Evaluation of cardiovascular function in women with a history of preeclampsia: a systematic review and meta-analysis

Maya Reddy[1,2], Leah Wright[3], Daniel Rolnik[1,2], Wentao Li[1], Ben Mol[1], Andre La Gerche[3], Fabricio Costa[1], Euan Wallace[1], Kirsten Palmer[1,2]

[1] Department of Obstetrics and Gynaecology, Monash University
[2] Monash Womens, Monash Health
[3] Baker Heart and Diabetes Institute
Email – Maya.Reddy@monash.edu

MonashHealth MONASH University

Background

Women with a history of preeclampsia (PE) are at a 2-4 fold increased risk of chronic hypertension, heart failure, coronary artery disease and cardiovascular disease (CVD) related death. In 2011, the American Heart Association identified PE as a major risk factor for CVD in women. However, women with PE receive no routine postpartum cardiovascular follow up.

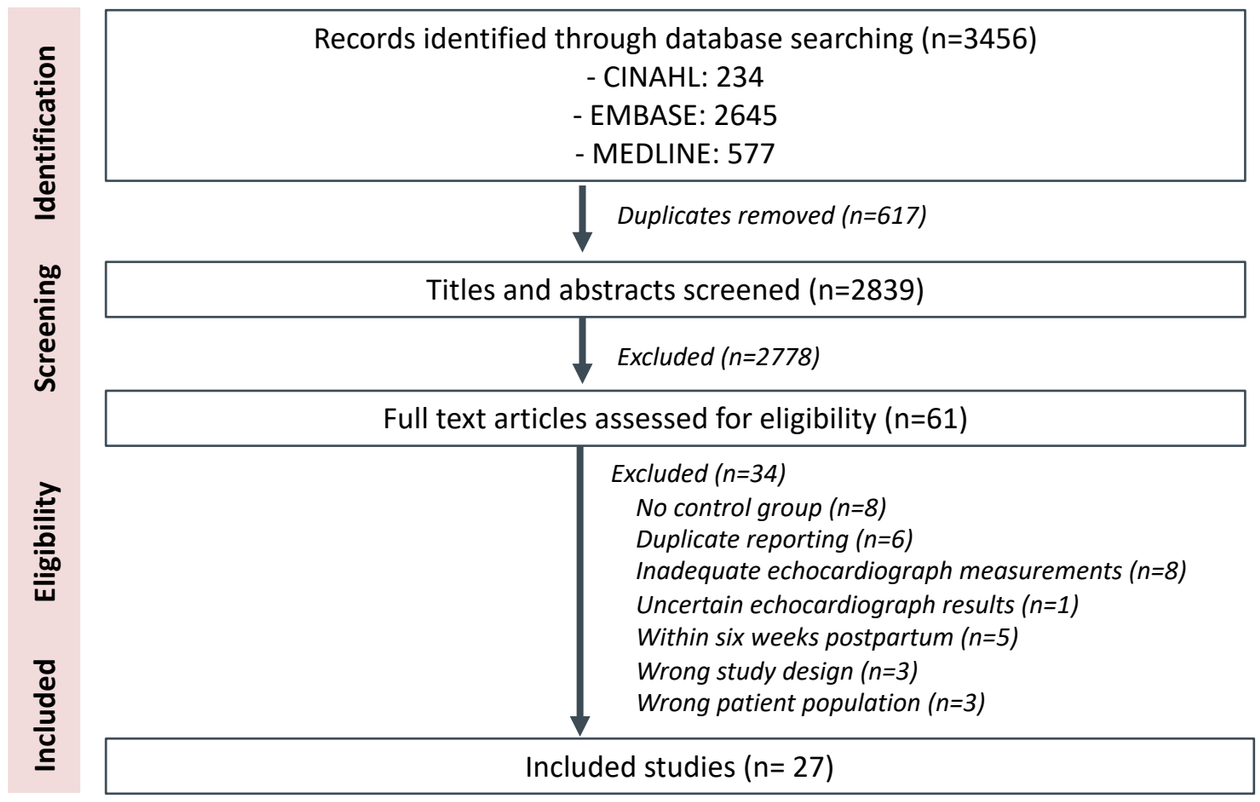
Objectives

To identify the echocardiograph changes seen in women with a history of PE in order to inform 1) further research, and 2) change in clinical practice guidelines to support or refute early cardiac investigations for women with a history of PE.

