Australian Government

Department of Health

Application 1467

(New and Amended

Requests for Public Funding)

(Version 0.1)

This application form is to be completed for new and amended requests for public funding (including but not limited to the Medicare Benefits Schedule (MBS)). It describes the detailed information that the Australian Government Department of Health requires in order to determine whether a proposed medical service is suitable.

Please use this template, along with the associated Application Form Guidelines to prepare your application. Please complete all questions that are applicable to the proposed service, providing relevant information only. Applications not completed in full will not be accepted.

Should you require any further assistance, departmental staff are available through the Health Technology Assessment Team (HTA Team) on the contact numbers and email below to discuss the application form, or any other component of the Medical Services Advisory Committee process.

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Fax: +61 2 6289 5540
Email: hta@health.gov.au
Website: http://www.msac.gov.au

PART 1 – APPLICANT DETAILS

1. Applicant details (primary and alternative contacts)

Corporation / partnership details *(where relevant)*: Corporation name: ABN: Business trading name:	The Royal Australian and New Zealand College of Radiologists
Primary contact name:	REDACTED
Primary contact numbers: Business: Mobile: Email:	 REDACTED REDACTED
Alternative contact name:	
Alternative contact numbers: Business: Mobile: Email:	

2. (a) Are you a lobbyist acting on behalf of an Applicant?

Yes:	
No:	N

(b) If yes, are you listed on the Register of Lobbyists?

Yes	
No:	N

PART 2 – INFORMATION ABOUT THE PROPOSED MEDICAL SERVICE

3. Application title

Obstetric MRI

4. Provide a succinct description of the medical condition relevant to the proposed service *(no more than 150 words – further information will be requested in Part 6 of the Application Form)*

1. MRI of the abdomen of a pregnant woman performed at or after 19 weeks of gestation to assess for fetal abnormalities following:
   a. Tertiary ultrasound performed by a fetal diagnostic specialist (COGU or equivalent) that has raised suspicion of such an abnormality where further characterisation, exclusion or confirmation are considered necessary by the COGU specialist to enable accurate pregnancy counselling and further management of the patient and fetus.
   b. Surgical planning for fetal or perinatal treatment of the fetus will be required due to abnormalities demonstrated by tertiary ultrasound and a specialist requires this information for patient counselling and / or treatment planning. This specialist may be a paediatric surgeon, maternal fetal medicine specialist, obstetrician, neurologist, neurosurgeon, geneticist, paediatrician, or any other specialist involved in the care of the pregnant woman and / or her fetus but will not be a radiologist.
   c. Assessment of the fetus with normal prenatal ultrasound but who is known to be at elevated risk for recurrence of a structural abnormality that is likely to be under – or non – diagnosed with ultrasound. Referral will be from a specialist (not a radiologist) who is involved in the care and counselling of the pregnant woman. Elevated risk will be most often identified as a result of a previously affected child or fetus or medical conditions in the patient, her partner or family members that increase the likelihood of a fetal abnormality that may be difficult or impossible to diagnose with prenatal ultrasound.

2. MRI of the abdomen of a pregnant woman performed at or after 19 weeks of gestation to diagnose and / or plan surgical management of placental adhesion disorder following prenatal ultrasound that has raised the suspicion of this disorder or failed to exclude it due to technical limitations of the examination.

3. MRI of the abdomen of a pregnant woman at any gestational age to elucidate the cause for acute and persistent abdominopelvic pain that has not been successfully diagnosed by ultrasound or other means and which would, under ordinary circumstances, be further investigated with CT. MR is indicated in this situation in order to avoid direct fetal exposure to the x- ray beam of the CT scanner.

5. Provide a succinct description of the proposed medical service *(no more than 150 words – further information will be requested in Part 6 of the Application Form)*

Targeted MRI to detected abnormality and further assess developmental abnormalities and find associated anomalies.

6. (a) Is this a request for MBS funding?

Yes:	X
No:	

(b) If yes, is the medical service(s) proposed to be covered under an existing MBS item number(s) or is a new MBS item(s) being sought altogether?

Amendment to existing MBS item(s):	
New MBS item(s):	X

(c) If an amendment to an existing item(s) is being sought, please list the relevant MBS item number(s) that are to be amended to include the proposed medical service:

(d) If an amendment to an existing item(s) is being sought, what is the nature of the amendment(s)?

i.	An amendment to the way the service is clinically delivered under the existing item(s)	
ii.	An amendment to the patient population under the existing item(s)	
iii.	An amendment to the schedule fee of the existing item(s)	
iv.	An amendment to the time and complexity of an existing item(s)	
v.	Access to an existing item(s) by a different health practitioner group	
vi.	Minor amendments to the item descriptor that does not affect how the service is delivered	
vii.	An amendment to an existing specific single consultation item	
viii.	An amendment to an existing global consultation item(s)	
ix.	Other (please describe below)	

(e) If a new item(s) is being requested, what is the nature of the change to the MBS being sought?

i.	A new item which also seeks to allow access to the MBS for a specific health practitioner group	
ii.	A new item that is proposing a way of clinically delivering a service that is new to the MBS (in terms of new technology and / or population)	X
iii.	A new item for a specific single consultation item	
iv.	A new item for a global consultation item(s)	

(f) Is the proposed service seeking public funding other than the MBS?

Yes:	
No:	X

(g) If yes, please advise:

7. What is the type of service:

Therapeutic medical service	
Investigative medical service	X
Single consultation medical service	
Global consultation medical service	
Allied health service	
Co-dependent technology	
Hybrid health technology	

8. For investigative services, advise the specific purpose of performing the service *(which could be one or more of the following)*:

i	To be used as a screening tool in asymptomatic populations	X
ii.	Assists in establishing a diagnosis in symptomatic patients	X
iii.	Provides information about prognosis	X
iv.	Identifies a patient as suitable for therapy by predicting a variation in the effect of the therapy	X
v.	Monitors a patient over time to assess treatment response and guide subsequent treatment decisions	X

9. Does your service rely on another medical product to achieve or to enhance its intended effect?

Pharmaceutical / Biological	
Prosthesis or device	
No	X

10. (a) If the proposed service has a pharmaceutical component to it, is it already covered under an existing Pharmaceutical Benefits Scheme (PBS) listing?

Yes	
No	

(b) If yes, please list the relevant PBS item code(s)?

(c) If no, is an application (submission) in the process of being considered by the Pharmaceutical Benefits Advisory Committee (PBAC)?

Yes (please provide PBAC submission item number below)	
No	

(d) If you are seeking both MBS and PBS listing, what is the trade name and generic name of the pharmaceutical?

Trade name	
Generic name	

11. (a) If the proposed service is dependent on the use of a prosthesis, is it already included on the Prostheses List?

Yes	
No	

(b) If yes, please provide the following information (where relevant):

Billing code(s)	
Trade name of prostheses	
Clinical name of prostheses	
Other device components delivered as part of the service	

(c) If no, is an application in the process of being considered by a Clinical Advisory Group or the Prostheses List Advisory Committee (PLAC)?

Yes	
No	

(d) Are there any other sponsor(s) and / or manufacturer(s) that have a similar prosthesis or device component in the Australian market place which this application is relevant to?

Yes	
No	

(e) If yes, please provide the name(s) of the sponsor(s) and / or manufacturer(s).

12. Please identify any single and / or multi-use consumables delivered as part of the service?

Single use consumables	
Multi-use consumables	

PART 3 – INFORMATION ABOUT REGULATORY REQUIREMENTS

13. (a) If the proposed medical service involves the use of a medical device, in-vitro diagnostic test, pharmaceutical product, radioactive tracer or any other type of therapeutic good, please provide the following details:

Type of therapeutic good	MRI Scanner.
Manufacturer's name	GE, Siemens, Philips (this list is not exhaustive and other MRI units are available and listed in the TGA register).
Sponsor's name	GE Healthcare Australia Pty Ltd, Siemens Healthcare Pty Ltd, Philips Electronics Australia Ltd.

(b) Is the medical device classified by the TGA as either a Class III or Active Implantable Medical Device (AIMD) against the TGA regulatory scheme for devices?

Class III	
AIMD	
N/A	X

14. (a) Is the therapeutic good to be used in the service exempt from the regulatory requirements of the *Therapeutic Goods Act 1989*?

Yes		If yes, please provide supporting documentation as an attachment to this application form
No		

(b) If no, has it been listed or registered or included in the Australian Register of Therapeutic Goods (ARTG) by the Therapeutic Goods Administration (TGA)?

Yes (please provide details below)	X
No	

ARTG listing, registration or inclusion number:	99713, 98485, 98887.
TGA approved indication(s), if applicable:	
TGA approved purpose(s), if applicable:	Digital Imaging and diagnosis of patients

15. If the therapeutic good has not been listed, registered or included in the ARTG, is the therapeutic good in the process of being considered for inclusion by the TGA?

Yes (please provide details below)	
No	

Date of submission to TGA	
Estimated date by which TGA approval can be expected	
TGA Application ID	
TGA approved indication(s), if applicable	
TGA approved purpose(s), if applicable	

16. If the therapeutic good is not in the process of being considered for listing, registration or inclusion by the TGA, is an application to the TGA being prepared?

Yes (please provide details below)	
No	

Estimated date of submission to TGA	
Proposed indication(s), if applicable	
Proposed purpose(s), if applicable	

PART 4 – SUMMARY OF EVIDENCE

17. Provide an overview of all key journal articles or research published in the public domain related to the proposed service that is for your application (limiting these to the English language only). ***Please do not attach full text articles, this is just intended to be a summary.***

1. Obstetric MRI for fetal abnormalities

Please note that the references cited below are intended to be an overview and not exhaustive literature review on the topic of comparative effectiveness of MRI and ultrasound for fetal diagnosis. There are many more comparative studies of the added value of MRI for specific fetal conditions as listed for point 27 where we have listed several common indications for fetal MRI as it is currently used in clinical practice in Australia.

Please note in particular the report of the Victorian Clinical Practice and Technology Committee who provided 3 years of funding to enable trialling of fetal MRI in the public sector in Victoria. This provides valuable locally contextualised and contemporary evidence regarding the effect of institution of such funding. One of the intents of the Victorian Fetal MRI program was to evaluate "real world" implementation of this new application of existing technology in order to inform an MSAC submission at a later date.

	Type of study design*	**Title of journal article or research project (including any trial identifier or study lead if relevant)**	**Short description of research (max 50 words)****	**Website link to journal article or research (if available)**	**Date of publication *****
1.		An assessment of the role of fetal MRI within the Victorian public health sector	This report provides a review of the published evidence in relation to the diagnostic accuracy of fetal MRI and also provides analysis and interpretation of the clinical and cost effectiveness of fetal MRI based on data collected in the Victorian Public sector. This report is provided to inform departmental consideration of ongoing policy and funding regarding the use of fetal MRI.	See Appendix A	May 2010

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
2.	Study of diagnostic accuracy	Comparative study of ultrasonography and magnetic resonance imagining in midline structures of fetal brain	32 fetuses tested with both US and MIR. The diagnostic accuracy rate of MRI compared to US was significantly higher, 100% and 93.8% respectively, and MRI modified 4/32 cases of US findings.	http://www.ncbi.nlm.nih.gov/pubmed/23230747	Sep 2012
3.	Study of diagnostic accuracy	Usefulness of additional fetal magnetic resonance imaging in the prenatal diagnosis of congenital abnormalities	81 cases to compare the value of fetal magnetic resonance imaging with detailed ultrasound in the prenatal diagnosis of congenital abnormalities; found Fetal MRI was not superior to ultrasound examination.	http://www.ncbi.nlm.nih.gov/pubmed/22875047	Dec 2012
4.	Study of diagnostic accuracy	The use of in utero MR imaging to delineate developmental brain abnormalities in multifetal pregnancies	Compared effectiveness of iuMR in singleton pregnancies to multifetal pregnancies, with fifty women with multifetal pregnancies carrying at least 1 fetus with a suspected developmental fetal CNS abnormality on sonography. Concluded that iuMR has similar rate of discrepancy to sonography in multifetal pregnancies compared to published data on singleton pregnancies.	http://www.ncbi.nlm.nih.gov/pubmed/?term=The+use+of+in+utero+MR+imaging+to+delineate+developmental+brain+abnormalities+in+multifetal+pregnancies	Feb 2012

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
5.	Study of diagnostic accuracy	Fetal MRI as a complement to US in the evaluation of cleft lip and palate	Investigated the role of fetal MRI as a complement to US and concluded that MRI is able to more accurately define degree of involvement of posterior palate and lateral extent of cleft compared to US. MRI also enables early detection of potential syndromic conditions. Study involved 24 pregnant women and 27 fetuses at a 23.7 mean gestational age.	http://www.ncbi.nlm.nih.gov/pubmed/21509548	Oct 2011
6.	Study of diagnostic accuracy	Second trimester fetal magnetic resonance imaging improves diagnosis of non-central nervous system anomalies	63 women with raised suspicion of fetal anomalies based on second trimester ultrasound compared to MRI findings. Concluded fetal MRI of non-CNS anomalies is valuable in adjunct to US diagnosis.	http://www.ncbi.nlm.nih.gov/pubmed/?term=second+trimester+fetal+magnetic+resonance+imaging+improves	Apr 2011
7.	Study of diagnostic accuracy	3D and 4D sonography and magnetic resonance in the assessment of normal and abnormal CNS development: alternative or complementary	Once CNS abnormality is suspected, use different technologies based on each abnormal CNS case. Magnetic resonance allows for viewing of the whole intracranial cavity, brainstem and cortical gyral/sulcal development. Neuro-sonography is best in detecting intracranial calcification, vascular abnormalities, intratumoral vascularity and bone dysplasia.	http://www.ncbi.nlm.nih.gov/pubmed/?term=3D+and+4D+sonography+and+magnetic+resonance+in+the+assessment+of+normal+and+abnormal+CNS	Jan 2011

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
8.	Study of diagnostic accuracy	Magnetic resonance imaging versus ultrasonography for the in utero evaluation of central nervous system anomalies	26 fetuses included in the study, ranging in gestational age of 17-25 weeks. Found fetal MRI is more sensitive in detecting CNS abnormalities but its abilitiy to provide correct diagnoses is only marginally superior to fetal ultrasonography.	http://www.ncbi.nlm.nih.gov/pubmed/20887106	Oct 2010
9.	Study of diagnostic accuracy	Role of fetal MRI in the diagnosis of cerebral ventriculomegaly assessed by ultrasonography	Studied 55 pregnant women via fetal MRI. Findings showed that MRI and US are substantially in agreement in defining the degree of VM and disagreement originated from possible progression of dilation between the two examinations. Fetal MRI is important as adjunctive measures to sonography in evaluation of cerebral ventriculomegaly.	http://www.ncbi.nlm.nih.gov/pubmed/?term=role+of+fetal+MRI+in+the+diagnosis+of+cerebral+ventriculomegaly+assessed+by+ultrasonography	Oct 2009
10	Study of diagnostic accuracy	Ultrasound versus MRI in the diagnosis of fetal head and trunk anomalies	40 pregnant women with fetal anomalies on US underwent MRI. More number of confident diagnoses obtained via MRI than with US in evaluation of fetal CNS and thoracic anomalies. MRI is an important supplementary tool for US in complex fetal anomalies.	http://www.ncbi.nlm.nih.gov/pubmed/19085633	Feb 2009

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
11	Study of diagnostic accuracy	What does magnetic resonance imaging add to the prenatal sonographic diagnosis of ventriculomegaly?	26 fetuses ranging in gestational age from 17-37 weeks with sonographically detected VM showed MRI adds important additional information compared to only sonography.	http://www.ncbi.nlm.nih.gov/pubmed/17957045	Nov 2007
12	Study of diagnostic accuracy	Comparison of prenatal and postnatal MRI findings in the evaluation of intrauterine CNS anomalies requiring postnatal neurosurgical treatment	13 fetal MRI scans perfomed in mothers that were suspected to have fetuses with congenital CNS defects requiring surgery after birth. Found fetal MRI scanning is effective, noninvase method of assessing in-utero CNS abnormalities with great diagnostic accuracy.	http://www.ncbi.nlm.nih.gov/pubmed/17710413	Feb 2008
13	Study of diagnostic accuracy	Fetal central nervous system anomalies: comparison of magnetic resonance imaging and ultrasonography for diagnosis	34 women with complicated pregnancies examined with MRI within 24 hours post-ultrasonography. MRI has advantages to US in detecting fetal CNS anomalies.	http://www.ncbi.nlm.nih.gov/pubmed/16919186	Aug 2006
14	Study of diagnostic accuracy	Comparative ultrasound and magnetic resonance diagnosis of fetal CNS malformations	144 fetuses with suspected CNS and facial malformations examined by a combination of US and MRI. The MRI changed the diagnosis in 33% of the cases. Using both US and MRI enhances the efficiency of diagnosis of congenital CNS and facial malformations in fetuses.	http://www.ncbi.nlm.nih.gov/pubmed/15587883	May-Jun 2004

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
15	Study of diagnostic accuracy	Potentialities of magnetic resonance imaging in the complex of prenatal radiation diagnosis of fetal malformations	Examined 28 female patients with suspected fetal malformations. Found use of MRI in the complex prenatal radiation diagnosis allows for clearer visualisation and more adequate prediction of pregnancy outcomes and management.	http://www.ncbi.nlm.nih.gov/pubmed/15462048	Jan-Feb 2004
16	Study of diagnostic accuracy	Magnetic resonance imaging and ultrasound in the assessment of the fetal central nervous system	MRI techniques appear to be safer due to the lack of radiation. MRI offers improved soft tissue contrast and can extend the sonographic diagnosis of CNS anomalies.	http://www.ncbi.nlm.nih.gov/pubmed/14711101	2003
17	Observational study	Diagnosis, outcome, and management of fetal abnormalities: fetal hydrocephalus	Morphological fetal CNS findings detected during early gestational age are not always the final features present after birth.	http://www.ncbi.nlm.nih.gov/pubmed/12920541	Aug 2003
18	Study of diagnostic accuracy	Prenatal screening: invasive diagnostic approaches	Invasive procedures carry risks of miscarriage and premature delivery. Invasive procedures are helpful in establishing diagnosis, etiology and prognosis when US and MRI show CNS anomaly.	http://www.ncbi.nlm.nih.gov/pubmed/12908114	Aug 2003
19	Study of diagnostic accuracy	Screening of fetal CNS anomalies by MR imaging	MR imaging has several superiorities including lack of radiation, freedom in selecting an imaging plane, production of standardized and easily reproducible images, great tissue contrast, no scanning dead space and no limit to penetration depth.	http://www.ncbi.nlm.nih.gov/pubmed/12820001	Aug 2003

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
20	Study of diagnostic accuracy	The diagnostic role of "in utero" magnetic resonance imaging	92 patients with US detection of abnormalities included and was scanned with fetal MRI techniques. Satisfactory imaging obtained in all but one case. MRI was no better than US for abnormalities of fetal contour and for large and complex distortion of CNS as holoprosencephaly. Subtle midbrain anomalies, neuronal migration disorders and for other anomalies, MRI was superior to US. MRI is a good adjunct to US for prenatal diagnosis for certain fetal anomalies.	http://www.ncbi.nlm.nih.gov/pubmed/10560083	1999
21	Study of diagnostic accuracy	Magnetic resonance imaging supplements ultrasonographic imaging of the posterior fossa, pharynx and neck in malformed foetuses	Study compares antepartum US and MRI in diagnosis and exclusion of malformations of fetal neck, pharynx, skull base and posterior fossa in late pregnancy using 26 women and 27 fetuses with suspected abnormalities. MRI proved to be a valuable supplement to US.	http://www.ncbi.nlm.nih.gov/pubmed/10380297	May 1999

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
22	Observational study	Cortical maturation in normal and abnormal fetuses as assessed with prenatal MR imaging	MR images of the brain in 53 normal and 40 abronal fetuses between 14-28 weeks gestational age were compared to gestational age guidelines from neuroanatomic studies. MR imaging of normal fetal cortical maturation follows predictable course slightly delayed to the descriptions in neuroanatomic specimens.	http://www.ncbi.nlm.nih.gov/pubmed/10207478	Mar 1999
23	Study of diagnostic accuracy	Evaluation of real-time single-shot fast spin-echo MRI for visualization of the fetal midline corpus callosum and secondary palate	Analysed 69 fetal MRI studies. Concluded RT SSFSE technique can aid in obtaining images in planes that are critical to evaluatiojn of moving fetus and may lead to improved diagnosis of CNS or orofacial abnormalities in fetuses.	http://www.ncbi.nlm.nih.gov/pubmed/17114544	Dec 2006

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
24	Study of diagnostic accuracy	Dynamic motion analysis of fetuses with central nervous system disorders by cine magnetic resonance imaging using fast imaging employing steady-state acquisition and parallel imaging: a preliminary result	25 fetuses with anomalies studied and imaging findings compared in fetuses with major CNS anomalies in five cases and minor CNS, non-CNS or no anomalies in twenty cases. Concluded that cine MR imaging illustrates fetal motion in utero with high clinical reliability, provides information on extremity motility in fetuses and serves as a good prognostic indicator of postnatal outcome and provides 4D information for making proper and timely obstetrical and postnatal management decisions.	http://www.ncbi.nlm.nih.gov/pubmed/16922069	Aug 2006
25	Study of diagnostic accuracy	Magnetic resonance signal intensity measurements in the diagnosis of fetal central nervous system anomalies	MR images of 110 fetal brains between 18-38 weeks gestational age studied. Found signal intensity measurements are useful to differentiate physiological and non-progressive ventriculomegaly from hydrocephalus and ACM-2.	http://www.ncbi.nlm.nih.gov/pubmed/21827341	Jun 2012

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
26	Study of diagnostic accuracy	The clinical impact of fetal magnetic resonance imaging on management of CNS anomalies in the second trimester of pregnancy	Evaluated the additional information given by MRI from 29 pregnant women in whom second trimester ultrasound identified or suspected fetal CNS anomalies. Fetal MRI in the second trimest may be clinically valuable as an adjunct to US for evaluation of CNS anomalies especially in cases of inconclusivity of US due to maternal obesity.	http://www.ncbi.nlm.nih.gov/pubmed/21080900	Dec 2010
27	Study of diagnostic accuracy	Prenatal ultrasound and fetal MRI: the comparative value of each modality in prenatal diagnosis	MRI has advantages in demonstrating pathology of brain, lungs, complex syndromes and conditions associated with reduction of amniotic fluid.	http://www.ncbi.nlm.nih.gov/pubmed/18790583	Nov 2008
28	Study of diagnostic accuracy	Additional value of fetal magnetic resonance imaging in the prenatal diagnosis of central nervous system anomalies: a systematic review of the literature	Identified 13 articles which included 710 fetuses that had both US and MRI results. MRI confirmed US-positive findings in 65.4% of fetsues, provided additional information in 22.1%, MRI disclosed CNS anomalies in 18.4% of fetuses. In 2% of cases US was more accurate. In 3-%, MRI was so different than US that clinical management changed. Concluded that MRI supplements information provided by US and should be considered in selected fetuses with US-detected CNS anomalies.	http://www.ncbi.nlm.nih.gov/pubmed/24890732	Oct 2014

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
29	Study of diagnostic accuracy	Outcomes Associated With Isolated Agenesis of the Corpus Callosum: A Meta-analysis	Objective is to ascertain the outcome in fetuses with isolated complete ACC and partial ACC.	http://pediatrics.aappublications.org/content/early/2016/08/29/peds.2016-0445	Aug 2016
30	Study of diagnostic accuracy	National Horizon Scanning Unit Horizon scanning prioritising summary	Microvolt T-wave alternans for the determination of patients likely to benefit from ICD therapy	http://www.horizonscanning.gov.au/internet/horizon/publishing.nsf/Content/6B81AEB3E7EE0001CA2575AD0080F344/$File/Volume15_2.pdf	Feb 2007
31	Study of diagnostic accuracy	Numerical study of RF exposure and the resulting temperature rise in the foetus during a magnetic resonance procedure	Numerical simulations of specific absorption rate (SAR) and temperature changes in a 26-week pregnant woman model within typical birdcage body coils as used in 1.5 T and 3 T MRI scanners are described in this review.	https://www.ncbi.nlm.nih.gov/pubmed/20090188	Feb 2010
32	Study of diagnostic accuracy	Prevalence of prenatal brain abnormalities in fetuses with congenital heart disease: a systematic review	The primary aim of this study was to perform a systematic review to quantify the prevalence of prenatal brain abnormalities in fetuses with CHDs	https://www.ncbi.nlm.nih.gov/pubmed/27062519	Sep 2016
33	Study of diagnostic accuracy	Letter From the Editor: Fetal Magnetic Resonance Imaging	A letter from the editor supporting the use of MRI for the detection and assessment of abnormalities.	https://www.ncbi.nlm.nih.gov/pubmed/26614128	Dec 2015

