

MAKING DIAGNOSIS MORE TIMELY AND ACCESSIBLE FOR PEOPLE WITH ENDOMETRIOSIS: THE IMAGENDO PROJECT



IMAGENDO

Dr Jodie Avery, PhD



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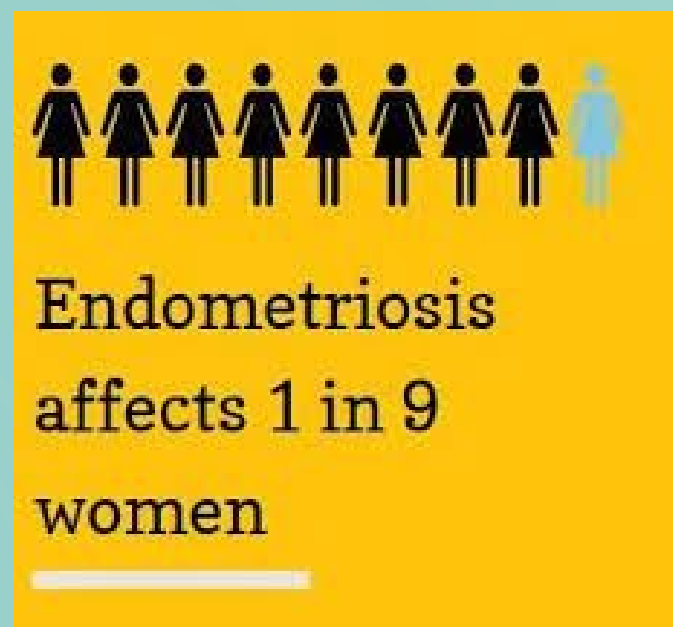


Endometriosis Research Group
Adelaide



Endometriosis

- Growth of tissue similar to the endometrium, outside the womb (usually pelvis)
- Occurrence: 1 in 7 reproductive aged women in Australia ~176 million women globally
- Costs Australia \$A7.4 billion annually
- direct costs and loss of productivity



News / National

Could Australia introduce menstrual leave? Some Melbourne businesses already have

By Allannah Sciberras, 9News Staff | 5:53pm May 23, 2022

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There are calls for more [Australian](#) businesses to offer menstrual leave, with Spain on track to legislate paid time away from work.

Many business have already taken on policies and it's being put on the bargaining table by unions as well.

For Melbourne woman Lucy Ballantyne it's a game changer.

Why is early diagnosis so important?

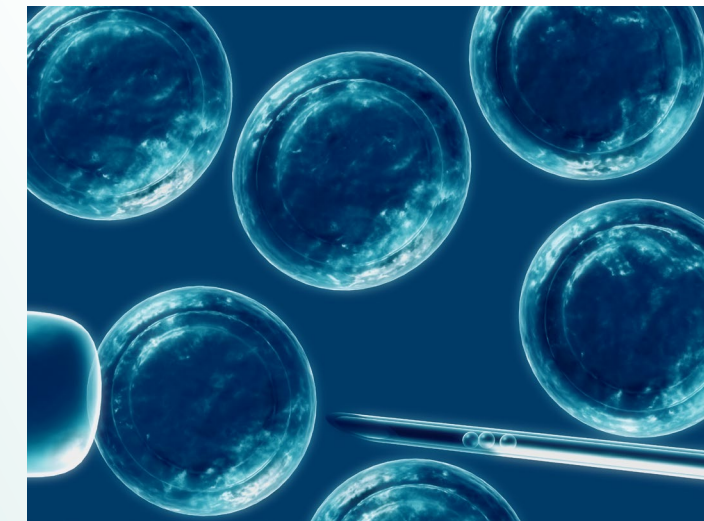
- Diagnostic delay¹
- Currently costs Australia >\$7.4 billion annually, after diagnosis²
- Reason for subfertility
- Optimisation of ART outcomes³

Women with endometriosis diagnosed after first ART were:

- more likely to use IUI (aOR: 2.14, 95% CI 1.48, 3.09)
 - have more cycles -11–36 cycles (aOR: 4.09, 95% CI 2.41, 6.95)
 - less likely to report a birth
- Surgical triage⁴

Utilising transvaginal ultrasound will lead to a significant cost saving of \$A1,562 per case, or \$A131,208 per year.

The total annual cost of the novel model (M2) is AU\$12,547,724.03, cheaper than the conventional model (M1), which cost AU\$13,472,161.67



1. O'Hara R et al. Managing endometriosis: a cross-sectional survey of women in Australia. *J Psychosom Obstet Gynaecol.* 2022;43(3):265-272.
2. Ernst & Young. The cost of Endometriosis in Australia: A report for EndoActive. 2019
3. Moss et al, Delayed diagnosis of endometriosis disadvantages women in ART: a retrospective population linked data study. 2021, *Hum Reprod*, 36(12): 3074-3082
4. Shakeri et al EP27.04: Cost-benefit analysis for the use of transvaginal ultrasound to avoid laparoscopy in women with minimal endometriosis disease *UOG* 2016;48, S1
5. Leonardi et al. Deep endometriosis transvaginal ultrasound in the workup of patients with signs and symptoms of endometriosis: a cost analysis. *BJOG* 2019;126:1499–1506



2022 - Significant change to the ESHRE guidelines

Are medical technologies reliable in diagnosing endometriosis and establishing the extent of the disease?

Clinicians should not use measurement of biomarkers in endometrial tissue, blood, menstrual or uterine fluids to diagnose endometriosis (Mol *et al.*, 1998; May *et al.*, 2010; May *et al.*, 2011; Liu *et al.*, 2015; Cosar *et al.*, 2016; Gupta *et al.*, 2016; Hirsch *et al.*, 2016; Nisenblat *et al.*, 2016a; Vanbieb *et al.*, 2019; Moustafa *et al.*, 2020).

Strong recommendation
⊕⊕⊕○

Clinicians are recommended to use imaging (ultrasound (US) or MRI) in the diagnostic work-up for endometriosis, but they need to be aware that a negative finding does not exclude endometriosis, particularly superficial peritoneal disease (Bazot *et al.*, 2009; Manganaro *et al.*, 2012; Guerriero *et al.*, 2014; Thomeer *et al.*, 2014; Nisenblat *et al.*, 2016b; Moura *et al.*, 2019).

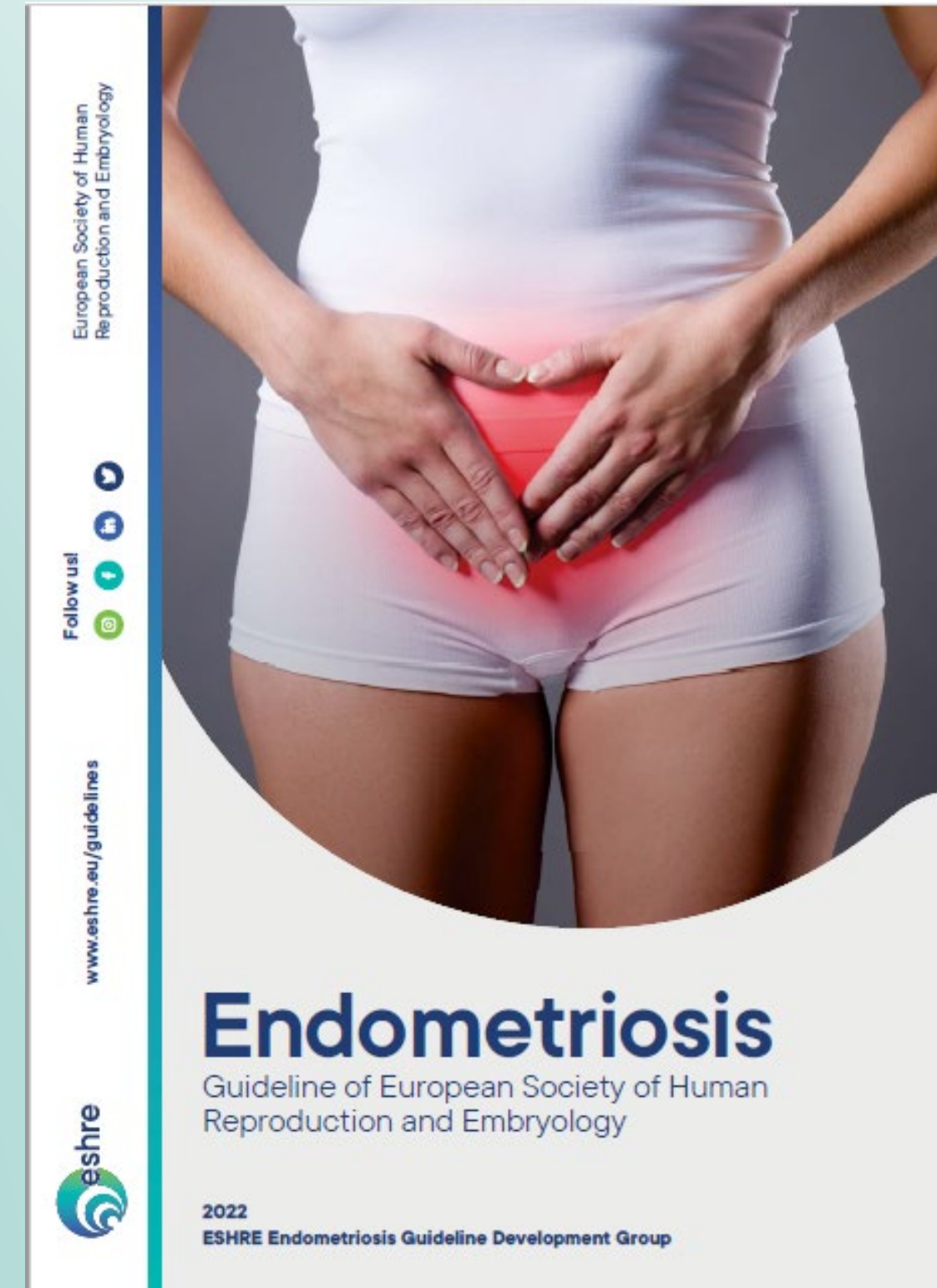
Strong recommendation
⊕⊕○○

In patients with negative imaging results or where empirical treatment was unsuccessful or inappropriate, the GDG recommends that clinicians consider offering laparoscopy for the diagnosis and treatment of suspected endometriosis.

