



STATISTICAL ANALYSIS PLAN

EMPOWaR

Efficacy of Metformin in Pregnant Obese Women, a Randomised Controlled Trial

MREC No. 10/MRE00/12

Funder: NIHR Efficacy and Mechanism Evaluation (EME) Programme

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Document Version History

Version Number	Reason for Update	Updated By:	Date
0.0	Creation of new statistical analysis plan	Gordon Murray	20 Nov 2012
1	Additional clarification text	Jane Norman	8 Oct 2014

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EMPOWaR: Efficacy of Metformin in Pregnant Obese Women, a Randomised Controlled Trial
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Statistical Report

Population = Intention to treat (ITT) - AllocatedTreatment used for analysis
Report number: 02

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Data set analysed as it was on:

29 April 2015

Section 1. Disposition / data checks

1.1 Patient disposition before randomisation - All Centres

		---Overall---
<i>Parameter(s)</i>	<i>Categories</i>	<i>Count (n(%))</i>
All patients in DB (n(%))	Yes	4867 (100)
Declined reason (n(%))	Subject participate has declined	2861 (58.8)
	Other Reason	57 (1.2)
	Failed Exclusion	100 (2.1)
	Failed Inclusion	626 (12.9)
	Failed both Exclu and Inclu	4 (0.1)
	Did not decline and pass IN_EX but not rand*	10 (0.2)
	Did not attend appointment	8 (0.2)
	Unable to contact	752 (15.5)
	Did not decline and pass IN_EX and rand	449 (9.2)

Section 1. Disposition / data checks

1.2.1.1 Patient disposition after randomisation - All Centres

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Consented/randomised (n(%))	Yes	223 (100)	226 (100)	449 (100)
Disposition in database (n(%))	Active	196 (87.9)	191 (84.5)	387 (86.2)
	Declined	2 (0.9)	2 (0.9)	4 (0.9)
	Withdrawn by clinician	0	1 (0.4)	1 (0.2)
	Lost to follow up	9 (4.0)	7 (3.1)	16 (3.6)
	Participant withdrawn	15 (6.7)	24 (10.6)	39 (8.7)
	Serious Adverse Event	1 (0.4)	1 (0.4)	2 (0.4)
Outcome (z score) available* (n(%))	Yes - Live Birth	218 (97.8)	213 (94.2)	431 (96.0)
	Yes - Live Birth-followed by neonatal death	2 (0.9)	1 (0.4)	3 (0.7)
	Yes - Stillbirth	0	2 (0.9)	2 (0.4)
	No - Miscarriage	0	4 (1.8)	4 (0.9)
	No - Termination of Pregnancy	2 (0.9)	1 (0.4)	3 (0.7)
	No - Not available	1 (0.4)	5 (2.2)	6 (1.3)
Outcome (Glucose test) available# (n(%))	Yes	148 (66.4)	142 (62.8)	290 (64.6)
	No	75 (33.6)	84 (37.2)	159 (35.4)

Section 1. Disposition / data checks

1.2.1.2 Patient disposition after randomisation - All Centres - Consort figures

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Treatment distributed(n(%))	Data available	222 (99.6)	225 (99.6)	447 (99.6)
	Withdrawn pre treatment	1 (0.4)	1 (0.4)	2 (0.4)
Outcome (z score) available* (n(%))	Data available	220 (98.7)	214 (94.7)	434 (96.7)
	Stillbirth	0	2 (0.9)	2 (0.4)
	Miscarriage (<24 weeks)	0	4 (1.8)	4 (0.9)
	Withdrawn pre treatment	1 (0.4)	1 (0.4)	2 (0.4)
	Withdrawn post treatment	0	3 (1.3)	3 (0.7)
	Lost to follow up	0	1 (0.4)	1 (0.2)
	Termination of Pregnancy	2 (0.9)	1 (0.4)	3 (0.7)

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 00:26

By: Aryelly Rodriguez - ECTU Statistician

N = number of patients randomised, n = number of observations

*Available at visit 8 (Delivery)

IMPORTANT NOTES on manual identification:

Patients 12046 and 12047 withdrawn pre treatment

Patients 17063, 27317 and 18113 withdrawn post treatment

Patients 12041, 12086 and 21119 were identified as miscarriage but they were termination of pregnancies TOP

Section 1. Disposition / data checks

1.2.1.2 Patient disposition after randomisation - All Centres - Consort figures (Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Follow up Visit 9 data available* (n(%))	Data available	128 (57.4)	132 (58.4)	260 (57.9)
	Miscarriage (<24 weeks)	0	4 (1.8)	4 (0.9)
	Did not attend the visit	65 (29.1)	54 (23.9)	119 (26.5)
	Decline to further participate	16 (7.2)	20 (8.8)	36 (8.0)
	Lost to follow up	9 (4.0)	7 (3.1)	16 (3.6)
	Withdrawn pre treatment	1 (0.4)	1 (0.4)	2 (0.4)
	Withdrawn post treatment	0	3 (1.3)	3 (0.7)
	Withdrawn by clinician	0	1 (0.4)	1 (0.2)
	Stillbirth	0	2 (0.9)	2 (0.4)
	Termination of Pregnancy	2 (0.9)	1 (0.4)	3 (0.7)
	Live Birth followed by neonatal death	2 (0.9)	1 (0.4)	3 (0.7)

Section 1. Disposition / data checks
 1.2.2 Study Populations - All Centres

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo</i>	<i>Metformin</i>	<i>Overall</i>
Randomised - ITT population (n(%))*	Yes	223 (100)	226 (100)	449 (100)
IMP at least once (n(%))#	Missing	46	59	105
	No	8 (4.5)	9 (5.4)	17 (4.9)
	Yes	169 (95.5)	158 (94.6)	327 (95.1)
Compliant - PP population (n(%))\$	Missing	46	59	105
	No	59 (33.3)	58 (34.7)	117 (34.0)
	Yes	118 (66.7)	109 (65.3)	227 (66.0)

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 00:26

By: Aryelly Rodriguez - ECTU Statistician

N = number of patients randomised, n = number of observations

*The intention to treat (ITT) population will comprise all randomised subjects

#Members of the ITT population who took IMP at least once

\$The per-protocol (PP) population will comprise those members of the ITT population who completed the study without a major protocol violation and who complied adequately with the randomised treatment, further details of treatment compliance are in table 3.2.2 of this report

Section 1. Disposition / data checks

1.3 Patient disposition - Minimisation variables

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Centres (n(%))	Royal Infirmary of Edinburgh	60 (26.9)	59 (26.1)	119 (26.5)
	Coventry	49 (22.0)	49 (21.7)	98 (21.8)
	Liverpool Womens Hospital	38 (17.0)	39 (17.3)	77 (17.1)
	Sheffield	24 (10.8)	24 (10.6)	48 (10.7)
	Notts City	7 (3.1)	6 (2.7)	13 (2.9)
	Notts QMC	8 (3.6)	6 (2.7)	14 (3.1)
	Bradford	4 (1.8)	4 (1.8)	8 (1.8)
	St Helens	1 (0.4)	3 (1.3)	4 (0.9)
	Chelsea and Westminster	0	1 (0.4)	1 (0.2)
	Preston	18 (8.1)	18 (8.0)	36 (8.0)
	Arrow Park Wirral	3 (1.3)	4 (1.8)	7 (1.6)
	Chesterfield	11 (4.9)	12 (5.3)	23 (5.1)
Blackburn	0	1 (0.4)	1 (0.2)	
BMI band at randomisation*(n(%))	30-39 Kg/m ²	152 (68.2)	152 (67.3)	304 (67.7)
	>40 Kg/m ²	71 (31.8)	74 (32.7)	145 (32.3)

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Section 1. Disposition / data checks

1.4 Data Completeness by time point

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Patients CRF Completeness by CRF SECTIONS</i>	<i>Allocated Regimen</i>			
	<i>METFORMIN</i>		<i>PLACEBO</i>	
	<i>Visit attended</i>		<i>Visit attended</i>	
	<i>Yes</i>	<i>No</i>	<i>Yes</i>	<i>No</i>
<i>VISIT 1 (SCREENING)</i>	226	0	223	0
<i>VISIT 2 (BASELINE)</i>	226	0	223	0
<i>VISIT 3 (RANDOMISATION)</i>	226	0	223	0
<i>VISIT 4 (18 TO 20 WEEKS)</i>	194	32	188	35
<i>VISIT 5 (28 WEEKS)</i>	175	51	183	40
<i>VISIT 6 (36 WEEKS)</i>	145	81	158	65
<i>VISIT 7 (TERM)</i>	73	153	76	147
<i>VISIT 8 (DELIVERY)</i>	201	25	206	17
<i>VISIT 9 (FINAL)</i>	132	94	128	95

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Section 1. Disposition / data checks

1.4 Data Completeness by time point

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Patients CRF Completeness by CRF SECTIONS</i>	<i>Allocated Regimen</i>	
	<i>OVERALL</i>	
	<i>Visit attended</i>	
	<i>Yes</i>	<i>No</i>
<i>VISIT 1 (SCREENING)</i>	449	0
<i>VISIT 2 (BASELINE)</i>	449	0
<i>VISIT 3 (RANDOMISATION)</i>	449	0
<i>VISIT 4 (18 TO 20 WEEKS)</i>	382	67
<i>VISIT 5 (28 WEEKS)</i>	358	91
<i>VISIT 6 (36 WEEKS)</i>	303	146
<i>VISIT 7 (TERM)</i>	149	300
<i>VISIT 8 (DELIVERY)</i>	407	42
<i>VISIT 9 (FINAL)</i>	260	189

Section 2. Baseline - Visit 2 (10-16 Weeks) - Demographics and Lifestyle

2.1.1 Maternal Age

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
Maternal Age at consent (years)	Mean	28.9	28.7	28.8
	Median	29.0	28.0	29.0
	SD	5.1	5.8	5.5
	MIN,MAX	17,43	18,43	17,43
	Q1,Q3	25,33	24,33	24,33
	n	223	226	449
	Nmiss	0	0	0

Section 2. Baseline - Visit 2 (10-16 Weeks) - Demographics and Lifestyle

2.1.2 Maternal Life Style Status

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Smoking Status (n%)	ACTIVE	31 (13.9)	40 (17.7)	71 (15.8)
	PREVIOUSLY	13 (5.8)	15 (6.6)	28 (6.2)
	NOT SMOKING	179 (80.3)	171 (75.7)	350 (78.0)
Alcohol During Pregnancy (n%)	Yes	9 (4.0)	3 (1.3)	12 (2.7)
	No	214 (96.0)	223 (98.7)	437 (97.3)
Illicit Drug Status (n%)	USING	1 (0.4)	0	1 (0.2)
	NOT USING	222 (99.6)	226 (100)	448 (99.8)

Section 2. Baseline - Visit 2 (10-16 Weeks) - Demographics and Lifestyle

2.1.3 Maternal Education

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Educational Qualifications (n(%))	No formal qualifications	17 (7.6)	8 (3.5)	25 (5.6)
	Entry level certification/foundation diploma	7 (3.1)	12 (5.3)	19 (4.2)
	GCSE, Standard grade, "O" grades	55 (24.7)	55 (24.3)	110 (24.5)
	A level, A/S level, Highers or BTEC Dip/Cert.	49 (22.0)	37 (16.4)	86 (19.2)
	Cert. higher Education, City & Guilds	15 (6.7)	14 (6.2)	29 (6.5)
	Diploma HE/FE or HND/HNC	30 (13.5)	30 (13.3)	60 (13.4)
	Graduate certificate or Diploma	4 (1.8)	9 (4.0)	13 (2.9)
	Degree	32 (14.3)	47 (20.8)	79 (17.6)
	Professional Qualification	3 (1.3)	4 (1.8)	7 (1.6)
	PGCE/Postgraduate certificate or Diploma, Masters. Doctorate	11 (4.9)	10 (4.4)	21 (4.7)
Educational Qualifications coded (n(%))	None	17 (7.6)	8 (3.5)	25 (5.6)
	School up to 16 years	62 (27.8)	67 (29.6)	129 (28.7)
	School 16 to 18 years	64 (28.7)	51 (22.6)	115 (25.6)
	College or Uni degree or Higher	80 (35.9)	100 (44.2)	180 (40.1)

Section 2. Baseline - Visit 2 (10-16 Weeks) - Demographics and Lifestyle

2.1.4.1 Previous pregnancy status* PARITY 1

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
PARITY1 (n(%))	0	84 (37.7)	100 (44.2)	184 (41.0)
	=>1	139 (62.3)	126 (55.8)	265 (59.0)

Section 2. Baseline - Visit 2 (10-16 Weeks) - Demographics and Lifestyle

2.1.4.2 Previous pregnancy status*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Number of Previous Pregnancies (n(%))	Missing	3	0	3
	0	59 (26.8)	79 (35.0)	138 (30.9)
	1	66 (30.0)	61 (27.0)	127 (28.5)
	2	46 (20.9)	47 (20.8)	93 (20.9)
	3	20 (9.1)	21 (9.3)	41 (9.2)
	4	12 (5.5)	9 (4.0)	21 (4.7)
	5	11 (5.0)	2 (0.9)	13 (2.9)
	6	3 (1.4)	3 (1.3)	6 (1.3)
	7	2 (0.9)	3 (1.3)	5 (1.1)
	8	0	1 (0.4)	1 (0.2)
	9	1 (0.5)	0	1 (0.2)
At least one Prev Preg* (n(%))	Missing	3	0	3
	Yes	161 (73.2)	147 (65.0)	308 (69.1)
	No	59 (26.8)	79 (35.0)	138 (30.9)

Section 2. Baseline - Visit 2 (10-16 Weeks) - Demographics and Lifestyle

2.1.4.3 Previous Pregnancy details*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo	Metformin	Overall
Multiple Pregnancy#(%)	Missing	3	0	3
	Yes	4 (2.5)	6 (4.1)	10 (3.2)
	No	157 (97.5)	141 (95.9)	298 (96.8)
Gestation of Pregnancy#(weeks)(n(%))	Missing	3	0	3
	<12	40 (24.8)	38 (25.9)	78 (25.3)
	12<22	2 (1.2)	5 (3.4)	7 (2.3)
	>22	119 (73.9)	104 (70.7)	223 (72.4)
Last Pregnancy Outcome#(%)	Missing	3	0	3
	Miscarriage	31 (19.3)	32 (21.8)	63 (20.5)
	Ectopic	1 (0.6)	1 (0.7)	2 (0.6)
	Termination of Pregnancy	9 (5.6)	10 (6.8)	19 (6.2)
	Live Birth	120 (74.5)	103 (70.1)	223 (72.4)
	Live Birth followed by neonatal death	0	1 (0.7)	1 (0.3)
Pre term Birth#(n(%))	Missing	26	27	53
	Yes	8 (5.8)	6 (5.0)	14 (5.4)
	No	130 (94.2)	114 (95.0)	244 (94.6)

Section 2. Baseline - Visit 2 (10-16 Weeks) - Demographics and Lifestyle

2.1.5 Maternal Blood Pressure at baseline

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Maternal Systolic BP (mmHg)	Mean	119.4	117.6	118.5
	Median	120.0	118.0	120.0
	SD	10.4	10.8	10.6
	MIN,MAX	90,142	91,148	90,148
	Q1,Q3	111,127	110,126	110,126
	n	223	226	449
	Nmiss	0	0	0
Maternal Diastolic BP (mmHg)	Mean	68.9	68.0	68.5
	Median	69.0	69.0	69.0
	SD	7.3	7.8	7.6
	MIN,MAX	50,90	49,86	49,90
	Q1,Q3	64,74	60,74	62,74
	n	223	226	449
	Nmiss	0	0	0

Section 2. Baseline - Visit 2 (10-16 Weeks) - Demographics and Lifestyle

2.1.6 Current pregnancy details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Ultrasound Confirmation (n(%))	Yes	219 (98.2)	224 (99.1)	443 (98.7)
	No	4 (1.8)	2 (0.9)	6 (1.3)
Gestation at baseline* (days)	Mean	98.9	99.1	99.0
	Median	100.0	99.0	100.0
	SD	8.7	8.1	8.4
	MIN,MAX	71,112	70,112	70,112
	Q1,Q3	92,106	94,106	93,106
	n	223	226	449
	Nmiss	0	0	0

Section 2. Baseline - Visit 2 (10-16 Weeks) - Putative father

2.2.1 Putative father Age

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
Paternal age (years)	Mean	31.5	31.3	31.4
	Median	31.0	31.0	31.0
	SD	6.3	6.7	6.5
	MIN,MAX	15,50	20,60	15,60
	Q1,Q3	27,35	26,36	26,36
	n	221	221	442
	Nmiss	2	5	7

Section 2. Baseline - Visit 2 (10-16 Weeks) - Putative father

2.2.2 Putative father Height and Weight

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Paternal height (cm)	Mean	178.5	177.1	177.8
	Median	178.0	178.0	178.0
	SD	8.3	13.7	11.3
	MIN,MAX	156,207	63,196	63,207
	Q1,Q3	173,185	173,185	173,185
	n	204	202	406
	Nmiss	19	24	43
Paternal weight (Kg)	Mean	92.3	93.5	92.9
	Median	89.3	89.0	89.0
	SD	22.5	25.8	24.2
	MIN,MAX	57,154	57,205	57,205
	Q1,Q3	74,105	76,105	76,105
	n	187	188	375
	Nmiss	36	38	74

Section 2. Baseline - Visit 2 (10-16 Weeks) - Putative father

2.2.3 Putative father Ethnicity

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
Ethnic Origin (n(%))	Missing	0	2	2
	White	214 (96.0)	210 (93.8)	424 (94.9)
	Non-White	9 (4.0)	14 (6.3)	23 (5.1)
Ethnic Origin-More detail (n(%))	Missing	0	2	2
	White	214 (96.0)	210 (93.8)	424 (94.9)
	Mixed	4 (1.8)	4 (1.8)	8 (1.8)
	Asian	0	3 (1.3)	3 (0.7)
	Black	4 (1.8)	6 (2.7)	10 (2.2)
	Othe Ethnic group	1 (0.4)	1 (0.4)	2 (0.4)

Section 2. Baseline - Visit 2 (10-16 Weeks) - Mother Medical history

2.3.1 Preeclampsia or Hypertension / Hypertension Requiring Treatment

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Preeclampsia or Hypertension (n(%))	Yes	7 (3.1)	10 (4.4)	17 (3.8)
	No	216 (96.9)	216 (95.6)	432 (96.2)
Currently taking Medication (n)	Yes	0	1	1
	No	7	9	16
Hypertension Require Treatment (n(%))	Yes	2 (0.9)	1 (0.4)	3 (0.7)
	No	221 (99.1)	225 (99.6)	446 (99.3)
Currently taking Medication (n)	No	2	1	3

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Section 2. Baseline - Visit 2 (10-16 Weeks) - Mother Medical history

2.3.2 Polycystic Ovarian Syndrome / Depression Requiring Treatment

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
Polycystic Ovarian Syndrome (n(%))	Yes	21 (9.4)	28 (12.4)	49 (10.9)
	No	201 (90.1)	196 (86.7)	397 (88.4)
	Unk	1 (0.4)	2 (0.9)	3 (0.7)
Currently taking Medication (n)	No	21	28	49
Depression Require Treatment (n(%))	Yes	71 (31.8)	48 (21.2)	119 (26.5)
	No	152 (68.2)	178 (78.8)	330 (73.5)
Currently taking Medication (n)	Yes	9	11	20
	No	62	37	99

Section 2. Baseline - Visit 2 (10-16 Weeks) - Mother Medical history

2.3.3 Anxiety Requiring Treatment / Use of Steroids

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Anxiety Require Treatment (n(%))	Yes	20 (9.0)	15 (6.6)	35 (7.8)
	No	203 (91.0)	211 (93.4)	414 (92.2)
Currently taking Medication (n)	Yes	5	4	9
	No	15	11	26
Use of Steroids (n(%))	Yes	22 (9.9)	13 (5.8)	35 (7.8)
	No	201 (90.1)	213 (94.2)	414 (92.2)
Currently taking Medication (n)	Yes	18	11	29
	No	4	2	6

