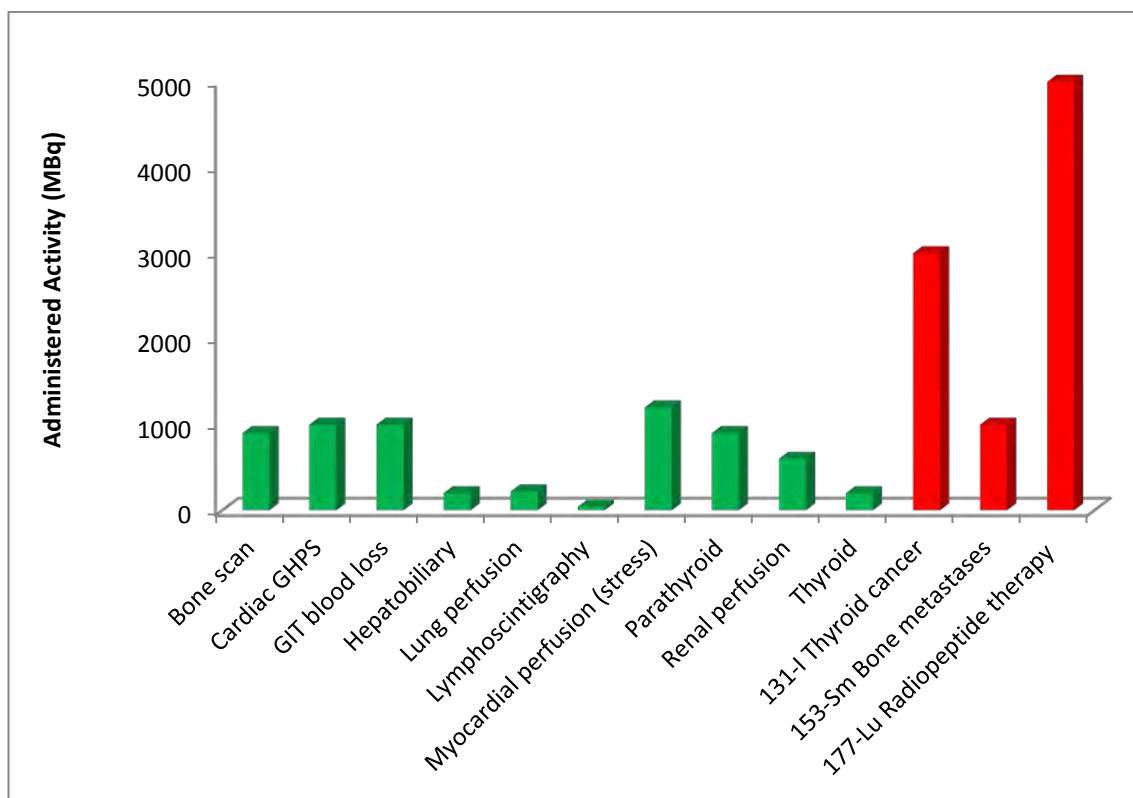


Figure 1.3: Comparison of administered activities for ^{99m}Tc diagnostic imaging (green) and minimum activities for therapy (red)

Table 1.2: Approximate radiation doses to adults from diagnostic nuclear medicine procedures (5)

Effective Dose (mSv)	Procedure
< 1mSv	GIT motility, lymphoscintigraphy,
1-5 mSv	Hepatobiliary, liver/spleen, Lung V/Q, renal, thyroid,
5-10 mSv	Bone, parathyroid, GHPs, infection, blood pool, brain
10-20 mSv	Myocardial perfusion with ^{99m}Tc , PET/CT & SPECT/CT

1.3.3 BIOLOGICAL EFFECTS OF IONISING RADIATION

The ionising radiation used in nuclear medicine has the potential to cause biological harm to those who are exposed (10). The biological effects of ionising radiation are categorised into deterministic and stochastic effects (11, 12). Deterministic effects are characterised by a threshold dose. The threshold dose for deterministic effects varies depending on the type of effect but it is always greater than 100 mGy (13). Below the threshold dose deterministic effects are not seen however, as dose rises above the threshold, the frequency and severity of the effect increases (11). Due to the relatively low doses used in diagnostic nuclear medicine (typically <20 mSv) (Table 1.2) (5), these types of effects are not usually seen (14).

On the other hand, stochastic effects have no threshold dose assumed and, rather than the severity of the effect increasing with dose, the probability of the effect increases with dose. Stochastic effects occur due to cellular changes resulting from interaction with ionising radiation. These changes may cause malignant transformations or genetic changes (14). The basis of radiation protection programs is that the risk of radiation effects increases with dose so exposures should be kept as low as reasonably achievable (ALARA) to minimise possible biological effects (15).

Foetal Irradiation

The developing embryo is extremely sensitive to ionising radiation because they are highly dynamic systems, characterised by rapid cell proliferation, migration, and differentiation (14). ICRP 84 states that radiation risk to the foetus is greatest in the period of organogenesis (weeks 2 to 8 of gestation) and the early foetal growth period (weeks 8 to 15 of gestation) (6). The foetal doses associated with maternal diagnostic nuclear medicine procedures are lower than the levels where developmental and neurological effects are known to occur. However, there is evidence to suggest that there may be an increased risk of childhood cancer or leukaemia following a foetal dose of 10mGy (16, 17).

1.4 RATIONALE FOR STUDY

During the early stages of pregnancy women are often unaware they are pregnant. A review of national and international policies and regulations regarding the safe use of ionising radiation in medical imaging revealed that while all documents recommended that female patients of child bearing age be questioned about their pregnancy status prior to **DIAGNOSTIC** imaging procedures to ensure that unnecessary foetal irradiation does not occur. However, there were **no guidelines** on what constitutes child bearing age or any advice to assist the NMS in how to question their patients (5, 6).

In the absence of evidence, health practices can often develop based on the experiences of practitioners. Consistent approaches to practice are essential to ensure all individuals receive quality health care (18). The author's 25 years of clinical experience and discussions with NMS provided anecdotal evidence that suggested a range of methods of questioning were being used; from a simple verbal question to a written questionnaire. This *ad hoc* approach may lead to inconsistencies in individual patient care and the possibility of unnecessary foetal irradiation.

For the therapeutic application of radionuclides, there are recommendations in radiation protection documents on how to confirm the absence of pregnancy prior to administration of the therapy. ARPANSA Safety Guide for Radiation Protection in Nuclear Medicine No 14.2 (5) clearly states that pregnancy must be excluded by "definitive biochemical test, e.g. serum or urinary bHCG, within 24 hours before the commencement of the treatment". Given the strength of readily available and clear statements, the research reported in this thesis does **not** comment on pregnancy screening strategies prior to the therapeutic use of radionuclides.

1.5 AIMS

The aims of the research are to:

1. Investigate current practice in Australia and New Zealand in how nuclear medicine scientists determine the pregnancy status of their female patients prior to performing diagnostic imaging procedures.

2. Develop a set of consensus statements to allow nuclear medicine scientists to consistently and accurately determine a patient's pregnancy status prior to diagnostic nuclear medicine imaging procedures.

1.6 OBJECTIVES

A number of steps were required to address these aims. Thus the key objectives of this research were to:

- Undertake a comprehensive literature search to understand what research had been done and what needs to be done (gap analysis) and identify appropriate methodology
- Complete systematic literature review on pregnancy screening strategies
- Obtain ethics approval for research
- Formulate semi-structured interview guide
- Recruit participants and conduct interviews
- Analysis of interview transcripts using thematic detail
- Develop questionnaire for nationwide online survey
- Analysis of questionnaire data
- Develop consensus statements

1.7 RESEARCH ETHICS

Ethics applications and variations for all phases of the research were approved by the University of Newcastle Human Research Ethics Committee (approval number H-2009-0270).

1.8 SCOPE OF RESEARCH

This thesis concentrates on the approaches used to determine pregnancy status prior to **DIAGNOSTIC** imaging studies in nuclear medicine only. Approaches used prior to the therapeutic use of radiopharmaceuticals in nuclear medicine and other uses of ionising radiation for medical imaging have not been considered.

The participants in the research were nuclear medicine scientists, physicians and physicists working in Australia and New Zealand. The research was conducted over a

five year period, which is within the typical timeframe and funding limitations of a part-time doctoral study. Interviews for Phase 2 of the research were conducted between March and October 2010 and the online survey (Phase 3) was open for 2 months in November and December 2011. The Delphi study (Phase 4) was conducted between November 2013 and June 2014.

1.9 LIMITATIONS AND ASSUMPTIONS

There are several limitations of this research. It focused upon diagnostic nuclear medicine imaging procedures and therefore conclusions are not transferable to therapeutic applications of nuclear medicine or other uses of ionising radiation. The small semi-structured-interview study, potentially a major limitation (Chapter 4) provided a foundation and informed the development of the online survey (Chapter 5). This survey provided data from a large representative sample of nuclear medicine personnel from Australia and New Zealand which reinforced the interview findings. The Delphi study (Chapter 6) was a convenience sample of relevant experts chosen for their expertise and experience in the field. As these experts were either known to the researcher or recommended to the researcher there was potential for a bias of agreement with the researcher. The inclusion criteria for all three studies potentially limited the results as participants from countries other than Australia and New Zealand, who may have relevant expert knowledge, were unable to contribute to the research. The existing knowledge and expertise of the researcher may produce potential bias when interpreting the qualitative aspects of the study. To minimise the possible effect of this bias, coding books and secondary reviewers were used to analyse data.

1.10 SIGNIFICANCE

The number of nuclear medicine procedures performed each year is steadily increasing and the use of hybrid imaging systems, which have the potential to significantly increase patient radiation exposure, are becoming more prevalent. NMS have a responsibility to ensure the safe use of ionising radiation. This research has identified that the current practice for determining pregnancy status prior to diagnostic nuclear medicine procedures in Australia and New Zealand varies from department to

department, and even within departments. This research revealed variations in the method of questioning female patients, the age range and determination of the age range to question, and the circumstances for the use of pregnancy testing. It highlighted the need for a consistent and standardised approach to questioning patients about pregnancy status, thereby reducing potential foetal irradiation.

Consensus statements for pregnancy screening strategies have been developed to provide NMS with a standardised approach to questioning female patients about their pregnancy status. These statements will assist NMS to more confidently question their female patients about their pregnancy status and achieve a more accurate response. Implementation of the statements into nuclear medicine practice in Australia and New Zealand will ensure that patients who are in the early stages of pregnancy are identified prior to administration of any radiopharmaceutical, preventing any unnecessary foetal irradiation.

1.11 REFERENCES

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CHAPTER TWO

LITERATURE REVIEW

2.1 OVERVIEW

Diagnostic nuclear medicine procedures use radiopharmaceuticals that emit ionising radiation in the form of gamma rays to image the physiological pathways of the body. As the ionising radiation has the potential to cause biological harm, precautions must be taken to minimise the radiation exposure to all patients. Importantly, any exposure that may potentially damage foetal health or development should be avoided during pregnancy because foetal tissue is especially sensitive to the effects of ionising radiation. Therefore, accurate assessment of the pregnancy status of child-bearing women is essential prior to diagnostic nuclear medicine procedures to minimise any foetal irradiation from maternal examinations. In the early stages of pregnancy women are often unaware they are pregnant. Simply asking a woman if she might be pregnant may not elicit an accurate or truthful answer so the use of pregnancy screening strategies, such as questionnaires and HCG pregnancy tests, should be employed.

This chapter provides a review of current literature discussing the biological effects of ionising radiation, in particular regarding foetal exposure to ionising radiation. The review also examines national and international radiation protection documents for advice on how to determine pregnancy status prior to diagnostic nuclear medicine imaging procedures. The accuracy of pregnancy tests and other screening strategies for the diagnosis of early pregnancy is discussed.

Due to the lack of guidance in the radiation protection recommendations on how to question patients about their pregnancy status prior to diagnostic nuclear medicine procedures, Phase Four of the research develops consensus statements to assist nuclear medicine personnel (Chapter 6). In order to select the most appropriate research method to develop consensus, a review of formal research methods for developing consensus in health was conducted.

This chapter includes two embedded published papers: a systematic review on the diagnostic accuracy of pregnancy screening strategies used in health care; and a narrative review discussing formal research methods for developing consensus guidelines.

2.2 NUCLEAR MEDICINE

Nuclear medicine is a medical specialty that utilises radioactive materials for the diagnosis and treatment of disease. Therapeutic nuclear medicine involves the administration of large amounts of radioactive materials to treat specific diseases (1). The radiation emitted from therapy radiopharmaceuticals is of a type and magnitude that will effectively kill diseased cells, eg thyroid cancer cells. There are clearly defined radiation protection guidelines for therapy applications in pregnant, or potentially pregnant, women (1, 2). Therefore, this thesis does not discuss the therapeutic applications of nuclear medicine.

Diagnostic nuclear medicine procedures involve the administration of relatively small amounts of radiopharmaceuticals to image the physiological pathways of the body. The radiopharmaceutical consists of a biological compound attached to a radioactive isotope (3, 4). The biological compound enables the radiopharmaceutical to localise in a specific organ or system of the body. The radioactive compound emits radiation, usually in the form of gamma rays, which can be externally detected by an imaging detector called a gamma camera. The radiopharmaceuticals are designed not to affect the physiological status of the patient; only to trace the pathways and allow for imaging to determine if any abnormalities or pathological changes are present. For example to image bone, a phosphate compound attached to ^{99m}Tc -Technetium is used. The ^{99m}Tc -phosphate is administered intravenously, extracted from the blood, and incorporated into the bone cells in the same way as calcium and phosphates (3).

Conventional diagnostic nuclear medicine includes planar, Single Photon Emission Computed Technology (SPECT) imaging, and Positron Emission Tomography (PET) imaging. The radioisotopes used for these types of imaging are selected on the basis of their physical characteristics and mode of decay (3). Planar and SPECT imaging use radioisotopes that decay by gamma emissions; ideally with an energy between 100-300 keV which is most appropriate for emission from the body (4). In PET imaging the annihilation process between a positron and an electron is utilised and a specially designed detector is used to create the images.

The radiopharmaceuticals used in diagnostic nuclear medicine procedures are primarily administered intravenously, and also via inhalation or ingestion (3-5). After administration, the radioactive material circulates within the blood prior to being taken up by the desired physiological pathway (eg the bones). Therefore the whole body of the patient is being irradiated from the moment of administration until the radioactive material either decays completely or is excreted from the body usually via the renal system or bowel (3). This process can typically take approximately 24 hours for radiopharmaceuticals using ^{99m}Tc -Technetium, which has a physical half-life of 6 hours ($T_{1/2} = 6$ hours), and even longer for radioisotopes with long physical or biological half-lives such as ^{67}Ga -Gallium ($T_{1/2} = 78$ hours) and ^{111}In -Indium ($T_{1/2} = 67$ hours)(3).

2.3 HUMAN PREGNANCY

The human gestation period lasts approximately 40 weeks. Gestational age is usually expressed as the time elapsed after conception (6). However, in clinical situations, the time is often counted from the date of the beginning of the last menstrual period, which occurs about two weeks prior to conception (7). The timing of ovulation and conception in relation to the menstrual cycle varies between individual women and even between cycles, making the estimation of the date of conception problematic. The gestation period is divided into a several broad stages for the consideration of teratogenic agents:

1. Pre-implantation
2. Organogenesis
3. Foetal growth period

Pre-implantation

The pre-implantation stage begins with fusion of the ovum and sperm (creating what is called a zygote) and continues through day nine in humans. This stage is marked by high mitotic activity with the zygote dividing into multiple cells (7). The growing cluster of cells, called a blastocyst, moves into the uterus and implants in the uterine

lining on the tenth or eleventh day post fertilisation. Here the blastocyst begins to develop into the embryo and its extraembryonic structures.

Organogenesis

The period known as organogenesis occurs between the 2nd and 8th week after conception. During this period the primordial organ systems of the embryo are developed, including the primordial central nervous system, circulatory system and digestive system (6). External characteristics of the embryo begin to develop and the formation of the specific organs and organ systems occur during organogenesis. In the fourth week, the heart begins to beat and rapid growth causes the longitudinal and transverse folding of the embryonic disc. By the end of the fourth week the embryo has the rudiments of ears, arms, legs and facial structures (7). During the fifth week the brain develops rapidly causing extensive growth of the head and the eyes begin development. Continued growth and development occurs during the next few weeks and by the end of the eighth week, and the period of organogenesis, all essential internal and external structures are present. This period of development is most susceptible to exposure to teratogens which may be lethal or cause congenital malformations (Figure 2.1) (7).

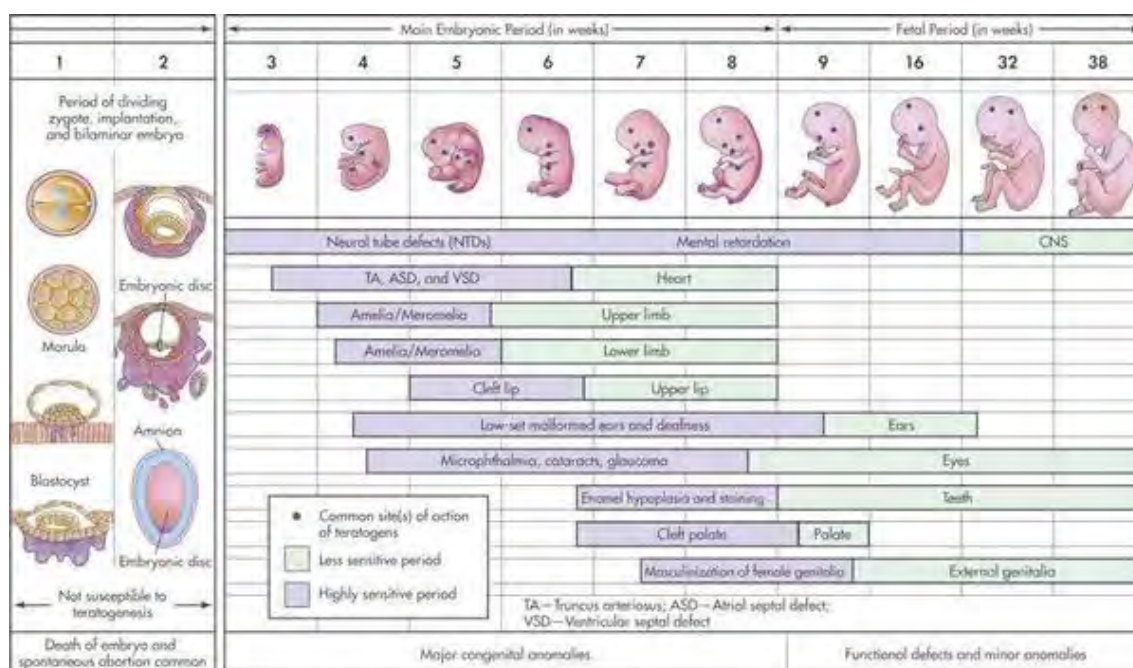


Figure 2.1: Critical stages of foetal development and effect of teratogens (8)

Foetal Growth

The later stage of pregnancy is known as the foetal growth period. This stage takes up approximately two thirds of the human prenatal period and is characterised by growth and histogenesis (6). By the end of the tenth week post fertilisation, the foetus begins to look undeniably human and it can perform certain physiological functions such as swallowing, urination, and moving specific parts of the body. The sex of the foetus is clearly evident by the twelfth week. Bone development rapidly progresses. As the pregnancy progresses the foetus continues to develop and grow in size (7).

2.4 RADIATION BIOLOGY

2.4.1 INTERACTIONS OF IONISING RADIATION

Gamma rays, or photons, are a form of electromagnetic radiation emitted from a nucleus in an excited state in order to transition to a lower (more stable) energy state (9). Gamma rays with sufficient energy per photon can remove bound electrons from atomic shells, thereby producing ionised atoms and molecules. Hence, they are known as **ionising radiation**. When traversing matter, photons will either penetrate without interaction (this allows for external detection and imaging), scatter, or be absorbed. In human tissue, photon interactions result in the production of secondary photons and energetic electrons which deposit their energy into the cells and molecules via ionisation, excitation and thermal heating. The energy is deposited randomly and secondary interactions may occur creating more electrons (9). The energy transferred from the electrons is responsible for the radiobiologic effects such as molecular changes and DNA damage (9).

The three main processes that need to be considered in nuclear medicine are:

- Photoelectric effect
- Compton scattering
- Annihilation (4, 9, 10).

Photoelectric Effect

The photoelectric effect is an interaction that takes place between an incident photon and an inner orbital shell electron. In order for photoelectric absorption to occur, the incident photon energy must be greater than or equal to the binding energy of the electron that is ejected (10). In the photoelectric effect, all of the incident photon energy is transferred to an electron, which is ejected from the atom (Figure 2.2). Photoelectric interactions predominate at energies lower than 25keV in soft tissue.

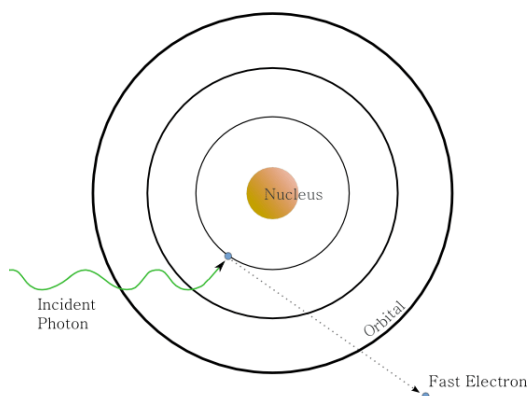


Figure 2.2 Photoelectric Effect(11)

The ejection of an electron from the atom leaves an inner shell vacancy which may be filled by a higher energy electron “dropping down” resulting in the emission of characteristic x-rays. As the incident photon’s energy increases, the probability for photoelectric effect interaction decreases (10). The electrons and characteristic x-rays produced by the photoelectric interaction have the potential to create subsequent interactions and deposit their energy into the cells and molecules of human tissue causing possible damage.

Compton Scattering

Compton scattering is the main interaction of photons with tissue in the diagnostic nuclear medicine energy range (10). This process results in the ionization of an atom and the division of the incident photon's energy between a recoil electron (which is ejected from the atom) and a scattered lower energy photon (Figure 2.3).

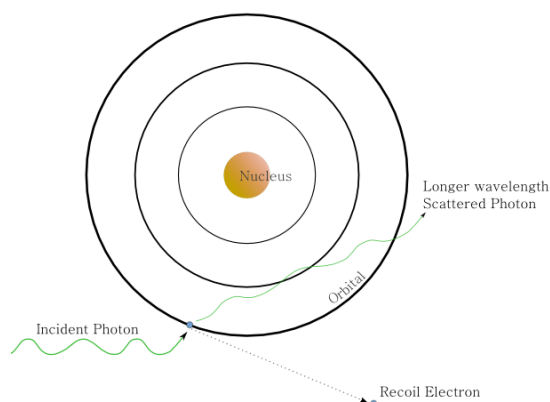


Figure 2.3: Compton Scattering (11)

Compton events occur with loosely bound outer –shell electrons, which have negligible binding energy compared to the energy of the incident photon. Therefore, the probability of a Compton scattering event occurring is independent of the atomic number of the material (10). The ejected electron and scattered photon have the potential to create multiple subsequent interactions and ionisation events which can cause radiobiologic damage.

Annihilation

Positron Emission Tomography (PET) imaging utilises proton-rich radioisotopes that decay via positron emission. A proton in the nucleus will decay to a neutron, a positron and a neutrino. The net energy released during positron emission is shared between the nucleus, the positron and the neutrino. Positrons are therefore emitted with a range of energies up to a maximum endpoint energy E_{\max} (12). The positron is emitted from the nucleus and travels a short distance in matter depending on its kinetic energy and the material (9). In tissue, the distance is several millimetres at most because the positron rapidly loses its kinetic energy through multiple inelastic interactions with electrons (12). The positron then undergoes annihilation with electron, producing a pair of 511 keV photons traveling at 180° to each other (Figure 2.4). These annihilation photons are used in the creation of PET images.

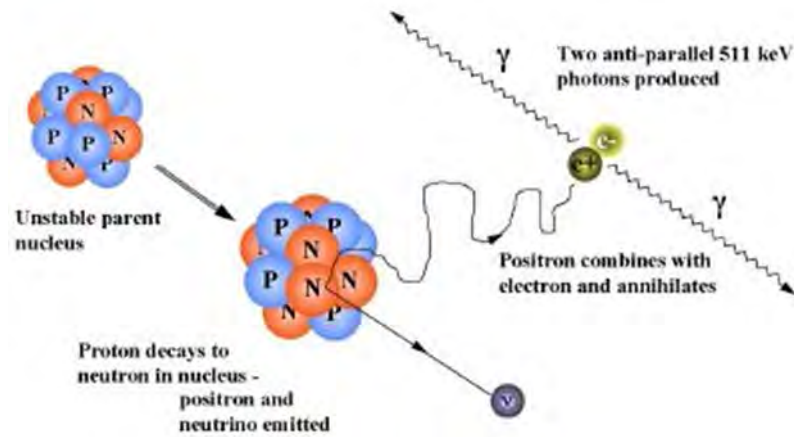


Figure 2.4: Positron annihilation (13)

2.4.2 RADIATION DOSE QUANTITIES

The ICRP has established several different SI units of measurement to describe the amount of energy deposited into tissue when ionisation occurs.

The *absorbed dose* (D_T) is defined as the energy (E) imparted by ionising radiation per unit mass of irradiated material (m). The SI unit for absorbed dose is the Gray (Gy) (3, 9).

$$D_T = \frac{E}{m}$$

Not all types of ionising radiation cause the same biological damage per unit absorbed dose. Therefore, the ICRP established a radiation weighting factor W_R (Table 2.1) which is applied to calculate the *equivalent dose* (H_T). This is measured in Sieverts (Sv).

$$H_T = \sum_R [D_T * W_R]$$

For x-rays and gamma rays the radiation weighting factor is 1, therefore 1 Gy of absorbed dose is equivalent to 1 Sv of equivalent dose.

Table 2.1 Radiation weighting factors (14)

Type of Radiation	Radiation Weighting Factor (W_R)
X-rays, gamma rays, beta particles, and electrons	1.0
Protons	2.0
Neutrons (energy dependent)	2.5-20
Alpha particles and other multiple-charged particles	20

The *effective dose* (E) takes into account the radiosensitivity of specific tissues and applies a tissue weighting factor W_T (Table 2.2) to the equivalent dose. The sum of the products of the equivalent dose to each organ or tissue irradiated (H_T) and the corresponding weighting factor (W_T) for that organ or tissue is called the effective dose (E). Effective dose is also measured in Sieverts (3, 9).

$$E = \sum_T [W_T * H_T]$$

Table 2.2: Tissue Weighting Factors (14)

Organ or tissue	Tissue Weighting Factor (W_T)
Breast, bone marrow, colon, lung, stomach, remainder.	0.12
Gonads	0.08
Bladder, oesophagus, liver, thyroid	0.04
Bone surface, brain, salivary gland, skin	0.01

It is important to note that the tissue weighting factors were developed by the ICRP for a reference population of equal numbers of both genders and a wide range of ages. Therefore, they should not be used to calculate individual patient doses (9). As the knowledge of radiation effects develop over time the tissue weighting factors have changed. The most recent update of tissue weighting factors were published in ICRP Publication 103 (2007) (14).

2.4.3 BIOLOGICAL EFFECTS OF IONISING RADIATION

Since the discovery of x-rays and radioactivity in the late 1800's, scientists have reported on adverse effects of radiation exposure to human tissue. The study of radiation biology has continued over the years and radiation protection guidelines have been developed to provide advice to help minimise these effects. However, despite more than one hundred years of research on the biological effects of ionising radiation, the exact consequences of radiation exposure on the early stages of human pregnancy is not clearly understood (15). The major reason is the problem of obtaining direct information for humans. Data from Oxford Study of Childhood Cancer (16), Japanese atomic bomb survivors and more recently, workers exposed in radiation accidents in Chernobyl, have been used by UNSCEAR to estimate biological effects following radiation exposure (5). Also the information obtained from animal experiments has been extrapolated to the human situation (17).

There are a variety of factors that contribute to the biological effects caused by the interaction of matter with ionising radiation. These include the type of radiation, absorbed dose, rate of exposure and the radiosensitivity of the tissues being irradiated (9). When ionising radiation interacts with tissue, it deposits energy into the tissues and damage can occur at a cellular or molecular level. Changes such as the formation of free radicals, damage to DNA and impaired repair, chromosomal aberrations, genomic instability and other cellular effects may occur (Figure 2.5). Clinically observable effects may take years or even decades to manifest.

There are two broad categories of biological effects of ionising radiation:

- deterministic effects, and
- stochastic effects (18).

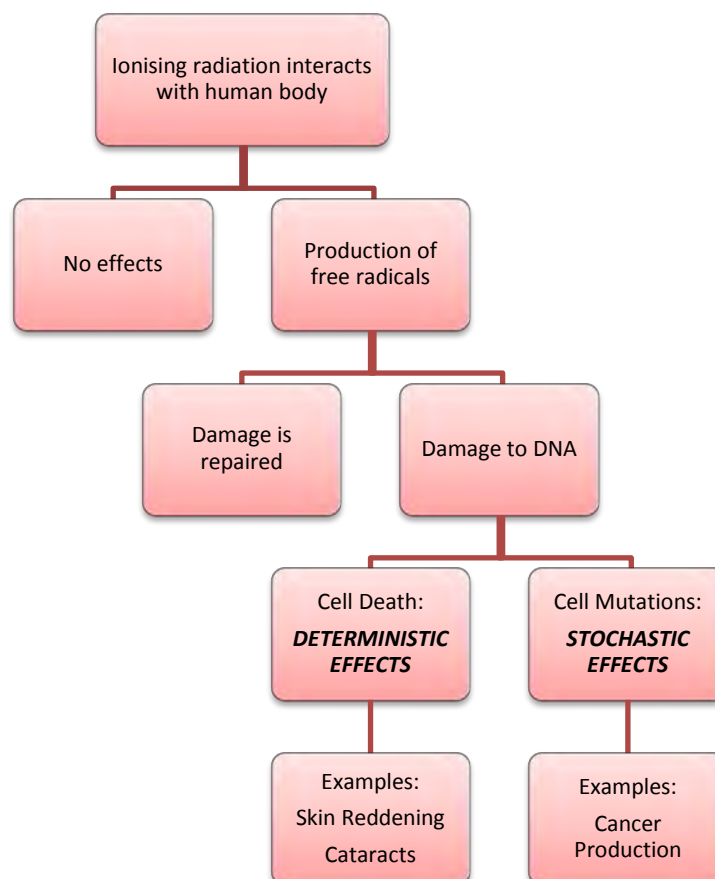


Figure 2.5: Biological effects of ionising radiation

Deterministic Effects

Deterministic effects are those caused by cell damage or cell killing in the exposed tissue. Threshold doses exist for these effects (Table 2.3). Below the threshold dose these effects are not seen (Figure 2.6) and as the dose increases so does the severity of the effect. Examples of deterministic effects include erythema (skin reddening), dermatitis, alopecia and radiation-induced cataract formation (9). Due to the relatively low doses used (Table 2.4), these types of effects are not seen in diagnostic nuclear medicine as the threshold dose is not achieved.

Table 2.3: Threshold doses for deterministic effects (9)

Effect	Organ/Tissue	Time to develop	Threshold Dose (Gy)
Temporary sterility	Testes	3-9 weeks	0.1
Permanent sterility	Testes	3 weeks	6
Permanent sterility	Ovaries	< 1 week	3
Skin reddening	Skin	1-4 weeks	< 3-6
Skin burns	Skin	2-3 weeks	5-10
Cataract formation	Eye	>20 year	0.5
Acute pneumonitis	Lung	1-3 month	6-7

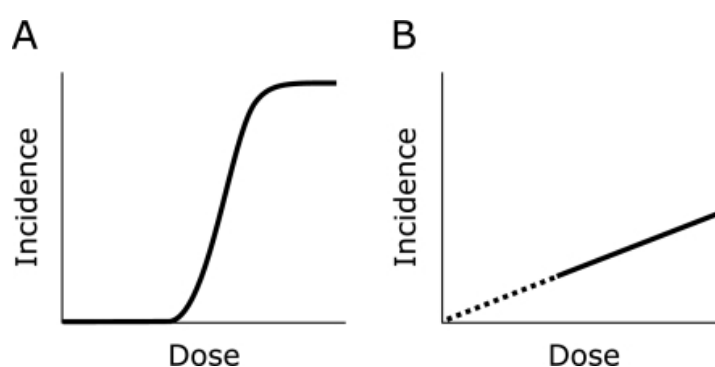


Figure 2.6: Dose response for (A) deterministic effects and (B) stochastic effects (19)

Table 2.4: Foetal dose estimates for some commonly used radiopharmaceuticals (5)

Radiopharmaceutical	Administered Activity (MBq)	Estimated Foetal Dose (mGy)			
		Early	3 mths	6 mths	9 mths
^{99m}Tc -DMSA	220	1.1	1.0	0.88	0.75
^{99m}Tc -DTPA	750	9.0	6.5	3.1	3.5
^{99m}Tc -MAA	200	0.56	0.8	1.0	0.8
^{99m}Tc MDP	750	4.6	4.0	2.0	1.8
^{99m}Tc red blood cells	930	6.3	4.4	3.2	2.6
^{99m}Tc sestamibi	1100	17.0	13.0	9.2	5.9
^{99m}Tc sodium pertechnetate	400	4.4	8.8	5.6	3.7
^{123}I -sodium iodide	30	0.6	0.42	0.33	0.29
^{111}In - pentetreotide	230	19.0	14.0	8.0	7.0
^{67}Ga Citrate	190	18.0	38.0	34.0	25.0
^{18}F -FDG	370	8.1	8.1	6.3	6.3

Stochastic Effects

Stochastic effects are those that result from radiation changes in cells that retain their ability to divide. These modified cells may sometimes initiate a malignant transformation of a cell. The period between the irradiation and the manifestation of the disease varies and may extend from a few years to several decades (9). In addition, genetic effects may be initiated due to the irradiation of germ cells. This type of damage may cause hereditary effects that are not seen until future generations. No threshold dose is assumed for stochastic effects (Figure 2.6). The linear non-threshold (LNT) model is used for the purposes of radiation protection as it recognises that even at low doses there is a possibility for biological effects. The probability of the effect occurring increases as the dose increases, rather than the severity of the effect (9, 20). Therefore, in medical imaging the probability of the induction of stochastic effects should be reduced by keeping the dose to the patient as low as possible. Stochastic effects are regarded as the principal health risk from low-dose radiation, including exposures of patients and staff to radiation from diagnostic imaging procedures (9).

The basic assumption that risks from ionising radiation exposure increase with dose and that there is no threshold dose below which risks cease is the basis of radiation protection programs. The goal of radiation protection is to keep exposures as low as reasonably achievable (ALARA) to minimise any possible effects (20). Radiation protection policies achieve this by:

1. providing dose limits below which deterministic effects should not occur
2. recommending the reduction of doses using the ALARA principle to lower the possibility of stochastic effects occurring.

2.4.4 FACTORS AFFECTING RADIOSENSITIVITY

In 1906, Bergonie and Tribondeau (21) performed a series of experiments that evaluated the relative radiosensitivity of germ cells at different stages. From these experiments, some of the fundamental characteristics of cells that affect the relative radiosensitivity were established. Basically the law by Bergonie and Tribondeau states that:

- Stem cells are radiosensitive. The more mature a cell is, the more resistant to radiation it is.
- The younger tissues and organs are, the more radiosensitive they are.
- When the level of metabolic activity is high, radiosensitivity is also high.
- As the proliferation rate for cells and the growth rate for tissues increase, the radiosensitivity increases also.

Developing organisms are highly dynamic systems characterised by rapid cell proliferation, migration and differentiation (22). A developing embryo or foetus is therefore highly radiosensitive. After exposure to ionising radiation, the response is dependent on several factors including total dose, dose rate, type of radiation, and the stage of development at the time of exposure (20). These factors determine the type and extent of damage that may occur.

2.5 BIOLOGICAL EFFECTS DURING PREGNANCY

As previously discussed, the gestation period of humans can be divided into three stages: a relatively short pre-implantation stage, followed by an extended period of major organogenesis, and finally the foetal growth stage, during which differentiation is complete and growth mainly occurs (20). Each of these stages is characterised by different responses to radiation exposure, owing principally to the relative radiosensitivities of the tissues at the time of exposure.

2.5.1 PRE-IMPLANTATION STAGE

The embryo is extremely sensitive during this stage and radiation damage can result in prenatal death. During this period the incidence of congenital abnormality is low, although not completely absent. Embryos exhibit the so-called "all or none" response in

which, if prenatal death does not occur, the damage cells are repaired or replaced to the extent that there are unlikely to be visible signs of abnormalities even though radiation may have killed several cells (23).

2.5.2 ORGANOGENESIS

The risk of foetal death decreases substantially during this period, while the risk of congenital malformation coincides with the peak developmental periods of various organ systems. The type and extent of radiation damage is dependent on the timing of radiation delivery and the developmental stage of the cells (23). The critical periods and relative sensitivities for radiation-induced birth defects in humans over the three stages of pregnancy are shown in Figure 2.7 and Figure 2.8.

ICRP 84 (2) states that radiation risk to the foetus is greatest in the period of organogenesis and early foetal growth. Foetal malformation and other significant biological effects, such as mental retardation, are unlikely below a threshold dose of 100-200 mGy (2).

2.5.3 FOETAL GROWTH

The foetal growth stage in humans begins after the end of the major organogenesis and continues until term. During this period the incidence of radiation-induced prenatal death and congenital anomalies is, for the most part, negligible for doses less than 100 mGy. During the early foetal stage (weeks 9-17), the central nervous system is particularly sensitive to ionising radiation. Mental retardation is the most likely consequence of exposure at this time. (23) A threshold dose for mental retardation has been estimated from Japanese radiation data at approximately 500 mGy, which is well above the dose expected from diagnostic nuclear medicine procedures. In the mid and late foetal stages, exceptionally high doses (greater than 1000 mGy) are required to induce deterministic effects.

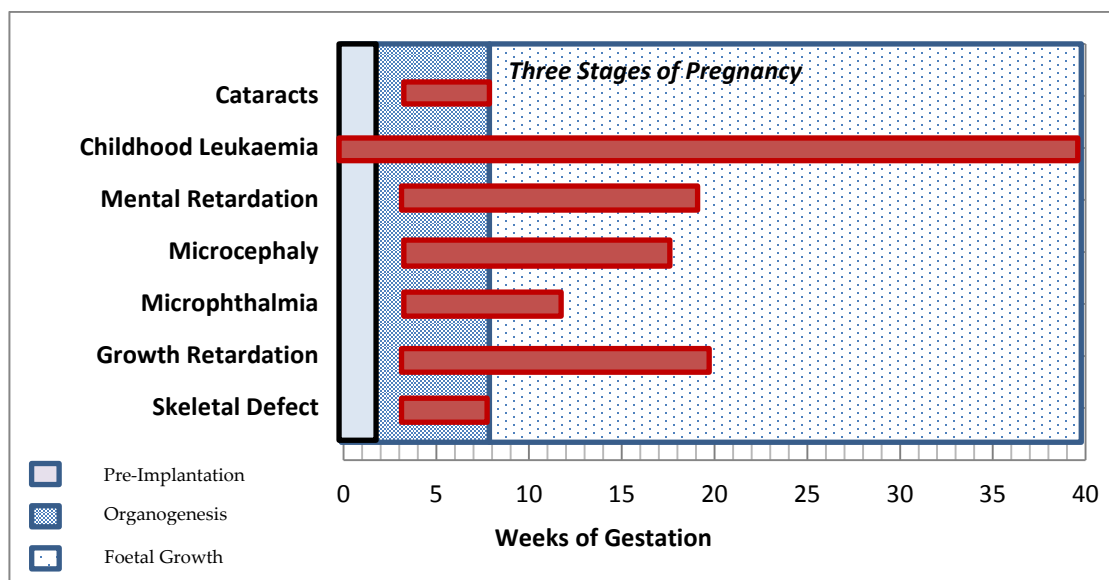


Figure 2.7: Critical periods for radiation induced birth defects in humans

(Adapted from Bushberg JT et al, The Essential Physics of Medical Imaging 2nd Ed. Philadelphia : Wolters Kluwer Health/Lippincott Williams & Wilkins, 2002)

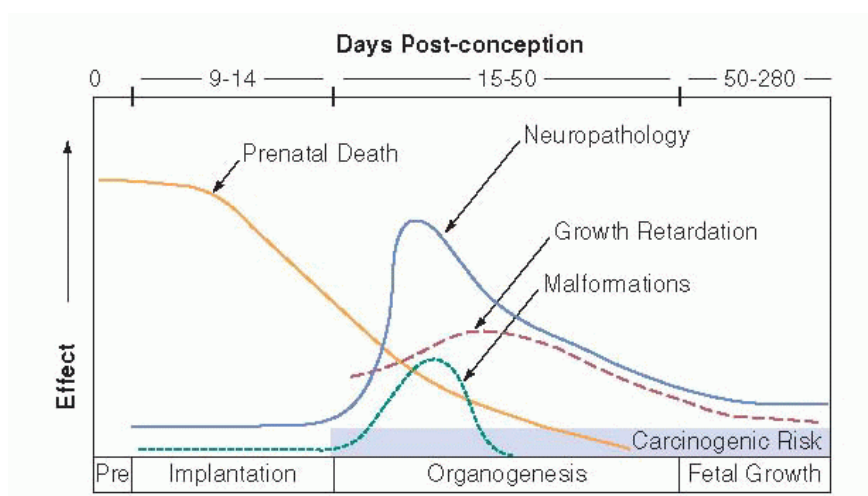


Figure 2.8: Relative sensitivity for radiation-induced effects during different stages of foetal development (9)

2.5.4 RISK OF CANCER INDUCTION FOLLOWING FOETAL IRRADIATION

Stochastic effects have no threshold dose and as such, any radiation exposure has the potential to induce cancer. Risk may be expressed as absolute or relative risk. Relative risk relates to the risk as a function of background cancer risk. Absolute risk indicates the numbers of excess cancer cases in a population. Studies have shown that foetal doses greater than 10 mGy result in a relative risk of 1.4 (40% above background risk)

for childhood leukaemia and other cancers. (2) Although this represents a very small increase, because the background incidence of childhood cancers is very low, it is approximately equivalent to an absolute risk of 1 cancer death per 1700 children exposed in utero to 10 mGy. The relationship of risk of cancer production with gestational age is uncertain but is estimated to be relatively constant from organogenesis to term (23).