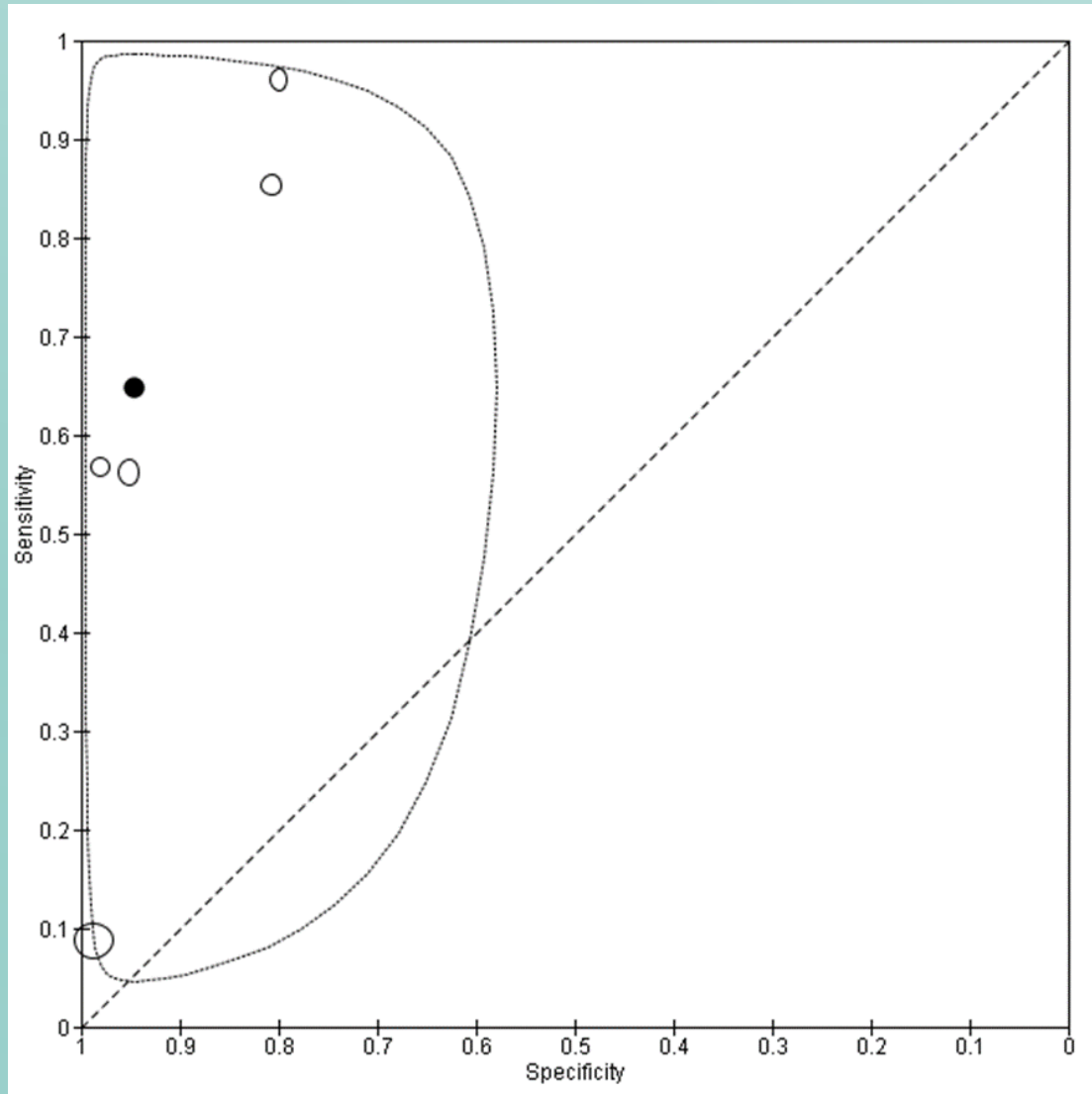
GPP

The GDG recommends that laparoscopic identification of endometriotic lesions is confirmed by histology although negative histology does not entirely rule out the disease.

GPP



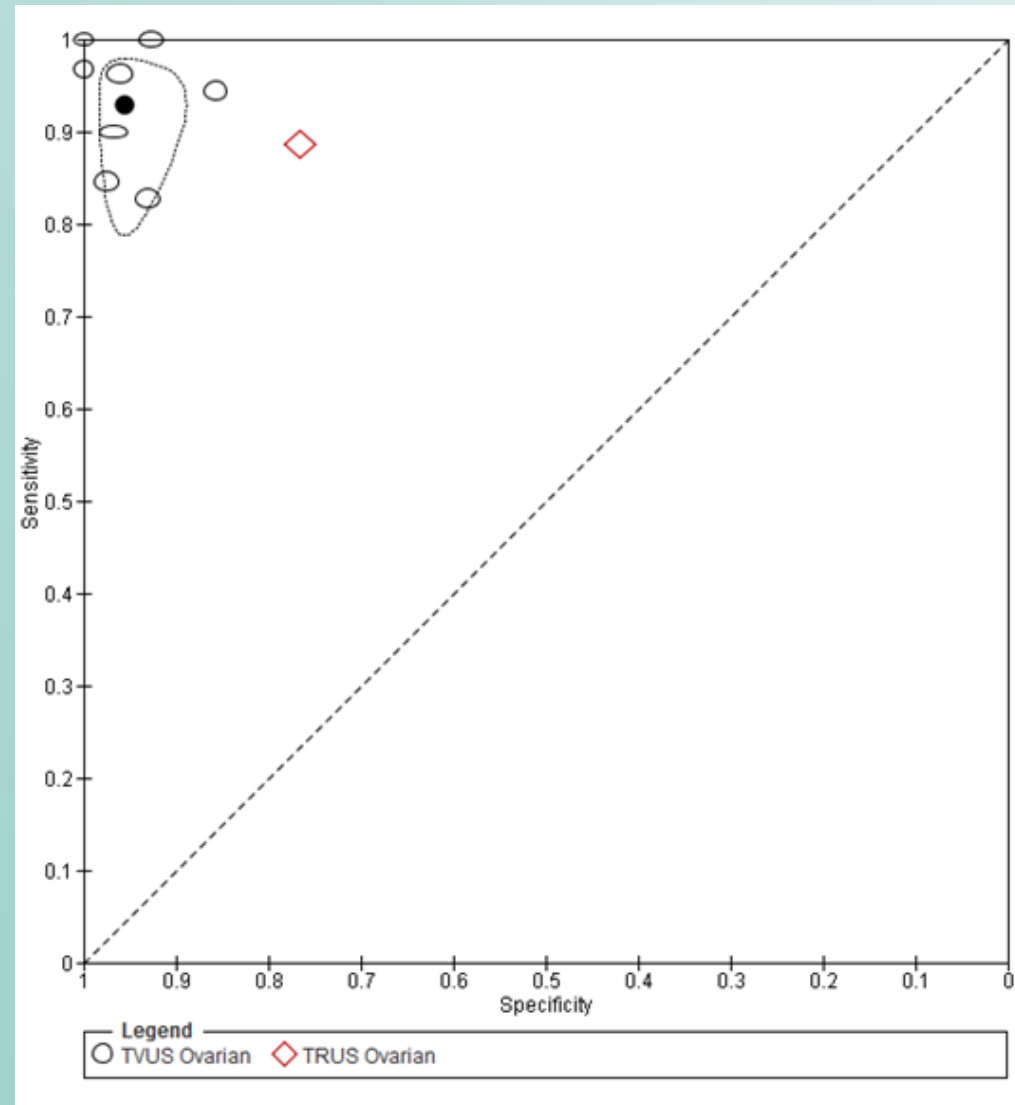
Transvaginal Ultrasound



Pelvic lesions :

Sens : 0.65 (0.27, 1.00)

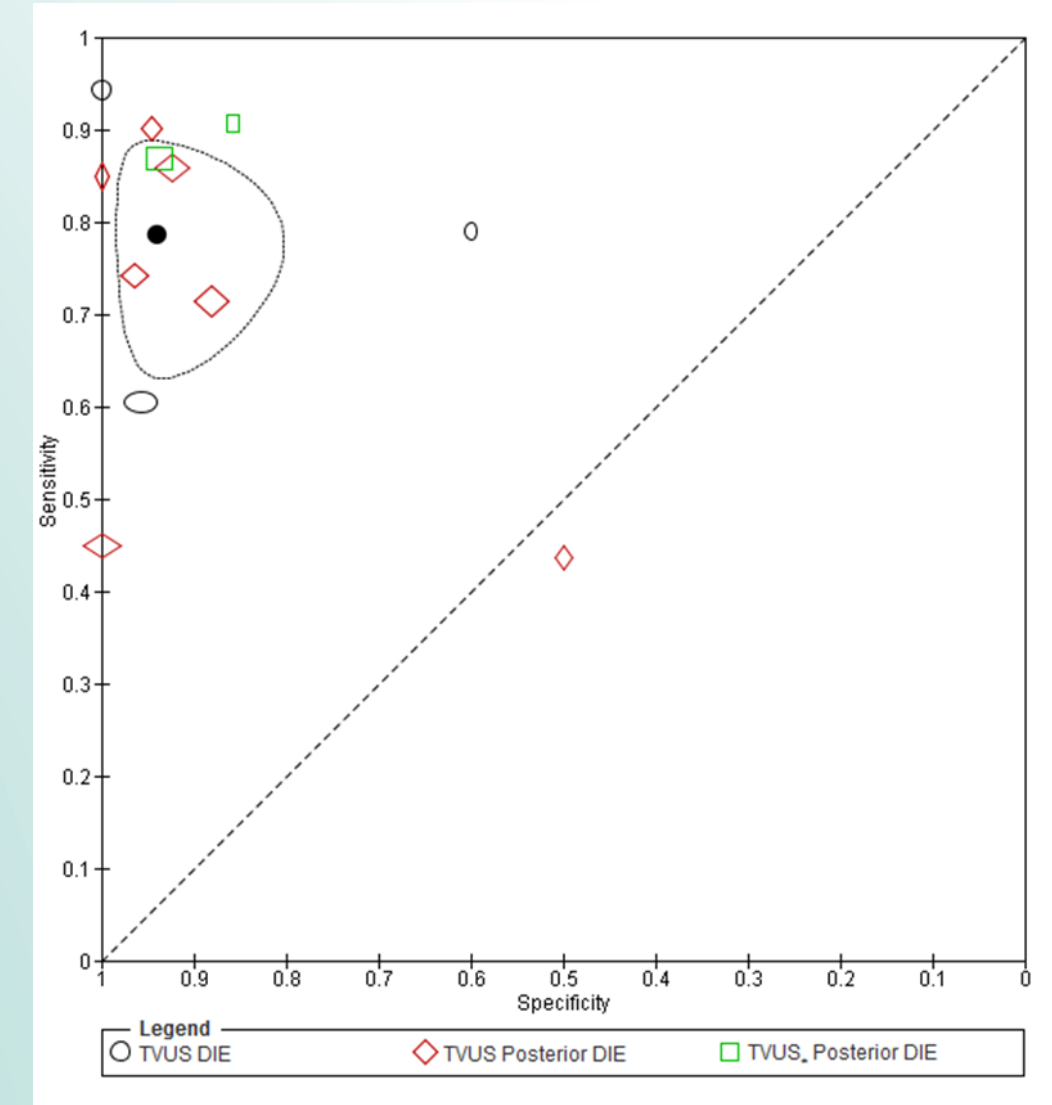
Spec : 0.95 (0.89, 1.00)



Ovarian :

Sens : 0.93 (0.87, 0.99)

Spec : 0.96 (0.92, 0.99)