Section 2. Baseline - Visit 2 (10-16 Weeks) - Mother Family history

2.4 Any family history for the following conditions

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Any Medical History* (n(%))	Yes	142 (63.7)	157 (69.5)	299 (66.6)
	No	78 (35.0)	67 (29.6)	145 (32.3)
	Unk	3 (1.3)	2 (0.9)	5 (1.1)
Cardiovascular disease (n(%))	Yes	69 (30.9)	71 (31.4)	140 (31.2)
	No	150 (67.3)	152 (67.3)	302 (67.3)
	Unk	4 (1.8)	3 (1.3)	7 (1.6)
Diabetes(n(%))	Yes	101 (45.3)	99 (43.8)	200 (44.5)
	No	120 (53.8)	124 (54.9)	244 (54.3)
	Unk	2 (0.9)	3 (1.3)	5 (1.1)
Preeclampsia(n(%))	Yes	22 (9.9)	19 (8.4)	41 (9.1)
	No	198 (88.8)	200 (88.5)	398 (88.6)
	Unk	3 (1.3)	7 (3.1)	10 (2.2)
Any other medical history(n(%))	Yes	96 (43.0)	109 (48.2)	205 (45.7)
	No	127 (57.0)	117 (51.8)	244 (54.3)

Section 2. Baseline - Visit 2 (10-16 Weeks) - Mother details

2.5.1 Mother Anthropometry / Height and Weight*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Maternal Height (cm)	Mean	165.1	165.5	165.3
	Median	165.0	165.0	165.0
	SD	5.9	5.9	5.9
	MIN,MAX	149,184	152,182	149,184
	Q1,Q3	161,170	162,170	161,170
	n	223	226	449
	Nmiss	0	0	0
Maternal Weight (kg)	Mean	102.94	103.60	103.27
	Median	99.20	101.35	100.20
	SD	17.00	15.50	16.25
	MIN,MAX	72.0,170.4	74.0,154.8	72.0,170.4
	Q1,Q3	90.1,111.9	93.0,113.5	92.0,112.1
	n	223	226	449
	Nmiss	0	0	0

Section 2. Baseline - Visit 2 (10-16 Weeks) - Mother details

2.5.2 Mother Anthropometry / BMI_c and Waist*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Maternal BMI Calculated (kg/m ²)	Mean	37.699	37.751	37.725
	Median	36.659	36.882	36.787
	SD	5.598	4.935	5.269
	MIN,MAX	30.12,61.27	30.03,57.23	30.03,61.27
	Q1,Q3	33.14,40.88	34.17,41.10	33.61,41.01
	n	223	226	449
	Nmiss	0	0	0
Maternal Waist (cm)	Mean	108.69	110.09	109.39
	Median	106.00	109.00	108.00
	SD	13.50	11.86	12.71
	MIN,MAX	64.0,152.0	84.0,145.0	64.0,152.0
	Q1,Q3	99.0,117.0	102.0,117.0	100.0,117.0
	n	222	225	447
	Nmiss	1	1	2

Section 2. Baseline - Visit 2 (10-16 Weeks) - Mother details

2.5.3 Mother Anthropometry / Hip and MidArm*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Maternal Hip (cm)	Mean	126.38	127.39	126.89
	Median	125.00	126.00	125.00
	SD	12.12	11.78	11.95
	MIN,MAX	95.0,159.0	100.0,160.5	95.0,160.5
	Q1,Q3	117.0,133.5	119.0,135.0	118.0,134.0
	n	222	225	447
	Nmiss	1	1	2
Maternal Mid Arm (cm)	Mean	36.29	36.74	36.51
	Median	36.00	36.00	36.00
	SD	5.01	4.65	4.83
	MIN,MAX	20.0,54.0	27.5,52.0	20.0,54.0
	Q1,Q3	33.0,39.0	34.0,39.4	33.5,39.0
	n	220	221	441
	Nmiss	3	5	8

Section 2. Baseline - Visit 2 (10-16 Weeks) - Mother details

2.5.4 Mother Anthropometry / Mid Thigh and Tricep Skinfold*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Maternal Mid Thigh (cm)	Mean	64.15	64.24	64.20
	Median	64.00	63.00	64.00
	SD	7.67	6.91	7.29
	MIN,MAX	25.0,84.0	50.0,89.0	25.0,89.0
	Q1,Q3	60.0,69.0	60.0,68.0	60.0,68.5
	n	219	222	441
	Nmiss	4	4	8
Maternal Tricep Skinfold (mm)	Mean	31.176	31.936	31.556
	Median	30.550	31.000	30.800
	SD	9.666	10.793	10.241
	MIN,MAX	5.00,62.00	8.00,66.00	5.00,66.00
	Q1,Q3	25.00,37.80	24.00,39.00	24.50,38.00
	n	222	222	444
	Nmiss	1	4	5

Section 2. Baseline - Visit 2 (10-16 Weeks) - Mother details

2.5.5 Mother Anthropometry / Bicep Skinfold and Subscapular Skinfold*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Maternal Bicep Skinfold (mm)	Mean	25.707	27.432	26.570
	Median	24.200	25.800	25.000
	SD	9.998	10.890	10.478
	MIN,MAX	1.00,60.00	9.00,61.00	1.00,61.00
	Q1,Q3	20.00,31.00	20.00,34.00	20.00,32.00
	n	222	222	444
	Nmiss	1	4	5
Maternal Subscapular Skinfold (mm)	Mean	31.997	32.555	32.275
	Median	32.700	31.300	32.000
	SD	12.205	11.805	11.998
	MIN,MAX	3.00,67.80	8.00,71.00	3.00,71.00
	Q1,Q3	24.00,40.00	24.50,39.00	24.00,39.00
	n	222	220	442
	Nmiss	1	6	7

Section 3. Compliance

3.1 Gestation by timepoint - Visit 1 Screening (10-16 Weeks), Visit 2 Consent/Baseline (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Calculated* Gestation - Visit 1 (days)	Mean	86.1	86.0	86.1
	Median	87.0	88.0	88.0
	SD	14.0	13.6	13.8
	MIN,MAX	47,112	51,112	47,112
	Q1,Q3	79,97	77,95	79,96
	n	223	226	449
	Nmiss	0	0	0
Recorded# Gestation - Visit 2 (days)	Mean	98.9	99.1	99.0
	Median	100.0	99.0	100.0
	SD	8.7	8.1	8.4
	MIN,MAX	71,112	70,112	70,112
	Q1,Q3	92,106	94,106	93,106
	n	223	226	449
	Nmiss	0	0	0

Section 3. Compliance

3.1 Gestation by timepoint - Visit 3 Randomisation (10-16 Weeks), Visit 4 (18-20 Weeks) (Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Calculated* Gestation - Visit 3 (days)	Mean	101.1	100.8	101.0
	Median	102.0	101.0	102.0
	SD	8.1	7.4	7.7
	MIN,MAX	84,118	84,113	84,118
	Q1,Q3	95,108	96,108	95,108
	n	223	226	449
	Nmiss	0	0	0
Calculated* Gestation - Visit 4 (days)	Mean	142.0	143.7	142.9
	Median	141.0	141.0	141.0
	SD	13.9	29.1	22.9
	MIN,MAX	102,252	114,498	102,498
	Q1,Q3	135,145	134,145	135,145
	n	197	202	399
	Nmiss	26	24	50

Section 3. Compliance

3.1 Gestation by timepoint - Visit 5 (28 Weeks), Visit 6 (36 Weeks) (Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Calculated* Gestation - Visit 5 (days)	Mean	197.6	197.6	197.6
	Median	197.0	197.0	197.0
	SD	9.0	6.0	7.7
	MIN,MAX	155,275	167,226	155,275
	Q1,Q3	195,200	195,200	195,200
	n	192	184	376
	Nmiss	31	42	73
Calculated* Gestation - Visit 6 (days)	Mean	252.9	251.4	252.2
	Median	253.0	253.0	253.0
	SD	8.7	24.4	18.0
	MIN,MAX	155,264	-43,268	-43,268
	Q1,Q3	251,256	251,256	251,256
	n	165	154	319
	Nmiss	58	72	130

Section 3. Compliance

3.1 Gestation by timepoint - Visit 7 Term (Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Calculated* Gestation - Visit 7 (days)	Mean	284.3	278.8	281.5
	Median	278.0	279.0	278.0
	SD	72.8	18.6	52.4
	MIN,MAX	155,1011	250,419	155,1011
	Q1,Q3	273,281	274,280	274,280
	n	109	115	224
	Nmiss	114	111	225
Calculated* Gestation - Visit 8 (days)	Mean	278.9	278.3	278.6
	Median	281.0	280.0	280.0
	SD	26.1	30.5	28.4
	MIN,MAX	132,459	99,527	99,527
	Q1,Q3	272,288	271,287	271,287
	n	218	218	436
	Nmiss	5	8	13

Section 3. Compliance

3.1 Gestation by timepoint - Visit 8 Delivery (Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	<i>Overall N=449</i>
Recorded* Gestation - Visit 8 (days)	Mean	274.7	275.0	274.9
	Median	277.5	278.0	278.0
	SD	20.4	18.3	19.3
	MIN,MAX	130,298	126,297	126,298
	Q1,Q3	271,286	271,285	271,286
	n	222	218	440
	Nmiss	1	8	9
Coded R_gestation - Visit 8 (n(%))	Missing	1	8	9
	<= 24 WEEKS	2 (0.9)	2 (0.9)	4 (0.9)
	>24 and <=37 WEEKS	14 (6.3)	19 (8.7)	33 (7.5)
	>37 WEEKS	206 (92.8)	197 (90.4)	403 (91.6)

Section 3. Compliance

3.2.1 Treatment compliance / Tablets returned by study visit

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
Tablets Returned Visit 5 (28 Weeks) (n(%))	Missing	66	80	146
	Yes	13 (8.3)	9 (6.2)	22 (7.3)
	No	144 (91.7)	137 (93.8)	281 (92.7)
Tablets Returned Visit 8 (Delivery) (n(%))	Missing	42	37	79
	Yes	69 (38.1)	79 (41.8)	148 (40.0)
	No	112 (61.9)	110 (58.2)	222 (60.0)

Section 3. Compliance

3.2.2 Treatment compliance Calculated using the patient diary (as per SAP)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Calculated Compliance* (n(%))	Missing	46	59	105
	No	59 (33.3)	58 (34.7)	117 (34.0)
	Yes	118 (66.7)	109 (65.3)	227 (66.0)

N = number of patients randomised, n = number of observations

*The number of weeks that a patient was pregnant within the study period was calculated using the gestation at baseline and the gestation at delivery, this value was then halved and compared to the number of weeks recorded in the diary, if a patient has less week diary entries than the halved total weeks then she is non-compliant straight away. If a patient had equal or more week diary entries than halved total weeks then it was required that she taken at least one pill for 4 days in order to declare a compliant week. Finally for being treatment compliant the patient should have equal or more than 50% of compliant weeks out of all available weeks

Section 3. Compliance

3.2.3.1 Cross Check* of Treatment compliance Calculated# vs tablets returned - Visit 5 (28 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Compliance by tablets returned at visit 5</i>	<i>Allocated Regimen</i>			
	<i>METFORMIN</i>		<i>PLACEBO</i>	
	<i>Tablets returned</i>		<i>Tablets returned</i>	
	<i>Yes</i>	<i>No</i>	<i>Yes</i>	<i>No</i>
<i>Compliance</i>				
<i>No</i>	3	30	3	38
<i>Yes</i>	6	92	9	89

<i>Compliance by tablets returned at visit 5</i>	<i>Allocated Regimen</i>	
	<i>OVERALL</i>	
	<i>Tablets returned</i>	
	<i>Yes</i>	<i>No</i>
<i>Compliance</i>		
<i>No</i>	6	68
<i>Yes</i>	15	181

Section 3. Compliance

3.2.3.2 Cross Check* of Treatment compliance Calculated# vs tablets returned - Visit 8 Delivery

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Compliance by tablets returned at visit 8</i>	<i>Allocated Regimen</i>			
	<i>METFORMIN</i>		<i>PLACEBO</i>	
	<i>Tablets returned</i>		<i>Tablets returned</i>	
	<i>Yes</i>	<i>No</i>	<i>Yes</i>	<i>No</i>
<u><i>Compliance</i></u>				
<i>No</i>	15	34	11	37
<i>Yes</i>	57	43	53	46

<i>Compliance by tablets returned at visit 8</i>	<i>Allocated Regimen</i>	
	<i>OVERALL</i>	
	<i>Tablets returned</i>	
	<i>Yes</i>	<i>No</i>
<u><i>Compliance</i></u>		
<i>No</i>	26	71
<i>Yes</i>	110	89

Section 3. Compliance

3.3 Treatment compliance / Metformin level in blood samples at Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Metformin level (ng/mL)	Mean	2.3	61.5	31.2
	Median	0.0	7.0	0.0
	SD	16.2	172.5	124.5
	MIN,MAX	0,154	0,1611	0,1611
	Q1,Q3	0,0	0,48	0,10
	n	137	131	268
	Nmiss	86	95	181
Any Metformin level coded (n(%))	Missing	86	95	181
	Yes	12 (8.8)	80 (61.1)	92 (34.3)
	No	125 (91.2)	51 (38.9)	176 (65.7)

Section 3. Compliance

3.4 Cross Check* of Treatment compliance Calculated# vs Metformin level in blood samples at Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Compliance by metformin level at visit 6</i>	<i>Allocated Regimen</i>			
	<i>METFORMIN</i>		<i>PLACEBO</i>	
	<i>Any Metformin</i>		<i>Any Metformin</i>	
	<i>Yes</i>	<i>No</i>	<i>Yes</i>	<i>No</i>
<i>Compliance</i>				
<i>No</i>	13	20	3	28
<i>Yes</i>	63	20	7	86

<i>Compliance by metformin level at visit 6</i>	<i>Allocated Regimen</i>	
	<i>OVERALL</i>	
	<i>Any Metformin</i>	
	<i>Yes</i>	<i>No</i>
<i>Compliance</i>		
<i>No</i>	16	48
<i>Yes</i>	70	106

Section 4. Secondary Outcome - All Patients

4.1.1.1.1.1 Delivery Details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Delivery Method (n(%))	Missing	1	7	8
	Spontaneous vaginal delivery	126 (56.8)	133 (60.7)	259 (58.7)
	LSCS in labour	34 (15.3)	25 (11.4)	59 (13.4)
	LSCS pre labour	42 (18.9)	40 (18.3)	82 (18.6)
	Forceps/ventouse	18 (8.1)	21 (9.6)	39 (8.8)
	Vaginal breech	2 (0.9)	0	2 (0.5)
C-SECTION index pregnancy (n(%))	Missing	1	7	8
	Yes	76 (34.2)	65 (29.7)	141 (32.0)
	No	146 (65.8)	154 (70.3)	300 (68.0)
Primary C-SECTION in index pregnancy (n(%))	Missing	1	7	8
	Yes	46 (20.7)	42 (19.2)	88 (20.0)
	No	176 (79.3)	177 (80.8)	353 (80.0)

Section 4. Secondary Outcome - All Patients

4.1.1.1.1.2 Birth Outcome - C-SECTION current pregnancy - Statistical analysis - POST-HOC*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of CSECTIONYN by AllocatedTreatment</i>			
		<i>AllocatedTreatment(Allocated Treatment)</i>			
<i>CSECTIONYN(C-section coded (Y/N))</i>		<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>	
<i>Missing</i>		7	1	.	
<i>Yes</i>		65	76	141	
<i>No</i>		154	146	300	
<i>Total</i>		219	222	441	
<i>Frequency Missing = 8</i>					

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
c_section_itt	AllocatedTreatment METFORMIN vs PLACEBO	0.811	0.543	1.211	0.3056	0.3095

Section 4. Secondary Outcome - All Patients

4.1.1.1.3 Birth Outcome - First ever C-SECTION - Statistical analysis - POST-HOC*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Table of first_c_section by AllocatedTreatment</i>			
<i>first_c_section(First ever c-section in current pregnancy (Y/N))</i>	<i>AllocatedTreatment(Allocated Treatment)</i>		<i>Total</i>
	<i>METFORMIN</i>	<i>PLACEBO</i>	
<i>Missing</i>	7	1	.
<i>Yes</i>	42	46	88
<i>No</i>	177	176	353
<i>Total</i>	219	222	441

Frequency Missing = 8

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
first_csec_itt	AllocatedTreatment METFORMIN vs PLACEBO	0.908	0.569	1.449	0.6853	0.7216

Section 4. Secondary Outcome - All Patients

4.1.1.1.2.1 Delivery Details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Delivery Blood Loss (mL)	Mean	494.9	486.7	490.8
	Median	400.0	400.0	400.0
	SD	405.5	453.7	429.5
	MIN,MAX	100,2500	50,5000	50,5000
	Q1,Q3	250,600	300,580	250,600
	n	216	212	428
	Nmiss	7	14	21
Hemorrhage* (n(%))	Missing	7	14	21
	Yes	21 (9.7)	20 (9.4)	41 (9.6)
	No	195 (90.3)	192 (90.6)	387 (90.4)
SAE recorded due to Hemorrhage# (n(%))	Missing	1	1	2
	Yes	10	8	18
	No	10	11	21

Section 4. Secondary Outcome - All Patients

4.1.1.1.2.2 Birth Outcome - Hemorrhage - Statistical analysis - POST-HOC*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Frequency</i>		<i>Table of HEMORRHAGE by Allocated Treatment</i>			
<i>HEMORRHAGE(Heamorrhage (Y/N))</i>		<i>Allocated Treatment(Allocated Treatment)</i>			
		<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>	
<i>Missing</i>		14	7	.	
<i>Yes</i>		20	21	41	
<i>No</i>		192	195	387	
<i>Total</i>		212	216	428	
<i>Frequency Missing = 21</i>					

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
HEMORRHAGE_itt	Allocated Treatment METFORMIN vs PLACEBO	0.967	0.508	1.842	0.9193	1.0000

Section 4. Secondary Outcome - All Patients

4.1.1.1.3 Delivery Details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Labour Type (n(%))	Missing	2	6	8
	Spontaneous	89 (40.3)	97 (44.1)	186 (42.2)
	Induced	98 (44.3)	82 (37.3)	180 (40.8)
	C-section	34 (15.4)	41 (18.6)	75 (17.0)
Non Spontaneous Reason* (n(%))	Missing	3	8	11
	Post dates	24 (18.3)	16 (13.2)	40 (15.9)
	Pre-eclampsia	3 (2.3)	6 (5.0)	9 (3.6)
	Abruption	0	1 (0.8)	1 (0.4)
	Other maternal condition	45 (34.4)	48 (39.7)	93 (36.9)
	Previous C-section	20 (15.3)	16 (13.2)	36 (14.3)
	Previous obstetric history (other)	4 (3.1)	2 (1.7)	6 (2.4)
	Maternal request	10 (7.6)	5 (4.1)	15 (6.0)
	Suspected fetal compromise	13 (9.9)	13 (10.7)	26 (10.3)
	Malpresentation	5 (3.8)	8 (6.6)	13 (5.2)
	Suspected IUGR	3 (2.3)	2 (1.7)	5 (2.0)
	Suspected Macrosomia	4 (3.1)	4 (3.3)	8 (3.2)

Section 4. Secondary Outcome - All Patients

4.1.1.1.4 Delivery Details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Gesta_coded by method* (n(%))	Missing	1	6	7
	Sponta_vaginal_delivery_<=37 WEEKS	3 (1.4)	8 (3.6)	11 (2.5)
	Sponta_vaginal_delivery_>37 WEEKS	121 (54.5)	119 (54.1)	240 (54.3)
	LSCS in labour_<=37 WEEKS	2 (0.9)	1 (0.5)	3 (0.7)
	LSCS in labour_>37 WEEKS	32 (14.4)	24 (10.9)	56 (12.7)
	LSCS pre labour_<=37 WEEKS	7 (3.2)	8 (3.6)	15 (3.4)
	LSCS pre labour_>37 WEEKS	35 (15.8)	32 (14.5)	67 (15.2)
	Forceps/ventouse_<=37 WEEKS	1 (0.5)	1 (0.5)	2 (0.5)
	Forceps/ventouse_>37 WEEKS	17 (7.7)	20 (9.1)	37 (8.4)
	Vaginal breech_<=37 WEEKS	1 (0.5)	0	1 (0.2)
	Vaginal breech_>37 WEEKS	1 (0.5)	0	1 (0.2)
	TOP_Stillbirth_Miscarriage	2 (0.9)	7 (3.2)	9 (2.0)

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Section 4. Secondary Outcome - All Patients

4.1.1.1.5 Delivery Details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	<i>Overall N=449</i>
Gesta_coded by labour* (n(%))	Missing	2	5	7
	Spontaneous_<=37 WEEKS	4 (1.8)	3 (1.4)	7 (1.6)
	Spontaneous_>37 WEEKS	85 (38.5)	92 (41.6)	177 (40.0)
	Induced_<=37 WEEKS	4 (1.8)	7 (3.2)	11 (2.5)
	Induced_>37 WEEKS	92 (41.6)	71 (32.1)	163 (36.9)
	C-section_<=37 WEEKS	6 (2.7)	8 (3.6)	14 (3.2)
	C-section_>37 WEEKS	28 (12.7)	33 (14.9)	61 (13.8)
	TOP_Stillbirth_Miscarriage	2 (0.9)	7 (3.2)	9 (2.0)

