

# SOMANZ EVOLVE

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# What is Evolve?

Part of a global movement, Evolve is an initiative led by physicians and the RACP to drive high-value, high-quality care in Australia and New Zealand.

Evolve is a founding member of the Choosing Wisely campaigns in Australia and New Zealand.

Through a rigorous peer-review process, Evolve identifies a specialty's **Top 5** clinical practices that, in particular circumstances, may:

- be overused;
- provide little or no benefit; or
- cause unnecessary harm.

# Creating our Top-Five

- SOMANZ Council Meeting 2015
  - Individual council members researched potential interventions
- Potential list presented at SOMANZ conference in 2016
- Survey Monkey to all SOMANZ members

# Ranking

1. The clinical practice being targeted by this recommendation is still being undertaken in significant numbers
  2. This recommendation is evidence based
  3. This recommendation is important in terms of reducing harm to patients and/or costs to the healthcare system
- 118 responses – just over 25% of the membership

# Do not measure MTHFR gene testing as part of a routine evaluation for thrombophilia in pregnancy

- Prevalence of thermolabile variant in the Caucasian population
  - Homozygous variants: 11%
  - Heterozygous variants: 40-50%
- Women with pregnancy-associated venous thromboembolism do not have an increased rate of the 'thermolabile' variant of the MTHFR gene<sup>1</sup>

1. McLintock et al. Recommendations for the prevention of pregnancy-associated venous thromboembolism.

ANZJOG 2012;52:3-13

# Do not measure ESR in pregnancy

- Non-specific test to identify inflammation
  - Infection/cancer/autoimmune process
  - Women 18-50 years should be <20mm/hr
- 'Normal' range in pregnancy varies from 4-70mm/hr

# Do not repeat testing for proteinuria in established Preeclampsia

- Proteinuria is a diagnostic not prognostic factor in pre-eclampsia
- Various models: PIERS model (Preeclampsia integrated estimate of risk of adverse maternal outcomes)
  - gestational age,
  - chest pain or dyspnoea,
  - oxygen saturation,
  - platelet count,
  - serum creatinine,
  - AST.

# Degree of proteinuria is not an indication for delivery

*Table 4. Indications for delivery in women with preeclampsia or gestational hypertension*

<b>Maternal</b>	<b>Fetal</b>
Gestational age $\geq$ 37 weeks	Placental abruption
Inability to control hypertension	Severe FGR
Deteriorating platelet count	Non-reassuring fetal status
Intravascular haemolysis	
Deteriorating liver function	
Deteriorating renal function	
Persistent neurological symptoms	
Persistent epigastric pain, nausea or vomiting with abnormal LFTs	
Pulmonary edema	



# Do not test for inherited thrombophilia for placental mediated complications

- Retrospective studies found an 'association' between inherited thrombophilia and adverse pregnancy outcomes
- Prospective studies have either failed to find an association or found a weak association only.

**Table 4. Association Between Inherited Thrombophilia Polymorphisms and Composite Primary Outcome**

Thrombophilia	Univariable Odds Ratio (95% CI)	<i>P</i>	Multivariable Odds Ratio* (95% CI)	<i>P</i>
Factor V Leiden (homozygous or heterozygous)	0.94 (0.42–2.06)	.87	1.24 (0.49–3.15)	.64
Prothrombin gene mutation (heterozygous)	2.45 (1.06–5.64)	<b>.04<sup>†</sup></b>	3.58 (1.20–10.61)	<b>.02<sup>†</sup></b>
MTHFR C677T mutation (heterozygous)	1.01 (0.70–1.48)	.93	1.08 (0.65–1.77)	.77
MTHFR C677T mutation (homozygous)	1.09 (0.63–1.93)	.74	0.97 (0.44–2.13)	.94
MTHFR A1298C mutation (heterozygous)	0.83 (0.57–1.18)	.30	0.73 (0.44–1.19)	.20
MTHFR A1298C mutation (homozygous)	0.44 (0.20–0.98)	.04 <sup>†</sup>	0.26 (0.08–0.86)	.03 <sup>†</sup>
Thrombomodulin gene mutation (heterozygous)	1.31 (0.90–1.91)	.16	1.28 (0.77–2.12)	.34
Thrombomodulin gene mutation (homozygous)	1.14 (0.45–2.93)	.78	1.24 (0.36–4.35)	.73