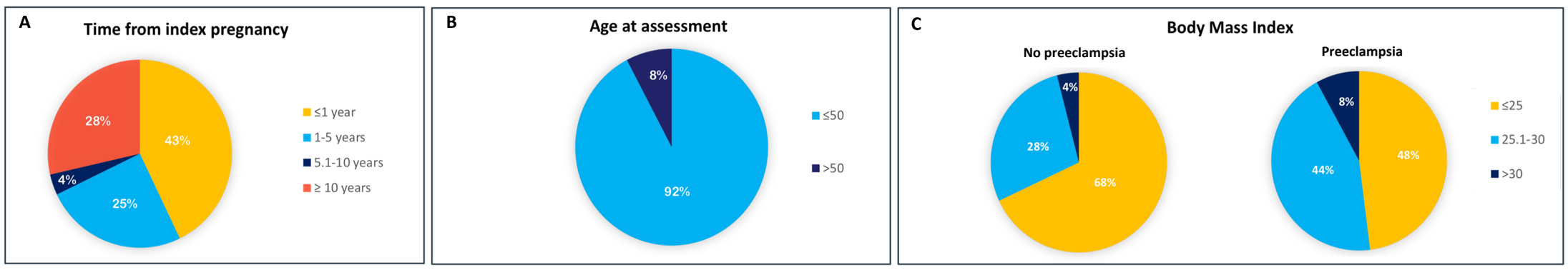
Methods

A systematic search of MEDLINE, EMBASE and CINAHL databases was performed to identify studies that examined cardiovascular function in women with a history of preeclampsia in comparison to those with normotensive pregnancies.

Methods



Results - Demographics



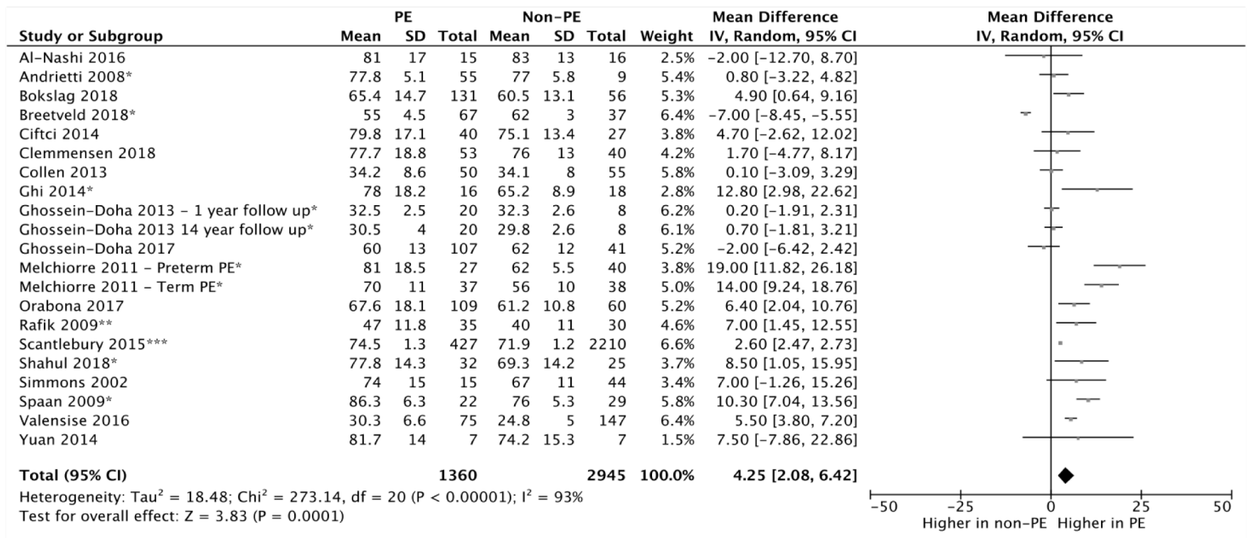
Most studies assessed women within 1 year or ≥10 years after the index pregnancy.

The mean age of assessment was less than 50 in most studies.

The mean BMI was less than 30 in both PE and control groups in most studies.