UNSCEAR 2000 Report (24) clearly states the prenatal exposure to ionising radiation may induce cancer and that even low doses of radiation may initiate tumourigenesis due to damaged DNA. It states there is a clear relationship between radiation exposure and increased risk for leukaemia. The report notes that although increased risk at low doses is difficult to detect, it does not mean the risk does not exist. In addition, as the relative risk increases with decreasing age at exposure, as demonstrated among atomic bomb survivors, it raises concerns regarding a potentially higher sensitivity to cancer induction for those exposed in utero.

ICRP 103 (14) concludes that studies show there is an appreciable lifetime risk from irradiation in utero but, at this time, the size of the risk remains uncertain due to limitations in the major datasets: Japanese atomic bomb survivors data and the Oxford Study of Childhood Cancers (OSCC) diagnostic radiation study. The report recommends that careful consideration be given to protecting the foetus in the early weeks after conception when medical exposures may occur in the context of unknown pregnancies.

2.5.5 FOETAL DOSE ESTIMATION FOR NUCLEAR MEDICINE EXAMINATIONS

The direct measurement of radiation dose to the organs and tissues in the individual human body from nuclear medicine procedures is rarely possible. Dose estimations are made using complex Monte Carlo simulations and basic physics probability models. The Society of Nuclear Medicine and Molecular Imaging (SNMMI) Committee on Medical Internal Radiation Dose (MIRD) develops standards, models, assumptions and mathematical schema for assessing internal radiation doses from radiopharmaceuticals (25). The committee aims to provide relatively simple dosimetry analyses for clinical

use. The MIRD Committee publishes reports on dose estimations for radiopharmaceuticals and provides internet software tools to assist in calculating individual doses in the clinical environment.

Estimation of foetal dose from maternal nuclear medicine examinations can be difficult. Many factors need to be considered when calculating foetal dose estimates. Some of the factors that are required include the physical properties of the radionuclide (such as its half-life, type and energy of emissions), the administered activity of radiopharmaceutical and the stage of the foetal development (5). The chemical and biological properties of the radiopharmaceutical must also be taken into account to determine the amount of placental transfer and the biodistribution of the radiopharmaceutical in the foetal tissues (5). Also adding to the dose is external irradiation to the foetus from the maternal organs (such as the urinary bladder) (26). Dose calculations for nuclear medicine are not dependent on the type of imaging equipment unless hybrid scanners with CT are used.

The estimated foetal doses for some of the most commonly used radiopharmaceuticals for diagnostic nuclear medicine are displayed in Table 2.4 (5). This clearly shows that foetal dose is not just related to the administered activity of the radionuclide.

2.5.6 HYBRID IMAGING

In recent years, hybrid imaging systems, such as SPECT/CT and PET/CT, have been introduced and rapidly incorporated into general nuclear medicine practice. In Australia, the number of CT scans performed on SPECT/CT systems increased significantly from 7597 procedures in 2007, to 91924 in 2010, and 194668 in 2013 (27). Hybrid imaging systems combine the functional imaging capabilities of a gamma camera with the anatomical imaging of a CT (1). The use of SPECT/CT and PET/CT increases the patient's radiation exposure, and hence the dose to the foetus, by combining the exposure from the radiopharmaceutical with that of the CT scans. Depending on the CT exposure factors used, "the effective dose to the patient from CT component may be larger than that of the radiopharmaceutical" (1).

If a CT is performed over the abdomen or pelvis of a pregnant woman there will be a significantly increased risk to the foetus because these procedures involve exposures of 10 mGy or greater depending on the exposure factors (28). Angel et al (2008) conducted a study using Monte Carlo simulations to estimate foetal dose from abdominal and pelvic CT examinations performed on multi-detector CT scanners (29). The study used actual pregnant patient's CT scans with anatomy that represented a range of gestational ages. The estimated mean foetal dose was 10.8 mGy/100mAs with a range of 7.3-14.3 mGy/100 mAs.

The CT scan performed on hybrid systems, in conjunction with SPECT and PET imaging, is generally performed as a low-dose examination to assist with anatomical localisation and attenuation correction. These CT scans provide considerably less exposure than diagnostic quality CT (30). Sawyer et al (2008) (31) reported average effective adult doses from low dose abdominal CT of 1.5 mSv compared to 8 mSv reported by Mettler et al for diagnostic quality abdominal CT (32). CT dose is dependent on several parameters which can be controlled by the operator, such as current (mAs), energy (kVp), scan length, slice thickness and pitch. Therefore, imaging protocols which minimise the dose from CT in hybrid imaging should be implemented to reduce patient exposure and in the case of pregnant or potentially pregnant women reduce possible foetal exposure. CT dose can be further minimised using dose modulation software such as CareDose (Siemens (Munich, Germany)) and DoseRight (Philips (Amsterdam, Netherlands)).

2.6 RECOMMENDATIONS AND REGULATIONS REGARDING IONISING RADIATION AND PREGNANCY

Several well-recognised published documents provide guidance regarding the radiologic imaging of pregnant and potentially pregnant women. These include documents and reports released by international and national organisations such as the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), International Commission on Radiation Protection (ICRP), National Council on Radiation Protection and Measurements (NCRP), the Society of Nuclear Medicine and Molecular Imaging (SNMMI), and the Australian Radiation Protection and Nuclear

Safety Agency (ARPANSA). All of the professional and regulatory bodies governing the use of ionising radiation for diagnostic imaging procedures recommend that the pregnancy status of all females of child-bearing age should be verified prior to any procedure utilising ionising radiation. However, there are no clear guidelines on what constitutes childbearing age or how to determine the patient's pregnancy status in the documents.

2.6.1 UNITED NATIONS SCIENTIFIC COMMITTEE ON THE EFFECTS OF ATOMIC RADIATION

Across the world, radiation protection recommendations regarding the radiologic imaging of pregnant or potentially pregnant women are based on UNSCEAR Reports (Figure 2.9). UNSCEAR was established by the General Assembly of the United Nations in 1955 with a mandated purpose to assess and report levels and effects of exposure to ionizing radiation. Scientists from 27 countries serve as members of the Committee. UNSCEAR publishes scientific reports assessing the effects of exposure to ionising radiation. These reports are used by other international organisations, such as ICRP and IAEA, as a basis for estimating radiation risk and establishing radiation protection recommendations. (33) In Australia, the Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) provides guidance for Nuclear Medicine personnel on the radiation protection of the patient.

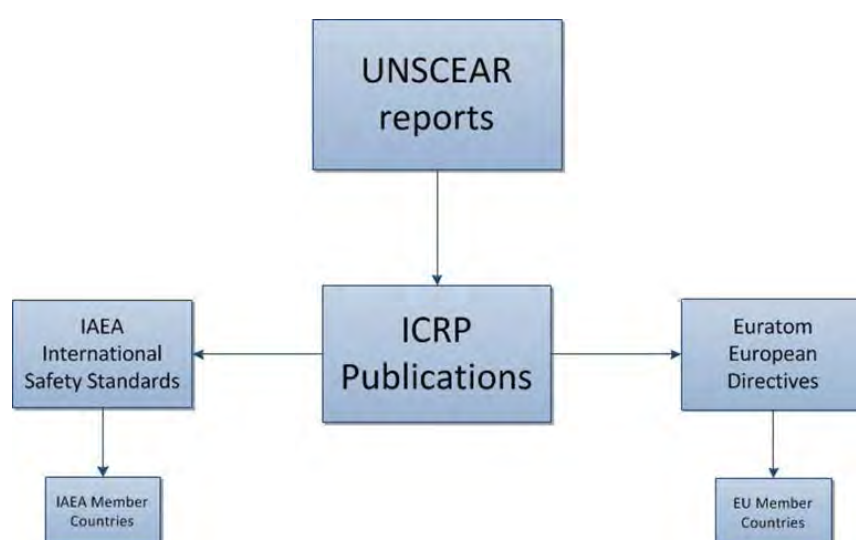


Figure 2.9: International Radiation Protection

2.6.2 INTERNATIONAL COMMISSION ON RADIATION PROTECTION

The ICRP system of radiation protection is based on three fundamental principles: justification, optimisation and dose limitation. In medical imaging, the exposure is intentional but the aim is to “do more good than harm to the patient” (14). Thus, the use of medical radiation must always be justified to ensure the benefits outweigh the risks and the most appropriate procedure is performed. The process of optimisation of radiation protection for medical imaging involves ensuring that exposures are as low as reasonably achievable below the dose constraints (14). For the medical use of radiation, justification of the procedure and optimisation of protection are emphasised; as dose limits are not set for patients.

ICRP 84 (2) and ICRP 103 (14) state that the risk to a foetus from ionising radiation is most significant during organogenesis (weeks 3-8) and in the early foetal period. On the basis of data from animal studies and the Japanese atomic bomb survivors, it is judged that physical malformations have a threshold dose 100mGy or higher and severe mental retardation has a threshold dose of around 300mGy (14). These doses are well above those used in diagnostic nuclear medicine. However, a 40% increase in the incidence of leukaemia and other cancers from a foetal dose of 10 mGy or more has been reported (34). Nuclear medicine examinations have the potential to deliver doses above 10 mGy (Table 2.4), especially when hybrid imaging is performed (5) .

ICRP 84 provides advice regarding the use of radionuclides for diagnostic nuclear medicine procedures in potentially pregnant women (2). The report recommends that patients undergoing any procedure that may result in a foetal dose of greater than 1 mGy should receive a detailed explanation of the relative risks to a foetus. Patients of childbearing age should be interviewed and if pregnancy status is uncertain, or the menstrual period is overdue, a pregnancy test should be performed (2).

2.6.3 AUSTRALIAN AND NEW ZEALAND GUIDELINES

In 2008, the Australian Radiation Protection and Nuclear Safety Agency ARPANSA published the Safety Guide for Radiation Protection in Nuclear Medicine (1) which provides advice and guidance on radiation practice. Section 5 (p24-28) discusses the

protection of the embryo or foetus. The Guide states that “illustrated signs” advising patients to inform staff if they may be pregnant are to be placed in prominent places within a nuclear medicine department. It also states that “staff have a responsibility to enquire about the possibility of pregnancy in all female patients of childbearing age”. ARPANSA recommends the patient is given an explanation as to why the question is being asked to ensure full cooperation and a truthful response. This is identified as a sensitive issue which requires “tact and discretion”, especially with teenagers and if language barriers exist.

When pregnancy status is deemed uncertain, ARPANSA recommends consulting the nuclear medicine physician to decide if the procedure should be postponed or whether to perform a pregnancy test. This report advises that reasonable steps must be taken to ascertain the pregnancy status of a patient if the foetal dose is estimated to exceed 1 mGy.

The Australian and New Zealand Society of Nuclear Medicine (ANZSNM) has a Code of Nuclear Medicine Technologists Practice (35) document which is available on their web site. It advises nuclear medicine technologists of the obligations and responsibilities of their work. It does not mention checking for pregnancy prior to commencing a procedure. This document is currently under review.

2.6.4 UNITED KINGDOM GUIDELINES

In the UK, the Administration of Radioactive Substances Advisory Committee (ARSAC) provides guidance on the radiation protection of patients undergoing nuclear medicine examinations. The British Nuclear Medicine Society (BNMS) refers its members to the ARSAC publications for information regarding pregnancy and foetal irradiation.

In March 2006, ARSAC published “Notes for Guidance on the Clinical Administration of Radiopharmaceuticals and Use of Sealed Radioactive Sources” (36). This document has been revised several times, most recently in 2014. Section 7 deals with Conception, pregnancy and breastfeeding. If pregnancy cannot be excluded, the report recommends asking the patient if her menstrual period is overdue and if the period is

not overdue, low dose procedures can continue. If the period is overdue, confirmation of pregnancy is recommended for higher dose procedures that result in foetal doses in the order of tens of milligrays. The report states that an age range for females to be questioned should be established and suggests 12 to 55 years.

2.6.5 UNITED STATES OF AMERICA GUIDELINES

In 2013, the National Council on Radiation Protection and Measurement (NCRP) released NCRP Report no 174 - an updated report on the potential effects and protection from ionising radiation exposure during pregnancy (37). The report provides a comprehensive review of current state-of-knowledge regarding risks and effects of ionising radiation exposure to the developing foetus. It discusses assessment of dose and protective measures for medical, occupational and environmental exposures. However it does not provide any specific advice on how to question patients regarding their pregnancy status prior to diagnostic nuclear medicine procedures.

The Society of Nuclear Medicine and Molecular Imaging (SNMMI) is the primary professional organisation for Nuclear Medicine Scientists in the USA. In 2007, the SNMMI approved and published a Procedure Guideline for the Use of Radiopharmaceuticals 4.0 (38). This guideline is intended for nuclear medicine practitioners to assist in establishing policies regarding the use of radiopharmaceuticals. It briefly states that female patients who are “postmenarcheal and premenopausal” should be asked about pregnancy. It does not provide any information on an age range to ask or how to question the patient. Pregnancy testing is recommended before any procedure that could potentially result in a foetal dose of 50 mGy or greater.

In 2007, Applegate (39) suggested that the American College of Radiology (ACR) develop a national guideline to address pregnancy screening of patients prior to diagnostic radiology procedures to provide a standardised approach to identifying pregnant patients. The article highlighted the lack of any survey data investigating current practice and an apparent wide variation in departmental procedure. Topics

suggested for the proposed guidelines included how the patient should be questioned, age range for screening, use of urine and blood pregnancy testing, and documentation. In 2008, the ACR released “ACR Practice Guideline for Imaging Pregnant or Potentially Pregnant Adolescents and Women with Ionizing Radiation”. (40) These guidelines address the possible radiation risks to the foetus and how to screen for pregnancy. The guidelines were developed for diagnostic radiology and specifically state that “it does not address issues for nuclear medicine”.

2.6.6 EUROPEAN GUIDELINES

The European Commission is the executive body for the European Union (EU). It represents the interests of Europe as a whole and sets priorities for action, drafts legislation and manages and implements policy. In the EU, radiation protection legislation relating to ionising radiation derives from the Euratom Treaty. Its common objective is to establish uniform safety standards to protect the health of workers, patients and the general public and to ensure that they are applied. The specific requirements for radiation protection are found in Chapter 3 "Health and Safety". This system has been embodied in various European Directives most notably the Basic Safety Standards (BSS, originally adopted in 1959 and last revised by Council Directive 96/29/EURATOM) and the Medical Exposure Directive (MED, 97/43/EURATOM). The Medical Exposure Directive deals with the health protection of individuals against the dangers of ionising radiation in relation to medical exposure. This is the main legal instrument dealing with the protection of patients undergoing diagnostic and therapeutic procedures which utilise ionising radiation.

The European Commission publishes radiation protection reports for use by members of the EU. In 1998, Radiation Protection 100 (18) was released providing guidance for the protection of unborn children irradiated due to parental medical exposures. It recognised that unborn children are particularly vulnerable to ionising radiation and that there are increased risks to the foetus for malformation, mental retardation and radiation induced cancer. The report recommends questioning women regarding their pregnancy status verbally or in writing, and recording the response. It states that this should apply to all women of childbearing potential from puberty until menopause

and suggests an age range of 12-50 years, and that if any doubt exists regarding the women's pregnancy status, the procedure should be postponed until a pregnancy test can confirm the pregnancy or otherwise. The report also comments on the use of oral contraceptives and stresses that their use does not guarantee that a patient is not pregnant.

Schreiner-Karoussou (41) conducted a preliminary review of European practice concerning ionising radiation and pregnancy in 2009 and concluded that there was "no harmonisation on this issue at the European level" (p81). The report suggested that there was a lack of consistent practice and thinking in this area among health professionals and that more research is required to give it the merit it deserves.

2.7 DIAGNOSIS OF PREGNANCY IN EARLY PREGNANCY: A SYSTEMATIC REVIEW (PAPER ONE).

This paper was submitted for publication to the *Medical Journal of Australia* in February 2015 and is currently under review.

The co-author of this paper is the principal supervisor of the PhD.

ABSTRACT

Objective: To explore the literature to identify the diagnostic accuracy of pregnancy testing in early pregnancy, and the reliability of patient history to identify early pregnancy.

Study design: Systematic review of peer reviewed literature.

Data sources: Electronic databases were searched to identify articles published in English from 1975. Original articles investigating the diagnostic accuracy of pregnancy testing or pregnancy screening strategies and comparing results to a reference test were included. Reference lists of included articles were searched for relevant unpublished articles and reports.

Data synthesis: Ten papers out of 2041 titles met the inclusion criteria. Five articles reported on the sensitivity and accuracy of pregnancy testing in early pregnancy. Sensitivity, specificity and accuracy for pregnancy testing have all improved to >99% over the past 20 years. Five articles discussed the use of a questionnaire to predict the pregnancy status of patients presenting to the ED.

Conclusion: Diagnosing early pregnancy can be problematic and although the detection limits for HCG in urine and serum testing have decreased, false-negative results may still occur if testing is used prior to the date of missed menses. Patient prediction of pregnancy status is reliable however; pregnancy testing should be used when any uncertainty exists.

Keywords: Pregnancy, diagnostic test use, general practice

INTRODUCTION

Diagnosing or excluding early pregnancy in women is an important step in primary care and emergency departments. Early pregnancy can be defined as the period known as organogenesis which lasts from weeks two to eight post conception (42, 43). Women are often unaware they are pregnant at this stage and since the foetus is highly sensitive to the harmful effects of teratogenic drugs and ionising radiation it is often necessary to determine a patient's pregnancy status prior to performing surgical and diagnostic procedures or prescribing treatment (39, 44).

Preoperative pregnancy testing has been a topic of interest in anaesthesiology for some time (45). Although the possible teratogenic and abortive effects of commonly used anaesthesia are widely acknowledged, routine pregnancy testing prior to surgery has not been mandated. The National Institute for Health and Care Excellence (NICE) *Preoperative tests: The use of routine preoperative tests for elective surgery [CG3]* (2003) recommends pregnancy testing on women “who says it is possible that she may be pregnant” and to consider pregnancy testing for women “with history of last menstrual period” or “who says that it is not possible for her to be pregnant”. Obviously, the need for pregnancy testing prior to surgery depends on the risk from the anaesthetic and surgery, and the urgency of the procedure.

Exposure to ionising radiation from medical imaging procedures during organogenesis may induce teratogenic, mutagenic or carcinogenic changes (2). In order to protect the foetus the regulatory and professional bodies involved with the use of ionising radiation for medical imaging recommend checking patient pregnancy status prior to performing procedures using ionising radiation (2). Certain medications can induce adverse effects on a fetus if taken by the mother in the early stage of pregnancy. Isotretinoin, an effective acne treatment widely prescribed for severe cystic acne in Australia and the UK, is a known teratogen causing fetal abnormalities in rodent and primate models (46). Other known teratogenic medications, such as ACE (angiotensin converting enzyme) inhibitors, high dose Vitamin A, lithium and warfarin can adversely affect the health of the fetus so pregnancy checking is recommended before treatment (47).

There is a perception that the ability of the patient to self-diagnose pregnancy is unreliable. Without a clinical examination or pregnancy test, explicit questions regarding the patient's sexual activity, menstrual history and use of contraceptives must be undertaken. In some cases, such as young teenagers, verbal questioning may not illicit a truthful or accurate response, particularly if a parent is present at the time of questioning (48).

The aim of this review is to explore literature that reported on accuracy of:

- pregnancy testing for identifying early pregnancy, and
- patient history to identify early pregnancy; including verbal questioning, written questionnaires and use of last menstrual period dates.

METHODS

A three step search strategy was used for the review. A preliminary search of MEDLINE and CINAHL identified keywords and index terms. A second search using these terms was conducted in MEDLINE, CINAHL, EMBASE, SCOPUS, Web of Science, and the Cochrane Library. Thirdly, the reference list of all identified reports and articles were searched for any additional studies. A systematic review protocol with full details of the search strategy and data analysis is registered with, and published by, the Joanna Briggs Institute (#JBL000702) (49).

The review included studies that report on strategies for identifying early pregnancy (index test) and compared results to a pregnancy test (reference test). The search was restricted to studies published in English from January 1975, when immunoassay pregnancy tests were introduced. The outcome measures considered were urine or serum HCG pregnancy test results, and medical history and/or physical examination.

All articles selected for full text review were assessed by two independent reviewers for methodological quality using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) checklist. The QUADAS checklist includes 14 items related to known areas of bias and it is a recognised indicator of methodological quality (50). Data was extracted from included papers, using the Standards for Reporting Studies of

Diagnostic Accuracy (STARD) checklist (51), including specific details regarding study population, setting, methods, sensitivity, specificity and accuracy of the index test compared to HCG pregnancy test results (reference test).

RESULTS

The search identified 2041 potentially relevant titles. A duplicate search identified 109 duplicate studies, leaving 1932 titles for review. Although the search terms were limited to “humans” and “English language”, a number of studies examining pregnancy in animals and studies published in other languages were identified. All 1932 studies were screened by title and keywords for relevance by two independent reviewers and 97 were retrieved for abstract review. Following careful consideration of the inclusion criteria, a further 53 studies were excluded following abstract review, leaving 44 studies for full text retrieval. A further 21 studies were excluded on full text review. The remaining 23 studies underwent methodological quality assessment by both reviewers using the QUADAS checklist. Ten articles were deemed to be suitable for data extraction. The process of study selection is displayed as a flowchart (Figure 2.10). The articles selected for data extraction included five articles describing the use pregnancy tests and five articles describing other screening strategies, such as questionnaire, to identify pregnant patients (Table 2.5 and Table 2.6). Nine of the included studies were conducted in the USA and one from France. Only 3 studies were published after 2010. A total of 3832 female patients participated in the studies. Participant ages ranged from 12-53 years.

Only five studies were identified that investigated the diagnostic accuracy of pregnancy tests according to our criteria. Four of these were from the USA and the other from France. Two of these studies, performed in 1986 and 1993, compared the index test to a urine HCG reference test rather than a serum HCG test (Table 2.5).

Five studies using a questionnaire as a pregnancy screening strategy were selected for review. All were conducted in the USA, between 1984 and 2011, and investigated the ability of women presenting to an emergency department to predict their pregnancy

status. Study data including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy have been tabulated (Table 2.6).

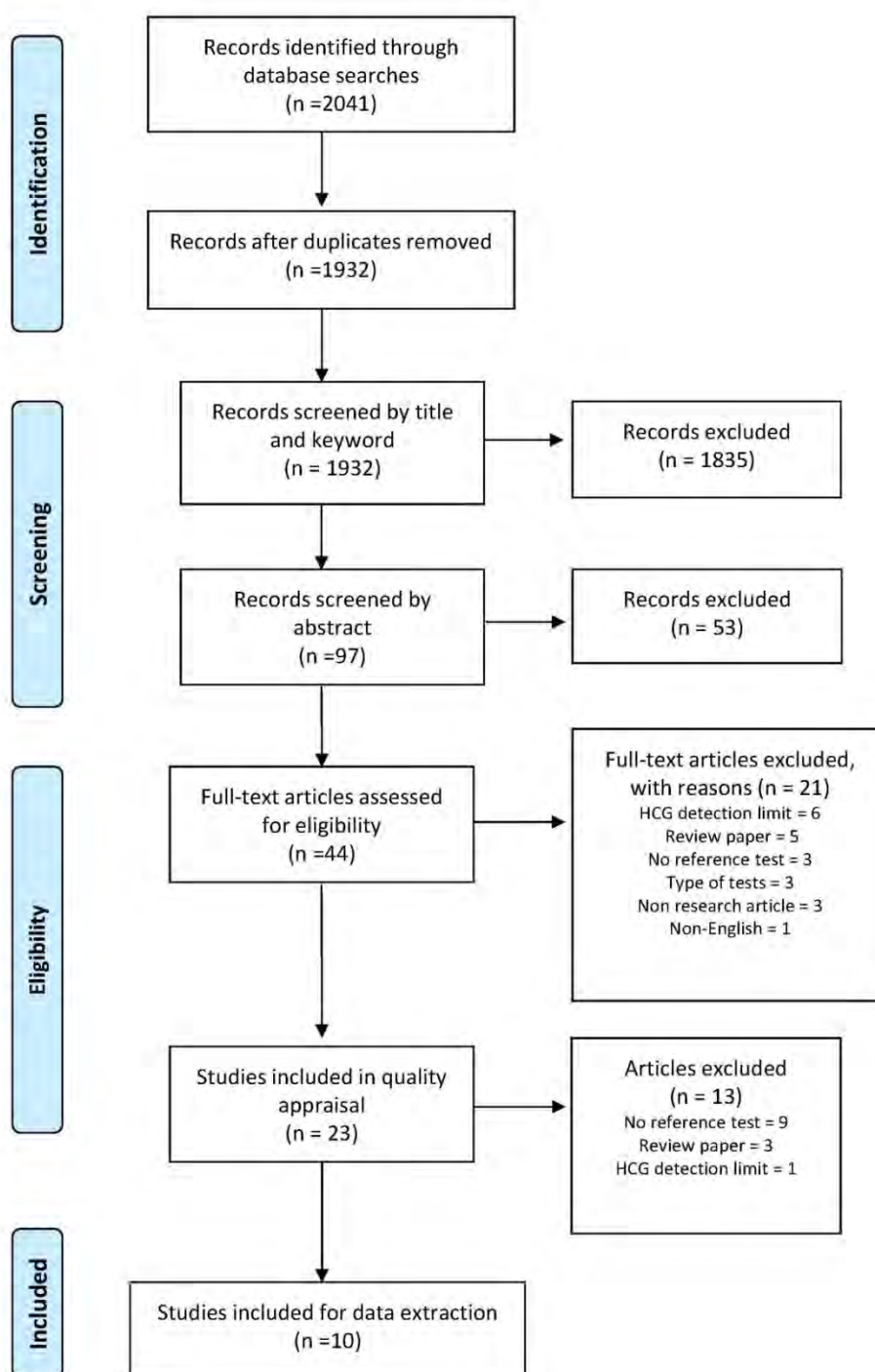


Figure 2.10: Study selection

Table 2.5: Included studies - Pregnancy testing

Date	Authors	Country	Participants			Ref test	Index tests	Reported Results					
			Number	Age	History			Sens		Spec	PPV	NPV	Accuracy
1986	Doshi	USA	109	18-30	Physican ordered preg test - late menses 6-20 d	Urine - Sensi-Tex	Daisy 2	82		64	78	69	75
							EPT	81		*	84	62	83
							Answer	78		64	78	64	73
1993	Daviaud et al	France	631	14-49	Coded urine samples	Urine - Abbott Testpack	11 qual urine kits (not named)	<i>U++</i>	<i>U+</i>			$Pr^{\delta} = 10\%$	
							Kit 9	36	19	94	*	91	*
							Kit 11	100	93	100	*	99	*
							Kit 12	47	14	100	*	91	*
							Kit 14	20	0	92	*	89	*
							Kit 15	93	100	93	*	100	*
							kit 19	93	52	100	*	95	*
							Kit 22	31	33	77	*	91	*
							Kit 23	38	22	87	*	91	*
							Kit24	86	70	100	*	97	*
							Kit 26	94	54	100	*	95	*
							Kit 27	20	7	86	*	89	*
1993	O'Connor et al	USA	186	*	Physican ordered preg test	Tandem Icon II - qual serum	Tandem Icon II - qual urine	100		99	98	100	99
2012	Fromm et al	USA	633	18-51	Physican ordered preg test	Serum total hCG - ADVIA Centaur	ICON 25 rapid hCG - Urine	95		100	100	98	98
2012	Furtado et al	USA	740	18+	Physican ordered serum test	Quant serum Total βhCG - UniCel DxI800	QuickVue One-Step hCG combo - qual serum	97		100	91	100	99
* Not reported δ Prevalance rate U+ HCG concentration the same as the detection limit of the test U++ HCG concentration twice the detection limit of the test													

Table 2.6: Included studies - Questionnaire

Date	Authors	Country	Participants			Ref test	Index tests	Reported Results				
			Number	Age	History			Sens	Spec	PPV	NPV	Accuracy
1984	Bachmann	USA	283	16-28	Physican ordered preg test - late menses	Urine - Neocept	Questionnaire	92	42	53	89	63 [#]
1989	Ramoska et al	USA	208	13-49	Physican ordered serum test	Serum HCG (not specified)	Questionnaire	69 [#]	80 [#]	63 [#]	84 [#]	76 [#]
1994	Stengel et al	USA	191	Av 27 yrs	Present to ED and require preg test	Urine - Tandem ICON	Questionnaire	92	*	*	*	*
2006	Strote & Chen	USA	474	16-53	Present to ED and require preg test	Urine - Mainline Tech OR Serum Abbot AxSYM	Questionnaire	55	95	20 [#]	99	94 [#]
2011	Minnerop et al	USA	377	Med 29	Present to ED and require preg test	Quant serum or urine (not specified)	Questionnaire	100	74 [#]	34 [#]	100 [#]	77 [#]
[#] Calculated result [*] Insufficient data to calculate												

Pregnancy Testing

Doshi (1986) (52) reported on a study of 109 women in USA presenting to doctor's office and health clinics whose menses were late by at least 6 days, but not more than 20 days. They tested 3 qualitative urine home pregnancy tests. The study revealed a marked decrease in the sensitivity (88% to 56%) and accuracy (81% to 65%) for all 3 tests combined when menses was less than 9 days late. Manufacturers of the tests had claimed 98-99% accuracy as early as 6 days after the missed menses date. The decreased sensitivity and accuracy resulted in a larger false negative rate when the tests were used early. The study concluded by suggesting the manufacturers should "re-evaluate their claims" and for women to wait longer before using the tests.

Daviaud et al (1993) (53) conducted a large study in France on home-use pregnancy tests. They tested the sensitivity and specificity of 27 tests under laboratory conditions. Kits which showed 100% accuracy (11 kits) were then tested by 638 volunteers. The women were given coded urine samples which were either negative for HCG, had a concentration of HCG the same as the detection limit of the test (U+), or an HCG concentration twice the detection limit of the test (U++). Each woman was given a sample and a kit to test. They conducted 58 assays for each of the 11 kits. The majority of negative samples were correctly classified as negative (93.7%) however the sensitivity for the positive samples was 42.5% for U+ and 58.5% for U++. They reported that when tested with a U+ sample only 2 kits had a diagnostic sensitivity of >90% and only 5 kits had a sensitivity of >85% for U++. They concluded that a possible cause of the high rate of false negative results was that the volunteers, all lay-woman, had difficulty understanding the instruction leaflet and therefore did not perform the test properly.

O'Connor et al (1993) (54) compared HCG levels in the urine and serum of 186 women presenting to an emergency department (ED) who had a pregnancy test requested. No information regarding the reasons the test was requested or the menstrual history of the patients were reported. They utilised the Tandem Icon II HCG which used monoclonal antibody technology with a detection limit of 10IU/L in serum and 20IU/L in urine with 100% sensitivity, according to the manufacturer. The study reported a

98.4% concordance between the urine test and qualitative serum assay and concluded the tests may be used interchangeably, with the urine test preferable as it was less invasive and cheaper.

In a more recent study, Fromm et al (2012) (55) investigated the use of whole blood instead of urine for HCG bedside testing. This study was conducted in an ED on a convenience sample of women who had a pregnancy test requested. They collected whole blood and urine samples and tested the samples using the ICON 25 rapid HCG immunoassay kit with a detection limit of 25 IU/L. They also performed a quantitative serum HCG test with a positive test criterion of >5 IU/L. In accordance with our review criteria, we extracted data comparing the urine and serum tests only. This study reported a high sensitivity (95%) and specificity (100%) for the urine HCG test and PPV and NPV of 100% and 98% respectively.

In 2012 Furtado et al (56) investigated whether qualitative HCG serum tests were obsolete. They compared the results of the qualitative serum QuickVue One-Step HCG Combo test (detection limit 25 IU/L) with a quantitative serum HCG test (detection limit 1 IU/L) on 740 samples which had been sent to the laboratory for HCG testing. They reported sensitivity (96.8%), specificity (99.6%), PPV (90.9%) and NPV (99.9%) and concluded that qualitative serum tests have similar performance characteristics and turn-around times to quantitative tests, and are cheaper to perform thereby validating their use.

Questionnaires

Gloria Bachmann (1984) (57) evaluated the ability of women to self-diagnose pregnancy. She studied 283 women who requested a pregnancy test due to late menses. Each woman completed a comprehensive questionnaire and had a urine HCG test performed which indicted a positive test at approximately 200 IU/mL. Bachmann concluded that self-diagnosis of pregnancy is not accurate and reported sensitivity of 53% and specificity of 89%.

Ramoska et al (1989) (58) conducted a similar study on 208 patients in an ED comparing questionnaire results to a qualitative serum HCG test. They reported a

pregnancy rate of 7% in patients whose LMP was on time and normal and who stated there was no chance she could be pregnant. They concluded that patient history is unreliable in predicting pregnancy (sensitivity 69%, specificity 80%, NPV 84%) in the ED patient and recommended the liberal use of pregnancy testing.

Stengel et al (1994) (59) investigated the prevalence of undiagnosed pregnancy in an ED and whether patient history effectively detects pregnancy. Their study used a menstrual/sexual history questionnaire and compared the results to qualitative urine HCG test with a reported sensitivity and specificity of 100% for HCG concentrations of >20 IU/L. They reported a pregnancy rate of 6.3% and sensitivity of 92% when asked "Is there any chance you could be pregnant now?" However, the article lacked sufficient data to calculate specificity or accuracy.

Strote and Chen (2006) (60) conducted a similar study of 474 patients in an ED. A questionnaire was completed and either a urine and serum HCG test ordered. The study reported a pregnancy rate of 2.3%. Although the calculated sensitivity was low (55%), the NPV and accuracy were high – 99% and 94% respectively. The study concluded that an affirmative answer to questions regarding pregnancy status had a high likelihood of predicting pregnancy and that an absence of sexual activity or a response of "no chance" was an excellent predictor of a negative pregnancy test.

Minnerop et al (2011) (61) reported another study comparing questionnaires and quantitative HCG tests in 377 patients in an ED setting. The women were asked to estimate the likelihood of pregnancy as impossible, possible or definite. This study reported a pregnancy rate of 12% and a NPV of 100%. They reached a similar conclusion to Strote and Chen.

DISCUSSION

The diagnosis of early pregnancy can be challenging when evaluating patients presenting to primary care and emergency departments. Our study provides a systematic review of the literature and summarises the diagnostic accuracy of pregnancy screening strategies for early pregnancy. Many pharmaceutical interventions and diagnostic tests, such as those that utilise ionising radiation, have the

potential to cause adverse fetal effects. It is important to accurately diagnose or exclude early pregnancy before providing treatment or ordering such tests.

All of the studies reviewed comparing pregnancy tests demonstrated that a low detection limit is needed to maximise diagnostic sensitivity and minimise the false-negative results. The minimum detection limits for HCG testing has decreased over the past 20-30 years. In 1984 Bachmann (57) reported using a urine pregnancy test with a detection limit of 200 IU/L, whereas by 2013 Greene et al (62) reported using qualitative urine tests with a limit of 20 IU/L and quantitative serum test with a detection limit of 1 IU/L. Greene et al reported excellent performance for two point of care (POC) urine tests for specimens with an HCG concentration > 300IU/l. However, the analytic and diagnostic sensitivity for HCG concentrations in the “sub-optimal performance” range of 20-300 IU/L was reported as poor. They estimate the expected false negative rate in a typical patient population to be approximately 2%. For early pregnancy (2-5 weeks gestation) they recommend using quantitative serum HCG tests which have a lower detection limit and are therefore more accurate in diagnosing pregnancy in the early stage.

Studies investigating the ability of women to predict their pregnancy status reported varying rates of unrecognised pregnancy (2.3% up to 12%). All reported good sensitivity, except Strote and Chen (60) whose study reported the lowest pregnancy rate, and excellent NPV for asking a woman if they might be pregnant. Ramoska (1989) suggested that patient history was unreliable in diagnosing or excluding early pregnancy (58). However later studies performed by Strote and Chen (60) and Minnerop et al (61) reported that sexual history and self-assessment were effective predictors of pregnancy. These studies suggest that women are better at predicting when they are not pregnant, especially in the absence of sexual activity. Also oral contraceptive pill (OCP) use was not considered a good means of excluding pregnancy. Although OCP manufacturers advertise 99% or greater efficacy, typical user failure rates within the first year of use have been reported at around 9% (63). All studies recommend taking into consideration a patient’s self-assessment of pregnancy status,

while erring on the side of caution and ordering pregnancy testing when suspicion of undiagnosed pregnancy exists.

Interpretation

Point of care (POC) pregnancy tests using serum and urine samples are frequently performed to identify possible pregnancy (56). Home pregnancy testing (HPT) kits have been reported to be ineffective in identifying early pregnancy. While manufacturers claim greater than 97% accuracy, when performed in the home, the real accuracy may be as low as 77% (64). In particular, there is a high rate of false-negatives reported in early pregnancy. There are many reported possible causes for this including testing prior to the date of missed menses, tests with differing detectable concentrations of human chorionic gonadotropin (HCG), operator error, and dilution of the urine sample (65, 66). Other physiological factors that may inhibit the accuracy of the test include: variation in menstrual cycle length and calculation of expected day of menses, variation in timing of implantation and the HCG concentration in urine (66-68). False negative pregnancy test results, where the woman is assessed to be not pregnant, when in fact she is pregnant, are most concerning as the woman may undergo interventions that could potentially harm the fetus.

Other pregnancy screening strategies, such as questionnaires and medical history, are also used to identify early pregnancy. There is conflicting evidence in the literature regarding the accuracy of these types of strategies to identify the pregnant patient in early pregnancy. A review article by Bastian and Piscitelli (64) looked at articles published between 1966 and 1996 concerning the diagnosis of pregnancy focussing on the use of patient history and clinical examination to rule out early pregnancy. Their search identified nine studies and they used the findings from these to create likelihood ratios to predict the likelihood of pregnancy in certain situations. The review recommended laboratory pregnancy testing is used, rather than clinical history or examination, to accurately rule out pregnancy prior to any treatment or procedure that could adversely affect a foetus. However, it is impractical and expensive to perform serum pregnancy testing on all female patients of child-bearing age presenting for medical imaging or elective surgery.

The WHO Guidelines for Safe Surgery 2009 do not include information regarding pre-operative pregnancy testing. Clinical guidelines for preoperative testing recommend pregnancy checking or pregnancy testing for women prior to surgery (44, 69). An abstract from Euroanaesthesia 2011 reported that pregnancy checking should be performed preoperatively and that a “clear definition of what makes an adequate preoperative pregnancy status check would help in assessment and achievement of standards as well as reducing inter-hospital variability” (70).

CONCLUSION

Although we identified many studies discussing the accuracy of pregnancy tests or pregnancy screening strategies, the review focussed on those that compared outcomes to a reference test. Over the past 30 years, the sensitivity and accuracy of urine pregnancy tests has improved. However, testing in the early stage of pregnancy is still associated with high false negative rates.

A negative urine HCG test prior to the date of missed menses should be followed up with a repeat test a week later or with serum pregnancy test to ensure pregnancy is accurately diagnosed. Patient’s self-assessment of their pregnancy status is reliable for predicting pregnancy however pregnancy testing should be used whenever any uncertainty exists. The lack of studies that met the criteria for review, in particular recent studies, indicates the need for further research in this area.

FUNDING

This systematic review forms part of the doctoral studies of Daphne James. Funding for the review was provided by the University of Newcastle Research Training Scheme.

2.8 REVIEW OF FORMAL METHODS FOR CONSENSUS DEVELOPMENT (PAPER TWO)

This paper has been published in *Nurse Researcher*.

Citation:

James DJ, Warren-Forward HM. Research methods for formal consensus development in health. *Nurse Researcher* 2015; 22(3):35-40.

The co-author of this paper is the principal supervisor of the PhD.

ABSTRACT

Aim: This paper provides a review of three research methods for consensus development.

Background: Consensus statements and guidelines are increasingly used to clarify and standardise practice, and inform health policy when relevant and rigorous evidence is lacking. Clinicians need to evaluate the quality of practice guidelines to determine whether to incorporate them into clinical practice or reject them. Formal methods of consensus development provide a scientific method, using expert panel members, to evaluate current evidence and expert opinions to produce consensus statements for clinical problems.

Data Sources: Online search for relevant literature was conducted in Medline and CINAHL.

Review Methods: A literature review on consensus, consensus development and research methods papers published in peer-reviewed journals and written in English.

Discussion: The three methods of consensus development discussed are the Delphi technique, nominal group technique and the consensus development conference. The techniques and their respective advantages are described, and examples from the literature are provided. The three methods are compared and a flowchart to assist researchers selecting an appropriate method is included. Online resources with information on the development and evaluation of clinical guidelines are reviewed.

Conclusion: This paper will assist researchers to select an appropriate research method for development of consensus statements and guidelines.

Implications for research/practice: When developing consensus guidelines for clinical practice, researchers should use a formal research method to ensure rigour and credibility.

INTRODUCTION

Consensus statements and guidelines are frequently used in health care to inform practice and ensure appropriate practice policies for specific patient conditions. Clinical practice guidelines are used to assist clinicians in decision making and to provide a consistent approach across health departments (71). Ideally these guidelines should be based on sound scientific evidence, however in practice most are derived from the opinions and experiences of clinicians or an expert in the area at the time. In areas where there is a lack of evidence or where evidence is contradictory, practice can vary widely (72). These variations in practice patterns are a significant concern in the health professions as they may result in inconsistencies in patient care and treatment. Expert consensus panels are increasingly used as a decision-making tool to develop practice guidelines and treatment policies (71).

Consensus development methods have been used in health since the 1950's (73). This type of research method uses a quantitative approach to organise the opinions and judgements of a group of people, i.e., qualitative data. Formal methods bring together a group of experts to evaluate evidence, comment on statements and ideas, and ultimately come to a consensus opinion on a clinical problem (74). They attempt to identify all relevant issues and frame these into a series of explicit statements which the group participants rank as to their level of agreement with each statement (73). Formal methods attempt to overcome the disadvantages found in informal group decision making processes such as domination of the discussion by a particular individual or pressure to agree to a majority or powerful person's opinion (72).

Consensus development methods are not a method of creating new scientific knowledge, rather they serve as a process to improve clinical decision-making and assist in the development of health policy (75). Their objective is to determine a central tendency and grade the level of agreement reached (76). Consensus is not necessarily defined as complete agreement between participants. Instead consensus may be defined by a final vote with a pre-determined percentage of agreement (e.g. 80%) (77) or by a rating scale where a specified mean rating is achieved for each topic. (76)

All methods of formal consensus development consist of several key features:

1. Experts are provided with an independent summary of all scientific and research evidence pertaining to the issue.
2. Experts provide their views privately so other members are unaware of their judgements.
3. Experts are given the opportunity to change their initial opinions after seeing the group views.
4. Statistical analysis is used to derive a group decision (73).