Section 4. Secondary Outcome - All Patients

4.1.1.1.6 Delivery Details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Labour by method* <=37 Weeks (n(%))	Spontaneous_vaginal_deliv	2 (12.5)	3 (14.3)	5 (13.5)
	Spontaneous_LSCS in labour	1 (6.3)	0	1 (2.7)
	Spontaneous_Vaginal breech	1 (6.3)	0	1 (2.7)
	Induced_vaginal_deliv	1 (6.3)	5 (23.8)	6 (16.2)
	Induced_LSCS in labour	1 (6.3)	1 (4.8)	2 (5.4)
	Induced_LSCS pre labour	1 (6.3)	0	1 (2.7)
	Induced_Forceps/ventouse	1 (6.3)	1 (4.8)	2 (5.4)
	C-section_LSCS pre labour	6 (37.5)	8 (38.1)	14 (37.8)
	TOP_Stillbirth_Miscarriage	2 (12.5)	3 (14.3)	5 (13.5)

Section 4. Secondary Outcome - All Patients

4.1.1.1.7 Delivery Details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo</i>	<i>Metformin</i>	<i>Overall</i>
Labour by method* >37 Weeks (n(%))	Missing	1	1	2
	Spontaneous_vaginal_deliv	64 (31.2)	70 (35.7)	134 (33.4)
	Spontaneous_LSCS in labour	11 (5.4)	9 (4.6)	20 (5.0)
	Spontaneous_Forceps/ventouse	9 (4.4)	13 (6.6)	22 (5.5)
	Spontaneous_Vaginal breech	1 (0.5)	0	1 (0.2)
	Induced_vaginal_deliv	57 (27.8)	49 (25.0)	106 (26.4)
	Induced_LSCS in labour	21 (10.2)	15 (7.7)	36 (9.0)
	Induced_LSCS pre labour	6 (2.9)	0	6 (1.5)
	Induced_Forceps/ventouse	8 (3.9)	7 (3.6)	15 (3.7)
	C-section_LSCS pre labour	28 (13.7)	32 (16.3)	60 (15.0)
	TOP_Stillbirth_Miscarriage	0	1 (0.5)	1 (0.2)

Section 4. Secondary Outcome - All Patients

4.1.1.2.1.1 Delivery Outcome

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Baby Gestational age (Days)*	Mean	274.7	275.0	274.9
	Median	277.5	278.0	278.0
	SD	20.4	18.3	19.3
	MIN,MAX	130,298	126,297	126,298
	Q1,Q3	271,286	271,285	271,286
	n	222	218	440
	Nmiss	1	8	9
Baby Gestational age coded (n(%))*	Missing	1	8	9
	<= 24 WEEKS	2 (0.9)	2 (0.9)	4 (0.9)
	>24 and <=37 WEEKS	14 (6.3)	19 (8.7)	33 (7.5)
	>37 WEEKS	206 (92.8)	197 (90.4)	403 (91.6)

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Section 4. Secondary Outcome - All Patients

4.1.1.2.1.1 Delivery Outcome (Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	<i>Overall N=449</i>
Baby Gender (n(%))	NA	2	9	11
	Male	110 (49.8)	109 (50.2)	219 (50.0)
	Female	111 (50.2)	107 (49.3)	218 (49.8)
	Indeterminate	0	1 (0.5)	1 (0.2)
<hr/>				
Birth Outcome (n(%))	NA	1	5	6
	Live Birth	218 (98.2)	213 (96.4)	431 (97.3)
	Stillbirth (intrauterine death)	0	2 (0.9)	2 (0.5)
	Miscarriage (<24 weeks)	0	4 (1.8)	4 (0.9)
	Termination of Pregnancy	2 (0.9)	1 (0.5)	3 (0.7)
	Live Birth-followed by neonatal death	2 (0.9)	1 (0.5)	3 (0.7)

Section 4. Secondary Outcome - All Patients

4.1.1.2.1.2 Birth Outcome - Statistical analysis - POST-HOC*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Frequency</i>		<i>Table of Birth_Out_Ana by AllocatedTreatment</i>				
<i>Birth_Out_Ana(Birth Outcome categorised for analysis)</i>	<i>AllocatedTreatment(Allocated Treatment)</i>		<i>Total</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>Fisher exact P-value#</i>
	<i>METFORMIN</i>	<i>PLACEBO</i>				
<i>NA</i>	5	1	.			
<i>Live Birth</i>	214	220	434			
<i>TOP_Stillbirth_Miscarriage</i>	7	2	9			
<i>Total</i>	221	222	443			
<i>Frequency Missing = 6</i>						
<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
BirthOut_itt	AllocatedTreatment METFORMIN vs PLACEBO	3.597	0.739	17.504	0.1129	0.1054

Section 4. Secondary Outcome - All Patients

4.1.1.2.2.1 Delivery Outcome - birth weight

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
Birth weight (g)	Mean	3449.3	3441.3	3445.4
	Median	3500.0	3500.0	3500.0
	SD	689.6	592.6	642.6
	MIN,MAX	400,4940	120,4900	120,4940
	Q1,Q3	3120,3850	3080,3780	3090,3836
	n	221	217	438
	Nmiss	2	9	11

Section 4. Secondary Outcome - All Patients

4.1.1.2.2.2 Delivery Outcome - birth weight split by gender

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight Males (g)	Mean	3530.3	3503.8	3517.1
	Median	3575.0	3500.0	3520.0
	SD	687.8	560.1	626.2
	MIN,MAX	400,4940	2230,4900	400,4940
	Q1,Q3	3240,3910	3170,3870	3180,3900
	n	110	109	219
	Nmiss	0	0	0
Birth weight Females(g)	Mean	3369.1	3408.8	3388.6
	Median	3460.0	3510.0	3465.0
	SD	685.1	535.5	615.1
	MIN,MAX	690,4550	1620,4650	690,4650
	Q1,Q3	3020,3740	3050,3700	3048,3730
	n	111	107	218
	Nmiss	0	0	0

Section 4. Secondary Outcome - All Patients

4.1.1.2.2.3 Delivery Outcome - birth weight split by gestation

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight <=24 WEEKS (g)	Mean	400.0	120.0	260.0
	Median	400.0	120.0	260.0
	SD	.	.	198.0
	MIN,MAX	400,400	120,120	120,400
	Q1,Q3	400,400	120,120	120,400
	n	1	1	2
	Nmiss	1	1	2
Birth weight >24 and <=37 WEEKS (g)	Mean	2102.4	2776.1	2490.2
	Median	2145.0	2730.0	2600.0
	SD	1126.5	569.2	901.2
	MIN,MAX	690,4800	1620,3740	690,4800
	Q1,Q3	1230,2750	2490,3180	2030,3110
	n	14	19	33
	Nmiss	0	0	0

Section 4. Secondary Outcome - All Patients

4.1.1.2.2.3 Delivery Outcome - birth weight split by gestation (Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight >37 WEEKS (g)	Mean	3555.7	3522.4	3539.4
	Median	3562.5	3530.0	3550.0
	SD	499.3	501.4	500.0
	MIN,MAX	2350,4940	2110,4900	2110,4940
	Q1,Q3	3235,3860	3160,3840	3190,3860
	n	206	197	403
	Nmiss	0	0	0

Section 4. Secondary Outcome - All Patients

4.1.1.2.2.4 Delivery Outcome - birth weight split by parity

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight parity=0 (g)	Mean	3364.9	3382.7	3374.3
	Median	3374.0	3390.0	3380.0
	SD	630.4	585.2	605.3
	MIN,MAX	690,4718	1620,4900	690,4900
	Q1,Q3	2993,3740	3000,3770	2995,3750
	n	84	94	178
	Nmiss	0	6	6
Birth weight parity=>1 (g)	Mean	3501.1	3486.1	3494.0
	Median	3610.0	3550.0	3575.0
	SD	720.9	596.6	663.8
	MIN,MAX	400,4940	120,4790	120,4940
	Q1,Q3	3240,3900	3180,3800	3190,3860
	n	137	123	260
	Nmiss	2	3	5

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Section 4. Secondary Outcome - All Patients

4.1.1.3 Delivery Outcome - Low birth weights

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Gestation (days) at delivery	Delivery date	Labour Type	Birth Outcome categorised as per CRF	Baby death date	Baby gender	Birth weight corrected from kg to g (g)
11880	METFORMIN	143	30NOV2013	Induced	Miscarriage (<24 weeks)	.	NA	120
21119	PLACEBO	152	10JAN2014	Induced	Termination of Pregnancy	10JAN2014	Male	400
14264	PLACEBO	191	12JAN2013	C-section	Live Birth	.	Female	690
14270	PLACEBO	181	07MAR2013	C-section	Live Birth	.	Female	832
11786	PLACEBO	211	04NOV2013	Spontaneous	Live Birth	.	Male	1120
15028	PLACEBO	200	13JUN2013	Spontaneous	Live Birth-followed by neonatal death	17JUN2013	Male	1230
12109	PLACEBO	218	19FEB2014	C-section	Live Birth	.	Female	1250
12059	PLACEBO	234	28JUN2013	C-section	Live Birth	.	Female	1490
11420	METFORMIN	222	03AUG2012	C-section	Live Birth	.	Female	1620
11881	METFORMIN	219	04JAN2014	C-section	Live Birth	.	Female	1800

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Section 4. Secondary Outcome - All Patients

4.1.1.4 Delivery Outcome - births before 24 weeks

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Gestation (days) at delivery	Delivery date	LabourType	Birth Outcome categorised as per CRF	Baby death date	Baby gender
12041	METFORMIN	126	09NOV2012	Induced	Termination of Pregnancy	.	NA
14186	METFORMIN	.	31AUG2012	Spontaneous	Miscarriage (<24 weeks)	.	NA
14302	METFORMIN	.	08MAR2013	Induced	Miscarriage (<24 weeks)	08MAR2013	Indeterminate
12086	PLACEBO	130	08SEP2013	Induced	Termination of Pregnancy	.	NA
11880	METFORMIN	143	30NOV2013	Induced	Miscarriage (<24 weeks)	.	NA
21119	PLACEBO	152	10JAN2014	Induced	Termination of Pregnancy	10JAN2014	Male

Section 4. Secondary Outcome - Only Alive Births

4.1.2.1.1 Delivery Details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Delivery Method(n(%))	Missing	0	1	1
	Spontaneous vaginal delivery	124 (56.4)	127 (59.6)	251 (58.0)
	LSCS in labour	34 (15.5)	25 (11.7)	59 (13.6)
	LSCS pre labour	42 (19.1)	40 (18.8)	82 (18.9)
	Forceps/ventouse	18 (8.2)	21 (9.9)	39 (9.0)
	Vaginal breech	2 (0.9)	0	2 (0.5)
C-SECTION index pregnancy(n(%))	Missing	0	1	1
	Yes	76 (34.5)	65 (30.5)	141 (32.6)
	No	144 (65.5)	148 (69.5)	292 (67.4)
Primary C-SECTION in index pregnancy(n(%))	Missing	0	1	1
	Yes	46 (20.9)	42 (19.7)	88 (20.3)
	No	174 (79.1)	171 (80.3)	345 (79.7)

Section 4. Secondary Outcome - Only Alive Births

4.1.2.1.2 Delivery Details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Delivery Blood Loss (mL)	Mean	496.7	488.5	492.7
	Median	400.0	400.0	400.0
	SD	405.5	455.4	430.4
	MIN,MAX	100,2500	50,5000	50,5000
	Q1,Q3	250,600	300,600	250,600
	n	215	210	425
	Nmiss	5	4	9
Hemorrhage* (n(%))	Missing	5	4	9
	Yes	21 (9.8)	20 (9.5)	41 (9.6)
	No	194 (90.2)	190 (90.5)	384 (90.4)
SAE recorded due to Hemorrhage# (n(%))	Missing	1	1	2
	Yes	10	8	18
	No	10	11	21

Section 4. Secondary Outcome - Only Alive Births

4.1.2.1.3 Delivery Details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Labour Type (n(%))	Missing	1	0	1
	Spontaneous	89 (40.6)	95 (44.4)	184 (42.5)
	Induced	96 (43.8)	78 (36.4)	174 (40.2)
	C-section	34 (15.5)	41 (19.2)	75 (17.3)
Non Spontaneous Reason* (n(%))	Missing	1	0	1
	Post dates	24 (18.5)	16 (13.4)	40 (16.1)
	Pre-eclampsia	3 (2.3)	6 (5.0)	9 (3.6)
	Abruption	0	1 (0.8)	1 (0.4)
	Other maternal condition	45 (34.6)	46 (38.7)	91 (36.5)
	Previous C-section	20 (15.4)	16 (13.4)	36 (14.5)
	Previous obstetric history (other)	4 (3.1)	2 (1.7)	6 (2.4)
	Maternal request	10 (7.7)	5 (4.2)	15 (6.0)
	Suspected fetal compromise	12 (9.2)	13 (10.9)	25 (10.0)
	Malpresentation	5 (3.8)	8 (6.7)	13 (5.2)
	Suspected IUGR	3 (2.3)	2 (1.7)	5 (2.0)
	Suspected Macrosomia	4 (3.1)	4 (3.4)	8 (3.2)

Section 4. Secondary Outcome - Only Alive Births

4.1.2.1.4.1 Delivery Details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo	Metformin	Overall
Gesta_coded by method* (n(%))	Missing	0	1	1
	Sponta_vaginal_delivery_<=37 WEEKS	3 (1.4)	8 (3.8)	11 (2.5)
	Sponta_vaginal_delivery_>37 WEEKS	121 (55.0)	119 (55.9)	240 (55.4)
	LSCS in labour_<=37 WEEKS	2 (0.9)	1 (0.5)	3 (0.7)
	LSCS in labour_>37 WEEKS	32 (14.5)	24 (11.3)	56 (12.9)
	LSCS pre labour_<=37 WEEKS	7 (3.2)	8 (3.8)	15 (3.5)
	LSCS pre labour_>37 WEEKS	35 (15.9)	32 (15.0)	67 (15.5)
	Forceps/ventouse_<=37 WEEKS	1 (0.5)	1 (0.5)	2 (0.5)
	Forceps/ventouse_>37 WEEKS	17 (7.7)	20 (9.4)	37 (8.5)
	Vaginal breech_<=37 WEEKS	1 (0.5)	0	1 (0.2)
	Vaginal breech_>37 WEEKS	1 (0.5)	0	1 (0.2)
Gesta_coded by labour# (n(%))	Missing	1	0	1
	Spontaneous_<=37 WEEKS	4 (1.8)	3 (1.4)	7 (1.6)
	Spontaneous_>37 WEEKS	85 (38.8)	92 (43.0)	177 (40.9)
	Induced_<=37 WEEKS	4 (1.8)	7 (3.3)	11 (2.5)
	Induced_>37 WEEKS	92 (42.0)	71 (33.2)	163 (37.6)
	C-section_<=37 WEEKS	6 (2.7)	8 (3.7)	14 (3.2)
	C-section_>37 WEEKS	28 (12.8)	33 (15.4)	61 (14.1)

Section 4. Secondary Outcome - Only Alive Births

4.1.2.1.4.2 Delivery Details (Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Labour by method* <=37 Weeks (n(%))	Spontaneous_vaginal_deliv	2 (14.3)	3 (16.7)	5 (15.6)
	Spontaneous_LSCS in labour	1 (7.1)	0	1 (3.1)
	Spontaneous_Vaginal breech	1 (7.1)	0	1 (3.1)
	Induced_vaginal_deliv	1 (7.1)	5 (27.8)	6 (18.8)
	Induced_LSCS in labour	1 (7.1)	1 (5.6)	2 (6.3)
	Induced_LSCS pre labour	1 (7.1)	0	1 (3.1)
	Induced_Forceps/ventouse	1 (7.1)	1 (5.6)	2 (6.3)
	C-section_LSCS pre labour	6 (42.9)	8 (44.4)	14 (43.8)
Labour by method* >37 Weeks (n(%))	Missing	1	1	2
	Spontaneous_vaginal_deliv	64 (31.2)	70 (35.9)	134 (33.5)
	Spontaneous_LSCS in labour	11 (5.4)	9 (4.6)	20 (5.0)
	Spontaneous_Forceps/ventouse	9 (4.4)	13 (6.7)	22 (5.5)
	Spontaneous_Vaginal breech	1 (0.5)	0	1 (0.3)
	Induced_vaginal_deliv	57 (27.8)	49 (25.1)	106 (26.5)
	Induced_LSCS in labour	21 (10.2)	15 (7.7)	36 (9.0)
	Induced_LSCS pre labour	6 (2.9)	0	6 (1.5)
	Induced_Forceps/ventouse	8 (3.9)	7 (3.6)	15 (3.8)
	C-section_LSCS pre labour	28 (13.7)	32 (16.4)	60 (15.0)

Section 4. Secondary Outcome - Only Alive Births

4.1.2.1.4.3 Delivery Details - Preterm Birth - Statistical analysis - POST-HOC*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of GESTA_2CODE by AllocatedTreatment</i>			
<i>GESTA_2CODE(Gestation Code 2)</i>		<i>AllocatedTreatment(Allocated Treatment)</i>			
		<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>	
<i>>24 and <=37 WEEKS</i>		18	14	32	
<i>>37 WEEKS</i>		196	206	402	
<i>Total</i>		214	220	434	

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
PRETERM_itt	AllocatedTreatment METFORMIN vs PLACEBO	1.345	0.651	2.777	0.4235	0.4658

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Section 4. Secondary Outcome - Only Alive Births

4.1.2.2.1.1 Delivery Outcome

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth Outcome (n(%))	Live Birth	218 (99.1)	213 (99.5)	431 (99.3)
	Live Birth-followed by neonatal death	2 (0.9)	1 (0.5)	3 (0.7)
Baby Gender (n(%))	Male	109 (49.5)	109 (50.9)	218 (50.2)
	Female	111 (50.5)	105 (49.1)	216 (49.8)

Section 4. Secondary Outcome - Only Alive Births

4.1.2.2.1.2 Delivery Outcome - Birth Outcome-Neonatal Death after delivery - Statistical analysis - POST-HOC*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of BirthOutcome by AllocatedTreatment</i>				
		<i>AllocatedTreatment(Allocated Treatment)</i>				
<i>BirthOutcome(Birth Outcome categorised as per CRF)</i>		<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>		
<i>Live Birth</i>		213	218	431		
<i>Live Birth-followed by neonatal death</i>		1	2	3		
<i>Total</i>		214	220	434		

<i>Parameter(s)</i>		<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
NEO_DEATH_itt	AllocatedTreatment	METFORMIN vs PLACEBO	0.512	0.046	5.686	0.5855	1.0000

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Section 4. Secondary Outcome - Only Alive Births

4.1.2.2.1.3 Delivery Outcome(Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Baby Gestational age (Days)*	Mean	275.9	276.6	276.3
	Median	278.0	278.0	278.0
	SD	15.9	11.7	14.0
	MIN,MAX	181,298	219,297	181,298
	Q1,Q3	271,286	271,285	271,286
	n	220	214	434
	Nmiss	0	0	0
Baby Gestational age coded (n(%))*	>24 and <=37 WEEKS	14 (6.4)	18 (8.4)	32 (7.4)
	>37 WEEKS	206 (93.6)	196 (91.6)	402 (92.6)

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Section 4. Secondary Outcome - Only Alive Births

4.1.2.2.2.1 Delivery Outcome - birth weight

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight (g)	Mean	3463.2	3461.8	3462.5
	Median	3505.0	3510.0	3510.0
	SD	659.6	548.1	606.5
	MIN,MAX	690,4940	1620,4900	690,4940
	Q1,Q3	3130,3855	3090,3800	3110,3840
	n	220	214	434
	Nmiss	0	0	0

Section 4. Secondary Outcome - Only Alive Births

4.1.2.2.2.2 Delivery Outcome - birth weight split by gender

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight Males (g)	Mean	3559.0	3503.8	3531.4
	Median	3580.0	3500.0	3525.0
	SD	621.2	560.1	590.7
	MIN,MAX	1120,4940	2230,4900	1120,4940
	Q1,Q3	3260,3910	3170,3870	3190,3900
	n	109	109	218
	Nmiss	0	0	0
Birth weight Females(g)	Mean	3369.1	3418.3	3393.0
	Median	3460.0	3520.0	3470.0
	SD	685.1	534.5	615.6
	MIN,MAX	690,4550	1620,4650	690,4650
	Q1,Q3	3020,3740	3080,3700	3049,3730
	n	111	105	216
	Nmiss	0	0	0