Results – Cardiac Indices

Left Ventricular Mass Index (g/m²)



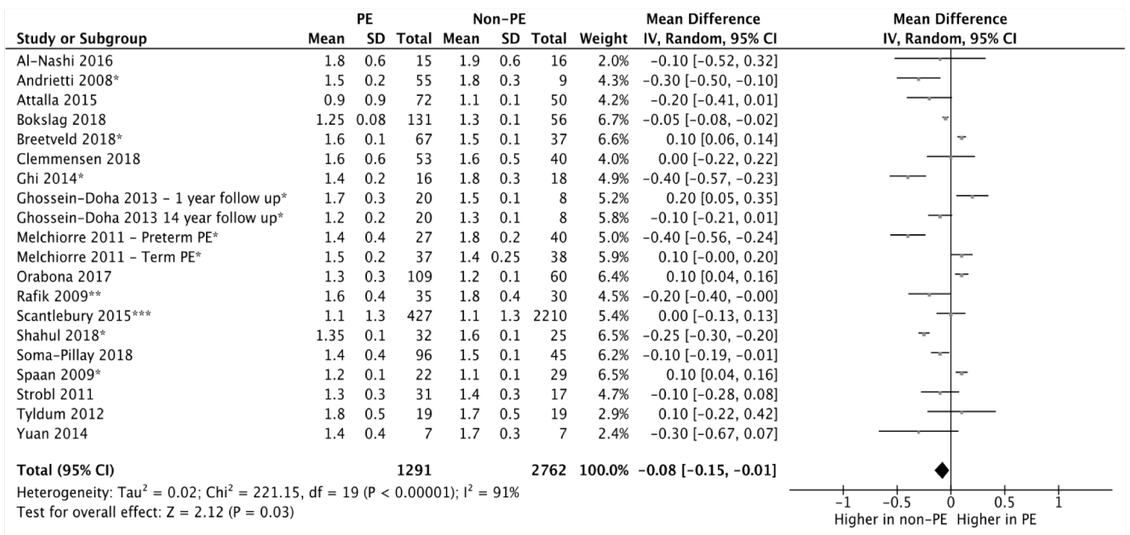
Study or Subgroup	PE Mean	PE SD	PE Total	Non-PE Mean	Non-PE SD	Non-PE Total	Weight	Mean Difference IV, Random, 95% CI
Al-Nashi 2016	81	17	15	83	13	16	2.5%	-2.00 [-12.70, 8.70]
Andrietti 2008*	77.8	5.1	55	77	5.8	9	5.4%	0.80 [-3.22, 4.82]
Bokslag 2018	65.4	14.7	131	60.5	13.1	56	5.3%	4.90 [0.64, 9.16]
Breetveld 2018*	55	4.5	67	62	3	37	6.4%	-7.00 [-8.45, -5.55]
Ciftci 2014	79.8	17.1	40	75.1	13.4	27	3.8%	4.70 [-2.62, 12.02]
Clemmensen 2018	77.7	18.8	53	76	13	40	4.2%	1.70 [-4.77, 8.17]
Collen 2013	34.2	8.6	50	34.1	8	55	5.8%	0.10 [-3.09, 3.29]
Ghi 2014*	78	18.2	16	65.2	8.9	18	2.8%	12.80 [2.98, 22.62]
Ghossein-Doha 2013 - 1 year follow up*	32.5	2.5	20	32.3	2.6	8	6.2%	0.20 [-1.91, 2.31]
Ghossein-Doha 2013 14 year follow up*	30.5	4	20	29.8	2.6	8	6.1%	0.70 [-1.81, 3.21]
Ghossein-Doha 2017	60	13	107	62	12	41	5.2%	-2.00 [-6.42, 2.42]
Melchiorre 2011 - Preterm PE*	81	18.5	27	62	5.5	40	3.8%	19.00 [11.82, 26.18]
Melchiorre 2011 - Term PE*	70	11	37	56	10	38	5.0%	14.00 [9.24, 18.76]
Orabona 2017	67.6	18.1	109	61.2	10.8	60	5.2%	6.40 [2.04, 10.76]
Rafik 2009**	47	11.8	35	40	11	30	4.6%	7.00 [1.45, 12.55]
Scantlebury 2015***	74.5	1.3	427	71.9	1.2	2210	6.6%	2.60 [2.47, 2.73]
Shahul 2018*	77.8	14.3	32	69.3	14.2	25	3.7%	8.50 [1.05, 15.95]
Simmons 2002	74	15	15	67	11	44	3.4%	7.00 [-1.26, 15.26]
Spaan 2009*	86.3	6.3	22	76	5.3	29	5.8%	10.30 [7.04, 13.56]
Valensise 2016	30.3	6.6	75	24.8	5	147	6.4%	5.50 [3.80, 7.20]
Yuan 2014	81.7	14	7	74.2	15.3	7	1.5%	7.50 [-7.86, 22.86]
Total (95% CI)			**1360**			**2945**	**100.0%**	**4.25 [2.08, 6.42]**