Several factors attribute to the success of a consensus method. Selection of appropriate participants is important in determining the outcomes of the group process. Participants should be considered experts in the field, either by virtue of clinical experience or a thorough knowledge of the literature (78). Often patients or other lay persons are incorporated into the group because they have personal experience of the impact of the disease or intervention in question. A diverse group may be able to consider all aspects of the topic; however this may lead to increased levels of disagreement (76). The size of the group should be selected carefully. Larger groups can make the process difficult to manage but may result in an increased reliability of the final decisions. Once recruited, participants should be provided with a summary of current literature to ensure all participants begin with a common level of understanding and that the process remains evidence based (72).

Health care is increasingly influenced by economics, politics, and social and cultural factors (75). The use of research methods designed to achieve consensus across a range of stakeholders are frequently being used. This paper provides a review of three formal consensus development methods used in health care: the Delphi technique, consensus development conference, and nominal group technique (NGT); and offers guidance on which method to use for particular situations before providing information on how to evaluate the quality of guidelines prior to incorporation into clinical practice.

FORMAL CONSENSUS METHODS

The Delphi Technique

The Delphi technique was first developed by the Rand Corporation in the 1950's and named after the oracle at Delphi (79). It was originally used in technological forecasting and to synthesise expert opinion on new technology (72). Since the 1970's it has been used extensively in health, in particular in the nursing profession. There are a number of modified versions of this technique and over the years it has often been criticised for a lack of methodological rigour (80).

The Delphi technique is characterised by the following factors: expert panel, iteration with feedback, statistical group response, and anonymity (79). It utilises a series of questionnaires; each followed by analysis and feedback. The Delphi can be conducted via email with online surveys or via post. Therefore, it can be applied to groups with large numbers of participants from different geographical areas when it is not practical to bring them together (76).

Prior to the first round the goal of the Delphi and a definition of consensus should be defined by the research team. A thorough literature search should be completed to evaluate any existing evidence and a summary should be provided to each participant. The participants, or expert panel, are selected based on their clinical and/or research expertise (79). Typically 3-4 survey rounds are completed with iterative analysis and feedback. Some areas of consensus may emerge from each round and any areas not reaching consensus are developed into subsequent rounds. When an acceptable level of consensus has been achieved, the process will end and final results are presented to the participants. (76).

The advantages of the Delphi technique are:

- the ability to gain the opinions of large numbers of experts,
- participants are able to express their opinions freely due to anonymity,
- reduction in the potential for moderator bias or dominance by an individual,
- cost effectiveness and convenience,

- application to a diverse range of topics, and
- it can be used preceding a nominal group technique in a modified Delphi version.

Some disadvantages of the method include: reliance on questionnaire design and selection of “expert” panel, no personal contact between experts, possible lack of generalizability or scientific validation of findings, and difficulties coordinating large groups (76, 77). Also due to the required number of rounds and their iterative nature, it can be a lengthy process.

The Delphi technique has been utilised in a wide variety of applications in health care to establish consensus opinion, identify research priorities, and develop clinical guidelines. A table of examples of recent studies that have used the Delphi technique is provided (Table 2.7) showing the diversity of its application. The Delphi should be the research method of choice when there is little scientific evidence or conflicting evidence on the topic, and when the cost and practicalities of bringing the participants together is prohibitive.

Table 2.7: Examples of Applications of the Delphi Technique in Health

Study	Purpose	Rounds & completion time	Panel	Outcomes	Consensus definition
USA (81)	Identify and standardise the core clinical knowledge and skills required to care for patients receiving mechanical ventilation	4 rounds 26 months	14 participants Content experts and educators	List of learning objectives in 8 categories	Not reported
South Africa (82)	Obtain consensus on the biggest challenges and important priorities for rural health care delivery in South Africa	3 rounds Time frame not reported	53 participants Health workers, academics	List of top 5 priorities and challenges	Not reported
Australia (83)	Establish consensus regarding clinical identifiers for early stage primary adhesive capsulitis	3 rounds Time frame not reported	70 participants Musculoskeletal experts	List of 8 clinical identifiers established	Not reported
USA (84)	Establish consensus on case history questions and eye examinations for patients with mild traumatic brain injury	2 rounds Time frame not reported	16 participants Optometrists	17 history questions and 7 examination procedures	80%
Sweden (85)	Describe core competencies for nursing practice in renal care in Sweden	4 rounds 6 months	17 participants Renal care nurses	List of 43 core competencies	75%

Consensus Development Conference (CDC)

This method was devised by the US National Institutes of Health and differs from other consensus approaches by providing a public forum for the discussion of issues (79). A decision-making group of participants (usually about 10 people) are chosen for their methodological expertise rather than expertise in the area of concern (74). They are presented with evidence from a small group of experts in the topic who are not involved in the decision making process. In this method any type of evidence, including research evidence, clinical expertise and consumer experiences can be presented to the decision-making panel (75). The meeting is chaired and the panel discuss the evidence and attempt to reach consensus through questioning and discussion. Similar to a legal trial, the group, like a jury, hear evidence and later deliberate, make judgements and produce a definitive consensus statement by the conclusion of the conference proceedings (86). However, unlike a jury, the panel are able to ask questions to clarify ideas and perceptions, and any audience members may also contribute to the discussion. The chairperson, or facilitator, controls the proceedings, directing discussion and delegating tasks (72, 74). It is important that the facilitator moderating the discussion is independent and experienced (75). The facilitator should ensure that all panel members are given an opportunity to contribute to the discussion and that any potential conflicts are managed appropriately. The optimal panel size is reported to be between six and twelve participants, as reliability declines with less than six, and more than twelve becomes difficult to manage (72, 87).

The main advantage of the CDC is that it “fosters dialogue, debate and discussion”. It allows for interaction between participants which is important when multiple perspectives are being considered (75). Another advantage of this method is that bias is reduced as the decision-making panel are not involved in research in the topic of concern and that all panel members have an equal opportunity to influence outcomes (75). A disadvantage of not using experts to make the decisions is that there is a possibility that some meaning of data may be lost, and as the topic experts only have a limited time to present their evidence, not all evidence may be delivered. Also as the

panel members meet, this method does not have the anonymity of the Delphi technique (73). Table 2.8 provides examples of applications of CDC.

Table 2.8: Examples of applications of CDC in Health

Study	Purpose
Sorrel et al 2009 USA (88)	Management of hepatitis B
Signore and Spong 2010 USA (89)	Vaginal birth after Cesarean: New insights
Daviglus et al 2010 USA (90)	Preventing Alzheimer disease and cognitive decline
Berry et al 2011 Australia (91)	Oral hygiene in the critically ill
Wolff et al 2011 Germany (92)	Chronic graft-versus-host disease

Nominal Group Technique (NGT)

Delbecq and Van de Ven devised this technique in 1971 for committee decision making (79). In this method the group consists of a small number of members, typically 6-9 people (86), and the final views are an aggregation of the members' views rather than a communal viewpoint (73). The NGT method is conducted in several iterative stages over one session. The first stage consists of each panel member suggesting any relevant issues surrounding the topic. These suggestions are collated and used to develop a questionnaire covering all identified issues. The questionnaire is circulated and members are asked to rate their agreement on each suggestion using a Likert scale. Finally, the aggregated responses are distributed and members engage in a structured group discussion facilitated by an independent researcher. Each suggestion is discussed by the group and members record their judgements or level of agreement. Further discussion and voting may ensue until a group judgement is decided on (72, 73).

Membership of the NGT group should include representation from the full range of people to which the guidelines will apply. This gives this technique the advantage of including patient opinions in the development of clinical guidelines (93). The technique may be used as part of a "modified Delphi" technique where the first rounds are completed by email and then the panel are brought together for a face-to-face

discussion (74). An advantage of the NGT is that each member is given an equal opportunity to generate and present suggestions, preventing individual members from either dominating the idea generation or leaving it to the rest of the group. Also as the generation of ideas and the discussion and evaluation phases are separated, a greater number of ideas may be potentially developed (72). Limitations of the NGT are the small number of participants involved and the practicalities and cost of arranging at least one face-to-face meeting for all participants (86). Due to the relatively small number of participants contributing their views, this technique has been criticised for its ability to be representative (73). A major concern regarding the NGT is that it does not specifically allow for integration of evidence from literature and thus it has been criticised for a lack of rigour (74). To ensure greater scientific validity for this technique, any clinical recommendations should be developed using systematic reviews or meta-analysis and the expertise of key stakeholders to whom the guidelines may apply including clinicians, academics and patients (93). Table 2.9 provides examples of the applications of NGT.

Table 2.9: Examples of applications of NGT.

Study	Purpose	Participants
Netherlands (94)	Selection of attributes for discrete choice experiments – drug treatment choice in osteoporosis	4-8 patients
Canada (95)	Design of an oral mucositis assessment instrument for use in children	9 health care professionals
Australia (96)	Characteristics of dialysis important to patients and family caregivers	6 groups – 17 patients and 17 caregivers
Canada (97)	Defining Quality Criteria for Online Continuing Medical Education Modules	9 clinical educators

Selecting an Appropriate Method

The decision to use a particular research method should be based on the purpose of the study, the availability of scientific evidence in the field, time and cost factors, and the number of participants and the model of participant interaction (75). Initially a search of the current literature should be completed and all evidence summarised. The level of available evidence will help select the most appropriate method. The CDC is more

appropriate for areas where higher, and more varied, levels of evidence are found (75). The Delphi or NGT are used when low, or conflicting, levels of evidence are available (73). Selection of the “experts” is the next key step which has a direct impact on the credibility and reliability of the research findings (78). There is little consensus in the literature about what constitutes an “expert” however they are usually people who have considerable knowledge or experience in the specific field of study. There is potential for bias when selecting experts who are known to the researcher, although this is sometimes unavoidable when studying small, very specific topics. Researchers should define what “expert” means in the context of their research and thus be able to justify their decision for the selection and rejection of panel members (78). The number of participants and whether they will meet face-to-face is another consideration. This will impact on the costs involved. The Delphi is the most cost effective method as it can be conducted completely via email and online.

A comparison of some of the features of these three research methods is given in Table 2.10 and a flowchart for selecting a method is provided (Figure 2.11).

Table 2.10: Comparison of consensus methods

	Delphi Technique	Consensus Development Conference	Nominal Group Technique
Purpose	Postal or email surveys to assist in prioritisation of issues relating to policy and practice	Presentation of current evidence and subsequent discussion of issues relating to policy and practice	Generation and collation of ideas with subsequent discussion and voting on priorities
Location	Distance	Local	Local
Time Frame	Several rounds conducted over months	One to three days	One day
Anonymity	Yes	No	No
Panel size	Variable	6-12 panel members	6-9 panel members
Analysis	Variable Statistical and descriptive	Variable Majority voting and levels of agreement	Statistical Ranking

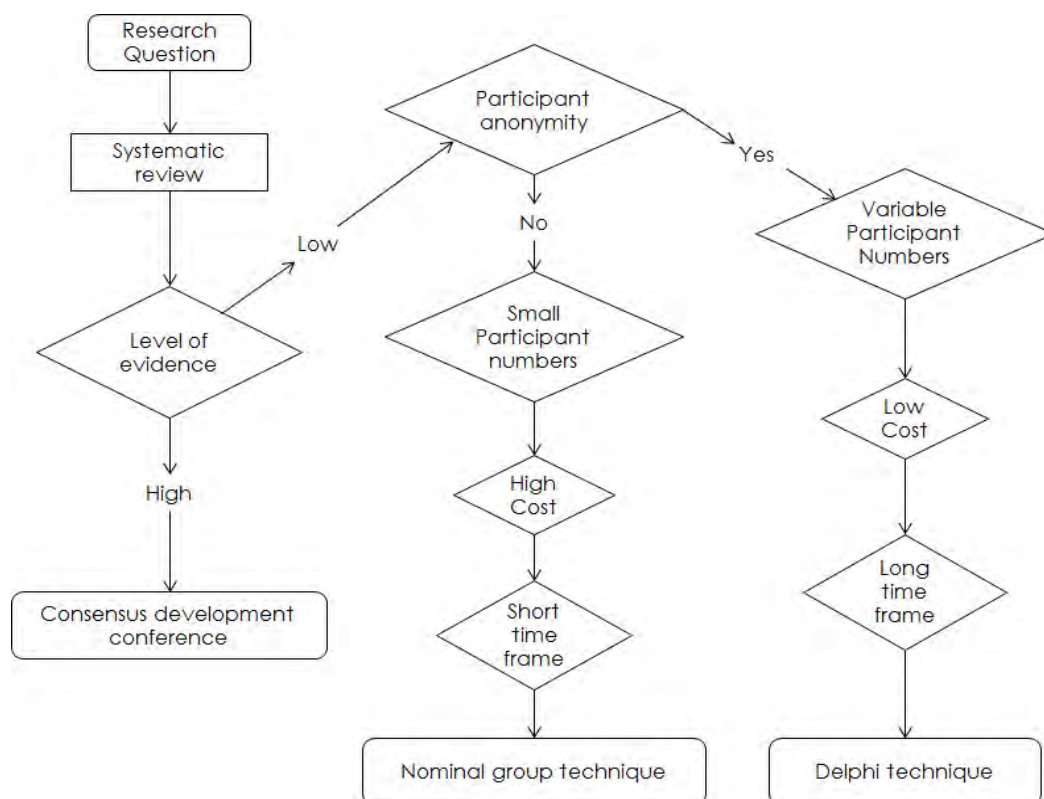


Figure 2.11: Flowchart for selection of a consensus development method

Evaluation of Consensus Guidelines

In all areas of health, clinical consensus guidelines are increasingly being developed to inform and guide practice to ensure consistent, quality care. Clinicians must be able to evaluate these guidelines to decide whether to incorporate them into their day to day clinical practice (74). The method used to develop clinical guidelines should be explicitly detailed and a formal research method should be used to ensure the guidelines reflect the available evidence and the views of experts in the area. A rigorous method helps reduce bias and increases guideline credibility (75). Several national government agencies have created online resources to assist clinicians on how to develop and evaluate clinical guidelines. Some also serve as an open access repository for clinical practice guidelines.

In Australia, the National Health and Medical Research Council (NHMRC) launched the *Clinical Practice Guidelines Portal* (98) in February 2010, and it now has over 300

guidelines registered. The NHMRC web site includes information on how to develop clinical guidelines to the NHMRC standard (99). The web site contains a link to the NHMRC policy on clinical guideline development and conflict of interest published in 2012, which aims to provide guidance and transparency in the declaration of interests. A lack of information on managing conflict of interest in the NHMRC principles of guideline development had been reported (100) and so this policy was developed in recognition that many experts involved in clinical guideline development have interests which may be conflicting and therefore should be appropriately managed and declared.

The U.S. Department of Health and Human Services, Agency for Healthcare Research and Quality (AHRQ), runs the *National Guideline Clearinghouse* which is a “public resource for evidence-based clinical practice guidelines” (101). It has over 2,700 guideline summaries available and also enables the comparison of guidelines on similar topics (101). In the UK, the National Institute for Health and Care Excellence (NICE) provides guidance and advice to improve health care and their web site contains access to over 180 clinical guidelines and information on guideline implementation (102). The Canadian Institutes of Health Research funds the AGREE Enterprise website (Appraisal of Guidelines Research and Evaluation) (103). The original AGREE instrument was developed in 2003 to assess the quality of clinical guidelines using six quality domains: scope and purpose, stakeholder involvement, rigour of development, clarity of presentation, applicability, and editorial independence. The tool was updated in 2010 and the new AGREE II can be used to evaluate the process of practice guideline development, components of final recommendations and the quality of reporting (104).

CONCLUSION

Formal consensus methods are used widely in health to assist in the development of clinical practice guidelines and health policy. There are several methodologies available; each with its own advantages and disadvantages. The Delphi technique is the method of choice when participant anonymity is required and cost is a concern.

Consensus development conferences are useful when there is a large, but conflicting amount of evidence in the literature. The nominal group technique is best for small groups of participants and when of patient opinions are desirable. Researchers should choose the research method and the group participants carefully to ensure credibility and any outcomes should remain closely tied to evidence based literature to ensure rigour and credibility. Once consensus statements or guidelines have been developed, clinicians should carefully evaluate not only their outcomes, but also their method of development prior to incorporating into clinical practice.

2.9 SUMMARY

This review of the current literature discusses nuclear medicine, pregnancy, ionising radiation, radiobiology, and the radiation protection guidelines for pregnant and potentially pregnant women. It highlights the increased radiosensitivity of the foetus in early pregnancy and the potential biological effects of foetal irradiation during maternal diagnostic nuclear medicine examinations. Although many national and international radiation protection documents provide recommendations for the use of ionising radiation in pregnant and potentially pregnant women, none give clear guidelines on how to accurately assess the pregnancy status of women prior to diagnostic nuclear medicine procedures.

This research aims to address the lack of guidelines for the Australian and New Zealand nuclear medicine community by investigating current practice for determining pregnancy status prior to diagnostic nuclear medicine procedures and developing consensus statements to assist nuclear medicine personnel in confidently and accurately assessing the pregnancy status of their patients.

A systematic review on the accuracy of pregnancy screening strategies for early pregnancy revealed that both serum and urine HCG pregnancy tests are highly sensitive however, urine HCG test have a high false negative rate when used prior to the date of missed menses. A number of factors may contribute to the false negative rate in particular urine dilution and variations in menstrual cycle length and timing of implantation. The review also revealed that women are able to reliably self-assess their pregnancy status especially when not pregnant. The review concluded by recommending the use of serum HCG pregnancy tests whenever there is uncertainty as to a woman's pregnancy status.

A narrative review of formal research methods for developing consensus in health was conducted to aid in the selection of a research method for Phase Four of the research. Three methods were reviewed and guidance was provided on how to select the most appropriate for particular situations.

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CHAPTER THREE

INTERVIEW STUDY

3.1 CHAPTER OVERVIEW

This chapter describes Phase Two of the research – a semi-structured interview study.

Nuclear medicine utilises ionising radiation to perform diagnostic imaging and therapeutic applications. The safe use of ionising radiation is a responsibility of nuclear medicine scientists (NMS). Radiation protection regulations recommend all women of child-bearing age are questioned regarding their pregnancy status prior to the administration of a radiopharmaceutical. There are clearly defined guidelines in the literature and radiation protection documents on how to determine pregnancy status prior to therapeutic applications. However, the literature review from Phase One revealed that no guidelines for use in diagnostic imaging procedures have been reported.

Phase 2 of the research consisted of an interview study which aimed to investigate current practice and identify any problems associated with determining the pregnancy status of patients prior to **diagnostic** nuclear medicine procedures. A series of semi-structured interviews were conducted with Chief and Staff NMS employed in a small number of departments in Australia. Invitations to participate were sent to two departments in New Zealand however they did not respond. The Chief NMS was interviewed to investigate the departmental policy, while the Staff NMS interview responses represented staff involved in the department's day-to-day patient examinations.

This chapter consists of one published paper. The paper describes findings from the interviews. These findings were used to develop a questionnaire for Phase 3 of the research - a nationwide survey.

More detailed information regarding the research methodology for the study which was not able to be included in the paper, including participant information sheets, consent forms, demographic questionnaire, and interview schedule, can be found in Appendix C.

3.2 DETERMINING THE PREGNANCY STATUS OF PATIENTS PRIOR TO DIAGNOSTIC NUCLEAR MEDICINE PROCEDURES: THE AUSTRALIAN EXPERIENCE (PAPER THREE)

This paper has been published in the *Journal of Nuclear Medicine Technology*.

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The co-authors of this paper are supervisors of the PhD.

Determining the Pregnancy Status of Patients Before Diagnostic Nuclear Medicine Procedures: The Australian Experience

Daphne J. James¹, Paul Cardew^{1,2}, and Helen M. Warren-Forward¹

¹School of Health Sciences, University of Newcastle, Newcastle, Australia; and ²Hunter New England Imaging, Hunter New England Area Health Service, Newcastle, Australia

Ionizing radiation used in diagnostic nuclear medicine procedures has the potential to have biologic effects on a fetus. Nuclear medicine technologists (NMTs) therefore have a responsibility to ensure that they question all patients of child-bearing age about their pregnancy status before starting any procedure, to avoid unnecessary fetal irradiation. In Australia, there are no clearly defined practice guidelines to assist NMTs in determining whom to question or how to question their patients. **Methods:** Semistructured interviews were conducted with chief NMTs and staff NMTs in 8 nuclear medicine departments in Australia. Questions were based around 5 areas: regulations and policy, fetal radiation exposure, questioning of the patient, difficulties in determining pregnancy status, and the impact of the use of hybrid imaging. Audio files of the interviews were transcribed and coded. **Results:** Topics were coded into 5 themes: policy and awareness of guidelines, questioning the patient, radiation knowledge, decisions and assumptions made by NMTs, and the use of pregnancy testing. There was a wide variation in practice between and within departments. NMTs demonstrated a lack of knowledge and awareness of the possible biologic effects of radiation. **Conclusion:** This study identified a need in Australia for nuclear medicine to arrive at a consensus approach to verifying a patient's pregnancy status so that NMTs can successfully question patients about their pregnancy status. Continuing education programs are also required to keep NMTs up to date in their knowledge.

Key Words: ionizing radiation; pregnancy status; fetal exposure; qualitative

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Diagnostic nuclear medicine procedures involve the administration of radioactive materials, usually intravenously. These radiopharmaceuticals emit ionizing radiation, which

has the potential to have biologic effects on humans. The injected radiopharmaceutical circulates within the bloodstream of the patient and irradiates the entire body. In Australia, nuclear medicine technologists (NMTs) administer the radiopharmaceutical for most nuclear medicine procedures. Although the radiation dose from these procedures is relatively small, the potential for biologic effects on injected patients is recognized (1).

Care must be taken not to administer radiopharmaceuticals to a patient who is pregnant, as biologic damage to the developing fetus may result (2). The response after exposure to ionizing radiation depends on several factors, including total dose, dose rate, radiation quality, and the stage of fetal development at the time of exposure; together, these factors determine the type and extent of damage that may occur (3). Developmental consequences can be teratogenic, mutagenic, or carcinogenic (3). The most radiosensitive period for the fetus is during organogenesis, which occurs at weeks 2–8 after conception (4,5). At this early stage of the pregnancy, many patients are unaware that they are pregnant, and therefore, to protect the developing fetus, it is important that the NMTs have clear guidelines for ascertaining the pregnancy status of their patients. Several well-recognized published documents provide guidance on the radiologic imaging of pregnant patients. These include documents from international and national organizations such as the International Commission on Radiation Protection (2), the Society of Nuclear Medicine (6), and the Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) (7).

In 2008, ARPANSA published the *Safety Guide for Radiation Protection in Nuclear Medicine* (7), which provides advice and guidance on radiation practice. Section 5 discusses the protection of the embryo or fetus. The guide states that “illustrated signs” advising patients to inform staff if they may be pregnant are to be placed in prominent places within a nuclear medicine department. The guide also states that “staff have a responsibility to enquire about the possibility of pregnancy in all female patients of child-bearing age.” ARPANSA recommends that the patient be given an explanation of why the question is being asked to ensure full cooperation and a truthful response. The guide

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For correspondence or reprints contact: Daphne J. James, School of Health Sciences, University of Newcastle, University Dr., Callaghan, NSW 2308, Australia.
E-mail: Daphne.James@newcastle.edu.au
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identifies this questioning as a sensitive issue that requires "tact and discretion," especially with teenagers and if language barriers exist. When pregnancy status is deemed uncertain, ARPANSA recommends that the nuclear medicine physician be consulted to decide whether to postpone the procedure or perform a pregnancy test.

All professional and regulatory bodies governing the use of ionizing radiation for diagnostic imaging procedures recommend verification of the pregnancy status of all female patients of childbearing age before any procedure using ionizing radiation (7). It is thus the NMT's responsibility to perform this verification; however, the documents contain no clear guidelines on what constitutes childbearing age or how to determine the patient's pregnancy status.

All NMTs are trained to question their female patients, but it became evident from talking to NMT colleagues around Australia that the methods used vary greatly between departments and even between staff members within a department. Typically, the NMT will verbally question the patient immediately before administering the radiopharmaceutical. Some departments ask patients to sign a form stating they are not pregnant and may also require them to provide the date of their last menstrual period. Urine and serum pregnancy tests can be used to determine whether a patient is pregnant, but they are not routinely applied.

In recent years, hybrid imaging systems such as SPECT/CT and PET/CT have been introduced and rapidly incorporated into general nuclear medicine practice in Australia. The use of CT combined with SPECT or PET can increase the patient's radiation exposure and hence the dose to the fetus by combining the exposure from the radiopharmaceutical with that from CT. Depending on the CT exposure factors used, "the effective dose to the patient from the CT component may be larger than that of the radiopharmaceutical" (7). If the CT is performed over the abdomen or pelvis of a pregnant patient, there will be an increased risk to the fetus.

In 2007, Applegate (8) suggested that the American College of Radiology develop a national guideline on screening patients for pregnancy before diagnostic radiology procedures to provide a standardized approach. The article highlighted the lack of any survey data investigating current practice and an apparent wide variation in departmental procedures. Topics suggested for the proposed guidelines included how the patient should be questioned, the age range for screening, the use of urine and blood pregnancy testing, and documentation. In 2008, the American College of Radiology released the *ACR Practice Guideline for Imaging Pregnant or Potentially Pregnant Adolescents and Women with Ionizing Radiation* (9). This guideline addresses the possible radiation risks to the fetus and how to screen for pregnancy. The guideline was developed for diagnostic radiology and specifically states that "it does not address issues for nuclear medicine."

In 2009, Schreiner-Karoussou (10) published a preliminary review of European practice concerning ionizing radiation and pregnancy that concluded there was "no harmonisation

on this issue at the European level." The report suggested that there was a lack of consistent practice and thinking in this area among health professionals and that more research was required to give it the merit it deserves.

Our paper describes the findings from a qualitative study investigating current practice in Australia for determining the pregnancy status of a patient before diagnostic nuclear medicine procedures.

MATERIALS AND METHODS

Ethics approval for the study was granted by the University of Newcastle Human Research Ethics Committee in September 2009 (approval H-2009-0270).

After a literature review, interview questions were developed to investigate current departmental policies and practice, NMT knowledge of the biologic effects of radiation and fetal exposure, and problems NMTs associate with determining a patient's pregnancy status. These questions formed the basis of semistructured interviews conducted with chief NMTs and members of their staff.

Eighteen nuclear medicine departments were invited to participate. These included departments from each state of Australia and covered a variety of metropolitan and rural, and public and private, centers. A package sent to the chief NMT of each department contained an information sheet and consent form for the chief NMT, as well as several letters to be distributed among the NMTs working in the department. These letters contained an information sheet, a consent form, and a short demographic questionnaire. If the NMTs wished to participate, they were asked to return the consent form and questionnaire to us. Interviews were conducted at a time and place convenient to the participants.

A guidebook was used during all interviews to ensure that each interviewee was asked similar questions on a series of themes: regulations and policy, fetal radiation exposure, questioning of the patient, difficulties in determining pregnancy status, and impact of the use of hybrid imaging.

All interviews were recorded using a DS-50 digital voice recorder (Olympus). The audio files were transcribed using an online service, and the identity of each participant was masked during transcription. The transcripts were returned to interviewees for review and editing before analysis. After review, each transcript was printed and a paper copy stored for review and analysis. Initial topic coding was performed on the paper transcripts, and computer coding was performed using NVivo software (version 8.0; QSR International).

RESULTS

A total of 16 interviews were conducted from March to October 2010 with 8 nuclear medicine departments. Four departments were within public hospitals, and 4 were private practices. All staff NMTs had a minimum of 3 y of experience working as an Australian and New Zealand Society of Nuclear Medicine-accredited NMT. Table 1 summarizes the demographic information for all departments and participants.

TABLE 1
Participant Information

Department	Australian state	Public or private	Participant ID	Sex	Years as NMT	NMT position	Method of questioning
1	Australian Capital Territory	Private	C1	M	>5	Chief	Verbal and signature
			S1	M	>2	Staff	Verbal and signature
2	Queensland	Private	C2	M	>25	Chief	Verbal and signature
			S2	F	>2	Staff	Verbal and signature
3	New South Wales	Private	C3	F	>15	Chief	Verbal only
			S3	F	>2	Staff	Verbal only
4	Western Australia	Private	C4	F	>5	Chief	Verbal only
			S4	F	>10	Staff	Verbal only
5	Australian Capital Territory	Public	C5	M	>25	Chief	Verbal and signature
			S5	F	>5	Staff	Verbal and signature
6	Victoria	Public	C6	M	>25	Chief	Verbal, LMP, and signature
			S6	F	>2	Staff	Verbal, LMP, and signature
7	Queensland	Public	C7	M	>10	Chief	Written form and signature
			S7	M	>2	Staff	Written form and signature
8	Western Australia	Public	C8	M	>25	Chief	Verbal, LMP, and signature
			S8	F	>10	Staff	Verbal, LMP, and signature

LMP = last menstrual period.

Topic coding identified 37 free nodes (topics), which were further categorized into 5 free nodes (themes). The themes were policy and awareness of guidelines, questioning the patient, radiation knowledge, decisions and assumptions made by NMTs, and use of pregnancy testing.

Three of these themes were aligned with those used at the interview, and the additional themes—decisions and assumptions made by NMTs and the use of pregnancy testing—were related to the question theme of difficulties in determining pregnancy status. The impact of the use of hybrid imaging was included in the theme of “radiation knowledge.”

Policy and Awareness of Guidelines

All interviewees were asked if they knew whether their department had a written policy on verifying the patient's pregnancy status. Only 1 participant (C6) said his department had a written policy but it was “not that readily available” to the NMT working in the department. Nine participants thought that their procedure protocol documents, radiation safety manuals, or consent forms would have information on this.

“In our protocol manual and I think there is also a blurb written with the Radiation Safety Manual as well.” (S1)

“We don't have a written policy as such however it is written into all of our consent forms.” (C7)

Fifteen of the 16 participants (94%) were not aware of any guidelines or policy statements from the Australian and New Zealand Society of Nuclear Medicine, ARPANSA, or other professional bodies that dealt specifically with how to verify a patient's pregnancy status.

Questioning the Patient

Australian policy and guidelines referring to the use of ionizing radiation in medical imaging state that all female

patients of childbearing age must be questioned about their pregnancy status. However “childbearing age” does not have a clearly defined range. Participants were asked what age range of patients they questioned and how they determined which patients would be considered within childbearing age.

There were varied responses from all departments and between the chief and staff NMTs of each department. In 6 of the 8 departments, the responses from the chief and staff NMTs differed. Eight (50%) NMTs specified age ranges from 12, 14, or 16 y to 50–55 y. Eight participants (50%) stated that an age range was not specified in their department, and thus, each NMT made the decision on which patients to question.

“I don't believe we have guidelines for the age. That's just up to the tech at the time.” (C2)

“Pretty much from 16 to 50, but anything under that, and depending where you work, we have a lower class area around us that—you have your suspicions when a young girl comes through, we usually ask the parent to leave the room, and we will question them under the age of 15, 16, if we feel it's necessary” (S6)

“There's a lot of people doing IVF and things these days and having children in their 40s and even into their late 40s sort of thing.” (C6)

Interviewees were asked to describe how they questioned their female patients about pregnancy status. Fourteen participants (87.5%) said that they verbally questioned the patient, and 2 participants (12.5%) said they used a written form that the patient completed and signed. Twelve participants said they required the patient to sign or initial some type of document that indicated she was not pregnant at the time of administration of the radiopharmaceutical. This was stored as part of the patient referral documents. Only verbal

questioning was used by 4 participants, who all worked in private practice. Only 4 participants routinely asked the patient when her menstrual period was. There was 100% agreement between the answers of the chief NMT and the staff NMTs in all departments. The method of questioning used in each department is displayed in Table 1.

All participants using verbal questioning, with or without a signed document, were doubtful that there was any legal validity to this method if challenged in a court of law. Verbal questioning alone left the NMT open to a possible “he said, she said” scenario. According to ARPANSA (7), the “ultimate decision to perform or reject each individual nuclear medicine procedure” lies with the nuclear medicine specialist (the radiation medical practitioner). The referring doctor also has a responsibility to alert the nuclear medicine specialist if a patient may be pregnant.

The participants in the study felt that when the patient gave her signature or initials, it was more a case of the patient agreeing to document that she had been asked about her pregnancy status rather than declaring that she was not pregnant.

“I guess we think it adds, like I say, more the evidence that we’ve asked the question because if someone says I don’t remember that question or we’ve got at least proof that we did ask it and they must have read—it’s a simple statement. So it’s more that that gives us confidence that we’ve checked. Whether it will help our case further in a legal setting, I think we would have to wait and see.” (C5)

In most instances the patient would be asked “Is there any chance you could be pregnant?” or something similar. If the patient responded “No” and was “100% sure,” the NMT would usually go ahead with the procedure with no further questioning. Only when the patient seemed unsure or said she was trying to conceive did the NMT consider asking questions about her last menstrual period, contraceptive methods, or sexual activity.

Several types of patients were identified as potentially problematic. Teenagers were the main group discussed, with most NMTs stating it was difficult not only to decide which young girls to question but also to get a reliable, truthful answer from a girl, especially if she was accompanied by her parents. In some departments, they attempt to take the girl to a private area without the parent and question her there.

“The difficulties obviously are young females with parents in attendance. If they’re around the age of 13/14 you try to separate them from the parents so you can actually get them to answer truthfully.” (C2)

“If the father is standing right next to you when you’re asking quite a young girl, I find that quite difficult. I also find it difficult because it’s very uncomfortable for the young girl as well because the father’s standing there looking at them going, I’m hoping you’re not sexually active. But I do find that quite difficult.” (S3)

Other patients identified as potentially difficult were those with language barriers, different cultural backgrounds, or mental disability and inpatients on certain medications. With

these patients, the NMT was not always sure the patient understood the question being asked or the reasons for it.

“The other group I guess would be the ones who come in who don’t speak English, maybe from a different cultural background” (C7)

“I suppose if you’ve got a patient of childbearing age who’s got any sort of mental or—mental retardation—they’re always difficult to ascertain. Just because they’ve got a disability, you can’t rule them out from being pregnant.” (C2)

“We have so many inpatients we get a lot of people that are on morphine and all sorts of analgesia and are not aware that they’ve actually signed something, or that we’ve given them something or why we’ve given it to them, even though we have described why.” (S5)

Radiation Knowledge

The interviews included direct questions aimed at ascertaining the NMT’s knowledge of, and attitudes toward, ionizing radiation and in particular fetal radiation exposure. Most participants (81%) thought that the most radiosensitive time during gestation was in the first trimester, and only 1 participant could narrow that down to a more discrete time frame. When questioned about the possible consequences of fetal irradiation, only 1 NMT (S8) could give specific information on the biologic effects that may occur. Four participants said they did not know the possible consequences, and 11 participants gave vague responses.

“I guess it could lead to some sort of congenital defect.” (C1)

“Deformities in the fetus and developmental problems and stuff like that.” (S2)

“I guess there would be increased chances of childhood cancers and whatnot like that, but outside of that I don’t know.” (S7)

The NMTs were asked whether they would be concerned if they or their partner were irradiated while unknowingly pregnant. Eight participants (50%) said they would be concerned, and 1 of these said they would terminate the pregnancy. The reasons given for their concern were the same as the reasons the other NMTs gave for not being concerned. Almost all of them said that their knowledge of radiation was sufficient to make them believe that either the fetus would be safe, or that possible biologic damage could ensue.

“I’d be concerned. It’s the sort of thing that because you sort of work in radiation safety and radiation you’re a bit more sort of switched on about it.” (S1)

“I don’t think I would, and I don’t know whether that meant I’m too blasé about radiation or just informed enough to not be concerned about the risk.” (C6)

Decisions and Assumptions Made by NMTs

There were many comments suggesting that NMTs rely on the patient’s word when she says that she is not pregnant. The NMT has a professional responsibility to question the patient about her pregnancy status; however, the patient also has a responsibility to answer truthfully to the best of

her knowledge. If a patient confidently answers that she does not think she could be pregnant, most NMTs said they would accept that response and proceed with the procedure without any further questioning.

"It's not a direct written formal questionnaire; it's purely just based on someone's word." (S1)

"As a rule the patient's word is usually enough and then they sign that form." (C6)

Use of Pregnancy Testing

The routine use of serum pregnancy testing on all female patients would be time-consuming, expensive, and impractical. Patients would have to be sent to a pathology service to have blood withdrawn. In a hospital department that provides this service, obtaining a result could take approximately 1 h. This delay would be inconvenient for the patient and disrupt department workflow schedules. Urine pregnancy tests are a quick way to check if a patient is pregnant, but the results may be unreliable if performed before the date of missed menses and hence are appropriate in only certain cases (11).

Participants were asked whether they used pregnancy testing, under which circumstances they tested, and which types of tests they used. All NMTs except 1 said they had used pregnancy tests but not routinely. Most used the tests when a patient expressed uncertainty about her pregnancy status. Seven participants said they had used only serum β -human chorionic gonadotropin (hCG) tests, whereas 6 used only urine tests. One participant could not recall ever using a pregnancy test on a patient. In 3 departments, the chief and staff NMTs gave differing answers as to the type of testing they used.

DISCUSSION

Nuclear medicine procedures use ionizing radiation, which potentially can have a biologic effect on a fetus. The various organizations that provide radiation protection information and guidance recommend, but do not regulate, how NMTs question female patients of childbearing age about their pregnancy status. This preliminary study investigating NMT practice regarding pregnancy status has highlighted the need for reeducation and an Australia-wide consensus approach to questioning female patients.

This study has shown that a variety of methods of questioning is used across Australia and that NMTs show a lack of awareness of departmental and national policy. Verbal questioning is still widely used but is not usually documented and hence may lead to possible legal complications in the event a patient is irradiated in the early phases of pregnancy.

Although it is recommended that all female patients of childbearing age be questioned, this age range has not been clearly defined. There appears to be no set age limits to which NMTs adhere, and the lower age limit varies within and between departments. A patient from 12 to 16 y old may be questioned, depending on the NMT's assessment of the patient. Women delaying pregnancy until later in life and

the increasing number of older women having in vitro fertilization pregnancies are seen as a reason to ask women up until the age of 55 or 60 y. However, it may be more prudent to question patients about the date of their last menstrual period. This method would identify younger patients who have not begun menstruation and older patients who have completed menopause.

NMTs identified teenagers as one of the most difficult patient groups to question about pregnancy status. The NMTs require tact and sensitivity to ensure a truthful response to questions about pregnancy, especially if the parents are present. Removing the girl to another area, often under the guise of weighing her, is a common tactic used to allow the question to be asked in private without the parent. NMTs in this study reported using visual assessment of the patient and their own discretion to decide which young girls to question. Teenage pregnancy rates are declining across the industrialized world (12). However, both the age at menarche and the age of first sexual experience are also reported to be declining (13), making it imperative for NMTs to ensure that all their younger patients are adequately informed of the risks of radiation and questioned about possible pregnancy.

In Australia, NMTs are required to complete radiation protection and radiation biology education as part of their training courses (14). This study identified a lack of knowledge of the possible biologic effects of fetal irradiation. The fact that all participants had completed their training more than 2 y before the study indicates a need for emphasis on ongoing education in this area.

Pregnancy testing is not routinely used in Australia to screen for pregnancy before diagnostic imaging. hCG is produced after implantation of the conceptus. Detecting hCG levels in early pregnancy is made difficult by variability in the timing of implantation (6–12 d after ovulation) and in the timing of ovulation after the onset of the last menstrual period (11). Urine pregnancy test kits are widely available and relatively inexpensive. However, they have a high rate of false-negative results when used before the date of missed menses (15,16) and hence may fail to identify a pregnant patient if the test is performed too early. Serum hCG tests are able to detect smaller concentrations of hCG than urine tests (17) and therefore are more accurate when used before the date of missed menses. Nuclear medicine practices should carefully assess their use of pregnancy testing to ensure patients in the early stages of pregnancy are identified before they undergo a procedure using ionizing radiation.

CONCLUSION

There appears to be a wide variation in the approaches NMTs use to determine a patient's pregnancy status in nuclear medicine departments in Australia. Verbal questioning is the most common approach used; with or without the addition of a patient's signature to document her response. The age range for childbearing needs to be clearly defined, and NMTs should ensure that all patients within this range

are questioned. A surprising finding of the study was that NMTs often visually assess patients and use their own discretion when deciding whom to question. NMTs also place a great deal of reliance on the patient's word when she says she is not pregnant. The use of pregnancy testing before the date of missed menses should be carefully assessed to determine the most accurate test to detect early pregnancy. This study has identified a lack of a consistent approach by NMTs in Australia when questioning female patients about their pregnancy status before diagnostic nuclear medicine procedures. There is a need for reeducation and a consensus approach to ensure that pregnant patients are not irradiated unnecessarily.

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CHAPTER FOUR

SURVEY

4.1 CHAPTER OVERVIEW

This chapter describes Phase Three of the research – a nationwide survey.

A cross-sectional survey was considered the most effective way to gather data to investigate current practice in Australia and New Zealand for determining a patient's pregnancy status prior to diagnostic nuclear medicine procedures. The findings for the interview study (Chapter 4) revealed a wide variation in the methods used to question patients about their pregnancy status. Interview participants reported using both verbal questioning and written questionnaires. Also the types of questions being asked, the age range for questioning, and the circumstances for using pregnancy testing all varied between, and sometimes within, nuclear medicine departments. The aim of the survey was to capture the opinions of a large, representative sample of nuclear medicine personnel, including nuclear medicine scientists, medical physicists and nuclear medicine physicians, to investigate current practice, and to determine if standardised practice guidelines are required.

This chapter consists of two published papers. The first paper describes the quantitative survey results. The second paper describes the findings from the qualitative data regarding four clinical scenarios identified in the interviews as potentially challenging.

More detailed information regarding the research methodology for the survey which was not able to be included in the papers, including the Invitation to Participate, participant information sheets, survey questionnaire and the coding book for the qualitative analysis can be found in Appendix D.

4.2 PREGNANCY SCREENING STRATEGIES FOR DIAGNOSTIC NUCLEAR MEDICINE: SURVEY RESULTS FROM AUSTRALIA AND NEW ZEALAND (PAPER FOUR)

This paper has been published in the *Journal of Nuclear Medicine Technology*.

Citation:

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The co-authors of this paper are supervisors of the PhD.