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
34	Study of diagnostic accuracy	Association Between MRI Exposure During Pregnancy and Fetal and Childhood Outcomes	To evaluate the long-term safety after exposure to MRI in the first trimester of pregnancy or to gadolinium at any time during pregnancy.	https://www.ncbi.nlm.nih.gov/pubmed/27599330	Sep 2016
35	Study of diagnostic accuracy	Airway compromise in the fetus and neonate: Prenatal assessment and perinatal management	Identifies benefit of the use of fetal MRI in airway obstruction.	https://www.ncbi.nlm.nih.gov/pubmed/27084444	Aug 2016
36	Study of diagnostic accuracy	Perinatal and long-term outcome in fetuses diagnosed with isolated unilateral ventriculomegaly: systematic review and meta-analysis	The aim of this study was to undertake a systematic review and meta-analysis to quantify the perinatal and long-term outcome of fetuses diagnosed with isolated unilateral ventriculomegaly during the second- or third- trimester of pregnancy	https://www.ncbi.nlm.nih.gov/pubmed/27091707	Apr 2016
37	Study of diagnostic accuracy	The use of magnetic resonance imaging in the obstetric patient	To review the biological effects and safety of magnetic resonance imaging (MRI) in the obstetric patient and to review procedural issues, indications, and contraindications for obstetrical MRI	https://www.ncbi.nlm.nih.gov/pubmed/24798674	Apr 2014

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
38	Study of diagnostic accuracy	Evaluations of Specific Absorption Rate and Temperature Increase Within Pregnant Female Models in Magnetic Resonance Imaging Birdcage Coils	Paper presents a detailed numerical study of specific absorption rate (SAR) and temperature increase calculations within pregnant female models exposed to magnetic resonance imaging (MRI)	http://www.mrisafetymodeling.com/pub/P2_IEEE-TMTT_2006.pdf	Dec 2006
39	Study of diagnostic accuracy	Prenatally diagnosed fetal tumors of the head and neck: a systematic review with antenatal and postnatal outcomes over the past 20 years	The aim of this study was to review prenatally diagnosed tumors of the head and neck in the fetus and to report antenatal and postnatal outcomes.	https://www.ncbi.nlm.nih.gov/pubmed/27508950	Aug 2016
40	Study of diagnostic accuracy	Prognostic usefulness of derived T2-weighted fetal magnetic resonance imaging measurements in congenital diaphragmatic hernia	To determine the usefulness of various parameters based on T2-weighted fetal magnetic resonance (MR) imaging measurements of the uninvolved lung for the neonatal prognosis of congenital diaphragmatic hernia (CDH).	https://www.ncbi.nlm.nih.gov/pubmed/25011437	May 2015
41	Study of diagnostic accuracy	Comparison of ultrasound and magnetic resonance imaging parameters in predicting survival in isolated left-sided congenital diaphragmatic hernia	To compare test characteristics of ultrasound- and magnetic resonance imaging (MRI)-derived parameters in predicting newborn survival in cases of isolated left-sided congenital diaphragmatic hernia (CDH)	https://www.ncbi.nlm.nih.gov/pubmed/24307080	Jun 2014

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
42	Study of diagnostic accuracy	Fetal lung volume and quantification of liver herniation by magnetic resonance imaging in isolated congenital diaphragmatic hernia	To determine associations between fetal lung and liver herniation volumes measured by magnetic resonance imaging (MRI) and mortality/need for extracorporeal membrane oxygenation (ECMO) in cases of isolated congenital diaphragmatic hernia (CDH)	https://www.ncbi.nlm.nih.gov/pubmed/24127326	Jun 2014
43	Study of diagnostic accuracy	The use of magnetic resonance imaging in the obstetric patient	To review the biological effects and safety of magnetic resonance imaging (MRI) in the obstetric patient and to review procedural issues, indications, and contraindications for obstetrical MRI	https://www.ncbi.nlm.nih.gov/pubmed/24798674	Apr 2014
44	Study of diagnostic accuracy	Fetal magnetic resonance imaging: jumping from 1.5 to 3 tesla (preliminary experience)	This paper presents the preliminary experience of evaluating the developing fetus at 3 T and discusses several artifacts encountered and techniques to decrease them, as well as safety concerns associated with scanning the fetus at higher magnetic strength.	https://www.ncbi.nlm.nih.gov/pubmed/24671739	Apr 2014
45	Study of diagnostic accuracy	Techniques, terminology, and indications for MRI in pregnancy	In this article, the authors provide a brief overview of the physical principles involved in fetal MRI imaging, the sequences that are used in clinical practice today, current indications, and limitations	https://www.ncbi.nlm.nih.gov/pubmed/24176156	Oct 2013

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
46	Study of diagnostic accuracy	Benefits and risks of MRI in pregnancy	This review discusses the benefits ad potential risks of fetal MRI.	https://www.ncbi.nlm.nih.gov/pubmed/24176150	Oct 2013
47	Study of diagnostic accuracy	Prenatal diagnosis of spinal dysraphism		https://www.ncbi.nlm.nih.gov/pubmed/24013324	Sep2013
48	Study of diagnostic accuracy	MRI: is there a role in obstetrics?	Outlines the findings supporting MRI in its ability to provide additional information that cannot be obtained by US and is invaluable in central nervous system anomaly evaluation, airway management, and planning for postnatal intervention.	https://www.ncbi.nlm.nih.gov/pubmed/22343250	Mar 2012
49	Study of diagnostic accuracy	Prenatal detection of pulmonary hypoplasia in fetuses with congenital diaphragmatic hernia: a systematic review and meta-analysis of diagnostic studies	To determine the value of prenatal imaging parameters for predicting lethal pulmonary hypoplasia in fetuses with CDH.	https://www.ncbi.nlm.nih.gov/pubmed/20085507	Jul 2010
50	Study of diagnostic accuracy	ACR–SPR PRACTICE PARAMETER FOR THE SAFE AND OPTIMAL PERFORMANCE OF FETAL MAGNETIC RESONANCE IMAGING (MRI)	This practice parameter addresses the use of MRI in fetal diagnosis.	http://www.acr.org/~/media/CB384A65345F402083639E6756CE513F.pdf	2015

2. Obstetric MRI at or after 28 weeks' gestation for diagnosis of and surgical planning for suspected placental adhesion disorders (placenta accrete, increta, or percreta) following incomplete, inconclusive or non diagnostic uterine and pelvic ultrasound, especially in the setting of a placenta located on the posterior uterine wall.

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
1.	Study of diagnostic accuracy	MRI Significantly Improves Disease Staging to Direct Surgical Planning for Abnormal Invasive Placentation: A Single Centre Experience	To describe the role of ultrasound and MRI in defining the extent of disease and guiding perioperative and surgical management of abnormal invasive placentation (AIP). Cohort study with gold standard.	http://www.jogc.com/article/S1701-2163(16)00046-3/abstract	Mar 2016
2.	Study of diagnostic accuracy	Invasive placental disorders: a prospective US and MRI comparative analysis.	To compare the role of various imaging modalities used in current practice for evaluation of invasive placental disorders, and evaluate the validity of certain imaging signs for prediction of invasive placenta. Cohort study with gold standard.	https://www.ncbi.nlm.nih.gov/pubmed/26993291	Mar 2016
3.	Study of diagnostic accuracy	Evaluation of interobserver variability and diagnostic performance of developed MRI-based radiological scoring system for invasive placenta previa	To evaluate the interobserver variability and diagnostic performance of a developed magnetic resonance imaging (MRI)-based scoring system for invasive placenta previa. Cohort study with gold standard.	https://www.ncbi.nlm.nih.gov/pubmed/26898236	Sep 2016
4.	Study of diagnostic accuracy	Utility of ultrasound and magnetic resonance imaging in prenatal diagnosis of placenta accreta: A prospective	To summarize our experience in the antenatal diagnosis of placenta accreta on imaging in a tertiary care setup. To compare the accuracy of ultrasound (USG) with color Doppler (CDUS)	https://www.ncbi.nlm.nih.gov/pubmed/26752827	Oct 2015

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
		study.	and magnetic resonance imaging (MRI) in prenatal diagnosis of placenta accrete.		
5.	Study of diagnostic accuracy	[Accuracy of placenta accreta prenatal diagnosis by ultrasound and MRI in a high-risk population]	Main objective was to compare accuracy of ultrasonography and MRI for antenatal diagnosis of placenta accreta. Secondary objectives were to specify the most common sonographic and RMI signs associated with diagnosis of placenta accreta.	https://www.ncbi.nlm.nih.gov/pubmed/26321608	Aug 2015
6.	Study of diagnostic accuracy	Morbidly Adherent Placenta: Ultrasound Assessment and Supplemental Role of Magnetic Resonance Imaging	Review article discusses the ultrasound image findings in placenta accreta, its limitations and pitfalls, and the supplemental role of magnetic resonance imaging in the imaging evaluation of placenta accreta	https://www.ncbi.nlm.nih.gov/pubmed/26296483	Aug 2015
7.	Study of diagnostic accuracy	When Timing Is Everything: Are Placental MRI Examinations Performed Before 24 Weeks' Gestational Age Reliable?	The objective of our study was to determine if placental MRI examinations performed for the detection of abnormal placentation earlier than 24 weeks' gestational age (GA) are more or less reliable than examinations performed at a later GA.	https://www.ncbi.nlm.nih.gov/pubmed/26295658	Sep 2015
8.	Study of diagnostic accuracy	Counseling in fetal medicine: evidence-based answers to clinical questions on morbidly adherent	Aim of this review is to provide up-to-date and evidence-based answers to common clinical questions regarding the diagnosis and management of	http://onlinelibrary.wiley.com/doi/10.1002/uog.14950/abstract	Mar 2016

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
		placenta	MAP.		
9.	Study of diagnostic accuracy	Prenatal identification of invasive placentation using magnetic resonance imaging: systematic review and meta-analysis	To assess systematically the performance of prenatal magnetic resonance imaging (MRI) in diagnosing the presence, degree and topography of disorders of invasive placentation and to explore the role of the different MRI signs in predicting these disorders. Systematic review.	https://www.ncbi.nlm.nih.gov/pubmed/24515654	Jul 2014
10	Study of diagnostic accuracy	Comparing the diagnostic value of ultrasound and magnetic resonance imaging for placenta accreta: a systematic review and meta-analysis	The aim of this study was to evaluate the diagnostic value of ultrasound (US) as compared with magnetic resonance imaging (MRI) in the detection of placenta accreta.	https://www.ncbi.nlm.nih.gov/pubmed/23972487	Nov 2013
11	Study of diagnostic accuracy	Diagnostic value of ultrasonography and magnetic resonance imaging in pregnant women at risk for placenta accreta	The purpose of this study was to evaluate whether ultrasonography and magnetic resonance imaging can detect placenta accreta reliably in at-risk patients	https://www.ncbi.nlm.nih.gov/pubmed/23489020	Sep 2013
12	Study of diagnostic accuracy	Accuracy of ultrasonography and magnetic resonance imaging in the diagnosis of placenta accreta	To evaluate the accuracy of ultrasonography and magnetic resonance imaging (MRI) in the diagnosis of placenta accreta and to define the most relevant specific ultrasound and MRI features that may predict placental invasion	https://www.ncbi.nlm.nih.gov/pubmed/24733409	Apr 2014
13	Study of	MRI in the	To determine the	https://www.ncbi	Apr 2013

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
	diagnostic accuracy	diagnosis and surgical management of abnormal placentation	usefulness of placental magnetic resonance imaging (MRI) in the diagnosis and surgical management of abnormal placentation. Cohort study with gold standard.	.nlm.nih.gov/pubmed/22881062	

3. Obstetric MRI for evaluation of acute maternal abdominopelvic pain following incomplete, inconclusive or non diagnostic abdominopelvic ultrasound

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication**
1	Study of diagnostic accuracy	Magnetic resonance evaluation of pregnant patients with acute abdominal pain	Study to identify the benefit of MR over ultrasound and CT when patients demonstrates acute abdominal pain in pregnancy.	http://www.semultrasoundctmri.com/article/S0887-2171(05)00034-X/abstract?cc=y=	Aug 2005
2	Study of diagnostic accuracy	Imaging of acute abdomen in pregnancy	Article discusses test selection and underlying reasoning, with a description of common imaging features of different causes of acute abdominal pain in pregnancy. Narrative review.	https://www.ncbi.nlm.nih.gov/pubmed/24210441	Nov 2013
3	Study of diagnostic accuracy	Evaluating the Acute Abdomen in the Pregnant Patient	MR imaging has been shown to be useful in the diagnosis of gynecologic and obstetric problems and in the setting of acute abdomen during pregnancy. MR imaging is often used when ultrasound is inconclusive. Narrative review.	https://www.ncbi.nlm.nih.gov/pubmed/26526440	Nov 2015
4	Study of diagnostic accuracy	MR imaging evaluation of abdominal pain during pregnancy: appendicitis and other nonobstetric causes	Review of MR imaging technique used for evaluating abdominal pain in the pregnant patient.	http://pubs.rsna.org/doi/full/10.1148/rg.322115057	Jul 2011
5	Study of diagnostic accuracy	Acute abdominal and pelvic pain in pregnancy: ESUR	Article reviews the evolving imaging and clinical literature on appropriate investigation of acute	https://www.ncbi.nlm.nih.gov/pubmed/23990045	Dec 2013

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
		recommendations	abdominal and pelvic pain during established intrauterine pregnancy, addressing its common causes. Clinical practice guideline.		
6	Study of diagnostic accuracy	MR imaging evaluation of acute abdominal pain during pregnancy	Article reviews the MR imaging technique and findings of various abnormalities causing acute abdominal pain in pregnant patients	https://www.ncbi.nlm.nih.gov/pubmed/17433979	Nov 14
7	Study of diagnostic accuracy	Magnetic resonance imaging for the evaluation of acute abdominal pain in pregnancy	Narrative review that details the MRI technique required to image the pregnant abdomen and describes the MRI features of common causes of acute abdominal pain in pregnancy	https://www.ncbi.nlm.nih.gov/pubmed/20974361	Oct 2010
8	Study of diagnostic accuracy	MR imaging of maternal diseases of the abdomen and pelvis during pregnancy and the immediate postpartum period	Narrative review to discuss the view that MR imaging should be reserved for cases in which results of ultrasonography are inconclusive and patient care depends on further imaging.	https://www.ncbi.nlm.nih.gov/pubmed/15371610	Sep 2004
9	Study of diagnostic accuracy	Imaging of abdominal pain in pregnancy	Article reviews the evolving radiology and clinical literature on imaging of suspected common and relatively common maternal nonobstetric conditions of the abdomen and pelvis.	https://www.ncbi.nlm.nih.gov/pubmed/22099493	Jan 2012
10	Study of diagnostic accuracy	Non-obstetrical acute abdomen during pregnancy	Study that identifies the risk of acute abdomen in pregnancy.	https://www.ncbi.nlm.nih.gov/pubmed/16982130	Mar 2007
11	Study of diagnostic accuracy	Magnetic resonance imaging of acute abdominal and pelvic pain in pregnancy	Review presents a practical approach to common obstetric and nonobstetric causes of acute abdominal and pelvic pain during	https://www.ncbi.nlm.nih.gov/pubmed/25099561	Aug 2014

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
			pregnancy, as well as safety considerations for performing MRI in this patient population		
12	Study of diagnostic accuracy	MRI of acute abdominal and pelvic pain in pregnant patients	The purpose of this study was to show the usefulness of MRI in the evaluation of pregnant women with acute abdominal or pelvic pain.	https://www.ncbi.nlm.nih.gov/pubmed/15671363	Feb 2005
13	Study of diagnostic accuracy	Acute abdomen in pregnancy requiring surgical management: a 20-case series	This study presents the experience of the authors in pregnant patients with acute abdomen.	https://www.ncbi.nlm.nih.gov/pubmed/21831513	Nov 2011
14	Study of diagnostic accuracy	MRI evaluation of acute appendicitis in pregnancy	A discussion on a comprehensive MRI protocol for evaluation of pregnant women with abdominal pain. Narrative review.	https://www.ncbi.nlm.nih.gov/pubmed/23423797	Mar 2013
15	Study of diagnostic accuracy	Comparing the diagnostic performance of MRI versus CT in the evaluation of acute nontraumatic abdominal pain during pregnancy	Objectives of this study were to document the utilization of MRI compared with CT in pregnant patients presenting with acute nontraumatic abdominal pain at our institution and to compare the diagnostic performance of the two modalities.	https://www.ncbi.nlm.nih.gov/pubmed/22886287	Dec 2012

** Categorise study design, for example meta-analysis, randomised trials, non-randomised trial or observational study, study of diagnostic accuracy, etc.*

***Provide high level information including population numbers and whether patients are being recruited or in post-recruitment, including providing the trial registration number to allow for tracking purposes.*

**** If the publication is a follow-up to an initial publication, please advise.*

18. **Identify yet to be published research that may have results available in the near future that could be relevant in the consideration of your application by MSAC (limiting these to the English language only).** ***Please do not attach full text articles, this is just intended to be a summary.***

	Type of study design*	Title of research (including any trial identifier if relevant)	Short description of research (max 50 words)**	Website link to research (if available)	Date***
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** Categorise study design, for example meta-analysis, randomised trials, non-randomised trial or observational study, study of diagnostic accuracy, etc.*

***Provide high level information including population numbers and whether patients are being recruited or in post-recruitment.*

****Date of when results will be made available (to the best of your knowledge).*

PART 5 – CLINICAL ENDORSEMENT AND CONSUMER INFORMATION

19. **List all appropriate professional bodies / organisations representing the group(s) of health professionals who provide the service (please attach a letter of support for each group nominated).**

The Royal Australian and New Zealand College of Radiologists
The Royal Australian and New Zealand College of Obstetricians and Gynaecologists.

20. **List any professional bodies / organisations that may be impacted by this medical service (i.e. those who provide the comparator service).**

Royal Australian and New Zealand College of Obstetricians and Gynaecologists

21. **List the relevant consumer organisations relevant to the proposed medical service (please attach a letter of support for each consumer organisation nominated).**

We are unaware of a consumer advocacy group specific to pregnant women but would be pleased to seek their support should such organisations be identified by MSAC.

22. List the relevant sponsor(s) and / or manufacturer(s) who produce similar products relevant to the proposed medical service.

None. Any current generation MRI scanner (1.5T or 3T) with appropriate surface coils and trained technologists can provide this service. Many such scanners already exist in Australia in the public and private sector.

23. Nominate two experts who could be approached about the proposed medical service and the current clinical management of the service(s):

Name of expert 1	REDACTED
Telephone number(s)	REDACTED
Email address	REDACTED
Justification of expertise	REDACTED

Name of expert 2	REDACTED
Telephone number(s)	REDACTED
Email address	REDACTED
Justification of expertise	REDACTED

Please note that the Department may also consult with other referrers, proceduralists and disease specialists to obtain their insight.

PART 6 – POPULATION (AND PRIOR TESTS), INDICATION, COMPARATOR, OUTCOME (PICO)

PART 6a – INFORMATION ABOUT THE PROPOSED POPULATION

24. Define the medical condition, including providing information on the natural history of the condition and a high level summary of associated burden of disease in terms of both morbidity and mortality.

MRI involves no exposure to ionising radiation and is thus ideal for diagnostic imaging during pregnancy where imaging of the fetus, uterus, uterine contents, abdomen or pelvis is required and the pathological process is demonstrable with MRI. Current scientific knowledge indicates that MRI is safe during pregnancy and current international guidelines and position statements support this (SPR – ACR position statement attached).

Ultrasound is, and will likely remain, the initial imaging test of choice for the three indications for abdominopelvic MRI during pregnancy to which this application relates and it is a necessary precursor to MRI for these indications. Performance of MRI in the three described situations has the potential to improve the timeliness, appropriateness, safety and accuracy of the counselling and treatment delivered to pregnant women and to obviate the need for repeated ultrasound examinations that can be driven by incomplete or indeterminate findings. This has the potential to result in savings to the health system and improved patient care and experience.

1. **Obstetric MRI for further evaluation of suspected or incompletely characterised fetal structural abnormality**
2. **Obstetric MRI for diagnosis of and surgical planning for suspected placental adhesion disorders (placenta accreta, increta, or percreta) following incomplete, inconclusive or non-diagnostic uterine and pelvic ultrasound, especially in the setting of a placenta located on the posterior. This will most often, but not always be performed after 28 weeks and always after 20 weeks.**
3. **Obstetric MRI for evaluation of acute and persistent maternal abdominopelvic pain following incomplete, inconclusive or non-diagnostic abdominopelvic ultrasound**

25. Specify any characteristics of patients with the medical condition, or suspected of, who are proposed to be eligible for the proposed medical service, including any details of how a patient would be investigated, managed and referred within the Australian health care system in the lead up to being considered eligible for the service.

Patient characteristics / demographics vary with the three indications for obstetric MRI for which funding through the Medicare system is sought:

Pregnant patients > 18 weeks gestation for suspected fetal abnormality following indeterminate / incomplete or non-diagnostic tertiary ultrasound by a maternal fetal medicine specialist service

Pregnant patients > 18 weeks gestation for suspected placental adhesion disorder following indeterminate / incomplete or non-diagnostic ultrasound performed at a centre providing obstetric / surgical care for pregnant women with placental adhesion disorders

Pregnant patients of any gestation with acute abdominal pain following indeterminate / incomplete or non-diagnostic ultrasound referred by an obstetrician, emergency medicine, surgical or general medical specialist

26. Define and summarise the current clinical management pathway *before* patients would be eligible for the proposed medical service (supplement this summary with an easy to follow flowchart [as an attachment to the Application Form] depicting the current clinical management pathway up to this point).

1. Suspected fetal abnormality

Pregnant women in Australia are recommended to have obstetric ultrasound at 20 weeks of gestation to assess their fetus for abnormalities and to check their placenta and uterus for abnormalities that may complicate delivery or change the mode or location of delivery. For most women (>90% of the 200,00 or so women who give birth each year, most of whom have the midtrimester prenatal US), this provides sufficient information for routine pregnancy care and no fetal or placental abnormality of concern is identified. The 20-week scan is most often performed in Australia in hospital or community radiology practices by radiologists or by obstetricians who have subspecialised in diagnostic ultrasound by undertaking COGU or DDU training and achieving an additional qualification. The 18 – 20 week ultrasound is generally not performed as a point – of – care examination by obstetricians without this subspecialty qualification due to the complexity of the examination.

Approximately 2% of well pregnant women (approximately 4,000 women per year in Australia) who have a 20 week pregnancy screening ultrasound in the community will have a fetal abnormality demonstrated, and many of these women, depending on the nature and severity of the abnormality, are routinely referred to a specialist maternal fetal medicine service affiliated with a tertiary referral maternity hospital in the State they live in as each State has at least one such centre and the larger States 2 or 3.

At this point, the ultrasound will be repeated to confirm or further evaluate the abnormality. The woman may receive further testing of themselves or their fetus (e.g. blood tests for infection, sampling of the amniotic fluid for evidence of genetic abnormalities or infection) prior to being counselled regarding the significance of the abnormality for their unborn child and potential treatment options both during the pregnancy and following birth. In some cases, repeat ultrasound evaluation will be recommended in order to refine treatment planning and prognostic counselling. Referral to other specialists such as paediatric surgeons, cardiologists, cardiothoracic surgeons, geneticists, and paediatric neurologists may occur or be recommended.