Section 4. Secondary Outcome - Only Alive Births

4.1.2.2.2.3 Delivery Outcome - birth weight split by gestation

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight >24 and <=37 WEEKS (g)	Mean	2102.4	2751.9	2467.8
	Median	2145.0	2685.0	2590.0
	SD	1126.5	575.7	906.1
	MIN,MAX	690,4800	1620,3740	690,4800
	Q1,Q3	1230,2750	2490,3170	1915,3053
	n	14	18	32
	Nmiss	0	0	0
Birth weight >37 WEEKS (g)	Mean	3555.7	3527.0	3541.7
	Median	3562.5	3535.0	3550.0
	SD	499.3	498.4	498.4
	MIN,MAX	2350,4940	2110,4900	2110,4940
	Q1,Q3	3235,3860	3170,3845	3200,3860
	n	206	196	402
	Nmiss	0	0	0

Section 4. Secondary Outcome - Only Alive Births

4.1.2.2.2.4 Delivery Outcome - birth weight split by parity

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Birth weight parity=0 (g)	Mean	3364.9	3391.0	3378.6
	Median	3374.0	3400.0	3380.0
	SD	630.4	582.8	604.2
	MIN,MAX	690,4718	1620,4900	690,4900
	Q1,Q3	2993,3740	3000,3770	3000,3750
	n	84	93	177
	Nmiss	0	0	0
Birth weight parity=>1 (g)	Mean	3523.9	3516.2	3520.3
	Median	3615.0	3560.0	3580.0
	SD	672.1	515.7	602.4
	MIN,MAX	832,4940	2110,4790	832,4940
	Q1,Q3	3240,3903	3180,3800	3200,3860
	n	136	121	257
	Nmiss	0	0	0

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Section 4. Secondary Outcome - Only Alive Births

4.1.2.3 Delivery Outcome - Low birth weights

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Gestation (days) at delivery	Delivery date	Labour Type	Birth Outcome categorised as per CRF	Baby death date	Baby gender	Birth weight corrected from kg to g (g)
14264	PLACEBO	191	12JAN2013	C-section	Live Birth	.	Female	690
14270	PLACEBO	181	07MAR2013	C-section	Live Birth	.	Female	832
11786	PLACEBO	211	04NOV2013	Spontaneous	Live Birth	.	Male	1120
15028	PLACEBO	200	13JUN2013	Spontaneous	Live Birth-followed by neonatal death	17JUN2013	Male	1230
12109	PLACEBO	218	19FEB2014	C-section	Live Birth	.	Female	1250
12059	PLACEBO	234	28JUN2013	C-section	Live Birth	.	Female	1490
11420	METFORMIN	222	03AUG2012	C-section	Live Birth	.	Female	1620
11881	METFORMIN	219	04JAN2014	C-section	Live Birth	.	Female	1800

Section 4. Outcomes - Only Alive Births

4.2.1.1 PRIMARY EFFICACY: Birth weight centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight centile	Mean	57.271	56.870	57.073
	Median	57.659	62.943	58.986
	SD	27.862	28.587	28.190
	MIN,MAX	0.11,99.95	0.03,99.83	0.03,99.95
	Q1,Q3	35.35,80.17	33.41,81.96	34.53,81.86
	n	220	214	434
	Nmiss	0	0	0

Section 4. Outcomes - Only Alive Births

4.2.1.2 PRIMARY EFFICACY: Birth weight centile split by gender

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight centile Males	Mean	57.219	55.116	56.168
	Median	58.710	56.130	57.613
	SD	28.993	29.452	29.175
	MIN,MAX	1.27,99.95	1.94,99.76	1.27,99.95
	Q1,Q3	34.15,81.92	33.26,82.48	33.26,82.48
	n	109	109	218
	Nmiss	0	0	0
Birth weight centile Females	Mean	57.323	58.690	57.987
	Median	56.465	64.308	60.840
	SD	26.837	27.684	27.197
	MIN,MAX	0.11,99.34	0.03,99.83	0.03,99.83
	Q1,Q3	35.35,79.87	38.37,81.86	36.11,81.06
	n	111	105	216
	Nmiss	0	0	0

Section 4. Outcomes - Only Alive Births

4.2.1.3 PRIMARY EFFICACY: Birth weight centile split by gestation

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight centile >24 and <=37 WEEKS	Mean	45.277	61.655	54.490
	Median	47.213	65.106	59.095
	SD	28.994	27.900	29.113
	MIN,MAX	11.51,99.95	20.03,97.59	11.51,99.95
	Q1,Q3	14.96,67.66	33.26,86.71	27.60,78.90
	n	14	18	32
	Nmiss	0	0	0
Birth weight centile >37 WEEKS (g)	Mean	58.086	56.430	57.279
	Median	57.932	62.943	58.986
	SD	27.668	28.679	28.142
	MIN,MAX	0.11,99.89	0.03,99.83	0.03,99.89
	Q1,Q3	35.73,82.48	33.53,81.91	35.24,81.96
	n	206	196	402
	Nmiss	0	0	0

Section 4. Outcomes - Only Alive Births

4.2.1.4 PRIMARY EFFICACY: Birth weight centile split by parity

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight centile parity=0 (g)	Mean	54.271	54.718	54.506
	Median	50.234	54.451	50.563
	SD	28.134	29.603	28.834
	MIN,MAX	1.27,98.99	3.91,99.83	1.27,99.83
	Q1,Q3	32.12,79.21	30.99,81.26	31.64,80.87
	n	84	93	177
	Nmiss	0	0	0
Birth weight centile parity=>1 (g)	Mean	59.124	58.524	58.841
	Median	60.547	64.228	62.996
	SD	27.634	27.791	27.655
	MIN,MAX	0.11,99.95	0.03,99.70	0.03,99.95
	Q1,Q3	38.88,81.20	38.37,82.77	38.44,81.96
	n	136	121	257
	Nmiss	0	0	0

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Section 4. Outcomes - Only Alive Births

4.2.2.1.1 PRIMARY EFFICACY: Birth weight centile categorised

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Split Birth weight Centile (n(%))	<=3rd	3 (1.4)	3 (1.4)	6 (1.4)
	>3rd and <=5th	4 (1.8)	3 (1.4)	7 (1.6)
	>5th and <=10th	4 (1.8)	8 (3.7)	12 (2.8)
	>10th and <=90th	171 (77.7)	169 (79.0)	340 (78.3)
	>90th and <=95th	16 (7.3)	14 (6.5)	30 (6.9)
	>95th and <=97th	7 (3.2)	5 (2.3)	12 (2.8)
	>97th	15 (6.8)	12 (5.6)	27 (6.2)

Section 4. Secondary Outcome - Only Alive Births

4.2.2.1.2 PRIMARY EFFICACY: Birth weight centile categorised - Statistical analysis - POST-HOC*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of centile_03b by AllocatedTreatment</i>					
		<i>AllocatedTreatment(Allocated Treatment)</i>					
<i>centile_03b</i>	<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>				
<i>No</i>	211	217	428				
<i>Yes</i>	3	3	6				
<i>Total</i>	214	220	434				

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
centile_03b_itt	AllocatedTreatment METFORMIN vs PLACEBO	1.028	0.205	5.152	0.9728	1.0000

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 00:26
 *Analysed using logistic regression (binary logit), probability modeled is centile_03b='Yes'
 #Significance level set at p<0.05
 Fisher's exact test should be used for reporting due to low cell count
 Detailed analysis in file 'Empowar_4_2_2_1_weight_centile.lst'

By: Aryelly Rodriguez - ECTU Statistician

Section 4. Secondary Outcome - Only Alive Births

4.2.2.1.3 PRIMARY EFFICACY: Birth weight centile categorised - Statistical analysis - POST-HOC*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of centile_10b by AllocatedTreatment</i>			
		<i>AllocatedTreatment(Allocated Treatment)</i>			
<i>centile_10b</i>	<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>		
<i>No</i>	200	209	409		
<i>Yes</i>	14	11	25		
<i>Total</i>	214	220	434		

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
<i>centile_10b_itt</i>	<i>AllocatedTreatment METFORMIN vs PLACEBO</i>	1.330	0.590	2.999	0.4918	0.5408

Section 4. Outcomes - Only Alive Births

4.2.2.2 PRIMARY EFFICACY: Birth weight centile categorised split by gender

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Split Birth weight Centile Males(n(%))	<=3rd	2 (1.8)	2 (1.8)	4 (1.8)
	>3rd and <=5th	2 (1.8)	3 (2.8)	5 (2.3)
	>5th and <=10th	3 (2.8)	4 (3.7)	7 (3.2)
	>10th and <=90th	81 (74.3)	86 (78.9)	167 (76.6)
	>90th and <=95th	8 (7.3)	6 (5.5)	14 (6.4)
	>95th and <=97th	5 (4.6)	4 (3.7)	9 (4.1)
	>97th	8 (7.3)	4 (3.7)	12 (5.5)
Split Birth weight Centile Females(n(%))	<=3rd	1 (0.9)	1 (1.0)	2 (0.9)
	>3rd and <=5th	2 (1.8)	0	2 (0.9)
	>5th and <=10th	1 (0.9)	4 (3.8)	5 (2.3)
	>10th and <=90th	90 (81.1)	83 (79.0)	173 (80.1)
	>90th and <=95th	8 (7.2)	8 (7.6)	16 (7.4)
	>95th and <=97th	2 (1.8)	1 (1.0)	3 (1.4)
	>97th	7 (6.3)	8 (7.6)	15 (6.9)

Section 4. Outcomes - Only Alive Births

4.2.2.3 PRIMARY EFFICACY: Birth weight centile categorised split by gestation

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Split Birth weight Centile >24 and <=37 WEEKS(n(%))	>10th and <=90th	13 (92.9)	14 (77.8)	27 (84.4)
	>90th and <=95th	0	1 (5.6)	1 (3.1)
	>95th and <=97th	0	1 (5.6)	1 (3.1)
	>97th	1 (7.1)	2 (11.1)	3 (9.4)
Split Birth weight Centile >37 WEEKS(n(%))	<=3rd	3 (1.5)	3 (1.5)	6 (1.5)
	>3rd and <=5th	4 (1.9)	3 (1.5)	7 (1.7)
	>5th and <=10th	4 (1.9)	8 (4.1)	12 (3.0)
	>10th and <=90th	158 (76.7)	155 (79.1)	313 (77.9)
	>90th and <=95th	16 (7.8)	13 (6.6)	29 (7.2)
	>95th and <=97th	7 (3.4)	4 (2.0)	11 (2.7)
	>97th	14 (6.8)	10 (5.1)	24 (6.0)

Section 4. Outcomes - Only Alive Births

4.2.2.4 PRIMARY EFFICACY: Birth weight centile categorised split by parity

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Split Birth weight Centile parity=0 (n(%))	<=3rd	1 (1.2)	0	1 (0.6)
	>3rd and <=5th	2 (2.4)	3 (3.2)	5 (2.8)
	>5th and <=10th	1 (1.2)	5 (5.4)	6 (3.4)
	>10th and <=90th	67 (79.8)	72 (77.4)	139 (78.5)
	>90th and <=95th	5 (6.0)	7 (7.5)	12 (6.8)
	>95th and <=97th	4 (4.8)	1 (1.1)	5 (2.8)
	>97th	4 (4.8)	5 (5.4)	9 (5.1)
Split Birth weight Centile parity=>1 (n(%))	<=3rd	2 (1.5)	3 (2.5)	5 (1.9)
	>3rd and <=5th	2 (1.5)	0	2 (0.8)
	>5th and <=10th	3 (2.2)	3 (2.5)	6 (2.3)
	>10th and <=90th	104 (76.5)	97 (80.2)	201 (78.2)
	>90th and <=95th	11 (8.1)	7 (5.8)	18 (7.0)
	>95th and <=97th	3 (2.2)	4 (3.3)	7 (2.7)
	>97th	11 (8.1)	7 (5.8)	18 (7.0)

Section 4. Outcomes - Only Alive Births

4.3.1 PRIMARY EFFICACY: Calculated Z score

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
Z-score for birth weight centile	Mean	0.2680	0.2464	0.2573
	Median	0.1932	0.3304	0.2272
	SD	1.0055	1.0179	1.0105
	MIN,MAX	-3.071,3.299	-3.428,2.929	-3.428,3.299
	Q1,Q3	-0.376,0.848	-0.429,0.914	-0.398,0.910
	n	220	214	434
	Nmiss	0	0	0

Section 4. Outcomes - Only Alive Births

4.3.2 PRIMARY EFFICACY: Calculated Z score - Statistical Analysis

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
z-score - itt	0.358	0.1267	220	0.329	0.1231	214	-0.029	-0.217	0.158	0.094	0.7597

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 00:26

By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in table 4.3.1 of this report

Outcome analysed using a linear regression model, adjusted by BMI band and centre. Significance level set at p<0.05

Estimated mean represents the adjusted means for the z score by allocated treatment,

SE represents standard error of the estimated mean and N represents number of observations

*Represents the difference between the estimated means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_4_3_2_primary_outcome_z_analysis.lst'

Parameter shown normal behavior

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.1 Fasted Glucose - Visit 3 Randomisation (12-16 Weeks)*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
GTT - V3 - base (mmol/L)	Mean	4.39	4.41	4.40
	Median	4.40	4.40	4.40
	SD	0.34	0.40	0.37
	MIN,MAX	3.5,5.6	3.1,5.6	3.1,5.6
	Q1,Q3	4.2,4.6	4.1,4.7	4.1,4.6
	n	223	226	449
	Nmiss	0	0	0
GTT - V3 - 2 hr (mmol/L)	Mean	5.50	5.20	5.35
	Median	5.40	5.20	5.30
	SD	1.09	1.08	1.10
	MIN,MAX	2.4,7.8	1.7,7.7	1.7,7.8
	Q1,Q3	4.8,6.3	4.6,6.0	4.7,6.1
	n	223	226	449
	Nmiss	0	0	0

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.2 Fasted Glucose - Visit 5 (28 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
GTT - V5 - base (mmol/L)	Mean	4.49	4.38	4.44
	Median	4.40	4.40	4.40
	SD	0.47	0.41	0.44
	MIN,MAX	2.9,5.6	3.4,6.0	2.9,6.0
	Q1,Q3	4.2,4.8	4.1,4.7	4.1,4.7
	n	184	175	359
	Nmiss	39	51	90
GTT - V5 - 2 hr (mmol/L)	Mean	5.85	5.58	5.72
	Median	5.80	5.50	5.60
	SD	1.20	1.32	1.27
	MIN,MAX	2.4,8.9	3.0,12.3	2.4,12.3
	Q1,Q3	5.0,6.7	4.8,6.0	4.9,6.4
	n	184	174	358
	Nmiss	39	52	91

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.3 Fasted Glucose - Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
GTT - V6 - base (mmol/L)	Mean	4.42	4.35	4.39
	Median	4.30	4.30	4.30
	SD	0.48	0.45	0.47
	MIN,MAX	2.7,5.8	3.4,5.9	2.7,5.9
	Q1,Q3	4.0,4.7	4.0,4.6	4.0,4.7
	n	151	143	294
	Nmiss	72	83	155
GTT - V6 - 2 hr (mmol/L)	Mean	5.96	5.70	5.83
	Median	5.70	5.70	5.70
	SD	1.46	1.32	1.40
	MIN,MAX	3.0,10.3	2.7,9.1	2.7,10.3
	Q1,Q3	4.9,6.9	4.8,6.4	4.9,6.7
	n	148	142	290
	Nmiss	75	84	159

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.4.1 Fasted Glucose - Visit 6 (36 Weeks) - Statistical Analysis

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
Glucose_V6_Baseline - itt	4.420	0.0660	151	4.360	0.0624	143	-0.060	-0.163	0.043	1.330	0.2498
Glucose_V6_Two_Hour - itt	6.083	0.2001	148	5.832	0.1890	142	-0.251	-0.565	0.062	2.487	0.1159

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 00:26

By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in table 5.1.3 of this report

Outcome analysed using a linear regression model. Significance level set at p<0.05

Estimated mean represents the adjusted means for the glucose in blood by allocated treatment,

SE represents standard error of the estimated mean and N represents number of observations

*Represents the difference between the estimated means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_5_1_4_glucose_outcome_analysis.lst'

Parameters shown normal or near-normal behavior

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.4.2 Fasted Glucose - Visit 5 (28 Weeks) - Statistical Analysis - POST-HOC

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Lower CI*	Estimated Mean Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
Glucose_V5_Baseline - itt	4.468	0.0599	184	4.363	0.0570	175	-0.105	-0.193	-0.016	5.383	0.0209
Glucose_V5_Two_Hour - itt	5.787	0.1716	184	5.537	0.1633	174	-0.250	-0.504	0.005	3.724	0.0545

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 00:26

By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in table 5.1.2 of this report

Outcome analysed using a linear regression model. Significance level set at p<0.05

Estimated mean represents the adjusted means for the glucose in blood by allocated treatment,

SE represents standard error of the estimated mean and N represents number of observations

*Represents the difference between the estimated means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_5_1_4_glucose_outcome_analysis_v5.lst'

Parameters shown normal or near-normal behavior

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.1 Fasted Glucose - Visit 5 (28 Weeks) split by C-section

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Yes C-section - GTT - V5 - base (mmol/L)	Mean	4.56	4.46	4.51
	Median	4.55	4.40	4.50
	SD	0.51	0.44	0.48
	MIN,MAX	3.6,5.6	3.5,6.0	3.5,6.0
	Q1,Q3	4.2,5.0	4.2,4.8	4.2,4.8
	n	64	52	116
	Nmiss	6	9	15
Yes C-section - GTT - V5 - 2 hr (mmol/L)	Mean	6.10	5.86	5.99
	Median	6.00	5.60	5.85
	SD	1.44	1.41	1.42
	MIN,MAX	2.4,8.9	4.2,12.3	2.4,12.3
	Q1,Q3	5.2,7.4	5.1,6.3	5.1,7.0
	n	64	52	116
	Nmiss	6	9	15

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.1 Fasted Glucose - Visit 5 (28 Weeks) split by C-section

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
No C-section - GTT - V5 - base (mmol/L)	Mean	4.45	4.35	4.40
	Median	4.40	4.30	4.40
	SD	0.44	0.40	0.42
	MIN,MAX	2.9,5.6	3.4,5.6	2.9,5.6
	Q1,Q3	4.2,4.7	4.1,4.6	4.1,4.7
	n	120	122	242
	Nmiss	21	21	42
No C-section - GTT - V5 - 2 hr (mmol/L)	Mean	5.71	5.47	5.59
	Median	5.70	5.50	5.60
	SD	1.03	1.27	1.16
	MIN,MAX	3.0,8.7	3.0,10.0	3.0,10.0
	Q1,Q3	4.9,6.4	4.6,6.0	4.9,6.3
	n	120	121	241
	Nmiss	21	22	43

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.2 Fasted Glucose - Visit 6 (36 Weeks) split by C-section

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Yes C-section - GTT - V6 - base (mmol/L)	Mean	4.43	4.39	4.41
	Median	4.50	4.30	4.30
	SD	0.50	0.47	0.49
	MIN,MAX	2.7,5.6	3.6,5.5	2.7,5.6
	Q1,Q3	4.1,4.8	4.0,4.7	4.0,4.7
	n	52	43	95
	Nmiss	17	16	33
Yes C-section - GTT - V6 - 2 hr (mmol/L)	Mean	6.18	5.79	6.00
	Median	6.10	5.80	6.00
	SD	1.58	1.20	1.43
	MIN,MAX	3.0,10.3	2.7,8.5	2.7,10.3
	Q1,Q3	4.9,7.4	5.0,6.6	5.0,6.9
	n	52	43	95
	Nmiss	17	16	33

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.2 Fasted Glucose - Visit 6 (36 Weeks) split by C-section

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall
		Placebo	Metformin	
No C-section - GTT - V6 - base (mmol/L)	Mean	4.41	4.34	4.37
	Median	4.30	4.30	4.30
	SD	0.47	0.45	0.46
	MIN,MAX	3.4,5.8	3.4,5.9	3.4,5.9
	Q1,Q3	4.0,4.7	4.0,4.6	4.0,4.6
	n	99	100	199
	Nmiss	40	40	80
No C-section - GTT - V6 - 2 hr (mmol/L)	Mean	5.84	5.65	5.75
	Median	5.55	5.40	5.50
	SD	1.38	1.38	1.38
	MIN,MAX	3.5,9.8	3.2,9.1	3.2,9.8
	Q1,Q3	4.9,6.8	4.7,6.3	4.8,6.5
	n	96	99	195
	Nmiss	43	41	84