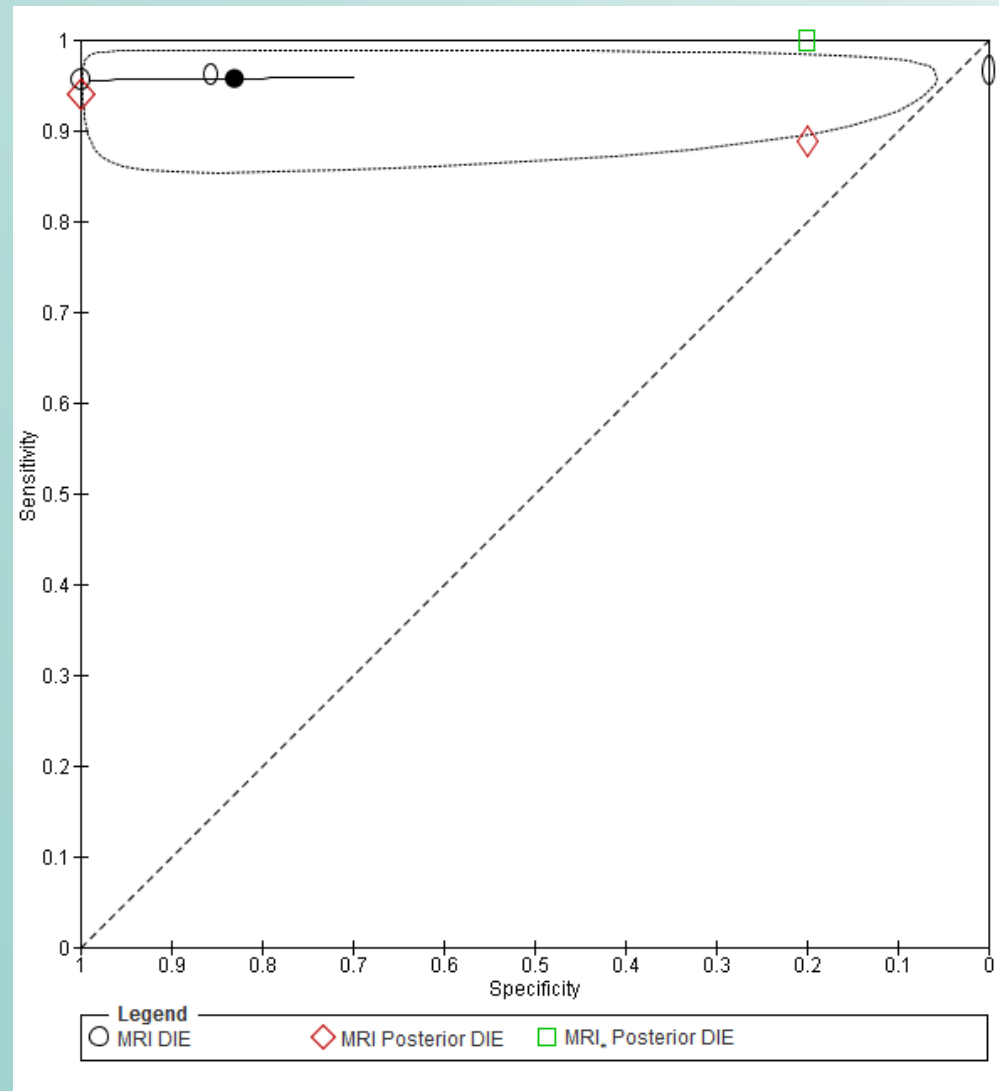
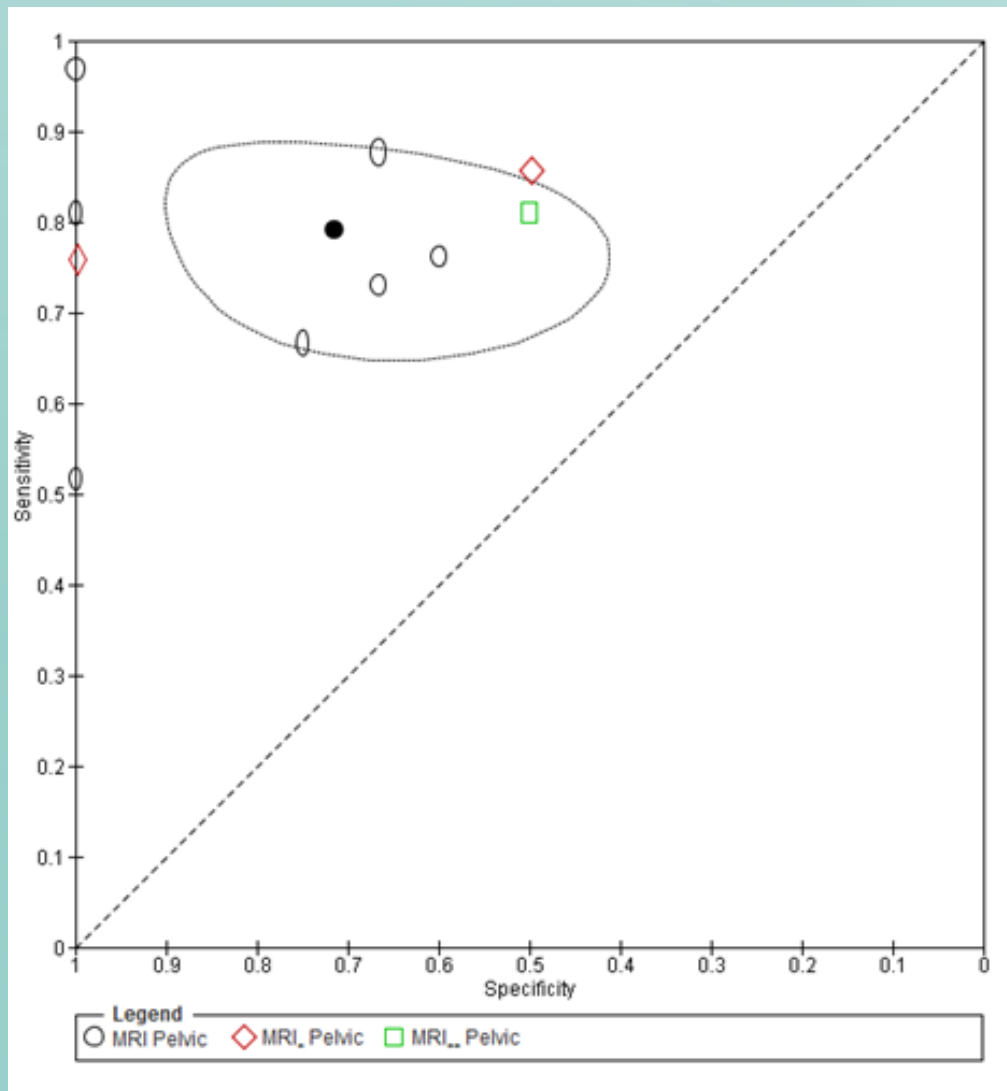
Deep Infiltrating Endometriosis:

Sens : 0.95 (0.81, 1.00)

Spec : 0.90 (0.76, 1.00)



Magnetic Resonance Imaging

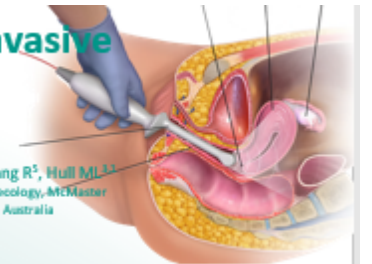


Pelvic lesions:
 Sens: 0.79 (0.70, 0.88)
 Spec: 0.72 (0.51, 0.92)

DIE:
 Sens: 0.96 (0.93, 0.99),
 Spec: 0.83 (0.50, 1.00)

Imaging modalities for the non-invasive diagnosis of Endometriosis: A Cochrane review update

Avery J¹, Leonardi M², Abeygunasekara N^{1,3}, Bliss E³, Johnson N¹, Condous G^{4,5}, Wang R¹, Hull ML^{1,4}
 1. Robinson Research Institute, University of Adelaide, Australia, 2. Department of Obstetrics and Gynecology, McMaster University, Hamilton, Canada, 3. SA Health, Australia, 4. Omni Gynaecare, Sydney, 5. Monash University, Australia



Introduction

Partly based on our original 2016 Cochrane review¹, ESHRE 2022 guidelines recommend imaging for diagnosing endometriosis, providing negative findings do not exclude disease. Forty-one additional publications, and improvements in imaging modalities and methods, prompted an updated review. Here we describe some initial results.

Aim

To determine the diagnostic accuracy of imaging modalities for the diagnosis of pelvic, ovarian endometrioma and deep endometriosis (DE).

Materials and Methods

Key databases as per Cochrane methodology were searched again in January 2022. Diagnostic test accuracy studies undertaken in reproductive aged women (18-45 years), with both index and reference standard tests (endometriosis visualisation at surgery) were included. QUADAS-2 assessed risk of bias, and bivariate random-effects meta-analyses were performed.

MRI	Pelvic Endometriosis		Ovarian Endometrioma		Deep Endometriosis	
	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
2016	0.79	0.72	0.95	0.91	0.94	0.77
	[0.70-0.88]	[0.51-0.90]	[0.90-1.00]	[0.86-0.97]	[0.90-0.97]	[0.44-1.00]
2023	0.82	0.84	0.93	0.95	0.94	0.92
	[0.68-0.90]	[0.58-0.95]	[0.87-0.97]	[0.87-0.98]	[0.88-0.97]	[0.27-1.00]

Figure 1. MRI Pooled Estimates



Results

Ninety studies (10,936 participants) were included: 22 assessing pelvic endometriosis, 14 ovarian endometriomas and 45 Deep endometriosis (DE). Sensitivities and specificities for pelvic endometriosis, endometriomas and DE are shown for and Magnetic Resonance Imaging (MRI) (Fig 1) and Transvaginal ultrasound (TVUS) (Fig 2).