This small number of women necessarily limits the projected demand for this service, even when a minority of women who access it may require MRI more than once to monitor abnormalities that may progress or regress in utero. In practice, about 80% of women will require prenatal MRI for fetal abnormality (suspected based on ultrasound or risk profile of the fetus) only once during the pregnancy.

Based on the results of further testing and specialist advice regarding fetal prognosis, some women may choose to terminate the pregnancy if local laws permit this. Women who continue their pregnancy will often receive subspecialised care during the remainder of the pregnancy and after the baby is born, depending on the nature and severity of the abnormality. They may be advised to give birth in a specialist centre rather than a hospital in their community due to anticipated need for additional medical support for themselves or their baby following birth. This can result in reduced maternal and fetal morbidity and mortality and thus reduced downstream costs to the health system that can be lifelong.

Some women, based on their family history or previously affected children, will know their baby is at an increased risk of an abnormality and while they will routinely receive a 20 week screening ultrasound, they may have more intensive monitoring with ultrasound during their pregnancy.

2. Suspected placental adhesion disorder

Abnormal placental adhesion prevents normal separation of the placenta from the uterus after birth. If unrecognised it increases the risk of peripartum haemorrhage, which may be life threatening in amount for mother and baby especially if delivery occurs in a situation where this complication cannot be dealt with using maximal medical support.

Placenta praevia and one or more prior caesarean deliveries increase the risk of placental adhesion disorders (PADs) including placenta accreta, increta and percreta. The risk increases with the number of previous caesarean deliveries. As this mode of delivery has become more common in developed countries, so the occurrence of PADs has risen.

Ultrasound in experienced hands is usually adequate for the diagnosis of a PAD. However, maternal obesity, or a posteriorly located placenta, may prevent adequate placental visualisation with ultrasound.

MR is useful in this situation but is now being used at specialist centres that manage these pregnancies to plan delivery, the chief alternatives being:

I. peripartum hysterectomy – while this has been the conventional treatment in order to reduce maternal morbidity and mortality from post partum haemorrhage that complicates partial placental separation in PADs, this approach is technically challenging with large parametrial vessels that have enlarged due to stimulation by pregnancy – associated hormones, being potentially difficult to control. It is common, when PAD is diagnosed during the 3rd trimester on ultrasound, for delivery to be planned at a centre where specialist gynaecological oncology surgical expertise is available. Dissection of extrauterine placental tissue away from the bladder, when such tissue is present, and control of adnexal vessel haemorrhage as well as peripartum balloon occlusion of iliac vessels are all utilised in varying combinations to reduce blood loss when the decision is made to perform hysterectomy immediately after delivery of the baby rather than expectantly managing the retained placenta in hospital, with contingent hysterectomy in the event of major postnatal bleeding some weeks later when parametrial vascularity that is driven by pregnancy – related hormones, has regressed, making hysterectomy easier and safer. However, this requires management in hospital, with emergency hysterectomy available should the woman develop post partum haemorrhage while waiting for the vascularity to regress and the placenta to shrink.
II. expectant in – hospital management after delivery of the baby without hysterectomy or planned delayed hysterectomy (this is associated with risk of post partum haemorrhage due to placental retention and potential partial separation over the days after delivery. However it can decrease the risk of blood loss associated with immediate peripartum hysterectomy in the setting of PADs and offers fertility preservation in appropriate women).
III. Interventional radiological support for i) with temporary balloon occlusion of internal iliac vessels is required in many cases of immediate peripartum hysterectomy.

3. Acute persistent abdominal pain during any stage of pregnancy

Depending upon the result of the MRI and other tests (e.g. urine dipstick, CRP, full blood examination, bilirubin, urea and electrolytes etc) the underlying cause for the pain may or may not be specifically diagnosed. The commonest abnormalities found on a positive MRI in this situation are in approximate descending order of frequency: acute appendicitis, ovarian torsion, cholecystitis / common bile duct obstruction by calculus, ureteric obstruction by the gravid uterus or a calculus, pyelonephritis, and inflammatory bowel disease, and small bowel mechanical obstruction. Treatment will depend on the diagnosis.

PART 6b – INFORMATION ABOUT THE INTERVENTION

27. Describe the key components and clinical steps involved in delivering the proposed medical service.

Not all congenital abnormalities are easily detectable or accurately diagnosed with ultrasound due to:

- fetal position,
- maternal body habitus and obesity,
- the nature of the malformation. This applies particular to some types of brain malformation.

Not all malformations that are suspected on the 20 week screening ultrasound can be fully characterised and specifically diagnosed with ultrasound. A subset of the women who are referred to tertiary maternal fetal medicine specialty units because of a suspected abnormality are currently referred for fetal MRI, and this has been the case in most States of Australia for more than 10 years, in order to improve diagnostic certainty and thus provide more accurate counselling and pre and postnatal care to the small number of pregnant women in this situation.

Fetal MRI is not currently used as a standalone screening test and always follows tertiary ultrasound. Sometimes, a woman with a fetus who appears normal at the 20 week ultrasound but who has a high genetic risk of producing a fetus with a specific abnormality that is known to be difficult to diagnose with ultrasound, but more easily diagnosed with MRI, will be referred for MRI by a maternal fetal medicine unit or geneticist involved in her pregnancy care.

Current indications for fetal MRI include but are not limited to:

1. Isolated fetal ventriculomegaly on antenatal ultrasound
2. Suspected absence / abnormality of the corpus callosum
3. Suspected brainstem or cerebellar abnormality
1. Suspected malformation of cortical development (e.g. lissencephaly, polymicrogyria)
2. Following treatment for twin transfusion syndrome or cotwin demise in a monochorionic pregnancy
3. Evaluation of the fetal airway in the setting of fetal neck mass to facilitate delivery planning
4. Confirmation of diagnosis, assessment of prognosis, and treatment planning in congenital diaphragmatic hernia
5. Diagnosis of lung masses
6. Diagnosis of the cause for and prognosis of abdominal masses, cysts, and dilated bowel when this is uncertain on ultrasound
7. Diagnosis the cause(s) of kidney and bladder malformations / obstruction
8. Evaluation of any abnormality of the fetal cranium when abnormality is suspected but not fully characterised on ultrasound
9. Evaluation of the fetus at increased risk of a genetic abnormality that is completely or inaccurately diagnosed with ultrasound
10. Evaluation of cardiac or vascular abnormalities/malformations not fully characterised with ultrasound

28. Does the proposed medical service include a registered trademark component with characteristics that distinguishes it from other similar health components?

No

29. If the proposed medical service has a prosthesis or device component to it, does it involve a new approach towards managing a particular sub-group of the population with the specific medical condition?

N/A

30. If applicable, are there any limitations on the provision of the proposed medical service delivered to the patient (i.e. accessibility, dosage, quantity, duration or frequency).

The indications outlined in this application are once-off examinations performed only during pregnancy. There is therefore a limit use for these examinations and do not allow for ongoing or life-time utilisation by patients.

Studies can be performed on a 1.5T or 3T MRI scanner and many of these exist in Australia.

Training is required, as for all other subspecialty radiology practice, in order to accurately interpret fetal, placental, and pregnancy MRI studies. The "learning curve" is longest for fetal MRI compared with the other indications due to the small number of studies performed and the wide range of pathological conditions encountered, many of which are rare by virtue of the subspecialist referral pathway that leads to a patient proceeding to fetal MRI.

As a result, provision of fetal MR services is currently concentrated in a small number of mostly tertiary, mainly but not exclusively, public hospitals and these services are provided by a small number of radiologists. Building and maintenance of skills requires a critical mass of ongoing experience and due to the necessarily small caseload, it is not practical for large numbers of radiologist at many centres to gain or maintain the required level of expertise.

Placental MRI is similarly conducted mainly at centres that specialise in managing the pregnancies of pregnant women with this disorder. MRI for abdominal pain in pregnancy that is undiagnosed by ultrasound is provided more widely, mainly in conjunction with emergency medicine departments within public and private hospitals.

31. If applicable, identify any healthcare resources or other medical services that would need to be delivered <u>at the same time</u> as the proposed medical service.

Women having fetal MRI should have this in the context of a comprehensive maternal – fetal medicine diagnostic service with availability of counselling and further testing and treatment delivered by people with the appropriate expertise. It is not appropriate for women with an abnormal 20 week screening ultrasound to receive direct referral by their managing obstetrician or GP to fetal MRI.

Women with acute abdominal pain and indeterminate ultrasound are appropriately referred by those managing their symptoms – an emergency doctor, surgeon, or obstetrician for example.

Women with suspected placental adhesion disorder will generally have been first referred to a specialist centre that treats this condition before being referred for MRI. In other words, direct referral following obstetric ultrasound in the community that raises the possibility of an adhesion disorder at or after 28 weeks is undesirable from a comprehensive clinical management viewpoint. Almost invariably, women with suspected placental adhesion disorders have placenta praevia and as such are planned for caesarean delivery. Diagnosis of a coexisting placental adhesion disorder places them at risk of significant postpartum haemorrhage which can be life threatening for both them and their baby, and thus they are most often referred to a specialist centre for pregnancy management and delivery when this diagnosis is made.

32. If applicable, advise which health professionals will primarily deliver the proposed service.

Radiologists.

33. If applicable, advise whether the proposed medical service could be delegated or referred to another professional for delivery.

N/A

34. If applicable, specify any proposed limitations on who might deliver the proposed medical service, or who might provide a referral for it.

See previous responses for training requirements and referral pathways / pre requisites

35. If applicable, advise what type of training or qualifications would be required to perform the proposed service as well as any accreditation requirements to support service delivery.

There is currently no credentialing or formal training program. FRANZCR is a minimum requirement. Obstetric specialists are not trained or examined in MRI interpretation. Post FRANZCR Part II fellowship training in fetal MRI is not yet formalized, occurs in conjunction with some paediatric MRI fellowships, but not all, because fetal MRI is currently performed in only a few centres around Australia and New Zealand. These are currently almost exclusively in metropolitan centres and mainly in public hospitals with formal or informal affiliations with tertiary referral maternal fetal medicine diagnosis / treatment units. In the smaller states, tertiary fetal diagnostic units usually serve the entire State or territory whereas in larger states there may be 2 or 3 recognised centres. Fetuses with congenital abnormalities revealed on ultrasound or women with complex pregnancy management issues either as a result of fetal abnormalities or maternal conditions are referred to these centres by obstetricians involved in their care when subspecialist expertise in fetal diagnosis or treatment or management of maternal medical conditions is required during the pregnancy. While these centres may not have an official designation by State or Federal government bodies, it is locally well known how to refer patients to these facilities.

Training of radiologists who currently provide these services has been to date through attending courses and short term observerships at centres overseas and through experience on the job. The background and subspecialty interests of these radiologists often includes paediatric radiology and / or obstetric ultrasound and / or paediatric neuroimaging.

Placental Adhesion Disorder / Abdominal Pain in Pregnancy: These indications require less training and a lower amount of continual exposure to maintain skills as the range of pathology is limited for placental adhesion disorders.

For acute abdominal pain, the relevant conditions and imaging findings are familiar to radiologists who routinely interpret a wide range of adult non - pregnant MRI (unlike fetal imaging) in the non-pregnant patient for the acute abdominal pain indication.

36. (a) Indicate the proposed setting(s) in which the proposed medical service will be delivered (select all relevant settings)

Inpatient private hospital	X
Inpatient public hospital	X
Outpatient clinic	X
Emergency Department	
Consulting rooms	
Day surgery centre	
Residential aged care facility	
Patient's home	
Laboratory	
Other – please specify	

(b) Where the proposed medical service is provided in more than one setting, please describe the rationale related to each.

Patients receive their prenatal ultrasounds in all of these settings, including private radiology practices and with the implementation of fetal MRI. The service would remain accessible at the same locations.

37. Is the proposed medical service intended to be entirely rendered in Australia?

Yes	X
No (please specify below)	

PART 6c – INFORMATION ABOUT THE COMPARATOR(S)

38. Nominate the appropriate comparator(s) for the proposed medical service, i.e. how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian health care system (including identifying health care resources that are needed to be delivered at the same time as the comparator service).

At present there are no direct comparators listed on the MBS that manage the three indications identified in this application. Ultrasound services can and, at present, are used on an ongoing basis, however the efficacy of these tests are not to the standard of those outlined in this application. Multiple ultrasound scans would be required over the term to manage the 3 indications should MRI services not be available to the patient.

There are a number of similar MRI items that perform scans in the same anatomical region, however they differ significantly in terms of the time required to perform the scan, the complexity of the scan and the oversight required by the radiologist throughout the performing of the scan.

By way of example, the item number for MRI Abdomen and Pelvis is somewhat comparable based on the anatomical region. However, in order to perform a Fetal MRI, an experienced radiologist must be present due to the fetus being mobile which may cause the pathology and anatomy to be missed. The complexity of performing the MRI is also significantly higher so despite appearing to be an appropriate comparator, many other aspects of the scan need to be taken into consideration.

Question 39 outlines both the ultrasound item numbers that are likely to be substituted for the indications in this application, and the combination of MRI comparators (in MBS items numbers) that we believe represent the anatomical region, complexity and time taken to perform the scan. However, the combination of these items are not used to treat the indications in this application and are therefore a proxy for a comparators to the indications in this application.

39. Does the medical service that has been nominated as the comparator have an existing MBS item number(s)?

Yes (please provide all relevant MBS numbers below)	X
No	

MBS ultrasound items seen as comparators in terms of examinations that are currently administered when the examinations outlined in this application are not available to the patient (despite the lower efficacy, and need for multiple examinations):

55706, 55709, 55712, 55713, 55715, 55717, 55719, 55720- 55727, 55729, 55730, 55762-55765, 5576-55775.

MBS items that are comparators in terms of complexity, modality and anatomical region:

1) Suspected fetal abnormality
    a. Item 63473: staging of histologically diagnosed cervical cancer; *plus*,
    b. Item 63052: congenital malformation of the brain or meninges; *plus*,
    c. Item 63385: congenital disease of the heart or a great vessel.

2) Suspected placental adhesion disorder
    a. Item 63473: staging of histologically diagnosed cervical cancer; *plus*,
    b. Item 63482: suspected biliary or pancreatic pathology.

3) Acute abdominal pain in pregnancy
    a. Item 63473: staging of histologically diagnosed cervical cancer; *plus*,
    b. Item 63482: suspected biliary or pancreatic pathology.

40. Define and summarise the current clinical management pathways that patients may follow *after* they receive the medical service that has been nominated as the comparator (supplement this summary with an easy to follow flowchart [as an attachment to the Application Form] depicting the current clinical management pathway that patients may follow from the point of receiving the comparator onwards including health care resources).

Pathways for the 3 indications in this application are provided in Appendix B.

41. (a) Will the proposed medical service be used in addition to, or instead of, the nominated comparator(s)?

Yes	X
No	

(b) If yes, please outline the extent of which the current service/comparator is expected to be substituted.

The three described indications for ultrasound will be supplemented with obstetric MRI (the proposed service) in a specific subset of women with indeterminate results on ultrasound, to:

- increase specificity and sensitivity of prenatal diagnosis, pregnancy outcome, planning of delivery and fetal therapy
- improve diagnosis and maternal / fetal outcomes in women with placental adhesion disorders
- improve diagnose and avoid ionising radiation exposure in pregnant women with abdominal pain not diagnosed with ultrasound

42. Define and summarise how current clinical management pathways (from the point of service delivery onwards) are expected to change as a consequence of introducing the proposed medical service including variation in health care resources (Refer to Question 39 as baseline).

Clinical management for all three scenarios is improved due to greater diagnostic accuracy which has the potential to reduce maternal and fetal morbility and mortality, assist with medical and surgical pregnancy management, and contribute to prognostic genetic and family counselling.

PART 6d – INFORMATION ABOUT THE CLINICAL OUTCOME

43. Summarise the clinical claims for the proposed medical service against the appropriate comparator(s), in terms of consequences for health outcomes (comparative benefits and harms).

Severe anomalies are better delineated with fetal MRI and aide in decision making for clinicians and families. Fetal MRI can improve quality and accuracy of information provided to patients about fetal prognosis. It can also be used to assist planning of the location and support needed for safe delivery in fetuses with specific abnormalities.

44. Please advise if the overall clinical claim is for:

Superiority	X
Non-inferiority	

45. List the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be specifically measured in assessing the clinical claim of the proposed medical service versus the comparator:

Safety Outcomes

MRI when performed at 1.5T or 3T is safe during all trimesters of pregnancy[iii]. However, it is generally avoided during the first trimester unless the anticipated benefits for the mother outweigh the potential risks to the fetus. The theoretical risks, which have not yet been proven to exist in human fetuses, arise from static and changing magnetic and radiofrequency fields, and are thought to result mainly from the effects these produce on the temperature of the fetus and its environment (the amniotic fluid). Potential biological effects have been modelled using animal fetuses and temperature measurements of phantoms of the maternal abdomen in order to try to simulate these heating effects on a human fetus with the aim of constructing safe limits for SAR deposition, and thus machine settings / operating parameters during clinical scanning. MR technologists engaged in MRI during pregnancy are aware of this and operate the scanner within SAR (specific absorption rate) limits that have been set for pregnancy women.
Clinical Effectiveness Outcomes
Improved diagnostic specificity and sensitivity when compared with ultrasound for specific clinical problems or when ultrasound is inconclusive with regard to the presence of fetal abnormality or placental attachment disorder.
MRI can more accurately assess the abnormalities and associated lesions. This helps clinicians and patients with prognosticating and decision making.

[i] ACR–SPR PRACTICE PARAMETER FOR THE SAFE AND OPTIMAL PERFORMANCE OF FETAL MAGNETIC RESONANCE IMAGING (MRI), ACR and SPR, 2015. http://www.acr.org/~/media/CB384A65345F402083639E6756CE513F.pdf

[ii] The use of magnetic resonance imaging in the obstetric patient, Patenaude Y et al; Society of Obstetricians and Gynaecologists of Canada, J Obstet Gynaecol Can. 2014 Apr;36(4):349-63. Review. English, French. PMID: 24798674 [PubMed - indexed for MEDLINE].

PART 7 – INFORMATION ABOUT ESTIMATED UTILISATION

46. Estimate the prevalence and/or incidence of the proposed population.

1-2% of 18-20 week ultrasounds return with a major anomaly finding. Ultrasounds detect anomalies at approximately 60% accuracy.

The incidence of placental adhesion disorders is 3: 1000 deliveries or about 600 women per annum in Australia.

The incidence of severe persistent abdominal pain during pregnancy is hard to estimate, but:

i. Clinical experience suggests that fewer than 5% of pregnant women ~(10,000 per annum nationwide) experience this
ii. Most of these will have diagnosis and treatment based on ultrasound findings and blood test results as well as history and physical exam
iii. Many others will be managed on clinical grounds and if their symptoms and signs settle, no further investigation will occur
iv. Therefore, a conservative estimate of perhaps less than 5,000 women per annum Australia wide might be referred for MRI in the event of inconclusive ultrasound.
v. Overwhelmingly the commonest reason for this scenario is acute appendicitis. Undiagnosed, appendicitis with perforation / rupture into the peritoneal cavity substantially increases fetal mortality. Less common causes for this scenario are ovarian torsion, ureteric obstruction by a calculus or by the gravid uterus, pelvic inflammatory disease, pyelonephritis, and first presentation inflammatory bowel disease (e.g. Crohn's disease).

Exposure of the fetus to one prenatal abdominopelvic CT doubles the risk of childhood cancer (stochastic effect) from 1:1000 to 1:500 but has an almost unmeasurable effect on lifetime cancer risk and no measurable effect on the incidence of fetal malformation (deterministic effect). Source: Tirada et al, Radiographics 2015.

47. Estimate the number of times the proposed medical service(s) would be delivered to a patient per year.

Less than 10 fetal MRI studies are performed per week in Victoria. Therefore approximately 1000 per year in Australia. Based on our local experience in Victoria, about 20% of women with indications for fetal MR will need two MRIs in the situation of a potentially progressing or regressing problem (e.g. dural sinus malformation, brain injury following twin transfusion syndrome). 10% or less will need 3 or more

Less than 3 obstetric MRI studies are performed per week in Victoria for suspected placental adhesion disorder.

It is uncertain how many pregnant women may be potential candidates for MRI for abdominal pain that is still undiagnosed following ultrasound – based on 200,000 births per year in Australia and the above response to Question 47. as well as local experience in major maternity centres in Victoria, an upper limit approximate estimate would be 1000 per year.

48. How many years would the proposed medical service(s) be required for the patient?

Fetal MRI: During each affected pregnancy the service would generally be performed only once in about 20% twice and in less than 10% more than twice. Once the fetus is born, other existing Medicare items (MRI, US, CT, fluoroscopy or combinations of all of these, depending on the nature of the problem, apply to both mother and baby should follow up imaging be required.

Placental MRI: 1 – 2 times during each affected pregnancy.

Abdominal pain MRI: usually once, occasionally twice during each affected pregnancy.

Thus, even in combination, these three indications are by their nature and by the restricted population they apply to, low volume procedures relative to current utilisation of MRI of the spine or head in adults and children.

49. Estimate the projected number of patients who will utilise the proposed medical service(s) for the first full year.

3000 – 4000 for all three indications broken down as indicated above.

50. Estimate the anticipated uptake of the proposed medical service over the next three years factoring in any constraints in the health system in meeting the needs of the proposed population (such as supply and demand factors) as well as provide commentary on risk of 'leakage' to populations not targeted by the service.

1. Fetal MRI

We expect the current 250 fetal MRIs per year performed in Victoria to increase to 400 by the end of the three years – this translates to approximately 1,000 per annum nationally at the end of the three years. This is limited by the number of pregnancies per year. According to the ABS, registered births in 2014 came in at 299,697 (the ABS does not have data on total pregnancies, therefore this figure would understate total pregnancies). As stated earlier in the application, approximately 1% of pregnancies have congenital abnormalities detected on ultrasound (i.e. about 3000 women per annum in Australia) and in over half of these, cardiac abnormalities are the problem – these are currently better imaged with ultrasound than fetal MRI in the vast majority of cases and fetal MR is not used for this purpose. We do not expect this to change in the foreseeable future due to the ability of ultrasound to depict motion of the heart and direction of blood flow which are essential to the diagnosis of congenital heart disease in the fetus. MR is currently not able to do this as well as ultrasound can in the fetus.

Fetal MRI by its nature will not become a large volume procedure in the future due to the number of pregnancies placing an upper limit on eligible patients. Demographic trends do not predict a dramatic increase in current birth rates in the near future.

2. Placental adhesion disorders (PAD)

The chief predictors of the development of PAD are current placenta praevia and a past history of one or more caesarian section deliveries, with the risk of PAD being close to 50% in a woman with placenta praevia and 2 previous caesarians. Between 1:500 and 1:1000 women (or 200 – 500 women per annum in Australia) will have PAD but most of these will be diagnosed and managed with ultrasound alone as the usual treatment is peripartum hysterectomy. This treatment prevents the potentially catastrophic bleeding and maternal and fetal morbidity and mortality that can complicate PADs due to defective detachment of the placenta during the 3rd stage of labour.

Placental adhesion disorders are becoming more common due to increased use of caesarian delivery. However, even in a specialist centre such as the Royal Women's Hospital in Melbourne, less than one of these procedures is done per week – this may mean that 150 per year are done in Australia at present. Ultrasound remains the mainstay of diagnosis. MR is reserved for indeterminate ultrasound or surgical planning especially if the traditional treatment of peripartum hysterectomy is NOT to be performed because the woman wants fertility preservation or delayed hysterectomy (after regression of high parametrial vascularity resulting from pregnancy – associated hormonal changes – in this setting MR can be very useful when referred by a specialist gynaecological surgery unit to assist with planning whether fertility preservation is feasible and/or safe by assessing whether or not there is extrauterine placental tissue.

Most pregnant women will have only one MR between 28 and 32 weeks to confirm the diagnosis and aid surgical planning when ultrasound is inadequate or surgical planning requires the additional information provided by MRI.