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.3 Fasted Glucose - Visit 5 (28 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
3%<=_GTT_V5_base (mmol/L)	Mean	4.03	4.13	4.08
	Median	4.00	4.20	4.10
	SD	0.25	0.12	0.18
	MIN,MAX	3.8,4.3	4.0,4.2	3.8,4.3
	Q1,Q3	3.8,4.3	4.0,4.2	4.0,4.2
	n	3	3	6
	Nmiss	0	0	0
3%<=_GTT_V5_2 hr (mmol/L)	Mean	4.60	6.13	5.37
	Median	4.80	5.70	4.95
	SD	0.35	1.31	1.20
	MIN,MAX	4.2,4.8	5.1,7.6	4.2,7.6
	Q1,Q3	4.2,4.8	5.1,7.6	4.8,5.7
	n	3	3	6
	Nmiss	0	0	0

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.3 Fasted Glucose - Visit 5 (28 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
5%<=_GTT_V5_base (mmol/L)	Mean	4.04	4.08	4.06
	Median	4.00	4.15	4.10
	SD	0.18	0.27	0.22
	MIN,MAX	3.8,4.3	3.6,4.4	3.6,4.4
	Q1,Q3	4.0,4.1	4.0,4.2	4.0,4.2
	n	5	6	11
	Nmiss	1	0	1
5%<=_GTT_V5_2 hr (mmol/L)	Mean	4.24	5.18	4.75
	Median	4.80	5.40	4.80
	SD	1.07	1.63	1.43
	MIN,MAX	2.4,5.0	3.0,7.6	2.4,7.6
	Q1,Q3	4.2,4.8	3.8,5.9	3.8,5.7
	n	5	6	11
	Nmiss	1	0	1

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.3 Fasted Glucose - Visit 5 (28 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
10%<=_GTT_V5_base (mmol/L)	Mean	4.30	4.22	4.25
	Median	4.20	4.20	4.20
	SD	0.42	0.30	0.34
	MIN,MAX	3,8,5,0	3,6,4,7	3,6,5,0
	Q1,Q3	4,0,4,6	4,0,4,4	4,0,4,4
	n	8	11	19
	Nmiss	2	2	4
10%<=_GTT_V5_2 hr (mmol/L)	Mean	4.60	4.91	4.78
	Median	4.80	5.10	4.80
	SD	1.09	1.37	1.23
	MIN,MAX	2,4,6,2	3,0,7,6	2,4,7,6
	Q1,Q3	4,2,5,1	3,7,5,9	3,8,5,7
	n	8	11	19
	Nmiss	2	2	4

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.3 Fasted Glucose - Visit 5 (28 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
10%> AND 90%<=_GTT_V5_base (mmol/L)	Mean	4.47	4.37	4.42
	Median	4.40	4.35	4.40
	SD	0.46	0.41	0.44
	MIN,MAX	2.9,5.5	3.4,6.0	2.9,6.0
	Q1,Q3	4.2,4.8	4.1,4.6	4.2,4.7
	n	142	134	276
	Nmiss	21	25	46
10%> AND 90%<=_GTT_V5_2 hr (mmol/L)	Mean	5.85	5.61	5.73
	Median	5.85	5.50	5.70
	SD	1.20	1.30	1.25
	MIN,MAX	3.0,8.9	3.1,12.3	3.0,12.3
	Q1,Q3	4.9,6.7	4.9,6.1	4.9,6.5
	n	142	133	275
	Nmiss	21	26	47

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.3 Fasted Glucose - Visit 5 (28 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
90%>_GTT_V5_base (mmol/L)	Mean	4.60	4.51	4.56
	Median	4.60	4.40	4.60
	SD	0.50	0.43	0.47
	MIN,MAX	3.7,5.6	3.7,5.6	3.7,5.6
	Q1,Q3	4.3,4.9	4.3,4.7	4.3,4.8
	n	34	29	63
	Nmiss	2	2	4
90%>_GTT_V5_2 hr (mmol/L)	Mean	6.14	5.75	5.96
	Median	5.90	5.40	5.70
	SD	1.08	1.36	1.22
	MIN,MAX	4.4,8.3	3.6,9.8	3.6,9.8
	Q1,Q3	5.3,7.1	5.0,6.0	5.1,6.5
	n	34	29	63
	Nmiss	2	2	4

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.3 Fasted Glucose - Visit 5 (28 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
95%>_GTT_V5_base (mmol/L)	Mean	4.71	4.50	4.61
	Median	4.60	4.45	4.60
	SD	0.51	0.37	0.45
	MIN,MAX	4.0,5.6	4.0,5.5	4.0,5.6
	Q1,Q3	4.3,5.2	4.3,4.7	4.3,4.8
	n	19	16	35
	Nmiss	1	2	3
95%>_GTT_V5_2 hr (mmol/L)	Mean	6.11	5.75	5.95
	Median	5.90	5.35	5.90
	SD	1.03	1.51	1.27
	MIN,MAX	4.4,8.3	3.6,9.8	3.6,9.8
	Q1,Q3	5.3,7.0	5.0,6.1	5.2,6.4
	n	19	16	35
	Nmiss	1	2	3

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.3 Fasted Glucose - Visit 5 (28 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
97%>_GTT_V5_base (mmol/L)	Mean	4.78	4.49	4.64
	Median	4.70	4.30	4.60
	SD	0.45	0.43	0.46
	MIN,MAX	4.1,5.6	4.0,5.5	4.0,5.6
	Q1,Q3	4.5,5.2	4.2,4.7	4.3,4.9
	n	12	11	23
	Nmiss	1	2	3
97%>_GTT_V5_2 hr (mmol/L)	Mean	5.88	5.78	5.83
	Median	5.80	5.90	5.90
	SD	0.82	1.58	1.21
	MIN,MAX	4.8,7.5	3.6,9.8	3.6,9.8
	Q1,Q3	5.3,6.4	5.0,6.1	5.2,6.3
	n	12	11	23
	Nmiss	1	2	3

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.4 Fasted Glucose - Visit 6 (36 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
3%<=_GTT_V6_base (mmol/L)	Mean	3.90	.	3.90
	Median	3.50	.	3.50
	SD	0.78	.	0.78
	MIN,MAX	3.4,4.8	..	3.4,4.8
	Q1,Q3	3.4,4.8	..	3.4,4.8
	n	3	0	3
	Nmiss	0	3	3
3%<=_GTT_V6_2 hr (mmol/L)	Mean	5.17	.	5.17
	Median	4.50	.	4.50
	SD	1.99	.	1.99
	MIN,MAX	3.6,7.4	..	3.6,7.4
	Q1,Q3	3.6,7.4	..	3.6,7.4
	n	3	0	3
	Nmiss	0	3	3

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.4 Fasted Glucose - Visit 6 (36 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
5%<=_GTT_V6_base (mmol/L)	Mean	3.90	3.90	3.90
	Median	3.90	3.90	3.90
	SD	0.55	0.30	0.45
	MIN,MAX	3.4,4.8	3.6,4.2	3.4,4.8
	Q1,Q3	3.5,3.9	3.6,4.2	3.6,4.1
	n	5	3	8
	Nmiss	1	3	4
5%<=_GTT_V6_2 hr (mmol/L)	Mean	4.80	4.90	4.84
	Median	4.50	4.60	4.55
	SD	1.73	1.18	1.45
	MIN,MAX	3.0,7.4	3.9,6.2	3.0,7.4
	Q1,Q3	3.6,5.5	3.9,6.2	3.8,5.9
	n	5	3	8
	Nmiss	1	3	4

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.4 Fasted Glucose - Visit 6 (36 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
10%<=_GTT_V6_base (mmol/L)	Mean	4.14	4.41	4.28
	Median	4.10	4.50	4.35
	SD	0.54	0.49	0.52
	MIN,MAX	3,4,4,8	3,6,5,1	3,4,5,1
	Q1,Q3	3,7,4,7	4,1,4,8	3,9,4,7
	n	8	8	16
	Nmiss	2	5	7
10%<=_GTT_V6_2 hr (mmol/L)	Mean	5.45	5.26	5.36
	Median	5.65	5.55	5.65
	SD	1.71	1.48	1.55
	MIN,MAX	3,0,7,9	2,7,7,3	2,7,7,9
	Q1,Q3	4,1,6,7	4,3,6,3	4,2,6,3
	n	8	8	16
	Nmiss	2	5	7

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.4 Fasted Glucose - Visit 6 (36 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
10%> AND 90%<=_GTT_V6_base (mmol/L)	Mean	4.39	4.33	4.36
	Median	4.30	4.20	4.30
	SD	0.46	0.45	0.46
	MIN,MAX	2.7,5.8	3.4,5.9	2.7,5.9
	Q1,Q3	4.0,4.7	4.0,4.6	4.0,4.6
	n	116	111	227
	Nmiss	44	45	89
10%> AND 90%<=_GTT_V6_2 hr (mmol/L)	Mean	5.83	5.73	5.78
	Median	5.70	5.70	5.70
	SD	1.38	1.38	1.38
	MIN,MAX	3.2,9.5	3.2,9.1	3.2,9.5
	Q1,Q3	4.7,6.8	4.7,6.5	4.7,6.6
	n	113	111	224
	Nmiss	47	45	92

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.4 Fasted Glucose - Visit 6 (36 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
90%>_GTT_V6_base (mmol/L)	Mean	4.63	4.45	4.55
	Median	4.60	4.35	4.40
	SD	0.49	0.46	0.48
	MIN,MAX	3.8,5.6	3.9,5.5	3.8,5.6
	Q1,Q3	4.3,5.0	4.1,4.6	4.2,4.8
	n	27	24	51
	Nmiss	9	5	14
90%>_GTT_V6_2 hr (mmol/L)	Mean	6.67	5.70	6.22
	Median	6.50	5.70	5.90
	SD	1.55	0.98	1.39
	MIN,MAX	3.9,10.3	3.6,8.3	3.6,10.3
	Q1,Q3	5.5,7.5	5.0,6.2	5.2,7.2
	n	27	23	50
	Nmiss	9	6	15

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.4 Fasted Glucose - Visit 6 (36 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
95%>_GTT_V6_base (mmol/L)	Mean	4.79	4.28	4.54
	Median	4.70	4.30	4.40
	SD	0.49	0.31	0.48
	MIN,MAX	4.0,5.6	3.9,5.1	3.9,5.6
	Q1,Q3	4.4,5.1	4.0,4.4	4.2,4.8
	n	14	13	27
	Nmiss	6	3	9
95%>_GTT_V6_2 hr (mmol/L)	Mean	6.52	5.63	6.11
	Median	6.30	5.55	5.85
	SD	1.52	0.82	1.30
	MIN,MAX	3.9,9.8	4.5,7.2	3.9,9.8
	Q1,Q3	5.5,7.5	5.0,6.0	5.1,7.2
	n	14	12	26
	Nmiss	6	4	10

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.4 Fasted Glucose - Visit 6 (36 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
97%>_GTT_V6_base (mmol/L)	Mean	4.93	4.28	4.58
	Median	4.85	4.30	4.40
	SD	0.40	0.35	0.49
	MIN,MAX	4.4,5.6	3.9,5.1	3.9,5.6
	Q1,Q3	4.7,5.2	4.0,4.3	4.3,5.0
	n	8	9	17
	Nmiss	5	2	7
97%>_GTT_V6_2 hr (mmol/L)	Mean	6.90	5.60	6.25
	Median	6.65	5.15	5.70
	SD	1.63	0.98	1.46
	MIN,MAX	5.2,9.8	4.5,7.2	4.5,9.8
	Q1,Q3	5.6,7.9	5.0,6.4	5.1,7.4
	n	8	8	16
	Nmiss	5	3	8

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.6.1 Gestational diabetes mellitus (GDM) - OGTT Test*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
GDM WHO CRITERIA*# (n(%))	Missing	73	83	156
	No	124 (82.7)	124 (86.7)	248 (84.6)
	Yes	26 (17.3)	19 (13.3)	45 (15.4)
GDM WHO CRITERIA CODED# (n(%))	Missing	73	83	156
	GDM first at visit 5 (28 weeks)	12 (8.0)	10 (7.0)	22 (7.5)
	GDM first at visit 6 (36 weeks)	14 (9.3)	9 (6.3)	23 (7.8)
	NO GDM	124 (82.7)	124 (86.7)	248 (84.6)
GDM IADPSG CRITERIA*\$ (n(%))	Missing	70	84	154
	No	117 (76.5)	116 (81.7)	233 (79.0)
	Yes	36 (23.5)	26 (18.3)	62 (21.0)
GDM IADPSG CRITERIA CODED\$ (n(%))	Missing	70	84	154
	GDM first at visit 5 (28 weeks)	26 (17.0)	11 (7.7)	37 (12.5)
	GDM first at visit 6 (36 weeks)	10 (6.5)	15 (10.6)	25 (8.5)
	NO GDM	117 (76.5)	116 (81.7)	233 (79.0)

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N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*Once GDM is present in visit 5 then it will stay present in visit 6

#WHO criteria: Fasting glucose \geq 7.0 mmol/l or 2hr glucose \geq 7.8 mmol/l\$IADPSG criteria: Fasting glucose \geq 5.1 mmol/l or 2hr glucose \geq 8.5 mmol/l

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.6.2 Gestational diabetes mellitus (GDM) IADPSG\$ - OGTT Test* - Statistical Analysis - POST-HOC*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Frequency</i>		<i>Table of GDM_IAD by Allocated Treatment</i>					
<i>GDM_IAD(GDM calculated using IADPSG criteria (Y/N))</i>	<i>Allocated Treatment(Allocated Treatment)</i>			<i>Total</i>			
	<i>METFORMIN</i>	<i>PLACEBO</i>					
<i>Missing</i>	84	70					
<i>No</i>	116	117		233			
<i>Yes</i>	26	36		62			
<i>Total</i>	142	153		295			
<i>Frequency Missing = 154</i>							

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
GDMIAD_itt	Allocated Treatment METFORMIN vs PLACEBO	0.728	0.414	1.283	0.2726	0.3174

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.6.3 Gestational diabetes mellitus (GDM) IADPSG\$ - OGTT Test* - Statistical Analysis - POST-HOC*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Frequency</i>	<i>Table of GDM_CODE_IAD by AllocatedTreatment</i>		
	<i>GDM_CODE_IAD(GDM calculated using IADPSG criteria by visit)</i>	<i>AllocatedTreatment(Allocated Treatment)</i>	
	<i>METFORMIN</i>	<i>PLACEBO</i>	
<i>Missing</i>	84	70	.
<i>GDM first at visit 5 (28 weeks)</i>	11	26	37
<i>GDM first at visit 6 (36 weeks)</i>	15	10	25
<i>NO GDM</i>	116	117	233
<i>Total</i>	142	153	295

Frequency Missing = 154

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Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.6.3 Gestational diabetes mellitus (GDM) IADPSG\$ - OGTT Test* - Statistical Analysis - POST-HOC*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Statistics for Table of GDM_CODE_IAD by Allocated Treatment

Statistic	DF	Value	Prob
Chi-Square	2	6.6845	0.0354
Likelihood Ratio Chi-Square	2	6.8605	0.0324
Mantel-Haenszel Chi-Square	1	3.2419	0.0718
Phi Coefficient		0.1505	
Contingency Coefficient		0.1489	
Cramer's V		0.1505	

Effective Sample Size = 295

Frequency Missing = 154

WARNING: 34 % of the data are missing.

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Summary statistics are presented in table 5.1.6.1 of this report

*Analysed using The Mantel-Haenszel chi-square statistic tests

#Significance level set at $p < 0.05$. Detailed analysis in file 'Empowar_5_1_6_glucose_GDM_analysis.lst'

\$IADPSG criteria: Fasting glucose ≥ 5.1 mmol/l or 2hr glucose ≥ 8.5 mmol/l

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Section 5. Maternal insulin resistance (Secondary Outcome)

5.2.1 Insulin - Visit 2 Consent/Baseline (10-16 Weeks), Visit 5 (28 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Insulin - Visit 2 (mIU/ml)	Mean	22.077	21.953	22.015
	Median	19.457	19.765	19.679
	SD	10.201	12.264	11.262
	MIN,MAX	3.73,71.22	2.00,106.02	2.00,106.02
	Q1,Q3	15.51,26.41	14.93,26.72	15.26,26.60
	n	189	188	377
	Nmiss	34	38	72
Insulin - Visit 5 (mIU/ml)	Mean	27.487	26.313	26.920
	Median	25.015	23.158	24.014
	SD	14.282	19.053	16.740
	MIN,MAX	6.86,121.29	6.82,196.84	6.82,196.84
	Q1,Q3	19.46,31.33	17.18,30.29	17.99,30.73
	n	154	144	298
	Nmiss	69	82	151

Section 5. Maternal insulin resistance (Secondary Outcome)

5.2.1 Insulin - Visit 6 (36 Weeks) (Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
Insulin - Visit 6 (mIU/ml)	Mean	30.086	32.794	31.419
	Median	27.342	27.088	27.222
	SD	13.123	24.547	19.605
	MIN,MAX	6.46,91.87	9.78,204.26	6.46,204.26
	Q1,Q3	20.91,35.86	20.36,36.61	20.73,35.86
	n	131	127	258
	Nmiss	92	99	191

Section 5. Maternal insulin resistance (Secondary Outcome)

5.2.2.1 Fasted Insulin - Visit 6 (36 Weeks) - Statistical Analysis - POST-HOC

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
Insulin_log_visit_6 - itt	3.438	0.0759	131	3.442	0.0724	127	0.005	-0.104	0.113	0.007	0.9342

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Summary statistics are presented in table 5.2.1 of this report

Outcome analysed using a linear regression model. Significance level set at p<0.05

Estimated mean represents the adjusted means of the log transformed insulin in blood by allocated treatment, SE represents standard error of the estimated log transformed mean and N represents number of observations

*Represents the difference between the estimated log transformed mean and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_5_2_2_INSULIN_RES_outcome_analysis.lst'

Parameter shown normal or near-normal behavior

Section 5. Maternal insulin resistance (Secondary Outcome)

5.2.2.2 Fasted Insulin - Visit 5 (28 Weeks) - Statistical Analysis - POST-HOC

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
Insulin_log_visit_5 - itt	3.305	0.0694	154	3.214	0.0656	144	-0.091	-0.189	0.007	3.374	0.0673

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By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in table 5.2.1 of this report

Outcome analysed using a linear regression model. Significance level set at p<0.05

Estimated mean represents the adjusted means of the log transformed insulin in blood by allocated treatment,

SE represents standard error of the estimated log transformed mean and N represents number of observations

*Represents the difference between the estimated log transformed mean and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_5_2_2_INSULIN_RES_outcome_analysis_v5'.lst

Parameter shown normal or near-normal behavior

Section 5. Maternal insulin resistance (Secondary Outcome)
5.3.1 HOMA-IR - Visit 2 Consent/Baseline (10-16 Weeks) and Visit 5 (28 Weeks)
 Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	<i>Overall N=449</i>
HOMA - visit 2 - base	Mean	4.360	4.363	4.362
	Median	3.855	3.903	3.857
	SD	2.157	2.755	2.470
	MIN,MAX	0.71,14.24	0.34,24.02	0.34,24.02
	Q1,Q3	2.94,5.16	2.74,5.16	2.88,5.16
	n	189	188	377
	Nmiss	34	38	72
HOMA - visit 5 - base	Mean	5.563	5.234	5.404
	Median	4.862	4.651	4.735
	SD	3.298	4.173	3.745
	MIN,MAX	1.10,28.57	1.23,41.12	1.10,41.12
	Q1,Q3	3.72,6.46	3.21,6.13	3.31,6.28
	n	153	144	297
	Nmiss	70	82	152

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 N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations
 HOMA-IR was calculated using the following formula: $HOMA-IR \text{ (units)} = (\text{glucose} \times \text{insulin} / 22.5)$

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Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.2 HOMA-IR - Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
HOMA - visit 6 - base	Mean	5.978	6.298	6.133
	Median	5.345	5.056	5.175
	SD	2.888	4.777	3.914
	MIN,MAX	1.15,16.74	1.73,34.50	1.15,34.50
	Q1,Q3	4.04,7.18	3.72,7.26	3.87,7.18
	n	131	123	254
	Nmiss	92	103	195