Heterogeneity: $Tau^2 = 18.48$; $Chi^2 = 273.14$, df = 20 ($P < 0.00001$); $I^2 = 93\%$
Test for overall effect: Z = 3.83 (P = 0.0001)

Mean Difference IV, Random, 95% CI
-50 -25 0 25 50
Higher in non-PE Higher in PE

Women with a history of preeclampsia (PE) have a higher left ventricular mass index in comparison to the non-PE population.

E/A ratio



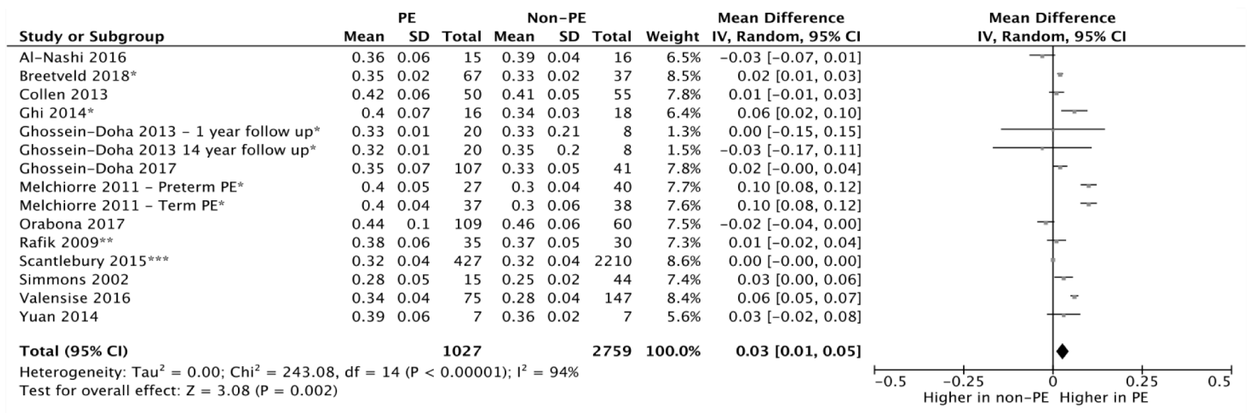
Study or Subgroup	PE Mean	PE SD	PE Total	Non-PE Mean	Non-PE SD	Non-PE Total	Weight	Mean Difference IV, Random, 95% CI
Al-Nashi 2016	1.8	0.6	15	1.9	0.6	16	2.0%	-0.10 [-0.52, 0.32]
Andrietti 2008*	1.5	0.2	55	1.8	0.3	9	4.3%	-0.30 [-0.50, -0.10]
Attalla 2015	0.9	0.9	72	1.1	0.1	50	4.2%	-0.20 [-0.41, 0.01]
Bokslag 2018	1.25	0.08	131	1.3	0.1	56	6.7%	-0.05 [-0.08, -0.02]
Breetveld 2018*	1.6	0.1	67	1.5	0.1	37	6.6%	0.10 [0.06, 0.14]
Clemmensen 2018	1.6	0.6	53	1.6	0.5	40	4.0%	0.00 [-0.22, 0.22]
Ghi 2014*	1.4	0.2	16	1.8	0.3	18	4.9%	-0.40 [-0.57, -0.23]
Ghossein-Doha 2013 - 1 year follow up*	1.7	0.3	20	1.5	0.1	8	5.2%	0.20 [0.05, 0.35]
Ghossein-Doha 2013 14 year follow up*	1.2	0.2	20	1.3	0.1	8	5.8%	-0.10 [-0.21, 0.01]
Melchiorre 2011 - Preterm PE*	1.4	0.4	27	1.8	0.2	40	5.0%	-0.40 [-0.56, -0.24]
Melchiorre 2011 - Term PE*	1.5	0.2	37	1.4	0.25	38	5.9%	0.10 [-0.00, 0.20]
Orabona 2017	1.3	0.3	109	1.2	0.1	60	6.4%	0.10 [0.04, 0.16]
Rafik 2009**	1.6	0.4	35	1.8	0.4	30	4.5%	-0.20 [-0.40, -0.00]
Scantlebury 2015***	1.1	1.3	427	1.1	1.3	2210	5.4%	0.00 [-0.13, 0.13]
Shahul 2018*	1.35	0.1	32	1.6	0.1	25	6.5%	-0.25 [-0.30, -0.20]
Soma-Pillay 2018	1.4	0.4	96	1.5	0.1	45	6.2%	-0.10 [-0.19, -0.01]
Spaan 2009*	1.2	0.1	22	1.1	0.1	29	6.5%	0.10 [0.04, 0.16]
Strobl 2011	1.3	0.3	31	1.4	0.3	17	4.7%	-0.10 [-0.28, 0.08]
Tyldum 2012	1.8	0.5	19	1.7	0.5	19	2.9%	0.10 [-0.22, 0.42]
Yuan 2014	1.4	0.4	7	1.7	0.3	7	2.4%	-0.30 [-0.67, 0.07]
Total (95% CI)			**1291**			**2762**	**100.0%**	**-0.08 [-0.15, -0.01]**

