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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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Supplementary Appendix

Contents

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Trial Definitions

Definition of preeclampsia (by the International Society for the Study of Hypertension in Pregnancy 2014 statement).[1]

New onset hypertension (≥ 140 mmHg systolic, or ≥ 90 mmHg diastolic) or worsening of existing hypertension with the coexistence of one or more of the following new-onset conditions: proteinuria (urine protein creatinine ratio of ≥ 30 mg/mmol, renal insufficiency (creatinine ≥ 90umol/L), liver involvement (elevated transaminases at least twice the upper limit of normal), neurological complications (eclampsia, blindness, hyperreflexia with clonus, severe headaches, persistent visual scotomata), haematological complications (platelet count ≤ 150 x 10^9 per litre, disseminated intravascular coagulation, haemolysis), evidence of uteroplacental dysfunction with fetal growth restriction.

Supplementary Tables

Table S1

Recruitment by centre

Centre	Number Recruited
Bradford Teaching Hospitals NHS Foundation Trust	50 (4.8%)
Central Manchester University Hospitals NHS Foundation Trust	126 (12.2%)
Guy's and St Thomas' NHS Foundation Trust	178 (17.2%)
Kingston Hospital NHS Foundation Trust	93 (9.0%)
Leeds Teaching Hospitals NHS Trust	102 (9.9%)
Liverpool Women's NHS Foundation Trust	116 (11.2%)
North Bristol NHS Trust	67 (6.5%)
St George's University Hospitals NHS Foundation Trust	79 (7.6%)
Royal United Hospitals Bath NHS Foundation Trust	50 (4.8%)
University Hospitals Bristol NHS Foundation Trust	84 (8.1%)
Chelsea and Westminster University Hospitals NHS Foundation Trust	90 (8.7%)
Total	**1035**

Table S2

Secondary Maternal Outcomes

	Revealed (intervention) N = 573	**Usual Care (non-intervention)** N = 446	
Maternal fullPIERS* adverse outcomes, n (%) (non-exclusive)	22 (3.8%)	24 (5.4%)	Odds ratio 0.32 (0.11-0.96)
Maternal Death	0 (0.0%)	0 (0.0%)	
Central nervous system n (%)			
Eclampsia	0 (0.0%)	2 (0.4%)	
Glasgow coma scale score < 13	0 (0.0%)	0 (0.0%)	
Stroke	0 (0.0%)	2 (0.4%)	
Transient Ischaemic Attack	0 (0.0%)	0 (0.0%)	
Cortical blindness or retinal detachment	0 (0.0%)	0 (0.0%)	
Posterior reversible encephalopathy	0 (0.0%)	0 (0.0%)	
Cardiovascular/ respiratory n (%)			
Positive inotropic support	0 (0.0%)	0 (0.0%)	
Infusion of third parenteral antihypertensive	1 (0.2%)	3 (0.7%)	
Myocardial infarction	0 (0.0%)	1 (0.2%)	
Blood oxygen saturation <90%	1 (0.2%)	1 (0.2%)	
50% oxygen administered >1 hour	0 (0.0%)	0 (0.0%)	
Intubation (other than for caesarean section)	0 (0.0%)	1 (0.2%)	
Pulmonary oedema	2 (0.3%)	0 (0.0%)	
Haematological n (%)			
Transfusion of blood products	9 (1.6%)	14 (3.1%)	
Platelets $<50\times10^9$/L	4 (0.7%)	4 (0.9%)	
Hepatic n (%)			
Dysfunction**	1 (0.2%)	0 (0.0%)	
Haematoma or rupture	0 (0.0%)	0 (0.0%)	
Renal n (%)			
Severe Acute Kidney Injury***	7 (1.2%)	6 (1.3%)	
Dialysis	0 (0.0%)	1 (0.2%)	
Other adverse events n (%)			
Placental Abruption	4 (0.7%)	5 (1.1%)	