3. Abdominopelvic pain in pregnancy not diagnosed successfully with ultrasound

Less than 5% of pregnant women (perhaps 2000 – 3000 per annum) will experience abdominal pain during pregnancy sufficient to make them seek medical attention. In most of these, no imaging is needed and appropriate treatment for urinary tract infection or gastroenteritis is all that is required. However, some will require ultrasound to confirm or exclude things like a ureteric or renal stone, appendicitis, ovarian torsion, inflammatory bowel disease etc. When ultrasound is unhelpful or equivocal in a subset of these patients, CT may be considered, so perhaps less than 1000 patients per year nationally. CT of the abdomen and pelvis exposes the fetus directly to ionizing radiation. While the dose from a single CT is insufficient to produce fetal malformations even if the CT occurs during the first trimester, there is a theoretical increased risk of childhood cancer that has been estimated to be an approximately doubled risk (from 1:1000 children not exposed to CT during fetal life to 1:500 if they are exposed to 1 maternal abdominopelvic CT) (Reference: Tirada N, Dreizin D, Khati NJ, Akin EA, Zeman RK. Imaging Pregnant and Lactating Patients. Radiographics. 2015 Oct;35(6):1751-65. doi: 10.1148/rg.2015150031. Review.). MR allows accurate diagnosis / exclusion of the commonest causes of abdominal pain in pregnancy when imaging is needed but ultrasound is equivocal or negative. While many causes of abdominal pain in pregnancy are self-limited and not requiring of investigation, others can lead to increased risk of fetal loss if not treated or maternal morbidity. These include appendicitis, renal calculus or other causes of renal obstruction, and ovarian torsion. CT may still be considered following or instead of MR in exceptional circumstances e.g. major abdominal trauma, clinical evidence of haemodynamic instability suggesting intraabdominal haemorrhage etc.

PART 8 – COST INFORMATION

51. Indicate the likely cost of providing the proposed medical service. Where possible, please provide overall cost and breakdown.

1. Fetal MRI (estimate in 2016 = $1400 - $1500)
2. Placental adhesion disorder (estimate in 2016 = $500 – 600)
3. Abdominal pain

Reporting and direct supervision throughout scanning are much more time consuming for the radiologist for fetal than for the other two obstetric indications.

Staff Costs

- Senior Radiologist – 2 hours (1 hour supervising study, 1 hour reporting for fetal MRI; 10 minutes to perform quality check at the end of the exam and 20 - 25 minutes to report the study for the other two indications). Other MRI procedures including the other two indications for Obstetric MRI in this submission require less direct involvement during the scanning process with checking for technical adequacy at the end of the exam only, and performance of a routine protocol, generally being all that is required. Fetal MRI, due to fetal movement, requires direct involvement of the radiologist throughout the exam in order to ensure each set of acquired images is diagnostic – if not, they are repeated on the spot before the exam is concluded. This monitoring is essential for limiting the duration of the study as most pregnant women find it somewhat uncomfortable to lie supine or decubitus on the scanner table for a considerable time. If this discomfort leads to them asking for the exam to stop, then critical diagnostic information will be missed with all of the attendant consequences for the patient and wasted resources.
- Senior MRI Radiographer – 1 hour (fetal MR), ½ hour (other two indications)

Equipment Costs

- MRI Scanner (lease, depreciation, maintenance). Same for all indications

Consumable Costs (same for all indications)

- In very rare circumstances, patient may require gadolinium contrast, but this is generally avoided during pregnancy.
- Sedation and/or general anaesthesia may be used, but is not routine.
- Usual consumables to perform MRI i.e. sheets, pyjamas etc.

52. Specify how long the proposed medical service typically takes to perform.

See above: fetal MR 1 hour to perform, 1 hour to report; the other two indications 10 minutes to check images and and 20 - 25 minutes to report respectively.

53. If public funding is sought through the MBS, please draft a proposed MBS item descriptor to define the population and medical service usage characteristics that would define eligibility for MBS funding.

Category (proposed category number) – (proposed category description)

Proposed item descriptor

MAGNETIC RESONANCE IMAGING performed under the professional supervision of an eligible provider at an eligible location for the following indications:

1. Pregnant woman 18 weeks gestation or greater with suspected fetal abnormality based on tertiary ultrasound or family / past pregnancy history referred by an appropriate specialist or maternal fetal medicine specialty unit.
2. Pregnant woman any gestation with acute abdominopelvic pain that has been evaluated with ultrasound where there is persistent diagnostic uncertainty
3. Pregnant woman 28 weeks gestation or greater with suspected placental adhesion disorder referred by specialist unit involved in treatment and pregnancy management where:
    a. Diagnosis is indeterminate on tertiary ultrasound
    b. MR is required for surgical planning of either hysterectomy or uterine conservation interventions

Fee: $(proposed fee)

PART 9 – FEEDBACK

The Department is interested in your feedback.

54. How long did it take to complete the Application Form?

~ 3 months spent on actual application.

55. (a) Was the Application Form clear and easy to complete?

Yes	X
No	

(b) If no, provide areas of concern.

56. (a) Are the associated Guidelines to the Application Form useful?

Yes	X
No	

(b) If no, what areas did you find not to be useful?

57. (a) Is there any information that the Department should consider in the future relating to the questions within the Application Form that is not contained in the Application Form?

Yes	
No	X

(b) If yes, please advise:

Appendix A

Fetal Magnetic Resonance Imaging

(Fetal MRI)

An assessment of the role of fetal MRI within the Victorian public health sector

May 2010

Deakin Health Evaluation Group

Contents

Tables

Figures

Executive summary

Victorian Policy Advisory Committee on Technology (VPACT) – role and approach

The Victorian Policy Advisory Committee on Technology (VPACT) was established by the Victorian Department of Health (DH) to consider and make recommendations regarding the application of new and existing technologies and clinical practices in Victorian Public Health services and hospitals.

VPACT approved temporary funding (for the 2007-08, 2008-09, and the 2009-10 financial years) of fetal magnetic resonance imaging (fetal MRI) at the Monash Medical Centre, the Royal Children's Hospital and the Austin Repatriation Hospital. One of the conditions of this funding was the collection of data to permit a review of the technology, and its suitability for ongoing funding.

This report has been undertaken in response to a request from the Integrated Care Branch of the Wellbeing, Integrated Care and Ageing Division of the Department of Health (DH) for an evidence review of fetal MRI that would include analyses of:

- Existing international literature on the clinical and cost effectiveness of fetal MRI
- Identifying the use of fetal MRI
- Clinically relevant outcomes following the use of fetal MRI
- Victorian public health sector activity using fetal MRI (and outcomes where available)
- Local costs for fetal MRI
- Local clinical and cost effectiveness of fetal MRI.

This report provides a review of the published evidence in relation to the diagnostic accuracy of fetal MRI and also provides analysis and interpretation of the clinical and cost effectiveness of fetal MRI based on data collected in the Victorian Public sector. This report is provided to inform departmental consideration of ongoing policy and funding regarding the use of fetal MRI.

Assessment of fetal MRI

Clinical need and proposed use of fetal MRI

In Australian practice, ultrasound is routinely performed in clinically normal pregnancies at 19-22 weeks gestation to confirm fetal normality and well being and to perform an anatomical evaluation of the fetus for significant structural abnormalities. Fetal MRI is proposed to be used as an ancillary or complementary imaging technique to ultrasound. The objective of fetal MRI is to elicit further information to confirm or exclude the presence of suspected or detected fetal abnormalities detected by ultrasound or by clinical assessment and to determine whether other abnormalities exist.

Fetal MRI is being proposed as an adjunct investigation rather than as a substitute for ultrasound because, although fetal MRI offers some advantages over ultrasound (e.g. fetal MRI produces images with superior contrast resolution and offers advantages in assessment of intracranial structures that are obscured by the calvarium in ultrasound or where ultrasound is difficult due to oligohydramnios, patient body habitus or fetal lie), fetal MRI is also associated with limitations compared to ultrasound in some respects. For example, fetal MRI is inferior to ultrasound for assessment of structures such as the spine, the skeleton and the fetal heart; unlike ultrasound, fetal MRI cannot currently be used to provide dynamic information (e.g. fetal heart activity and breathing); fetal MRI examination must be targeted to a specific area of interest (e.g. fetal head) and therefore is not an appropriate tool for providing an overview of the fetus; and the use of fetal MRI is limited by fetal movement.

The additional information obtained by fetal MRI may permit a more accurate assessment of fetal diagnosis and prognosis, which may result in improved counselling and decision- making with respect to treatment of the fetus, management of the pregnancy, planning of the delivery (e.g., in terms of location or timing).

Safety

From the limited amount of evidence available in regards to safety of fetal MRI, it appears that although there is a theoretical risk associated with the use of fetal MRI this has, to date, not translated to a detectable risk in practice at the field strengths used in this population. A positive aspect of MRI is that it does not use ionising radiation to obtain images, it is therefore considered to be a safe technology for use in pregnant women.

Effectiveness

The key evidence presented in this report are the results of analyses of data collected by the Monash Medical Centre, the Royal Children's Hospital and the Austin Repatriation Hospital following VPACT's approval of temporary funding (for the 2007-08, 2008-09, and the 2009-10 financial years) of fetal MRI.

Clinicians were asked to assess the likely outcome (prognosis) for the fetus prior to MRI and then again after the MRI for the following four categories:

- risk of spontaneous death of the fetus during pregnancy or neonatal life;
- risk of severe disability;
- risk of mild disability or;
- normal or near normal outcome.

Clinicians rated each outcome as unlikely [<10%], possible [10-50%], probable [51-70%] or very likely [>70%]). Outcomes that were rated “very likely” were assumed to be the anticipated prognosis. In the case that more than one outcome was rated “very likely”, then the more severe of these outcomes was assumed to be the anticipated prognosis. If no outcome was rated “very likely” but one or more outcomes was rated “probable”, then the most severe of the “probable” outcomes was assumed to be the anticipated prognosis. Where no outcome was rated “probable” or “very likely”, then the anticipated prognosis was considered to be "uncertain".

The primary outcome assessed was the frequency of change to the assessment of likely outcome (prognosis) for the fetus. Results are summarised in Table 1. The shaded cells represent concordance between the prognosis before MRI and the prognosis expected after MRI.

Table 1: Results for frequency of change to the assessment of likely outcome (prognosis) for the fetus – all patients

		Prognosis - post-MRI						
		Normal	Mild disability	Severe disability	Spontaneous death	Uncertain	Not recorded	Totals
Prognosis - pre-MRI	Normal	69 (62%)	7 (6%)	5 (5%)	2 (2%)	8 (7%)	20 (18%)	109 (40%)
	Mild disability	7 (25%)	4 (14%)	8 (29%)	1 (4%)	3 (11%)	5 (18%)	28 (10%)
	Severe disability	2 (3%)	6 (10%)	32 (52%)	4 (6%)	3 (5%)	15 (24%)	62 (23%)
	Spontaneous death	0	1 (10%)	1 (10%)	4 (40%)	0	4 (40%)	10 (4%)
	Uncertain	24 (47%)	2 (4%)	4 (8%)	1 (2%)	13 (25%)	7 (14%)	53 (20%)
	Not recorded	2 (25%)	0	0	0	1 (13%)	5 (63%)	8 (3%)
	Totals	104 (39%)	20 (7%)	50 (19%)	12 (4%)	30 (11%)	54 (20%)	270 (100%)

In summary, there was a change to prognosis in 89 (33%) of cases examined, no change to prognosis in 122 (45%) of cases examined. Fetal MRI is potentially particularly helpful in the case where prognosis for the fetus is uncertain prior to fetal MRI. As can be seen from Table 1, 53 (20%) of cases

were considered to have an uncertain prognosis at baseline but after fetal MRI, 24 (43%) of these fetuses were considered to have a "normal" prognosis. This change in prognosis is likely to provide substantial peace of mind in these women.

Table 2 presents results indicating the proportion of patients in whom changes to diagnosis as a result of fetal MRI were correct, partially correct (i.e., where the fetal MRI provided further but incomplete information compared with the ultrasound) or incorrect. Results are presented only for a subgroup of 12 patients who had either a change to diagnosis predicted and in whom a final diagnosis was able to be determined from the findings of post-natal or post-mortem assessment.

Table 2: Results indicating whether predicted changes to diagnosis as a result of fetal MRI were correct according to post-natal or post-mortem assessment

Total number of patients with a change to diagnosis (N)	Patients with a change to diagnosis for whom diagnosis could be determined from a post-natal or post-mortem assessment n/N (%)	Proportion of patients with post-natal or post-mortem assessments in whom predicted change in diagnosis was correct		
		Correct	MRI added incomplete information	Incorrect
64	12 (19%)	7/12 (58%)	3/12 (25%)	2/12 (17%)

Economic considerations

As shown in Table 3, an analysis of incremental cost-effectiveness of fetal MRI suggests, that considering all patients who undergo fetal MRI (on the basis of a recommendation that fetal MRI is indicated by a fetal/maternal medicine unit), the incremental cost per additional patient with a correct diagnosis after MRI is approximately $4,475.

Table 3: Results for impact of MRI on diagnosis (excluding patients where certainty around diagnosis was not reported and excluding patients where the effect of the MRI on diagnosis was not reported.

	Fetal MRI conducted	Fetal MRI not conducted	Increment
Cost per patient	$623	-	$623
Proportion of patients achieving a correct diagnosis following fetal MRI	13.9% (=24% x 58%)	-	13.9%
Incremental cost per additional patient with an accurate diagnosis following fetal MRI:			$4,475

It is the remit of decision-makers to consider whether this result represents value for money. Ideally, a cost-effectiveness ratio should be presented in a metric that permits comparison with other health interventions (e.g., incremental cost per QALY) however, as discussed above, such an analysis has not been conducted in this case due to the ethical and practical issues (e.g., difficulties in determining the value of an accurate diagnosis [e.g., this might involve avoiding the birth of a child with an abnormality]).

Introduction

Victorian Policy Advisory Committee on Technology (VPACT) – role and approach

Health technology is rapidly changing. In order to ensure the Victorian public health system stays at the forefront of health technology investment, and to ensure a smooth transition of new health technology into routine clinical practice, and retirement of a health technology that offers little or no health gain, the Victorian Department of Health (DH) established the Victorian Policy Advisory Committee on Technology (VPACT) in 2004. VPACT comprises a diverse group of individuals, including specialists from the health sector, academic sector and consumer representation.

The activities of VPACT complement and supplement those being undertaken by the Health Policy Advisory Committee on Technology (HealthPACT) at the national level. HealthPACT advises the Australian Health Ministers' Advisory Committee, the Medical Services Advisory Committee (MSAC) and all jurisdictions, through horizon scanning activities, on new and emerging health technologies that have the potential to impact on the Australian health care system over the next three years.

The role of VPACT is to advise and make recommendations on:

- New technologies with potential implications for public health services
- Nationally Funded Centre applications put forward by Victorian health services
- Priorities for the introduction and use of new health technologies
- Identification and consideration of areas and health technologies for investment
- Policy and procedures for best practice for introduction and use of new and existing health technologies in public health services
- Requirements for evaluating and monitoring the introduction and use of new health technologies in public health services
- The assessment of clinical effectiveness and cost-effectiveness of new and of existing health technologies
- Dissemination of information regarding the introduction and use of emerging, new and existing health technologies
- Strategies for the recognition and management of Health technologies that may be ineffective or offer little health gain

The use of evidence based medicine is the basis for decision making when reimbursement is sought from DH. A team from the Deakin Health Economics Unit was engaged to conduct an evidence review of fetal MRI. Contributors to this review from the Deakin Health Economics Unit include Liliana Bulfone, Sandra Younie, Stephen Colgan, Bridie Murphy and Grace Kabaniha. The Deakin Health Economics team would like to acknowledge the significant contributions made to this report by Jenni Clark (the Database Manager for the data captured in the Victorian public sector), Stacy

Goergen (radiologist) and Luisa Chaves and Paul Fennessy from the Wellbeing, Integrated Care and Ageing Division of the Department of Health in Victoria.

Department of Health (Corporate Background information)

The Department of Health is responsible for a wide range of services to the diverse client groups across Victoria. The principle function of the Department is to ensure the delivery of a range of health, housing and community services.

The Department's mission statement is:

> "To enhance and protect the health and well being of all Victorians, emphasising vulnerable groups and those most in need."

Wellbeing, Integrated Care and Ageing Division (WICA)

WICA is responsible for state-wide policy and program direction for acute, sub-acute and ambulance services. WICA is also accountable for the delivery of all health and aged care services within Metropolitan Melbourne.

The Programs Branch of WICA has a key role in developing policies, standards, guidelines and projects to improve delivery of ambulance, maternity, cancer, radiotherapy, sub-acute services and continuity of care for patients. The branch also has responsibility for co-ordinating the provision and funding of blood and blood products in Victoria, the organ donation program, the Commonwealth/State Highly Specialised Drug program and Pharmaceutical reform as well as development and implementation of private hospital and day procedure centre policy and regulations.

Background

Intervention name

The intervention assessed by this health technology assessment (HTA) is the addition of a fetal MRI examination to the current management algorithm for fetuses considered by a fetal/maternal medicine unit to be at high risk of an abnormality of the head, selected masses of the neck, chest or abdomen

The procedure/test

The test is fetal magnetic resonance imaging using real-time single-shot fast spin-echo (RT SSFSE) imaging at 1.5T.

In the Victorian public sector, MRIs were performed using Siemens 1.5T Avanto scanners with mothers in the supine or left lateral decubitus position. 12 channel phased body array and small flex coils were used. Where compliance by mothers and fetus permitted, the following protocol was administered:

- T2 half fourier acquisition single shot turbo spin echo (HASTE) 3-4 mm slices preformed in 3 orthogonal planes to fetal anatomy (axial, coronal and sagittal).
- T1 weighted fast spoiled gradient recalled acquisition (FSPGR) in axial plane for fetal head and coronal plane for fetal body

- T2 star echo planar imaging (EPI) and diffusion weighted imaging.
- A thick slab (40-55 mm) MRCP haste sequence.
- Dependent on pathology demonstrated, a T2 steady state free precession (True Fisp) and T2 True Fisp cine were acquired. The planes best demonstrating the pathology were performed.

Proposed clinical place for fetal MRI

In Australian practice, ultrasound is routinely performed in clinically normal pregnancies at 19-22 weeks gestation to confirm fetal normality and well being and to perform an anatomical evaluation of the fetus for significant structural abnormalities. Fetal MRI is proposed to be used as an ancillary or complementary imaging technique to ultrasound. The objective of fetal MRI is to elicit further information to confirm or exclude the presence of suspected or detected fetal abnormalities detected by ultrasound or by clinical assessment and to determine whether other abnormalities exist.

Fetal MRI is being proposed as an adjunct investigation rather than as a substitute for ultrasound because, although fetal MRI offers some advantages over ultrasound (e.g. fetal MRI produces images with superior contrast resolution and offers advantages in assessment of intracranial structures that are obscured by the calvarium in ultrasound or where ultrasound is difficult due to oligohydramnios, patient body habitus or fetal lie), fetal MRI is also associated with limitations compared to ultrasound in some respects. For example, fetal MRI is inferior to ultrasound for assessment of structures such as the spine, the skeleton and the fetal heart; unlike ultrasound, fetal MRI cannot currently be used to provide dynamic information (e.g. fetal heart activity and breathing); fetal MRI examination must be targeted to a specific area of interest (e.g. fetal head) and therefore is not an appropriate tool for providing an overview of the fetus; and the use of fetal MRI is limited by fetal movement.

The additional information obtained by fetal MRI may permit a more accurate assessment of fetal diagnosis and prognosis, which may result in improved counselling and decision- making with respect to treatment of the fetus, management of the pregnancy, planning of the delivery (e.g., in terms of location or timing).

It has been proposed that the provision of fetal MRI should be limited to a select group of large public hospitals because of the specialised clinical expertise necessary and the requirement for access to specialised counselling. Fetal imaging is mainly undertaken on an outpatient basis.

Clinical Need

In Australia, data pertaining to rates of birth defects is obtained by different state registries. In Victoria, the Victorian Peri-natal Data Collection Unit is responsible for the collection of data of birth defects.

In Victoria, birth defects as a proportion of peri-natal mortality account for almost 25% of deaths (Riley, 2005). In 2003, the rate of birth defects, if only birth defects terminated after 20 weeks of gestation are included, was 4.0% (Consultative Council on Obstetric and Paediatric Mortality and Morbidity, 2005). This is comparable to the 5.0% rate of birth defects in Western Australia (Bower et

al, 2004) but twice as high as the birth defect rate of 2.0% in New South Wales in the same year (Centre for Epidemiology and Research, 2004).

The clinical implications of fetal abnormalities vary with the type and severity of the abnormality. While some abnormalities such as anencephaly are invariably fatal, other conditions such as hypospadia or obstructive disorders of the pelvis are rarely fatal, and other conditions such as neural tube defects are associated with developmental delay and poor quality of life (Riley andHalliday, 2008).

Ultrasound has been the mainstay of pre-natal diagnosis of fetal abnormalities for many years. It is capable of producing real-time, dynamic images with high anatomical and spatial resolution. It is also safe, relatively inexpensive and widely available (Ismail et al, 2002; Whitby et al, 2004a). It is, however, limited by the presence of maternal obesity and/or oligohydramnios and the fact that it is an operator dependent technique (Ismail et al, 2002; Blaicher et al, 2005).

Although the use of fetal MRI was initially constrained by concerns about safety, maternal anxiety and poor image quality resulting from maternal or fetal movement during imaging, in recent years the use of rapid acquisition imaging modalities such as single-shot fast spin echo (SSPE) and half-Fourier acquisition turbo spin echo (HASTE) have led to dramatic improvements in image quality. This improvement in image quality and evidence from studies suggesting that fetal MRI may have some advantages over ultrasound for some anatomical systems and disease processes has resulted in an increase in the use of fetal MRI as an adjunct to ultrasound in Europe and USA. Although fetal MRI is not an operator dependent technique, its use requires an excellent understanding of normal fetal anatomy (Whitby et al, 2004a; Perrone et al, 2008).

Existing procedures /tests

In Australia current recommended practice for screening for developmental abnormalities during pregnancy is for fetal ultrasound between 18-22 weeks of gestation. The purpose of this ultrasound is to assess fetal morphology and localisation of the placenta (The Royal Australian and New Zealand College of Obstetricians and Gynaecologists, 2009).

Marketing status of device / technology

Magnetic resonance devices by Toshiba, GE Medical, WIG 2005, Siemens Ltd., and Phillips & Taylor are currently registered with and approved by the TGA for full body imaging.

Current reimbursement arrangements

Ultrasound remains the gold standard for the detection of fetal abnormality. Ultrasound screening for fetal abnormalities is reimbursed through Medicare from the first trimester. Reimbursement for fetal MRI is not currently available through Medicare.

Review of the published evidence

Safety

Most of the evidence regarding the safety of fetal MRI comes from studies in animals. The three potential sources of known adverse effects are the three components of the MRI system. These are the static magnetic field, time-varying gradient fields and the pulse radio-frequency fields (De Wilde et al, 2005).

The static magnetic field strengths used in routine clinical practice range from 0.2 to 2 teslas (T). Some specialist sites may use field strengths of 3T, and some research sites have up to 8T systems. However, it is still not clear what danger these fields pose for the fetus, as most of the available evidence comes from animal studies. The major dangers of the static magnetic field are biological effects, implant and monitoring device malfunction and movement (De Wilde et al, 2005).

The effect of interest in fetal MRI is biological. Studies of the effect of static magnetic fields on human cultured cells show a lack of effect on growth, cell division, multiplication and differentiation (Sato et al, 1992; Kula et al, 1996). This is supported by the findings of the study of Kanal et al (1993) in which pregnant women working with MRI showed no statistically significant difference, between those exposed and those not exposed, in terms of fertility, length of gestation, birth weight and other pregnancy outcomes.

The danger to the fetus from the pulse radio-frequency fields generated by MRI is mainly due to thermal heating. An increase in embryonic temperature of 2°C over a 24 hour period, especially during organogenesis, can result in fetal brain damage and neural tube defects (Edwards, Saunders & Shiota, 2003). However, animal studies conducted do not show any evidence of this effect in pregnant animals at different sequences using HASTE (Kawabata et al, 2003; Levine et al, 2001).