Pregnancy Screening Strategies for Diagnostic Nuclear Medicine: Survey Results from Australia and New Zealand

Daphne J. James¹, Paul Cardew^{1,2}, and Helen M. Warren-Forward¹

¹School of Health Sciences, University of Newcastle, New South Wales, Australia; and ²Hunter New England Imaging, Hunter New England Area Health Service, Newcastle, Australia

The ionizing radiation used in diagnostic nuclear medicine procedures has the potential to cause biologic harm to a fetus. Although the risks are relatively small, it is recommended that all female patients of childbearing age be questioned regarding their pregnancy status before administration of the radiopharmaceutical. This can be a sensitive situation especially for certain types of patients, such as teenagers. Currently, there are no guidelines that detail how to question the patient. Previous studies have revealed the lack of a consistent approach in this area. The aim of this study was to investigate current practice for pregnancy screening before diagnostic nuclear medicine procedures in Australia and New Zealand and to determine whether a standardized practice guideline is required. **Methods:** An online survey was administered via SurveyMonkey from October to December 2011. Members of the Australian and New Zealand Society of Nuclear Medicine were invited to participate. The survey consisted of 30 questions divided into 4 sections: demographics, policy and regulations, current practice, and open-ended clinical scenarios. **Results:** Three hundred thirty-five responses were recorded from participants in all states and territories of Australia and New Zealand; 90% were nuclear medicine technologists. Participants reported a low awareness of radiation policy and regulations but demonstrated good knowledge of the relative risk to the fetus from commonly performed procedures. The most common minimum and maximum age to question patients was 12 y (32%) and 55 y (42%), respectively, although the range was from 10 to 60 y. Verbal questioning (44%) was the most commonly used approach. Pregnancy testing was used by 72%, usually if the patient indicated she was unsure of her pregnancy status. Responses to clinical scenarios were varied, and these will be discussed in a subsequent paper. **Conclusion:** The survey revealed a lack of awareness of government regulations and departmental policy regarding radiation protection. The study demonstrated wide variety in pregnancy screening strategies used to determine the pregnancy status of patients before diagnostic nuclear medicine procedures, indicating that a standardized practice guideline is required for Australia and New Zealand.

Key Words: ionizing radiation; pregnancy; fetal exposure

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Received Apr. 3, 2013; revision accepted Jun. 4, 2013.
For correspondence or reprints contact: Daphne James, School of Health Sciences, University of Newcastle, University Dr., Callaghan New South Wales 2308 Australia.

E-mail: Daphne.James@newcastle.edu.au

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Radioactive materials that emit ionizing radiation are used in nuclear medicine to perform diagnostic imaging procedures and therapeutic dose administration. Measures for the protection of the fetus are necessary because ionizing radiation has the potential to cause biologic damage in humans, and fetal tissue is particularly sensitive to these effects (1). The potential biologic effects from irradiating a fetus with ionizing radiation can be “teratogenic, mutagenic or carcinogenic” (2).

Therapeutic nuclear medicine entails the administration of large doses of a radiopharmaceutical designed to destroy specific cells, whereas diagnostic nuclear medicine procedures involve considerably smaller doses to image the physiology and anatomy of the body. It is imperative to determine whether a female patient could be pregnant before administration of the therapeutic dose to protect the fetus. Guidelines published by government and regulatory bodies, such as the International Commission on Radiological Protection (ICRP) (publication 84, *Pregnancy and Medical Radiation* (3)) and the Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) (14.2, *Safety Guide for Radiation Protection in Nuclear Medicine* (4)), contain instructions on how to determine the pregnancy status of the patient before radiopharmaceutical dose administration. Because of the size of the doses used, pregnancy testing within 24 h of therapy administration is mandatory to ensure any unborn fetus is not irradiated (4). However, for diagnostic imaging procedures, where the amount of radiation administered is considerably smaller and the risk to the fetus is less, the guidelines are less clear. It is recommended that all women of childbearing age be questioned regarding their pregnancy status before diagnostic imaging procedures and that signs be placed around nuclear medicine departments asking patients to notify staff if they think they may be pregnant (4). However, there are no instructions on how to question the patient or how to determine which patients should be classed as within childbearing age.

In 2008, the American College of Radiology developed a practice guideline to provide information regarding fetal risk from ionizing radiation and instructions to assist radiographers on how to screen for pregnancy before radiologic examinations (5). These guidelines did not include information for nuclear medicine procedures. In

2009, a review of European procedures suggested that there was a lack of consistent practice in this area and that more research was required (6).

In 2011, James et al. conducted an interview study in Australia to identify the methods used to question female patients about their pregnancy status before diagnostic nuclear medicine procedures and any problems that nuclear medicine scientists (NMSs) associated with these methods. The study reported that a variety of approaches to questioning were used in different departments, and even within departments, and that the most common form of questioning was a verbal approach, with the NMSs often using their discretion as to which patients to question (7). A limited number of interviews were conducted; therefore, the authors decided to investigate whether the findings were representative of current practice in nuclear medicine across Australia and New Zealand. A questionnaire was developed from the findings to investigate knowledge of pertinent regulations, methods of questioning, determination of age range for screening, use of pregnancy testing, and knowledge of fetal risk from ionizing radiation. The questionnaire was used to conduct a nationwide survey of nuclear medicine personnel in Australia and New Zealand.

The aim of the current study was to investigate current practice for pregnancy screening before diagnostic nuclear medicine procedures in Australia and New Zealand and to determine whether a standardized practice guideline is required.

MATERIALS AND METHODS

Ethics approval was gained from the University of Newcastle Human Research Ethics Committee before the study commenced (approval number H-2009-0270).

A SurveyMonkey questionnaire (supplemental data file; supplemental materials are available at <http://jnm.snmjournals.org>) consisting of 30 items divided into 4 sections was developed from the findings of the interview study (7). Questions in sections 1–3 were mainly closed responses, whereas section 4 sought open-ended responses to 4 clinical scenario questions. In section 1, the demographic questions (items 1–8) asked about sex, profession, years of experience, and place of practice to help categorize participants and determine whether the study sample was representative of the nuclear medicine professional community in Australia and New Zealand. Section 2 (items 9–13) investigated participants' awareness of departmental policy and government regulations relating to pregnancy and medical radiation. Section 3 (items 14–25) investigated current practice in determining pregnancy status in nuclear medicine. Participants were asked to nominate the minimum and maximum ages that they routinely questioned their patients and give a rationale for this age. The questions asked which method of questioning was used—verbal, verbal with a signature, or a written form—and whether any questions about last menstrual period (LMP), contraceptive use, or menopause and hysterectomy were included. Participants were asked if they used pregnancy tests in their department and how often they were used, which type (serum or urine) was used, and

in which circumstances they were used. Question 25 asked participants to rank 8 diagnostic procedures in order of risk to a fetus from the exposure to ionizing radiation from each procedure.

Section 4 (items 26–30) included 4 open-response questions on how to question the patient in a series of clinical scenarios and 1 open-response asking for any additional comments. The results from this section will be discussed in a subsequent paper.

The questionnaire was administered as an online survey via SurveyMonkey and was open for 2 mo from October 11 to December 12, 2011. An invitation to participate was published in the September 2011 issue of the *Gamma Gazette* (the journal of the Australian and New Zealand Society of Nuclear Medicine [ANZSNM]). It was also emailed to members of the ANZSNM with a link to the survey. In April 2011, there were 1,115 members of the ANZSNM, of which 839 were NMSs (J. Anderson, written e-mail communication, 2011).

Data analysis was performed using descriptive statistics, and open-ended responses were manually coded using thematic analysis.

RESULTS

Demographics

Three hundred thirty-five responses were recorded, and 66% were from women. Most participants were NMSs (90%). The remainder consisted of 6 physicists and 33 nuclear medicine physicians. Most participants were experienced nuclear medicine professionals, with almost half (48%) reporting that they had more than 10 y of experience in their profession and 88% with more than 3 y of experience. The type of practice that participants were in was relatively evenly split between public (48%) and private (52%) practice departments. Most participants practiced in New South Wales (38%) and Victoria (25%), although responses were recorded from all states and territories of Australia and New Zealand. The survey participants are believed to be representative of the nuclear medicine community in Australia and New Zealand. (J. Anderson, written e-mail communication, 2011).

Policy and Regulations

In response to the question asking if they were aware of a written policy regarding checking for pregnancy before diagnostic procedures in their department, 65% (193/295) indicated yes, with 63% (121/193) having read the policy within the last 12 mo (Fig. 1). When asked if they were aware of any government regulations regarding how to determine the pregnancy status of patients before diagnostic imaging procedures, only 28% (85/298) answered yes. Participants who answered that they were aware of government regulations were asked to briefly state, in their own words, what was included in the regulations (Fig. 2). Participants were then asked if they had read relevant sections in either ICRP 84 (3) or ARPANSA 14.2 (4). Most participants (76% and 64%, respectively) indicated that they had not read these documents.

Current Practice

Age. The most common minimum age reported to be used for questioning a patient about pregnancy was 12 y,

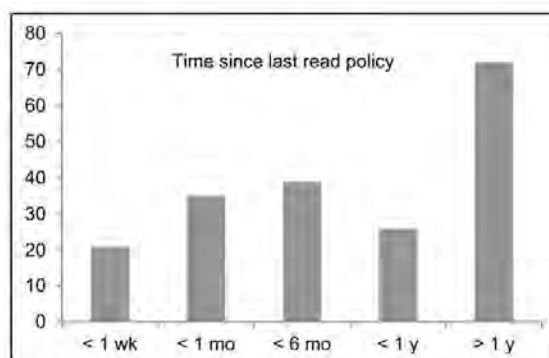


FIGURE 1. Time since participants had read department policy.

and the most common maximum age was 55 y. The age range for questioning was 10–60 y. The number of responses for each age category for male and female participants is displayed in Figure 3. There was no significant difference between the male and female responses ($P = 0.08$).

Participants were asked to state a rationale for using a particular minimum and maximum age to question their female patients about pregnancy. For the minimum age, 6 participants stated it was departmental policy, 6 had personal experience with a girl being pregnant at that age, and 18 said it depended on the maturity of the patient. The following were the most commonly used rationales for minimum age: age of menstruation (113), sexually active at this age (33), and at this age they would ask if the patient is menstruating first (21) (Fig. 4).

For the maximum age to question patients, 10 participants stated it was departmental policy and 7 had personal experience with a woman being pregnant at that age. The most commonly used rationales for maximum age were menopause (110) or unlikelihood of pregnancy at that age (26) (Fig. 5).

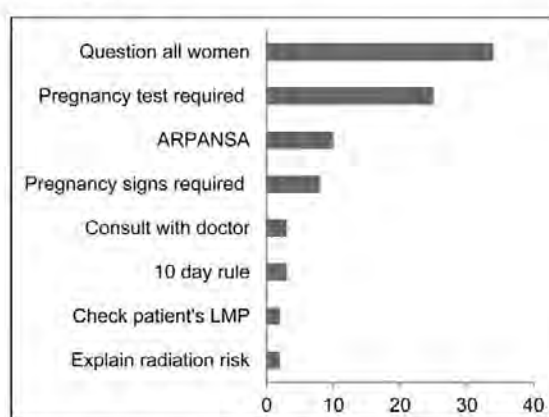


FIGURE 2. Open responses for content of regulations.

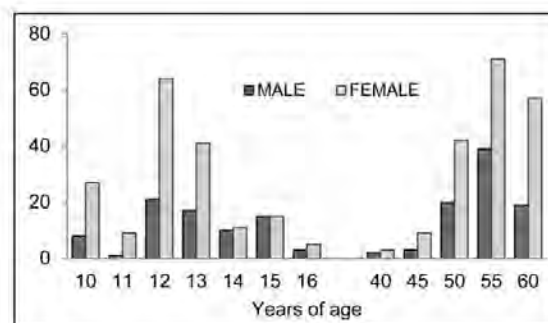


FIGURE 3. Age of questioning.

Method of Questioning. The most common method for determining pregnancy status was the use of verbal questioning (44%), followed by verbal questioning with the addition of the patient's signature (35%). Only 66 participants (21%) used a written form to ask the patients about their pregnancy status. Assuming that the written forms require the patient's signature, most patients (56%) are asked to verify that they have been questioned about their pregnancy status by providing their signature. Participants were asked to indicate if they used questions regarding LMP, contraceptive use, or menopause or hysterectomy history as part of their routine verbal or written questions. Questions about LMP were most commonly asked (89% if verbal; 93% on written form). Participants using verbal questioning were more likely to ask questions about contraceptive use and menopause or hysterectomy than those who used a written form (Table 1).

Use of Pregnancy Tests. Of 262 responses, 72% indicated that they used pregnancy tests in their department. Serum testing (69%) was most commonly used, with 50% using urine tests. The shared percentages are greater than 100% because some respondents ticked both serum and urine testing. Participants were asked to state in their own words in which circumstances they would use pregnancy tests.

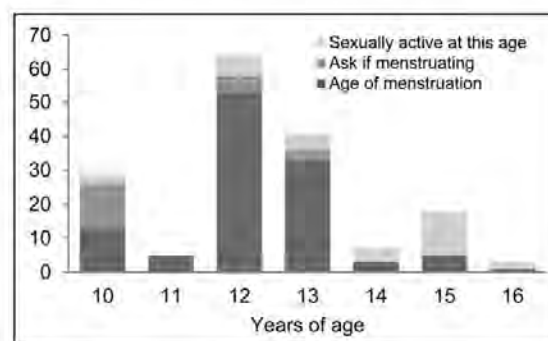


FIGURE 4. Rationale for minimum age.

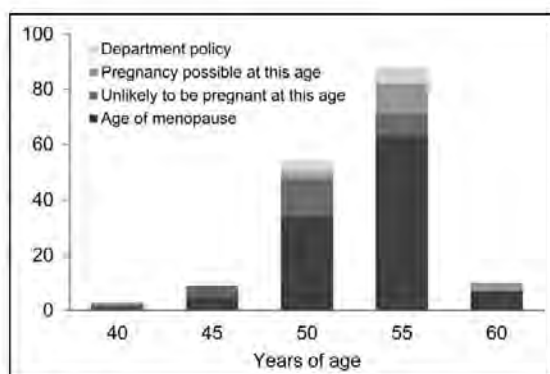


FIGURE 5. Rationale for maximum age.

The main reason cited for using pregnancy tests was if the patient was unsure or doubtful about her pregnancy status (45%). Other reasons cited were for therapeutic-dose patients, if pregnancy could not be excluded, if the patient had had unprotected sex, if their LMP was late, if there had been more than 10 d since their LMP, if the patient thought they could be pregnant, and if the radiation dose from the procedure was considered high (Fig. 6).

Radiation Risk to Fetus

Participants were asked to rank 8 diagnostic nuclear medicine procedures as to their risk to a fetus from ionizing radiation, with a ranking of 1 being the most risk and a ranking of 8 being the least risk. Only 18 of 238 (8%) participants correctly ranked all procedures according to fetal dose estimates reported by United Nations Scientific Committee on the Effects of Atomic Radiation (1). However, most participant responses were correctly ranked if the procedures were classified by relative risk as high (rank 1–3), 77% correct; medium (rank 4, 5), 66% correct; and low (rank 6–8), 75% correct (Table 2).

Table 2 displays the participant rankings for each procedure (i.e., 171 participants indicated that ^{18}F -FDG PET/CT was the highest-risk and 20 participants indicated that it was the lowest-risk procedure). The numbers marked by an asterisk show the correct ranking for each procedure which was also correctly identified by most participants.

TABLE 1
Routine Questions

Question	Verbal (n = 137)	Written (n = 69)
LMP	122 (89)	64 (93)
Contraceptive use	76 (55)	28 (41)
Menopause or hysterectomy	98 (72)	36 (52)

Data in parentheses are percentages.

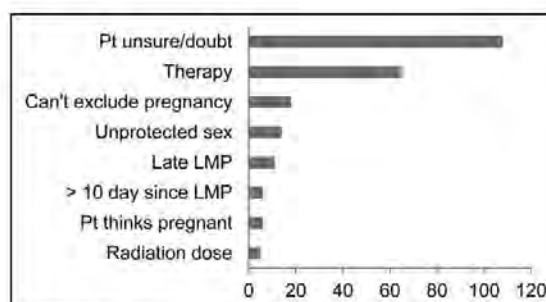


FIGURE 6. Reported circumstances for using pregnancy tests. Pt = patient.

DISCUSSION

Ionizing radiation is potentially harmful to a developing fetus. Although diagnostic nuclear medicine procedures use relatively small amounts of radiation, it is still imperative to determine whether a patient might be pregnant before commencing the procedure. Radiation protection documents such as ICRP 84 (3) and ARPANSA 14.2 (4) provide recommendations regarding the protection of patients undergoing diagnostic nuclear medicine procedures. These documents recommend that all females of childbearing age be questioned regarding their pregnancy status before administration of any radiopharmaceuticals. They do not, however, give instructions on what constitutes the childbearing age range, how to question the patient, or when to use pregnancy testing.

Policy and Regulations

This study revealed a low awareness of government and international regulations concerning pregnancy and medical radiation. Most participants reported that they had not read the relevant sections regarding pregnancy and diagnostic procedures in ICRP 84 (3) or ARPANSA 14.2 (4), which correlates with the findings from a previous interview study conducted by the authors (7).

ICRP publication 84, *Pregnancy and Medical Radiation*, is one of the primary international documents detailing recommendations for the use of ionizing radiation in pregnant and potentially pregnant women. Chapter 6 discusses radiation protection applicable to nuclear medicine. It states that for "women of childbearing age, the possibility of pregnancy and the justification for the examination should be considered." It recommends that patients be "carefully interviewed" to determine their pregnancy status and that "discretion" is required in the case of adolescents. It also states that "advisory notices should be posted" in the nuclear medicine department.

ARPANSA 14.2, *Safety Guide for Radiation Protection in Nuclear Medicine*, was published by the Australian government to provide advice on radiation practice. Section 5 discusses the protection of the embryo or fetus. It states that "all female patients of child bearing age" should be ques-

TABLE 2
Radiation Risk to Fetus

Relative risk	Procedure	Ranking (highest risk → lowest risk)							
		1	2	3	4	5	6	7	8
High	¹⁸ F-FDG PET/CT	171*	32	11	6	7	6	3	20
	Bone scanning with SPECT/CT of lumbar spine	37	131*	35	18	7	9	14	2
	^{99m} Tc-sestamibi myocardial perfusion scan	18	49	102*	31	21	12	13	5
Medium	Gated heart pool scan	2	9	34	85*	73	37	9	2
	Bone scan	1	9	38	81	94*	26	4	1
Low	Renal perfusion scan	5	7	23	21	30	105*	47	14
	Ventilation and perfusion lung scan	10	12	4	6	12	37	93*	81
	^{99m} Tc thyroid scan	14	9	7	5	4	19	68	127*

*Correct ranking for each procedure, which was also correctly identified by most participants.

tioned regarding their pregnancy status “immediately before the procedure”; the reason for asking should be explained to the patient “to avoid the patient taking offense and not answering fully”; this type of discussion “requires tact and discretion”; asking teenagers may be a “sensitive issue”; an interpreter may be required when language barriers exist; and that patient history alone “may not be reliable.” The guide lists several circumstances for when the likelihood of pregnancy is low or physically impossible. These include hysterectomy, tubal ligation, normal menstrual period within the last 10 d (if the patient has regular menstrual periods), contraceptive measures having been taken (providing they have been taken regularly), and no sexual relationship for several months. If pregnancy status is uncertain, “the nuclear medicine specialist should be consulted” to decide whether to postpone the study, perform a pregnancy test, or continue with the study. This decision may be influenced by the “level of radiation dose” from the procedure.

Current Practice

The age range to include for questioning about pregnancy has not been clearly defined. The use of the term “childbearing age” in radiation protection documents refers to any female capable of reproduction. Both the age at menarche and the age at menopause are individual and can vary greatly among women.

The age at menarche is primarily influenced by genetic factors but also by nutrition, geography, and altitude (8). In a study investigating age at menarche in 34 countries, Currie et al. (9) reported that “in 95% of individuals, age at menarche ranged between 10 y 6 mo and 14 y 11 mo.” Several studies (8,10,11) discuss whether there has been a decline in the age of menarche over the past 50 y. Declining age at menarche has been associated with obesity (11). Some studies report a decline in age from 13 to 12 y since the early 20th century, but that in the latter part of the century age of menarche appears stable (8,10). Posner (10)

reports that the “reference range for onset of menarche in the United States is now considered 10–14 y.”

The age at natural menopause varies greatly among women. Factors believed to influence age at menopause include ethnicity, location, smoking, body mass index, physical activity, and number of children (12). A large Australian study of 5,961 twin females by Do et al. reported the median age at natural menopause as 51 y (13). Another study of 5,288 women by Dratva et al., conducted in 9 European countries, reported the median age at menopause as 54 y (12). Surgically induced menopause (hysterectomy or tubal ligation) is associated with earlier timing of menopause (12).

Participants in our study reported using age at menarche as the rationale for applying a particular minimum age to question patients from 10 y and up to 16 y of age. Age of menopause was used as the rationale for choosing a particular maximum age between 40 and 60 y. These choices imply a lack of knowledge regarding these 2 aspects of female physiology and reproduction and possible reliance on personal interpretation and experience. Because both menarche and menopause can occur at different ages in individual women, it may be prudent to first ask whether the patient has either begun menstruating (for young teenagers) or completed menstruating (for women over 50 y of age) or ask the date of the LMP, rather than beginning with a question asking if the patient might be pregnant.

Although 65% of participants indicated they had a written department policy for questioning patients, few stated this as their rationale for the minimum or maximum age to question patients. This may be due to departmental policies that use wording similar to that used in radiation protection documents, which refer to women of childbearing age but do not define the age range or how to determine who is classed as childbearing. For minimum age, many participants commented that selection of patients to question was dependent on the patient’s perceived maturity, implying that some nuclear medicine per-

sonnel make assumptions about the patient when determining pregnancy status.

The American College of Radiology recommends that "all patients of menstrual age (typically ages 12 through 50 y) should be questioned about pregnancy status using a standardized form or through direct questioning by the technologist." In addition, it recommends the use of a standardized form to ensure uniformity in the questioning process (5). Variations in practice can lead to individual patients being treated differently and consequently not receiving the same level of care. Gabel and Shipan state that reducing practice variation is "a fundamental issue for increasing the quality of health care" (14). The development of a standardized form to determine pregnancy status may assist nuclear medicine personnel in ensuring that the appropriate patients are asked appropriate questions. Our study showed a wide variation in the methods used to determine which patients to question and which questions they were asked. Verbal questioning of the patient is still predominately used, with or without the addition of the patient's signature, and this may be a contributing factor to inconsistencies in practice.

Pregnancy testing is not routinely used before diagnostic nuclear medicine imaging procedures. Pregnancy testing for all female patients would be unnecessary, time-consuming, and expensive (7). Urine pregnancy tests are relatively inexpensive and easy to use; however, if used before the date of missed menses they have been reported to have a high false-negative rate (15). The most commonly reported circumstance for using pregnancy testing is when the patient is unsure of her pregnancy status. The reliability of patient history and self-assessment of pregnancy status has been reported with conflicting results (16,17). Minnerop et al. (18) investigated the reliability of patient assessment to exclude pregnancy and found that women are able to exclude pregnancy. They reported a 100% negative predictive value for women stating pregnancy was impossible. They suggest that history of tubal ligation, intrauterine device, or oral contraceptive use should not be relied on to exclude pregnancy. Minnerop et al. recommended using patient history and suspicion of pregnancy and weighing these against the risk associated with an undiagnosed pregnancy to decide if a pregnancy test is warranted.

A small number of participants indicated that they used pregnancy testing if the radiation dose from a procedure was considered high. This is recommended in ARPANSA 14.2 (4); however, a definition of higher dose is not provided. Diagnostic nuclear medicine procedures are generally considered low-dose procedures, with most ^{99m}Tc procedures giving an effective dose of less than 10 mSv to an adult patient (1). Because the dose is quite low for these procedures, it may be sufficient to rely on patient self-assessment of pregnancy status and to use pregnancy testing only where there is concern or doubt surrounding the patient's responses. Other procedures that use longer-lived

radioisotopes, positron emission, or hybrid CT imaging may provide a higher effective dose to the patient and therefore would warrant the use of pregnancy testing before administration of the radiopharmaceutical.

Radiation Risk to Fetus

Estimation of fetal dose from maternal examinations can be difficult. Calculation of fetal dose estimates must include factors such as the physical properties of the radionuclide, the administered activity, and the stage of fetal development. The chemical and biologic properties of the radiopharmaceutical must be considered to determine the amount of placental transfer and biodistribution in fetal tissues. External irradiation of the fetus from maternal organs also adds to the dose (19). The fetal doses from most diagnostic nuclear medicine procedures are "much lower than the levels where developmental and neurologic effects are known to occur" (4). However, the dose levels have been reported to be associated with "a slightly increased risk of childhood cancer or leukaemia" (4). Although the risks to the fetus are low, anxiety and distress may be caused if a woman is irradiated and subsequently finds out she is pregnant. The participants in this study ranked several commonly performed procedures according to their radiation risk to the fetus, and although only a small number of participants correctly ranked every procedure, most participants were able to identify the risks as low, medium, and high.

CONCLUSION

The results of the survey suggest that nuclear medicine personnel in Australia and New Zealand use a variety of methods to determine which female patients to question, and how they are questioned, regarding their pregnancy status before diagnostic imaging procedures. Although there is a lack of knowledge concerning radiation protection guidelines for the protection of the fetus, a good level of knowledge of the relative fetal risk from commonly performed procedures was demonstrated. We recommend that a standardized practice guideline be developed to ensure consistent practice and to reduce the possibility of any unnecessary fetal irradiation.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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4.3 PREGNANCY SCREENING STRATEGIES FOR POTENTIALLY CHALLENGING PATIENTS PRIOR TO DIAGNOSTIC NUCLEAR MEDICINE PROCEDURES: QUALITATIVE SURVEY ANALYSIS (PAPER FIVE)

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The co-authors of this paper are supervisors of the PhD.

Pregnancy Screening Strategies for Potentially Challenging Patients Before Diagnostic Nuclear Medicine Procedures: Qualitative Survey Analysis

Daphne J. James¹, Paul Cardew^{1,2}, and Helen M. Warren-Forward¹

¹School of Health Sciences, University of Newcastle, Australia; and ²Hunter New England Imaging, Hunter New England Area Health Service, Newcastle, Australia

Because of the ionizing radiation used in diagnostic nuclear medicine procedures, it is recommended that all female patients of childbearing age be questioned about their pregnancy status before the procedure begins. Several patient groups have been identified as potentially difficult to question: teenagers, unconscious or sedated patients, patients with language or cultural barriers, and patients with mental disability. Our aim was to capture the thoughts and opinions of nuclear medicine personnel in Australia and New Zealand regarding pregnancy screening strategies before diagnostic imaging procedures. **Methods:** Members of the Australian and New Zealand Society of Nuclear Medicine were invited to complete an online survey. Section 4 consisted of open-response questions asking participants to describe the strategies they use to question a patient about pregnancy status in 4 potentially difficult clinical scenarios. The content of the responses was analyzed. **Results:** For each question, 232 responses were recorded. The most commonly used strategies included questioning teenage girls away from their parents, referring to medical notes for unconscious patients, using an interpreter and visual aids for patients with language barriers, and asking a caregiver or relative of mentally disabled patients. Pregnancy testing was used when there was doubt about the patient's pregnancy status. Personal questions about menstrual and sexual history were often asked to determine the risk of pregnancy. **Conclusion:** The study revealed that a variety of strategies are used by nuclear medicine personnel in Australia and New Zealand to determine the pregnancy status of patients. A standardized practice guideline may be useful to ensure a consistent approach to questioning that would optimize the accuracy of pregnancy assessment and reduce the possibility of fetal irradiation.

Key Words: ionizing radiation; pregnancy; qualitative

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There have been several articles published discussing the difficulties associated with determining pregnancy status before diagnostic imaging procedures using ionizing radiation (1–4). Nuclear medicine imaging procedures using ^{99m}Tc as the radionuclide typically give an effective dose of less than 10 mSv for adults (5). However, doses of this size still pose a potential risk of biologic damage to a fetus if irradiated during maternal imaging procedures (6). Several international and national documents, such as publication 84 of the International Commission on Radiological Protection (6), report 128 of the National Council on Radiation Protection and Measurements (7), and publication 14.2 of the Australian Radiation Protection and Nuclear Safety Agency (8), provide information on protection of the fetus from radiation. These documents discuss the potential risks to a fetus from maternal medical imaging using ionizing radiation. They recommend that all women of childbearing age be questioned about their pregnancy status before the procedure begins, that the reason for asking be explained to the patient to avoid offense and illicit a more truthful answer, and that multilingual signs be placed around medical imaging departments asking patients to notify staff if they think they might be pregnant.

There are, however, no clearly defined guidelines to help nuclear medicine personnel determine which patients to question about pregnancy status or the best approach to questioning them. Teenagers and patients with language barriers are among several groups that have been identified as being potentially difficult to question and gain a truthful and accurate response (2,4).

A survey designed to investigate current practice and capture opinions about pregnancy determination in nuclear medicine in Australia and New Zealand was distributed to members of the Australian and New Zealand Society of Nuclear Medicine. The survey aimed to verify the findings from an earlier interview study (2), which had a limited number of participants. The design of the questionnaire and the results from sections 1–3 of the survey regarding demographic data, knowledge of regulations and policy, and current practice have been previously discussed in detail (7). The results revealed a lack of awareness of radiation protection guidelines

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For correspondence or reprints contact: Daphne James, School of Health Sciences, University of Newcastle, University Drive, Callaghan, N.S.W. 2308 Australia.

E-mail: daphne.james@newcastle.edu.au

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for the fetus and confirmed wide variations in current practice for questioning patients about their pregnancy status. Participants indicated that they used various methods of questioning, including verbal questioning, verbal questioning with the patient signing a form, and the use of written questionnaires. The age for questioning ranged from 10 to 60 y, with 12 y and 55 y being the most common minimum and maximum ages of patients to be questioned.

This paper concentrates on the content analysis of the open-response questions in section 4 of the survey, which asked participants to briefly describe how they would question the patient in 4 clinical scenarios: the young teenage patient, the unconscious or heavily sedated patient, the patient with language or cultural barriers, and the patient with mental disability.

MATERIALS AND METHODS

Ethics approval was provided by the University of Newcastle Human Research Ethics Committee before the study began (approval number H-2009-0270).

Four open ended questions were used to understand how nuclear medicine personnel deal with patients belonging to groups that have been described as potentially difficult to question about pregnancy status (2,4). Each question asked participants to "Briefly describe how you would question the patient in the following scenario": young teenager accompanied by a parent, unconscious or heavily sedated patient, patient with language or cultural barriers, and patient with a mental disability.

Content analysis (9) was used by the researchers to analyze the text and to identify several themes from the responses to each question. The analysis involved both quantitative and qualitative interpretation and analysis, allowing the data to be viewed in different yet complementary ways, with the outcome being the development of a range of distinct categories to describe the data. To eliminate potential bias by the primary researcher (a nuclear medicine technologist) and to ensure the validity of the theme categories, all responses were reviewed by the primary researcher and an independent researcher who had no working knowledge of nuclear medicine.

In the initial coding cycle, the researchers worked independently to examine the responses to each question with the intention

of categorizing the responses into a variety of themes. One or more themes or subthemes could be contained within each participant response because more than one strategy might be used when questioning the patient. As there were over 200 responses for each question, the researchers began by reviewing the first 50 responses for each question. The researchers discussed the developing categories of description from the first coding cycle, and several major themes and subthemes were created and agreed on by both researchers. These themes were used to develop a source code book, which was used by both researchers to examine all remaining responses (Tables 1–4).

RESULTS

There were 335 responses to the survey and 232 (69%) responses to each of the open-ended questions regarding the 4 clinical scenarios. The participants who responded to the scenario questions were predominately female (69%) and nuclear medicine technologists (93%). There was no statistically significant difference between the distribution of sex ($P = 0.58$) or profession ($P = 0.12$) for the main survey responses and the scenario responses. For all 4 questions, a 99% agreement rate between the 2 independent reviewers validated the source code books.

Direct quotes have been selected from the responses to illustrate the findings. The quotes are coded with a number relating to the participant's identity (e.g., C83), and any correction of spelling or grammar has been underlined; for example: "Assess patient's attitude and demeanor."

Young Teenager Accompanied by a Parent

A total of 404 comments were grouped into 4 major themes with 16 subthemes (Table 1). The major themes were method of questioning (81%), subjective assessment (5%), determining risk of pregnancy (12%), and pregnancy testing (2%).

Method of Questioning (Theme 1). The most common strategy used to question a young teenager accompanied by a parent was to ask the girl away from the parent (49%). This strategy could involve either asking the parent to leave

TABLE 1
Young Teenager Accompanied by Parent

Major theme	Subtheme	% (normalized to major theme)
1.1: Method of questioning (81%)	1.11: Ask away from parent	49
	1.12: Ask with parent present	15
	1.13: Ask parent directly	<1
	1.141: Same for all female patients, verbal question	18
	1.142: Same for all female patients, sign form	7
	1.15: Explain radiation risk	10
1.2: Subjective assessment (5%)	1.21: Assess parent-child relationship	25
	1.22: Assess response	65
	1.23: Assess maturity level	10
1.3: Determining risk of pregnancy (12%)	1.31: Question regarding LMP	38
	1.32: Question regarding start of menstruation	31
	1.33: Question regarding if sexually active	27
	1.34: Question regarding 10-d rule	4
1.4: Pregnancy testing (2%)	1.41: Pregnancy test	44
	1.42: Serum human chorionic gonadotropin	22
	1.43: Urine	33

TABLE 2
Unconscious or Heavily Sedated Patient

Major theme	Subtheme	% (normalized to major theme)
2.1: Method of obtaining information on pregnancy status (71%)	2.11: Consult patient notes	48
	2.12: Consult nurse/caregiver/doctor	27
	2.13: Consult partner/relative	18
	2.14: Ask patient	6
2.2: Pregnancy testing (14%)	2.21: Pregnancy test	23
	2.22: Serum human chorionic gonadotropin	62
	2.23: Urine	11
	2.24: Ultrasound	4
2.3: Unable to determine pregnancy status (13%)	2.31: Do not perform scan	27
	2.32: Postpone scan	42
	2.33: Refer to nuclear medicine physician	27
	2.34: Reduce radiation dose	3
2.4: Never been in this situation (2%)		

the room or remain in the waiting room, taking the girl to another room (often under the guise of weighing her or taking her to a bathroom), or asking quietly so the parent could not hear.

"Ask the parent to wait outside while you set up and then ask the patient." (C70)

"We take the patient out of the room to get their weight and ask them while away from their parent." (C37)

"Try to do it quietly and without the parent hearing." (C65)

Questioning with the parent present was reported by 15%, and 2 participants commented that they would ask the parent directly. Twenty-five percent commented that they question all female patients, regardless of age, in the same manner. Only 10% commented that they would explain the radiation risks from the procedure to the patient.

"Explain that radiation can have some risks to unborn fetus to child then mother, and explain that as a routine I ask all patients of childbearing age if they may be pregnant." (C193)

Subjective Assessment (Theme 2). Participants commented that in deciding whether to ask the patient about the possibility

of pregnancy, they would make a subjective judgment to assess the parent-child relationship (25%), the response from parent or child (65%), or the maturity of the girl (10%).

"Determine if they are comfortable talking in front of their parent." (C155)

"Assess patient's attitude and demeanor." (C163)

Determining Risk of Pregnancy (Theme 3). When attempting to determine the risk of the patient being pregnant, 3 main questions were asked: date of last menstrual period (LMP) (38%), whether the girl had commenced menstruating (31%), and whether the girl was sexually active (27%). Two participants (4%) commented that they would use the 10-d rule to assess the patient's risk of pregnancy.

"For younger teenagers we would ask first if they had gotten their period yet." (C90)

"Determine if sexually active and if so, use of contraceptive etc." (C79)

"Ask patient if menstruating. Ask date of LMP. If greater than 10 days determine if sexually active." (C118)

Pregnancy Testing (Theme 4). Comments regarding the use of pregnancy testing for teenagers made up only 2% of the comments. The type of pregnancy test used either was

TABLE 3
Patients with Language or Cultural Barrier

Major theme	Subtheme	% (normalized to major theme)
3.1: Method of questioning (91%)	3.11: Use interpreter/translator	67
	3.12: Use visual aids	27
	3.13: Speak slowly	1
	3.14: If cultural barrier, use female staff	2
	3.15: Same for all female patients	2
	3.16: Do not ask	<1
3.2: Pregnancy testing (4%)	3.21: Pregnancy test	40
	3.22: Serum human chorionic gonadotropin	47
	3.23: Urine	13
3.3: Unable to determine (4%)	3.31: Consult with doctor	38
	3.32: Postpone scan if patient does not understand	62
3.4: Determining risk of pregnancy (1%)	3.41: Question regarding LMP	50
	3.42: Question regarding contraception	25
	3.43: Question regarding sexual activity	25

TABLE 4
Patients with Mental Disability

Major theme	Subtheme	% (normalized to major theme)
4.1: Method of questioning (67%)	4.11: Ask patient (slowly, simple language)	26
	4.12: Ask caregiver/relative	50
	4.13: Ask nurse/doctor	11
	4.14: Consult notes	7
	4.15: Use visual aids	3
	4.16: Same for all female patients	2
	4.17: Do not ask	1
4.2: Determining risk of pregnancy (7%)	4.21: Question regarding LMP	38
	4.22: Question regarding contraception	26
	4.23: Question regarding if sexually active	35
4.3: Pregnancy testing (17%)	4.31: Pregnancy test	41
	4.32: Serum human chorionic gonadotropin	38
	4.33: Urine	21
4.4: Subjective assessment (7%)	4.41: Assume not sexually active	3
	4.42: Assess communication/understanding	97
4.5: Unable to determine (1%)	4.51: Do not perform scan	60
	4.52: Postpone scan	40

not specified (44%) or was reported to be serum or blood testing (22%) or urine testing (33%).

Unconscious or Heavily Sedated Patients

A total of 467 comments were grouped into 4 major themes with 12 subthemes (Table 2). The major themes were method of obtaining information on pregnancy status (71%), pregnancy testing (14%), unable to determine status (13%), and never been in this situation (2%).

Method of Obtaining Information (Theme 1). For an unconscious or heavily sedated patient, rather than questioning the patient, the participants used a variety of methods to obtain information about pregnancy status. The most common method was to consult the patient notes (48%). Participants commented that they would check the patient notes for information about recent pregnancy test results, contraceptive use, date of LMP, and length of stay in the hospital and to check for patient consent.

"Check medical records for LMP and length of stay in hospital and bHcg." (C7)

Other ways to obtain information were to consult with a medical professional (27%), nurse, caregiver, or doctor, about the patient's pregnancy status or to ask the patient's partner or relative (18%) if that person had accompanied the patient.

"Ask the nurse in charge of the patient the pregnancy status or last known menstrual period." (C55)

"Ask the partner if they are present." (C74)

Twenty participants (6%) commented that they would attempt to question the patient.

"Would try to get an answer from heavily sedated patient but if I was not confident on answer I would not do test." (C41)

"Talk loudly with using actions." (C85)

Pregnancy Testing (Theme 2). The comments of participants indicated that they were more likely to use pregnancy testing (14%) for patients who were unconscious or heavily

sedated, because the patient would be unable to answer their questions. Serum pregnancy tests were specified in 41 of 66 comments (62%) regarding pregnancy testing.

"I wouldn't be comfortable going ahead in this situation unless there was a negative BHCG test available." (C122)

Unable to Determine (Theme 3). There were 62 comments (13%) on what to do if the pregnancy status could not be determined. The most common response was to postpone the scan either until the patient was conscious and able to answer questions and provide consent or until pregnancy test results could be verified.

"Would not proceed—patient unable to consent for procedure." (C13)

"Depending on how urgent the scan was and the level of suspicion, a blood test should be done or wait until they were conscious." (C152)

An equal number of participants (27% each) stated that they would not proceed with the procedure or would defer to the nuclear medicine physician to make a decision as to whether to go ahead with the procedure.

Never Been in This Situation (Theme 4). There were 7 participants who commented that they had never faced this situation, usually because they worked in a private practice that did not cater to hospitalized patients.

Patients with Language or Cultural Barriers

A total of 371 comments were grouped into 4 major themes with 14 subthemes (Table 3). The major themes were method of questioning (91%), pregnancy testing (4%), unable to determine status (4%), and determining risk of pregnancy (1%).

Method of Questioning (Theme 1). The most common strategy for patients with a language barrier was to use an interpreter (67%). This could be either a professional interpreter or a family member who spoke English. The use of visual aids was quite common (28%). This category included referring to multilingual signage posted in the department, use of gestures or mime, drawing pregnant people,

and the use of Google Translate to print out the questions in the relevant language.

"I would ask the patient if they were pregnant using either translation or we have a poster with this question asked in different languages." (C17)

"Mime being pregnant or holding a baby." (C41)

"Draw a picture/mime it out/interpreter/point to poster on wall." (C84)

For patients with cultural barriers, the strategies suggested were to use female staff members to question the patient and to explain that the question needed to be answered because of the possible risk to the baby from radiation exposure.

"If it was cultural perhaps a female employee would do the questioning." (C227)

Pregnancy Testing (Theme 2). The major theme of pregnancy testing made up 4% of the total comments for this question. Serum pregnancy tests were most commonly recommended (47%), whereas 40% did not specify the type of test in their comment. Urine pregnancy tests were suggested in 2 comments (13%).

Unable to Determine Status (Theme 3). There were a small number of comments on what to do if pregnancy status could not be determined. In most cases (62%), the procedure would be postponed or referred to either the nuclear medicine physician or the referring doctor.

"I would not do the test if I didn't have an informed answer." (C41)

Being unable to gain consent for the procedure if the patient could not understand was also a reason cited to postpone the procedure.

"If I am unable to ask the patient this question then it would also be assumed that I would not be able to gain consent for the examination anyway hence would not undertake the examination without the ability to communicate with them. The examination would need to be rebooked with an interpreter." (C130)

Determining Risk of Pregnancy (Theme 4). Only 1% of comments were on trying to determine the risk that the patient was pregnant by asking questions about LMP, contraceptive use, or sexual activity.

Patients with Mental Disability

A total of 469 comments were grouped into 5 major themes with 17 subthemes (Table 4). The major themes were method of questioning (67%), subjective assessment (7%), determining risk of pregnancy (7%), unable to determine status (1%) and pregnancy testing (17%).

Method of Questioning (Theme 1). For patients with a mental disability, the most commonly used strategy to determine pregnancy status was to ask the caregiver or relative accompanying the patient (50%).

"Talk to their caregiver if the patient could not understand." (C26)

Speaking slowly and using simple language to directly question the patient (26%) was commonly used.

"Gesticulate, speak slowly and ask for understanding or ask them to repeat to you what they think you mean." (C68)

"Speak to the patient in simple and clear terms." (C158)

Consulting with a medical professional responsible for the patient's care, such as a nurse or doctor (11%), reviewing the patient's medical notes (7%), and using visual aids (3%) were some of the other strategies used to determine the pregnancy status for this type of patient.