	Revealed (intervention) N = 573	**Usual Care (non-intervention)** N = 446	
Time to diagnosis 0-23.9 hours n (%)	52 (20·3%)	31 (15·8%)	Odds ratio 3·6 (1·16-11·2)
Gestation at preeclampsia diagnosis (weeks) Mean (SD)	33·7 (3·6)	34·6 (3·4)	
Pre-eclampsia diagnosed within 4 weeks of trial entry n (%)	186 (90·1%)	133 (85·8%)	
Fetal growth abnormalities on ultrasound (non-exclusive) n (%)			
Any of the following:			Odds ratio
Scanned	438 (76·6%)	307 (69·3%)	-
Any growth abnormality identified	142 (32·4%)	67 (21·8%)	1·74 (0·87 to 3·47)
Abdominal circumference <10th centile	86 (19·6%)	41 (13·4%)	-
Estimated fetal weight <10th centile	117 (26·7%)	62 (20·2%)	1·49 (0·70 to 3·15)
Umbilical artery pulsatility index >95th	66 (15·1%)	27 (8·8%)	2·94 (1·07 to 8·11)
Absent or reversed end diastolic flow	43 (9·8%)	16 (5·2%)	-
Amniotic fluid index <5th centile	28 (6·4%)	15 (4·9%)	-
Use of magnesium sulfate n (%)	72 (12·6%)	64 (14·3%)	Odds ratio 0·95 (0·46 to 1·95)
Use of antenatal corticosteroids for fetal lung maturity n (%)	200 (34·9%)	132 (29·6%)	Odds ratio 1·26 (0·75 to 2·11)
Gestation at delivery, weeks Mean (SD)	36·6 (3·03)	36·8 (3·03)	Mean difference -0·52 (-0·63 to 0·73)
Time to delivery (all diagnoses), days Geometric mean (SD)	19·0 (3·1)	17·8 (3·1)	Ratio of means 1·10 (0·99-1·24)

***** as defined in fullPIERS consensus[2].

*** INR >1.2 in the absence of DIC or treatment with Warfarin (DIC is defined as having both: abnormal bleeding and consumptive coagulopathy [i.e., low platelets, abnormal peripheral blood film, or one or more of the following: increased INR, increased APTT, low fibrinogen, increased fibrin degradation products that are outside normal non-pregnancy ranges])

*** Defined as creatinine >150 μmol/L, or >200 μmol/L in women with chronic kidney disease

Table S3

Secondary Perinatal Outcomes

Perinatal adverse outcome*			Odds ratio
Non-exclusive n (%)	86 (15.0%)	63 (14.1%)	1.45 (0.73-2.90)
Central nervous system:			
Intraventricular haemorrhage	7 (1.3%)	11 (2.5%)	
Seizure (any grade)	0 (0.0%)	2 (0.4%)	
Retinopathy of prematurity (any grade)	9 (1.6%)	9 (2.1%)	
Respiratory:			
Respiratory distress syndrome	78 (14.2%)	54 (12.2%)	
Bronchopulmonary dysplasia	5 (0.9%)	3 (0.7%)	
Gastrointestinal:			
Necrotising enterocolitis (stage 2 or 3)	7 (1.2%)	7 (1.6%)	
Perinatal death** n (%)	6 (1.0%)	4 (0.9%)	
Late neonatal death*** (%)	3 (0.5%)	1 (0.2%)	
Birthweight < 10th centile	124 (21·8%)	98 (22·1%)	Odds ratio 0·82 (0·46 to 1·44)
Birthweight < 3rd centile	58 (10·2%)	43 (9·7%)	Odds ratio 0·89 (0·40 to 2·00)
Apgar <7 at 5 minutes	34 (6.0%)	22 (5.2%)	

*Composite of intraventricular haemorrhage (any grade), seizures, retinopathy of prematurity (any grade), respiratory distress syndrome, bronchopulmonary dysplasia, necrotising enterocolitis (stage 2 or 3), perinatal death and late neonatal death.