The main dangers posed to the fetus by the time varying magnetic gradient fields are due to the noise levels generated by Lorentz forces. According to Etzel et al (1997) these noise levels may result in a loss of fetal hearing, a shortening of the pregnancy or low infant birth weight. The intensity of the noise produced is proportion to the magnetic field intensity. In a 0.2T scan the intensity of the noise produced is only 75dB, whereas in a 3T scan it can be up to 115dB. No studies have been conducted that have established that the noise produced by fetal MRI at 1.5T can lead to damage to the fetus. One study attempted to measure the degree to which the pregnant abdomen would attenuate the noise of MRI, by introducing a microphone in the abdomen of a male volunteer. However, this does not faithfully reproduce the fetus in all phases of pregnancy (Glover et al, 1995).

In general, animal studies have looked at the effects of all the above risks working in concert and have reported that the likely effects of MRI on biologic factors such as fetal growth and postpartum mortality are likely to vary with the field strengths used.

There are few studies of the safety of MRI in humans. Baker et al (1994) conducted a three year follow up of 20 children examined in utero at 0.5T and reported no significant increase in morbidity in these children. Surveys of children exposed to MRI in utero have not detected any adverse outcomes later in life (Levine 2004; Sandrasegaran et al 2006). Myers et al (1998) found no statistically significant differences in intrauterine growth between a group of 74 women who underwent MRI and a control group of 148 women who did not.

From the limited amount of evidence available it appears that although there is a theoretical risk associated with the use of fetal MRI this has, to date, not translated to a detectable risk in practice at the field strengths used in this population. A positive aspect of MRI is that it does not use ionising radiation to obtain images, it is therefore considered to be a safe technology for use in pregnant women.

Effectiveness

The studies contained in the review are of the diagnostic accuracy of fetal MRI, located by a pragmatic search of the literature. Not all studies located by the search are included in the review (e.g., only prospective studies are presented as the evidence from retrospective studies is considered to be of poorer quality). Appendix A summarises the NHMRC designated levels of evidence and Appendix C provides a profile of all studies included in the review.

The available evidence groups studies for various types of fetal abnormalities and evidence for each type of abnormality (i.e., by body system) is discussed separately.

Central nervous system abnormalities

Twelve prospective studies are included in the evidence review which is provided at Table 4. Most of these studies are prospective diagnostic accuracy studies that compare the diagnosis obtained through the use of ultrasound to that obtained through the use of fetal MRI (level III-2 diagnostic evidence). As noted, the proposed use of fetal MRI in the Victorian public sector is as an adjunct to ultrasound in diagnosing fetal abnormalities. Therefore, the focus of the review presented in Table 4 is on the additional information provided by fetal assessment by MRI following detection of anomalies by prior ultrasound.

Table 4: Central nervous system abnormalities detected by fetal MRI

Study	Diagnostic level of evidence	Study design	Population	Outcomes
Manganaro et al (2009)	III-2	Prospective diagnostic accuracy on MRI and ultrasound Reference standard=post natal MRI, or biopsy	59 fetuses (4 twins), with 55 suspected of ventriculomegaly diagnosed on ultrasound.	29/55 suspected of isolated ventriculomegaly <u>Ultrasound</u> 26/55 ventriculomegaly 18/55 (33%) with CNS abnormalities 8/55 (15%) no CNS abnormalities. <u>MRI</u> 26/55 (47%) ventriculomegaly with CNS abnormalities 10/55 (18%) no CNS abnormalities

Study	Diagnostic level of evidence	Study design	Population	Outcomes
Saleem et al (2009)	III-2	Prospective diagnostic accuracy on MRI and ultrasound Reference standard=pathology in TOP, or combination of post-natal MRI, surgery, and post-natal clinical confirmation.	19 fetuses suspected of neural tube defects diagnosed on ultrasound	MRI 1/19 ruled out cephalocele 5/18 detailed topography and contents of neural tube sac 3/18 additional CNS abnormalities 3/18 confirmed non-CNS finds Change in diagnosis 3/19 change in diagnosis 5/19 minor change in diagnosis 11/19 concordant with ultrasound Change in management 4/19 (21%) changed/modified management decision
Levine et al (2008)	III-2	Prospective diagnostic accuracy on MRI and ultrasound Reference standard not stated	200 fetuses with suspected ventriculomegaly diagnosed on ultrasound	Final consensus diagnosis 198 ultrasound 198 MRI 196 ultrasound-MRI comparisons Prospective agreement on diagnosis 118/198 (60%) ultrasound 104/198 (53%) MRI 83/104 final diagnosis isolated 118/198 prospective agreement
Papadias et al (2008)	III-2	Prospective diagnostic accuracy on MRI and ultrasound Reference standard = post-natal clinical confirmation	13 fetuses with suspected CNS defects diagnosed by ultrasound that would require surgery after birth. Post-natal MRI performed to confirm pre-natal MRI findings	13/13 (100%) fetuses had a CNS defect confirmed by MRI 2/13 (15.4%) did not require post-natal surgery (The actual diagnosis of a particular condition was incorrect (discordant) in some cases but all had a confirmed post-natal CNS defect. Discordant diagnosis Total 3/13 (23.1%) Myelomeningocele 1/7 (14.3%) Meningocele 1/1 (100%) Occipital meningocele 0/1 (0%) Diastematomyelia 1/1 (100%) Isolated hydrocephalus 0/3 (0%)

Study	Diagnostic level of evidence	Study design	Population	Outcomes
Tilea et al (2007)	III-2	Prospective diagnostic accuracy on MRI and ultrasound Reference standard = post mortem confirmation	25 fetuses with suspected posterior fossa malformations diagnosed by ultrasound	25/25 (100%) fetuses had a malformation of the posterior fossa confirmed by MRI, resulting in the termination of the pregnancy at a mean gestational age of 33 weeks. The decision to terminate was correct in each case. <u>Discordant diagnosis</u> Total 9/25 (36%) Vermian hypoplasia 4/25 (16%) Partial vermian agenesis 0/25 (0%) Cerebellar hemisphere hypoplasia 3/25 (12%) Brain stem hypoplasia 1/25 (4%) Destructive lesions 1/25 (4%) 4/12 false positives for vermian hypoplasia, 0/6 dysplastic lesions diagnosed by MRI
Griffiths et al (2006)	III-2	Prospective diagnostic accuracy on MRI and ultrasound Reference standard = post-natal clinical or post-mortem confirmation	50 consecutive fetuses with suspected spine and spinal cord abnormalities diagnosed by ultrasound	40/50 (80%) ultrasound and MRI agreed 10/50 (20%) discordant diagnosis between ultrasound and MRI. Of these: 8/10 (80%) MRI identified as normal 2/10 (20%) misclassified diagnosis by ultrasound, MRI diagnosis confirmed by final reference diagnosis
Salomon et al (2006)	III-2	Prospective diagnostic accuracy on ultrasound and MRI. Reference standard = post-natal clinical confirmation	310 fetuses with suspected ventriculomegaly diagnosed by ultrasound. N=185 analysed (only those with isolated ventriculomegaly ≤12 mm	<u>Ultrasound</u> 114/185 (61.6%) suspected unilateral ventriculomegaly 71/185 (38.4%) suspected bilateral ventriculomegaly <u>MRI</u> 43/185 (23.2%) no abnormality 106/185 (57.3%) isolated ventriculomegaly (10-12 mm) 36/185 (MRI measured ventricle to be >12 mm MRI identified additional abnormalities in 5/106(4.7%) with isolated ventriculomegaly and 6/36 (16.7%) with measured ventricles >12 mm. Of these 6 underwent TOP (abnormalities conformed by pathology) and in 5 post-natal imaging confirmed pre-natal diagnosis
Garel et al (2004)	III-2	Prospective diagnostic accuracy on ultrasound and MRI.	28 fetuses with suspected cerebral ischemic lesions diagnosed by	24/28 (85.7%) findings additional to ultrasound findings 16/24 (66.7%) overlooked by ultrasound

Study	Diagnostic level of evidence	Study design	Population	Outcomes
		Reference standard = post-natal MRI confirmation	ultrasound	8/24 (33.3%) MRI revealed more extensive abnormality

Study	Diagnostic level of evidence	Study design	Population	Outcomes
Malinger et al (2004)	III-2	Prospective diagnostic accuracy on ultrasound, MRI and neurosonography Reference standard = post-natal clinical or post mortem confirmation	42 fetuses with suspected CNS abnormalities diagnosed by ultrasound	US NS MRI Sensitivity (%) 55 96 85 Specificity (%) 20 87 80 PPV (%) 55 93 88 NPV(%) 20 93 75 Measures of agreement Kappa p US/NS 0.105 0.73 US/MRI 0.175 0.33 US/post-natal 0.244 0.18 NS/MRI 0.483 0.002 NS/post-natal 0.842 <0.0001 MRI/post-natal 0.642 <0.0001
Whitby et al (2004b)	III-2	Prospective diagnostic accuracy on ultrasound and MRI Reference standard = post-natal clinical or post-mortem confirmation.	12 fetuses with suspected CNS abnormalities diagnosed by ultrasound	5/12 (42%) concordant diagnosis between MRI and ultrasound 7/12 (58%) discordant diagnosis between ultrasound and MRI 12/12 (100%) correct diagnosis on MRI χ 2= 9.88 (1 df), p< 0.01
Whitby et al (2004a)	III-2	Prospective diagnostic accuracy on ultrasound and MRI Reference standard = post-natal clinical or post mortem confirmation	100 fetuses with suspected CNS abnormalities diagnosed by ultrasound	52/100 (52%) concordant diagnosis with MRI and ultrasound 51/52 (98.1%) both ultrasound and MRI diagnoses agreed with definitive clinical or post-mortem diagnosis 12/100 (12%) MRI provided extra information which didn't affect clinical management 35/100 (35%) MRI diagnosis affected clinical management <u>Effect on clinical management</u> 6/100 (6%) MRI gave additional
Levine et al (2003a)	III-2	Prospective diagnostic accuracy on ultrasound and MRI Reference standard = post-natal clinical or post-mortem confirmation	214 fetuses diagnosed with suspected CNS abnormalities by ultrasound	Of the 214, confirmatory ultrasound normal in 69/214 Remaining 145 fetuses: 9/145 (6.2%) discordant diagnosis with MRI and confirmatory ultrasound 73/145 (50.3%) change in counselling 46/145 (31.7%) change in diagnosis 27/145 (18.6%) change in management
Ismail et al (2002)	III-2	Prospective diagnostic accuracy on ultrasound and MRI Reference standard = post-natal clinical or post-mortem confirmation	27 consecutive fetuses with suspected CNS abnormalities diagnosed by ultrasound	26/27 (96.3%) follow-up 15/26 (57.7%) concordant diagnosis with MRI and ultrasound 7/28 (26.9%) MRI changed diagnosis correctly 4/26 (15.4%) MRI misdiagnosed

Abbreviations : MRI=magnetic resonance imaging, CNS=central nervous system, TOP=termination of pregnancy, df=degree of freedom, NS=neurosonography, PPV=positive predictive value, NPV=negative predictive value

Manganaro et al (2009) report that an additional 14.5% of fetuses with ventriculomegaly with central nervous system (CNS) abnormalities and an additional 4% of fetuses with ventriculomegaly but no CNS abnormalities were detected by MRI compared to ultrasound alone. This was considered an important finding as the association of additional CNS diseases can markedly influence prognosis. Some studies report an increase in morbidity and mortality of 56% if CNS abnormalities are associated with ventriculomegaly (Manganaro et al, 2009).

Saleem et al (2009) report that, for fetuses referred with suspected findings of neural tube defects (NTD) on ultrasound, fetal MRI correctly established the diagnosis in all cases, including ruling out of an ultrasound diagnosis of cephalocele in a fetus with oligohydramnios and confirming the presence of NTDs in the other 18 cases. In a further 5 fetuses, MRI detected details of the NTD sac contents and topography that were hidden on ultrasound in five fetuses (however, these additional findings did not change the main diagnosis of the anomaly). In this study, fetal MRI correctly established the diagnosis made by fetal ultrasound and detected new findings unsuspected from the findings of ultrasound in 8/19 (42.1%) fetuses, although the new findings changed pre-natal diagnosis in only three cases (15.8%).

Griffiths et al (2006) report large numbers of changes in diagnosis when fetal MRI was used adjunctively to ultrasound. The study reported Griffiths et al (2006) was a prospective study although the aspect of the study that reported on clinical management was conducted retrospectively when it become clear that information gained from MRI impacted on clinical management. Of 50 consecutive fetuses with suspected spine and spinal cord abnormalities, there were 10 discordant diagnoses between diagnoses according to ultrasound and according to fetal MRI in the study. Based on the ultrasound diagnoses, termination was recommended in all 10 pregnancies as the fetuses were diagnosed as having category 3 abnormalities. Fetal MRI resulted in a revision to the ultrasound diagnoses in nine of the 10 fetuses - 8 of the 10 fetuses were reclassified as normal (category 1) and one was reclassified as category 2 abnormality (minor disability). All revised diagnoses were confirmed by post-natal clinical assessment.

Whitby et al (2004a) reported that in 35 of 100 (35%) fetuses with suspected CNS abnormalities, additional information was provided by MRI that modified the diagnosis and clinical management. The study reported by Levine et al (2003) included 145 fetuses with suspected abnormalities (145/214) after a confirmatory ultrasound. Fetal MRI changed the diagnosis in 46 (32%) cases, changed maternal counselling in 73 (50.3%) cases and changed clinical management in 27 (18.6%) cases. However, a weakness of this study, is that the ultrasound and fetal MRI findings could not be confirmed due to a lack of pathologic material after termination.

Sensitivity and specificity

One study reported the sensitivity and specificity of fetal MRI (Malinger et al, 2004). The purpose of this study was to determine if fetal MRI provided useful additional clinical information to that obtained by dedicated fetal neurosonography in fetuses with suspected brain anomalies. In this study, all 42 fetuses underwent ultrasound, fetal MRI and neurosonography for detection of CNS abnormalities at a mean gestational age of 30.2 weeks (range 23-37 weeks). Confirmation of abnormalities was provided by either post-mortem or post-natal findings. The study reported a

sensitivity and specificity for fetal MRI of 85% and 80% respectively, a positive predictive value (PPV) of 88% (abnormality correctly identified) and negative predictive value (NPV) of 75% (absence of abnormality correctly identified). The sensitivity, specificity PPV, and NPV for ultrasound in the same study was 55%, 20%, 55% and 20% respectively. Findings for neurosonography were higher than for MRI, with sensitivity, specificity, PPV and NPV of 96%, 87%, 93% and 93%. Although this study reports the rates of discordance between diagnoses made by fetal MRI and post-natal findings, it does not provide any information about a change in diagnosis as a result of the fetal MRI or whether these diagnoses were correct when compared to ultrasound.

Misdiagnosis by MRI

None of the prospective studies in Table 4 reported rates of misdiagnosis by fetal MRI. Only retrospective studies included results for this metric. Ismail et al (2002), which report that 15% of fetal MRI diagnoses were incorrect. Additionally, the study by Limperopoulos et al (2006) noted that 6/19 fetuses diagnosed with vermian hypoplasia were normal equating to a false positive rate of 32%. This study was conducted over a 5-year time frame, and the authors postulated that differences in fetal imaging technique and the accuracy of clinical interpretation may have improved with an increase in experience. This finding is supported by the study reported by Levine et al (2008), which found that a lack of experience in neuroradiology, as well as the use of different imaging techniques, increased variability in CNS diagnosis between ultrasound and fetal MRI.

Effect on clinical management

Saleem et al (2009) report that, following adjunctive fetal MRI in fetuses suspected of neural tube defects, 21% of patients (4/21) had a change/modification to clinical management. As discussed above, Griffiths et al (2006) reported on a change in management for 9/50 (18%) fetuses following fetal MRI. Whitby et al (2004a) report that fetal MRI provided additional information which effected clinical management in 6 of 100 cases and this information was confirmed by definitive clinical or post-mortem diagnosis. In another 29 out of the 100 cases, fetal MRI changed diagnosis; confirmed by either definite clinical or post-mortem diagnosis. Of these 29, the diagnosis was changed to normal for 11 fetuses. The study by Levine et al (2003), reported that 27 out of 145 fetus with suspected CNS abnormalities on confirmatory ultrasound, had a change in management post fetal MRI.

Abdominal and urinary tract malformations

Three prospective studies are included in the assessment of fetal MRI in detecting abdominal or urinary tract abnormalities (Table 5).

Table 5: Abdominal or urinary tract abnormalities detected by fetal MRI

Study	Diagnostic level of evidence	Study design	Population	Outcomes
Carcopino et al (2007)	III-2	Prospective diagnostic accuracy on ultrasound and MRI Reference standard = genetic (pre-natal) and post-natal clinical confirmation	17 fetuses with echogenic bowel diagnosed by ultrasound	Diagnosis 11/17 (64.7%) and MRI discordant diagnosis, normal 6/17 (35.3%) ultrasound and MRI concordant diagnosis, abnormal Of 11/17 MRI diagnosed as normal 11/11 (100%) were correctly diagnosed

Study	Diagnostic level of evidence	Study design	Population	Outcomes
				Of 1/17 MRI abnormal, incorrect diagnosis False positive rate =1/17 (5.9%)
Garel et al (2006)	III-2	Prospective diagnostic accuracy on ultrasound and MRI Reference standard = post-natal clinical or post-mortem confirmation	24 fetuses with suspected gastro-intestinal tract abnormalities diagnosed by ultrasound	Total discordant diagnosis by ultrasound compared to post-natal diagnosis 8/24 (33.3%) Total discordant diagnosis by MRI compared to post-natal diagnosis 3/24 (12.5%) <u>Duodenojejunal obstruction</u> 6/7 (85.7%) correctly diagnosed by ultrasound 6/7 (85.7%) diagnosis confirmed by MRI and post-natal diagnosis 1/7 (14.3%) discordant MRI diagnosis <u>Small bowel obstruction</u> 9/11 (81.9%) correctly diagnosed on ultrasound 10/11 (90.9%) correctly identified by MRI, confirmed by post-natal diagnosis 1/11 (9.1%) discordant MRI diagnosis <u>Large bowel obstruction</u> 3/3 (100%) discordant diagnosis on ultrasound 3/3 (100%) correctly diagnosed by MRI <u>Anorectal malformations</u> 2/3 (66.7%) discordant diagnosis on ultrasound 2/3 (66.7%) correctly identified by MRI, confirmed by post-natal diagnosis 1/3 (33.3%) discordant diagnosis on MRI MRI also overlooked 2/3 (66.7%) of associated recto urethral fistulas
Cassart et al (2004)	III-2	Prospective diagnostic accuracy on ultrasound and MRI Reference standard = post-natal clinical or post-mortem confirmation	16 fetuses with suspected urinary tract abnormalities diagnosed by ultrasound	11/16 (68.8%) MRI and ultrasound concordant diagnosis 5/16 (31.2%) MRI modified the diagnosis 4/5 (80%) of these resulted in a correct decision to terminate (n=3) or correct decision to continue the pregnancy (n=1).

The study by Carcopino et al (2007) reported that of 17 fetuses suspected on ultrasound of having an echogenic bowel (EB), 11 were correctly diagnosed by fetal MRI as being normal. However, fetal MRI also incorrectly diagnosed one case of echogenic bowel, a false positive rate of 5.9%. The study concluded that fetal MRI does not add significant data in cases of isolated EB, although in cases with bowel dilation, fetal MRI provides more accurate information than ultrasound. In the study of Garel et al (2006), when compared to post-natal diagnosis, fetal MRI was incorrect in 3/24 (12.5%) of cases

and ultrasound in 8/23 cases (33.3%). Fetal MRI and ultrasound performed similarly in the detection of gastrointestinal abnormalities. Concordant rates of diagnosis between ultrasound and fetal MRI were reported by Cassart et al (2004) in 11/16 (68%) of cases, but in 5 cases in disagreement fetal MRI correctly modified the initial ultrasound diagnosis, which resulted in 4/16 cases where pregnancy was terminated and 1/16 were it was continued the pregnancy.

High rates of discordance were found between ultrasound and fetal MRI in diagnosing gastrointestinal abnormalities (Carcopino et al, 2002 & Cassart et al, 2004). High rates of discordance for specific gastrointestinal conditions was also reported by Garel et al (2006), 67% for anorectal malformations but numbers in the study were small and in general this study reported good concordance between fetal MRI and ultrasound.

Multi-fetal gestations

Two studies, those of Kline-Fath et al (2007) and Hu et al (2006), are prospective cross classification studies on ultrasound and fetal MRI that include multiple pregnancies with suspected twin-twin transfusion system or various suspected complications. However, neither of the studies report outcomes with reference to post-natal clinical confirmation or another form of reference standard, so the reported diagnostic accuracy of fetal MRI is not verified.

Fetal abnormalities (various)

Two prospective studies are included in the assessment of fetal MRI in various fetal abnormalities (Table 6).

Table 6: Various fetal abnormalities detected by fetal MRI

Study	Diagnostic level of evidence	Study design	Population	Outcomes
Frates et al (2004)	III-2	Prospective diagnostic accuracy on ultrasound and MRI Reference standard = post-natal clinical confirmation	27* fetuses with suspected abnormalities (CNS, genitourinary system, thorax and facial) diagnosed by ultrasound	14/28 (50%) diagnoses by ultrasound and MRI correct when compared to post-natal diagnosis 7/28 (25%) MRI provided additional information to ultrasound 0/28 (0%) ultrasound provided additional information to MRI 3/28 (11%) MRI changed ultrasound diagnosis correctly 4/28 (14%) MRI diagnosis incorrect and ultrasound correct 7/28 (25%) both ultrasound and MRI incorrect diagnosis In total, MRI correct in 17/28 (61%) of cases.
Kubik-Huch et al (2000)	III-1	Prospective diagnostic accuracy on ultrasound and MRI Reference standard = post-natal pathology	27 fetuses (25 patients) (results are reported for 30 may reflect the spontaneous abortion and intrauterine death) Interpreters were blinded	1 Spontaneous abortion 2 labour induced due to intrauterine death 8/25 TOP 14/25 delivered normally Interpreters Agreement* Diagnostic accuracy Assessment of brain (A^z = 0.96) Spinal canal (A^z = 1.0) Uteroplacental unit (A^z = 0.93) Lungs (A^z = 0.91) Urinary tract ((A^z =0.79) Facial structures (A^z = 0.83) Extremities (A^z = 0.77), Heart (A^z = 0.63)

*One fetus had 2 diagnoses

#area under the curve, compared using Wilcoxon's signed rank test with Bonferroni adjustment. Score for each organ system, then correlated with the gestational age at the time of MR imaging using Spearman's rank correlation. MR imaging compared with ultrasound using the McNemar test, i.e. MR imaging scores categorised as either normal (1-3) or abnormal (scores 4 and 5).

The aim of the study of Frates et al (2004) was to compare ultrasound to MRI for the diagnosis of fetal abnormalities. Ultrasound and fetal MRI were performed within 15 days of each other and follow up information was available for a total of 27 fetuses with 28 diagnoses (1 fetus had 2 diagnoses). Fetal MRI and ultrasound were concordant in 50% of cases. In another 7/25 (25%) of cases, fetal MRI provided additional information to ultrasound and in three of these cases, fetal MRI correctly changed the diagnosis. However, the diagnosis made by fetal MRI was also found to be incorrect in 4/28 (14.3%) of cases. In total fetal MRI was correct in 17 (61%) of the 28 cases. In a reflection of the increased difficulty of a correct diagnosis where diverse abnormalities are present, both ultrasound and fetal MRI, were found to be incorrect in 7/28 (25%) of cases. A limitation of this study is the very small numbers of fetuses that were included in analysis of different body systems. Although 17 fetuses were examined for CNS abnormalities, there were only six with abnormalities of the thorax, four with abnormalities of the genitourinary system, and five, which were grouped as

'other', which was made up of one case of each of the following abnormalities; biliary tree, pelvic mass, complex facial cleft, cervical teratoma and sacrococcygeal teratoma.