Determining Risk of Pregnancy (Theme 2). Questions about the patient's LMP (38%), sexual activity (35%), or contraceptive use (26%) are asked to determine the risk that the patient is pregnant. These types of questions are asked to the patient, the caregiver or relatives, and medical professionals.

"Ask them if they have a boyfriend or if they are trying to make a baby." (C73)

"Ask when was the last period/contraceptive use or ask caregiver." (C120)

Pregnancy Testing (Theme 3). The use of pregnancy tests (17%) to verify the pregnancy status of a mentally disabled patient is common, particularly if there is doubt whether the patient can understand verbal or written questions.

"If they are not able to understand or communicate then I will show her the poster of pregnant woman. If that doesn't work then wait for pregnancy test." (C50)

"Depends on level of disability. If unable to comprehend get a pregnancy test done." (C58)

Subjective Assessment (Theme 4). There were several comments (7%) indicating that participants make subjective assessments and assumptions about the level of understanding or disability of the patient or about the sexual activity of mentally disabled people. These assumptions are then used to decide on the method of questioning to be used.

"This would be dependent on the level of disability and degree of independence. If the incapacitation is profound, I may waive the questioning altogether." (C94)

"I would assume the patient is not sexually active if their mental disability is extensive." (C109)

DISCUSSION

This survey has revealed that nuclear medicine personnel in Australia and New Zealand use of a variety of strategies when determining the pregnancy status of a patient before diagnostic imaging procedures. Although the paper identifies the main strategies used for each clinical scenario, the participants' responses may include several different strategies that are used concurrently to attempt to gain a more accurate response from the patient and provide greater confidence in the decision-making process. For example, in the case of a patient with a mental disability, the patient and caregiver may be asked and a pregnancy test performed.

The most commonly used strategy described by the participants for each category was to attempt to question young teenagers without their parent present, consult the patient notes for unconscious or sedated patients, use an interpreter if the patient has any language or cultural barriers, and question the caregiver of mentally disabled patients.

Establishing the pregnancy status of a patient is one of the fundamental tasks performed before beginning any diagnostic

nuclear medicine procedure using ionizing radiation to ensure the protection of any fetus. International and national radiation protection regulations (6–8) recommend that all women of child-bearing age be questioned on their pregnancy status, but the guidelines do not detail how the questioning should be performed. Our survey revealed wide variation in the methods used to question nuclear medicine patients in Australia and New Zealand (7). Variations in practice are a significant concern as they can lead to inconsistencies in the quality of health care and treatment received by individual patients. Clinical practice guidelines should be based on sound scientific evidence; however, in areas where there is a lack of evidence, practice patterns are often derived from the opinions or experience of the health professional (10).

Determining pregnancy status can be a sensitive issue and requires tact and discretion on the part of the health professional asking the questions. When attempting to determine pregnancy status before diagnostic imaging, the technologist tries to determine the risk of pregnancy by asking questions about the patient's menstrual cycle, sexual activity, and contraceptive use. The personal and intimate nature of this type of questioning can lead to embarrassment on the part of the patient, any accompanying persons, and even the technologist asking the questions. This is particularly so if the patient is unable to answer, such as for unconscious patients or patients with language barriers, and a relative or caregiver is asked the question instead. If the questioning is performed in an ad hoc manner, rather than using carefully developed protocols, a truthful answer or correct assessment may not be obtained, possibly resulting in irradiation of an unknown fetus. A study by James et al. (2) revealed that nuclear medicine technologists tend to assume that the patient is aware of her pregnancy status at the time of questioning, and a negative response may be accepted without any further questioning or testing.

There are conflicting reports in the literature concerning a woman's ability to self-assess her pregnancy status. Minnerop et al. (11) conducted a prospective, observational study on the ability of 377 adult women to exclude pregnancy without knowledge of a pregnancy test result. The researchers found that both patient history and physician suspicion could accurately exclude pregnancy. However, earlier studies by Strote and Chen (12) and Ramoska et al. (13) revealed that patient history alone was not adequate to exclude pregnancy, and both studies recommended that pregnancy testing be considered in emergency departments. In nuclear medicine, for which there is a real although relatively small risk that a fetus will receive ionizing radiation from a diagnostic maternal examination, it may be prudent to begin questioning patients about their history and to request a pregnancy test when there is any doubt.

Several patient groups have previously been identified as potentially difficult to question and obtain a truthful and accurate response (1–4). Young teenagers, especially when accompanied by a parent, are included in these groupings and may present a challenge for the nuclear medicine

technologist. The technologist must decide first whether to question the patient about the possibility of pregnancy. This issue may be decided by the patient's age, whether she has commenced menstruation, or her apparent maturity and possibility of sexual activity. The required questioning is of a personal nature, and in some cases, subjective judgments are made by the technologist (2). Our survey revealed that if the teenager is accompanied by a parent or caregiver the most commonly used strategy is to question the teenager in a separate room or out of earshot of the parent, as it is believed that the teenager may not provide a truthful answer in front of her parent. This strategy raises ethical questions about the age of medical consent, confidentiality, and the legality of questioning minors without a parent or guardian present. The age of consent for medical procedures and treatment varies with the country and state. In general, in Australia, the United Kingdom, and the United States, consent from a parent or guardian is required for minors (children under the age of 18 y) for medical procedures or treatment. However, some states in Australia (New South Wales, South Australia, and Australian Capital Territory) have specific laws allowing younger children to consent for procedures. For example, in New South Wales, the Minors (Property and Contracts) Act (14) allows a child of 14 y or older to consent to medical treatment. In states without consent laws, common law relating to the competency of a minor consenting to treatment may apply. This position was established by the English House of Lords decision in *Gillick v West Norfolk and Wisbech Area Health Authority* (15). "Gillick-competent" or "mature minor" children are deemed to be old enough or mature enough to make their own decisions and understand the issues and consequences regarding medical treatment. If children meet the Gillick definition, they are able to give consent and are entitled to the same confidentiality of medical information as an adult.

The survey responses regarding unconscious or heavily sedated patients, patients with language barriers, and patients with mental disabilities were often focused on the attempt to gain consent for a procedure as well as determine pregnancy status. Competency is considered a prerequisite for informed consent (16). However, there is a legal distinction between the requirement for capacity to consent and informed consent (17). The first focuses on the ability of a person to understand a proposed procedure or treatment, whereas the latter is concerned with the practitioner's duty to disclose information about the procedure. Informed consent is meaningful only when consenters are fully competent (meaning they possess the capacity to fully understand the situation and the ability to weigh potential outcomes and anticipate future consequences) and all relevant information regarding the procedure and any risks associated with the procedure have been conveyed to them (16).

CONCLUSION

This paper has discussed the methods used by nuclear medicine personnel in Australia and New Zealand to determine

pregnancy status for 4 groups of patients considered to be potentially difficult to question. The most common strategies used were questioning young teenagers away from their parent, consulting patient notes for unconscious or sedated patients, using an interpreter for patients with language barriers, and questioning the caregiver of patients with mental disability. The survey revealed variations in current practice for determining pregnancy status before diagnostic nuclear medicine procedures that may lead to inconsistencies in the care and treatment of individuals from these groups. The development of best practice guidelines on how to question patients about their pregnancy status is recommended to ensure a consistent approach to questioning, which would optimize the accuracy of pregnancy assessment and reduce the possibility of fetal irradiation.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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CHAPTER FIVE

DELPHI STUDY

5.1 OVERVIEW

This chapter describes Phase Four of the research – the development of consensus statements.

Phase Three, a cross-sectional survey of nuclear medicine personnel in Australia and New Zealand, revealed wide variations in the current practice for determining the pregnancy status of women prior to diagnostic nuclear medicine procedures. The results showed that there was no standardisation of age range for questioning or method of questioning. The qualitative data from the survey revealed a range of strategies used to question women from groups that may be considered potentially difficult to question, such as teenage girls. The survey results reinforced findings from the interview study and the need for a consistent approach to questioning women about their pregnancy status to optimise pregnancy assessment and reduce the possibility of unnecessary foetal irradiation.

Phase Four of the research involved developing consensus statements to ensure a consistent approach to determining the pregnancy status of women prior to diagnostic nuclear medicine procedures. In order to choose the most appropriate research design, a narrative review on formal research methods for developing consensus in health was completed (Chapter 2). The Delphi technique was selected for Phase Four because it can be conducted online and allows a panel of experts from a wide range of geographical locations to participate.

This chapter consists of a research paper describing the Delphi study and its results.

More detailed information regarding the research methodology for the study which was not able to be included in the paper, including the Invitation to Participate, participant information sheets, survey questionnaires, and analysis can be found in Appendix E.

5.2 DEVELOPMENT OF CONSENSUS STATEMENTS FOR PREGNANCY SCREENING IN DIAGNOSTIC NUCLEAR MEDICINE: A DELPHI STUDY (PAPER SIX)

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The co-author of this paper is the principal supervisor of the PhD.

ABSTRACT

Current radiation protection recommendations do not provide clear guidelines or advice on pregnancy screening strategies for diagnostic nuclear medicine procedures. Previous studies have reported on variations in current practice for pregnancy screening prior to diagnostic nuclear medicine procedures. The development of consensus statements aims to provide a consistent approach and assist nuclear medicine personnel to confidently question patients about their pregnancy status.

Method: The Delphi technique was chosen for the research design. A panel of “experts” was recruited based on their expertise and experience. Panel members were provided with a summary of existing research. Consensus agreement was pre-defined as 80%. Questionnaires were developed and distributed to the panel members with iterative analysis and feedback between survey rounds. The Round 1 questionnaire was developed from the results of a previous survey. It consisted of 30 questions designed to gather the opinions of the expert panel.

Results: An expert panel consisting of ten experienced nuclear medicine personnel from Australia and New Zealand was recruited. Three survey rounds were conducted online using SurveyMonkey between December 2013 and June 2014. Following analysis of the Round 1 responses, consensus statements were developed for Round 2 and revised in Round 3. Consensus was achieved for 16 statements. The statements recommend verbal questioning with patient signature, define age range for questioning as 12-55 years, and provide advice on the use of pregnancy testing and questioning potentially difficult groups, such as teenagers. A flowchart was included for comment in Round 3.

Conclusion: This is the first Australian study to develop consensus statements and a flowchart to assist nuclear medicine personnel in consistently and confidently questioning patients about their pregnancy status prior to diagnostic procedures. Implementation of these statements into clinical practice guidelines should reduce the possibility of inadvertent foetal irradiation.

Keywords: ionising radiation, pregnancy, consensus, Delphi

INTRODUCTION

Determining the pregnancy status of a female patient prior to a diagnostic nuclear medicine (NM) procedure is potentially problematic. Although the risk to a foetus from the ionising radiation is relatively small, radiation protection documents recommend all women of childbearing age be questioned regarding their pregnancy status prior to any procedure utilising ionising radiation to reduce the possibility of foetal irradiation (1, 2). James et al (3, 4) have previously shown that, in Australia and New Zealand, a variety of approaches are used by nuclear medicine personnel to question patients about their pregnancy status. The studies revealed that an ad hoc method of questioning (whether verbal or in writing) is being used. The types of questions asked, the age range questioned, and circumstances for the use of pregnancy testing varied across nuclear medicine departments. These variations in the approach used to identify women in the early stages of pregnancy may contribute to an increased number of cases of foetal irradiation and therefore the development of a consistent approach was recommended.

Consistency in health care practice is important to ensure all individuals are provided with the same standard of quality care (5). Formal consensus research methods are increasingly used to develop statements and guidelines for a range of health practices when evidence in the literature is lacking or conflicting (6). The Delphi technique is an established method for creating consensus statements or guidelines from expert opinion when there is a lack of evidence on a topic (7, 8).

The aim of this study is to gather the opinions of an expert panel of nuclear medicine personnel and develop consensus statements regarding the most appropriate methods to use to question female patients about their pregnancy status prior to diagnostic nuclear medicine procedures. The establishment and implementation of consensus statements into practice will ensure a more consistent approach to assist nuclear medicine personnel to confidently and accurately identify women in the early stages of pregnancy.

METHOD

Ethics approval for the study was provided by the University of Newcastle Human Research and Ethics Committee (Approval number 2009-H-0270).

Design

The Delphi technique was chosen to develop consensus statements on how to determine the pregnancy status of patient's prior to diagnostic nuclear medicine. The technique was first described in the 1950's by the RAND Corporation and since the 1970's it has been widely used in health to develop consensus statements and guidelines (7). The technique utilises a panel of experts, selected based on their expertise and experience, to explore important aspects of a topic whilst maintaining participant anonymity. The Delphi process involves a series of questionnaire rounds, each followed by iterative analysis and feedback. The process concludes when a pre-defined level of consensus is reached (6). As the Delphi does not require participants to physically meet, it can be conducted online making it a cost effective method to enable recruitment of participants from diverse geographical locations.

Expert panel members

The participants were nuclear medicine scientists, nuclear medicine physicians and medical physicists in Australia and New Zealand and who had at least 5 years of experience working in nuclear medicine. Potential participants were purposively selected from members of Special Interest Group committees of the Australian and New Zealand Society of Nuclear Medicine; the medical physicist register of the Australasian College of Physical Scientists and Engineers in Medicine; and the nuclear medicine clinical supervisors database from the School of Health Sciences at the University of Newcastle. A low response for participation was anticipated due to the on-going nature of the Delphi method and the time commitment required for the study. Hence, a total of 35 potential participants were invited to participate in the study via email with the aim of achieving a panel of at least 10 experts. A participant information sheet and consent form was attached to the invitation email.

Survey Rounds

Panellists were asked to participate in up to three rounds of web-based questionnaires. All questionnaires were conducted online using SurveyMonkey. To ensure all panel members began the process with an equivalent knowledge base, each member received an email containing published articles summarising issues surrounding the topic. The email also included a web link to the first round online survey. The questionnaire for Round 1 was developed from the results of a previous cross-sectional study conducted by the authors (4). The Round 1 questionnaire consisted of 30 questions with both closed and open responses to allow the participants to give their rationale for any answers. The questions covered a range of issues, including demographic information, method of questioning, and use of pregnancy testing. Round 2 and 3 provided panel members with a report on the analysis and feedback from the previous round, including quotes from participant responses and the level of agreement for each question. A series of statements were developed for each round and panel members were asked to agree or disagree with each one. A free text comment box was included after each statement. Consensus was pre-defined as achieving more than an 80% agreement on any statement. Areas of non-consensus were redeveloped according to the feedback and panel members were given the opportunity to revise their responses. Statements achieving consensus were reiterated in the following round and panel members asked to confirm their agreement and comment if needed.

RESULTS

Expert panel members

Ten people agreed to participate in the study: 8 nuclear medicine scientists, 1 medical physicist and 1 nuclear medicine physician. There were seven female participants. Nine participants worked in Australia and one in New Zealand. All participants had at least 5 years of experience working in nuclear medicine. All ten completed Round 1 however only 9 participants completed the Round 2 and 3 surveys. As all ten participants were emailed the links to Round 2 and 3 and their responses were

anonymous, it is not known if the same participant was the non-responder for both rounds.

Survey rounds

Three survey rounds were conducted between December 2013 and June 2014. Following Round 1 the results of the survey, including comments from the panel members, were tabulated and used to develop 12 statements for the Round 2 questionnaire. Ten of these 12 statements achieved consensus agreement in Round 2 (Table 1). Areas of non-consensus in Round 2 included questioning of teenage girls and women with “cultural barriers”, standard questions to ask, and use of pregnancy testing. These areas were further developed into 9 new statements for the Round 3 questionnaire. In Round 3, panel members were also asked to review and comment on the Round 2 consensus statements. The responses and comments from Round 3 resulted in 7 new statements achieving consensus and one statement from Round 2 being revoked (Table 1). Panel members disagreed (62.5%) with asking women about hysterectomy and commented that asking about hysterectomy was not necessary if LMP was asked first, as this would “prompt them to say that they have had a hysterectomy”.

Consensus Statements

All panel members agreed that the development of guidelines for pregnancy screening prior to diagnostic nuclear medicine procedures were needed to provide a consistent approach. Verbal questioning was agreed to be the most appropriate method prior to all diagnostic procedures, regardless of the potential radiation risk to the foetus. However the patient should be required to provide their signature to document that the procedure and risks had been explained and to verify their pregnancy status. All panel members agreed that standard questions should include date of last menstrual period (LMP). Childbearing age range was defined as 12-55 years.

For patients with cognitive impairment, the carer, medical records or medical personnel should be consulted to determine the possibility of pregnancy and whether a pregnancy test is required. An interpreter should be used to question women with

language barriers. The term “under normal circumstances” was included in these two statements to allow for flexibility and individual patient situations. Teenagers aged 12-17 years of age should be asked if they have started menstruation first and if yes, questioned regarding pregnancy. Therefore, if possible, and under normal circumstances, teenagers should be questioned away from accompanying parents or other adults. The term “culturally and linguistically diverse” should be used to describe women from different religious, spiritual, racial or ethnic backgrounds and where possible, under normal circumstances, they should be questioned by female personnel.

All panel members agreed that pregnancy testing should be used whenever there is any uncertainty regarding the patient’s pregnancy status and that if available in a reasonable time, serum HCG test should be used. If urine HCG testing is used prior to the date of missed menses and the result is negative, the procedure should be postponed until menstruation begins. Retesting with serum HCG test was also provided as an option however this statement only achieved 77.8% agreement.

Flowchart

In Round 3, panel members were provided with a flowchart that could be used by nuclear medicine personnel to assist in questioning women regarding their pregnancy status. The panel members commented that the flowchart would be “helpful” and was “a great idea” to support any guidelines and use as a “quick reference guide”. The flowchart questions initially separated women into three age groups 12-17, 18-49, and 50-55 however; the 2 older age groups were combined in the final version. Questions in the initial flowchart included: whether menstruation had started (12-17 years only), hysterectomy, LMP, if sexually active, and if they thought there was any chance they might be pregnant. Panel members made comments and suggested changes for the flowchart. The question about hysterectomy was considered unnecessary as the information is usually provided when asking LMP. Therefore, the first question for 18-55 years was changed to LMP. Questions regarding sexual activity were also considered unnecessary and removed. The flowchart was revised to reflect this feedback (Figure 5.1).

Table 5.1: Consensus Statements

Round	Consensus Statements
Two	Guidelines offering advice for pregnancy screening prior to DIAGNOSTIC nuclear medicine procedures would provide a more consistent approach.
	The procedure and any potential risks associated with it should be explained and female patients should be VERBALLY questioned regarding their pregnancy status AND required to provide their SIGNATURE to indicate the procedure and any radiation risks have been explained and indicate their pregnancy status.
	Childbearing age should be defined as 12-55 years for the purposes of questioning patients about their pregnancy status prior to diagnostic nuclear medicine procedures.
	Women up to 55 years of age should be questioned about their pregnancy status using the standard approach.
	Under normal circumstances, consultation with a carer, medical records or medical personnel should be initiated to determine the possibility of pregnancy for women with a cognitive impairment and to help decide if a pregnancy test is required.
	Under normal circumstances, an interpreter should be used to question women with a language barrier about their pregnancy status.
	Standard questions should include last menstrual period (LMP).
	<i>Standard questions should include both LMP and hysterectomy. Revoked in Round 3</i>
	Pregnancy testing should be used prior to diagnostic nuclear medicine procedures whenever there is uncertainty as to the patient's pregnancy status.
	Standard verbal questioning with patient signature is required to verify pregnancy status for all diagnostic nuclear medicine procedures regardless of the potential level of radiation risk to the foetus.
Three	If possible, when a teenage girl is accompanied by a parent or other adult, they should be taken to another room, without the parent, to be weighed for radiopharmaceutical dose calculation and questioned then.
	Teenage girls from age 12 to 17 years should be asked if they have begun menstruating and if yes, then questioned regarding pregnancy status.
	For girls aged 12-17 years: 1. Ask if they have begun menstruating. If no, proceed with examination. 2. If yes, continue with standard questioning
	The term "culturally and linguistically diverse" can be used to describe women who differ according to religion and spirituality, racial backgrounds and ethnicity as well as language.
	Whenever possible, a female staff member should question women from culturally and linguistically diverse backgrounds about their pregnancy status.
	If available in a reasonable time, serum pregnancy testing should be used in preference to urine pregnancy testing.
	If urine pregnancy testing is used PRIOR to the date of missed menses and the result is NEGATIVE, postpone the examination until menstruation begins

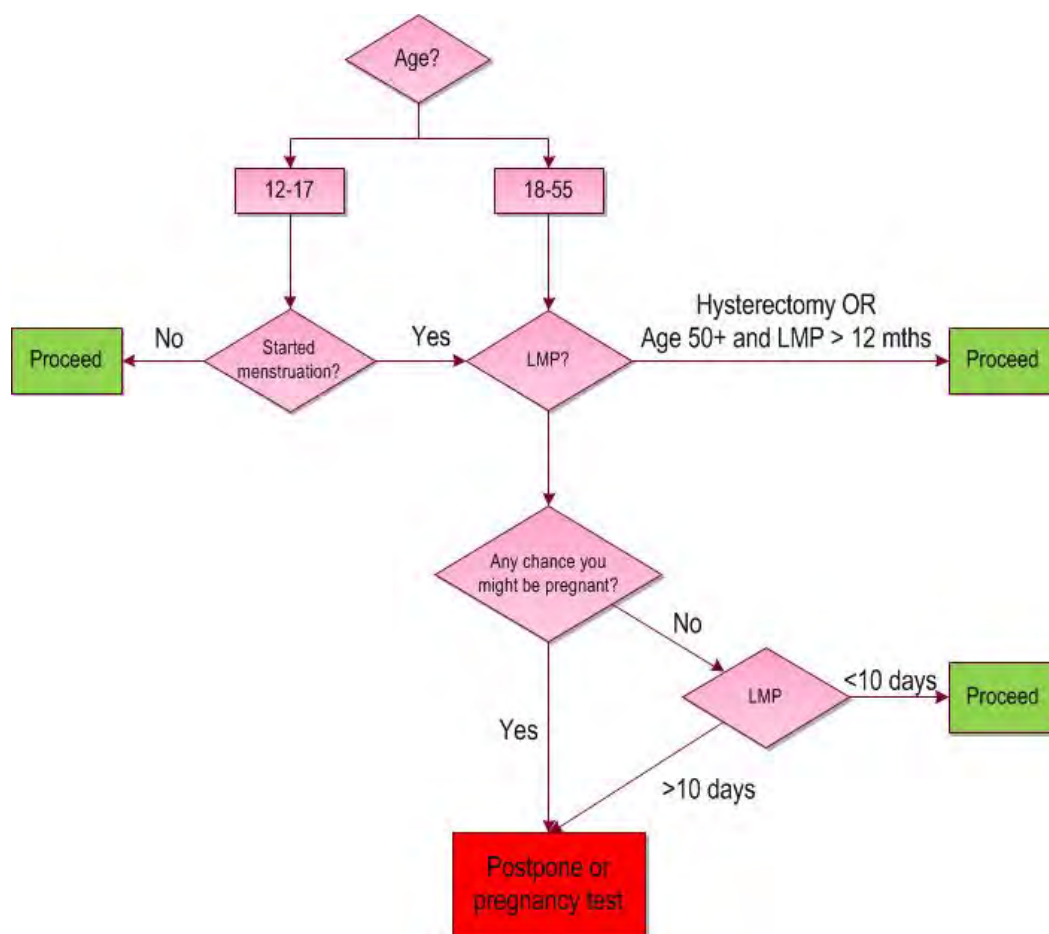


Figure 5.1: Final Flowchart

DISCUSSION

National and international radiation protection guidelines recognise the increased radiosensitivity of foetal tissue (1, 2, 9, 10). They recommend that all female patients of childbearing age be questioned regarding their pregnancy status prior to any procedure using ionising radiation to avoid foetal irradiation. However, the radiation protection guidelines do not provide clear instructions on how to question the patient or which patients to question. The age range for questioning has not previously been defined and there is no advice for questioning potentially difficult patient groups, such as teenagers. This study has developed 16 consensus statements to assist nuclear medicine personnel in Australia and New Zealand in confidently questioning patients and how to accurately assess pregnancy status.

Age range

The consensus statements developed in this study define the age range for questioning as 12-55 years. There are a very small number of cases of females under the age of 12 years or over 55 years falling pregnant. Australian birth statistics for 2012 show the total number of births at 309,582, with 405 (0.13%) from mothers aged 15 and under, and only 45 (0.01%) from mothers 50 years and over (Table 5.2) (11). These numbers only include the number of live births and do not include the number of miscarriages or induced abortions. Medicare Australia statistics for Item number 35643 *Evacuation of the contents of the gravid uterus by curettage or suction curettage* show that in 2012 there were over 61500 terminations performed in Australia, with 7145 of these performed in women aged 19 years or less and 15020 in women 35 years or more. The actual number of induced abortions performed is difficult to calculate because Medicare data does not include information on patients admitted to hospital and because it is estimated that approximately 15% of private patients do not claim a Medicare benefit (12). These factors, and the aggregation of data for ages 15 and under, make it difficult to calculate the number of pregnancies in very young teenage girls. However, assuming a worst case scenario where all of the 7145 terminations in the 19 years or less age group were conducted on teenagers under the age of 15, the estimated number of pregnancies in under 15 year olds accounts for less than 2.5% of all pregnancies.

Potentially difficult patient groups

Certain groups of patients, such as teenagers, women with cognitive impairment, or language or cultural barriers, have been identified as potentially problematic to question about their pregnancy status (4). When teenage girls are accompanied by an adult relative, they may be reluctant to provide truthful answers to questions about pregnancy for fear of embarrassment or recrimination (13). Removing the girl to another area under the guise of weighing her provides an opportunity to ask the relevant questions in privacy. This strategy may raise issues about the legality of questioning a minor without a parent or guardian present. However, if the girl is deemed Gillick competent, she is entitled to the same confidentiality for medical information as an adult (4, 13, 14).

Table 5.2: Births and age of mother - Australia 2012 (11)

5. Age of mother (years)	• Number of births
15 and under	405
16	887
17	2037
18	3255
20	6123
25	12685
30	21696
35	15545
40	5164
45	328
50 and over	45
Total Births	309852

In Round 2 of the Delphi study, participants commented on the use of the term "cultural barriers" as being "too non-specific". The Multicultural Health curriculum statement within the *Royal Australian College of General Practitioners Curriculum for Australian Practice 2011* (15) uses the term, "culturally and linguistically diverse", to define groups and individuals that differ according to religion and spirituality, racial backgrounds and ethnicity as well as language. They suggest the term "culturally and linguistically diverse background" can be used to reflect intergenerational and contextual issues, not only migrant experience. This term was agreed upon to replace "cultural barriers" by 8 out of the 9 participants in Round 3 of the Delphi study.

Pregnancy testing

In the early stages of pregnancy, especially prior to the date of missed menses, a serum HCG pregnancy test is the most accurate method to determine if a female is pregnant (16). Although the minimum detection limits for urine HCG pregnancy tests have decreased over the past 20 years to 10-20 IU/L, their performance in the lower range of HCG concentration is poor and false-negative results are common when used prior to the date of missed menses (16-19). This may be due to user error, urine sample dilution, variations in menstrual cycle duration and calculation of the date of missed

menses, and variations in the timing of implantation and therefore the concentration of HCG in urine (16-19)

A systematic review published in 2013 reported on the accuracy of pregnancy checklists to rule out pregnancy (20). The checklists were based on criteria defined by the World Health Organisation (WHO) Selected Practice Recommendations for Contraceptive Use (21, 22). The review reported on three studies of diagnostic accuracy assessing the validity of a pregnancy checklist when compared to a urine pregnancy test representing 2650 women. The review revealed a consistent 99-100% negative predictive value (NPV) across the included studies which mean that the checklists were able to confidently rule out pregnancy in women who are not pregnant. A number of other studies have reported on the ability of women to self-assess their pregnancy status (23, 24). These studies also report excellent NPV (99% & 100%) for questioning a woman if she “might be” pregnant.

Performing serum pregnancy tests on all females prior to diagnostic nuclear medicine procedures would be costly, time consuming, and unnecessary. The consensus guidelines and associated flowchart provide a simple, consistent process for pregnancy screening which should identify the majority of pregnancies and limit the number of pregnancy tests required. The current study demonstrates ongoing support for the development of consensus guidelines and reinforces the results from previous studies by the authors (3, 4, 25).

CONCLUSION

The consensus statements and flowchart developed in this study cover a range of issues which have not previously been discussed in radiation protection documentation for diagnostic nuclear medicine procedures. They provide a clear and consistent approach for nuclear medicine personnel to follow when questioning patients about their pregnancy status. The statements recommend the use of verbal questioning with documentation via the patient signature, define the age range to question, provide strategies for teenagers and other potentially difficult groups, and provide advice regarding the use of pregnancy testing.

In future research the results from this study will be used as a framework for the creation of “best practice” guidelines for pregnancy screening prior to diagnostic nuclear medicine procedures. Implementation of the guidelines into clinical practice will provide advice and a consistent approach for questioning patients which will assist nuclear medicine personnel to confidently and accurately determine pregnancy status and reduce the possibility of inadvertent foetal irradiation.

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CHAPTER SIX

FINAL DISCUSSION

6.1 OVERVIEW

This chapter examines the key findings of the research in this thesis. It includes a summary of the research findings for each phase of the research, final discussion, strengths and limitations, and the implications for clinical practice and future research. The chapter closes with the final conclusions of the thesis.

6.2 SUMMARY OF FINDINGS

Inadvertent foetal irradiation may occur during maternal diagnostic nuclear medicine procedures if the woman is unaware she is pregnant and the pregnancy is not identified. The ionising radiation used can potentially cause biological damage to the foetus, especially in the early stages of pregnancy (1). Foetal tissue is most sensitive to the effects of ionising radiation in this period. The research in this thesis explored the literature surrounding foetal irradiation and radiation protection recommendations for pregnant or potentially pregnant women undergoing diagnostic nuclear medicine procedures, and investigated current practice in Australia and New Zealand. Due to a lack of specific information and guidelines in the literature, and a lack of a consistent approach in practice in Australia and New Zealand, consensus statements were developed. The research in this thesis was conducted in four phases. A summary of the findings from each phase will follow.

6.2.1 PHASE ONE – LITERATURE REVIEW

The literature review (Chapter Two) consisted of four components:

1. Review of nuclear medicine, the stages of human pregnancy, and the biological effects of ionising radiation and foetal irradiation
2. Review of international and national radiation protection documents for advice on determining pregnancy status prior to diagnostic nuclear medicine procedures
3. Systematic review of the accuracy of pregnancy screening strategies for early pregnancy
4. Narrative review of formal research methods for developing consensus in health.

The review of the biological effects of foetal irradiation reported on the increased sensitivity of foetal tissue to the effects of ionising radiation, especially in the early phase of pregnancy known as organogenesis (1-5). Although the radiation exposure to the foetus from maternal diagnostic nuclear medicine procedures is relatively low, there is still a risk for biological damage and the induction of childhood cancers and leukaemia (1, 6). National and international radiation protection documents were reviewed and although all recommend that women of child-bearing age are questioned regarding their pregnancy status prior to any procedure using ionising radiation, there were no specific guidelines for diagnostic nuclear medicine procedures on how to question patients. This demonstrated a significant gap in the recommendations which the research in this thesis has attempted to bridge.

A systematic review of pregnancy screening strategies for early pregnancy was conducted to determine the accuracy of pregnancy testing and patient self-assessment of their pregnancy status. The review revealed that serum HCG pregnancy tests are highly sensitive and accurate in the early stage of pregnancy (7, 8). Urine HCG tests are also very sensitive however, due to a range of factors including variations in menstrual cycle length, timing of implantation, urine dilution and user errors, they have a high false negative rate prior to the date of missed menses (7, 9). The review also revealed that women are able to self-assess their pregnancy status, with the reliability of the self-assessment highest when they were not pregnant. Pregnancy testing using serum HCG tests was recommended if any uncertainty existed.

In order to select an appropriate research methodology for the development of consensus statements in Phase Four (Chapter Five), a narrative review of formal research methods for developing consensus in health was conducted. The review reported on three methods: the Delphi technique, the nominal group technique, and the consensus development conference; and offered guidance on the method to use for particular situations.

Two publications were produced as part of the literature review. A narrative review on methods for developing consensus was accepted for publication in *Nurse Researcher* in March 2014. A systematic review of pregnancy screening strategies for early pregnancy

was submitted to *BJOG: An International Journal of Obstetrics and Gynaecology* in July 2014 and is currently under review.

6.2.2 PHASE TWO – INTERVIEW STUDY

In 2010, a small semi-structured interview study (Chapter Three) was conducted in Australia. The Chief NMS and one staff NMS from eight nuclear medicine departments were interviewed to investigate current departmental policies and practice, knowledge of biological effects of radiation and foetal exposure, and problems NMS associate with determining a patients pregnancy status. The qualitative data from the 16 interviews was analysed using topic coding and five themes were identified. The themes were:

1. Policy and awareness of guidelines
2. Questioning the patient
3. Radiation knowledge
4. Decisions and assumptions made by the NMS
5. Use of pregnancy testing.

The study revealed a lack of awareness of national and departmental policies and a lack of knowledge and understanding of the possible biological effects of foetal irradiation. Approaches to questioning the patient varied both between, and within, departments. Verbal questioning of the patient, often with no documentation of the response, was the most commonly reported method to determine the pregnancy status of the patient. Definition of the age range to question varied; in particular the lower limit ranged from 12-16 years of age. Teenagers were identified as the most difficult group to question, along with patients with language barriers, different cultural backgrounds, patients with a mental disability, and patients on certain medications which would impair their ability to respond. The study revealed that NMS tend to rely on the patient's word regarding whether they might be pregnant and if she answered confidently that she wasn't pregnant that response was accepted without further investigation. Pregnancy testing is not routinely used however, all except one participant said they had used pregnancy tests in the past. The most common reason

for performing a pregnancy test was if the patient expressed uncertainty about their pregnancy status. Both serum and urine HCG were reported to be used.

The study concluded that there is wide variation in practice in nuclear medicine departments in Australia to determine pregnancy status. The study demonstrated the need for re-education regarding the possible effects of foetal exposure, and the development of a consensus approach to ensure pregnant patients are not irradiated unnecessarily.

An abstract of the results of the study (Appendix F) was accepted for oral presentation at the 42nd Annual Scientific Meeting of ANZSNM in Darwin in July 2011 and subsequently published in *Internal Medicine Journal*. The abstract was read by David Brill, a medical journalist for *Australian Doctor*, who contacted Daphne James for an interview. This interview was published in the issue of *Australian Doctor* dated 29 July 2011, under the title “Pre-radiation pregnancy checks ad hoc”.

The findings from the interview study were published in *Journal of Nuclear Medicine Technology* in September 2011 (10).

6.2.3 PHASE THREE – CROSS-SECTIONAL SURVEY

The results from the interview study were used to develop a questionnaire which was distributed in 2011 as an online cross-sectional survey (Chapter Four). The survey aimed to investigate current practice for pregnancy screening prior to diagnostic nuclear medicine procedures in Australia and New Zealand and determine if a standardised practice guideline was required. All members of the ANZSNM were invited to participate. The questionnaire consisted of 30 questions divided into 4 sections: demographics, policy and regulations, current practice, and clinical scenarios. There were 335 responses received from nuclear medicine scientists (n=296), physicians (n=33) and physicists (n=6) employed across Australia and New Zealand. The data was analysed using descriptive statistics and open-ended responses were coded using thematic analysis.

The survey results revealed that only 28% of participants were aware of national regulations regarding pregnancy screening for diagnostic nuclear medicine. Questions

about current practice revealed a wide age range with the most commonly reported minimum and maximum ages as 12 and 55 years respectively. Interestingly, age for menarche was reported as the rationale for choosing a minimum age to question, although the age ranged from 10-16 years. Age of menopause was the most common rationale for maximum age and that ranged from 40-60 years. This indicates a lack of knowledge regarding these aspects of female physiology.

An abstract of the results of the study was accepted for poster presentation at the 43rd Annual Scientific Meeting of ANZSNM in Melbourne in April 2012 and subsequently published in *Internal Medicine Journal*. A second abstract was accepted for poster presentation at the 60th Annual Meeting of SNMMI in Vancouver, Canada in June 2013 and published in *Journal of Nuclear Medicine*. Both abstracts and copies of the poster presentations are available in Appendix F.

The results from the survey were published as two articles in *Journal of Nuclear Medicine Technology* in September and December 2013 (11, 12).

6.2.4 PHASE FOUR – CONSENSUS DEVELOPMENT

The final stage of the research involved using a Delphi technique to develop consensus statement for determining a patient's pregnancy status prior to diagnostic nuclear medicine procedures (Chapter Five). A lack of consistent approach in current practice in Australia and New Zealand had been established in both the interview study and the cross-sectional survey. A review of formal research methods for developing consensus in health care was conducted (Chapter Two) and from this, the Delphi technique was selected for the study.

The 3 round Delphi study was conducted between December 2013 and June 2014 as a series of three online questionnaires. The expert panel members were recruited from nuclear medicine scientists, physicians and physicists employed in Australia and New Zealand. Ten experts agreed to participate in the study; 8 NMS, 1 physician and 1 physicist. Consensus was pre-defined as 80% agreement.

Round 1 consisted of a questionnaire designed to gather the thoughts and opinions of the panel members on a range of issues surrounding pregnancy screening in diagnostic

nuclear medicine. The results were analysed and tabulated and provided to the panellists in Round 2. The Round 2 questionnaire consisted of a series of 12 statements derived from the Round 1 results. Panel members were asked indicate their agreement or disagreement with each statement and were given an opportunity to provide comments if they wished. Round 2 resulted in 10 statements achieving consensus. These statements were restated for comment in Round 3 and a further 9 statements were developed from areas of non-consensus in Round 2. A flowchart for pregnancy screening was also developed and provided to participants for comment.

At the completion of Round 3, 16 statements achieved consensus (Table 6.1). These statements covered a range of issues such as method of questioning, standard questions to ask, age range to question, when to use pregnancy testing, how to effectively question potentially difficult patients such as teenagers and patients with diverse cultural and linguistic backgrounds. The flowchart was well received as a simple reference tool. However it needed some redesign to accommodate the panellists comments (Figure 6.1).

Table 6.1: Consensus statements

- 1 Guidelines offering advice for pregnancy screening prior to DIAGNOSTIC nuclear medicine procedures would provide a more consistent approach.
- 2 The procedure and any potential risks associated with it should be explained and female patients should be VERBALLY questioned regarding their pregnancy status AND required to provide their SIGNATURE to indicate the procedure and any radiation risks have been explained and indicate their pregnancy status.
- 3 Childbearing age should be defined as 12-55 years for the purposes of questioning patients about their pregnancy status prior to diagnostic nuclear medicine procedures.
- 4 Women up to 55 years of age should be questioned about their pregnancy status using the standard approach.
- 5 Under normal circumstances, consultation with a carer, medical records or medical personnel should be initiated to determine the possibility of pregnancy for women with a cognitive impairment and to help decide if a pregnancy test is required.
- 6 Under normal circumstances, an interpreter should be used to question women with a language barrier about their pregnancy status.
- 7 Standard questions should include last menstrual period (LMP).
- 8 Pregnancy testing should be used prior to diagnostic nuclear medicine procedures whenever there is uncertainty as to the patient's pregnancy status.
- 9 Standard verbal questioning with patient signature is required to verify pregnancy status for all diagnostic nuclear medicine procedures regardless of the potential level of radiation risk to the foetus.
- 10 If possible, when a teenage girl is accompanied by a parent or other adult, they should be taken to another room, without the parent, to be weighed for radiopharmaceutical dose calculation and questioned then.
- 11 Teenage girls from age 12 to 17 years should be asked if they have begun menstruating and if yes, then questioned regarding pregnancy status.
- 12 For girls aged 12-17 years:
 1. Ask if they have begun menstruating. If no, proceed with examination.
 2. If yes, continue with standard questioning.
- 13 The term "culturally and linguistically diverse" can be used to describe women who differ according to religion and spirituality, racial backgrounds and ethnicity as well as language.
- 14 Whenever possible, a female staff member should question women from culturally and linguistically diverse backgrounds about their pregnancy status.
- 15 If available in a reasonable time, serum pregnancy testing should be used in preference to urine pregnancy testing.
- 16 If urine pregnancy testing is used PRIOR to the date of missed menses and the result is NEGATIVE, postpone the examination until menstruation begins

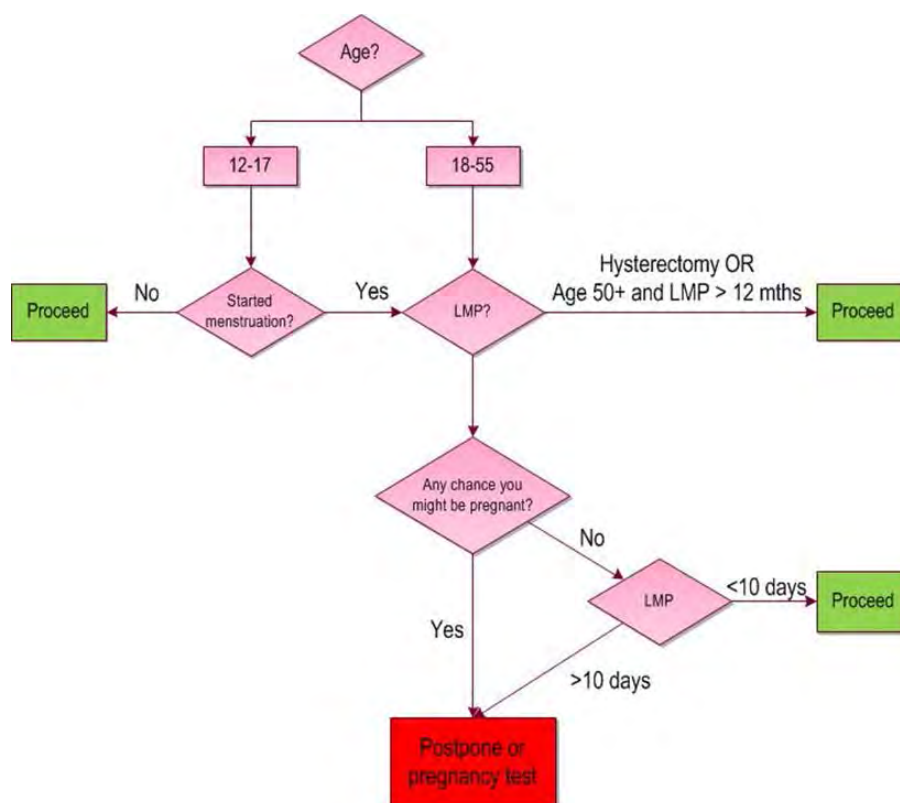


Figure 6.1: Revised flowchart for questioning

The consensus statements and flowchart developed in the Delphi study can be used in the future to produce “best practice” guidelines for pregnancy screening prior to diagnostic nuclear medicine procedures.