** Defined as stillbirths from 24 weeks' gestation to deaths up to seven completed days after birth

*** Death between 8 and 27 completed days of life

Table S4

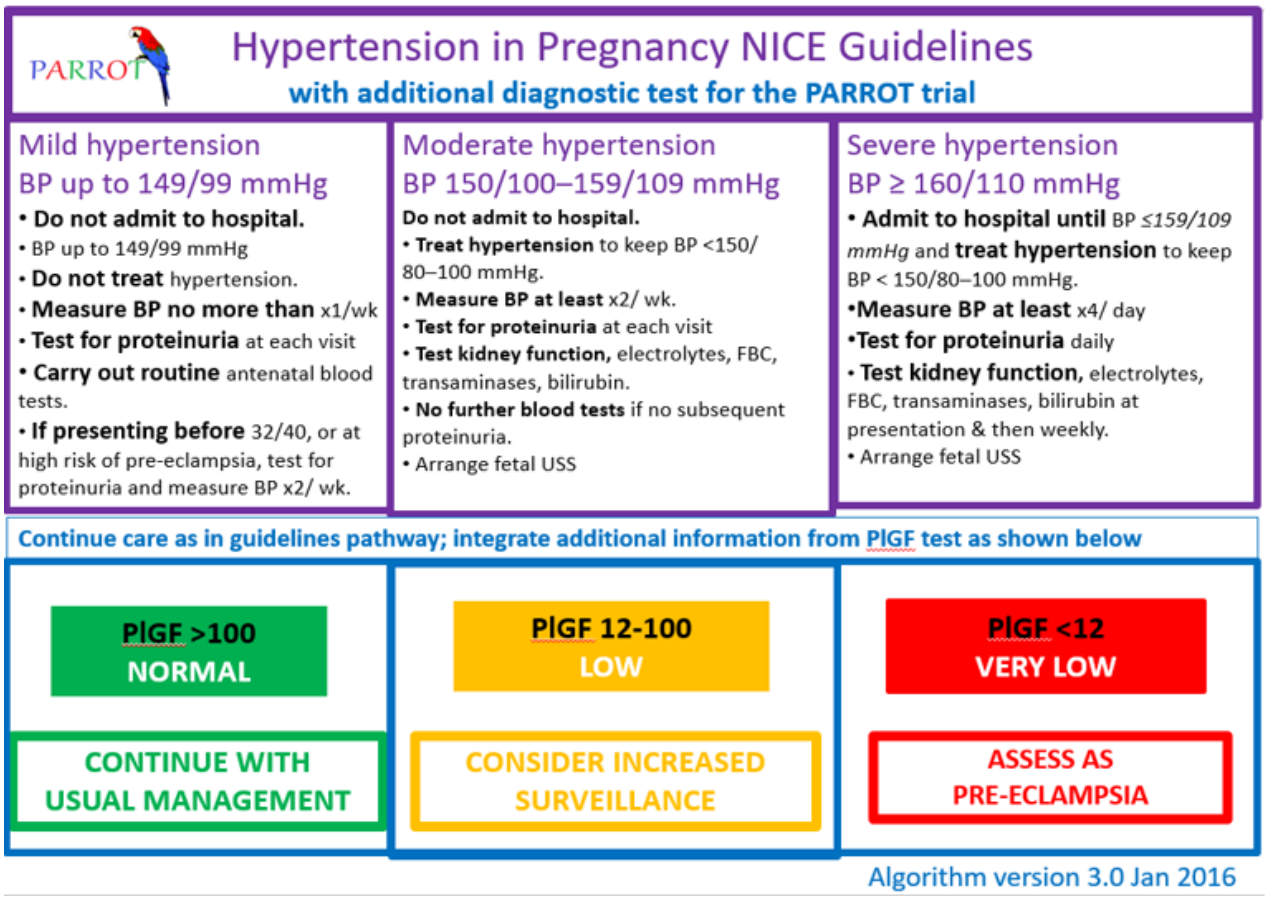
Test performance statistics in women allocated to usual care (concealed testing) for low Placental Growth Factor in prediction of preeclampsia

	Enrolled <35 weeks' gestation N=265	**Enrolled 35-36^{+6} weeks' gestation N= 170**
	Preeclampsia requiring delivery within 14 days	Preeclampsia requiring delivery before 37 weeks
PlGF <100 pg/mL		
Sensitivity (%; 95% CI) n/N	94·9 (82·7 to 99·4) 37/39	96·3 (81·0 to 99·9) 25/27
Specificity (%; 95% CI) n/N	52·7 (45·9 to 59·3) 119/226	23·8 (17·1 to 31·6) 34/143
Positive predictive value (%; 95% CI) n/N	25·7 (18·8 to 33·6) 37/144	19·3 (13·0 to 26·9) 26/135
Negative predictive value (%; 95% CI) n/N	98·3 (94·2 to 99·8) 119/121	97·1 (85·1 to 99·9) 34/35
Positive likelihood ratio (95% CI)	2·00 (1·71 to 2·34)	1·26 (1·12 to 1·42)
Negative likelihood ratio (95% CI)	0·10 (0·03 to 0·38)	0·16 (0·02 to 1·09)
PlGF <12 pg/mL		
Sensitivity (%; 95% CI) n/N	74·4 (57·9 to 87·0) 29/39	37·0 (19·4 to 57·6) 10/27
Specificity (%; 95% CI) n/N	84·1 (78·6 to 88·6) 190/226	78·3 (70·7 to 84·8) 12/143
Positive predictive value (%; 95% CI) n/N	44·6 (32·3 to 57·5) 29/65	24·4 (12·4 to 40·3) 10/41
Negative predictive value (%; 95% CI) n/N	95·0 (91·0 to 97·6) 190/200	86·8 (79·7 to 92·1) 112/129
Positive likelihood ratio (95% CI)	4·67 (3·28 to 6·64)	1·71 (0·95 to 3·06)
Negative likelihood ratio (95% CI)	0·30 (0·18 to 0·52)	0·80 (0·59 to 1·09)

Supplementary Figures

Figure S1

Clinical Management Algorithm



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