Severe PET

Fetal Growth Restriction < 5<sup>th</sup> centile

Placental Abruption

Still birth

Neonatal death

**Table 3** Association between placenta-mediated complications and thrombophilia exposure

Outcome N (%)	Without thrombophilia ( <i>n</i> = 6836)	With FVL and/or PGM ( <i>n</i> = 507)	RR (95% CI)	aRR (95% CI)
Any placenta-mediated complication (primary outcome)	768 (11.23)	59 (11.64)	1.04 (0.81, 1.33)	1.07 (0.83, 1.37)*
Small for gestational age (SGA)	469 (6.93)	36 (7.20)	1.04 (0.75, 1.44)	1.03 (0.75, 1.43)*
Preeclampsia	212 (3.10)	17 (3.35)	1.08 (0.66, 1.76)	1.14 (0.70, 1.85)†
Placental abruption	64 (0.94)	3 (0.59)	0.63 (0.20, 2.00)	0.60 (0.19, 1.91)‡
Pregnancy loss	80 (1.17)	6 (1.18)	1.01 (0.44, 2.31)	1.02 (0.45, 2.34)§

# Do not perform a D-Dimer test at any trimester in pregnancy

**Table V.** D-dimer values according to the duration of pregnancy. In all of the cited studies, the threshold for positive D-dimer was 500 mg/nL

Study group	D-dimer test	Study participants	1 <sup>st</sup> trimester	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester
Morse, 2004 [111]	IL-test D-dimer (IL)	N = 48, Healthy women	Mean: 191 Range: 45-553	Mean: 393 Range: 142 – 2210	Mean: 544 Range: 155 – 2782
Kline, 2005 [110]	MDA immuno- turbidometric assay (Organon Teknika)	N = 50, Healthy women	Mean ± SD: 579 ± 363 Normal D-dimer: 50 %	Mean ± SD: 832 ± 425 Normal D-dimer: 23 %	Mean ± SD: 1159 ± 573 Normal D-dimer: 0 %
Kovac, 2010 [118]	HemosIL D-dimer HS (IL)	N = 89, Healthy women	Mean ± SD: 222 ± 64 Range: 121 – 474 Normal D-dimer: 84 %	Mean ± SD: 326 ± 131 Range: 171 – 333 Normal D-dimer: 33 %	Mean ± SD: 475 ± 169 Range: 206 – 890 Normal D-dimer: 1 %
		N = 12, Confirmed DVT	Mean ± SD: 1596 ± 95 Range: 1500 – 1691	Mean ± SD: 1330 ± 700 Range: 524 – 1784	Mean ± SD: 1157 – 374 Range: 922 – 1818
Wang, 2013 [119]	Latex-based immu- noturbidimetry (Diagnostica Stago)	N = 1343 Healthy women	IQR: 200 – 410 Normal D-dimer: 85 %	IQR: 470 – 1030 Normal D-dimer: 29 %	IQR: 910 – 1870 Normal D-dimer: 4 %

Abbr.: SD: Standard deviation, IQR: Interquartile range.



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### D-dimers as a screening test for venous thromboembolism in pregnancy: Is it of any use?

M. Damodaram, M. Kaladindi, J. Luckit & W. Yoong

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# Study results

- Retrospective study of 37 women all in either 2<sup>nd</sup> or 3<sup>rd</sup> trimester
- D-Dimer - low probability PE on V/Q scan (0.25-2.2mg/L)
- D-Dimer - high probability PE on V/Q scan (0.31-1.74mg/L)
- Sensitivity of D-Dimer for PE - 0.73
- Specificity of D-Dimer for PE - 0.15
- Negative likelihood ratio = 1.8

# The Top Five

- Do not measure MTHFR gene testing as part of a routine evaluation for thrombophilia in pregnancy
- Do not measure ESR in pregnancy
- Do not repeat testing for proteinuria in established PET
- Do not test for inherited thrombophilia for placental-mediated complications
- Do not perform a D-Dimer test at any trimester in pregnancy