Kubik-Huch et al (2000) reported that the diagnostic confidence score in assessing the heart was significantly lower than that of the brain, liver and spleen, urinary tract, spinal canal, and uterus and placenta ($p<0.001$), however, except for the brain and face numbers were quite small. Fetal MRI images were assessed independently by assessors blinded to sonographic results and the standards of reference. Fetal MRI was reported to have performed similarly to ultrasound in detecting abnormalities but was reported to be slightly superior at detecting cerebral abnormalities. Ultrasound performed better in detecting abnormalities of the face. Diagnostic confidence scores were reported to have significantly increased with gestational age at the time of fetal MRI imaging for the lung and spinal canal, and there was a positive trend in the diagnoses of facial structures, liver, spleen and urinary tract.

Oesophageal atresia

One study is included in the assessment of oesophageal atresia (Table 7).

Table 7: Oesophageal atresia detected by MRI

Study	Diagnostic level of evidence	Study design	Population	Outcomes
Langer et al (2001)	III-2	Prospective diagnostic accuracy on ultrasound and MRI Reference standard=post-natal clinical confirmation	10 fetuses	MRI 4/10 (40%) negative 6/10 (60% positive) Sensitivity 100% Specificity 80% PPV 83% Ultrasound PPV 60%

In Langer et al (2001), the study population was made up of 10 fetuses that had an unexplained polyhydramnios on ultrasound. Ultrasound examination and fetal MRI examinations were undertaken at gestational ages of 23 weeks and 31 weeks respectively. Post-natal diagnosis was confirmed by the passage of a nasogastric tube or radiological studies. Fetal MRI was reported to have a PPV of 83%, compared to a PPV for ultrasound of 60%. The change in diagnosis post fetal MRI scan was not reported.

Appraisal of the published evidence

Most of the evidence found by the literature search addresses the use of MRI in detecting fetal abnormalities of the CNS. This is consistent with the population included in the Victorian fetal MRI database in which CNS abnormalities dominate.

Overall there was considerable variability in the quality of the studies, which limits the degree to which an appraisal of the evidence is possible. Studies varied in respect of whether the investigators were blinded, the time between ultrasound and fetal MRI and the gestational age. Some studies reported that patients had received a confirmatory ultrasound, similar to the use of fetal MRI in the Victorian public sector. Whether patients received a confirmatory ultrasound prior to fetal MRI is

reported to impact on the benefit of fetal MRI. For example, in the study by Levine et al (2003), women referred due to a suspect ultrasound, had a confirmatory ultrasound performed two days prior to their fetal MRI. The authors reported that without this confirmatory ultrasound, the benefit of fetal MRI would have been perceived as greater. However, even with this confirmatory ultrasound, Levine et al (2003) did report a benefit in the use of adjunct fetal MRI.

A number of studies, in response to a large change in the ultrasound diagnosis after fetal MRI, comment on the potential for selection bias, in that cases are only referred for fetal MRI after ultrasound if they present as problematic, i.e. difficult or equivocal, therefore in this population there is the potential to overestimate the benefit of fetal MRI (Griffith et al 2006; Whitby et al 2004a). Although these studies argue that the referral of these patients represents a selection bias, it is only true if the assessment of fetal MRI is in comparison to ultrasound. Where the assessment is the use of fetal MRI as an adjunct to ultrasound, then this population would be a representative of the target population for this technology, as it is used in the Victorian public health system.

The role of fetal MRI, in pre-natal screening, is to not only confirm or exclude possible lesions but also to define their full extent, aid in their characterization, and to demonstrate associated abnormalities. The diagnostic problems that can occur in the use of fetal MRI include, image acquisition and clinical interpretation. An investigation into the frequency and cause of disagreements in diagnoses between ultrasound and fetal MRI, for fetuses referred for ventriculomegaly found that there was a considerable variability in CNS diagnosis, in part due to errors in observation, lack of real-time ultrasound scanning, lack of neuroradiology experience, and modality differences in helping to depict abnormalities (Levine et al, 2008). The process by which fetal MRI has been implemented into the Victorian public health system and its location within large teaching hospitals, with access to specialists and interpretation undertaken by experienced radiologists, appears to have already addressed these issues.

The authors of the studies, presented in the evidence review, were generally supportive of the use of fetal MRI, with comments that it was a useful adjunctive tool to ultrasound in the evaluation of cerebral ventriculomegaly, for the additional information given to parents and for the possibility of change in the diagnosis, the counselling and the management of pregnancy (Manganaro et al, 2009), and an important adjunct to ultrasound in assessing NTDs (Saleem et al, 2009). Although supportive, Papadias et al 2008 cautioned that fetal MRI was not yet sufficiently accurate to allow counselling for termination of pregnancy.

In summary, the level of evidence in support of the use of MRI in the detection of fetal abnormalities is quite modest however the available literature is supportive of the use of fetal MRI as an adjunct to ultrasound, with positive comments about the ability of fetal MRI to provide improved visualisation and additional information to clinicians.

Clinically relevant outcomes following the use of fetal MRI

Uniform outcomes have not been reported in the literature. Most of the outcomes used in the studies would be considered to be clinically relevant, even if they didn't always result in a change in clinical management. Following the use of fetal MRI outcomes reported in studies assessing the diagnostic accuracy of fetal MRI were:

- In the studies, patients were referred for fetal MRI having already received an ultrasound and a suspected diagnosis. If interpretation of the fetal MRI

provided a diagnosis different to the ultrasound diagnosis, then this was reported as the *proportion of discordant diagnosis* and also often disaggregated in relation to the specific condition under investigation (if more than one condition was detected). This outcome did not rely on any reference standard.

- If after fetal MRI, the diagnosis was changed from that made through the use of ultrasound, then this was reported as the *proportion with a change to the diagnosis*. This outcome did not rely on any reference standard.
- If after screening with fetal MRI, additional information in the form of additional abnormalities or more extensive abnormalities than were reported by ultrasound, then this was reported as the *proportion with additional information from MRI*.
- If as a result of fetal MRI there was a change in diagnosis or additional information was made available and this lead to a change in management of the patient (a change in diagnosis or increase in available information did not always lead to a change in patient management) then this was reported in the studies as the *proportion with a change in management.*
- For some studies, if the reference standard confirmed the diagnosis, then this was reported as the *proportion with a correct diagnosis*, or true positive.
- If the reference standard did not confirm the diagnosis, then this was reported as the *proportion with an incorrect diagnosis*, or false positives.

The patient outcomes that are used in the studies of the efficacy of fetal MRI in the Victorian public sector, listed below, are consistent with the outcomes that were found in the published literature. Because outcome data, in the form of post-mortem is not available in the database, clinically relevant outcomes, such as the proportion of patients with a correct diagnosis were not able to be ascertained. The outcomes are however, more specific to the consequences of a change in the plan of management, in terms of further testing and potential resource use.

The following are patient outcomes used in studies of the efficacy of fetal MRI.

- Frequency of change in assessment of outcome for the fetus in terms of risk of spontaneous death of the fetus during pregnancy or neonatal life vs. risk of severe disability vs. risk of mild disability vs. normal or near normal outcome (% number of cases).
- Frequency of clinically significant change to clinical diagnosis
- Frequency of change to the plan of management. In patients, where a change to plan of management was reported:
    - Frequency of additional ante-natal testing being indicated;
    - Frequency of change to the surgical plan for the fetus;
    - Frequency of change to the site-or method or timing of delivery
- Assessment of change to certainty around likelihood of fetal outcome (i.e. prognosis); and
- Assessment of change in understanding of likely outcome for patient.

Cost Effectiveness Literature

No studies were identified that estimated the cost-effectiveness of fetal MRI in the detection of fetal abnormalities.

Fetal MRI in the Victorian public health sector

The Victorian Policy Advisory Committee on Clinical Practice and Technology (VPACT) approved temporary funding of fetal MRI at the Monash Medical Centre, the Royal Children's Hospital and the Austin Repatriation Hospital in the 2007-2008, 2008-2009 and the 2009-2010 financial years[iii,iv]. One of the conditions of the temporary funding was collection of data to permit review of the technology to permit a review of the suitability of the technology for ongoing funding. This section presents a summary of the data that was collected to satisfy this condition.

All women referred to Monash Medical Centre for further assessment from a tertiary level, multidisciplinary fetal/maternal medicine unit (either the Fetal Diagnostic Unit at Monash Medical Centre; the Fetal Management Unit at the Royal Women's Hospital or the Prenatal Medicine Department, Mercy Hospital for Women) were assessed by the hospital's multi disciplinary fetal/maternal medicine unit. Following assessment those women whose fetuses were suspected to have abnormality/abnormalities incompletely defined, equivocal or unconfirmed and in whom a fetal MRI was indicated were prospectively included in the study (unless MRI was contraindicated).

The overall research question that this collection of data is used to inform is "What is the incremental effectiveness, safety, and cost-effectiveness of adding a fetal MRI examination to the current management algorithm for fetuses considered by a fetal/maternal medicine unit to be at high risk of an abnormality of the head, selected masses of the neck, chest or abdomen?"

Overall study design and plan

The data collection exercise could be described as a prospective study with a pre and post observational design, with diagnosis and prognosis for the fetus based on the referrer's assessment prior to fetal MRI representing outcomes for the control and diagnosis and prognosis for the fetus post-fetal MRI representing outcomes for the intervention of interest.

The study population consists of women who were referred for further assessment to either the Fetal Diagnostic Unit at Monash Medical Centre; the Fetal Management Unit at the Royal Women's Hospital or the Perinatal Medicine Department, Mercy Hospital for Women and in whom the fetal/maternal medicine unit (with access to a multidisciplinary team of health professionals) determined an fetal MRI was indicated.

Patient privacy through this data collection exercise was protected through the de-identification of patient data and its storage in a password protected Microsoft Access database, with access to the database restricted to the Database Manager. Information that could be used to identify patients was stored in a locked office, with access restricted to the Database Manager.

The radiologists conducting the fetal MRI and interpreting the results of the fetal MRI were not blinded to assessments made prior to fetal MRI that led to the referral for fetal MRI.

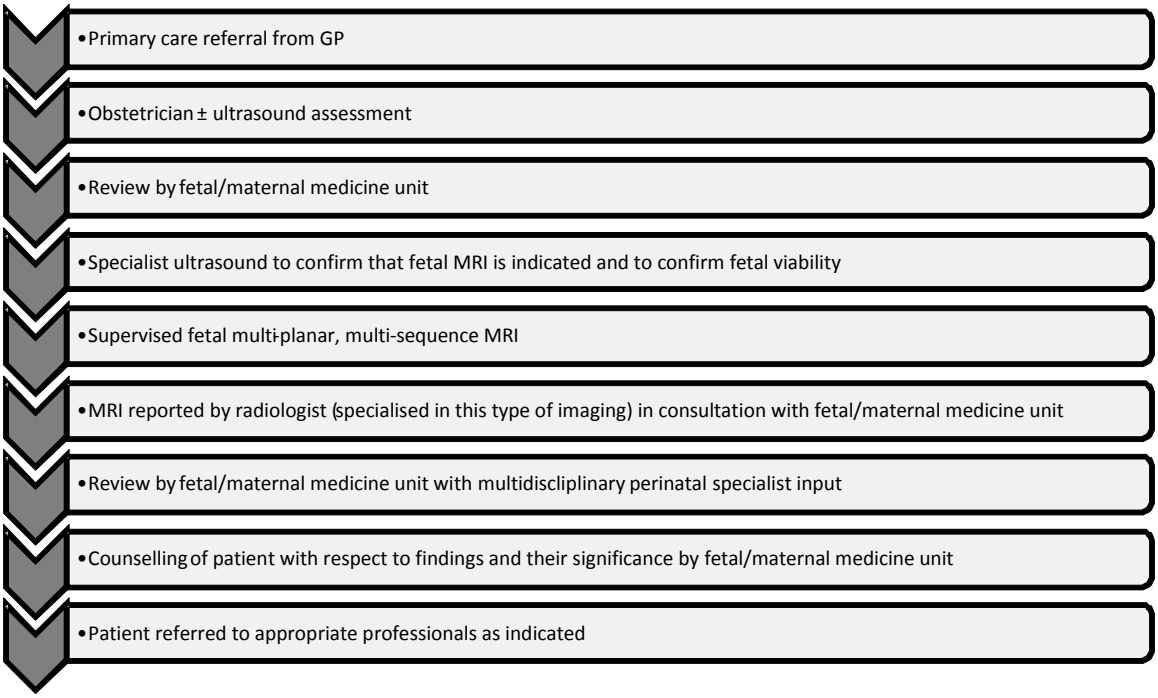
Important factors that may have influenced outcomes associated with fetal MRI delivered in the public sector, and which need to be considered in the application of the evidence in practice include:

[iii] http://www.health.vic.gov.au/newtech/documents/news0409.pdf [Last accessed: 8 March 2010]
[iv] http://www.health.vic.gov.au/newtech/documents/news0709.pdf [Last accessed: 8 March 2010]

- Referrals for fetal MRI were required to be made by a tertiary level, multidisciplinary, fetal/maternal medicine unit with access to obstetricians, fetal medicine specialists, obstetric sonologists, neonatologists, paediatric subspecialists, geneticists, genetic counsellors, social workers, pathologists, psychiatrists and paediatric/peri-natal radiologists.
- After referral to a fetal/maternal medicine unit the case was reviewed by a multi-disciplinary panel of clinicians, who decided whether or not a fetal MRI was indicated. In the majority of cases a repeat ultrasound was conducted.
- In patients for whom fetal MRI was considered indicated, the MRI was scheduled within two weeks of the assessment by the fetal/maternal medicine unit.
- Fetal MRI was only conducted by MRI units with specialist technical and clinical expertise in this type of imaging.
- To avoid distressing and expensive recall of patients due to technically deficient scans (which can occur as a result of fetal motion), fetal MRI studies were checked for technical quality on the operator's console prior to permitting the patient to leave the MRI suite.
- Interpretation of the MRI took place in the context of the findings of the full pre-referral clinical, sonographic, biochemical and genetic evaluation.
- Reporting of the MRI was conducted promptly (within 48 hours) to facilitate prompt counselling of the patient so that distress often experienced while waiting for test results was minimised.
- A continuous learning program was in place that involved regular peer review meetings where difficult or interesting cases were discussed.
- Results of the MRI were conveyed to the fetal/maternal medicine unit as the referrer and not directly to the patient so that the information provided by the MRI was placed in context with other available information and a plan of further management available to the patient.

Figure 1 illustrates the context in which fetal MRI was conducted in the Victorian public sector.

Figure 1: Illustration of care continuum incorporating fetal MRI as adopted in this study



Intervention

The intervention used in the Victorian public sector was second or third semester fetal MRI, without the use of an intravenous contrast agent. MRIs were performed using Siemens 1.5T Avanto scanners with mothers in the supine or left lateral decubitus position. 12 channel phased body array and small flex coils were used. Where compliance by mothers and fetus permitted, the following protocol was administered:

- T2 half fourier acquisition single shot turbo spin echo (HASTE) 3-4 mm slices preformed in 3 orthogonal planes to fetal anatomy (axial, coronal and sagittal).
- T1 weighted fast spoiled gradient recalled acquisition (FSPGR) in axial plane for fetal head and coronal plane for fetal body
- T2 star echo planar imaging (EPI) and diffusion weighted imaging.
- A thick slab (40-55 mm) MRCP haste sequence.
- Dependent on pathology demonstrated, a T2 steady state free precession (True Fisp) and T2 True Fisp cine were acquired. The planes best demonstrating the pathology were performed.

Assessments

Prior to the patient undertaking the fetal MRI, the clinician at the fetal/maternal medicine unit referring the patient was required to complete the data sheet provided at Appendix D. Assessments made by the referring clinician at the fetal/maternal medicine unit at this time included:

- Listing of clinically important diagnoses. For each diagnosis, the clinician was also requested to rate their confidence around the nature/extent of these abnormalities (rated as possible, probable, or definite)
- Assessment of likely outcome for fetus in terms of:
    - risk of spontaneous death of the fetus during pregnancy or neonatal life;
    - risk of severe disability;
    - risk of mild disability and;
    - normal or near normal outcome.

    Each outcome was requested to be rated as unlikely [<10%], possible [10-50%], probable [51-70%] or very likely [>70%]).

After the fetal MRI, the radiologist interpreting the results of the fetal MRI was requested to complete the questionnaire provided at Appendix E. Assessments made by the clinician at this time included:

- Clinically important diagnoses. For each diagnosis, the clinician was requested to rate their confidence around the nature/extent of the abnormalities (rated as possible, probable, or definite)
- Assessment as to whether any diagnoses that were not suspected (on ultrasound) were identified by the MRI (yes/no and if yes, list)
- Assessment as to whether any diagnoses that were suspected (on ultrasound) were excluded by the MRI (yes/no and if yes, list)

After the fetal MRI, the referring clinician at the fetal/maternal medicine unit was requested to complete the questionnaire provided at Appendix F. Assessments made by the referring clinician at this time included:

- Assessment of likely outcome for fetus based on results of both ultrasound and MRI in terms of:
    - risk of spontaneous death of the fetus during pregnancy or neonatal life;
    - risk of severe disability;
    - risk of mild disability or;
    - normal or near normal outcome.

    Each outcome was requested to be rated as unlikely [<10%], possible [10-50%], probable [51-70%] or very likely [>70%])

- Assessment as to whether there had been a significant change to the diagnosis as a consequence of information provided by the MRI (Yes/No)
- Assessment as to whether there had been a change to the plan for managing the patient as a consequence of information provided by the MRI (Yes/No)
- If the clinician indicated that there had been a change to the plan for managing the patient, the clinician was requested to provide a yes/no response to the following statements:
    - Further antenatal testing will be done / would have been recommended that would NOT have been done based on result of ultrasound alone;
    - Plans for fetal surgery have been / would have been made, cancelled or changed in some way;
    - Plans for the site OR method OR timing of delivery have been / would have been changed as a result of the MRI;
    - Assessment as to whether information provided by the MRI would have affect the counseling of the patient in regard to likelihood of fetal disability or fetal outcome (more certain/less certain/unchanged);
    - Assessment as to whether the patient's understanding of the likely outcome for fetus has changed (improved/unchanged/decreased) as a result of the findings of the MRI.

For a subset of patients with actual outcomes (as opposed to suspected or predicted), from the findings of autopsy and/or post-mortem assessment, or post-natal assessment, the following information was also collected:

- Outcome (birth, termination of pregnancy, fetal demise in utero, fetal demise in post-natal period) and;
- Diagnosis and severity of disability, based on findings of autopsy and/or post-mortem assessment or post-natal assessment.

Outcomes assessed

The primary outcome used to analyse the data collected in the Victorian public sector is:

- Frequency of change to assessment of outcome for fetus in terms of risk of spontaneous death of the fetus during pregnancy or neonatal life versus risk of severe disability versus risk of mild disability versus normal or near normal outcome (% number of cases)

This outcome has been nominated as the primary outcome as the assessment of outcome for the fetus represents the most patient-relevant outcome and is the basis for counseling of the patient and for parental decision-making. It is likely to be the most important factor taken into consideration by parents in deciding whether to continue or terminate the pregnancy and, if continuing with the pregnancy, planning for the time after the delivery.

The secondary outcomes analysed include:

- Frequency of clinically significant change to clinical diagnosis;
- Frequency of change to plan of management. In patients where a change to plan of management is reported:
  - Frequency of additional ante-natal testing being indicated;
  - Frequency of change to surgical plan for fetus;
  - Frequency of change to site or method or timing of delivery.
- Assessment of change to certainty around likelihood of fetal outcome (i.e., prognosis); and
- Assessment of change in understanding of likely outcome for patient.

In addition to the analyses above, as it was possible that a change to prognosis could occur where there was no change to diagnosis, (e.g., where further information about the severity of a condition might become available), the following assessments were also conducted:

- Frequency of change to prognosis; and
- Frequency of change to diagnosis or prognosis.

For the subgroup of patients for whom a final diagnosis was available from the findings of post-natal or post-mortem assessment, the frequency of difference between predicted diagnosis and actual diagnosis has also been estimated. The results from this analysis would generally be considered to permit an assessment of the accuracy (in terms of sensitivity and specificity) of an algorithm that incorporates fetal MRI in fetuses with suspected abnormalities.

Exploratory subgroup analysis of outcomes were planned to be conducted according to the following parameters:

- by certainty of assessment of diagnosis following confirmatory ultrasound (uncertain, probable, very likely/definite)
- by the location of the suspected abnormality (cranial, neck, chest, abdomen).

The purpose of these subgroup analyses is to examine whether fetal MRI may be more useful in some scenarios compared with others (e.g., fetal MRI may be more useful when the diagnosis/prognosis following confirmatory ultrasound is uncertain compared to when it is definite).

Statistical methods

Prior to commencement of the study, it was estimated that a total of approximately 400 women would be assessed by fetal RMI over the period of the study. The only baseline characteristics recorded for patients recruited to the study include was gestation at the time of the MRI. Descriptive statistics (specifically, mean, standard deviation, median, and range) have been used to describe the population in terms of this parameter.

To analyse the primary outcome, a matrix was constructed that summarised likely outcome for the fetus according to ultrasound and likely outcome for the fetus following fetal MRI.

Some patients were referred by the fetal/maternal medicine unit for a second MRI. Post-MRI questionnaires were not completed in these instances. Thus, analyses conducted above only take into consideration assessments and diagnoses made after the first MRI.

In the case of twin pregnancies, there is potential for an abnormality to be suspected in one or both of the fetuses. The analysis specifies details of number of twin pregnancies and whether one or both of the fetuses were suspected to have abnormalities.

The analysis assumes that data entry to the Microsoft Access Database is complete and accurate. Where data were missing (e.g., if confidence in the diagnosis of suspected abnormalities on ultrasound or MRI is not recorded), outcomes have been analysed on the basis of the total number of completed responses.

Results

Patient characteristics

A total of 269 women (and 270 fetuses) were referred, by either the Fetal Diagnostic Unit at Monash Medical Centre, the Fetal Management Unit at the Royal Women's Hospital, or the Perinatal Medicine Department at Mercy Hospital for Women to the Medical Imaging Departments at either the Monash Medical Centre, Royal Children's Hospital or the Austin Repatriation Hospital for assessment by fetal MRI in the period from 1 November 2006 to 19 November 2009. These women are all included in the Victorian fetal MRI Project. The baseline characteristics of these women are summarised in Table 8.

Table 8: Baseline characteristics of the women included in the Victorian fetal MRI project

Parameter	
Women (fetuses)	269 (270)
Mean gestation at MRI assessment (based on reported gestation for 247 women; gestation not reported for 22 women)	27.8 weeks (SD: 5.25 weeks) Range: 17 - 40 weeks
• Singleton pregnancy • Twin pregnancy	248 (92%) 21 (8%)
Centre where fetal MRI was performed • Monash Medical Centre • Royal Children's Hospital • Austin Repatriation Hospital	 90 (33%) 156* (58%) 23 (9%)
Body system in which abnormality was suspected (prior to fetal MRI) • Cranium • Neck • Chest • Abdomen • Other • Not recorded or not able to be determined	 194 (72%) 9 (3%) 30 (11%) 4 (1%) 29 (11%) 4 (1%)

* One of the records included in this statistic relates to outcomes for a twin pregnancy where both twins were suspected of having abnormalities

Evaluation of outcomes

Primary outcome

Clinicians were asked to assess the likely outcome (prognosis) for the fetus prior to MRI and then again after the MRI for the following four categories:

- risk of spontaneous death of the fetus during pregnancy or neonatal life;
- risk of severe disability;
- risk of mild disability or;
- normal or near normal outcome.

Clinicians rated each outcome as unlikely [<10%], possible [10-50%], probable [51-70%] or very likely [>70%]). Outcomes that were rated "very likely" were assumed to be the anticipated prognosis. In the case that more than one outcome was rated "very likely", then the more severe of these outcomes was assumed to be the anticipated prognosis. If no outcome was rated "very likely" but one or more outcomes was rated "probable", then the most severe of the "probable" outcomes was assumed to be the anticipated prognosis. Where no outcome was rated "probable" or "very likely", then the anticipated prognosis was considered to be "uncertain".

The primary outcome assessed was the frequency of change to the assessment of likely outcome (prognosis) for the fetus. Results are summarised in Table 9. The shaded cells represent concordance between the prognosis before MRI and the prognosis expected after MRI.