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.3.1 HOMA_IR - VISIT 6 (36 WEEKS) - Statistical Analysis

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
HOMA-IR_log_visit_6 - itt	1.808	0.0825	131	1.782	0.0787	123	-0.026	-0.145	0.093	0.187	0.6656

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Summary statistics are presented in table 5.3.2 of this report

Outcome analysed using a linear regression model. Significance level set at p<0.05

Estimated mean represents the adjusted means of the log transformed HOMA-IR in blood by allocated treatment,

SE represents standard error of the estimated log transformed means and N represents number of observations

*Represents the difference between the estimated log transformed means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_5_3_4_glucose_outcome_analysis.lst'

Parameter shown normal or near-normal behavior

Section 5. Maternal insulin resistance (Secondary Outcome)
 5.3.3.2 HOMA_IR - VISIT 5 (28 WEEKS) - Statistical Analysis - POST-HOC
 Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
HOMA-IR_log_visit_5 - itt	1.673	0.0774	153	1.563	0.0731	144	-0.111	-0.220	-0.002	3.984	0.0469

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By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in table 5.3.1 of this report

Outcome analysed using a linear regression model. Significance level set at p<0.05

Estimated mean represents the adjusted means of the log transformed HOMA-IR in blood by allocated treatment,

SE represents standard error of the estimated log transformed mean and N represents number of observations

*Represents the difference between the estimated log transformed means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_5_3_4_glucose_outcome_analysis_5v.lst'

Parameter shown normal or near-normal behavior

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.4.1 HOMA-IR - Visit 5 (28 Weeks) split by C-section

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Yes C-section - HOMA_IR - V5 - base	Mean	6.22	6.03	6.13
	Median	5.38	5.31	5.33
	SD	4.07	4.04	4.04
	MIN,MAX	1.6,28.6	1.8,23.1	1.6,28.6
	Q1,Q3	3.8,7.3	3.5,6.8	3.8,7.0
	n	50	46	96
	Nmiss	20	15	35
No C-section - HOMA_IR - V5 - base	Mean	5.25	4.86	5.06
	Median	4.69	4.25	4.51
	SD	2.82	4.22	3.56
	MIN,MAX	1.1,19.0	1.2,41.1	1.1,41.1
	Q1,Q3	3.4,6.1	3.1,5.7	3.2,5.8
	n	103	97	200
	Nmiss	38	46	84

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.4.2 HOMA-IR - Visit 6 (36 Weeks) split by C-section

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Yes C-section - HOMA_IR - V6 - base	Mean	6.52	5.74	6.17
	Median	5.88	5.20	5.46
	SD	3.06	2.79	2.95
	MIN,MAX	1.1,13.8	1.7,16.2	1.1,16.2
	Q1,Q3	4.4,7.8	3.9,7.2	4.2,7.2
	n	46	38	84
	Nmiss	23	21	44
No C-section - HOMA_IR - V6 - base	Mean	5.68	6.55	6.11
	Median	5.15	4.99	5.07
	SD	2.76	5.43	4.32
	MIN,MAX	1.6,16.7	1.7,34.5	1.6,34.5
	Q1,Q3	3.7,6.6	3.7,7.4	3.7,7.0
	n	85	85	170
	Nmiss	54	55	109

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.4.3 HOMA-IR - Visit 5 (28 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
3%<=_HOMA_IR_V5_base	Mean	3.55	4.30	3.85
	Median	4.04	4.30	4.04
	SD	1.73	2.77	1.90
	MIN,MAX	1.6,5.0	2.3,6.3	1.6,6.3
	Q1,Q3	1.6,5.0	2.3,6.3	2.3,5.0
	n	3	2	5
	Nmiss	0	1	1
5%<=_HOMA_IR_V5_base	Mean	3.63	3.41	3.52
	Median	4.04	2.83	3.14
	SD	1.39	1.68	1.46
	MIN,MAX	1.6,5.0	2.1,6.3	1.6,6.3
	Q1,Q3	2.8,4.7	2.3,3.5	2.3,4.7
	n	5	5	10
	Nmiss	1	1	2

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.4.3 HOMA-IR - Visit 5 (28 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
10%<=_HOMA_IR_V5_base	Mean	4.37	8.21	6.40
	Median	4.81	3.46	4.69
	SD	1.52	12.46	9.08
	MIN,MAX	1.6,6.5	2.1,41.1	1.6,41.1
	Q1,Q3	3.4,5.2	2.8,6.3	2.8,5.5
	n	8	9	17
	Nmiss	2	4	6
10%> AND 90%<=_HOMA_IR_V5_base	Mean	5.30	4.96	5.13
	Median	4.59	4.64	4.63
	SD	2.73	2.82	2.78
	MIN,MAX	1.1,19.0	1.2,23.1	1.1,23.1
	Q1,Q3	3.5,6.4	3.2,5.7	3.3,6.2
	n	117	109	226
	Nmiss	46	50	96

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.4.3 HOMA-IR - Visit 5 (28 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
90%>_HOMA_IR_V5_base	Mean	7.00	5.39	6.24
	Median	5.74	4.75	5.51
	SD	5.06	3.54	4.44
	MIN,MAX	2.7,28.6	1.5,19.4	1.5,28.6
	Q1,Q3	4.6,7.1	2.9,6.9	4.3,6.9
	n	28	25	53
	Nmiss	8	6	14
95%>_HOMA_IR_V5_base	Mean	7.10	5.34	6.16
	Median	5.79	4.50	5.53
	SD	6.34	4.18	5.28
	MIN,MAX	2.7,28.6	1.5,19.4	1.5,28.6
	Q1,Q3	4.5,6.6	2.6,6.6	3.3,6.6
	n	14	16	30
	Nmiss	6	2	8

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.4.3 HOMA-IR - Visit 5 (28 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
97%>_HOMA_IR_V5_base	Mean	8.32	5.61	6.83
	Median	5.95	4.48	5.73
	SD	7.71	4.93	6.30
	MIN,MAX	3.1,28.6	1.5,19.4	1.5,28.6
	Q1,Q3	5.7,6.6	2.5,6.9	3.7,6.7
	n	9	11	20
	Nmiss	4	2	6

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.4.4 HOMA-IR - Visit 6 (36 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
3%<=_HOMA_IR_V6_base	Mean	2.99	.	2.99
	Median	2.23	.	2.23
	SD	1.39	.	1.39
	MIN,MAX	2.1,4.6	..	2.1,4.6
	Q1,Q3	2.1,4.6	..	2.1,4.6
	n	3	0	3
	Nmiss	0	3	3
5%<=_HOMA_IR_V6_base	Mean	3.21	3.86	3.45
	Median	3.51	4.29	3.54
	SD	1.03	0.76	0.94
	MIN,MAX	2.1,4.6	3.0,4.3	2.1,4.6
	Q1,Q3	2.2,3.6	3.0,4.3	2.6,4.3
	n	5	3	8
	Nmiss	1	3	4

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.4.4 HOMA-IR - Visit 6 (36 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
10%<=_HOMA_IR_V6_base	Mean	4.90	5.27	5.09
	Median	3.57	4.31	4.30
	SD	3.19	2.25	2.66
	MIN,MAX	2.1,11.0	3.0,9.4	2.1,11.0
	Q1,Q3	2.2,7.3	3.7,7.3	3.5,7.3
	n	7	7	14
	Nmiss	3	6	9
10%> AND 90%<=_HOMA_IR_V6_base	Mean	5.74	6.50	6.10
	Median	5.34	5.06	5.20
	SD	2.54	5.24	4.08
	MIN,MAX	1.1,14.0	1.7,34.5	1.1,34.5
	Q1,Q3	4.1,6.7	3.8,7.3	3.9,7.0
	n	103	96	199
	Nmiss	57	60	117

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.4.4 HOMA-IR - Visit 6 (36 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
90%>_HOMA_IR_V6_base	Mean	7.52	5.69	6.63
	Median	5.99	6.05	6.05
	SD	3.89	2.54	3.39
	MIN,MAX	3.2,16.7	1.7,10.0	1.7,16.7
	Q1,Q3	4.8,10.7	3.9,7.3	4.1,8.2
	n	21	20	41
	Nmiss	15	9	24
95%>_HOMA_IR_V6_base	Mean	7.01	4.96	5.84
	Median	5.99	5.20	5.99
	SD	3.29	2.43	2.94
	MIN,MAX	3.6,12.7	1.7,10.0	1.7,12.7
	Q1,Q3	4.8,7.8	2.9,6.4	4.0,6.7
	n	9	12	21
	Nmiss	11	4	15

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.4.4 HOMA-IR - Visit 6 (36 Weeks) split by birth centile

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
97%>_HOMA_IR_V6_base	Mean	6.73	5.16	5.69
	Median	5.51	5.20	5.51
	SD	3.52	2.65	2.90
	MIN,MAX	4.0,11.9	1.7,10.0	1.7,11.9
	Q1,Q3	4.5,8.9	3.2,6.4	4.1,6.4
	n	4	8	12
	Nmiss	9	3	12

Section 5. Laboratory results (Secondary Outcome)

5.4.1 NEFA by study visit

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
NEFA - visit 2* (mmol/L)	Mean	0.519	0.481	0.500
	Median	0.500	0.460	0.480
	SD	0.200	0.177	0.190
	MIN,MAX	0.05,1.35	0.05,1.26	0.05,1.35
	Q1,Q3	0.38,0.65	0.36,0.59	0.37,0.61
	n	189	188	377
	Nmiss	34	38	72
NEFA - visit 5* (mmol/L)	Mean	0.420	0.427	0.423
	Median	0.420	0.410	0.410
	SD	0.139	0.161	0.150
	MIN,MAX	0.08,0.78	0.11,0.89	0.08,0.89
	Q1,Q3	0.31,0.52	0.30,0.53	0.31,0.52
	n	154	144	298
	Nmiss	69	82	151

Section 5. Laboratory results (Secondary Outcome)

5.4.1 NEFA by study visit (Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
NEFA - visit 6* (mmol/L)	Mean	0.465	0.455	0.460
	Median	0.450	0.430	0.440
	SD	0.181	0.194	0.187
	MIN,MAX	0.13,0.97	0.10,1.00	0.10,1.00
	Q1,Q3	0.33,0.60	0.31,0.56	0.32,0.57
	n	131	127	258
	Nmiss	92	99	191

Section 5. Laboratory results (Secondary Outcome)

5.4.2 IL_6 by study visit

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
IL_6 - visit 2* (pg/ml)	Mean	2.770	2.632	2.701
	Median	2.038	1.970	2.010
	SD	5.503	4.371	4.965
	MIN,MAX	0.73,75.20	0.62,58.25	0.62,75.20
	Q1,Q3	1.50,2.91	1.51,2.58	1.50,2.81
	n	189	188	377
	Nmiss	34	38	72
IL_6 - visit 5* (pg/ml)	Mean	2.733	2.379	2.562
	Median	2.243	2.142	2.199
	SD	2.158	1.186	1.763
	MIN,MAX	0.80,23.79	0.77,8.76	0.77,23.79
	Q1,Q3	1.68,3.36	1.62,2.76	1.64,2.96
	n	154	144	298
	Nmiss	69	82	151

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Section 5. Laboratory results (Secondary Outcome)

5.4.2 IL_6 by study visit (Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	<i>Overall N=449</i>
IL_6 - visit 6* (pg/ml)	Mean	3.856	2.926	3.399
	Median	2.904	2.499	2.709
	SD	4.101	1.374	3.106
	MIN,MAX	1.07,30.77	1.10,9.37	1.07,30.77
	Q1,Q3	2.28,4.05	1.99,3.75	2.09,3.83
	n	131	127	258
	Nmiss	92	99	191

Section 5. Laboratory results (Secondary Outcome)

5.4.3 Leptin by study visit

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Leptin - visit 2* (ng/ml)	Mean	93.610	98.499	96.048
	Median	87.734	89.443	88.352
	SD	42.077	40.296	41.217
	MIN,MAX	24.19,305.25	21.93,338.66	21.93,338.66
	Q1,Q3	65.00,111.76	73.26,115.63	69.36,113.41
	n	189	188	377
	Nmiss	34	38	72
Leptin - visit 5* (ng/ml)	Mean	104.417	102.250	103.369
	Median	96.360	94.544	94.892
	SD	46.427	50.533	48.384
	MIN,MAX	25.94,376.10	18.04,453.51	18.04,453.51
	Q1,Q3	76.14,125.11	71.87,125.33	71.99,125.11
	n	154	144	298
	Nmiss	69	82	151

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Section 5. Laboratory results (Secondary Outcome)

5.4.3 Leptin by study visit (Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
Leptin - visit 6* (ng/ml)	Mean	104.983	106.554	105.756
	Median	95.456	96.614	96.114
	SD	52.428	58.820	55.563
	MIN,MAX	21.49,397.20	31.85,505.21	21.49,505.21
	Q1,Q3	70.44,131.08	67.52,131.35	69.01,131.08
	n	131	127	258
	Nmiss	92	99	191

Section 5. Laboratory results (Secondary Outcome)

5.4.4 Cortisol by study visit

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Cortisol - visit 2* (nmol/l)	Mean	396.404	430.955	413.634
	Median	370.115	382.095	375.366
	SD	143.545	178.760	162.771
	MIN,MAX	154.11,869.93	145.01,1197.1	145.01,1197.1
	Q1,Q3	288.03,494.32	303.09,530.81	294.85,514.59
	n	189	188	377
	Nmiss	34	38	72
Cortisol - visit 5* (nmol/l)	Mean	716.481	777.227	745.835
	Median	673.822	738.567	720.696
	SD	230.814	252.761	243.167
	MIN,MAX	339.23,1922.5	234.30,1826.3	234.30,1922.5
	Q1,Q3	556.75,809.18	607.19,903.30	575.05,863.57
	n	154	144	298
	Nmiss	69	82	151

Section 5. Laboratory results (Secondary Outcome)

5.4.4 Cortisol by study visit (Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Cortisol - visit 6* (nmol/l)	Mean	821.701	867.039	844.018
	Median	781.602	831.024	800.864
	SD	232.879	225.416	229.914
	MIN,MAX	432.38,1903.3	432.71,1859.6	432.38,1903.3
	Q1,Q3	664.85,904.55	692.19,1003.0	680.38,967.38
	n	131	127	258
	Nmiss	92	99	191

Section 5. Laboratory results (Secondary Outcome)

5.4.5 PAI1/PAI2 ratio by study visit

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
PAI_ratio - visit 2*	Mean	1.476	1.771	1.622
	Median	1.053	0.977	0.997
	SD	1.393	5.222	3.798
	MIN,MAX	0.28,11.89	0.33,57.63	0.28,57.63
	Q1,Q3	0.76,1.70	0.71,1.43	0.73,1.54
	n	131	128	259
	Nmiss	92	98	190
PAI_ratio - visit 6*	Mean	3.203	2.965	3.085
	Median	2.246	1.828	2.040
	SD	2.611	2.791	2.699
	MIN,MAX	0.61,13.98	0.56,16.41	0.56,16.41
	Q1,Q3	1.27,4.43	1.18,3.77	1.24,4.04
	n	131	128	259
	Nmiss	92	98	190

Section 5. Laboratory results (Secondary Outcome)

5.4.6 NEFA, IL-6, Leptin, Cortisol, PAI1/PAI2 ratio Visit 6 (36 Weeks) - Statistical Analysis - POST-HOC

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Lower CI*	Estimated Mean Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
IL_6_log_Visit6 - itt	1.116	0.0819	131	0.950	0.0781	127	-0.166	-0.283	-0.049	7.778	0.0057
Leptin_log_Visit6 - itt	4.565	0.0757	131	4.570	0.0721	127	0.005	-0.103	0.113	0.008	0.9268
Cortisol_nmol_l_log_Visit6 - itt	6.673	0.0424	131	6.734	0.0404	127	0.060	-0.001	0.121	3.815	0.0519
NEFA_log_Visit6 - itt	-0.732	0.0684	131	-0.787	0.0652	127	-0.055	-0.152	0.043	1.206	0.2731
PAI_ratio_log_Visit6 - itt	1.000	0.1243	131	0.910	0.1153	128	-0.091	-0.259	0.078	1.119	0.2911

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By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in tables 5.4.1 to 5.4.5 of this report

Outcome analysed using a linear regression model, adjusted by BMI band and centre. Significance level set at p<0.05

Estimated mean represents the adjusted means of the log transformed variable by allocated treatment,

SE represents standard error of the estimated log transformed means and N represents number of observations

*Represents the difference between estimated log transformed means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_5_4_other_labs_analysis_v6.lst'

All parameters shown normal or near-normal behavior

Section 5. Laboratory results (Secondary Outcome)

5.5.1 B12# - Visit 2 Consent/Baseline (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
B12 (ng/l) - visit 2	Mean	260.2	266.3	263.2
	Median	249.0	251.0	249.0
	SD	101.3	92.4	96.8
	MIN,MAX	55,760	80,745	55,760
	Q1,Q3	195,325	214,315	205,317
	n	132	131	263
	Nmiss	91	95	186
B12 below 95th - visit 2 (n(%))*	Missing	91	95	186
	Yes	121 (91.7)	121 (92.4)	242 (92.0)
	No	11 (8.3)	10 (7.6)	21 (8.0)
B12 below 5th - visit 2 (n(%))*	Missing	91	95	186
	Yes	8 (6.1)	5 (3.8)	13 (4.9)
	No	124 (93.9)	126 (96.2)	250 (95.1)

Section 5. Laboratory results (Secondary Outcome)

5.5.1 B12# - Visit 6 (36 Weeks)(Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
B12 (ng/l) - visit 6	Mean	223.7	215.0	219.3
	Median	221.0	207.5	214.0
	SD	69.6	73.2	71.5
	MIN,MAX	60,482	38,564	38,564
	Q1,Q3	178,269	174,251	175,255
	n	130	132	262
	Nmiss	93	94	187
B12 below 95th - visit 6 (n(%))*	Missing	93	94	187
	Yes	127 (97.7)	129 (97.7)	256 (97.7)
	No	3 (2.3)	3 (2.3)	6 (2.3)
B12 below 5th - visit 6 (n(%))*	Missing	93	94	187
	Yes	6 (4.6)	7 (5.3)	13 (5.0)
	No	124 (95.4)	125 (94.7)	249 (95.0)

Section 5. Laboratory results (Secondary Outcome)

5.5.2 Serum folate# - Visit 2 Consent/Baseline (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Serum Folate (ug/l) - visit 2	Mean	13.84	13.77	13.81
	Median	16.45	16.40	16.40
	SD	4.57	4.83	4.69
	MIN,MAX	2.6,17.5	1.7,21.0	1.7,21.0
	Q1,Q3	10.7,17.5	10.4,17.5	10.5,17.5
	n	132	131	263
	Nmiss	91	95	186
Serum Folate below 95th - visit 2 (n(%))*	Missing	91	95	186
	Yes	71 (53.8)	75 (57.3)	146 (55.5)
	No	61 (46.2)	56 (42.7)	117 (44.5)
Serum Folate below 5th - visit 2 (n(%))*	Missing	91	95	186
	Yes	0	2 (1.5)	2 (0.8)
	No	132 (100)	129 (98.5)	261 (99.2)

Section 5. Laboratory results (Secondary Outcome)

5.5.2 Serum folate# - Visit 6 (36 Weeks) (Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Serum Folate (ug/l) - visit 6	Mean	8.29	8.54	8.42
	Median	5.60	6.60	5.95
	SD	5.61	5.64	5.61
	MIN,MAX	1.3,17.5	1.2,21.0	1.2,21.0
	Q1,Q3	3.8,14.2	3.9,14.0	3.9,14.2
	n	132	132	264
	Nmiss	91	94	185
Serum Folate below 95th - visit 6 (n(%))*	Missing	91	94	185
	Yes	110 (83.3)	110 (83.3)	220 (83.3)
	No	22 (16.7)	22 (16.7)	44 (16.7)
Serum Folate below 5th - visit 6 (n(%))*	Missing	91	94	185
	Yes	10 (7.6)	11 (8.3)	21 (8.0)
	No	122 (92.4)	121 (91.7)	243 (92.0)

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By: Aryelly Rodriguez - ECTU Statistician

N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*5th centile was set at 2.6 ug/l and 95th centile was set at 17.5 ug/l

#Reference range 3.1-17.5 ug/l, if Serum folate value was reported as greater than 17.5 ug/l, then the value was imputed at 17.5 ug/l for summarisation

Section 5. Laboratory results (Secondary Outcome)