An abstract of the results of the Delphi study (Appendix F) was accepted for oral presentation at the 45th Annual Scientific Meeting of ANZSNM in Adelaide in April 2014 and subsequently published in *Internal Medicine Journal*.

The results from the study were submitted for publication in *Journal of Nuclear Medicine Technology* in September 2014 and are currently under review.

6.3 STRENGTHS AND LIMITATIONS

In addition to the strengths and limitations of each phase of research outlined in the published/submitted papers, the collective strengths and limitations of the research as a whole are detailed below. This thesis only addressed issues relating to diagnostic

nuclear medicine procedures and is therefore not applicable to therapeutic application of nuclear medicine or other medical imaging using ionising radiation.

6.3.1 RESEARCH STRENGTHS

Previously there were no specific Australian guidelines available for pregnancy screening in diagnostic nuclear medicine. This research provides knowledge and advice for nuclear medicine personnel on how to determine the pregnancy status of women prior to diagnostic imaging procedures. The research considered a comprehensive range of issues relating to pregnancy screening for diagnostic nuclear medicine which included: policy and regulations, method of questioning, age range, use of pregnancy testing, and potentially difficult groups to question. This research provides a significant contribution to the limited evidence base available in this area. The cross-sectional survey is one of the largest and most comprehensive surveys of nuclear medicine practice conducted, with respect to determining pregnancy status. The findings of the research provide a valuable, practical contribution to the field of nuclear medicine which will potentially minimise the possibility of inadvertent foetal irradiation.

The research was conducted in four phases; with each phase building on the knowledge gained from the previous phase. Following a review of the current literature on foetal irradiation and guidelines for pregnancy screening in diagnostic nuclear medicine (Phase One), a small semi-structured interview study (Phase Two) was performed. The results from the interviews informed the development of a cross-sectional online survey (Phase Three) which was distributed to all members of the ANZSNM. The survey received a total of 335 responses from nuclear medicine scientists, physicians and physicists working in all states of Australia and New Zealand in both public hospital departments (48%) and private practices. This large sample is believed to be representative of the nuclear medicine workforce in Australia and New Zealand. The results of the survey demonstrated the need for a consistent approach to questioning women about their pregnancy status and therefore a Delphi technique study (Phase Four) was conducted to gather the opinions of a group of

experts and develop consensus statements. The iterative design of the four phases of research provides validity and credibility to the research.

6.3.2 RESEARCH LIMITATIONS

The research in this thesis was conducted in Australia and New Zealand only. This may limit the transferability of the findings for other countries. However, the research is underpinned by international radiation protection guidelines, such as UNSCEAR and ICRP reports (1, 6), which provide recommendations for the safe use of ionising radiation. The ICRP reports are used by national radiation protection agencies, such as NCRP (13) and ARPANSA (14), to guide practice in individual countries. Also, the biological effects caused by ionising radiation apply to all humans and do not vary according to race or ethnicity. Therefore the consensus guidelines developed by this research in Australia should be applicable for diagnostic nuclear medicine practice anywhere in the world.

The Delphi technique was chosen to develop consensus statements (Chapter Five). This is a validated research method which has been widely used in health. However it has been criticised for a lack of methodological rigour if not conducted properly (15). This was combatted by ensuring the study was grounded in evidence from the literature, and by careful selection of members of the expert panel. This study only involved a small number of participants (n=10) which may affect the validity of the results.

6.4 IMPLICATIONS FOR CLINICAL PRACTICE

This research has major implications for clinical practice in nuclear medicine. Worldwide, there are currently no published guidelines for pregnancy screening for diagnostic nuclear medicine. The research has highlighted variations in current practice in Australia and New Zealand and the lack of a consistent approach to questioning patients about their pregnancy status which may be leading to unnecessary foetal irradiation. Foetal irradiation, especially in the early stage of pregnancy, has the potential to cause biological harm. Therefore, the accurate identification of a pregnant or potentially pregnant woman prior to diagnostic imaging procedures using ionising radiation is a crucial step for the protection of the foetus.

This research provides important information and guidance regarding pregnancy screening which has now been published in the *Journal of Nuclear Medicine Technology*, the premier professional journal for nuclear medicine scientists in the world. The publication of this research should raise awareness of the existing variations in practice and prompt nuclear medicine scientists to reflect on their clinical practice.

6.5 FUTURE RESEARCH

This thesis has developed consensus statements and a flowchart for pregnancy screening in diagnostic nuclear medicine. Future research to be conducted includes the incorporation of the consensus statements and flowchart into “best practice” guidelines to assist nuclear medicine personnel to more accurately determine the pregnancy status of women having diagnostic nuclear medicine imaging procedures. The guidelines would provide a consistent approach and enable nuclear medicine personnel to be confident when questioning patients and ultimately, minimise the possibility of inadvertent and unnecessary foetal irradiation. Following dissemination and implementation into clinical practice in Australia and New Zealand, an evaluation of the impact of the guidelines could then be assessed.

This research in this thesis was limited to Australia and New Zealand. However it would be possible to extend the research to an international survey on current practice in nuclear medicine, based on the cross-sectional survey utilised in Phase Three, and compare the results to our results.

Another possible avenue for future research would be to extend the research to other areas of medical imaging using ionising radiation, such as computed tomography (CT), as it can have the potential to give relatively high exposures.

6.6 FINAL CONCLUSIONS

This research highlights the limited evidence base available to guide nuclear medicine practice in determining the pregnancy status of patients prior to diagnostic imaging procedures. Results from all phases of the research in this thesis support the development of pregnancy screening guidelines to minimise the possibility of inadvertent and unnecessary foetal irradiation. The results from the interview and

cross-sectional survey studies suggest an *ad hoc* approach to questioning patients about their pregnancy status exists in nuclear medicine in Australia and New Zealand. Variations in practice may lead to inconsistent patient care and the increased possibility of pregnant women undergoing diagnostic imaging using ionising radiation. The consensus statements developed in Phase Four provide a consistent approach to questioning which will assist nuclear medicine personnel to identify pregnant and potentially pregnant women prior to the commencement of diagnostic nuclear medicine procedures.

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Appendix A

AUTHOR CONTRIBUTION STATEMENTS

1. Determining the pregnancy status of patients prior to diagnostic nuclear medicine procedures: The Australian Experience

I attest that Research Higher Degree candidate, Daphne James, contributed to the paper/publication entitled:

Determining the pregnancy status of patients prior to diagnostic nuclear medicine procedures: The Australian Experience, published in *Journal of Nuclear Medicine Technology* 2011, 39(3):220-225

Daphne James contributed to the conception and design of the study, conducted data collection, analysed data, and drafted the manuscript. Paul Cardew and Associate Professor Helen Warren-Forward contributed to the conception and design of the study, and the preparation and critical review of the manuscript within the capacity of their role as PhD supervisors.

Paul Cardew

5/8/2014

Associate Professor Helen Warren-Forward

Date: 8/9/2014

Daphne James

Date: 8/9/2014

Professor Robert Callister

Date: 09/09/2014

Assistant Dean Research Training (ADRT)

2. Pregnancy screening strategies for diagnostic nuclear medicine: Survey results from Australia and New Zealand.

I attest that Research Higher Degree candidate, Daphne J James, contributed to the paper/publication entitled:

Pregnancy screening strategies for diagnostic nuclear medicine: Survey results from Australia and New Zealand., published in *Journal of Nuclear Medicine Technology* 2013; 41(3):216-222.

Daphne J James contributed to the conception and design of the study, conducted data collection, analysed data, and drafted the manuscript. Paul Cardew and Associate Professor Helen Warren-Forward contributed to the conception and design of the study, and the preparation and critical review of the manuscript within the capacity of their role as PhD supervisors.

Paul Cardew

5/8/2014

Associate Professor Helen Warren-Forward

8/9/2014

Daphne James
8/9/2014

Professor Robert Callister

Date: 09/09/2014

Assistant Dean Research
Training (ADRT)

3. Pregnancy screening strategies for potentially challenging patients prior to diagnostic nuclear medicine procedures: qualitative survey analysis

I attest that Research Higher Degree candidate, Daphne J James, contributed to the paper/publication entitled:

Pregnancy screening strategies for potentially challenging patients prior to diagnostic nuclear medicine procedures: qualitative survey analysis, published in Journal of Nuclear Medicine Technology 2013; 41(4):292-298

Daphne J James contributed to the conception and design of the study, conducted data collection, analysed data, and drafted the manuscript. Paul Cardew and Associate Professor Helen Warren-Forward contributed to the conception and design of the study, and the preparation and critical review of the manuscript within the capacity of their role as PhD supervisors.

Paul Cardew

5/8/2014

Associate Professor Helen Warren-Forward

8/9/2014

Daphne James

8/9/2014

Professor Robert Callister

Date:09/09/2014

Assistant Dean Research Training (ADRT)

4. **Development of consensus statements for pregnancy screening in diagnostic nuclear medicine: A Delphi study**

I attest that Research Higher Degree candidate, Daphne J James, contributed to the paper/publication entitled:

Development of consensus statements for pregnancy screening in diagnostic nuclear medicine: A Delphi study, submitted for publication in *Journal of Nuclear Medicine Technology*

Daphne J James contributed to the conception and design of the study, conducted data collection, analysed data, and drafted the manuscript.

Associate Professor Helen Warren-Forward contributed to the conception and design of the study, and the preparation and critical review of the manuscript within the capacity of her role as PhD supervisor.

Associate Professor Helen Warren-Forward

Date: 8/9/2014

Daphne James

Date: 8/9/2014

Professor Robert Callister

Date: 09/09/2014

Assistant Dean Research Training (ADRT)

5. Diagnosis of pregnancy in early pregnancy: a systematic review

I attest that Research Higher Degree candidate, Daphne J James, contributed to the paper/publication entitled:

Diagnosis of pregnancy in early pregnancy: a systematic review, submitted for publication in the *Medical Journal of Australia*

Daphne J James developed the review protocol, conducted the literature search and the identification of studies for inclusion, conducted the quality assessments and data extraction for included studies, and drafted the manuscript.

Associate Professor Helen Warren-Forward was the second reviewer for the systematic review, and therefore contributed to the selection of studies, conducted quality assessments and verified data extraction. Associate Professor Helen Warren-Forward contributed to the development and critical review of the manuscript within the capacity of her role as PhD supervisor.

Associate Professor Helen Warren-Forward

Date: 13/02/2015

Daphne James

Date: 13/02/2015

Professor Robert Callister

Date: 13/02/2015

Assistant Dean Research Training (ADRT)

6. Research methods for formal consensus development in health

I attest that Research Higher Degree candidate, Daphne J James, contributed to the paper/publication entitled:

Research methods for formal consensus development in health, accepted for publication in *Nurse Researcher* (in press).

Daphne J James conducted the literature search and the identification of studies for inclusion, conducted the data extraction for included studies, and drafted the manuscript. Associate Professor Helen Warren-Forward contributed to the development and critical review of the manuscript within the capacity of her role as PhD supervisor.

Associate Professor Helen Warren-Forward

Date: 8/9/2014

Daphne James

Date: 8/9/2014

Professor Robert Callister

Date: 09/09/2014

Assistant Dean Research Training

Appendix B

LITERATURE REVIEW

CONSENSUS DEVELOPMENT NARRATIVE REVIEW

A review of formal research methods for developing consensus was conducted using the following search strategy:

Search terms

Consensus

Consensus development

Research design

Delphi

Nominal group technique.

Data sources

Medline, CINAHL

Relevant peer-reviewed articles published in English were retrieved for review. The review was accepted for publication in Nurse Researcher in 2014 (Chapter 2).

SYSTEMATIC REVIEW

A systematic review was conducted on the diagnostic accuracy of pregnancy screening strategies for early pregnancy. The candidate completed a 5 day Joanna Briggs Institute (JBI) comprehensive systematic review training course in Adelaide in August 2011.

Protocol

A systematic review protocol was developed and approved by JBI (#JBL000702). The protocol as published by JBI is attached.

James, DJ., & Warren-Forward, HM. The diagnostic accuracy of strategies used to identify early pregnancy: a systematic review. JBI Library of Systematic Reviews 2012;10(56 Suppl),S303 - S312.

The protocol describes the background, search strategy, methodological quality assessment, and data extraction methods.

Review

The systematic review was conducted in 2013. The results of the review were submitted for publication in *BJOG: An International Journal of Obstetrics and Gynaecology* in July 2014 (Chapter 2).

James, DJ., & Warren-Forward, HM. Diagnostic accuracy of pregnancy screening strategies in early pregnancy: a systematic review.

The diagnostic accuracy of strategies used to identify early pregnancy: a systematic review.

Daphne James, PhD student, Ass Dip Nucl Med Tech^{1,2}

Contact: Daphne.James@newcastle.edu.au

Helen Warren-Forward, Associate Professor PhD^{1,2}

Contact: Helen.Warren-Forward@newcastle.edu.au

1. School of Health Sciences, Faculty of Health, The University of Newcastle
2. The University of Newcastle Evidence Based Health Care Group: a JBI Evidence Synthesis Group

Review question/objective

The objective of this review is to summarise and synthesise the evidence on the diagnostic accuracy of screening strategies used to identify early pregnancy in patients in the health care setting

More specifically, the objectives are to identify the diagnostic accuracy of:

1. patient history to identify early pregnancy; including verbal questioning, written questionnaires and use of last menstrual period dates, and
2. pregnancy testing in identifying early pregnancy

Background

Diagnosing or excluding early pregnancy is an important step in the evaluation of women of child-bearing age in primary care and emergency departments. Early pregnancy can be defined as the period known as organogenesis which last from weeks two to eight post conception^{1,2}. The foetus is highly sensitive to the harmful effects of teratogenic drugs and ionising radiation in the early stages of pregnancy so it is often necessary to determine a patient's pregnancy status prior to performing surgical and diagnostic procedures or prescribing treatment^{3,4}. This allows for appropriate clinical management and prenatal care to commence.

Preoperative pregnancy testing has been a topic of interest in anaesthesiology for some time⁵. Although the possible teratogenic and abortive effects of commonly used anaesthesia are widely acknowledged, routine pregnancy testing prior to surgery has not been mandated. The WHO Guidelines for Safe Surgery 2009 do not include information regarding pre-operative pregnancy testing. Routine pregnancy testing prior to elective surgery is also not an American Society of Anaesthesiologists standard. However, clinical guidelines for preoperative testing recommend pregnancy checking or pregnancy testing for women prior to surgery^{4,6}. An abstract from Euroanaesthesia 2011 reported that pregnancy checking should be performed preoperatively and that

a "clear definition of what makes an adequate preoperative pregnancy status check would help in assessment and achievement of standards as well as reducing interhospital variability"⁷.

The developing foetus is most sensitive to the biological effects from exposure to ionising radiation in the early period of pregnancy known as organogenesis which occurs during weeks two to eight after conception. Exposure to ionising radiation from medical imaging procedures in this early stage of pregnancy may induce teratogenic, mutagenic or carcinogenic changes. The type and extent of damage that may occur is dependent on factors such as the total dose, dose rate, type of radiation used, and the stage of foetal development. Women are often unaware they are pregnant in the early stage of pregnancy. In order to protect the foetus the regulatory and professional bodies involved with the use of ionising radiation for medical imaging recommend checking patient pregnancy status prior to performing procedures using ionising radiation⁸. These documents do not provide definitions for "child-bearing age" or guidelines on how to determine the pregnancy status of the patient.

Certain medications can induce adverse effects on a foetus if taken by the mother in the early stage of pregnancy. Isotretinoin is an effective acne treatment widely prescribed for severe cystic acne in Australia and the UK. As a member of the retinoid family, it is a known teratogen causing foetal abnormalities in rodent and primate models⁹. Craniofacial deformities, cardiac and eye abnormalities and spontaneous abortion are some of the major adverse effects of ingestion of isotretinoin during pregnancy. The Australian College of Dermatologists recommend that prior to commencing treatment, all women of child bearing age should be undergo a pregnancy test and be counselled regarding pregnancy, contraception and the possible dangers of falling pregnant during treatment. Other known teratogenic medications, such as ACE (angiotensin converting enzyme) inhibitors, high dose Vitamin A, some anticonvulsant medications, some antibiotics, chemotherapy drugs, lithium and warfarin can adversely affect the health of the foetus so pregnancy checking is recommended before treatment¹⁰.

There is a perception that the ability of the patient to self-diagnose pregnancy is unreliable. Without a clinical examination or pregnancy test, explicit questions regarding the patient's sexual activity, menstrual history and use of contraceptives must be undertaken. In some cases, such as young teenagers, verbal questioning may not illicit a truthful or accurate response, particularly if a parent is present at the time of questioning¹¹. Ramoska (1989)¹² suggested that patient history was unreliable in diagnosing or excluding early pregnancy. However later studies performed by Strote and Chen (2006)¹³ and Minnerop et al (2011)¹⁴ reported that sexual history and self-assessment were effective predictors of pregnancy. All studies recommended the liberal use of a laboratory pregnancy test in most cases.

Home pregnancy testing (HPT) kits have been found to be ineffective in identifying early pregnancy, especially if used prior to the date of missed menses. Manufacturers of HPT claim a greater than 97% accuracy in the detection of pregnancy however, when performed in the home, the real accuracy may be as low as 77%¹⁵. In particular, there is a high rate of false-negatives reported in early pregnancy. There are many reported possible causes for this including testing prior to the date of missed menses, tests with differing detectable concentrations of human chorionic gonadotrophin (HCG), operator error, and dilution of the urine sample^{16, 17}. Pregnancy tests (both urine and serum) performed in the laboratory have been found to be highly accurate in determining pregnancy during early pregnancy. However, it is impractical and expensive to perform serum pregnancy testing on all female patients of child-bearing age presenting for medical imaging or elective surgery.

A preliminary search performed of the JBI Library of Systematic Reviews and Cochrane Library did not find any systematic reviews regarding diagnosis of early pregnancy. A review article by Bastian and Piscitelli¹⁵ looked at articles published between 1966 and 1996 concerning the diagnosis of pregnancy focussing on the use of patient history and clinical examination to rule out early pregnancy. Their search identified nine studies and they used the findings from these to create likelihood ratios to predict the likelihood of pregnancy in certain situations. The review recommended laboratory pregnancy testing be used, rather than clinical history or examination, to accurately rule out pregnancy prior to any treatment or procedure that could adversely affect a foetus.

Keywords

Diagnostic accuracy, pregnancy, early pregnancy

Inclusion criteria***Types of participants***

This review will consider studies that include adolescent and adult female patients in the health care setting of childbearing age.

Focus of the review

The focus of the review is the correct identification of early pregnancy. This review will consider studies that compare the diagnostic accuracy of screening strategies to identify early pregnancy compared to HCG pregnancy test.

Types of outcomes

This review will consider studies that report on the sensitivity, specificity and accuracy of medical history and/or physical examination (index test), and urine or serum HCG pregnancy test (reference test) to identify early stage pregnancy. Likelihood ratios and/or predictive values will be generated to further describe the diagnostic test accuracy.

Types of studies

This review will consider any quantitative studies that examine the diagnostic accuracy of the index and/or reference tests.

Search strategy

The search strategy aims to find both published and unpublished studies. A three-step search strategy will be utilised in this review. An initial limited search of MEDLINE and CINAHL will be undertaken followed by analysis of the text words contained in the title and abstract, and of the index terms used to describe article. A second search using all identified keywords and index terms will then be undertaken across all included databases. Thirdly, the reference list of all identified reports and articles will be searched for additional studies. Studies published in English will be considered for inclusion in this review. Studies published from January 1975 will be considered for inclusion in this review because monoclonal antibody pregnancy assays were introduced during that year¹⁸.

The databases to be searched include:

MEDLINE, CINAHL, EMBASE, SCOPUS, Web of Science, Cochrane Library

The search for unpublished studies will include ProQuest, NOVA, TROVE, MedNar

Initial keywords to be used will be:

Female

Humans

Adolescent

All adult

Pregnancy tests

Pregnancy

Medical history

Physical Examination

Preoperative care

Diagnosis

Diagnostic accuracy

Sensitivity

Specificity

Likelihood ratio

Predictive value

Assessment of methodological quality

Papers selected for retrieval will be assessed by two independent reviewers for methodological quality prior to inclusion in the review. The Quality Assessment of Diagnostic Accuracy studies (QUADAS) ¹⁹ checklist will be used as an appraisal instrument. The checklist is presented in Appendix I. Any disagreements that arise between the reviewers will be resolved through discussion, or with a third reviewer.

Data collection

Data will be extracted from papers included in the review using the Standards for Reporting Studies of Diagnostic Accuracy (STARD) ²⁰ checklist (Appendix II). The data extracted will include specific details about the populations, setting, study methods, sensitivity, specificity and accuracy of the index test as compared with serum HCG pregnancy test results.

Data synthesis

The reported sensitivity, specificity and accuracy from individual studies will be tabulated. Predictive values and likelihood ratios will be calculated for each included study. Where statistical pooling is not possible the findings will be presented in narrative form including tables and figures to aid in data presentation where appropriate. Revman 5.1 and Microsoft Excel software will be used for data management and analysis.

Conflicts of interest

Nil

Acknowledgements

As this systematic review will form part of a PhD in Medical Radiation Science thesis, the secondary reviewer will be used for critical appraisal of studies only.

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Appendix I: Critical Appraisal Tool - The QUADAS checklist¹⁹

1. Was the spectrum of patient's representative of the patients who will receive the test in practice?
2. Were selection criteria clearly described?
3. Is the reference standard likely to correctly classify the target condition?
4. Is the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?
5. Did the whole sample or a random selection of the sample, receive verification using a reference standard of diagnosis?
6. Did patients receive the same reference standard regardless of the index test result?
7. Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)?
8. Was the execution of the index test described in sufficient detail to permit replication of the test?
9. Was the execution of the reference standard described in sufficient detail to permit its replication?
10. Were the index test results interpreted without knowledge of the results of the reference standard?
11. Were the reference standard results interpreted without knowledge of the results of the index test?
12. Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?
13. Were uninterpretable/ intermediate test results reported?
14. Were withdrawals from the study explained?

Appendix II: Data Extraction Tool - The STARD checklist²⁰

1. Was the study identified as being a diagnostic accuracy study?
2. Were research questions or study aims, such as estimating diagnostic accuracy or comparing accuracy between tests or across participant groups, detailed?
3. Does the study describe the study population, inclusion and exclusion criteria, setting and locations where the data were collected?
4. Does the study describe participant recruitment? Was recruitment based on presenting symptoms, results from previous tests, or the fact that the participants had received the index tests or the reference standard?
5. Describe participant sampling: Was the study population a consecutive series of participants defined by the selection criteria in items 3 and 4? If not, specify how participants were further selected
6. Describe data collection: Was data collection planned before the index test and reference standard were performed (prospective study) or after (retrospective study)?
7. Did the study describe the reference standard and its rationale?
8. Describe technical specifications of material and methods involved including how and when measurements were taken, and/or cite references for index tests and reference standard.
9. Describe definition of and rationale for the units, cut-offs and/or categories of the results of the index tests and the reference standard.
10. Describe the number, training and expertise of the persons executing and reading the index tests and the reference standard
11. Describe whether or not the readers of the index tests and reference standard were blind (masked) to the results of the other test and describe any other clinical information available to the readers.
12. Describe methods for calculating or comparing measures of diagnostic accuracy, and the statistical methods used to quantify uncertainty (e.g. 95% confidence intervals)
13. Describe methods for calculating test reproducibility, if done.
14. Report when study was done, including beginning and ending dates of recruitment.
15. Does the study report clinical and demographic characteristics of the study population (e.g. age, sex, spectrum of presenting symptoms, co-morbidity, current treatments, recruitment centres?)

16. Does the study report the number of participants satisfying the criteria for inclusion that did or did not undergo the index tests and/or the reference standard; describe why participants failed to receive either test (a flow diagram is strongly recommended) .
17. Does the study report time interval from the index tests to the reference standard, and any treatment administered between?
18. Does the study report distribution of severity of disease (define criteria) in those with the target condition; other diagnoses in participants without the target condition?
19. Does the study report a cross tabulation of the results of the index tests (including indeterminate and missing results) by the results of the reference standard; for continuous results, the distribution of the test results by the results of the reference standard?
20. Does the study report any adverse events from performing the index tests or the reference standard?
21. Does the study report estimates of diagnostic accuracy and measures of statistical uncertainty (e.g. 95% confidence intervals)?
22. Does the study report how indeterminate results, missing responses and outliers of the index tests were handled?
23. Does the study report estimates of variability of diagnostic accuracy between subgroups of participants, readers or centres?
24. Does the study report estimates of test reproducibility?
25. Does the study discuss the clinical applicability of the study findings?

Appendix C

INTERVIEW STUDY

ETHICS APPROVAL

Ethics approval for the study was submitted on 25th August 2009 to The University of Newcastle Human Research Ethics committee. The study was considered under **L1 Low Risk Research Expedited** review. Due to the inclusion of fieldwork, a *Safety Implications of Research Projects Involving Off-site Activity (RS/OSA Form)* was submitted to the University Health and Safety team and subsequently granted safety clearance. Ethics approval for the study was granted on 10th September 2009 (Approval number H-2009-0270).

The participant information sheets, consent forms, demographic questionnaire, and interview schedule can be found in Appendix 3.

INTERVIEW DESIGN

A review of current national and international literature and radiation protection documents was undertaken. Interview questions were developed to investigate current departmental policies and practice, NMS knowledge of the biological effects of radiation and foetal exposure, and potential problems NMS associated with determining a patient's pregnancy status. Semi-structured interviews were used to allow the researcher to guide the participant through a series of pertinent questions whilst allowing for additional information to be revealed in the interview.

An interview schedule was used during all interviews to ensure each interviewee was asked similar questions relating to a series of themes. The themes covered were:

- Regulations and policy
- Foetal radiation exposure
- Questioning of the patient
- Difficulties in determining pregnancy status
- Impact of the use of hybrid imaging

These themes were developed following a focus group conducted with NMS employed at the John Hunter Hospital in Newcastle, Australia in 2009. Conduction of the focus

group and analysis of the data formed part of the assessment for PUBH6210 Qualitative Methods in Health Research which the researcher completed in 2009.

The interviews were conducted at nuclear medicine departments in Canberra, Brisbane, Southport, Melbourne, Perth and Newcastle between March and October 2010. Each interview lasted approximately 45 minutes. The interviews were recorded using an Olympus DS-50 Digital Voice Recorder.

PARTICIPANT RECRUITMENT

The University of Newcastle School of Health Sciences Professional Placement Unit clinical placement site database was accessed to provide a list of nuclear medicine departments in Australia and New Zealand and their mailing address. Eighteen nuclear medicine departments were selected from the list and invited to participate in the study. The departments were selected to represent each state of Australia, New Zealand, and to cover a variety of metropolitan and rural, and public and private centres. The Chief NMS for each department was mailed a participant package which consisted of the Chief NMS Participant Information Statement, consent form, and several sealed envelopes to be distributed to their staff NMS. These envelopes contained the Staff NMS Participant Information Statement, consent form and demographic questionnaire. If they wished to participate in the study they were instructed to complete the forms and return to the researcher. Chief NMS and staff NMS from eight departments returned the completed forms and interviews were arranged at a mutually convenient time and place. Following these interviews, no further recruitment for interviews were deemed necessary as data saturation had been achieved and no new data was emerging.

ANALYSIS

After each interview set, the recordings were transcribed using an online transcription service. All data was de-identified during transcription. The transcripts were emailed to the interviewees prior to analysis for review and editing. No changes were identified. After review, each transcript was printed and a paper copy stored for review and analysis.

Each interview transcript was assigned a participant ID code. Chief NMS were coded C1, C2 etc, whilst the corresponding Staff NMS interview was coded S1, S2 respectively. Initial topic coding was performed by the researcher on each paper transcript to identify any emerging themes and to determine if the interview questions required refining for subsequent interviews. Following completion of all interviews, computer coding was conducted on the transcripts using QSR NVivo 8.0.

FUNDING

Funding for transcription of the recordings and travel to conduct the interviews was provided by a University of Newcastle New Staff Grant (G0190283).

ADDITIONAL ATTACHMENTS

- Participant Information Sheet – Chief NMS
- Consent form – Chief NMS
- Participant Information Sheet – Staff NMS
- Consent form – Staff NMS
- Demographic questionnaire – Staff NMS
- Interview schedule



Dr Helen Warren-Forward
 School of Health Sciences
 Faculty of Health
 Ph: 02 49217142
 Fax: 02 49217053
Helen.Warren-Forward@newcastle.edu.au

**Information Statement for the Research Project:
 Qualitative Review of the Problems Associated with the Verification of a Patient's Pregnancy
 Status prior to Diagnostic Imaging Procedures in Nuclear Medicine**

Chief Nuclear Medicine Scientist
 Document Version 3; dated 29/07/2009

You are invited to participate in the research project identified above which is being conducted by Dr Helen Warren-Forward and Daphne James, Lecturer, from the School of Health Sciences at the University of Newcastle. The research is part of Daphne James studies at the University of Newcastle, supervised by Dr Helen Warren-Forward from the School of Health Sciences and Paul Cardew from Hunter New England Health Service.

Why is the research being done?

The purpose of the research is to investigate current department policies and the problems Nuclear Medicine Scientists (NMS) associate with determining a patient's pregnancy status prior to a diagnostic Nuclear Medicine procedure.

Who can participate in the research?

Chief NMS have been selected from a list of Nuclear Medicine centres in Australia & New Zealand provided by the School of Health Sciences Professional Placement Unit. The Chief NMS from a maximum of 15 selected Nuclear Medicine departments will be interviewed.

One ANZSNM accredited member from the NMS staff of each Chief NMS will be interviewed at a separate time. To be eligible to participate, NMS must have a minimum of 2 years experience as an accredited NMS and be employed in Australia or New Zealand. Student NMS and Professional Development Year (PDY) NMS are excluded from participating.

What choice do you have?

Participation in this research is entirely your choice. Only those people who give their informed consent will be included in the project. Whether or not you decide to participate, your decision will not disadvantage you. If you do decide to participate, you may withdraw from the interview at any time without giving a reason and have the option of withdrawing any data which identifies you up to a period of 4 weeks after the interview.

What would you be asked to do?

If you agree to participate, you will be asked to participate in a semi-structured interview conducted by Daphne James. The interview may be conducted in person at a mutually convenient time and place, or by telephone. The interview will be recorded. The transcript will be sent to you for review and editing. The interview will investigate the department's policies regarding verifying a patient's pregnancy status prior to diagnostic Nuclear Medicine procedures.

You will be asked to distribute the provided letters to ANZSNM accredited NMS on your staff. These letters request their participation in the project. One member of your staff will be selected by the researcher to be interviewed. You will not be notified which staff member is to be interviewed.

How much time will it take?

The interview should take about 60 minutes to complete.

What are the risks and benefits of participating?

There are no risks or direct benefits to the participants.

How will your privacy be protected?

Any information collected by the researchers which might identify you will be stored securely and only accessed by the researchers. Data will be retained for at least 5 years in a locked cabinet in the office of Dr Helen Warren-Forward. The interview transcripts will be coded & de-identified prior to analysis. Interview transcripts on tape & paper will be stored in the locked cabinet when not in use. All computer records will be stored on a password-protected computer. Access will be by the researchers only. All tapes will be erased after transcription. Paper will be shredded after submission of the final thesis to the University with the original stored on the computer.

How will the information collected be used?

The results of this study will form part of a Research Higher Degree thesis for Daphne James. You will be able to review the transcript of the interview recording to edit or erase your contribution.

The information collected in the interviews will be used to formulate a questionnaire for the next phase of this project. The questionnaire will be distributed to all NMS practicing in Australia & New Zealand. The results of each phase of the project will be published in peer-reviewed journals. The articles will be written and submitted to journals with the participant population in mind. All interview participants will be sent a copy of the articles. Individual participants will not be identified in any reports arising from the project.

What do you need to do to participate?

Please read this Information Statement and be sure you understand its contents before you consent to participate. If there is anything you do not understand, or you have questions, contact the researcher.

If you would like to participate, please complete and return the attached consent form in the reply paid envelope provided. Daphne James will then contact you to arrange a time convenient to you for the interview.

Further information

If you would like further information please contact Daphne James by telephone on 02 49215596 or by email Daphne.James@newcastle.edu.au

Thank you for considering this invitation.

Dr Helen Warren-Forward
Associate Professor
School of Health Sciences

Complaints about this research

This project has been approved by the University's Human Research Ethics Committee, Approval No. H-2009-0270.

Should you have concerns about your rights as a participant in this research, or you have a complaint about the manner in which the research is conducted, it may be given to the researcher, or, if an independent person is preferred, to the Human Research Ethics Officer, Research Office, The Chancellery, The University of Newcastle, University Drive, Callaghan NSW 2308, Australia, telephone (02) 49216333, email Human-Ethics@newcastle.edu.au.



Dr Helen Warren-Forward
School of Health Sciences
Faculty of Health
Ph: 02 49217142
Fax: 02 49217053
Helen.Warren-Forward@newcastle.edu.au

Consent Form for the Research Project:

Qualitative Review of the Problems Associated with the Verification of a Patient's Pregnancy Status prior to Diagnostic Imaging Procedures in Nuclear Medicine

Chief Nuclear Medicine Scientist
Dr H Warren-Forward & Ms D James
Document Version 3; dated 29/07/2009

I agree to participate in the above research project and give my consent freely.

I understand that the project will be conducted as described in the Information Statement, a copy of which I have retained.

I understand that I can withdraw from the interview at any time and do not have to give any reason for withdrawing.

I consent to participating in an interview and having it recorded.

I understand that I will have the opportunity to review and edit the interview transcripts, which will be coded and de-identified prior to analysis.

I understand I can withdraw data up to 4 weeks after the interview.

I understand that my personal information will remain confidential to the researchers.

I have had the opportunity to have questions answered to my satisfaction.

Print Name: _____

Signature: _____ **Date:** _____

Contact Details to arrange interview:

Email address: _____ **Ph:** _____



Dr Helen Warren-Forward
 School of Health Sciences
 Faculty of Health
 Ph: 02 49217142
 Fax: 02 49217053
Helen.Warren-Forward@newcastle.edu.au

**Information Statement for the Research Project:
 Qualitative Review of the Problems Associated with the Verification of a Patient's Pregnancy
 Status prior to Diagnostic Imaging Procedures in Nuclear Medicine**

Staff Nuclear Medicine Scientist
 Document Version 3:dated 29/07/2009

You are invited to participate in the research project identified above which is being conducted by Dr Helen Warren-Forward and Daphne James, Lecturer, from the School of Health Sciences at the University of Newcastle. The research is part of Daphne James Research Higher Degree studies at the University of Newcastle, supervised by Dr Helen Warren-Forward from the School of Health Sciences and Paul Cardew from Hunter New England Health Service.

Why is the research being done?

The purpose of the research is to investigate current department policies and practice, and the problems Nuclear Medicine Scientists (NMS) associate with determining a patient's pregnancy status prior to a diagnostic Nuclear Medicine procedure.

Who can participate in the research?

Chief NMS have been selected from a list of Nuclear Medicine centres in Australia & New Zealand provided by the School of Health Sciences Professional Placement Unit. The Chief NMS from a maximum of 15 selected Nuclear Medicine departments will be interviewed. One ANZSNM accredited member from the NMS staff of each Chief NMS will be interviewed at a separate time. To be eligible to participate, NMS must have a minimum of 2 years experience as an accredited NMS and be employed in Australia or New Zealand. Student NMS and Professional Development Year (PDY) NMS are excluded from participating.

A short demographic questionnaire, completed by all NMS who would like to participate in the project, will be used to select the NMS to be interviewed from each department. This will ensure a cross reference of gender, age and experience.

What choice do you have?

Participation in this research is entirely your choice. Only those people who give their informed consent will be included in the project. Whether or not you decide to participate, your decision will not disadvantage you. If you do decide to participate, you may withdraw from the interview at any time without giving a reason and have the option of withdrawing any data which identifies you.

What would you be asked to do?

If you agree to participate, you will be asked to participate in a semi-structured interview conducted by Daphne James. The interview may be conducted in person at a mutually convenient time and place, or by telephone. The interview will be recorded. The transcript will be sent to you for review and editing. The interview will investigate your knowledge of regulations and department policies regarding verifying a patient's pregnancy status and your current practice.

If you choose to participate by returning the demographic questionnaire and consent form, you are not obligated to agree to an interview.

How much time will it take?

The interview should take about 60 minutes to complete.

What are the risks and benefits of participating?

There are no risks or direct benefits to the participants.

How will your privacy be protected?

The Chief NMS will not be informed which staff member is selected to be interviewed. Any information collected by the researchers will be stored securely and only accessed by the researchers unless you consent otherwise, except as required by law. Data will be retained for at least 5 years in a locked cabinet in the office of Dr Helen Warren-Forward. The interview transcripts will be coded & de-identified prior to analysis. Interview transcripts on tape & paper will be stored in the locked cabinet when not in use. All computer records will be stored on a password-protected computer. Access will be by the researchers only. All tapes will be erased after transcription. Paper will be shredded after submission of the final thesis to the University with the original stored on the computer.

How will the information collected be used?

The results of this study will form part of a Research Higher Degree thesis for Daphne James. You will be able to review the transcript of the interview recording to edit or erase your contribution.

The information collected in the interviews will be used to formulate a questionnaire for the next phase of this project. The questionnaire will be distributed to all NMS practicing in Australia & New Zealand. The results of each phase of the project will be published in peer-reviewed journals. The articles will be written and submitted to journals with the participant population in mind. All interview participants will be sent a copy of the articles. Individual participants will not be identified in any reports arising from the project.

What do you need to do to participate?

Please read this Information Statement and be sure you understand its contents before you consent to participate. If there is anything you do not understand, or you have questions, contact the researcher.

If you would like to participate, please complete and return the attached demographic questionnaire and the consent form in the reply paid envelope provided. Do not return it to your Chief NMS. Daphne James will then contact you to arrange a time convenient to you for the interview.

Further information

If you would like further information please contact Daphne James by telephone on 02 49215596 or by email Daphne.James@newcastle.edu.au

Thank you for considering this invitation.

Dr Helen Warren-Forward
Associate Professor
School of Health Sciences

Complaints about this research

This project has been approved by the University's Human Research Ethics Committee, Approval No. H-2009-0270.

Should you have concerns about your rights as a participant in this research, or you have a complaint about the manner in which the research is conducted, it may be given to the researcher, or, if an independent person is preferred, to the Human Research Ethics Officer, Research Office, The Chancellery, The University of Newcastle, University Drive, Callaghan NSW 2308, Australia, telephone (02) 49216333, email Human-Ethics@newcastle.edu.au



Dr Helen Warren-Forward
 School of Health Sciences
 Faculty of Health
 Ph: 02 49217142
 Fax: 02 49217053
Helen.Warren-Forward@newcastle.edu.au

Consent Form for the Research Project:

Qualitative Review of the Problems Associated with the Verification of a Patient's Pregnancy Status prior to Diagnostic Imaging Procedures in Nuclear Medicine

Staff Nuclear Medicine Scientist
 Dr H Warren-Forward & Ms D James
 Document Version 2; dated 29/07/2009

I agree to participate in the above research project and give my consent freely.

I understand that the project will be conducted as described in the Information Statement, a copy of which I have retained.

I understand that I can withdraw from the interview at any time and do not have to give any reason for withdrawing.

I understand that I will have the opportunity to review and edit the interview transcripts, which will be coded and de-identified prior to analysis.

I understand I can withdraw data up to 4 weeks after the interview.

I consent to (please circle):

- | | | |
|---|-----|----|
| • completing a demographic questionnaire; | Yes | No |
| • participating in an interview and having it recorded; | Yes | No |

I understand that my personal information will remain confidential to the researchers.

I have had the opportunity to have questions answered to my satisfaction.

Print Name: _____

Signature: _____ **Date:** _____

Contact Details to arrange interview:

Email address: _____ **Ph:** _____



Dr Helen Warren-Forward
 School of Health Sciences
 Faculty of Health
 Ph: 02 49217142
 Fax: 02 49217053
Helen.Warren-Forward@newcastle.edu.au

**Research Project: Verifying Pregnancy Status of Patients
 Questionnaire for Nuclear Medicine Scientists (NMS)**

Name: _____

Department: _____

Please circle the appropriate response.

1. Please indicate your gender

Male

Female

2. Number of years you have been an ANZSNM accredited Nuclear Medicine Scientist

<2

2-3

>3-5

>5-10

> 10

3. Which best describes your level of employment?

NMS

Senior NMS

NM Tutor/Educator

4. Where do you currently practice?

NSW

ACT

QLD

VIC

SA

WA

TAS

NZ

5. Which best describes your workplace?

Public Hospital

Private hospital

Private Practice

AND

Metropolitan

Rural

Thank you for completing this questionnaire.

Please return to the researcher, with your signed consent form, in the reply paid envelope supplied.

Interview Schedule for the Research Project:

Qualitative Review of the Problems Associated with the Verification of a Patient's Pregnancy Status prior to Diagnostic Imaging Procedures in Nuclear Medicine

Interview Schedule for all participants

Document Version 3: dated 29/07/2009

PREAMBLE

1. Introductions
2. Outline aim of project and interview
3. Clarify that the interviewee is aware that:
 - the interview will be recorded
 - all information will be confidential
 - the transcriptions will be coded and de-identified to protect the privacy of the interviewee
 - the transcript will be made available to them for editing after the interview
 - they can withdraw from the interview at any time
 - any information used will not personally identify them or their place of work.

QUESTION THEMES

Regulations & Policy

- Is there a written department policy?
- Aware of any regulations regarding testing for pregnancy prior to diagnostic imaging?
- ANZSNM guidelines?

Foetal exposure

- What are the dose limits for pregnant women & the foetus?
- What is the most radiosensitive time for the foetus during gestation?
- What may be the consequences of irradiating a foetus?
- Which diagnostic Nuclear Medicine procedures could give a potentially harmful dose to the foetus?

Questioning patients

- Who do you question?
 - Age range
- How do you question them?
 - Verbal or written
 - Signature
 - Storage of any document
- If verbal, what is the NMS instructed to ask the patient?
 - Do they ask the patient about hysterectomy or menopause or their method of contraception?
- Where are they questioned? Privacy issues

Difficulties in determining pregnancy status

- Do you use the "10 day rule"?
- What difficulties arise with teenage patients?
- Do you use of urine/blood pregnancy tests? In what circumstances?
- Do you ever postpone a procedure due to unclear pregnancy status?

Use of hybrid imaging (SPECT/CT or PET/CT)

- Has the introduction of hybrid imaging changed your department policy?