Table 9: Results for frequency of change to the assessment of likely outcome (prognosis) for the fetus – all patients

		Prognosis - post-MRI						
		Normal	Mild disability	Severe disability	Spontaneous death	Uncertain	Not recorded	Totals
Prognosis - pre-MRI	Normal	69 (62%)	7 (6%)	5 (5%)	2 (2%)	8 (7%)	20 (18%)	109 (40%)
	Mild disability	7 (25%)	4 (14%)	8 (29%)	1 (4%)	3 (11%)	5 (18%)	28 (10%)
	Severe disability	2 (3%)	6 (10%)	32 (52%)	4 (6%)	3 (5%)	15 (24%)	62 (23%)
	Spontaneous death	0	1 (10%)	1 (10%)	4 (40%)	0	4 (40%)	10 (4%)
	Uncertain	24 (47%)	2 (4%)	4 (8%)	1 (2%)	13 (25%)	7 (14%)	53 (20%)
	Not recorded	2 (25%)	0	0	0	1 (13%)	5 (63%)	8 (3%)
	Totals	104 (39%)	20 (7%)	50 (19%)	12 (4%)	30 (11%)	54 (20%)	270 (100%)

In summary, there was a change to prognosis in 89 (33%) of cases examined, no change to prognosis in 122 (45%) of cases examined. Fetal MRI is potentially particularly helpful in the case where prognosis for the fetus is uncertain prior to fetal MRI. As can be seen from Table 9, 53 (20%) of cases were considered to have an uncertain prognosis at baseline but after fetal MRI, 24 (43%) of these fetuses were considered to have a "normal" prognosis. This change in prognosis is likely to provide substantial peace of mind in these women. It was not possible to assess whether there was a change in prognosis for 59 (22%) cases due to missing data.

Although sub-group analyses had been planned that would assess the frequency of change to the assessment of likely outcome (prognosis) for the fetus by the location of the suspected abnormality (cranial, neck, chest, abdomen, etc), these analyses were not conducted as the large majority of fetuses had an abnormality suspected in the cranium. This meant that sample sizes for the other groups were small (see Table 8) and insufficient to conduct a meaningful analysis.

Sub-group analyses by degree of certainty around diagnosis prior to MRI were conducted and are presented in Table 10, Table 11 and Table 12. There was a change to prognosis in 39 (35%), 36 (30%) and 12 (39%) of cases where the diagnosis was “definite”, “probable” and “uncertain, respectively. There was no change to prognosis in 49 (44%), 56 (47%) and 15 (48%) of cases where the diagnosis was “definite”, “probable” and “uncertain, respectively. The results appear to suggest, somewhat unexpectedly, that fetal MRI is associated with similar frequencies of change to prognosis regardless of the certainty around the diagnosis.

Table 10: Results for frequency of change to the assessment of likely outcome (prognosis) for the fetus for the 111 fetuses in whom the diagnosis prior to MRI assessment was rated “definite”

		Prognosis - post-MRI						
		Normal	Mild disability	Severe disability	Spontaneous death	Uncertain	Not recorded	Totals
Prognosis - pre-MRI	Normal	25 (64%)	2 (5%)	1 (3%)	1 (3%)	3 (8%)	7 (18%)	39 (35%)
	Mild disability	2 (20%)	3 (30%)	1 (10%)	1 (10%)	1 (10%)	2 (20%)	10 (9%)
	Severe disability	1 (3%)	4 (13%)	15 (47%)	2 (6%)	2 (6%)	8 (25%)	32 (29%)
	Spontaneous death	0	1 (13%)	1 (13%)	4 (50%)	0	2 (25%)	8 (7%)
	Uncertain	13 (68%)	1 (5%)	1 (5%)	1 (5%)	2 (11%)	1 (5%)	19 (17%)
	Not recorded	0	0	0	0	1 (33%)	2 (67%)	3 (3%)
	Totals	41 (37%)	11 (10%)	19 (17%)	9 (8%)	9 (11%)	22 (20%)	111 (100%)

Table 11: Results for frequency of change to the assessment of likely outcome (prognosis) for the fetus for the 120 fetuses in whom the diagnosis prior to MRI assessment was rated "probable"

		Prognosis - post-MRI						
		Normal	Mild disability	Severe disability	Spontaneous death	Uncertain	Not recorded	Totals
Prognosis - pre-MRI	Normal	31 (61%)	1 (4%)	3 (6%)	0	4 (8%)	11 (22%)	51 (43%)
	Mild disability	4 (27%)	1 (7%)	6 (40%)	0	2 (13%)	2 (13%)	15 (13%)
	Severe disability	1 (3%)	2 (7%)	16 (55%)	2 (7%)	1 (3%)	7 (24%)	29 (24%)
	Spontaneous death	0	0	0	0	0	1 (100%)	1 (1%)
	Uncertain	7 (32%)	0	2 (9%)	0	8 (36%)	5 (23%)	22 (18%)
	Not recorded	1 (50%)	0	0	0	0	1 (50%)	2 (2%)
	Totals	44 (37%)	5 (4%)	27 (23%)	2 (2%)	15 (13%)	27 (23%)	120 (100%)

Table 12: Results for frequency of change to the assessment of likely outcome (prognosis) for the fetus for the 31 fetuses in whom the diagnosis prior to MRI assessment was rated "uncertain"

		Prognosis - post-MRI						
		Normal	Mild disability	Severe disability	Spontaneous death	Uncertain	Not recorded	Totals
Prognosis - pre-MRI	Normal	11 (65%)	3 (18%)	1 (6%)	0	0	2 (12%)	17 (55%)
	Mild disability	1 (33%)	0	1 (33%)	0	0	1 (33%)	3 (10%)
	Severe disability	0	0	1 (100%)	0	0	0	1 (3%)
	Spontaneous death	0	0	0	0	0	0	0
	Uncertain	4 (40%)	1 (10%)	1 (10%)	0	3 (30%)	1 (10%)	10 (32%)
	Not recorded	0	0	0	0	0	0	0
	Totals	16 (52%)	4 (13%)	4 (13%)	0	3 (10%)	4 (13%)	31 (100%)

Secondary outcomes

The secondary outcomes assessed include:

- Frequency of clinically significant change to clinical diagnosis;
- Frequency of change to prognosis;
- Frequency of change to diagnosis or prognosis.
- Frequency of change to plan of management. In patients where a change to plan of management is reported:
  - Frequency of additional ante-natal testing being indicated;
  - Frequency of change to surgical plan for fetus;
  - Frequency of change to site or method or timing of delivery.
- Assessment of change to certainty around likelihood of fetal outcome; and
- Assessment of change in understanding of likely outcome for patient.

Results for these analyses are summarized in

Table 13 and Table 14.

Table 13 summarises results where outcomes involved a dichotomous yes or no response. Table 14 summarises results for outcomes that involved a categorical response from clinicians.

Table 13: Results for secondary outcomes that involved a dichotomous response (N=270)

Secondary outcome	Yes	No	Not reported
Clinically significant change to clinical diagnosis	64 (24%)	150 (56%)	56 (21%)
Change to prognosis	89 (33%)	122 (45%)	59 (22%)
Change to clinical diagnosis or to prognosis	123 (46%)	92 (34%)	55 (20%)
Change to planned clinical management	50 (19%)	165 (61%)	55 (20%)
Where a change to clinical management is reported (N=50)			
• Further antenatal testing is indicated that was not previously considered indicated	10 (20%)	40 (80%)	0
• Change in surgical plan for fetus	8 (16%)	42 (84%)	0
• Change in site or method or timing of delivery	25 (50%)	24 (48%)	1 (2%)

Results for a subgroup of 119 fetuses with a pre-FMRI diagnosis that included ventriculomegaly were similar as those for the entire population - a clinically important change to diagnosis was reported for 30 (25%) of cases. A change to prognosis was reported for 39 (33%) of cases.

Table 14: Results for secondary outcomes that involved a categorical response (N=270)

Secondary outcome	Responses

	More certain	Less certain	Unchanged	Not reported
Change in certainty around likelihood of fetal outcome (prognosis)	148 (55%)	13 (5%)	52 (19%)	57 (21%)
	Improved	Unchanged	Decreased	Not reported
Understanding of outcome for patient	126 (47%)	74 (27%)	5 (2%)	65 (24%)

Table 15 provides further detail a sub-group analysis examining the impact of information from the MRI on diagnosis in patients by level of certainty around diagnosis prior to the MRI.

Table 15: Results for impact of MRI on diagnosis

Patient group	Effect of MRI on diagnosis						Totals
	Changed		Unchanged		Not reported		
	n	%	n	%	n	%	
Patients with a diagnosis that is "definite"	17	15%	72	65%	22	20%	111
Patients with a diagnosis that is "probable"	35	29%	58	48%	27	23%	120
Patients with a diagnosis that is "uncertain"	12	39%	15	48%	4	13%	31
Patients for whom certainty around diagnosis is not reported	0	0%	5	63%	3	38%	8
All patients	64	24%	150	56%	56	21%	270

If it is assumed that results for patients with data on change to diagnosis are generalisable to patients in whom the change to diagnosis was not reported (i.e., assuming there is no systematic difference across these patient populations), then the proportions in Table 16 could be applied in an economic analysis. Overall, the subgroup analysis suggests that a change in diagnosis as a result of information from an MRI is less likely in patients with a “probable” diagnosis prior to MRI, compared with those that have an “uncertain” diagnosis prior to MRI and is even less likely in patients who have a diagnosis that is considered “definite” prior to MRI.

Table 16: Results for impact of MRI on diagnosis (excluding patients where certainty around diagnosis was not reported and excluding patients where the effect of the MRI on diagnosis was not reported.

Patient group	Effect of MRI on diagnosis				Totals
	Changed		Unchanged		
	n	%	n	%	
Patients with a diagnosis that is "definite"	17	19%	72	81%	89
Patients with a diagnosis that is "probable"	35	38%	58	62%	93
Patients with a diagnosis that is "uncertain"	12	44%	15	56%	27
All patients	64	30%	150	70%	214

Table 17 presents results indicating the proportion of patients in whom changes to diagnosis as a result of fetal MRI were correct, partially correct (i.e., where the fetal MRI provided further but incomplete information compared with the ultrasound) or incorrect. Results are presented only for a subgroup of 12 patients who had either a change to diagnosis predicted and in whom a final diagnosis was able to be determined from the findings of post-natal or post-mortem assessment. Results from this analysis indicate that changes in diagnoses due to fetal MRI were accurate in 58% of cases where a change in diagnosis was reported. In a further 25% of cases, MRI provided additional diagnostic information compared to ultrasound alone but where the diagnosis was incomplete given post-natal or post-mortem assessments (e.g., in one case, the MRI was correct in indicating that an additional brain abnormality causing small hemispheres was present but was incorrect in diagnosing the exact cause; in the second case MRI was correct in diagnosing a brain injury that was not seen with ultrasound but underestimated the extent of the injury; in the third case the MRI was correct in identifying that a chest mass was of rib origin however the type of tumour was not accurately diagnosed by MRI). In relation to the 17% of cases where the diagnosis by MRI was incorrect - in one case both the ultrasound and MRI suggested a diagnosis of CMV but the infant exhibited no features of congenital CMV infection at birth; in the other case, both MRI and ultrasound failed to diagnose extensive facial vascular malformation that was diagnosed postnatally.

The results from this analysis would generally be considered to permit an assessment of the accuracy (in terms of sensitivity and specificity) of an algorithm that incorporates fetal MRI in fetuses with suspected abnormalities. However, an implicit assumption in this consideration is that final diagnosis from findings of post-mortem or post-natal examination represent the gold standard. This assumption is not entirely valid as there is potential for confounding between the fetus' health state at the time of MRI examination and at the time of delivery, death, miscarriage or abortion (e.g., there may be progression or resolution of an abnormality in the intervening period or an unrelated abnormality may develop in the intervening period that will affect future health status). In addition, there is considerable debate about the validity of fetal post mortem performed on 2nd trimester fetuses as a gold standard due to the difficulty in performance and interpretation of the examination of the fetus by the pathologist. For example, removal of the brain from the cranium can result in disruption of intracranial cysts so that they are no longer visible and sectioning of the brain for histological examination is problematic due to its high water content. Thus, results in Table 17 should be interpreted with caution

Table 17: Results indicating whether predicted changes to diagnosis as a result of fetal MRI were correct according to post-natal or post-mortem assessment

Total number of patients with a change to diagnosis (N)	Patients with a change to diagnosis for whom diagnosis could be determined from a post-natal or post-mortem assessment n/N (%)	Proportion of patients with post-natal or post-mortem assessments in whom predicted change in diagnosis was correct		
		Correct	MRI added incomplete information	Incorrect
64	12 (19%)	7/12 (58%)	3/12 (25%)	2/12 (17%)

Analysis of incremental cost effectiveness of fetal MRI in the Victorian public sector

There are a number of ethical issues that are raised in attempting to conduct an economic analysis of an intervention that aims to diagnose abnormalities in fetuses. For example, some metrics would necessitate ethical judgements as to the social value in avoiding the birth of a child with an abnormality, valuation of benefits of greater certainty in prognosis for the fetus, valuation of the life-time costs of caring for a child with an abnormality, etc. To avoid such problems, a simple cost-effectiveness analysis that includes only the cost of the additional test and the associated review by the fetal/maternal medicine unit and based on the outcome of additional patient with a clinically meaningful and accurate change in diagnosis is estimated based on the results of this study.

> The cost of a new MRI scanner in Australia has been estimated to be approximately $1.5-2.5 million depending on the options, specifications and building requirements (Source: ANZHN). The cost of an additional fetal MRI, has been estimated at $448 (estimated by Monash Medical Centre Finance Department; personal communication from Dr Goergen). Fetal scanning is predominantly undertaken on an outpatient basis. Additional costs associated with the introduction of use of fetal MRI include costs of an additional review by the fetal/maternal medicine unit. These have been difficult to ascertain. For the purposes of the cost-effectiveness analysis presented below, they have been estimated at $175.

An economic evaluation was conducted with a structure as summarised in Figure 2. Essentially all patients undergoing MRI are attributed with incremental costs of an MRI examination (costed at $448) and the costs of an additional review by the fetal/maternal medicine unit (estimated at $175). The proportion of patients with a change to diagnosis (24%; 64/270) are classified into three groups: (i) those in whom the diagnosis following fetal MRI is accurate compared with the diagnosis prior to fetal MRI (58%; 7/12); (ii) those in whom the diagnosis was correct prior to fetal MRI and incorrect after fetal MRI (0%); (iii) those in whom the diagnosis did not change as a result of fetal MRI or in whom although the MRI added some diagnostic information, it did not provide a completely accurate diagnosis. Patients who gain an accurate diagnosis are valued at 1 and those losing an accurate diagnosis are valued at -1. Patients who do neither gain an accurate diagnosis nor lose an accurate diagnosis are assigned a value of zero.

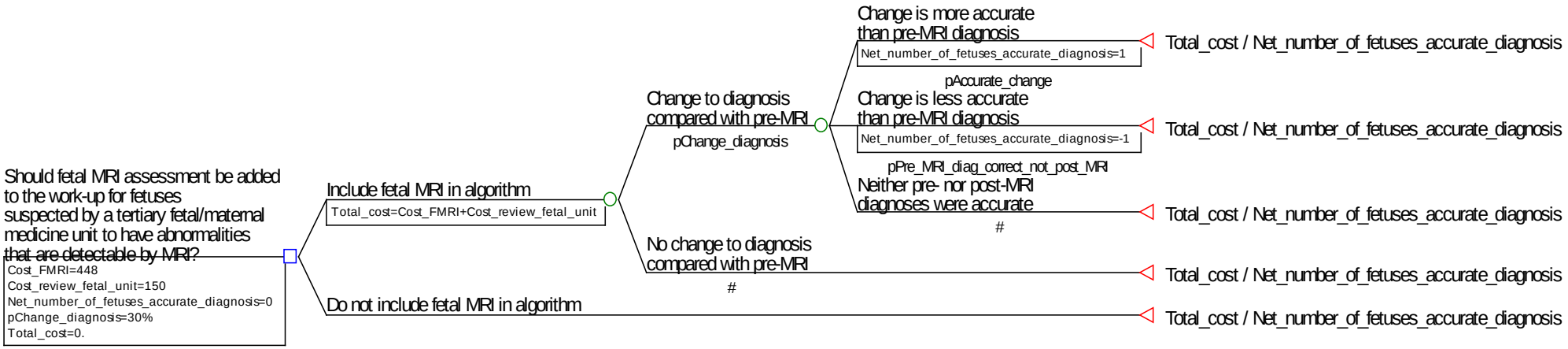
As shown in Table 18, an analysis of incremental cost-effectiveness of fetal MRI suggests, that considering all patients who undergo fetal MRI (on the basis of a recommendation that fetal MRI is indicated by a fetal/maternal medicine unit), the incremental cost per additional patient with a correct diagnosis after MRI is approximately $4,475.

Table 18: Results for impact of MRI on diagnosis (excluding patients where certainty around diagnosis was not reported and excluding patients where the effect of the MRI on diagnosis was not reported.

	Fetal MRI conducted	Fetal MRI not conducted	Increment
Cost per patient	$623	-	$623
Proportion of patients achieving a correct diagnosis following fetal MRI	13.9% (=24% x 58%)	-	13.9%
Incremental cost per additional patient with an accurate diagnosis following fetal MRI:			$4,475

It is the remit of decision-makers to consider whether this result represents value for money. Ideally, a cost-effectiveness ratio should be presented in a metric that permits comparison with other health interventions (e.g., incremental cost per QALY) however, as discussed above, such an analysis has not been conducted in this case due to the ethical and practical issues (e.g., difficulties in determining the value of an accurate diagnosis [e.g., this might involve avoiding the birth of a child with an abnormality]).

Figure 2: Structure for economic evaluation



Appendix A: Levels of evidence

Table 19: Designations of levels of evidence according to type of research question (including table notes) (NHMRC 2008).

Level	Intervention [1]	Diagnostic accuracy [2]	Prognosis	Aetiology [3]	Screening Intervention
I [4]	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies
II	A randomised controlled trial	A study of test accuracy with: an independent, blinded comparison with a valid reference standard,[5] among consecutive persons with a defined clinical presentation[6]	A prospective cohort study[7]	A prospective cohort study	A randomised controlled trial
III-1	A pseudo randomised controlled trial (i.e. alternate allocation or some other method)	A study of test accuracy with: an independent, blinded comparison with a valid reference standard,[5] among non-consecutive persons with a defined clinical presentation[6]	All or none[8]	All or none[8]	A pseudo randomised controlled trial (i.e. alternate allocation or some other method)
III-2	A comparative study with concurrent controls: ▪ Non-randomised, experimental trial[9] ▪ Cohort study ▪ Case-control study ▪ Interrupted time series with a control group	A comparison with reference standard that does not meet the criteria required for Level II and III-1 evidence	Analysis of prognostic factors amongst persons in a single arm of a randomised controlled trial	A retrospective cohort study	A comparative study with concurrent controls: ▪ Non-randomised, experimental trial ▪ Cohort study ▪ Case-control study
III-3	A comparative study without concurrent controls: ▪ Historical control study ▪ Two or more single arm study[10] ▪ Interrupted time series without a parallel control group	Diagnostic case-control study[6]	A retrospective cohort study	A case-control study	A comparative study without concurrent controls: ▪ Historical control study ▪ Two or more single arm study
IV	Case series with either post-test or pre-test/post-test outcomes	Study of diagnostic yield (no reference standard)[11]	Case series, or cohort study of persons at different stages of disease	A cross-sectional study or case series	Case series

Table notes

[1] Definitions of these study designs are provided on pages 7-8 How to use the evidence: assessment and application of scientific evidence (NHMRC 2000b).

[2] The dimensions of evidence apply only to studies of diagnostic accuracy. To assess the effectiveness of a diagnostic test there also needs to be a consideration of the impact of the test on patient management and health outcomes (Medical Services Advisory Committee 2005, Sackett and Haynes 2002).

[3] If it is possible and/or ethical to determine a causal relationship using experimental evidence, then the 'Intervention' hierarchy of evidence should be utilised. If it is only possible and/or ethical to determine a causal relationship using observational evidence (i.e. cannot allocate groups to a potential harmful exposure, such as nuclear radiation), then the 'Aetiology' hierarchy of evidence should be utilised.

[4] A systematic review will only be assigned a level of evidence as high as the studies it contains, excepting where those studies are of level II evidence. Systematic reviews of level II evidence provide more data than the individual studies and any meta-analyses will increase the precision of the overall results, reducing the likelihood that the results are affected by chance. Systematic reviews of lower level evidence present results of likely poor internal validity and thus are rated on the likelihood that the results have been affected by bias, rather than whether the systematic review itself is of good quality. Systematic review quality should be assessed separately. A systematic review should consist of at least two studies. In systematic reviews that include different study designs, the overall level of evidence should relate to each individual outcome/result, as different studies (and study designs) might contribute to each different outcome.

[5] The validity of the reference standard should be determined in the context of the disease under review. Criteria for determining the validity of the reference standard should be pre-specified. This can include the choice of the reference standard(s) and its timing in relation to the index test. The validity of the reference standard can be determined through quality appraisal of the study (Whiting et al 2003).

[6] Well-designed population based case-control studies (e.g. population based screening studies where test accuracy is assessed on all cases, with a random sample of controls) do capture a population with a representative spectrum of disease and thus fulfil the requirements for a valid assembly of patients. However, in some cases the population assembled is not representative of the use of the test in practice. In diagnostic case-control studies a selected sample of patients already known to have the disease are compared with a separate group of normal/healthy people known to be free of the disease. In this situation patients with borderline or mild expressions of the disease, and conditions mimicking the disease are excluded, which can lead to exaggeration of both sensitivity and specificity. This is called spectrum bias or spectrum effect because the spectrum of study participants will not be representative of patients seen in practice (Mulherin and Miller 2002).

[7] At study inception the cohort is either non-diseased or all at the same stage of the disease. A randomised controlled trial with persons either non-diseased or at the same stage of the disease in both arms of the trial would also meet the criterion for this level of evidence.

[8] All or none of the people with the risk factor(s) experience the outcome; and the data arises from an unselected or representative case series which provides an unbiased representation of the prognostic effect. For example, no smallpox develops in the absence of the specific virus; and clear proof of the causal link has come from the disappearance of small pox after large-scale vaccination.

[9] This also includes controlled before-and-after (pre-test/post-test) studies, as well as adjusted indirect comparisons (i.e. utilise A vs. B and B vs. C, to determine A vs. C with statistical adjustment for B).

[10] Comparing single arm studies i.e. case series from two studies. This would also include unadjusted indirect comparisons (i.e. utilise A vs. B and B vs. C, to determine A vs. C but where there is no statistical adjustment for B).

[11] Studies of diagnostic yield provide the yield of diagnosed patients, as determined by an index test, without confirmation of the accuracy of this diagnosis by a reference standard. These may be the only alternative when there is no reliable reference standard.

Note A: Assessment of comparative harms/safety should occur according to the hierarchy presented for each of the research questions, with the proviso that this assessment occurs within the context of the topic being assessed. Some harms are rare and cannot feasibly be captured within randomised controlled trials; physical harms and psychological harms may need to be addressed by different study designs; harms from diagnostic testing include the likelihood of false positive and false negative results; harms from screening include the likelihood of false alarm and false reassurance results.

Note B: When a level of evidence is attributed in the text of a document, it should also be framed according to its corresponding research question e.g. level II intervention evidence; level IV diagnostic evidence; level III-2 prognostic evidence.

Source: Hierarchies adapted and modified from: NHMRC 1999; Bandolier 1999; Lijmer et al. 1999; Phillips et al. 2001.