TVUS	Pelvic Endometriosis		Ovarian Endometrioma		Deep Endometriosis	
	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
2016	0.65	0.95	0.93	0.96	0.79	0.94
	[0.27-1.00]	[0.89-1.00]	[0.87-0.99]	[0.92-0.99]	[0.69-0.89]	[0.88-1.00]
2023	0.67	0.92	0.92	0.95	0.75	0.93
	[0.39-0.87]	[0.84-0.97]	[0.86-0.95]	[0.92-0.97]	[0.54-0.88]	[0.65-0.99]

Figure 2. TVUS Pooled Estimates

Conclusions and Impact

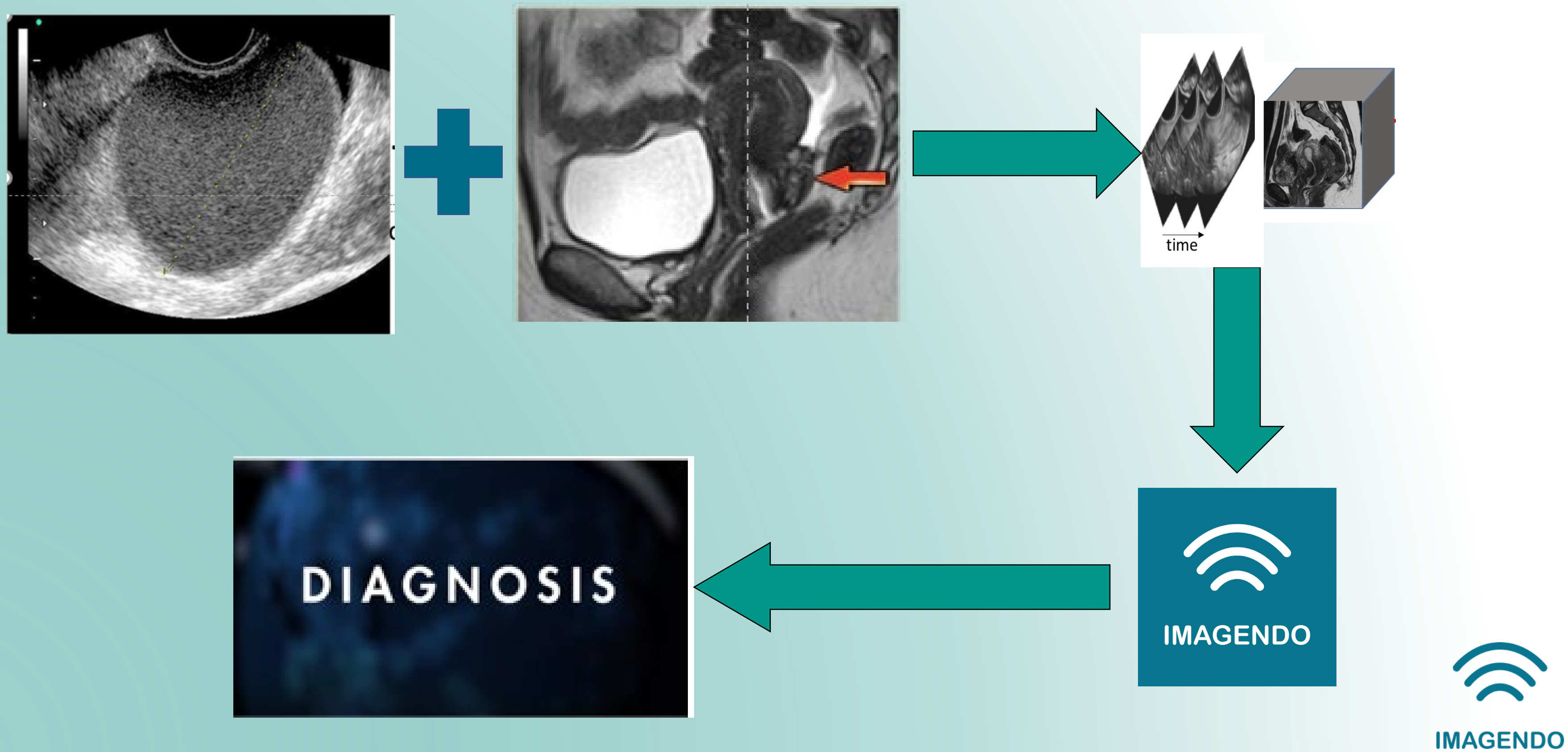
TVUS demonstrated high diagnostic accuracy for ovarian endometrioma and DE, but not for pelvic endometriosis. Compared to our 2016 findings, TVUS sensitivities and specificities were marginally lower, which may reflect regression to the mean. MRI showed improved sensitivities and specificities for pelvic endometriosis, suggesting more experienced reporting and a possible benefit over TVUS, in pelvic disease detection.



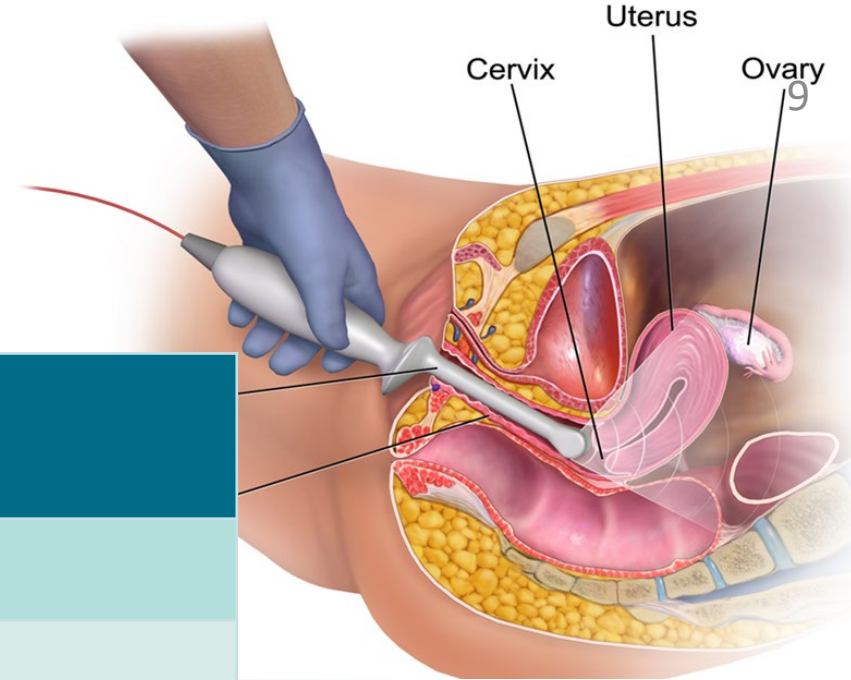
References

1. Leonardi M, Avery J, Wang R, Johnson N, Hull ML. Imaging modalities for the non-invasive diagnosis of endometriosis. Cochrane Database of Systematic Reviews 2016, Issue 2. Art. No.: CD009591. DOI: 10.1002/14651958.cd009591.pub1.

IMAGENDO Diagnostic Solution



Getting the right scan



eTVUS endometriosis markers	eMRI endometriosis markers
Endometrioma*	Endometrioma
Adenomyosis*	Upper rectal distortion
Question mark sign (anteverted, retroflexed uterus)	Fixed uterine anteversion and or retroflexion
Fixed or kissing ovaries (fixed together)	Thickened uterosacral ligaments
Fallopian tube distortion	Haematosalpinx
The sliding sign (rectum glides freely over cervix)	Posterior cul-de-sac obliteration
Endometriosis nodules	Uterine serosal plaques
	Elevated vaginal fornices
(* identified by standard TVUS)	

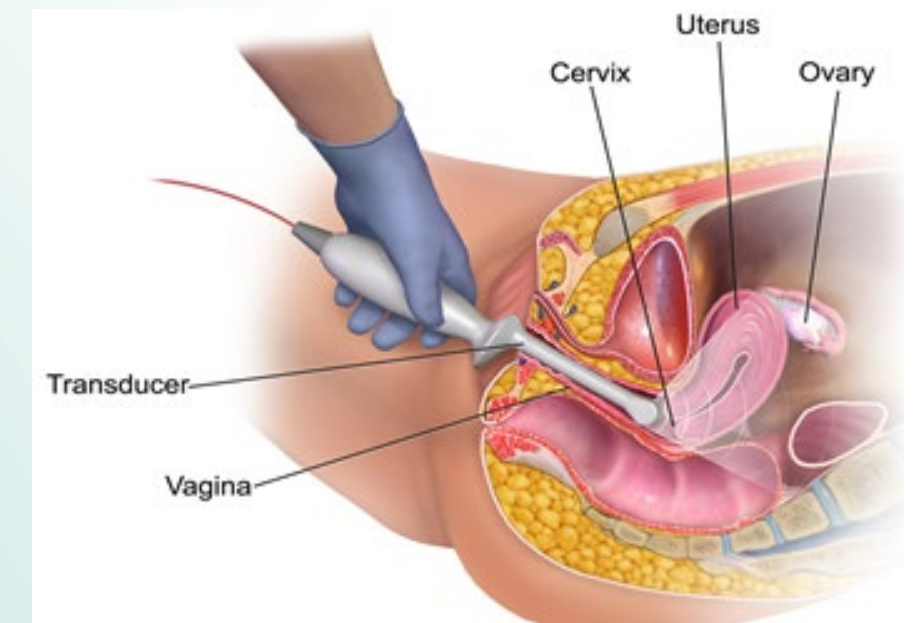
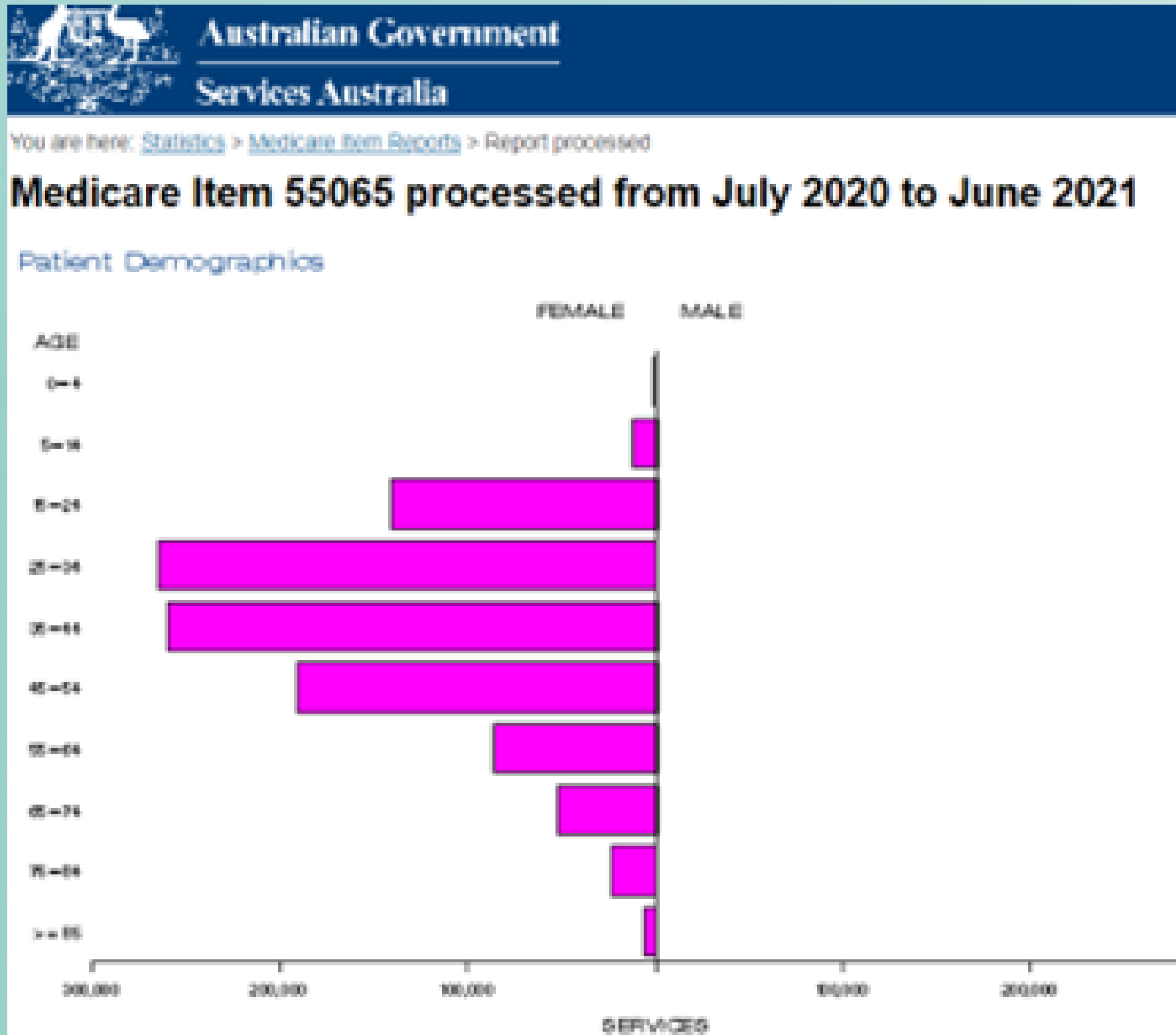
Guerriero et al. IDEA consensus statement, Ultrasound in O and G, 2016;48 (3): 318-32)

Thalluri AL, Knox S, Nguyen T. MRI findings in deep infiltrating endometriosis. J Med Imag Rad Onc. 2017;61(6):767-73.