Other

- Possible improvements/changes to department policy?
- Level of concern if partner or self were irradiated whilst pregnant?

Appendix D

SURVEY DOCUMENTS

ETHICS APPROVAL

A variation to the initial ethics application to include a nationwide online survey was submitted on 21st July 2011 to The University of Newcastle Human Research Ethics committee and approved on 12th August 2011.

SURVEY DESIGN

The questionnaire was developed from the interview study findings. Specific details of the questionnaire design are included in Chapter 4. The questionnaire consisted of 30 questions divided into four sections:

1. Demographics
2. Policy and regulations
3. Current practice
4. Clinical scenarios

Following approval from ethics, the questionnaire was entered into the online survey software tool, SurveyMonkey. It enables the creation, customised design, response collection, and data analysis of online surveys. A variety of question and response types are available. The School of Health Sciences has a paid subscription to SurveyMonkey and allows staff and research students to access the program at no cost.

A test run of the survey was completed by a small number of experts to provide feedback on the survey design to ensure validity prior to circulation. The questionnaire was administered online via SurveyMonkey between October and December 2011.

PARTICIPANT RECRUITMENT

Participants were recruited from the membership of the Australian and New Zealand Society of Nuclear Medicine (ANZSNM). Membership of the ANZSNM is available to any person working in nuclear medicine including NMS, medical physicists, nuclear medicine physicians, radiopharmacists, nursing staff and educators. A full page *Invitation to Participate* was published in the Gamma Gazette (the journal of the ANZSNM) in September 2011. An email inviting nuclear medicine personnel to participate in the study was distributed to all members of the ANZSNM by the

ANZSNM Secretariat on behalf of the researcher on 11th October 2011. The email included the participant information sheet and a link to the online survey. A reminder email was sent via the ANZSNM Secretariat on 23rd November 2011.

ANALYSIS

Data analysis was performed using descriptive statistics and open-ended responses were manually coded using thematic analysis.

The qualitative data from Section 4 was analysed by the researcher and an independent researcher with no experience in nuclear medicine to ensure validity of the themes and to eliminate potential bias by the primary researcher towards previously identified themes and personal experience. Content analysis was used to identify a number of themes and sub-themes from the responses to each of the four questions. The initial coding cycle was performed independently by each researcher. There were over 200 responses to each question so initially only the first 50 responses to each question were reviewed and categorised into a number of possible themes. The researchers then compared and discussed their analysis and developed a source code book which was used to analyse all responses. Following analysis of all responses, the researchers compared their coding analysis and if there was any disagreement, a third researcher was asked to deliberate.

ADDITIONAL ATTACHMENTS

- Invitation to Participate flyer - Gamma Gazette Sept 2011
- Participant Information Sheet
- Survey questionnaire
- Code Book for thematic analysis



RESEARCH STUDY

www.newcastle.edu.au

INVITATION TO PARTICIPATE

VERIFICATION OF THE PATIENT'S PREGNANCY STATUS PRIOR TO DIAGNOSTIC IMAGING PROCEDURES IN NUCLEAR MEDICINE

You are invited to participate in a research project investigating current practice and knowledge in determining the pregnancy status of a patient prior to diagnostic Nuclear Medicine procedures. The research is part of Daphne James Doctoral studies, within the School of Health Science at the University of Newcastle. Associate Professor Helen Warren-Forward (University of Newcastle) and Mr Paul Cardew from Hunter New England Health Service are supervisors.

We are conducting a survey of personnel working in Nuclear Medicine departments to determine the awareness of international and departmental policy, currently used methods of questioning patients and to identify any potential difficulties that may arise.

All members of the ANZSNM are invited to participate.

Ethics approval has been gained by the University of Newcastle Human Research Ethics Committee (Approval Number H-2009-0270 and variations).

The survey will be conducted online via SurveyMonkey and has been estimated to take no longer than 15 minutes to complete.

The survey will be open from August to 30th November, 2011. When the survey is open, the link to the survey will be displayed on the ANZSNM web site.

Your involvement in this project will assist in the first step of the development of practical guidelines for determining a patient's pregnancy status prior to diagnostic Nuclear Medicine procedures, so please take the time to participate. Your response will be entirely anonymous.

Thank you

Daphne James (PhD candidate)
Ass. Prof. Helen Warren-Forward
Paul Cardew

Associate Professor Helen Warren-Forward
School of Health Sciences
Faculty of Health
University of Newcastle
Ph: 02 49217142
Fax: 02 49217053
helen.warren-forward@newcastle.edu.au



Information Statement for the Research Project:

Qualitative Review of the Problems Associated with the Verification of a Patient's Pregnancy Status prior to Diagnostic Imaging Procedures in Nuclear Medicine

You are invited to participate in the research project identified above which is being conducted by Daphne James, Lecturer from the School of Health Sciences at the University of Newcastle. The research is part of Daphne James's Doctoral studies at the University of Newcastle, supervised by Associate Professor Helen Warren-Forward from the School of Health Sciences and Mr Paul Cardew, Chief Physicist in Nuclear Medicine, Hunter New England Health Service.

Why is the research being done?

The purpose of the research is to investigate current knowledge, department policies and practice, and the problems associated with determining a patient's pregnancy status prior to a diagnostic Nuclear Medicine procedure.

Who can participate in the research?

To be eligible to participate, participants must be a member of the Australian & New Zealand Society of Nuclear Medicine (ANZSNM).

What choice do you have?

Participation in this research is entirely your choice. Whether or not you decide to participate, your decision will not disadvantage you. Given the anonymous nature of the survey, you will be unable to withdrawing from the study after completion and submission of the survey.

What would you be asked to do?

If you agree to participate, you will be asked to complete an online survey conducted with SurveyMonkey.

How much time will it take?

It has been estimated that the survey should take about 15 minutes to complete.

What are the risks and benefits of participating?

There are no perceived risks or direct benefits to the participants. However, your participation will be the first step in the development of practical guidelines for the verification of pregnancy status prior to a diagnostic Nuclear Medicine procedure.

How will your privacy be protected?

All survey responses will be anonymous. Any information collected by the researchers will be stored securely and only accessed by the researchers, except as required by law. Data will be retained for at least 5 years in a locked cabinet in the office of Associate Professor Helen Warren-Forward. All computer records will be stored on a password-protected computer. Access will be by the researchers only.

How will the information collected be used?

The results of this study will form part of a Research Higher Degree thesis for Daphne James. The results of the survey will be reported at relevant conferences and published in peer-reviewed journals. The articles will be written and submitted to journals with the participant population in mind. Individual participants will not be identified in any reports arising from the project. The information collected will be the first step in the development of practical guidelines for the verification of pregnancy status prior to a diagnostic Nuclear Medicine procedure.

What do you need to do to participate?

Please read this Information Statement and be sure you understand its contents before you consent to participate. If there is anything you do not understand, or you have questions, contact the researcher.

If you would like to participate, copy and paste the link to the survey. The survey link can also be found on the ANZSNM web site.

Link: <http://www.surveymonkey.com/s/WY2TWYD>

Further information

If you would like further information please contact Daphne James by telephone on 02 49215596 or by email Daphne.James@newcastle.edu.au

Thank you for considering this invitation.

Helen Warren-Forward

Paul Cardew

Daphne James

Complaints about this research

This project has been approved by the University's Human Research Ethics Committee, Approval No. H- 2009-0270.

Should you have concerns about your rights as a participant in this research, or you have a complaint about the manner in which the research is conducted, it may be given to the researcher, or, if an independent person is preferred, to the Human Research Ethics Officer, Research Office, The Chancellery, The University of Newcastle, University Drive, Callaghan NSW 2308, Australia, telephone (02) 49216333, email Human-Ethics@newcastle.edu.au.

Current practice in determining pregnancy status prior to diagnostic Nuclear

Introduction

This survey has been designed to provide information regarding current practice in Nuclear medicine on determining the pregnancy status of patient's prior to diagnostic imaging.

This survey forms part of the PhD studies of Daphne James, from The University of Newcastle.

The survey should take approximately 10 mins to complete.

At the completion of the survey you will be redirected to a web page where, if you wish, you can enter your name & email address to enter the draw for one of five \$100 Westfield vouchers.

This information is kept separate to your survey responses to maintain anonymity.

Current practice in determining pregnancy status prior to diagnostic Nuclear**Participant Information****1. What is your gender?**

- ☐ Male
- ☐ Female

2. What is your profession?

- ☐ Physician
- ☐ Physicist
- ☐ Senior physicist
- ☐ PDY Nuclear Medicine Scientist
- ☐ Nuclear Medicine Scientist
- ☐ Senior Nuclear Medicine Scientist
- ☐ Chief Nuclear Medicine Scientist

3. How many years of experience do you have in your current profession?

- ☐ 0-2 years
- ☐ 3-5 years
- ☐ 6-10 years
- ☐ 11-15 years
- ☐ 16+ years

4. What type of practice are you employed in?

- ☐ Public
- ☐ Private

Current practice in determining pregnancy status prior to diagnostic Nuclear**5. Where do you practice?**

- ☐ NSW
☐ ACT
☐ VIC
☐ QLD
☐ SA
☐ WA
☐ NT
☐ TAS
☐ NZ

6. Did you obtain your University qualifications in Australia?

- ☐ Yes
☐ No

7. If Yes to Question 6, at which University?

- ☐ University of Sydney
☐ University of Newcastle
☐ University of South Australia
☐ Charles Sturt University
☐ RMIT
☐ Monash University
☐ Other (please specify)

8. If No to question 6, In which country did you obtain your University qualifications?

Current practice in determining pregnancy status prior to diagnostic Nuclear

Policy and Regulations

9. Does the department you work in have a written policy regarding how to determine the pregnancy status of female patients prior to diagnostic imaging procedures?

- ☐ Yes
☐ No
☐ Unsure

10. If Yes to question 9, when did you last read it?

- ☐ < 1 week
☐ < 1 month
☐ < 6 months
☐ < 1 year
☐ > 1 year

11. Are you aware of any government regulations regarding how to determine the pregnancy status of female patients prior to diagnostic imaging procedures?

- ☐ Yes
☐ No

12. If yes to question 11, briefly state what the regulations state regarding how to determine the pregnancy status of female patients prior to diagnostic imaging procedures?

13. Have you read the sections in the following government regulations regarding how to determine the pregnancy status of female patients prior to diagnostic imaging procedures?

	Yes	No
ARPANSA 14.2	<input type="radio"/>	<input type="radio"/>
ICRP 84: Pregnancy and Medical Radiation	<input type="radio"/>	<input type="radio"/>

Current practice in determining pregnancy status prior to diagnostic Nuclear**Current Practice**

14. Please indicate the minimum age of patient that you routinely question about their pregnancy status?

- ☐ 10 years
- ☐ 11 years
- ☐ 12 years
- ☐ 13 years
- ☐ 14 years
- ☐ 15 years
- ☐ 16 years
- ☐ 17 years
- ☐ 18 years
- ☐ Depends on how mature the patient appears

Other (please specify)

15. What the rationale for this age?

16. Please indicate the maximum age of patient that you routinely question about their pregnancy status?

- ☐ 40 years
- ☐ 45 years
- ☐ 50 years
- ☐ 55 years
- ☐ 60 years

Other (please specify)

17. What is the rationale for this age?

Current practice in determining pregnancy status prior to diagnostic Nuclear

18. Which method do you use to determine the pregnancy status of female patients prior to diagnostic imaging procedures?

- ☐ Verbal question
☐ Verbal + signature
☐ Written form

Other (please specify)

19. If you use verbal questioning, do you routinely ask the patient any questions regarding:

- ☐ Last menstrual period (LMP)
☐ Contraceptive Use
☐ Menopause/Hysterectomy

20. If you use a written form, does it ask the patient any questions regarding:

- ☐ Last menstrual period (LMP)
☐ Contraceptive Use
☐ Menopause/Hysterectomy

21. Do you use pregnancy tests in your department?

- ☐ Yes
☐ No

22. If yes to question 21, how often are they used?

- ☐ Routinely
☐ Occasionally

23. If yes to question 21, what type of pregnancy tests are used in your department?

- ☐ Urine
☐ Serum

24. If yes to question 21, in which circumstance are they used?

Current practice in determining pregnancy status prior to diagnostic Nuclear

25. Please rank the following diagnostic procedures from 1-8, with 1 having the most risk to a foetus from exposure to ionising radiation and 8 having the lowest risk.

	1	2	3	4	5	6	7	8
Bone scan	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Thyroid scan	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
V/Q Lung scan	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Renal Perfusion scan	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Gated Heart Pool scan	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Sestamibi Myocardial Perfusion scan	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bone scan with SPECT/CT of lumbar spine	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
¹⁸ F-FDG PET/CT	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Current practice in determining pregnancy status prior to diagnostic Nuclear**Scenarios**

26. Briefly describe how you would question the patient in the following scenario:

Young teenager accompanied by a parent

27. Briefly describe how you would question the patient in the following scenario:

Unconscious or heavily sedated patient

28. Briefly describe how you would question the patient in the following scenario:

Patient with a cultural or language barrier

29. Briefly describe how you would question the patient in the following scenario:

Patient with a mental disability

30. Is there anything you would like to add about the verification of pregnant patients prior to diagnostic nuclear medicine imaging?

Current practice in determining pregnancy status prior to diagnostic Nuclear**Thank you**

Thank you for completing this survey.

You will now be directed to a link to enter your name & email address to enter the draw for one of five \$100 Westfield vouchers.

Code Book for thematic analysis

Q26 - Teenagers

Code	Description
1.1	Method of questioning
1.11	Ask away from parent
1.111	- Take patient in separate room
1.112	- Ask parent to leave/wait in waiting room
1.12	Ask with parent present
1.121	- Ask discreetly/quietly
1.13	Ask parent directly
1.141	Same for all females - Verbal question
1.142	Same for all females - Sign form
1.15	Explain radiation risk
1.2	Subjective assessment
1.21	- Assess parent-child relationship
1.22	- Assess response
1.23	- Assess maturity level
1.3	Determining risk
1.31	Question Re: LMP
1.32	Question Re: Started menstruation
1.33	Question Re: If sexually active
1.34	Question Re: 10 day rule
1.4	Pregnancy test
1.41	- Serum HCG
1.42	- Urine

Q27- Unconscious/sedated patient

Code	Description
2.1	Method of obtaining information re pregnancy status
2.11	Consult patient notes
2.111	- check for pregnancy test results
2.112	- check contraception history
2.113	- check for LMP
2.114	- check length of stay
2.115	- check for consent
2.12	Consult nurse/carer/doctor
2.13	Consult partner/relative
2.14	Ask patient
2.2	Pregnancy test
2.21	- serum HCG
2.22	- urine
2.23	- ultrasound
2.3	Unable to determine
2.31	Don't do scan
2.32	Postpone scan
2.321	- until patient conscious
2.322	- until pregnancy test results available
2.33	Refer to NM physician
2.34	Reduce radiation dose
2.4	Never been in this situation

Q28 – Language/cultural barrier

Code	Description
3.1	Method of questioning
3.11	Interpreter/translator
3.111	- professional
3.112	- family member
3.12	Use visual aids
3.121	- Use of Multilingual signage
3.122	- Gestures/mime
3.123	- Drawings of pregnant people
3.124	- Google translate – print out
3.13	Speak slowly
3.14	Cultural barrier
3.141	- female staff to question
3.142	- explain radiation risk
3.15	Same for all females
3.16	Don't ask
3.2	Pregnancy test
3.21	- serum HCG
3.22	- urine
3.3	Unable to determine
3.31	Consult with doctor
3.32	Postpone scan if patient not understand
3.4	Determining risk
3.41	Question Re: LMP
3.42	Question Re: Contraception
3.43	Question Re: Sexual activity

Q29 – Mental disability

Code	Description
4.1	Method of questioning
4.11	Ask patient – slowly, simple language
4.12	Ask carer/relative
4.13	Ask nurse/doctor
4.14	Consult notes
4.15	Use visual aids
4.151	- poster/drawing
4.152	- gestures/mime
4.16	Same as all females
4.17	Don't ask
4.2	Determining risk
4.21	Question Re: LMP
4.22	Question Re: Contraception
4.23	Question Re: If sexually active
4.3	Pregnancy test
4.31	- serum HCG
4.32	- urine
4.4	Subjective assessment
4.41	Assume not sexually active
4.42	Assess communication/understanding
4.5	Unable to determine
4.51	Don't do scan
4.52	Postpone scan

Appendix E

DELPHI STUDY

ETHICS APPROVAL

A variation to the existing ethics application to include the Delphi study was submitted on 26th March 2013 to The University of Newcastle Human Research Ethics committee and approved on 18th April 2013.

STUDY DESIGN

A literature review of formal research methods for consensus development was completed (Chapter 2) and the Delphi technique selected for the study. The Delphi technique is a formal research method widely used to develop the consensus statements in health care. The technique utilises a panel of experts, selected based on their expertise and experience, to explore aspects of a topic whilst maintaining participant anonymity. It is a cost effective method that can be completed online allowing for participation of experts from a diverse geographical locations. The process of the Delphi involves a series of rounds of questionnaires followed by iterative feedback and analysis.

The Round 1 questionnaire was developed from the results of the nationwide survey. Panel members were asked to provide their thoughts and opinions regarding pregnancy screening strategies used for diagnostic nuclear medicine, and give a rationale for each of their comments. The questionnaire consisted of 30 questions covering a range of issues including demographic information, method of questioning, age range for questioning, and use of pregnancy testing. The Round 1 questionnaire was administered online via SurveyMonkey between 18th November 2013 and 30th January 2014.

The Round 2 questionnaire was developed from the previous round results. It consisted of 12 statements that panel members were asked to agree or disagree with and two questions were they were asked to rank responses in order of importance. The Round 2 questionnaire was administered by SurveyMonkey between 26th February and 21st March 2014.

Following Round 2, there were 10 statements that achieved consensus agreement. Round 3 was developed from the results from the previous rounds. The survey provided the participants with the ten statements which reached consensus and nine questions which they were asked to agree or disagree. A flowchart to assist in questioning patients was included and participants were asked to comment on this. The Round 3 questionnaire was administered by SurveyMonkey between 12th and 30th June 2014.

EXPERT PANEL

With an aim to recruit 10-12 participants for the expert panel, 35 nuclear medicine scientist, physicists and physician were purposively selected from members of Special Interest Group committees of the ANZSNM; the medical physicist register of the Australasian College of Physical Scientists and Engineers in Medicine; and the nuclear medicine clinical supervisors database from the School of Health Sciences at the University of Newcastle. An invitation to participate in the Delphi study as a member of the expert panel was emailed to each person with the participant information statement and a consent form. If they wished to participate they were asked to return the consent form to the researcher via email. A total of 10 people agreed to participate in the study: 8 NMS, 1 medical physicist and 1 nuclear medicine physician.

ANALYSIS

Following each survey round the results were analysed for level of agreement using descriptive statistics and open responses were manually coded using content analysis. Consensus agreement was pre-defined as 80% or greater. The results were summarised and returned to the participants with the next round survey. They were also provided with a complete set of responses to review their responses and compare to the other panel members.

ADDITIONAL ATTACHMENTS

Invitation to Participate email

Participant Information Statement

Consent form

Round 1 questionnaire

Round 1 Feedback and responses

Round 2 questionnaire

Round 3 questionnaire

Subject Heading: Invitation to participate in expert panel

Dear XXX

My name is Daphne James and I am a Lecturer from the School of Health Sciences at the University of Newcastle. I am also a PhD student studying at the University of Newcastle. My supervisors are Associate Professor Helen Warren-Forward from the School of Health Sciences and Mr Paul Cardew, Chief Physicist in Nuclear Medicine, Hunter New England Health Service.

The aim of my research is to develop best practice guidelines for determining a patient's pregnancy status prior to diagnostic nuclear medicine procedures. I conducted an interview study in 2010, and followed with a nationwide survey in 2011, investigating current practice in Australia and New Zealand. These studies revealed a wide variety of methods are being used to question patients about their pregnancy status and a lack of a consistent approach when determining which patients to question. Therefore, the next phase of the research will involve using a Delphi technique to gain expert opinion and form a consensus approach to questioning patients.

The Delphi technique is a well-recognised method of gaining consensus and it can be used to inform practice when there is a lack of evidence in the scientific literature. It has been used extensively in health areas, particularly in nursing, since the 1970's. The Delphi technique usually involves a series of iterative rounds. For each round an expert panel (approx 10 members) independently completes a questionnaire which is then analysed and the results used to inform subsequent rounds. Participants are selected based on their expertise and experience in the research area.

Due to your expertise in the research area, we would like to invite you to participate in the Delphi technique. Please find attached a participant information sheet, explaining the research and what would be required of you, and a consent form. I have also attached a copy of the published paper which describes the findings from the interview study.

If you would like to participate, please complete the attached consent form and return to Daphne James by either:

- Email - (Daphne.James@newcastle.edu.au)
- Fax - +61 2 49217053
- Mail – School of Health Sciences, Faculty of Health, University of Newcastle, Callaghan, NSW, 2308, Australia.

If you require any further information please contact me.

Kind regards

Daphne James

Associate Professor Helen Warren-Forward
School of Health Sciences
Faculty of Health
University of Newcastle
Ph: 02 49217142
Fax: 02 49217053
helen.warren-forward@newcastle.edu.au



Information Statement for the Research Project:

Guideline Development for the Verification of a Patient's Pregnancy Status prior to Diagnostic Imaging Procedures in Nuclear Medicine

You are invited to participate in the research project identified above which is being conducted by Daphne James, Lecturer from the School of Health Sciences at the University of Newcastle. The research is part of Daphne James's Doctoral studies at the University of Newcastle, supervised by Associate Professor Helen Warren-Forward from the School of Health Sciences and Mr Paul Cardew, Chief Physicist in Nuclear Medicine, Hunter New England Health Service.

Why is the research being done?

The purpose of the research is to obtain expert opinion to aid in the development of practice guidelines for determining a patient's pregnancy status prior to diagnostic Nuclear Medicine procedures.

Who can participate in the research?

Participants will be invited to participate based on their expertise in the research area.

What choice do you have?

Participation in this research is entirely your choice. Whether or not you decide to participate, your decision will not disadvantage you. You may withdraw from the research at any time and are not required to give a reason for withdrawing. However, as the responses to the SurveyMonkey questionnaires are anonymous, data cannot be withdrawn after completion of each survey round.

What would you be asked to do?

If you agree to participate, you will be an expert member in a Delphi technique of 3-5 rounds to gain consensus opinion on how to question female patients regarding their pregnancy status prior to diagnostic nuclear medicine imaging procedures. You will be asked to independently complete a series of online surveys conducted with SurveyMonkey. The data from each survey round will be analysed and used to inform the subsequent survey.

How much time will it take?

It has been estimated that each survey may take up to 30 minutes to complete.

What are the risks and benefits of participating?

There are no perceived risks or direct benefits to the participants. However, your participation will be an important step in the development of practical guidelines for the verification of pregnancy status prior to a diagnostic Nuclear Medicine procedure.

How will your privacy be protected?

All responses to the SurveyMonkey questionnaires will be anonymous. Any information collected by the researchers will be stored securely and only accessed by the researchers, except as required by law. Data will be retained for at least 5 years in a locked cabinet in the office of Associate Professor Helen Warren-Forward. All computer records will be stored on a password-protected computer. Access will be by the researchers only.

How will the information collected be used?

The results of this study will form part of a Research Higher Degree thesis for Daphne James. The results will be reported at relevant conferences and published in peer-reviewed journals. The articles will be written and submitted to journals with the participant population in mind. Individual participants will not be identified in any reports arising from the project. The information collected will be the final step in the development of practical guidelines for the verification of pregnancy status prior to a diagnostic Nuclear Medicine procedure.

What do you need to do to participate?

Please read this Information Statement and be sure you understand its contents before you consent to participate. If there is anything you do not understand, or you have questions, contact the researcher.

If you would like to participate, please complete the consent form and return to Daphne James by either:

- Email - Daphne.James@newcastle.edu.au
- Fax - +61 2 49217053
- Mail - School of Health Sciences, Faculty of Health, The University of Newcastle, Callaghan, NSW, 2308, Australia

Further information

If you would like any further information please contact Daphne James by telephone on +61 2 49215596 or by email Daphne.James@newcastle.edu.au

Thank you for considering this invitation.

Helen Warren-Forward

Paul Cardew

Daphne James

Complaints about this research

This project has been approved by the University's Human Research Ethics Committee, Approval No. H- 2009-0270.

Should you have concerns about your rights as a participant in this research, or you have a complaint about the manner in which the research is conducted, it may be given to the researcher, or, if an independent person is preferred, to the Human Research Ethics Officer, Research Office, The Chancellery, The University of Newcastle, University Drive, Callaghan NSW 2308, Australia, telephone (02) 49216333, email Human-Ethics@newcastle.edu.au.

□
Associate Professor Helen Warren-Forward
School of Health Sciences
Faculty of Health
Ph: 02 49217142
Fax: 02 49217053
helen.warren-forward@newcastle.edu.au



Consent Form for the Research Project:

Guideline Development for the Verification of a Patient's Pregnancy Status prior to Diagnostic Imaging Procedures in Nuclear Medicine

Associate Professor H Warren-Forward & Ms D James
Document Version 1; dated 19/02/2013

I agree to participate in the above research project and give my consent freely.

I understand that the project will be conducted as described in the Information Statement, a copy of which I have retained.

I understand that I can withdraw from the study at any time and do not have to give any reason for withdrawing.

I understand that my responses to the research can only be withdrawn up to the point of analysis of each survey round since the data will be used to inform subsequent rounds.

I consent to completing a series (between 3 and 5) of online questionnaires;

I understand that my personal information will remain confidential to the researchers.

I have had the opportunity to have questions answered to my satisfaction.

Print Name: _____

Signature: _____ **Date:** _____

Preferred E-mail Address: _____

Pregnancy screening in nuclear medicine - Delphi Round 1

Introduction

Thank you agreeing to participate in a Delphi research study about pregnancy screening strategies used in nuclear medicine prior to diagnostic imaging procedures.

This survey is the first in a series of rounds of questionnaires where you will be asked to give your opinions regarding issues concerning pregnancy screening.

This survey may take 30-45 minutes to complete as you will be asked to give your thoughts, opinions and provide rationales for answers.

The following rounds will be much shorter as they will consist of a series of statements which you will rank according to your agreement or disagreement.

Please read the two articles attached to the survey link email. These articles provide background information and discuss the results from a nationwide survey about pregnancy screening strategies used in Nuclear medicine.

Please limit your answers to DIAGNOSTIC nuclear medicine imaging procedures.

Demographics

*1. What is your gender?

- ☐ Male
☐ Female

*2. What is your profession?

- ☐ Nuclear medicine technologist
☐ Nuclear medicine physician
☐ Medical physicist

*3. How long have you been working in Nuclear medicine?

- ☐ < 5 years
☐ 5-10 years
☐ 10-15 years
☐ 15-20 years
☐ > 20 years

Standardised guidelines

Pregnancy screening in nuclear medicine - Delphi Round 1

***4. After reading the articles provided, do you think that a standardised guideline is needed for Australia and New Zealand to assist nuclear medicine personnel when questioning female patients about their pregnancy status prior to diagnostic nuclear medicine procedures?**

- ☐ Yes
☐ No
☐ Unsure

***5. Please provide a reason for your answer in Q4**

Pregnancy screening strategies

The questions on the following pages are designed to elicit your opinion on the most appropriate pregnancy screening strategies to use.

***6. How do you think nuclear medicine personnel should determine the pregnancy status of patients prior to diagnostic imaging?**

***7. Do you think verbal questioning of the patient is adequate and appropriate?**

- ☐ Yes
☐ No
☐ Unsure

***8. Please provide a rationale for your answer in Q7.**

Pregnancy screening in nuclear medicine - Delphi Round 1

***9. If verbal questioning is used, do you think the patient should provide their signature?**

- ☐ Yes
☐ No
☐ Unsure

***10. Please provide a reason for your answer in Q9.**

***11. Do you think the patient should complete a standardised written questionnaire?**

- ☐ Yes
☐ No
☐ Unsure

***12. Please provide a reason for your answer in Q11.**

Age to question

Radiation protection regulations state that all women of "child bearing age" should be questioned regarding their pregnancy status prior to diagnostic nuclear medicine procedures.

13. How do you define "child bearing" age?

14. How do you determine the minimum age to question?

15. How do you determine the maximum age to question?

Questioning strategies

Pregnancy screening in nuclear medicine - Delphi Round 1

*16. Do you think the routine strategy for questioning should be changed when questioning:

	Yes	No	Unsure
Young teens < 16 yrs	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Patients with cognitive impairment	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Patients with language barriers	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Patients with cultural barriers	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

*17. Select the most appropriate strategy for questioning a young teen (age < 16 years):

- ☐ Ask if she has started getting her period first and if yes, continue with routine verbal questioning
- ☐ Ask if she has started getting her period first and if yes, continue with standardised written questionnaire
- ☐ Verbal questioning asking routine questions
- ☐ Standardised written questionnaire
- ☐ Pregnancy test

Other (please specify)

*18. Select the most appropriate strategy for questioning women with cognitive impairment:

- ☐ Ask patient
- ☐ Consult with carer, medical records or other medical personnel
- ☐ Standardised written questionnaire
- ☐ Pregnancy test

Other (please specify)

*19. Select the most appropriate strategy for questioning women with a language barrier:

- ☐ Ask patient
- ☐ Ask accompanying person
- ☐ Use interpreter to ask patient
- ☐ Standardised written questionnaire
- ☐ Pregnancy test

Other (please specify)

Pregnancy screening in nuclear medicine - Delphi Round 1

***20. Select the most appropriate strategy for questioning women with a cultural barrier:**

- ☐ Use female staff member to ask patient
- ☐ Verbal questioning with routine questions
- ☐ Standardised written questionnaire
- ☐ Pregnancy test

Other (please specify)

***21. Do you think a standardised written questionnaire should include questions about:**

(please select all applicable answers)

- ☐ Last menstrual period
- ☐ Contraceptive use
- ☐ Hysterectomy
- ☐ Menopausal status

Other (please specify)

***22. Please provide a rationale for your response in Q21.**

Pregnancy testing

***23. In which circumstances should pregnancy testing be used?**

***24. Do you think urine or serum pregnancy tests should be used?**

- ☐ Urine
- ☐ Serum
- ☐ Either

***25. Please provide a reason for your answer in Q25.**

Radiation risk considerations

Pregnancy screening in nuclear medicine - Delphi Round 1

***26. Do you think the strategy used to determine pregnancy status should differ depending on the radiation risk to the foetus from the examination?**

- ☐ Yes
- ☐ No
- ☐ Unsure

***27. Select the most appropriate strategy for a low risk examination, such as a 99mTc thyroid scan.**

- ☐ Verbal question asking ONLY whether the patient thinks they might be pregnant
- ☐ Verbal question asking more details such as LMP
- ☐ Verbal question AND patient signature on referral next to written question or tick box
- ☐ Standardised written questionnaire

Other (please specify)

***28. Select the most appropriate strategy for a medium risk examination, such as a 99mTc bone scan without SPECT/CT.**

- ☐ Verbal question asking ONLY whether the patient thinks they might be pregnant
- ☐ Verbal question asking more details such as LMP
- ☐ Verbal question AND patient signature on referral next to written question or tick box
- ☐ Standardised written questionnaire

Other (please specify)

***29. Select the most appropriate strategy for a high risk examination, such as a 99mTc bone scan with SPECT/CT or a 99mTc Sestamibi scan**

- ☐ Verbal question asking ONLY whether the patient thinks they might be pregnant
- ☐ Verbal question asking more details such as LMP
- ☐ Verbal question AND patient signature on referral next to written question or tick box
- ☐ Standardised written questionnaire

Other (please specify)

Additional Comments

Pregnancy screening in nuclear medicine - Delphi Round 1**30. Please provide any additional comments for the researcher here.****Thank you**

Thank you for completing this survey.

The results will be analysed by the researchers and a second round survey will be distributed to you.

In the second round survey you be asked to provide your agreement ranking for a series of consensus statements derived from this survey.

Pregnancy Screening in Nuclear Medicine

Delphi Round 1 – Responses

Q1: What is your gender?

Male	30%
Female	70%

Q2. What is your profession?

Nuclear medicine technologist	80%
Nuclear medicine physician	10%
Nuclear medicine physicist	10%

Q3. How long have you been working in nuclear medicine?

<5 years	10%
5-10 years	20%
10-15 years	0%
15-20 years	20%
>20 years	50%

Q4. After reading the articles provided, do you think that a standardised guideline is needed for Australia and New Zealand to assist nuclear medicine personnel when questioning female patients about their pregnancy status prior to diagnostic nuclear medicine procedures?

Yes (80%)	Unsure (20%)
It seems a little hit and miss in the criteria used to determine pregnancy status	I think that a standardized guideline could lead to problems if it is not followed to the letter but it may be helpful to give an idea of the age cutoff for questioning.
I think there is too much ambiguity in some practices. A set in stone guideline is a necessity to consolidate knowledge, have an industry standard and as a basis for patients	It would be reassuring to have a standard approach to questioning as the expectation would be outlined, however there would also be a need to review this in each circumstance to determine adequacy.
Due to possible adverse medico legal ramifications.	
I would like to standardise the ages we should be asking our patients the pregnancy question	
Important to have a standard set of guidelines as there is too much discrepancy between departments and individuals regarding who and the way they ask patients of childbearing age. Also in regards to legalities, I think a standard set of protocols is needed.	
With registration of all personnel involved in the clinical procedure, guidelines will assist NM staff with addressing the issues of pregnancy in a professional manner and ensure consistency amongst patients, staff and departments. The guidelines will need to be generic and offer advice only, not mandate procedures such as plasma or urine tests	
A standardised guideline would remove the subjectivity in determining the pregnancy status of females. It lowers the risk of litigation associated with instances of radiation administration to pregnant females.	
To attempt to obtain some consistency in approach. However the guidelines will need to be sufficiently flexible to cover most scenarios.	

Q6. How do you think nuclear medicine personnel should determine the pregnancy status of patients prior to diagnostic imaging?

Verbal, followed by pregnancy test if it cannot be determined definitively
Ask them if they think there is any chance that they could be pregnant. If you are uncertain as to whether they are of child bearing age, ask them whether they get their periods or not.
A questionnaire for those patients that are eligible to handwrite. A witness (not relative) should also be present. There should also be a copy written in all languages (most common) as a means to communicate with the ethnic patients
Firstly by extensive questioning of pt, outlining menstrual cycle, sexual activity and if any ambiguity, then beta hcg blood testing.
I believe a woman should be asked directly. She should also be told the importance of this and lastly questioned as to if she is sexually active and if so why is she considered not pregnant. Some responsibility should remain with the patient.
We should have a consent form with questions and a patient signature
Identify if the patient is of childbearing age. Ask for verbal clarification if the patient is pregnant or breastfeeding. Have the patient sign a consent form to clarify this. If patient is a teenager, perhaps ask patient without an adult parent or guardian present as to not make patient uncomfortable.
We use a cutoff for pregnancy of 55years which complies with the higher age range for onset of menopause. Firstly ask when they had their LMP. Ascertain if the patient thinks that there is any chance that they could be pregnant, ensuring that you explain the reason why this question is being asked (eg. test involves an injection of radiation and that this test is usually not performed on pregnant patients without consultation between the referrer and the nuclear medicine physician. Caution must be taken when discussing radiation risk to the unborn foetus and the NM staff should only be quoting validated results from previous published data or guidelines. Use an interpreter if they are non-english speaking. If any uncertainty then perform a pregnancy test, urine or plasma based on the individual practice protocols
A verbal question (and response) and signature to declare their status. If there is doubt, then the test should be postponed until a blood test can be performed or until the patient menstruates.
It is impractical to test every patient, so testing should be limited to those cases where there is some uncertainty. Generally verbal questioning should be sufficient.

Q7. Do you think verbal questioning of the patient is adequate and appropriate?

Yes (70%)	No (30%)
Most patients are capable of answering this question honestly, but I think it needs to be explained to patient the importance of knowing pregnancy status	There needs to be written understanding and visual confirmation of the facts and the declaration. A simple my word versus yours is not sufficient
A verbal question and documentation of this should be satisfactory for diagnostic procedures.	I think the patients think more carefully when faced with signing a form to say they are not pregnant and seeing the answers to the questions
We are to a degree relying on the patients memory and honesty and can't necessarily assume they are not being truthful.	I think verbal questioning is appropriate but not adequate. I think patient should also have to sign a consent form confirming their response. I think sometimes patients can not fully take in the verbal question but when someone is made to sign something, it is a good double check. I think would also have act as a backup down the track, should a patient return and say that they were pregnant when the scan was performed, there would be physical documented evidence that the patient was asked. A lot harder to prove verbal confirmation compared to physical documentation
Please see answer 6. I believe a woman should be asked directly. She should also be told the importance of this and lastly questioned as to if she is sexually active and if so why is she considered not pregnant. Some responsibility should remain with the patient. But as long as the patient is suitably informed of the potential risks as well as the risk of being pregnant if you are sexually active. Then she can answer the questions appropriately. The risks are relatively small except with therapy. In the situation of therapy a urine pregnancy test and verbal questioning should be performed.	
For a diagnostic procedure, verbal questioning is sufficient, however I do believe that consent to proceed and having the patient sign-off to say that they are not pregnant or breastfeeding is the best option. We have a section on our request form that requires the patient to consent to proceed and acknowledge that they are not breastfeeding or pregnant, witnessed by the registrar, consultant or technologist. This will often prompt the patient to think about their response rather than just stating no	
If the technologist assesses the patient as being aware, understanding and responsive to the explanation of the test and risk to pregnancy, then the verbal question should be adequate as long as there is no doubt in the mind of the patient AND technologist	
See answer to Q6 - It is impractical to test every patient, so testing should be limited to those cases where there is some uncertainty. Generally verbal questioning should be sufficient.	

Q9. If verbal questioning is used, do you think the patient should provide their signature?

Yes (90%)	No (10%)
Legally accept the answer they give	The signature won't mean anything more than their answer to the question
As proof they have understood and stated their status	
Their signature is acknowledgement and agreement of their statement.	
To ensure they have given consent for the investigation.	
Always get the patient to sign to prevent fall back on the technologist and to prove that the patient has been questioned	
Like previous answer, as a backup to confirming their pregnancy status, also should an issue arise in the future and the patient realises at the time of the scan they were pregnant then they can't say they were not asked.	
As per previous question, this is easy to implement and provides evidence that you have asked the question before proceeding	
To provide evidence of the question being asked and acknowledged. For litigious purposes it is also necessary as proof of the question being approached.	
Provides some medico-legal protection for the NM practice. This is not fool-proof as the patient could claim that she had misinterpreted the questions.	

Q11. Do you think the patient should complete a standardised written questionnaire?

Yes (60%)	No (30%)	Unsure (10%)
Good idea!!!	It becomes too complicated and time consuming	This may help in some cases but the questions may need to be further explained by the technologist
As an industry standard. It should be implemented across the board for crosscheck and standardisation	This is time consuming and will have significant implications on workflow. From my experience, patients are honest and they will let you know if there is a chance of pregnancy	
This written questionnaire further documents hence clarifying the answers to questions regarding pregnancy and or breast feeding.	A full written questionnaire is not necessary - it forces the patient to divulge personal information that they may not be comfortable discussing on paper. Further questioning (verbal) should be sufficient to establish a yes/no response to pregnancy	
I think that is a great idea. The questions I have previously outlined could be used.		
As said before this makes the patient think very carefully about their status		
Important to have physical documentation/evidence to confirm the patients' pregnancy status.		

Q13. How do you define "child bearing" age?

Ask patient if they are menstruating yet
I ask the patient if they still get their periods or if they are a child or teen, I ask them if they are getting their periods
Women who are physically able to conceive a child
I believe from the start of menses until 6/12 after periods have finally ceased and this could be after periods have been irregular for 12/12.
>18, Between 13-18 a brief conversation away from the parents would be appropriate.
After reading the articles I am concerned that we not asking 10 year olds. We have department policy 12-50yr olds.
12 - 55 years of age
Upper limit of 55years based on the quoted upper age range for onset of menopause Lower limit not clearly defined but we generally use either 15 or 16 years as a starting point
Any female who menstruates, ie can fall pregnant
Generally 12-55 years of age.

Q14. How do you determine the minimum age to question?

If they are menstruating then ask pregnancy status
Hard one but I don't usually ask this of patients under 11
The age at where young females reach pubescent age
From time patients periods have commenced, however, this is a grey area as patient could have become pregnant just prior to onset of menses.
Menstruation.
Department protocol
It is our standard within our department, determined by our doctor and chief.
Usually 15 or 16 years and this is often based on non-measurable factors such as maturity, physical development of the patient
Young teens (or pre-teens - 11 and 12) are asked if they've begun menstruating to ascertain whether they need to declare their pregnancy status
Ask if menstruating

Q15. How do you determine the maximum age to question?

Ask if patient has gone through menopause or has had a hysterectomy
I ask the patient if they still get their periods. I will do this up to age 65.
Where a woman has started menopause
Age is not necessarily relevant but if periods have gradually ceased over prior 12/12 and absent for 6/12.
Menopause.
Department protocol
It is our standard within our department, determined by our doctor and chief.
Standard 55 years for both diagnostic and therapeutic procedures
Any female up to the age of 50. Over 50, ask if they've gone through menopause yet and determine status accordingly
Ask if past the menopause

Q16. Do you think the routine strategy for questioning should be changed when questioning:

	Yes	No	Unsure
Young teens <16 years	60%	30%	10%
Patients with cognitive impairment	60%	30%	10%
Patients with language barriers	60%	40%	0%
Patients with cultural barriers	60%	40%	0%

Q17. Select the most appropriate strategy for questioning a young teen (age < 16 years):

Answer Choices –	Responses
Ask if she has started getting her period first and if yes, continue with routine verbal questioning	70%
Ask if she has started getting her period first and if yes, continue with standardised written questionnaire	0%
Verbal questioning asking routine questions	0%
Standardised written questionnaire	20%
Pregnancy test	10%
Other	
Ask if period and then with sensitivity ask if she is sexually active and that if she is pregnant that we could not do the test. Is she using contraception with sexual activity? If no then consider a pregnancy test.	
This should be performed with the patient being away from an accompanying family member	

Q18. Select the most appropriate strategy for questioning women with cognitive impairment:

Answer Choices –	Responses
Ask patient	10%
Consult with carer, medical records or other medical personnel	90%
Standardised written questionnaire	0%
Pregnancy test	0%
Other	
Consult with carer if appropriate otherwise urine pregnancy test most likely.	
This all depends on the patient but if they are in a shared house facility then a pregnancy test may well be required	
Depending on the extent of the cognitive impairment, perhaps a combination of asking patient, written questionnaire and consultation of carer and medical records.	