5.5.3 B12 and Serum Folate Visit 6 (36 Weeks) - Statistical Analysis - POST-HOC

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
B12_log_99_Visit6 - itt	5.397	0.0588	130	5.348	0.0545	132	-0.049	-0.129	0.031	1.451	0.2296
SFOLATE_log_99_Visit6 - itt	1.898	0.1264	132	1.947	0.1174	132	0.049	-0.122	0.221	0.317	0.5737

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 00:26

By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in tables 5.5.2 and 5.6.2 of this report

Outcome analysed using a linear regression model, adjusted by BMI band and centre. Significance level set at p<0.05

Estimated mean represents the adjusted means of the log transformed variable by allocated treatment,

SE represents standard error of the estimated log transformed means and N represents number of observations

*Represents the difference between the estimated log transformed means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_5_5_B12_folate_continuo_analysis_v6.lst'

All parameters shown normal or near-normal behavior

Section 5. Laboratory results (Secondary Outcome)

5.5.4.1 B12* - Patients below 5th centile - Visit 6 (36 Weeks) - Statistical Analysis - POST-HOC

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Frequency</i>		<i>Table of B12_N5TH by Allocated Treatment</i>				
<i>B12_N5TH(Patients with B12 below 5th centile (Y/N))</i>	<i>Allocated Treatment(Allocated Treatment)</i>		<i>Total</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>Fisher exact P-value#</i>
	<i>METFORMIN</i>	<i>PLACEBO</i>				
<i>Missing</i>	94	93	.			
<i>Yes</i>	7	6	13			
<i>No</i>	125	124	249			
<i>Total</i>	132	130	262			
<i>Frequency Missing = 187</i>						
<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
b12_n5th_itt	Allocated Treatment METFORMIN vs PLACEBO	1.157	0.378	3.541	0.7979	1.0000

Section 5. Laboratory results (Secondary Outcome)

5.5.4.2 Serum Folate* - Patients below 5th centile - Visit 6 (36 Weeks) - Statistical Analysis - POST-HOC

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of SFOL_N5TH by AllocatedTreatment</i>			
	<i>SFOL_N5TH(Patients with Serum Folate below 5th centile (Y/N))</i>	<i>AllocatedTreatment(Allocated Treatment)</i>		<i>Total</i>	
		<i>METFORMIN</i>	<i>PLACEBO</i>		
<i>Missing</i>		94	91	.	
<i>Yes</i>		11	10	21	
<i>No</i>		121	122	243	
<i>Total</i>		132	132	264	
<i>Frequency Missing = 185</i>					

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
sfol_n5th_itt	AllocatedTreatment METFORMIN vs PLACEBO	1.109	0.454	2.708	0.8201	1.0000

Section 6. Mother Anthropometry

6.1.1 Maternal Height at Visit 2 Consent/Baseline (10-16 Weeks)*#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Height (cm) at Visit 2	Mean	165.1	165.5	165.3
	Median	165.0	165.0	165.0
	SD	5.9	5.9	5.9
	MIN,MAX	149,184	152,182	149,184
	Q1,Q3	161,170	162,170	161,170
	n	223	226	449
	Nmiss	0	0	0

Section 6. Mother Anthropometry

6.1.2 Maternal Height at Visit 6 (36 Weeks) and its change from baseline*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Height (cm) at Visit 6	Mean	166.0	166.3	166.1
	Median	166.0	166.0	166.0
	SD	6.0	5.6	5.8
	MIN,MAX	149,184	155,183	149,184
	Q1,Q3	162,170	163,171	162,170
	n	153	142	295
	Nmiss	70	84	154
Height (cm) change V6 baseline	Mean	0.1	0.2	0.2
	Median	0.0	0.0	0.0
	SD	0.8	0.8	0.8
	MIN,MAX	-2,3	-3,3	-3,3
	Q1,Q3	0,0	0,0	0,0
	n	153	142	295
	Nmiss	70	84	154

Section 6. Mother Anthropometry

6.1.3 Maternal Height at Visit 9 (Final 3 months postnatal) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Height (cm) at Visit 9	Mean	165.3	166.1	165.7
	Median	165.5	166.0	166.0
	SD	5.9	5.8	5.8
	MIN,MAX	149,184	154,180	149,184
	Q1,Q3	163,169	162,171	162,170
	n	125	127	252
	Nmiss	98	99	197
Height (cm) change V9 baseline	Mean	-0.2	-0.2	-0.2
	Median	0.0	0.0	0.0
	SD	0.8	0.8	0.8
	MIN,MAX	-3,2	-3,3	-3,3
	Q1,Q3	0,0	0,0	0,0
	n	125	127	252
	Nmiss	98	99	197

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Section 6. Mother Anthropometry

6.2.1 Maternal Weight at Visit 2 Consent/Baseline (10-16 Weeks)*#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
Weight (kg) at Visit 2	Mean	102.94	103.60	103.27
	Median	99.20	101.35	100.20
	SD	17.00	15.50	16.25
	MIN,MAX	72.0,170.4	74.0,154.8	72.0,170.4
	Q1,Q3	90.1,111.9	93.0,113.5	92.0,112.1
	n	223	226	449
	Nmiss	0	0	0

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N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is a repeat from section 2.5 in this report

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

Section 6. Mother Anthropometry

6.2.2.1 Maternal Weight at Visit 6 (36 Weeks) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Weight (kg) at Visit 6	Mean	111.67	112.52	112.08
	Median	107.30	111.00	109.90
	SD	17.33	16.02	16.69
	MIN,MAX	79.8,166.4	79.1,165.7	79.1,166.4
	Q1,Q3	99.7,121.4	102.4,121.5	100.6,121.5
	n	156	143	299
	Nmiss	67	83	150
Weight (kg) change V6 baseline	Mean	7.23	6.70	6.97
	Median	6.93	6.50	6.80
	SD	4.91	6.00	5.45
	MIN,MAX	-5.1,19.0	-5.7,35.7	-5.7,35.7
	Q1,Q3	4.2,9.6	2.6,10.0	3.3,10.0
	n	156	143	299
	Nmiss	67	83	150

Section 6. Mother Anthropometry

6.2.2.2 Maternal Weight at Visit 6 (36 Weeks) change from baseline - Statistical Analysis - POST-HOC

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
Weight-DIFF-Visit_6 - itt	7.342	0.7601	156	6.661	0.7209	143	-0.680	-1.863	0.503	1.282	0.2585

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By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in table 6.2.2.1 of this report

Outcome analysed using a linear regression model. Significance level set at p<0.05

Estimated mean represents the means for the Weight Difference by allocated treatment,

SE represents standard error of the estimated means and N represents number of observations

*Represents the difference between the estimated means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_6_2_2_Mother Anthropometry_weight_gain_v6.lst'

Parameter shown normal or near-normal behavior

Section 6. Mother Anthropometry

6.2.3 Maternal Weight at Visit 9 (Final 3 months postnatal) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Weight (kg) at Visit 9	Mean	102.14	105.91	104.02
	Median	98.70	105.00	102.32
	SD	15.29	18.41	16.99
	MIN,MAX	72.7,145.8	72.9,193.0	72.7,193.0
	Q1,Q3	92.0,111.0	94.6,115.2	92.4,112.3
	n	124	124	248
	Nmiss	99	102	201
Weight (kg) change V9 baseline	Mean	-0.13	0.07	-0.03
	Median	-0.35	-0.50	-0.50
	SD	6.22	9.82	8.20
	MIN,MAX	-15.5,18.2	-19.2,79.5	-19.2,79.5
	Q1,Q3	-3.6,3.2	-4.9,2.5	-4.0,2.8
	n	124	124	248
	Nmiss	99	102	201

Section 6. Mother Anthropometry

6.3.1 Maternal Waist at Visit 2 Consent/Baseline (10-16 Weeks)*#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Waist (cm) at Visit 2	Mean	108.7	110.1	109.4
	Median	106.0	109.0	108.0
	SD	13.5	11.9	12.7
	MIN,MAX	64,152	84,145	64,152
	Q1,Q3	99,117	102,117	100,117
	n	222	225	447
	Nmiss	1	1	2

Section 6. Mother Anthropometry

6.3.2 Maternal Waist at Visit 6 (36 Weeks) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Waist (cm) at Visit 6	Mean	120.0	119.0	119.5
	Median	120.0	119.0	119.0
	SD	13.2	11.1	12.2
	MIN,MAX	95,168	88,148	88,168
	Q1,Q3	109,128	111,126	110,127
	n	155	142	297
	Nmiss	68	84	152
Waist (cm) change V6 baseline	Mean	10.4	8.3	9.4
	Median	10.0	8.3	9.0
	SD	10.4	8.9	9.8
	MIN,MAX	-20,78	-22,29	-22,78
	Q1,Q3	5,16	4,14	4,14
	n	155	142	297
	Nmiss	68	84	152

Section 6. Mother Anthropometry

6.3.3 Maternal Waist at Visit 9 (Final 3 months postnatal) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Waist (cm) at Visit 9	Mean	109.2	109.9	109.5
	Median	107.0	109.0	107.5
	SD	12.8	13.9	13.3
	MIN,MAX	80,142	79,147	79,147
	Q1,Q3	100,117	101,117	100,117
	n	124	125	249
	Nmiss	99	101	200
Waist (cm) change V9 baseline	Mean	1.5	-0.2	0.6
	Median	0.5	0.0	0.0
	SD	9.5	9.6	9.6
	MIN,MAX	-21,55	-29,34	-29,55
	Q1,Q3	-4,6	-6,4	-5,5
	n	124	125	249
	Nmiss	99	101	200

Section 6. Mother Anthropometry

6.4.1 Maternal Hip at Visit 2 Consent/Baseline (10-16 Weeks)*#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Hip (cm) at Visit 2	Mean	126.4	127.4	126.9
	Median	125.0	126.0	125.0
	SD	12.1	11.8	11.9
	MIN,MAX	95,159	100,161	95,161
	Q1,Q3	117,134	119,135	118,134
	n	222	225	447
	Nmiss	1	1	2

Section 6. Mother Anthropometry

6.4.2 Maternal Hip at Visit 6 (36 Weeks) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Hip (cm) at Visit 6	Mean	130.1	131.3	130.7
	Median	128.0	130.0	129.5
	SD	12.3	11.8	12.1
	MIN,MAX	108,169	107,174	107,174
	Q1,Q3	122,139	123,140	122,139
	n	155	142	297
	Nmiss	68	84	152
Hip (cm) change V6 baseline	Mean	2.9	2.7	2.8
	Median	3.0	2.0	2.5
	SD	6.0	6.8	6.4
	MIN,MAX	-14,18	-12,21	-14,21
	Q1,Q3	-1,6	-2,7	-1,7
	n	155	142	297
	Nmiss	68	84	152

Section 6. Mother Anthropometry

6.4.3 Maternal Hip at Visit 9 (Final 3 months postnatal) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Hip (cm) at Visit 9	Mean	127.3	128.6	128.0
	Median	126.0	128.0	127.0
	SD	12.2	13.4	12.8
	MIN,MAX	99,166	79,167	79,167
	Q1,Q3	120,135	121,137	120,136
	n	124	125	249
	Nmiss	99	101	200
Hip (cm) change V9 baseline	Mean	1.1	-0.0	0.5
	Median	1.3	0.0	1.0
	SD	6.8	7.8	7.3
	MIN,MAX	-19,17	-41,23	-41,23
	Q1,Q3	-3,6	-4,5	-4,5
	n	124	125	249
	Nmiss	99	101	200

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Section 6. Mother Anthropometry

6.5.1 Maternal Mid Arm at Visit 2 Consent/Baseline (10-16 Weeks)*#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	<i>Overall N=449</i>
Mid Arm (cm) at Visit 2	Mean	36.3	36.7	36.5
	Median	36.0	36.0	36.0
	SD	5.0	4.7	4.8
	MIN,MAX	20,54	28,52	20,54
	Q1,Q3	33,39	34,39	34,39
	n	220	221	441
	Nmiss	3	5	8

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N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is a repeat from section 2.5 in this report

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

Section 6. Mother Anthropometry

6.5.2 Maternal Mid Arm at Visit 6 (36 Weeks) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Mid Arm (cm) at Visit 6	Mean	36.5	36.5	36.5
	Median	36.0	36.0	36.0
	SD	4.9	4.4	4.7
	MIN,MAX	22,56	22,52	22,56
	Q1,Q3	33,39	34,39	34,39
	n	154	142	296
	Nmiss	69	84	153
Mid Arm (cm) change V6 baseline	Mean	-0.1	-0.8	-0.4
	Median	0.0	-0.5	-0.4
	SD	3.8	4.0	3.9
	MIN,MAX	-10,12	-20,9	-20,12
	Q1,Q3	-2,2	-2,1	-2,1
	n	153	140	293
	Nmiss	70	86	156

Section 6. Mother Anthropometry

6.5.3 Maternal Mid Arm at Visit 9 (Final 3 months postnatal) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Mid Arm (cm) at Visit 9	Mean	37.1	37.4	37.2
	Median	36.5	37.0	37.0
	SD	4.7	4.4	4.5
	MIN,MAX	28,53	28,54	28,54
	Q1,Q3	34,39	34,40	34,40
	n	123	125	248
	Nmiss	100	101	201
Mid Arm (cm) change V9 baseline	Mean	0.7	0.0	0.3
	Median	0.3	0.0	0.0
	SD	4.4	3.8	4.1
	MIN,MAX	-7,25	-9,13	-9,25
	Q1,Q3	-2,3	-2,2	-2,3
	n	122	123	245
	Nmiss	101	103	204

Section 6. Mother Anthropometry

6.6.1 Maternal Mid Thigh at Visit 2 Consent/Baseline (10-16 Weeks)*#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Mid Thigh (cm) at Visit 2	Mean	64.2	64.2	64.2
	Median	64.0	63.0	64.0
	SD	7.7	6.9	7.3
	MIN,MAX	25,84	50,89	25,89
	Q1,Q3	60,69	60,68	60,69
	n	219	222	441
	Nmiss	4	4	8

Section 6. Mother Anthropometry

6.6.2 Maternal Mid Thigh at Visit 6 (36 Weeks) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Mid Thigh (cm) at Visit 6	Mean	65.3	65.2	65.3
	Median	65.0	65.0	65.0
	SD	7.4	6.8	7.1
	MIN,MAX	29,85	45,83	29,85
	Q1,Q3	60,70	60,69	60,70
	n	154	139	293
	Nmiss	69	87	156
Mid Thigh (cm) change V6 baseline	Mean	0.8	0.1	0.5
	Median	0.0	1.0	0.6
	SD	5.7	6.1	5.9
	MIN,MAX	-12,28	-30,14	-30,28
	Q1,Q3	-3,4	-4,4	-3,4
	n	152	137	289
	Nmiss	71	89	160

Section 6. Mother Anthropometry

6.6.3 Maternal Mid Thigh at Visit 9 (Final 3 months postnatal) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Mid Thigh (cm) at Visit 9	Mean	64.3	65.8	65.1
	Median	64.3	65.0	64.8
	SD	6.7	6.8	6.8
	MIN,MAX	51,84	52,84	51,84
	Q1,Q3	59,68	61,70	60,70
	n	122	124	246
	Nmiss	101	102	203
Mid Thigh (cm) change V9 baseline	Mean	0.7	0.7	0.7
	Median	0.0	1.0	0.5
	SD	6.8	5.7	6.3
	MIN,MAX	-10,47	-19,21	-19,47
	Q1,Q3	-4,4	-3,4	-4,4
	n	120	122	242
	Nmiss	103	104	207

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Section 6. Mother Anthropometry

6.7.1 Maternal Tricep Skinfold at Visit 2 Consent/Baseline (10-16 Weeks)*#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
Tricep Skinfold (mm) at Visit 2	Mean	31.2	31.9	31.6
	Median	30.6	31.0	30.8
	SD	9.7	10.8	10.2
	MIN,MAX	5,62	8,66	5,66
	Q1,Q3	25,38	24,39	25,38
	n	222	222	444
	Nmiss	1	4	5

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By: Aryelly Rodriguez - ECTU Statistician

N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is a repeat from section 2.5 in this report

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

Section 6. Mother Anthropometry

6.7.2 Maternal Tricep Skinfold at Visit 6 (36 Weeks) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Tricep Skinfold (mm) at Visit 6	Mean	30.4	31.3	30.9
	Median	30.5	30.0	30.0
	SD	10.3	12.0	11.1
	MIN,MAX	9,65	9,80	9,80
	Q1,Q3	23,36	24,36	23,36
	n	155	143	298
	Nmiss	68	83	151
Tricep Skinfold (mm) change V6 baseline	Mean	-1.0	-0.3	-0.7
	Median	-1.2	0.4	-0.3
	SD	10.3	12.2	11.2
	MIN,MAX	-31,32	-44,34	-44,34
	Q1,Q3	-7,5	-6,6	-6,5
	n	154	141	295
	Nmiss	69	85	154

Section 6. Mother Anthropometry

6.7.3 Maternal Tricep Skinfold at Visit 9 (Final 3 months postnatal) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Tricep Skinfold (mm) at Visit 9	Mean	32.2	33.4	32.8
	Median	32.0	32.0	32.0
	SD	10.8	11.4	11.1
	MIN,MAX	8,77	13,110	8,110
	Q1,Q3	25,38	27,39	26,39
	n	123	125	248
	Nmiss	100	101	201
Tricep Skinfold (mm) change V9 baseline	Mean	1.0	1.3	1.2
	Median	0.0	0.0	0.0
	SD	10.5	11.5	11.0
	MIN,MAX	-32,37	-26,64	-32,64
	Q1,Q3	-6,6	-6,7	-6,6
	n	122	124	246
	Nmiss	101	102	203

Section 6. Mother Anthropometry

6.8.1 Maternal Bicep Skinfold at Visit 2 Consent/Baseline (10-16 Weeks)*#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Bicep Skinfold (mm) at Visit 2	Mean	25.7	27.4	26.6
	Median	24.2	25.8	25.0
	SD	10.0	10.9	10.5
	MIN,MAX	1,60	9,61	1,61
	Q1,Q3	20,31	20,34	20,32
	n	222	222	444
	Nmiss	1	4	5

Section 6. Mother Anthropometry

6.8.2 Maternal Bicep Skinfold at Visit 6 (36 Weeks) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Bicep Skinfold (mm) at Visit 6	Mean	26.0	26.9	26.5
	Median	25.0	25.0	25.0
	SD	10.5	11.6	11.0
	MIN,MAX	8,66	7,71	7,71
	Q1,Q3	19,33	19,31	19,33
	n	155	143	298
	Nmiss	68	83	151
Bicep Skinfold (mm) change V6 baseline	Mean	-0.2	-0.5	-0.3
	Median	-0.1	-1.0	-0.6
	SD	11.1	10.7	10.9
	MIN,MAX	-42,35	-26,35	-42,35
	Q1,Q3	-7,7	-6,4	-7,5
	n	154	141	295
	Nmiss	69	85	154

Section 6. Mother Anthropometry

6.8.3 Maternal Bicep Skinfold at Visit 9 (Final 3 months postnatal) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Bicep Skinfold (mm) at Visit 9	Mean	27.2	29.7	28.5
	Median	25.0	27.0	25.8
	SD	12.1	15.1	13.7
	MIN,MAX	9,70	8,120	8,120
	Q1,Q3	20,31	21,35	20,34
	n	123	125	248
	Nmiss	100	101	201
Bicep Skinfold (mm) change V9 baseline	Mean	0.6	2.4	1.5
	Median	-0.9	2.0	0.5
	SD	11.8	12.6	12.2
	MIN,MAX	-35,39	-20,76	-35,76
	Q1,Q3	-7,8	-4,7	-6,7
	n	122	124	246
	Nmiss	101	102	203

Section 6. Mother Anthropometry

6.9.1 Maternal Subscapular Skinfold at Visit 2 Consent/Baseline (10-16 Weeks)*#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Subscapular Skinfold (mm) at Visit 2	Mean	32.0	32.6	32.3
	Median	32.7	31.3	32.0
	SD	12.2	11.8	12.0
	MIN,MAX	3,68	8,71	3,71
	Q1,Q3	24,40	25,39	24,39
	n	222	220	442
	Nmiss	1	6	7

Section 6. Mother Anthropometry

6.9.2 Maternal Subscapular Skinfold at Visit 6 (36 Weeks) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Subscapular Skinfold (mm) at Visit 6	Mean	32.7	34.5	33.5
	Median	31.4	34.0	32.0
	SD	13.5	13.9	13.7
	MIN,MAX	3,71	5,77	3,77
	Q1,Q3	24,40	25,41	25,41
	n	154	141	295
	Nmiss	69	85	154
Subscapular Skinfold (mm) change V6 base	Mean	-0.2	1.3	0.5
	Median	-1.5	1.0	0.0
	SD	12.0	10.7	11.4
	MIN,MAX	-32,39	-23,38	-32,39
	Q1,Q3	-7,6	-5,7	-6,7
	n	153	137	290
	Nmiss	70	89	159