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Availability of Ultrasounds



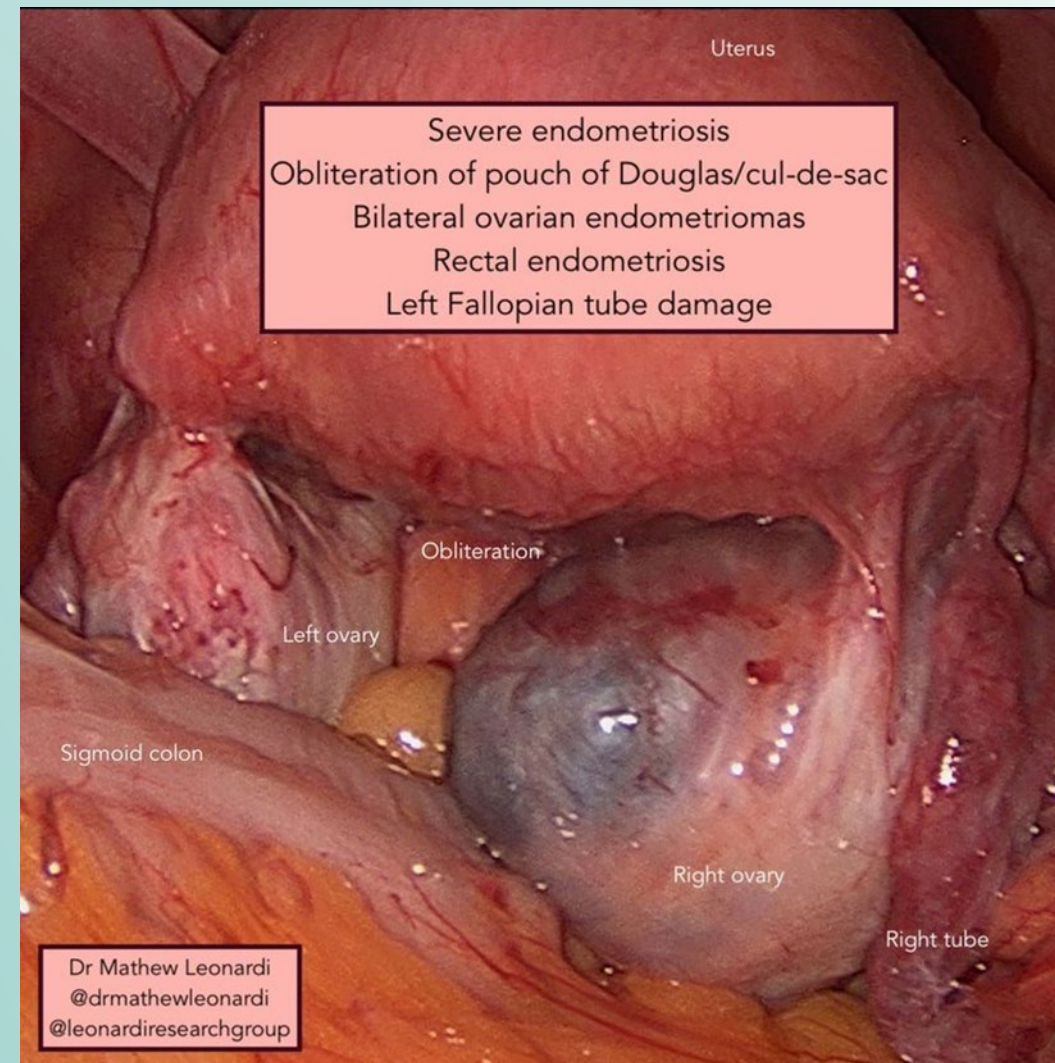
eTVUS

- Convenient, cheaper, accessible
- Frontline tool in gynaecological assessment
- Few trained highly skilled sonographers
- Access to tuition difficult
- Further contributes to diagnostic delay

Pouch of Douglas (POD) obliteration

Aim

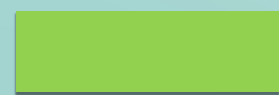
- To improve eMRI detection of POD obliteration, by leveraging detection results from unpaired eTVUS data.



Maicas, Leonardi, Avery, Panuccio, Carneiro, Hull, and Condous. "Deep learning to diagnose pouch of Douglas obliteration with ultrasound sliding sign." *Reproduction & Fertility* 2, no. 4 (2021): 236.

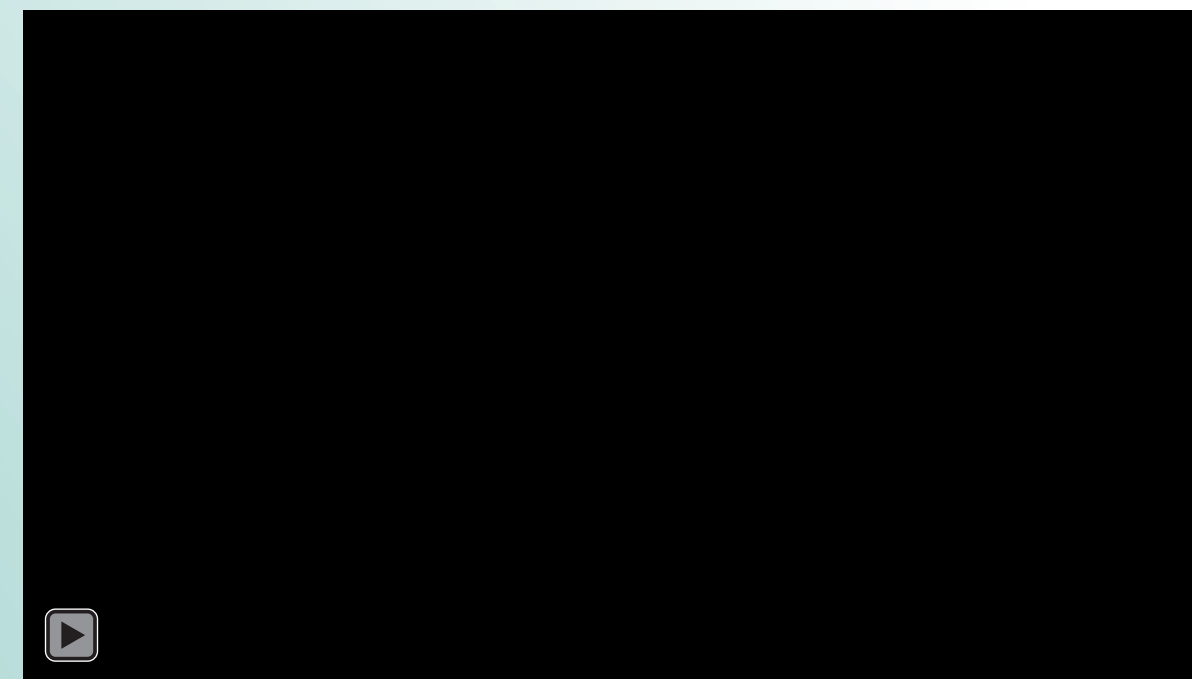
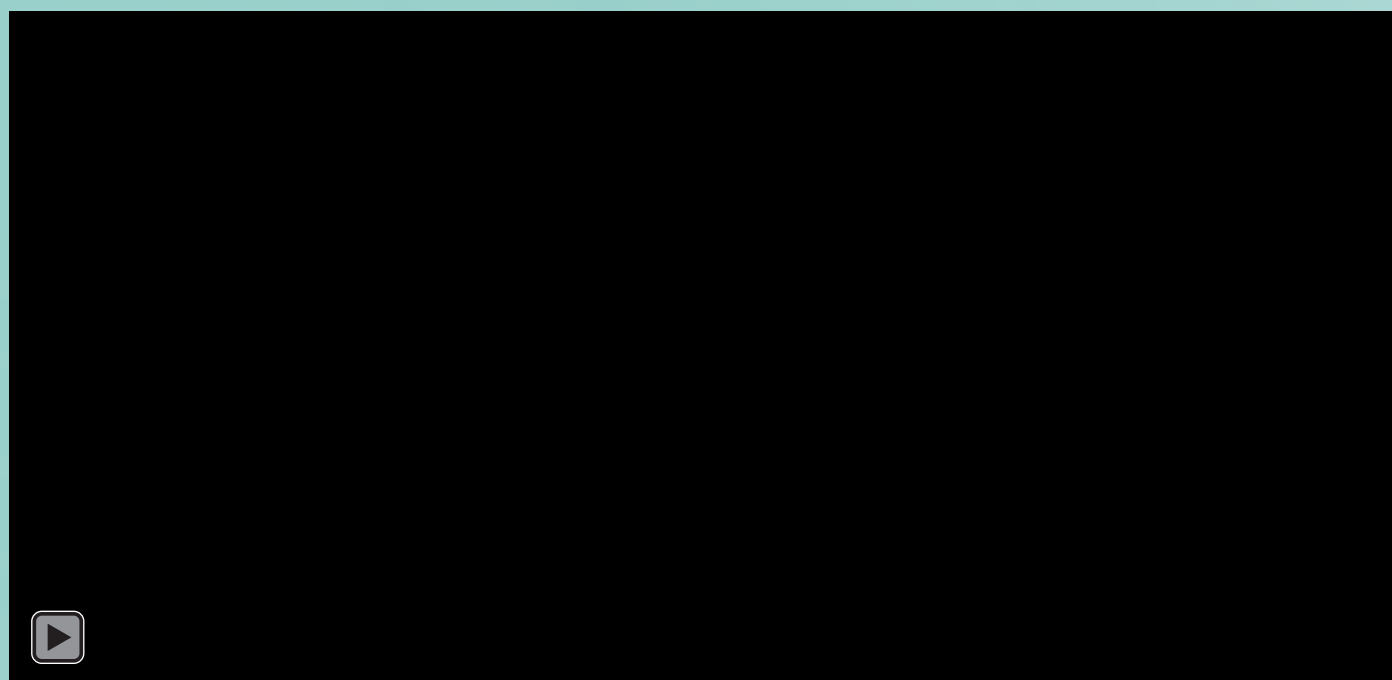
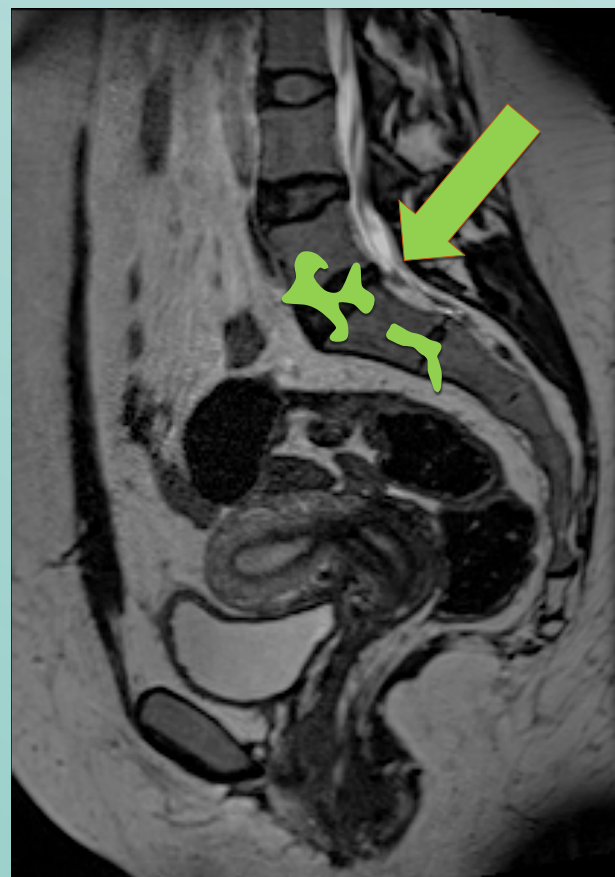