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 221.15$, df = 19 ($P < 0.00001$); $I^2 = 91\%$
Test for overall effect: Z = 2.12 (P = 0.03)

Mean Difference IV, Random, 95% CI
-1 -0.5 0 0.5 1
Higher in non-PE Higher in PE

Women with a history of preeclampsia (PE) have a lower E/A ratio in comparison to the non-PE population.

Relative Wall Thickness



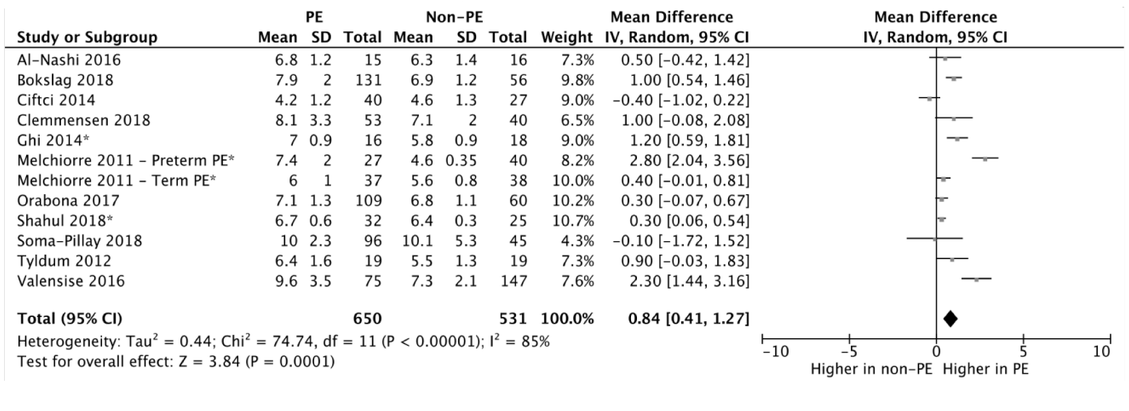
Study or Subgroup	PE Mean	PE SD	PE Total	Non-PE Mean	Non-PE SD	Non-PE Total	Weight	Mean Difference IV, Random, 95% CI
Al-Nashi 2016	0.36	0.06	15	0.39	0.04	16	6.5%	-0.03 [-0.07, 0.01]
Breetveld 2018*	0.35	0.02	67	0.33	0.02	37	8.5%	0.02 [0.01, 0.03]
Collen 2013	0.42	0.06	50	0.41	0.05	55	7.8%	0.01 [-0.01, 0.03]
Ghi 2014*	0.4	0.07	16	0.34	0.03	18	6.4%	0.06 [0.02, 0.10]
Ghossein-Doha 2013 - 1 year follow up*	0.33	0.01	20	0.33	0.21	8	1.3%	0.00 [-0.15, 0.15]
Ghossein-Doha 2013 14 year follow up*	0.32	0.01	20	0.35	0.2	8	1.5%	-0.03 [-0.17, 0.11]
Ghossein-Doha 2017	0.35	0.07	107	0.33	0.05	41	7.8%	0.02 [-0.00, 0.04]
Melchiorre 2011 - Preterm PE*	0.4	0.05	27	0.3	0.04	40	7.7%	0.10 [0.08, 0.12]
Melchiorre 2011 - Term PE*	0.4	0.04	37	0.3	0.06	38	7.6%	0.10 [0.08, 0.12]
Orabona 2017	0.44	0.1	109	0.46	0.06	60	7.5%	-0.02 [-0.04, 0.00]
Rafik 2009**	0.38	0.06	35	0.37	0.05	30	7.3%	0.01 [-0.02, 0.04]
Scantlebury 2015***	0.32	0.04	427	0.32	0.04	2210	8.6%	0.00 [-0.00, 0.00]
Simmons 2002	0.28	0.05	15	0.25	0.02	44	7.4%	0.03 [0.00, 0.06]
Valensise 2016	0.34	0.04	75	0.28	0.04	147	8.4%	0.06 [0.05, 0.07]
Yuan 2014	0.39	0.06	7	0.36	0.02	7	5.6%	0.03 [-0.02, 0.08]
Total (95% CI)			**1027**			**2759**	**100.0%**	**0.03 [0.01, 0.05]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 243.08$, df = 14 ($P < 0.00001$); $I^2 = 94\%$
Test for overall effect: Z = 3.08 (P = 0.002)