Appendix B: Search strategy

Table 20: Search terms used

Search Terms
Fetal diagnosis, fetal abnormalities, pre-natal imaging, pre-natal diagnosis, magnetic resonance imaging

Table 21: Selection criteria for included studies

Research question:		
Selection criteria	Inclusion	Exclusion
Study design	Prospective studies	
Population	Pregnant women in 2nd or 3rd trimester referred to specialist centre following ultrasound	Women in the first trimester of their pregnancy
Prior tests	Ultrasound scan to assess fetal morphology	N/A
Index test/Intervention	MRI for diagnosis of fetal abnormality following ultrasound	N/A
Reference standard	Intrauterine surgery findings, post-natal imaging using ultrasound and MRI. Post-natal surgical findings Post-mortem findings Post-natal Clinical Confirmation	
Comparator	Ultrasound alone for screening of fetal abnormalities	
Outcomes	Sensitivity and specificity of imaging modalities Proportion of cases with changes in diagnosis Proportion of cases with incorrect diagnosis Proportion of cases with improvement in counselling Proportion of cases with change in clinical management.	
Publication type	Comparative studies	

Appendix C: Studies included in review

Profiles of included studies

Study	Location	Study design	Study population	Gestation	Study details	Outcomes assessed
Carcopino, X. Chaumoitre, K. Shojai, R. Akkawai, R. Panuel, M. et al (2007)	Marseille, France	Diagnostic evidence level III-2	17 fetuses with suspected echogenic bowel diagnosed by ultrasound	Mean 24 weeks (range 21-32 weeks)	All fetuses underwent MRI after ultrasound	Genetic (pre-natal) and post-natal clinical confirmation of cranio-synostosis
Cassart, M. Massex, A. Metens, T. Rypens, F. Lambot, M.A. et al (2004)	Brussels, Belgium	Diagnostic evidence level III-2	16 fetuses with suspected urinary tract abnormalities diagnosed by ultrasound	Mean 31 weeks (range 27-37)	All fetuses underwent MRI after ultrasound	Post-natal clinical (n=12) or post-mortem (n=4) confirmation of abnormality.
Frates, M.I. Kumar, A.J. Benson, C.B. Ward, V.L. Tempany, C.M. (2004)	Boston, USA	Diagnostic evidence level III-2	27 fetuses with suspected abnormalities (CNS, genitourinary, system, thorax and facial) diagnosed by ultrasound	18-37 weeks.	All fetuses underwent MRI after ultrasound within 15 days.	Post-natal clinical confirmation of diagnosis
Garel, C. Dreux, S. Phillipe-Chomette, P. Vuillard, E. et al (2006)	Paris, France	Diagnostic evidence level III-2	24 fetuses with suspected gastro-intestinal tract abnormalities diagnosed by ultrasound	Median 33 weeks (range 30-39 weeks)	All fetuses underwent MRI after ultrasound	Post natal clinical or post-mortem confirmation of abnormality.
Garel, C. Delezolde, A-L. Elmaleh-Berges, M. et al (2004)	Paris, France	Diagnostic evidence level III-2	28 fetuses with suspected cerebral ischemic lesions diagnosed by ultrasound	median of 31.8 ±3.3 weeks (range 23-39 weeks)	All fetuses underwent MRI after ultrasound	Post-natal neurofeto-pathologic confirmation of abnormality
Griffiths, P.D. Widjala, E. Paley, M.N.J. Whitby, E.H. (2006)	Sheffield, United Kingdom	Diagnostic evidence level III-2	50 consecutive fetuses with suspected spine and spinal cord abnormalities diagnosed by ultrasound	Median 26.5 weeks (range 18-37)	All fetuses underwent MRI after ultrasound	Post-natal clinical or post-mortem confirmation of abnormality
Hu, L.S. Caire, J. Twickler, D.M. (2006)	Texas, USA	Diagnostic evidence level III-2	32 multiple pregnancies (30 twin, 2 triplet) with suspected complications diagnosed by ultrasound	18-34 weeks gestation	All fetuses underwent MRI after ultrasound	Post-natal confirmation of findings were not reported. Only results of MRI
Ismail, K. Ashworth, J.	Stoke-on-Trent	Diagnostic evidence	27 consecutive fetuses, with suspected CNS	Median 27 weeks	All fetuses underwent MRI after	Postpartum findings or post-mortem confirmation of

Study	Location	Study design	Study population	Gestation	Study details	Outcomes assessed
Martin, W. Chapman, S et al (2002)	UK	level III-2	abnormalities diagnosed by ultrasound	(range 20-34)	ultrasound All scans within 10 days of ultrasound 4-yr retrospective study	abnormality
Kline-Fath, B.M. Calvo-Garcia, M.A. O'Hara, S.M. Crombleholme, T.M. Racadio, J.M. (2007)	Cincinnati, USA	Diagnostic evidence level III-2	37 multiple pregnancies (36 twin, 1 triplet) with suspected twin-twin transfusion syndrome diagnosed by ultrasound	Mean 20 weeks (range 18-23)	All fetuses underwent MRI after ultrasound	Post-natal confirmation of findings were not reported. Only results of MRI.
Kubik-Huch , R.A. Huisman, T. Wisser, J. Gottstein-Aalame, N. et al (2000).	Zurich, Switzerland	Diagnostic evidence level III-2	30 women with complicated pregnancies	Mean 190±54 days	All fetuses underwent MRI after ultrasound	Post-natal clinical or post mortem confirmation of abnormality
Levin, D. Feldman, H.A. Tannus, J.F. Estroff, J.A. et al (2008)	Boston, USA	Diagnostic evidence level III-2	200 fetuses with suspected ventriculomegaly diagnosed on ultrasound		All fetuses underwent MRI after ultrasound Final diagnosis by consensus	Assessment of the frequency and cause of disagreements in diagnoses at ultrasonography for ventriculomegaly
Levin, D. Barnes, P.D. Robertson, R.R. Wong, G. Mehta, T.S. (2003)	Boston, USA	Diagnostic evidence level III-2	214 fetuses diagnosed with suspected CNS abnormalities by ultrasound	Mean 24.7±6.1 weeks (range 14-40)	214 fetuses (20 sets of twins) underwent confirmatory ultrasound followed by 242 MRI examinations	Post-natal clinical or post-mortem confirmation of abnormality
Manganaro, L. Savelli, S. Francioso, A. Di Maurizio, M. et al (2009)	Rome, Italy	Diagnostic evidence level III-2	55 fetuses diagnosed with suspected ventriculomegaly diagnosed by ultrasound	Mean 27 weeks (19-38)	59 fetus (4 sets of twins) underwent MRI after ultrasound 2days-2 wks after ultrasound	50/55 post natal imaging or biopsy to confirm abnormality 5/55 patient history from mother or paediatrician
Malinger, G. Ben-Sira, L. Lev, D. Ben-Aroya, Z. Kidron, D. et al (2004)	Tel Aviv, Israel	Diagnostic evidence level III-2	42 fetuses with suspected CNS abnormalities diagnosed by ultrasound	Mean 30.2 weeks (range 23-37 weeks)	All fetuses underwent MRI after neurosonography after ultrasound	Post-natal clinical or post mortem confirmation of abnormality
Papadis, A. Miller, C. Martin, W.L. Kilby, M.D. Sgouros, S. (2008)	Birmingham UK	Diagnostic evidence level III-2	13 fetuses with suspected CNS defects diagnosed by ultrasound, which may require immediate post-natal surgery		All fetuses underwent MRI after ultrasound	Post-natal MRI to confirm pre-natal MRI findings
Saleem, S.N.	Cairo,	Diagnostic evidence	19 fetuses with neural tube		All fetuses underwent MRI after	Post-natal MRI, clinical and pathology

Study	Location	Study design	Study population	Gestation	Study details	Outcomes assessed
Said, A.H. Abdel-Raouf, M. El-Kattan, E.A. et al (2009)	Eygpt	level III-2	defects diagnosed by ultrasound		ultrasound	to confirm pre-natal MRI findings

Study	Location	Study design	Study population	Gestation	Study details	Outcomes assessed
Salomon, L.J. Quahba, J. Vuillard, E. Oury, J-F. et al (2006)	Paris, France	Diagnostic evidence level III-2	310 fetuses with suspected ventriculomegaly diagnosed by ultrasound.	Mean 33.2 weeks (±2.03, range 30-38 weeks)	All fetuses underwent MRI after ultrasound Post-natal MRI done at 2 and 24 months and clinical follow-up at 2,6,9,12,18 and 24 months	Post-natal clinical confirmation of ventriculomegaly
Tilea, B. Delezoide, A.L. Khung-Savalovski, S. Guimot, G. et al (2007)	Paris, France	Diagnostic evidence level III-2	25 fetus with suspected posterior fossa malformation diagnosed by ultrasound	Mean 31 weeks Autopsy at 33 weeks	All fetuses underwent MRI after ultrasound	All fetuses terminated and the fetus underwent fetopathological examination. Post-mortem confirmation of posterior fossa malformation at a mean gestational age of 33 weeks
Whitby, E.H. Paley, M.N.J. Sprigg, A. Rutter, S. et al (2004a)	Sheffield, UK	Diagnostic evidence level III-2	100 fetuses with suspected CNS abnormalities diagnosed by ultrasound		All fetuses underwent MRI after ultrasound	Post mortem post-natal MRI or post-natal clinical confirmation of diagnosis.

Appendix D: Fetal MRI referral data sheet

Fetal MRI Referral Data Sheet

VICTORIAN FETAL MRI PROGRAM

Southern Health, Austin Health, Royal Children's Hospitals, Melbourne

Version 3 September 4 2006

(To be completed by fetal medicine specialist who is referring the patient for MRI. Data will be de-identified and stored in a password protected electronic database at Monash Medical Centre, Department of Diagnostic Imaging)

Name of Patient _____

UR _____

Patient's Phone Numbers **(H)**_____

(W)_____

(M)_____

Date of MFM unit confirmatory ultrasound_____

Name / qualification of clinician providing counselling_____

Name / qualification of clinician performing confirmatory ultrasound_____

Hospital_____

Gestational age at time of referral_____

Has patient had previous MRI of this fetus? Y _____ N_____

If yes, WHERE was this done_____

If yes, WHEN was this done (approximate date YYYY/MM/DD) _____/____/____

De-identified patient number _____ /_____ (this will be filled in on each page by the MRI radiologist)

1.THIS DATA SHEET REPRESENTS A REQUEST FOR FETAL MRI. THERE ARE **TWO** PAGES TO BE COMPLETED BY THE MATERNAL FETAL MEDICINE SPECIALIST WHO IS MAKING THE REFERRAL. THE REMAINDER OF THE FORM WILL BE COMPLETED BY THE RADIOLOGIST REPORTING THE MRI.

2. THE DATA SHEET / REQUEST FOR MRI SHOULD BE POSTED OR FAXED TO THE MRI DEPARTMENT OF MONASH MEDICAL CENTRE, ROYAL CHILDREN'S HOSPITAL OR AUSTIN HOSPITAL FOR AN APPOINTMENT .

DO NOT SEND THIS SECTION TO THE DATA MANAGER AT MONASH MEDICAL CENTRE. IT WILL BE FILED IN A SECURED FILE BY THE REPORTING RADIOLOGIST AT THE HOSPITAL WHERE THE MRI IS PERFORMED.

De-identified patient number _____ /_____

Please indicate specialists other than yourself who you or the patient have consulted regarding this pregnancy :

1.Medical Geneticist **4.Pediatric surgeon**

2.Clinical obstetrician **5.Pediatric neurologist**

3.Fetal surgery specialist **6.Other pediatric medical specialist**

1. Diagnosis based on ultrasound (fill in as many as needed from a. - e.)

a._____

This diagnosis is (circle) Possible Probable Definite

b._____

This diagnosis is (circle) Possible Probable Definite

c. _____

This diagnosis is (circle) Possible Probable Definite

d. _____

This diagnosis is (circle) Possible Probable Definite

e. _____

This diagnosis is (circle) Possible Probable Definite

f. Additional diagnoses_____

De-identified Patient Number _____/_____

COUNSELLING AND PREGNANCY OUTCOME

2. Fetal outcome in this pregnancy based on ultrasound results :

a. Spontaneous death of fetus during pregnancy or neonatal life (CIRCLE ONE ONLY)

Unlikely (0-10% chance) Possible (11-50% chance)

Probable (51 – 70% chance) Very Likely (71-100% chance)

b. Severe disability of neonate OR child (CIRCLE ONE ONLY)

Unlikely Possible Probable Very likely

De-identified patient number _____ /_____

c. Mild disability of neonate OR child (CIRCLE ONE ONLY)

Unlikely Possible Probable Very likely

d. Normal or near normal outcome of neonate OR child (CIRCLE ONE ONLY)

Unlikely Possible Probable Very likely

END OF SECTION TO BE COMPLETED BY REFERRING MATERNAL – FETAL MEDICINE SPECIALIST REQUESTING MRI

Appendix E: Radiologist questionnaire

De-identified patient number _____ /_____

THIS SECTION TO BE COMPLETED BY MR RADIOLOGIST

4. Diagnosis based on MR

Note: <u>all</u> diagnoses referred to above must be addressed below

a._____

This diagnosis is Possible Probable Definite

b._____

This diagnosis is Possible Probable Definite

c._____

This diagnosis is Possible Probable Definite

d._____

This diagnosis is Possible Probable Definite

e. _____

This diagnosis is Possible Probable Definite

f.Additional diagnoses_____

5. Have other abnormalities been found that were not indicated above

Yes No

De-identified patient number _____ /_____

If YES, please list

1._____

2._____

3._____

4._____

5._____

6.Have any abnormalities suspected on ultrasound (see Question 3) been shown NOT to be present on MRI?

Yes **No**

If YES please list

1._____

2._____

3._____

4._____

Appendix F: Post MRI questionnaire

VICTORIAN FETAL MRI PROGRAM

Southern Health, Austin Health, Royal Children's Hospitals, Melbourne

POST FETAL MRI QUESTIONNAIRE

Patient Name: **Study ID number:**

Date of MRI:

This is to be completed by the maternal / fetal medicine specialist who originally requested the MRI even if the patient does not return for further counselling.

1. Fetal outcome in this pregnancy based on MRI + ULTRASOUND results :

a. Spontaneous death of fetus during pregnancy or neonatal life (CIRCLE ONE ONLY)

Unlikely (0-10% chance) Possible (11-50% chance)

Probable (51 – 70% chance) Very Likely (71-100% chance)

b. Severe disability of neonate OR child (CIRCLE ONE ONLY)

Unlikely Possible Probable Very likely

c. Mild disability of neonate OR child (CIRCLE ONE ONLY)

Unlikely Possible Probable Very likely

d. Normal or near normal outcome of neonate OR child (CIRCLE ONE ONLY)

Unlikely Possible Probable Very likely

Study ID number _____ /_____

2.

a. In my opinion, the clinical DIAGNOSIS has been changed in a significant way by the result of the MRI in this patient

Yes No

b. In my opinion, the clinical MANAGEMENT has been / would have been changed in a significant way by the result of the MRI in this patient

Yes No

c. If the management has been / would have been changed as a result of the MR being performed please state HOW (CIRCLE YES or NO FOR ALL QUESTIONS):

- **Further antenatal testing will be done/ would have been recommended that would NOT have been done based on US result alone**

Yes No

- **Plans for fetal surgery have been / would have been made, cancelled or changed in some way**

Yes No

- **Plans for the site OR method OR timing of delivery have been / would have been changed as a result of the MRI**

Yes No

d. As a result of the information provided by MRI, my counselling of the patient regarding likely fetal disability(ies) or fetal outcome is (please circle ONE) is or would have been

More certain Less certain Unchanged

e. It is my impression that the patient's *understanding of the likely outcome* for her fetus has been (please circle ONE)

Improved Unchanged Decreased

as a result of the MRI findings.

END – THANK YOU FOR COMPLETING THIS QUESTIONNAIRE

Completed questionnaires may be emailed to Jenni.Clark@southernhealth.org.au

or faxed as below

Your fax or email will be acknowledged if email address is included below

---

Fax To:

VICTORIAN FETAL MRI PROJECT

A/Prof Stacy Goergen

Fax: 9594 6009

Attention: Jenni Clark, Data Manager, Victorian Fetal MRI Project

From:

Dr_____

Hospital_____

Date_____

Phone_____

Fax_____

Email _____

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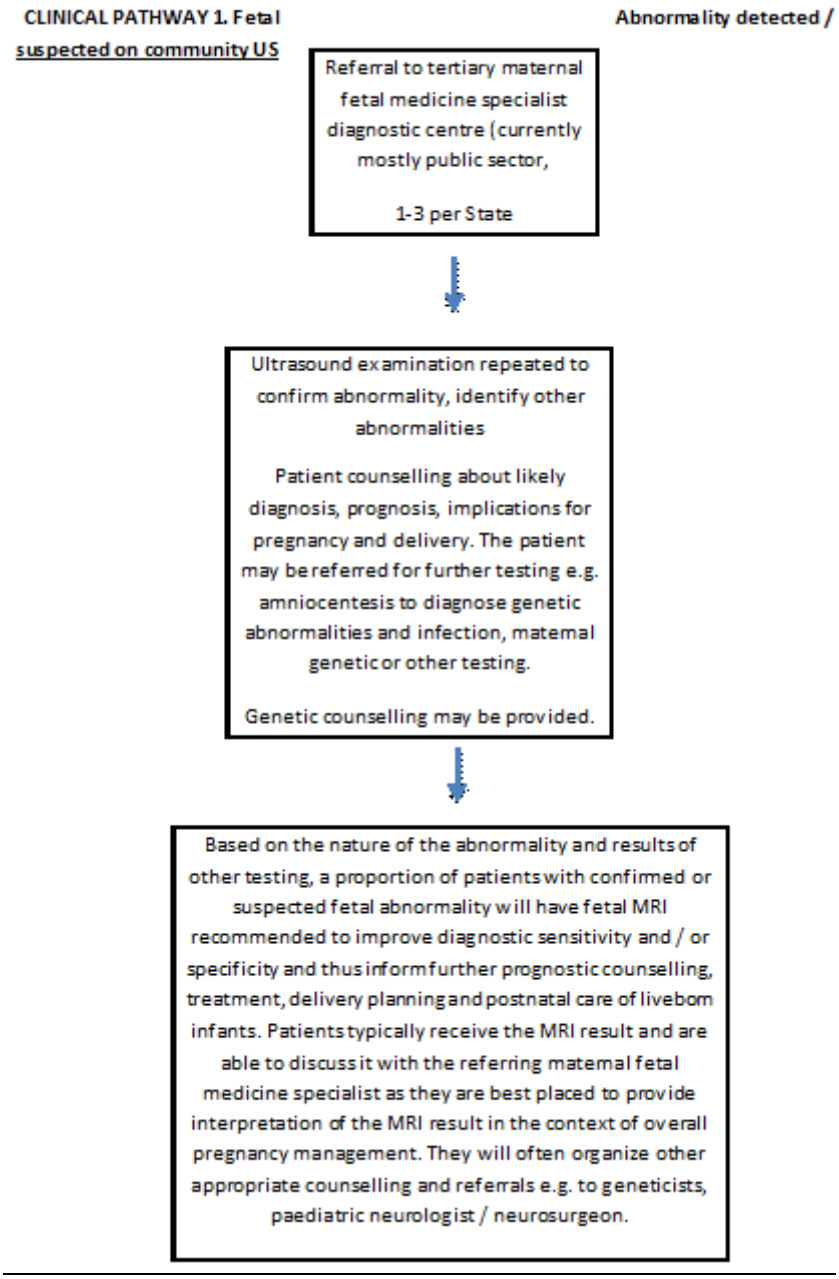
Appendix B

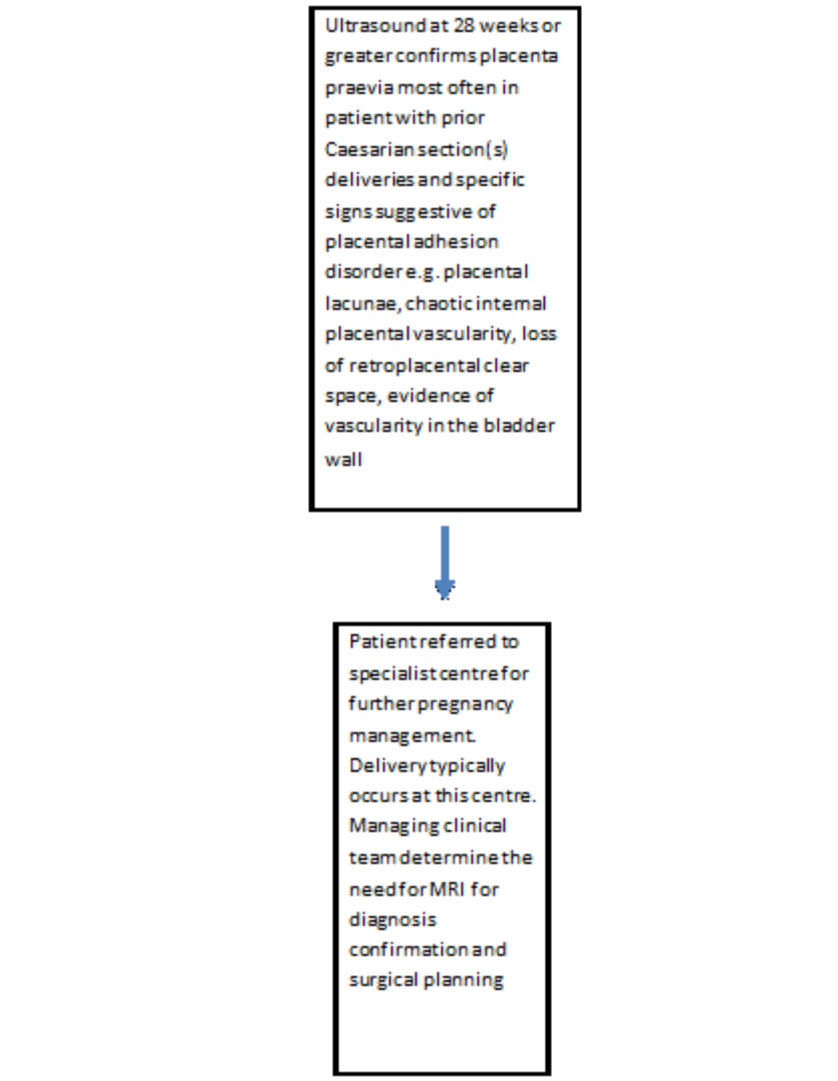

CLINICAL PATHWAY 1. Fetal suspected on community US
Abnormality detected /
Referral to tertiary maternal fetal medicine specialist diagnostic centre (currently mostly public sector,
1-3 per State
Ultrasound examination repeated to confirm abnormality, identify other abnormalities
Patient counselling about likely diagnosis, prognosis, implications for pregnancy and delivery. The patient may be referred for further testing e.g. amniocentesis to diagnose genetic abnormalities and infection, maternal genetic or other testing.
Genetic counselling may be provided.
Based on the nature of the abnormality and results of other testing, a proportion of patients with confirmed or suspected fetal abnormality will have fetal MRI recommended to improve diagnostic sensitivity and / or specificity and thus inform further prognostic counselling, treatment, delivery planning and postnatal care of livebom infants. Patients typically receive the MRI result and are able to discuss it with the referring maternal fetal medicine specialist as they are best placed to provide interpretation of the MRI result in the context of overall pregnancy management. They will often organize other appropriate counselling and referrals e.g. to geneticists, paediatric neurologist / neurosurgeon.

CLINICAL PATHWAY 2.

Patient at increased risk of congenital abnormality based on family history or prior affected pregnancy may be referred for fetal MRI in the presence of normal midtrimster screening exam if the pathology is known to be more difficult / impossible to demonstrate with ultrasound e.g. molar tooth malformation of the brain, lissencephaly, pontocerebellar atrophy and hypoplasia, absent pituitary etc. Referral may be direct from geneticist, paediatric neurologist, obstetrician or other relevant specialist

Depending on the result, the patient may be referred to a maternal fetal medicine specialist service for further counseling or treatment.

CLINICAL PATHWAY 3. Suspected placental adhesion disorder



CLINICAL PATHWAY 4. Abdominal pain during pregnancy, cause indeterminate after ultrasound

Woman at any gestational stage of pregnancy with abdominal pain and inconclusive ultrasound. Usual causes include appendicitis, ovarian torsion, ureteric obstruction, inflammatory bowel disease, bowel obstruction.

Referral will most often come from an emergency department, surgeon, or obstetrician.

This clinical problem is common in both community and tertiary referral settings. Ruptured appendicitis, colitis, and urosepsis that go undiagnosed are associated with increased fetal mortality and morbidity