Endometriosis eMRI and eTVUS

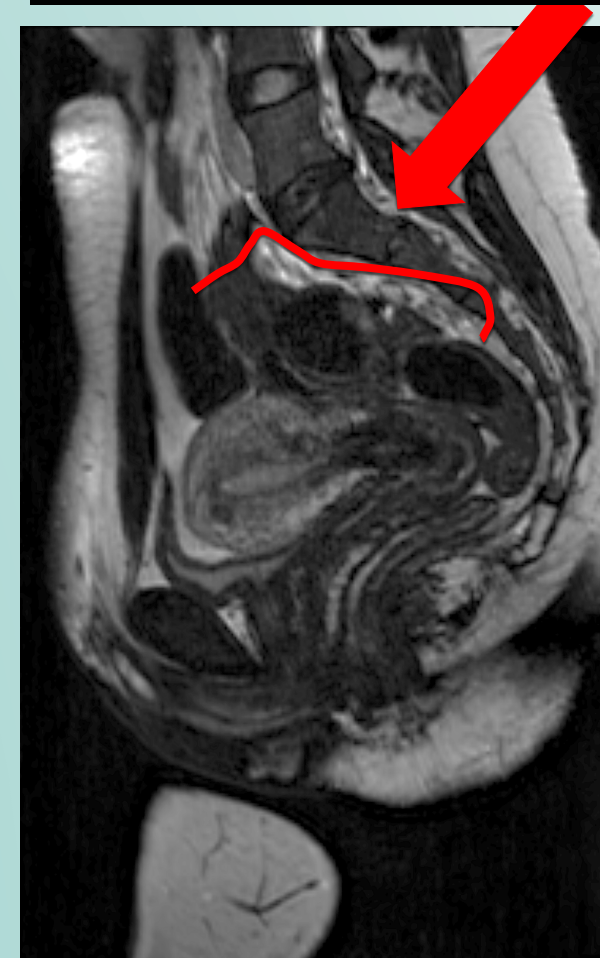


Disease absent

MRI: Normal POD
TVUS: Positive sliding sign



MRI: POD obliterated
TVUS: Negative sliding sign



+
Disease present



Motivation and Contributions



- Unpaired MRI and TVUS dataset
- Combining TVUS and MRI may allow the identification of distinct and complementary markers

Motivation

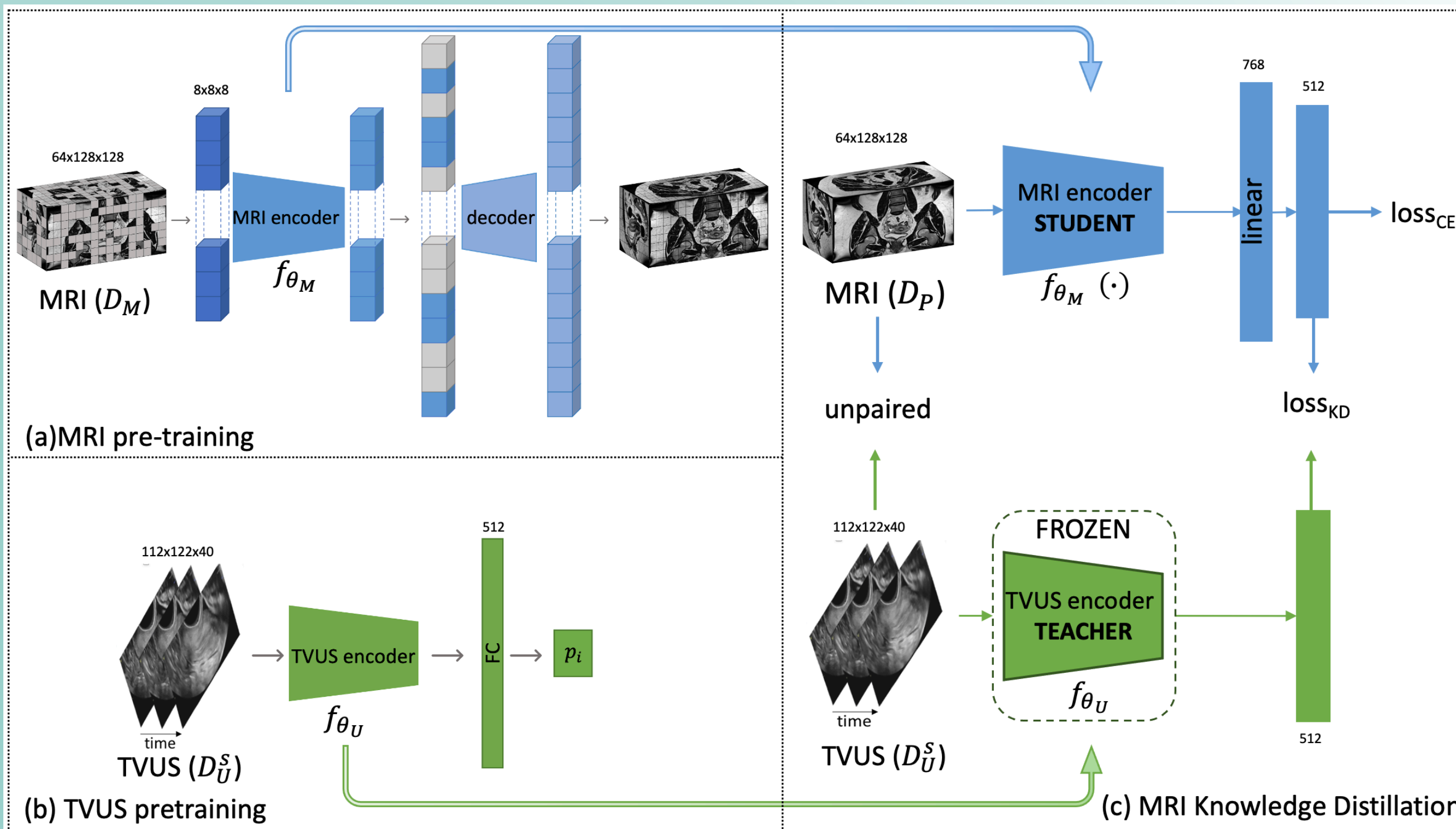
- Leveraging TVUS POD obliteration detection to improve the automated detection accuracy with MRI using an unpaired training set containing scans from both modalities.

Contributions

- The first method that distills knowledge from unpaired TVUS and MRI data for POD obliteration detection¹
- The first machine learning method that can automatically detect POD obliteration from MRI data¹

1. Zhang Y, Wang H, Butler D, To MS, Avery J, Hull ML, Carneiro G. 20th IEEE International Symposium on Biomedical Imaging (ISBI): April, 2023 Cartagena de Indias Colombia: (Oral) “Distilling Missing Modality Knowledge from Ultrasound for Endometriosis Diagnosis with Magnetic Resonance Images”. - Best Oral Presentation

Two-stage Knowledge Distillation



Stage 1. Pre-training

Stage 2. Knowledge distillation



Our Datasets

MRI Endo dataset

- 89 T2_SPC scans
 - 19 complete POD obliteration,
 - 70 negative POD cases

Pretraining datasets:

TVUS Endo dataset

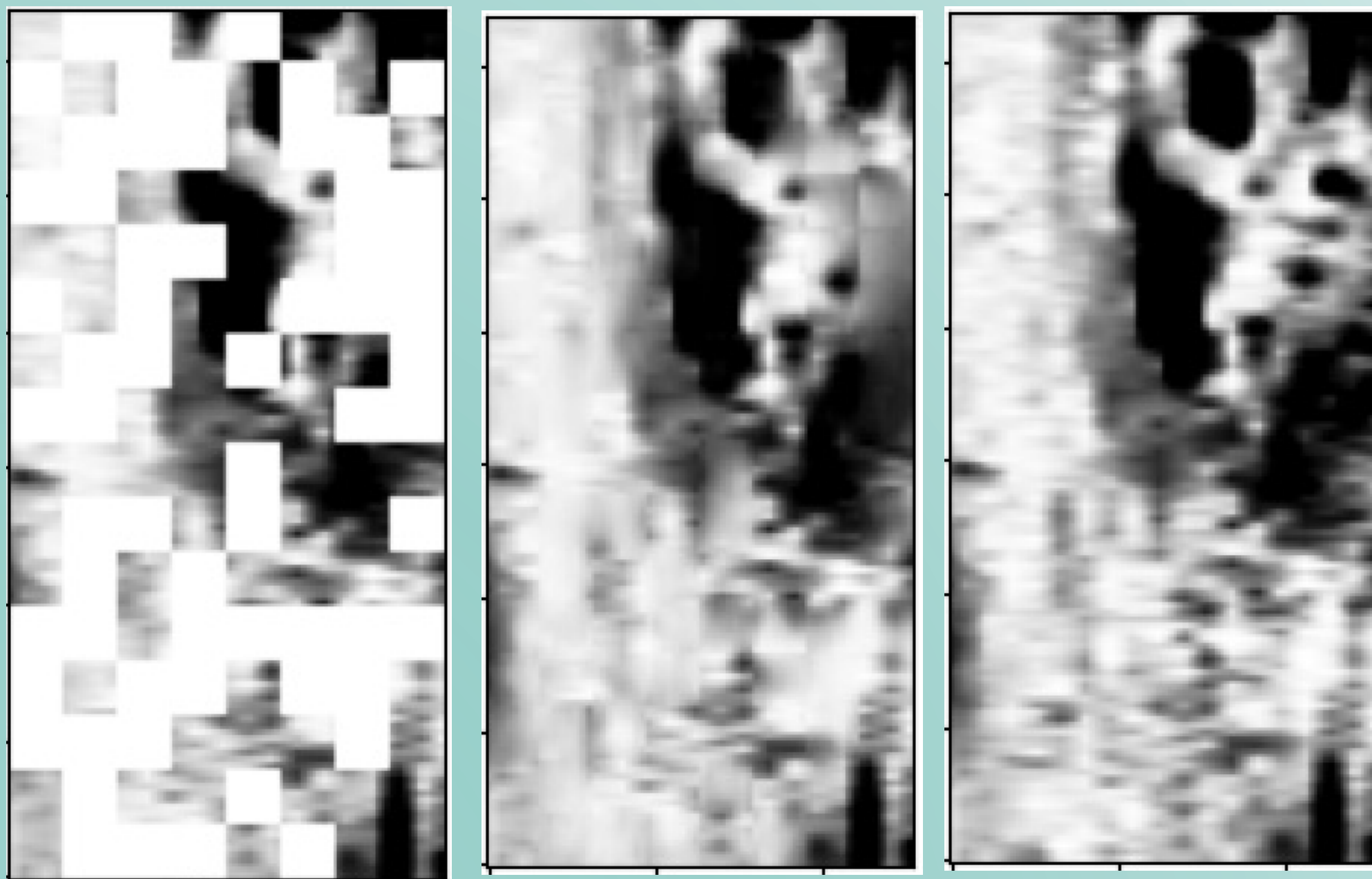
- 749 TVUS
 - 103 complete POD obliteration
 - 646 negative POD cases

Public hospital female pelvic MRI dataset

- 8984 T2 scans'



Results: pretraining



Masked Input

Reconstruction

Original

Masked autoencoder (MAE):

Unsupervised learning which learns to reconstruct masked data

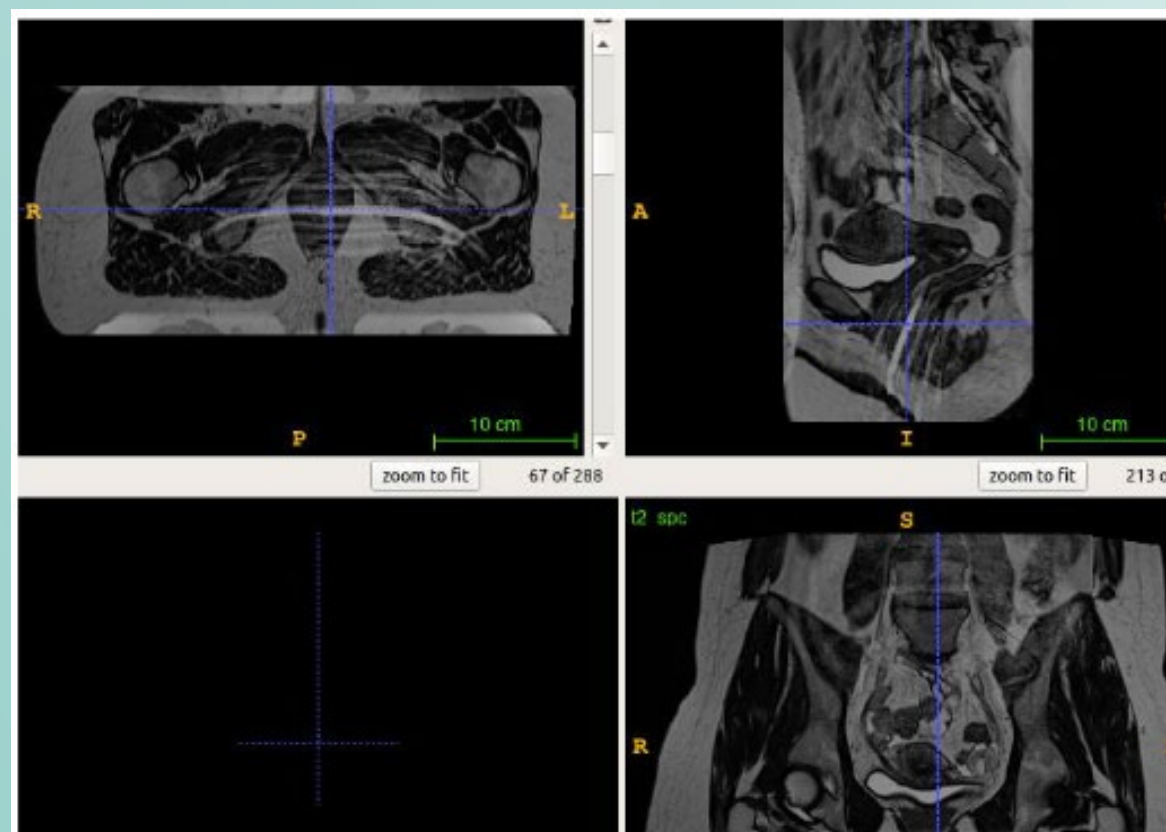
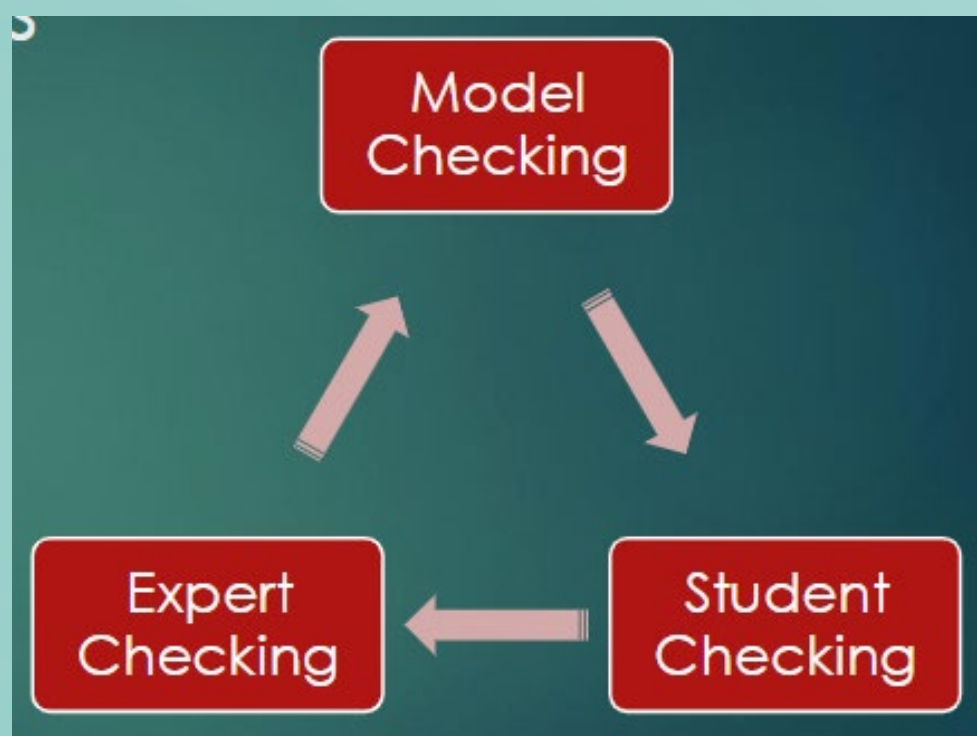
Embedding:

Compressing a large dataset into a small representation with the most salient features



Challenges

- Artefacts, mislabelling, and misreporting confounded our eMRI datasets



Dr Steven Knox
Radiologist, Bensons Radiology

Results: POD Obliteration Classification

Method	Training Modality	Testing Modality	AUC mean \pm stddev
3D ViT	MRI	MRI	0.650 \pm 0.102
3D ViT + MAE Pretraining	MRI	MRI	0.872 \pm 0.094
3D ViT + Knowledge Distillation	MRI, TVUS	MRI	0.667 \pm 0.107
3D ViT + MAE Pretraining + Knowledge Distillation	MRI, TVUS	MRI	0.772 \pm 0.087
3D ViT + MAE Pretraining + FT + Knowledge Distillation	MRI, TVUS	MRI	0.906 \pm 0.099



Conclusion

- We developed a two-stage algorithm to distil the knowledge from an ultrasound to an MRI classifier, which improves the POD obliteration classification accuracy for the MRI classifier.
- Through MAE pre-training, knowledge distillation and fine-tuning, we were able to significantly improve the diagnostic accuracy of MRI for endometriosis using unpaired ultrasound and MRI data.
- our approach shows improved diagnostic efficacy in our experimental results using our endometriosis datasets.



Ms Yuan Zhang
PhD Candidate, AIML

IMAGENDO[®] – recruitment

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 **IMAGENDO**

09 September 2021

We are seeking women who are 18 to 45 years to take part in the IMAGENDO study



ARE YOU HAVING SURGERY FOR PELVIC PAIN?

Participation involves:

- Having an MRI scan (approx. 1 hour)
- Having a transvaginal ultrasound (approx. 1 hour)
- Completing two online questionnaires (approx. 10 mins)

Let your doctor or sonographer know if you would like to take part

Or, scan the QR code now!

Link: <https://is.gd/imagendostudy>



Contact Jodie or Nicola if you want more information...

- Study Manager, Dr Jodie Avery, 0410 519 941 or endostudy@adelaide.edu.au or
- Research Assistant, Nicola Mathews, nicola.mathews@Adelaide.edu.au

This project has received Ethics approval from the University of Adelaide Human Research Ethics Committee [H-2020-051]

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 **IMAGENDO**

Do you want to improve the diagnosis of endometriosis with a FREE MRI?

We are seeking participants 18-45 years old, who are planning surgery to take part in the IMAGENDO study...