Q19. Select the most appropriate strategy for questioning women with a language barrier:

Answer Choices	Responses
Ask patient	0%
Ask accompanying person	20%
Use interpreter to ask patient	70%
Standardised written questionnaire	10%
Pregnancy test	0%
Other	
Written questionnaire with an interpreter	
Interpreter if the accompanying person doesn't appear to understand	

Q20. Select the most appropriate strategy for questioning women with a cultural barrier:

Answer Choices	Responses
Use female staff member to ask patient	50%
Verbal questioning with routine questions	30%
Standardised written questionnaire	20%
Pregnancy test	0%
Other	
Standardised written questionnaire with a female staff member and phone interpreter if necessary.	
Use female staff member and using great sensitivity determine risk of pregnancy. Specific questions are likely to vary greatly. Possibly use female staff	
There will often be a language barrier as well so a female interpreter will be needed	

Q21. Do you think a standardised written questionnaire should include questions about: (please select all applicable answers)

Answer Choices	Responses
Last menstrual period	100%
Contraceptive use	70%
Hysterectomy	100%
Menopausal status	80%
<i>Other</i>	
On any IVF programme	

Q22. Please provide a rationale for your response in Q21.

These are all relevant questions to ask a patient and in some cases would definitively give the answers required
All are relevant and if you are standardizing it they need to be included
They are all important to determine whether or not the female patient can conceive
Cannot proceed to perform the study without a comprehensive history of the menstrual status.
You would need to cover all bases or directly question patient.
All of the above are crucial for the Technologist to know prior
Those 2 questions can be helpful in determining whether a pregnancy test is required if the patient is unsure. Contraceptive not totally 100%
All of the above listed factors are relevant when determining the pregnancy status of a patient. Obviously some of the questions may not be relevant to all age groups but that can be accounted for in the design of the questionnaire
Asking about contraceptive use is extremely personal and patients (especially young ones) may not be truthful if forced to write it down on record. Menopausal status may be irrelevant if asking about last menstrual period and/or hysterectomy. Unnecessary personal information for the patient to divulge - also patients may have an unclear definition of when menopause actually takes place
Questions about contraceptive use can be very unreliable as you don't know how conscientiously the patient has followed the instructions.

Q23. In which circumstances should pregnancy testing be used?

When the patient is unsure of their pregnancy status or if there is a chance the patient maybe pregnant
When a patient is unsure or if they are undergoing a therapy procedure
Before administration of a radiotracer
If patient is 10/7 into her cycle or more and does not wish to re book the study until after period has arrived.
In those that are unable to sign with confidence and inform with confidence that they are not pregnant.
Every diagnostic and therapeutic procedure
When patients within childbearing age are unsure whether they could be pregnant or not. Definitely on all patients undergoing ablative therapy.
Patient is unsure when questioned. Inability to understand the questions being asked. Performed routinely prior to all therapeutic procedures in women of childbearing age
When the scan is urgent and cannot be postponed long enough to wait for the patient to get her period.
Whenever there is an uncertainty as to the pregnancy status.

Q24. Do you think urine or serum pregnancy tests should be used?

Urine 20%	Serum 60%	Either 20%
Urine test is sufficient and it is quicker to get a result	The serum will give you a number as well as a yes or no	Serum for therapy and urine for diagnostic
Less invasive.	They are more accurate	A serum test will usually be formed in a hospital practice due to the availability of pathology services. In private practices it will often take too long to get the result from a serum test, so a urine one should suffice. (I'm not aware of the current accuracy data of urine tests)
	Serum beta HCG will give a more precise and accurate result in the first days of pregnancy.	
	Urine testing not always 100% accurate	
	Serum is more accurate in the window period (or the first 2 weeks)	
	Improper use and understanding of urine tests by the technologist can lead to false results. If a pregnancy test is required, serum is the definitive test.	

Q26. Do you think the strategy used to determine pregnancy status should differ depending on the radiation risk to the foetus from the examination?

Yes	20%
No	70%
Unsure	10 %

If Yes to Q26:

Q27. Select the most appropriate strategy for a low risk examination, such as a 99mTc thyroid scan.

Verbal question asking ONLY whether the patient thinks they might be pregnant
Verbal question AND patient signature on referral next to written question or tick box

Q28. Select the most appropriate strategy for a medium risk examination, such as a 99mTc bone scan without SPECT/CT.

Verbal question asking more details such as LMP
Verbal question AND patient signature on referral next to written question or tick box

Q29. Select the most appropriate strategy for a high risk examination, such as a 99mTc bone scan with SPECT/CT or a 99mTc Sestamibi scan

Verbal question asking more details such as LMP
Verbal question AND patient signature on referral next to written question or tick box

Q30. Please provide any additional comments for the researcher here.

I have a concern with written questions adding to the time for studies. Also, I think that we have to start putting some of the responsibility back on the patient. Yes or no- is there any chance you could be pregnant.
This is a great topic to research. It is new and touches base with all NM depts. I look forward to the publication
We cannot waiver in our standard regarding this issue however inconvenient it may appear to be. I had a situation of a 19 yr old mother with a 5/12 old bub she was currently breast feeding. Whilst happy to cease breast feeding and denying any possibility of being pregnant, as her friends had told her she could not possibly get pregnant whilst Breast feeding and not having any periods. I felt it was prudent to pursue the situation and sent her for bloods to be done. Sure enough she was pregnant. As this took place in a remote department I then organised a counsellor to come to the department and offer help and assistance to the young mum who was in total disbelief that she could be pregnant again and was petrified at what her family reaction would be.
Whatever scan there will always be some element of risk
Whenever there is exposure to ionizing radiation there is some risk involved. It shouldn't depend on the isotope used or the overall exposure to the foetus, a standard set of protocols should be used on all nuclear medicine procedures. All of the departments I have worked in have a different set of procedures for determining the patient's pregnancy status. I think a standardised set of procedures needs to be implemented.
All female patients of childbearing age undergoing a diagnostic procedure should have their pregnancy status ascertained prior to proceeding with the study
It's important to strike the balance between ascertaining pregnancy status for the female without forcing her to divulge personal information that may not be necessary. While it may assist the technologist to be certain, it may also mean the patient will view the experience in the department as being a negative one and therefore make them unlikely to return.
Re Q26. Although the risk to the foetus may be scientifically negligible, the "perceived" risk by the woman (if the patient was later found to be pregnant) would bear no relation to the actual risk, so it is better to stick to a common strategy, irrespective of the actual foetal dose.

Round 2 Delphi - Pregnancy screening in Nuclear medicine

Introduction

Thank you for completing Round 1 of the Delphi study. You have received a document containing detailed responses from Round 1 which should inform your responses in Round 2. Consensus (agreement of 80% or more) was achieved in several areas.

The Round 2 questionnaire provides summarized feedback from Round 1 for each question. You will be asked to indicate your agreement or disagreement for a series of statements.

This survey should only take 10-15 minutes to complete.

Round 2 Delphi - Pregnancy screening in Nuclear medicine

Standardised guidelines

In round 1 Q4, 80% agreed that standardised guidelines are required and 20% were unsure.

Comments included that standardised guidelines would:

- provide a more consistent approach,
- consolidate knowledge and provide an industry standard
- remove subjectivity,
- standardize age ranges,
- help lower risk of litigation,
- standardised guideline may lead to problems if not followed exactly
- need to be flexible to cover individual patient scenarios

***1. Please indicate if you agree or disagree with the following statement:**

Guidelines offering advice for pregnancy screening prior to DIAGNOSTIC nuclear medicine procedures would provide a more consistent approach.

☐ Agree

☐ Disagree

2. Please add any comments if you wish.

Round 2 Delphi - Pregnancy screening in Nuclear medicine

Questioning strategies

In Round 1 Q7, Q9 & Q11:

70% agreed that "verbal questioning is adequate and appropriate"

90% agreed that if verbal questioning is used, the patient should provide their signature.

60% agreed that patients should complete a standard written form.

Comments included that:

- verbal questioning is appropriate for diagnostic imaging as long as the patient is suitably informed of the risks
- most patients capable of answering honestly
- verbal questioning followed by the patient signing a form confirming their response makes the patient think more carefully about their response
- written documentation provides evidence that the questions have been asked and acknowledgement of patient
- written documentation provides medico-legal protection - proof of questions been asked
- standardised written form is time consuming and not necessary
- standardised written form provides documentation, clarifies questions, and makes patient think carefully about their responses.

***3. Please rank the following statements to indicate which is most appropriate approach prior to DIAGNOSTIC nuclear medicine procedures:**

☐

The procedure and any potential risks associated with it should be explained and female patients should be VERBALLY questioned regarding their pregnancy status AND required to provide their SIGNATURE to indicate the procedure and any radiation risks have been explained and indicate their pregnancy status.

☐

The procedure and any potential risks associated with it should be explained and female patients should complete and sign a WRITTEN QUESTIONNAIRE indicating the procedure and any radiation risks have been explained and answering questions regarding their pregnancy status.

4. Please add any comments if you wish.

Round 2 Delphi - Pregnancy screening in Nuclear medicine

Age to question

In Round 1 Q13,14,15:

Childbearing age definition:

- 50% defined "childbearing age" as females who are menstruating
- 50% defined "childbearing age" as an age range
- 12-55 years most common range
- other responses included 15-16 years as minimum and 50 years as maximum

Minimum age:

- 60% determined the minimum age by asking if the patient had begun menstruating
- 20% used department protocol to determine minimum age
- 20% used a specific age

Maximum age:

- 70% determined the maximum age by asking if the patient had completed menopause
- 20% used department protocol to determine maximum age
- 10 % used a specific age

***5. Please indicate if you agree or disagree with the following statements:**

Childbearing age should be defined as 12-55 years for the purposes of questioning patients about their pregnancy status prior to diagnostic nuclear medicine procedures.

☐

Agree

☐

Disagree

***6. Teenage girls aged over 12 years of age should be asked if they have begun menstruating first, and if yes then questioned about whether they could be pregnant.**

☐

Agree

☐

Disagree

***7. Women up to 55 years of age should be questioned about their pregnancy status using the standard approach.**

☐

Agree

☐

Disagree

8. Please add any comments if you wish.

Round 2 Delphi - Pregnancy screening in Nuclear medicine

Patients with Cognitive Impairment

In Round 1 Q16, 60% indicated that the pregnancy screening strategies should change for specific scenarios.

For women with cognitive impairment:

- 90% thought consultation with a carer, medical records or other medical personnel was the most appropriate strategy
- 10% thought the patient should be asked.

Comments included that, depending on the level of impairment:

- a pregnancy test may be required as well
- a combination approach may be needed - consult patient, medical records, ask carer and possibly pregnancy test.

***9. Please indicate if you agree or disagree with the following statement:**

Under normal circumstances, consultation with a carer, medical records or medical personnel should be initiated to determine the possibility of pregnancy for women with a cognitive impairment and to help decide if a pregnancy test is required.

☐ Agree

☐ Disagree

10. Please add any comments if you wish.

Round 2 Delphi - Pregnancy screening in Nuclear medicine**Women with a Language Barrier**

In Round 1 Q19, for women with a language barrier:

- 70% thought that an interpreter should be used to question the patient
- 20% thought an accompanying person should be asked, but if they don't understand then use an interpreter
- 10% thought a standard form should be used.

Comments included:

- to use an interpreter if the accompanying person doesn't understand
- use written questionnaire with an interpreter

***11. Please indicate if you agree or disagree with the following statement:**

Under normal circumstances, an interpreter should be used to question women with a language barrier about their pregnancy status.

☐ Agree

☐ Disagree

12. Please add any comments if you wish.

Round 2 Delphi – Pregnancy screening in Nuclear medicine**Women with a Cultural Barrier**

In Round 1 Q20, for women with a cultural barrier:

- 50% thought that a female staff member should question the patient
- 30% thought a standard form should be used.
- 20% thought routine questioning should be used.

Comments included:

- if possible use female staff to provide cultural sensitivity
- language barriers may also be present so use a female interpreter if needed

***13. Please indicate if you agree or disagree with the following statement:**

Under normal circumstances, a female staff member should question women with cultural barriers about their pregnancy status.

☐ Agree

☐ Disagree

14. Please add any comments if you wish.

Round 2 Delphi - Pregnancy screening in Nuclear medicine

Standard questions

In round 1 Q21:

- 100% thought standard questions should include questions about LMP
- 100% thought standard questions should include questions about hysterectomy
- 80% thought standard questions should include questions about menopausal status
- 70% thought standard questions should include questions about contraceptive use

Comments included:

- all questions are relevant and needed to make an decision
- all questions are relevant although some not to specific age ranges - can be accounted for in questionnaire design
- need comprehensive menstrual history to make decision
- LMP and hysterectomy are helpful in determining if a pregnancy test is required
- Contraceptive use is extremely personal and may responses may be unreliable
- Menopausal status is irrelevant if LMP and hysterectomy included

***15. Please rank the following statements, in order of importance for determining pregnancy status.**

Standard questions should include:

<input type="text"/>	LMP
<input type="text"/>	Hysterectomy
<input type="text"/>	Menopausal status
<input type="text"/>	Contraceptive use

***16. Standard questions should include both LMP and hysterectomy.**

- ☐ Agree
- ☐ Disagree

***17. Questions regarding menopausal status and contraceptive use are not required if both LMP and hysterectomy are included in standard questions.**

- ☐ Agree
- ☐ Disagree

18. Please add any comments if you wish.

Round 2 Delphi – Pregnancy screening in Nuclear medicine

Pregnancy testing

In Round 1 Q23 & 24,

- 60% thought pregnancy testing should be used whenever there is any uncertainty as to the pregnancy status
- 20% thought pregnancy testing should be used when a scan is medically urgent and cannot be postponed long enough to wait until her period begins
- 20% thought pregnancy testing should be used for every diagnostic and therapeutic procedure

- 60% indicated that serum pregnancy tests should be used
- 20% indicated either serum or urine tests should be used
- 20% indicated urine testing should be used

Comments regarding the type of pregnancy test included:

- serum is more accurate in early pregnancy period
- urine testing is less accurate and improper use may lead to false results
- urine test is sufficient and quicker
- serum usually more available in hospital departments
- serum for therapy and urine for diagnostic

Comments were made that pregnancy testing should be used for all therapeutic procedures however this study is only concerned with diagnostic procedures.

***19. Please indicate if you agree or disagree with the following statements:**

Pregnancy testing should be used prior to diagnostic nuclear medicine procedures whenever there is uncertainty as to the patients pregnancy status.

- ☐ Agree
- ☐ Disagree

***20. If available, serum pregnancy testing should be used in preference to urine pregnancy testing.**

- ☐ Agree
- ☐ Disagree

21. Please add any comments if you wish.

Round 2 Delphi - Pregnancy screening in Nuclear medicine

Radiation risk considerations

In Round 1 Q26:

- 70% thought that the strategy for determining pregnancy status should NOT differ depending on the radiation risk to the foetus from the examination.
- 20% thought it should differ
- 10% were unsure.

Those that indicated the strategy should differ selected verbal questioning with a signature or verbal questioning with details such as LMP.

A comment was made that although the scientific risk may be small, the "perceived risk" by a woman who later found out she was pregnant, would bear no relationship to the actual risk.

***22. Please indicate if you agree or disagree with the following statement:**

Standard verbal questioning with patient signature is required to verify pregnancy status for all diagnostic nuclear medicine procedures regardless of the potential level of radiation risk to the foetus.

☐ Agree

☐ Disagree

23. Please add any comments if you wish.

Round 2 Delphi - Pregnancy screening in Nuclear medicine

Thank you

Thank you for completing Round 2 of the Delphi study. Your time and effort is greatly appreciated.

The responses will be analysed and a final round distributed if necessary.

Round 3 Delphi - Pregnancy screening in Nuclear medicine

Introduction

Thank you for continuing to support and participate in this research. We anticipate this will be the final round of the Delphi technique.

Round 2 results have been analysed and included in the survey.

We achieved consensus (>80% agreement) for 10 statements in Round 2 (see next page). This round will concentrate on the areas that have not yet achieved consensus. You will be asked to agree or disagree with a series of statements.

This survey should take approximately 20 minutes to complete.

Thank you.

Round 3 Delphi - Pregnancy screening in Nuclear medicine

Round 2 Consensus Statements

These are the 10 statements for which consensus has been achieved:

1. Guidelines offering advice for pregnancy screening prior to DIAGNOSTIC nuclear medicine procedures would provide a more consistent approach.
2. The procedure and any potential risks associated with it should be explained and
 - female patients should be VERBALLY questioned regarding their pregnancy status AND
 - required to provide their SIGNATURE to indicate the procedure and any radiation risks have been explained and indicate their pregnancy status
3. Childbearing age should be defined as 12-55 years for the purposes of questioning patients about their pregnancy status prior to diagnostic nuclear medicine procedures.
4. Women up to 55 years of age should be questioned about their pregnancy status using the standard approach.
5. Under normal circumstances, consultation with a carer, medical records or medical personnel should be initiated to determine the possibility of pregnancy for women with a cognitive impairment and to help decide if a pregnancy test is required.
6. Under normal circumstances, an interpreter should be used to question women with a language barrier about their pregnancy status.
7. Standard questions should include last menstrual period (LMP).
8. Standard questions should include both LMP and hysterectomy.
9. Pregnancy testing should be used prior to diagnostic nuclear medicine procedures whenever there is uncertainty as to the patients pregnancy status.
10. Standard verbal questioning with patient signature is required to verify pregnancy status for all diagnostic nuclear medicine procedures regardless of the potential level of radiation risk to the foetus.

Round 3 Delphi - Pregnancy screening in Nuclear medicine

Teenage girls

Teenage girls have been identified previously as potentially difficult to question regarding pregnancy.

Child-bearing age has been defined by consensus in this study as 12-55 years.

In Round 2, 67% of participants agree that from 12 years of age teenage girls should be asked if they have begun menstruating first before asking if they might be pregnant.

There were no comments from participants for this question however one comment received regarding childbearing age was that:

"although rare, cases have been reported of children 8-12 falling pregnant, and women 60-70... Determining how to phrase the question in these groups can be tricky."

Concern surrounding the truthfulness of a response from a teen accompanied by a parent or other adult has been previously reported. A common tacit is to take the girl to another room, without the parent, to weigh her and ask the girl there. The weight can then be used for radiopharmaceutical dose calculations.

Please indicate if you agree or disagree with the following statements:

***1. If possible, when a teenage girl is accompanied by a parent or other adult, they should be taken to another room, without the parent, to be weighed for radiopharmaceutical dose calculation and questioned then.**

☐

Agree

☐

Disagree

Please comment if you wish:

***2. Teenage girls from age 12 to 17 years should be asked if they have begun menstruating and if yes, then questioned regarding pregnancy status.**

☐

Agree

☐

Disagree

Please comment if you wish:

Round 3 Delphi - Pregnancy screening in Nuclear medicine

Women with a Cultural Barrier

In Round 2, 67% of participants agreed that under normal circumstances women with cultural barriers should be questioned by a female staff member.

Comments raised concerns about the term "cultural barriers" as being "too non-specific", and that sometimes there more male staff on duty which makes this unachievable.

In their curriculum statements for multicultural health, The Royal Australian College of General Practitioners (2011) defines "culturally and linguistically diverse" as groups and individuals differ according to religion and spirituality, racial backgrounds and ethnicity as well as language. The term 'culturally and linguistically diverse background' is used to reflect intergenerational and contextual issues, not only migrant experience.

Please indicate if you agree or disagree with the following statements:

***3. The term "culturally and linguistically diverse" can be used to describe women who differ according to religion and spirituality, racial backgrounds and ethnicity as well as language.**

☐ Agree

☐ Disagree

Please comment if you wish.

***4. Whenever possible, a female staff member should question women from culturally and linguistically diverse backgrounds about their pregnancy status.**

☐ Agree

☐ Disagree

Please comment if you wish.

Round 3 Delphi - Pregnancy screening in Nuclear medicine

Standard questions

Questions often used to determine pregnancy status include:

- date of last menstrual period
- whether a hysterectomy has been performed
- use of contraception
- whether menopause is complete.

In Round 2:

- 100% ranked LMP as the most important question
- 90% agreed that LMP and hysterectomy should be included in standard questions
- 56% disagreed that menopausal status and contraceptive use are not required if both LMP and hysterectomy are included in standard questions.

Comments:

- If there has been a hysterectomy you can stop there, but LMP just doesn't cut it
- Order of questioning would vary according to the age of the patient. Menopausal status would normally be first for >50 year olds

In light of these results and comments, and previous national survey data, a set of standard questions have been developed with variations for women 12-17 and 50-55 years.

The final phase of the research will incorporate the standard questions into a best practice guide using a simple flowchart.

Please agree or disagree with the following statements:

Round 3 Delphi - Pregnancy screening in Nuclear medicine***5. The standard questioning strategy for women aged 18-49 years:**

Explain the procedure to the patient and that it uses radiation which could affect an unborn baby if she happened to be pregnant. Explain that you need to ask a series of questions before starting the procedure to determine if she might be pregnant.

All information should be recorded in the patient file. The patient and the person questioning them should sign underneath to confirm the responses.

- 1. Ask if they have had a hysterectomy. If yes, proceed with examination.**
- 2. If no, ask date of LMP.**
- 3. Ask if she is sexually active. If no, proceed with examination.**
- 4. If yes, ask "Is there is any chance you might be pregnant?"**
- 5. If yes or maybe, examination should be postponed while a pregnancy test is performed.**
- 6. If no, and LMP was less than 10 days prior, proceed with examination.**
- 7. If no, and LMP greater than 10 days prior, either:**
 - postpone examination until menstruation begins OR**
 - perform pregnancy test.**

☐ Agree

☐ Disagree

Please comment if you wish:

Round 3 Delphi - Pregnancy screening in Nuclear medicine***6. For girls aged 12-17 years:**

- 1. Ask if they have begun menstruating. If no, proceed with examination.**
- 2. If yes, continue with standard questioning.**

☐ Agree

☐ Disagree

Please comment if you wish.

***7. For women aged 50-55 years:**

- 1. Ask if they have had a hysterectomy. If yes, proceed with examination.**
- 2. If no, ask date of LMP**
- 3. If LMP is greater than 12 months prior (definition of completion of menopause), proceed with examination.**
- 4. If LMP is less than 12 months, continue with standard questioning.**

☐ Agree

☐ Disagree

Please comment if you wish.

Round 3 Delphi - Pregnancy screening in Nuclear medicine

Pregnancy testing

In Round 2:

- 100% agreed that pregnancy testing should be used whenever there is any uncertainty as to the patients pregnancy status.
- 78% agreed that "If available, serum pregnancy testing should be used in preference to urine pregnancy testing."

Comments included that:

- serum tests were more accurate but require more time and cost. May slow the work flow.
- To add "If available in a reasonable time" to the statement.

High rates of false negative results have been reported when using urine pregnancy tests prior to the date of missed menses.

Please agree or disagree with the following statements:

***8. If available in a reasonable time, serum pregnancy testing should be used in preference to urine pregnancy testing.**

☐ Agree

☐ Disagree

Please comment if you wish.

***9. If urine pregnancy testing is used PRIOR to the date of missed menses and the result is NEGATIVE:**

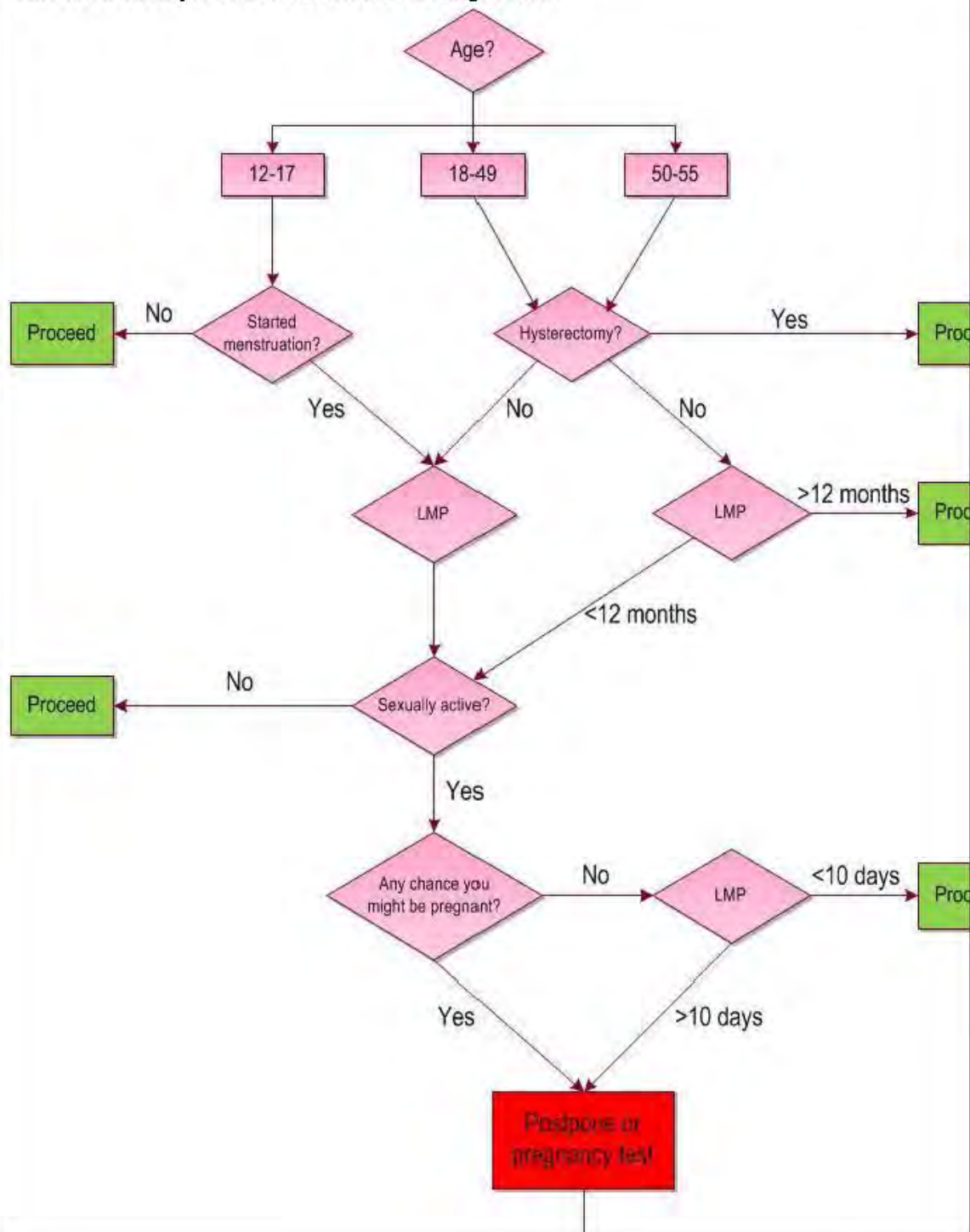
	Agree	Disagree
Postpone the examination until menstruation begins.	<input type="radio"/>	<input type="radio"/>
Retest using serum pregnancy test.	<input type="radio"/>	<input type="radio"/>

Please comment if you wish.

Round 3 Delphi - Pregnancy screening in Nuclear medicine

Flowchart

This is an example of how the flowchart might look



Round 3 Delphi - Pregnancy screening in Nuclear medicine

↓
If urine pregnancy test used
prior to date of missed
menses, postpone or retest
with serum pregnancy test

10. Please comment on the flowchart if you wish

Round 3 Delphi - Pregnancy screening in Nuclear medicine**Comments**

11. Please provide any further comments if you wish:

Round 3 Delphi – Pregnancy screening in Nuclear medicine**Thank you**

Thank you for completing this survey and contributing to the research.

Finals results will be emailed to you when available.

Appendix F

CONFERENCE PRESENTATIONS

42ND ANNUAL SCIENTIFIC MEETING OF A.N.Z.S.N.M. DARWIN 2011**Oral presentation**

Title: Determining A Patient's Pregnancy Status Prior to Diagnostic Nuclear Medicine Imaging.

James DJ, Cardew P, Warren-Forward HM.

Abstract

BACKGROUND: Ionising radiation used in diagnostic nuclear medicine procedures has the potential to cause biological effects to a foetus. Nuclear medicine scientists (NMS) have a responsibility to ensure all women of childbearing age are questioned regarding their pregnancy status before commencing any procedure to avoid unnecessary foetal irradiation. In Australia, there are no clearly defined practice guidelines to assist NMS in who to question or how to question their patients.

AIM: The aim of this study was to investigate current practice for verifying a patient's pregnancy status in Australia and NMS knowledge of policy and foetal radiation exposure.

METHODS: Semi-structured interviews were conducted with Chief NMS's and staff NMS in eight (8) nuclear medicine departments throughout Australia. Questions were based around five areas: regulations and policy, foetal radiation exposure, questioning of the patient, difficulties in determining pregnancy status, and the impact of the use of hybrid imaging. Audiotapes of the interviews were transcribed and coded using QSR NVivo8.

RESULTS: Questioning of the patient was performed via a written form in one department. Two departments used verbal questioning only whilst the majority used a combination of verbal and a signature. Only four participants (25%) routinely asked for last menstrual period dates. Routine pregnancy testing was not performed. Ninety four percent of participants were unaware of any national guidelines or policy. Fifty percent of participants said there was no specified age range to question in their department. Teenage patients were considered to be the most problematic for questioning. One participant could provide specific information on the possible biological effects of foetal irradiation.

CONCLUSION: There is a wide variation in practice between, and within, departments. Participants demonstrated a lack of knowledge and awareness of departmental and national policy and of foetal radiation exposure and its possible biological effects. This study identified a need for a consensus approach to verifying a patient's pregnancy status across the profession. Continuing education programs are also required to keep NMS knowledge up-to-date.

43RD ANNUAL SCIENTIFIC MEETING OF A.N.Z.S.N.M. MELBOURNE 2012**Poster presentation**

Title: Pregnancy Screening Prior to Diagnostic Nuclear Medicine Procedures.

James DJ, Cardew P, Warren-Forward HM

Abstract

BACKGROUND: Semi-structured interviews were conducted in eight Nuclear Medicine (NM) departments in Australia to identify the methods nuclear medicine scientists (NMS) used to question patients about their pregnancy status prior to diagnostic NM procedures. The interviews revealed that a variety of methods are used and the most common form of questioning was a verbal approach. Due to the limited number of interviews conducted, a questionnaire was developed for circulation to NM personnel in Australia and New Zealand.

AIM: To investigate whether the interview findings are representative of current practice in NM throughout Australia and New Zealand.

METHOD: A questionnaire consisting of 30 questions was administered via SurveyMonkey from October to December 2011. An invitation to participate was posted on the ANZSNM web page and emailed to all ANZSNM members. The survey consisted of 4 sections: demographics, policy and regulations, current practice, and clinical scenarios.

RESULTS: NMS made up 90.2% (302/335) of respondents. Responses were recorded from all states and territories of Australia and New Zealand. When asked if their department had a written policy 65.4% of respondents indicated “Yes” with 62.7% of these having read in it the last 6 months. Only 28% of participants were aware of government regulations. The most common minimum and maximum age to question patients was 12 years (32.4%) and 55 years (42.0%) respectively. Verbal questioning was used by 53.8% of participants. Although pregnancy tests were not routinely used, both serum and urine testing was used.

CONCLUSION: This study revealed a lack of awareness of government regulations and departmental policy regarding radiation protection, reinforcing the need for continuing education programs in this area. The study demonstrated a wide variety in current practice for determining the pregnancy status of patients prior to diagnostic NM procedures, indicating a consensus approach to pregnancy screening is required.

Pregnancy Screening Prior to Diagnostic Nuclear Medicine Procedures

D James¹, P Cardew^{1,2}, H Warren-Forward¹

1.School of Health Sciences, Faculty of Health, The University of Newcastle

2.Dept of Nuclear Medicine, John Hunter Hospital, HNEHS



INTRODUCTION: Ionising radiation has the potential to cause biological harm to a foetus. An interview study conducted in 8 nuclear medicine departments in Australia in 2010 revealed a variety of methods of questioning was used to identify pregnancy in patients prior to diagnostic NM procedures⁽¹⁾. A questionnaire was developed to investigate whether the interview findings are generalisable to current practice in Australia and New Zealand.

METHOD

- Ethics approval:
 - University of Newcastle Human Research Ethics Committee (H-2009-0270)
- Questionnaire developed with 30 items divided into 4 sections (Figure 1):
 - Section 1-3: closed responses
 - Section 4: open responses to 4 clinical scenarios (Table 1)
- Questionnaire administered online via SurveyMonkey from Oct to Dec 2011
- Link emailed to ANZSNM members (n=1115)⁽²⁾



Figure 1: Flowchart of questionnaire

RESULTS

Demographics

- 335 responses
 - Representing all states & territories of Australia, and NZ
 - 90% NM scientists
 - 66% female
 - 51% employed in private practice

RESULTS (Continued)

Policy & Regulation

- 65% had a policy, with 62% of these having read it in last 12 months
- More than 60% had NOT read relevant sections of ARPANSA 14.2 or ICRP 84

Current practice

- Most common minimum & maximum age to question:
 - 12 yrs (range 10-18 yrs)
 - 55 yrs (range 40-60 yrs)
- Method of questioning:
 - Verbal 53%
- Pregnancy testing:
 - 71% used pregnancy tests
 - 68% use serum test
 - 49% use urine test

Clinical scenarios

- The most commonly used strategies are given in Table 1:

Table 1: Clinical Scenarios and most common strategies used for presenting patient

Clinical Scenario	Pregnancy Screening Strategy
Young teenager	Separate child from parent to question
Unconscious/sedated patient	Consult notes or medical staff; serum pregnancy test
Patient with language barrier	Use interpreter & multilingual signage
Patient with mental disability	Consult carer; serum pregnancy test

DISCUSSION

- NMS are required to question all patients of child-bearing age about their pregnancy status prior to diagnostic NM procedures^(3,4).
- However, there are no guidelines outlining specific strategies for pregnancy screening in NM for diagnostic imaging.
- This study revealed that many NM personnel have not read the relevant departmental policies or government regulations.
- A wide variety of screening strategies are being used including verbal questioning, verbal plus a signature, written form, and urine and serum pregnancy testing.
- The age range used for "child-bearing age" varies from 10-60 years, indicating the need for a definition for practice.
- The screening strategies used for potentially difficult patients, as identified by James et al (2011), vary depending on the situation.
- Subjective assessments are used by staff to evaluate:
 - patient maturity,
 - parent-child relationship,
 - patient level of understanding,
 - truth of response, and
 - if they are sexually active.
- This study forms part of the PhD thesis of Daphne James

CONCLUSION: This study confirmed the findings of the interview study. It revealed a lack of awareness of government regulations and departmental policy regarding radiation protection of the potentially pregnant patient attending a diagnostic NM scan, reinforcing the need for continuing education programs in this area. The study demonstrated a wide variety in current practice for determining the pregnancy status of patients prior to diagnostic NM procedures, indicating a consensus approach to pregnancy screening is required.

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1. James D, Cardew P, Warren-Forward H. Determining the pregnancy status of patients before diagnostic nuclear medicine procedures: The Australian experience. *JNMT* 2011;39(3):220-225
2. ANZSNM Sec mrlarlet (personal communication, April 14, 2011)
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60TH ANNUAL MEETING OF S.N.M.M.I., VANCOUVER, CANADA. JUNE 2013

Poster Presentation

Title: Is a standardised practice guideline needed for pregnancy screening in diagnostic nuclear medicine?

James DJ, Cardew P, Warren-Forward HM

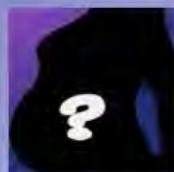
Abstract

OBJECTIVES: Although the risks to a fetus from ionising radiation are relatively small, all female patients should be questioned about their pregnancy status prior to administration of a radiopharmaceutical. However there are no guidelines detailing how to question these patients prior to diagnostic procedures in nuclear medicine. The study aimed to investigate current practice for pregnancy screening prior to diagnostic nuclear medicine procedures in Australia and New Zealand and to determine whether a standardised practice guideline is required.

METHODS: An online survey was administered from October to December 2011. All members of the Australian and New Zealand Society of Nuclear Medicine were invited to participate. The survey consisted of 30 questions divided into four sections: demographics, policy and regulations, current practice, and open-response clinical scenarios.

RESULTS: 335 responses were recorded; 90% from nuclear medicine technologists. Participants reported using various methods to question patients about their pregnancy status; verbal, verbal and a signature, and written forms. The most common minimum and maximum age to question patients was 12 years (32%) and 55 years (42%) respectively (range 10-60 years). 72% reported using serum and/or urine pregnancy tests. Clinical scenario questions revealed a variety of strategies to question potentially problematic patients such as young teenagers and those with language or cultural barriers including: separating the parent and child to gain a truthful response, and using gestures, mime and multilingual signs. Assumptions are frequently made regarding the patient's maturity, sexual history, and their ability to understand the question and its relevance.

CONCLUSION: Given the wide variation in questioning and the methods used to determine pregnancy status, a standardised practice guideline is recommended.



Is a standardised practice guideline needed for pregnancy screening in diagnostic nuclear medicine?

D James¹, P Cardew^{1,2}, H Warren-Forward¹

¹School of Health Sciences, Faculty of Health, The University of Newcastle, Australia

²Dept of Nuclear Medicine, John Hunter Hospital, HNEHS, Newcastle, Australia



OBJECTIVES

The risks to a foetus from the ionising radiation from maternal diagnostic nuclear medicine (NM) procedures are relatively small. However, all female patients should be questioned about their pregnancy status prior to administration of a radiopharmaceutical.

This study aimed to investigate current practice for pregnancy screening prior to diagnostic NM procedures in Australia and New Zealand and to determine whether a standardised practice guideline is required.

METHOD

- University of Newcastle Human Research Ethics Committee (H-2009-0270)
- Questionnaire administered online via SurveyMonkey from Oct to Dec 2011.
- Link emailed to ANZSNM members (n=1115)⁽¹⁾



Figure 1: Flowchart of questionnaire

REFERENCES

1. ANZSNM Secretariat (Personal communication April 14, 2011)
2. James D, Cardew P, Warren-Forward H. Determining the pregnancy status of patients before diagnostic nuclear medicine procedures: The Australian experience. JNM 2011;39(5):220-223
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5. Gabel, M.J. and C.R. Shipen. A split choice approach to expert consensus panels. Journal of Health Economics 2004;23:343-346

RESULTS

- 335 responses - representing all states & territories of Australia, and New Zealand
- 90% NM scientists
- 66% female

Policy & Regulation

- 65% had a departmental policy
- > 60% had NOT read relevant sections of ICRP 84 or ARPANSA 14.2

Current practice

- Pregnancy testing used by 72%

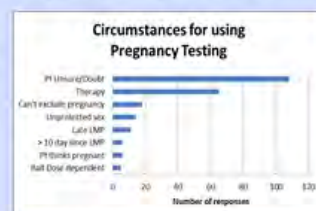


Figure 2: Circumstances for pregnancy testing

- Verbal questioning used by 44%
- Personal questions regarding LMP, contraceptive use and sexual activity were commonly asked

RESULTS

- Most common minimum age = 12 years
- Most common maximum age = 55 years

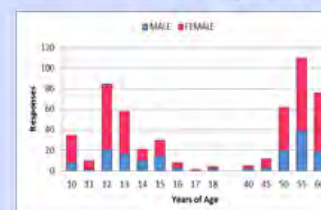


Figure 3: Min & max age questioned by participant gender

Clinical scenarios

- Participants described strategies they used for 4 patient groups identified as potentially difficult to question⁽²⁾

Table 1: Commonly used strategies

Clinical Scenario	Pregnancy Screening Strategy
Young teenager	Separate child from parent to question.
Unconscious/sedated patient	Consult notes or medical staff; serum pregnancy test
Patient with language barrier	Use interpreter & multilingual signage
Patient with mental disability	Consult carer; serum pregnancy test

DISCUSSION

- Radiation protection documents recommend all patients of child-bearing age should be questioned prior to diagnostic NM procedures^(3,4) but there are no specific guidelines on how to question the patient.

- This study revealed low awareness of relevant departmental policies or government regulations.

- A wide variety of screening strategies are being used including verbal questioning, verbal plus a signature, and written form.

- Both serum and urine pregnancy tests are used. Urine tests should be used with caution as they have a high false negative rate if used prior to the date of missed menses.

- "Child-bearing age" has not been clearly defined. Age at menarche and age at menopause varies between individuals.

- Screening strategies used for potentially difficult patients, as identified by James et al (2011)⁽²⁾, vary depending on the clinical scenario.

- Variations in practice can lead to individual patients being treated differently and subsequently not receiving the same level of care⁽⁶⁾.

CONCLUSION: The development of a standardised practice guideline for questioning patients about their pregnancy status prior to diagnostic NM procedures is recommended to ensure consistent practice and reduce the possibility of foetal irradiation.

45TH ANNUAL SCIENTIFIC MEETING OF A.N.Z.S.N.M. ADELAIDE 2014

Oral presentation

Title: Development of consensus statements for pregnancy screening in diagnostic nuclear medicine: A Delphi technique

James DJ, Warren-Forward HM.

Abstract

BACKGROUND: Consistent approaches in clinical practice are essential to ensure quality health care for all individuals. Previous studies have revealed a wide variation in the strategies used to determine pregnancy status prior to diagnostic nuclear medicine (NM) procedures in Australia and New Zealand including the method of questioning (verbal or written), age range to question, routine questions to ask, and when to use of pregnancy testing.

AIMS: To develop consensus statements for pregnancy screening prior to diagnostic NM procedures.

METHOD: An expert panel of 35 NM staff were invited to participate in a Delphi study. Three online survey rounds were conducted over 4 month period. Iterative analysis and feedback was performed between each round. Consensus was defined as >75% agreement. The first round questionnaire consisted of 30 questions designed to gain the opinions of the expert panel. Rounds 2 and 3 contained feedback and statements derived from the previous rounds and required the panel members to agree or disagree with each statement.

RESULTS: Following round 1, consensus was achieved in 6 key areas: 1) that a standardised guideline is needed; 2) when questioned verbally the patient should provide their signature; 3) standard questions should include last menstrual period and hysterectomy; 4) that the strategy used for diagnostic NM procedures should not differ based on the radiation risk; 5) that for women with cognitive impairment the carer or other medical personnel should be consulted; and 6) that serum pregnancy testing should be used if there is any uncertainty. Round 2 and 3 focused on defining the age range to question and strategies for specific scenarios.

CONCLUSIONS: Consensus statements for diagnostic NM pregnancy screening strategies will be presented. These will enable future development of clinical practice guidelines to ensure more consistent and accurate identification of pregnancy prior to diagnostic NM procedures.