Mean Difference IV, Random, 95% CI
-0.5 -0.25 0 0.25 0.5
Higher in non-PE Higher in PE

Women with a history of preeclampsia (PE) have a higher relative wall thickness in comparison to the non-PE population.

E/e' ratio



Study or Subgroup	PE Mean	PE SD	PE Total	Non-PE Mean	Non-PE SD	Non-PE Total	Weight	Mean Difference IV, Random, 95% CI
Al-Nashi 2016	6.8	1.2	15	6.3	1.4	16	7.3%	0.50 [-0.42, 1.42]
Bokslag 2018	7.9	2	131	6.9	1.2	56	9.8%	1.00 [0.54, 1.46]
Ciftci 2014	4.2	1.2	40	4.6	1.3	27	9.0%	-0.40 [-1.02, 0.22]
Clemmensen 2018	8.1	3.3	53	7.1	2	40	6.5%	1.00 [-0.08, 2.08]
Ghi 2014*	7	0.9	16	5.8	0.9	18	9.0%	1.20 [0.59, 1.81]
Melchiorre 2011 - Preterm PE*	7.4	2	27	4.6	0.35	40	8.2%	2.80 [2.04, 3.56]
Melchiorre 2011 - Term PE*	6	1	37	5.6	0.8	38	10.0%	0.40 [-0.01, 0.81]
Orabona 2017	7.1	1.3	109	6.8	1.1	60	10.2%	0.30 [-0.07, 0.67]
Shahul 2018*	6.7	0.6	32	6.4	0.3	25	10.7%	0.30 [0.06, 0.54]
Soma-Pillay 2018	10	2.3	96	10.1	5.3	45	4.3%	-0.10 [-1.72, 1.52]
Tyldum 2012	6.4	1.6	19	5.5	1.3	19	7.3%	0.90 [-0.03, 1.83]
Valensise 2016	9.6	3.5	75	7.3	2.1	147	7.6%	2.30 [1.44, 3.16]
Total (95% CI)			**650**			**531**	**100.0%**	**0.84 [0.41, 1.27]**

Heterogeneity: $Tau^2 = 0.44$; $Chi^2 = 74.74$, df = 11 ($P < 0.00001$); $I^2 = 85\%$
Test for overall effect: Z = 3.84 (P = 0.0001)

Mean Difference IV, Random, 95% CI
-10 -5 0 5 10
Higher in non-PE Higher in PE

Women with a history of preeclampsia (PE) have a higher E/e' ration in comparison to the non-PE population.

Conclusion

In comparison to normotensive pregnancies, women with a history of PE show a trend to a higher left ventricular mass index, relative wall thickness and E/e' ratio, and a lower E/A ratio. However the studies included are small in sample size and show significant heterogeneity. Further studies with larger sample sizes, consistent echocardiograph reporting, and the use of more sensitive pre-clinical markers are required to assess the role of echocardiography in monitoring women with a history of PE.