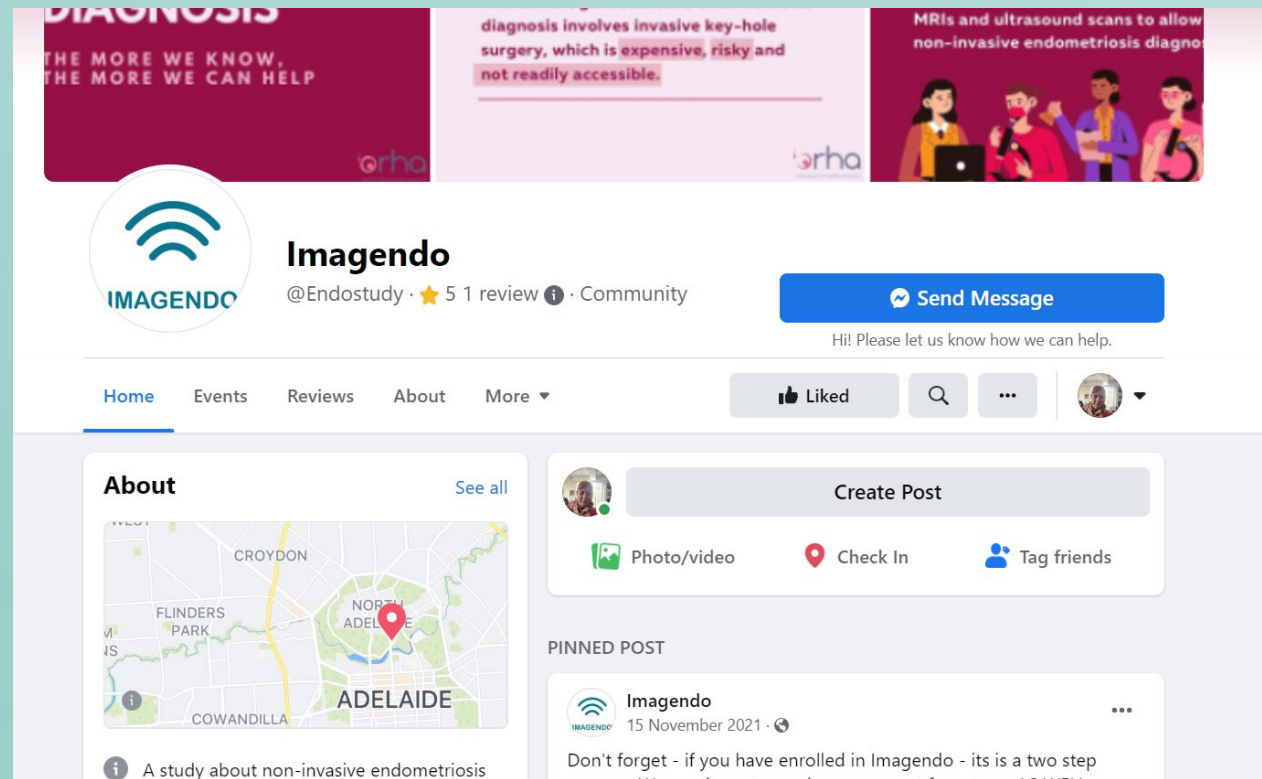
For more information contact: endostudy@adelaide.edu.au
or 0450 534 950

Or go to our website: www.imagendo.org.au



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Non-invasive endometriosis diagnosis using machine learning

Dear IMAGENDO Study Participant,
You are invited to participate in the research project described below.
Thank you!

If you wish to participate, please complete the following questions and click submit.
Please note: you will not be able to continue with the survey unless you select 'yes' to 'Consent to participate'

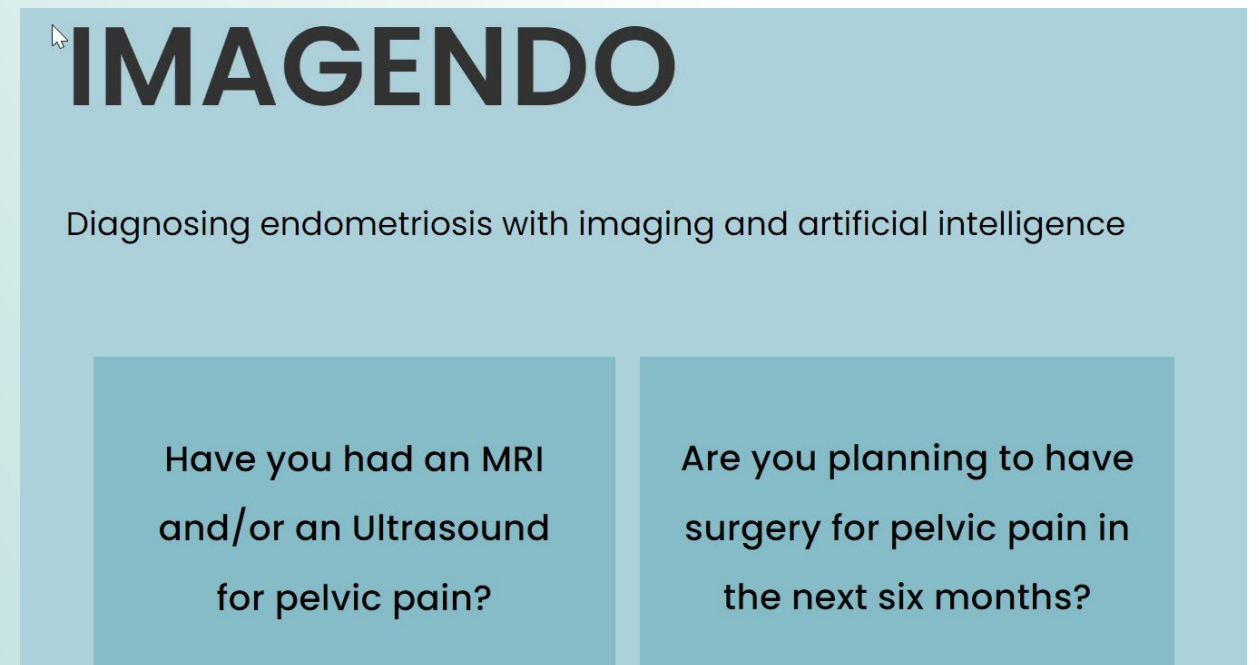
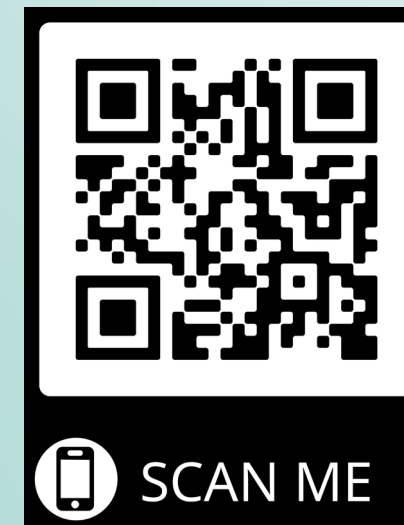
Today's date: Today D-M-Y

I agree to participate in the activities as outlined in the participant information sheet Yes No reset

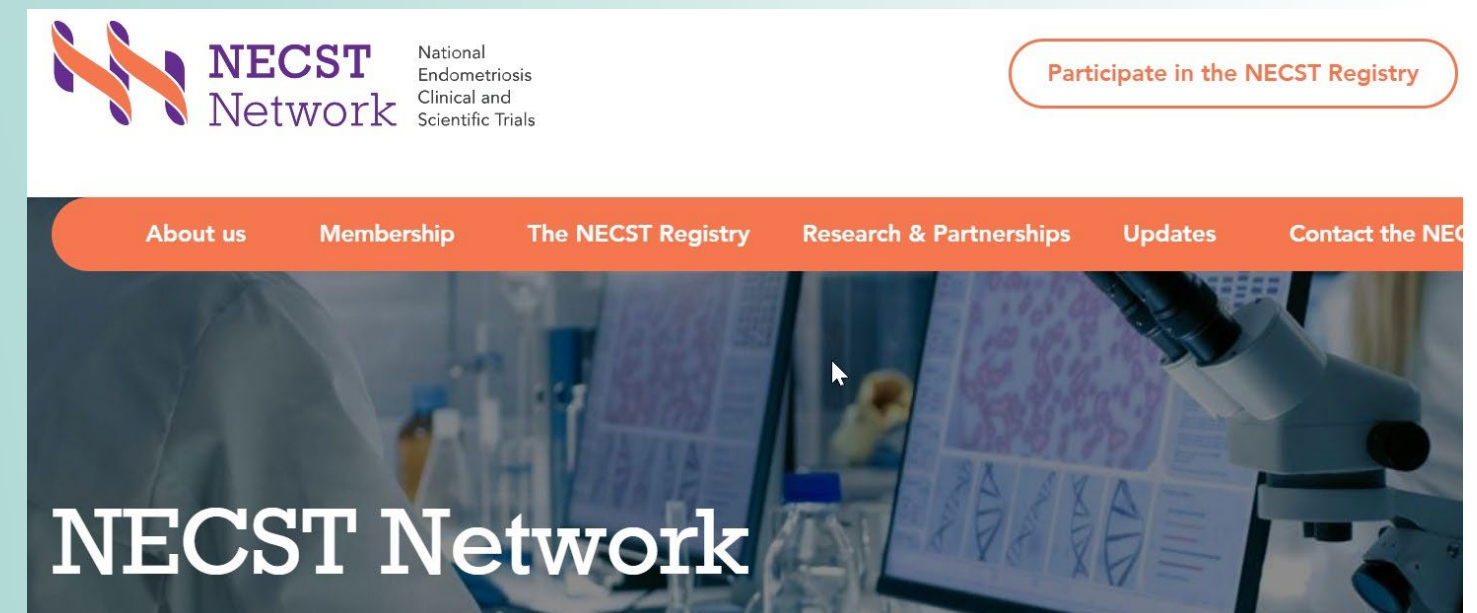
Finding Imagendo



<https://imagendo.org.au/>



<https://www.jeanhailes.org.au/necst-network/home>



IMAGENDO® Team



Dr Jodie Avery



Dr Beck O'Hara



Ms Aisha Sirop



Prof Mary Louise Hull



Prof Gustavo Carneiro



Dr Tim Chen



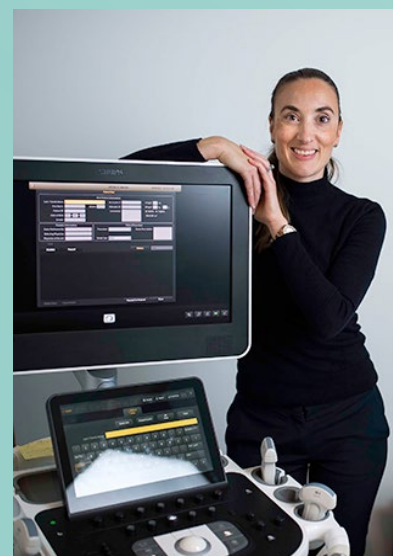
Dr Hu Wang



Ms Yuan Zhang



A/ Prof David Gonzalez Chica



Ms Catrina Panuccio



Dr Jane Woolcock



Dr Steven Knox



A/ Prof George Condous



Dr Mathew Leonardi



Ms Alison Deslandes

Winner!

AUSTRALIAN MUSEUM EUREKA PRIZES 2023 WINNER



IMAGENDO® Contact

IMAGENDO® has received funding from the Australian Government, the Australasian Society of Ultrasound in Medicine (ASUM), Endometriosis Australia, The Australian Gynaecological Endoscopy Association and the Lions Club.

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