Section 6. Mother Anthropometry

6.9.3 Maternal Subscapular Skinfold at Visit 9 (Final 3 months postnatal) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Subscapular Skinfold (mm) at Visit 9	Mean	33.2	35.9	34.6
	Median	31.0	34.0	33.0
	SD	13.1	13.2	13.2
	MIN,MAX	6,83	9,81	6,83
	Q1,Q3	24,40	28,44	26,42
	n	123	124	247
	Nmiss	100	102	202
Subscapular Skinfold (mm) change V9 base	Mean	1.2	1.7	1.4
	Median	-0.2	2.6	1.0
	SD	11.6	12.6	12.1
	MIN,MAX	-28,47	-31,56	-31,56
	Q1,Q3	-6,7	-7,9	-6,9
	n	122	122	244
	Nmiss	101	104	205

Section 6. Mother Anthropometry

6.10.1 Maternal Calculated BMI at Visit 2 Consent/Baseline (10-16 Weeks)*#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Calculated BMI (kg/m ²) at Visit 2	Mean	37.7	37.8	37.7
	Median	36.7	36.9	36.8
	SD	5.6	4.9	5.3
	MIN,MAX	30,61	30,57	30,61
	Q1,Q3	33,41	34,41	34,41
	n	223	226	449
	Nmiss	0	0	0

Section 6. Mother Anthropometry

6.10.2 Maternal Calculated BMI at Visit 6 (36 Weeks) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Calculated BMI (kg/m ²) at Visit 6	Mean	40.4	40.6	40.5
	Median	39.6	39.8	39.7
	SD	5.4	4.9	5.2
	MIN,MAX	31,56	32,55	31,56
	Q1,Q3	36,44	37,44	37,44
	n	153	141	294
	Nmiss	70	85	155
Calculated BMI (kg/m ²) change V6 baseli	Mean	2.5	2.4	2.5
	Median	2.4	2.5	2.4
	SD	1.8	2.1	2.0
	MIN,MAX	-3,7	-2,12	-3,12
	Q1,Q3	2,4	1,3	1,4
	n	153	141	294
	Nmiss	70	85	155

Section 6. Mother Anthropometry

6.10.3 Maternal Calculated BMI at Visit 9 (Final 3 months postnatal) and ist change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Calculated BMI (kg/m ²) at Visit 9	Mean	37.4	38.3	37.8
	Median	37.3	37.9	37.5
	SD	5.2	5.6	5.4
	MIN,MAX	28,61	29,61	28,61
	Q1,Q3	34,40	34,42	34,41
	n	124	124	248
	Nmiss	99	102	201
Calculated BMI (kg/m ²) change V9 baseli	Mean	0.0	0.1	0.0
	Median	-0.0	-0.2	-0.1
	SD	2.2	3.3	2.8
	MIN,MAX	-5,5	-7,25	-7,25
	Q1,Q3	-1,1	-2,1	-1,1
	n	124	124	248
	Nmiss	99	102	201

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Section 6. Mother Anthropometry

6.11 Maternal body percentage fat (Edinburgh)*#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Fat (%) Visit 1	Mean	46.82	48.19	47.54
	Median	46.85	48.00	47.50
	SD	5.62	5.18	5.41
	MIN,MAX	33.9,59.0	34.3,58.7	33.9,59.0
	Q1,Q3	42.6,50.4	45.3,51.7	44.8,51.1
	n	48	53	101
	Nmiss	12	7	19
<hr/>				
Fat (%) Visit 6	Mean	46.30	47.48	46.88
	Median	47.10	47.65	47.30
	SD	4.84	4.63	4.74
	MIN,MAX	34.3,53.9	39.1,56.3	34.3,56.3
	Q1,Q3	43.9,48.8	43.9,51.2	43.9,50.2
	n	31	30	61
	Nmiss	29	30	59

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By: Aryelly Rodriguez - ECTU Statistician

N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is only applicable to Edinburgh patients

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

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Section 6. Mother Anthropometry

6.11 Maternal body percentage fat (Edinburgh) (Cont.)*#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Fat (%) Visit 9	Mean	47.45	48.35	47.91
	Median	48.10	47.30	48.00
	SD	4.97	5.31	5.12
	MIN,MAX	36.6,54.6	37.9,58.6	36.6,58.6
	Q1,Q3	43.6,51.9	44.6,53.1	44.4,52.0
	n	29	30	59
	Nmiss	31	30	61

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 00:26

By: Aryelly Rodriguez - ECTU Statistician

N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is only applicable to Edinburgh patients

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

Section 6. Mother Anthropometry

6.12 Maternal Body fat mass (Edinburgh)*#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
FatMass (kg) Visit 1	Mean	47.927	50.325	49.185
	Median	45.854	49.384	47.509
	SD	12.054	11.787	11.916
	MIN,MAX	29.91,96.83	26.82,76.17	26.82,96.83
	Q1,Q3	38.65,54.37	42.17,59.48	41.17,55.54
	n	48	53	101
	Nmiss	12	7	19
FatMass (kg) Visit 6	Mean	50.827	54.372	52.570
	Median	50.278	54.583	50.690
	SD	10.944	12.172	11.606
	MIN,MAX	27.38,89.22	30.52,76.38	27.38,89.22
	Q1,Q3	46.87,55.44	46.75,65.08	46.86,57.92
	n	31	30	61
	Nmiss	29	30	59

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Section 6. Mother Anthropometry

6.12 Maternal Body fat mass (Edinburgh) (Cont.)*#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
FatMass (kg) Visit 9	Mean	49.063	50.086	49.583
	Median	51.265	48.549	50.263
	SD	9.011	13.726	11.562
	MIN,MAX	26.64,63.25	13.56,75.76	13.56,75.76
	Q1,Q3	46.31,55.43	45.10,59.07	45.10,56.26
	n	29	30	59
	Nmiss	31	30	61

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By: Aryelly Rodriguez - ECTU Statistician

N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is only applicable to Edinburgh patients

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

Section 6. Mother Anthropometry

6.13 Maternal Body mass (Edinburgh)*#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
BodyMass (kg) Visit 1	Mean	101.388	103.322	102.413
	Median	97.810	104.018	100.077
	SD	16.190	15.961	16.017
	MIN,MAX	74.97,170.25	73.54,140.37	73.54,170.25
	Q1,Q3	89.72,111.83	92.19,112.90	90.53,112.40
	n	47	53	100
	Nmiss	13	7	20
BodyMass (kg) Visit 6	Mean	108.794	113.366	111.043
	Median	105.046	111.525	108.272
	SD	14.871	16.740	15.853
	MIN,MAX	79.82,165.47	78.11,147.87	78.11,165.47
	Q1,Q3	100.32,117.60	104.43,124.68	102.65,118.64
	n	31	30	61
	Nmiss	29	30	59

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Section 6. Mother Anthropometry

6.13 Maternal Body mass (Edinburgh) (Cont.)*#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
BodyMass (kg) Visit 9	Mean	102.821	106.471	104.677
	Median	102.540	105.399	104.190
	SD	12.759	16.507	14.772
	MIN,MAX	72.74,126.73	73.76,146.86	72.74,146.86
	Q1,Q3	96.36,112.37	98.50,115.30	96.80,114.25
	n	29	30	59
	Nmiss	31	30	61

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 00:26

By: Aryelly Rodriguez - ECTU Statistician

N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is only applicable to Edinburgh patients

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

Section 6. Mother Anthropometry

6.2.2.2.extra Maternal Weight at Visit 6 (36 Weeks) - Statistical Analysis - POST-HOC

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
Weight-Visit_6 - itt	112.473	0.7582	156	111.836	0.7209	143	-0.637	-1.819	0.544	1.127	0.2893

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 00:26

By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in table 6.2.2.1 of this report

Outcome analysed using a linear regression model, adjusted by weight_V2, BMI band and centre.

Significance level set at p<0.05. Estimated mean represents the means for the Weight by allocated treatment,

SE represents standard error of the estimated means and N represents number of observations

*Represents the difference between the estimated means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_6_2_2_Mother_Anthropometry_weight_v6.lst'

Parameter shown normal or near-normal behavior

Section 7. Baby Anthropometry - All Patients

7.1.1.1 Baby Age and Weight at Visit 8 (Delivery)#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Neonatal Age (days)-V8	Mean	1.04	0.95	1.00
	Median	1.00	0.00	0.00
	SD	2.44	2.42	2.43
	MIN,MAX	0.0,26.0	0.0,23.0	0.0,26.0
	Q1,Q3	0.0,1.0	0.0,1.0	0.0,1.0
	n	157	147	304
	Nmiss	66	79	145
Baby Weight* (g)-V8	Mean	3687.72	3447.81	3574.28
	Median	3510.00	3432.50	3460.00
	SD	2689.82	546.15	1989.47
	MIN,MAX	400.0,37141	2110.0,4900.0	400.0,37141
	Q1,Q3	3110.0,3860.0	3077.5,3810.0	3090.0,3850.0
	n	165	148	313
	Nmiss	58	78	136

Section 7. Baby Anthropometry - All Patients

7.1.1.2 Baby Length and Ponderal Index at Visit 8 (Delivery)#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Baby Length (cm)-V8	Mean	50.23	49.64	49.94
	Median	51.50	50.00	51.00
	SD	8.16	7.98	8.06
	MIN,MAX	0.0,63.5	0.0,61.0	0.0,63.5
	Q1,Q3	49.5,53.0	48.0,53.0	49.0,53.0
	n	153	143	296
	Nmiss	70	83	153
Baby ponderal index* -V8	Mean	3.01	2.67	2.85
	Median	2.54	2.61	2.57
	SD	3.68	0.50	2.69
	MIN,MAX	1.7,40.6	1.5,5.0	1.5,40.6
	Q1,Q3	2.3,2.8	2.4,2.9	2.3,2.9
	n	145	131	276
	Nmiss	78	95	173

Section 7. Baby Anthropometry - All Patients

7.1.1.3 Baby Head Circumference and Skinfold Triceps at Visit 8 (Delivery)*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Baby Head Circumfe (cm)-V8	Mean	34.71	34.78	34.74
	Median	35.00	35.00	35.00
	SD	4.20	3.55	3.89
	MIN,MAX	0.0,41.5	0.0,53.0	0.0,53.0
	Q1,Q3	34.0,36.0	34.0,36.0	34.0,36.0
	n	164	153	317
	Nmiss	59	73	132
Baby Skinfold Triceps (mm)-V8	Mean	14.34	16.42	15.32
	Median	7.00	6.50	6.75
	SD	20.63	27.87	24.28
	MIN,MAX	0.0,90.0	0.0,162.0	0.0,162.0
	Q1,Q3	5.0,9.5	5.0,10.0	5.0,9.5
	n	111	99	210
	Nmiss	112	127	239

Section 7. Baby Anthropometry - All Patients

7.1.1.4 Baby Skinfold Subscapular and fat at Visit 8 (Delivery)#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Baby Skinfold Subscapular (mm)- V8	Mean	13.46	15.69	14.49
	Median	6.00	6.15	6.00
	SD	20.44	27.96	24.19
	MIN,MAX	0.0,100.0	0.0,158.0	0.0,158.0
	Q1,Q3	5.0,9.5	5.0,9.0	5.0,9.5
	n	113	98	211
	Nmiss	110	128	238
BABY_FAT* (%)-V8	Mean	12.08	12.86	12.46
	Median	10.95	12.30	12.30
	SD	5.74	4.47	5.11
	MIN,MAX	1.0,24.3	5.7,20.6	1.0,24.3
	Q1,Q3	8.1,17.1	10.0,16.2	8.1,16.5
	n	22	21	43
	Nmiss	201	205	406

Section 7. Baby Anthropometry - All Patients

7.1.1.5 Baby Fat Mass and Body mass at Visit 8 (Delivery)#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
BABY_FatMass* (kg)-V8	Mean	0.43259	0.44833	0.44028
	Median	0.39545	0.44260	0.43290
	SD	0.24801	0.19505	0.22121
	MIN,MAX	0.0247,0.9767	0.1421,0.7902	0.0247,0.9767
	Q1,Q3	0.2703,0.6053	0.2933,0.5896	0.2703,0.6053
	n	22	21	43
	Nmiss	201	205	406
BABY_BodyMass* (kg)-V8	Mean	3.39626	3.37760	3.38715
	Median	3.38680	3.42610	3.41780
	SD	0.50097	0.41133	0.45403
	MIN,MAX	2.4244,4.4472	2.5026,3.9902	2.4244,4.4472
	Q1,Q3	3.0944,3.6853	3.1039,3.7412	3.0944,3.7141
	n	22	21	43
	Nmiss	201	205	406

Section 7. Baby Anthropometry - All Patients

7.1.2.1 Baby Age and Weight at Visit 9 (Final 3 months postnatal)*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Neonatal Age (days)-V9	Mean	99.59	97.72	98.65
	Median	96.00	94.00	95.00
	SD	13.12	14.01	13.58
	MIN,MAX	59.0,143.0	53.0,172.0	53.0,172.0
	Q1,Q3	92.0,105.5	91.0,103.0	91.0,104.0
	n	128	129	257
	Nmiss	95	97	192
Baby Weight (g)-V9	Mean	6085.04	5971.97	6027.64
	Median	6205.50	6075.00	6156.60
	SD	1276.59	1724.20	1518.54
	MIN,MAX	666.0,8883.0	90.2,12500	90.2,12500
	Q1,Q3	5598.0,6845.0	5556.4,6735.0	5580.0,6795.0
	n	128	132	260
	Nmiss	95	94	189

Section 7. Baby Anthropometry - All Patients

7.1.2.2 Baby Length and Ponderal Index at Visit 9 (Final 3 months postnatal)#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Baby Length (cm)-V9	Mean	66.47	61.69	64.08
	Median	62.00	62.00	62.00
	SD	48.75	6.33	34.77
	MIN,MAX	41.0,605.0	5.7,74.0	5.7,605.0
	Q1,Q3	60.0,64.5	60.0,64.0	60.0,64.3
	n	125	125	250
	Nmiss	98	101	199
Baby ponderal index* -V9	Mean	2.58	28.76	15.72
	Median	2.53	2.54	2.54
	SD	0.82	293.42	207.90
	MIN,MAX	0.0,8.9	0.0,3283.1	0.0,3283.1
	Q1,Q3	2.4,2.8	2.3,2.8	2.3,2.8
	n	124	125	249
	Nmiss	99	101	200

Section 7. Baby Anthropometry - All Patients

7.1.2.3 Baby Head Circumference and Skinfold Triceps at Visit 9 (Final 3 months postnatal)*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Baby Head Circumfe (cm)-V9	Mean	41.30	41.02	41.16
	Median	41.00	41.00	41.00
	SD	2.87	4.42	3.72
	MIN,MAX	34.8,62.0	4.0,62.0	4.0,62.0
	Q1,Q3	40.0,42.6	39.8,42.5	40.0,42.5
	n	124	122	246
	Nmiss	99	104	203
BabySkinfoldTriceps (mm)-V9	Mean	22.05	24.61	23.32
	Median	10.40	11.00	11.00
	SD	33.17	34.59	33.82
	MIN,MAX	0.7,160.2	0.8,170.2	0.7,170.2
	Q1,Q3	8.0,15.0	9.0,15.0	9.0,15.0
	n	106	104	210
	Nmiss	117	122	239

Section 7. Baby Anthropometry - All Patients

7.1.2.4 Baby Skinfold Subscapular and fat at Visit 9 (Final 3 months postnatal)#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
BabySkinfoldSubscapular (mm)-V9	Mean	17.00	23.11	20.05
	Median	8.65	10.00	9.00
	SD	23.95	31.33	27.99
	MIN,MAX	0.5,106.0	0.7,162.0	0.5,162.0
	Q1,Q3	7.0,11.0	7.4,14.9	7.0,13.0
	n	104	104	208
	Nmiss	119	122	241
BABY_FAT* (%) -V9	Mean	25.88	23.19	24.58
	Median	24.10	23.50	23.55
	SD	6.13	5.91	6.13
	MIN,MAX	15.1,41.6	12.0,32.3	12.0,41.6
	Q1,Q3	21.5,29.7	19.6,27.8	21.2,28.8
	n	31	29	60
	Nmiss	192	197	389

Section 7. Baby Anthropometry - All Patients

7.1.2.5 Baby Fat Mass and Body mass at Visit 9 (Final 3 months postnatal)#

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
BABY_FatMass* (kg)-V9	Mean	3.00671	1.41993	2.23977
	Median	1.53930	1.42560	1.49110
	SD	8.04716	0.50009	5.80390
	MIN,MAX	0.8625,46.309	0.5693,2.4550	0.5693,46.309
	Q1,Q3	1.1952,1.9387	1.0391,1.7338	1.1552,1.8330
	n	31	29	60
	Nmiss	192	197	389
BABY_BodyMass* (kg)-V9	Mean	9.68262	6.01111	7.91017
	Median	6.22815	6.10320	6.16140
	SD	19.4087	0.92006	13.9814
	MIN,MAX	4.8014,112.37	4.4105,8.0110	4.4105,112.37
	Q1,Q3	5.6061,6.5379	5.2742,6.5058	5.4949,6.5379
	n	30	28	58
	Nmiss	193	198	391

Section 7. Baby Anthropometry - Only Alive Births

7.2.1.1 Baby Age and Weight at Visit 8 (Delivery)#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Neonatal Age (days)-V8	Mean	1.04	0.97	1.00
	Median	1.00	0.00	0.00
	SD	2.44	2.44	2.44
	MIN,MAX	0.0,26.0	0.0,23.0	0.0,26.0
	Q1,Q3	0.0,1.0	0.0,1.0	0.0,1.0
	n	157	145	302
	Nmiss	63	69	132
Baby Weight* (g)-V8	Mean	3707.76	3455.18	3588.80
	Median	3515.00	3437.50	3460.00
	SD	2685.66	545.08	1990.02
	MIN,MAX	1490.0,37141	2110.0,4900.0	1490.0,37141
	Q1,Q3	3115.0,3865.0	3080.0,3820.0	3090.0,3860.0
	n	164	146	310
	Nmiss	56	68	124

Section 7. Baby Anthropometry - Only Alive Births

7.2.1.2.1 Baby Length and Ponderal Index at Visit 8 (Delivery)#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Baby Length (cm)-V8	Mean	50.23	49.66	49.95
	Median	51.50	50.00	51.00
	SD	8.16	8.00	8.07
	MIN,MAX	0.0,63.5	0.0,61.0	0.0,63.5
	Q1,Q3	49.5,53.0	48.0,53.0	49.0,53.0
	n	153	142	295
	Nmiss	67	72	139
Baby ponderal index* -V8	Mean	3.01	2.67	2.85
	Median	2.54	2.61	2.57
	SD	3.68	0.50	2.69
	MIN,MAX	1.7,40.6	1.5,5.0	1.5,40.6
	Q1,Q3	2.3,2.8	2.4,2.9	2.3,2.9
	n	145	130	275
	Nmiss	75	84	159

Section 7. Baby Anthropometry - Only Alive Births

7.2.1.2.2 Ponderal index #,\$ - Statistical Analysis - POST-HOC

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
baby_ponderal_alive_log - itt	0.954	0.0241	143	0.986	0.0244	130	0.031	-0.004	0.066	3.007	0.0841

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 00:26

By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in table 7.2.1.2.1 of this report

Outcome analysed using a linear regression model, adjusted by BMI band and centre. Significance level set at p<0.05. Estimated mean represents the mean of the log transformed variable by allocated treatment, Parameter shown normal or near-normal behavior

SE represents standard error of the estimated log transformed mean and N represents number of observations

*Represents the difference between the estimated log means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_7_2_2_Baby_Ponderal_delivery.lst'

#Ponderal index was calculated using the following formula: $(100 * (\text{baby_weight_in_g})) / ((\text{baby_length_in_cm})^3)$,

\$Data have been checked, inaccuracies happened at time and point of recording and there are not other sources

for further checks, outliers outside +/- 6SD were removed to exclude extreme errors in data entry

Section 7. Baby Anthropometry - Only Alive Births

7.2.1.3 Baby Head Circumference and Skinfold Triceps at Visit 8 (Delivery)*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Baby Head Circumfe (cm)-V8	Mean	34.71	34.80	34.75
	Median	35.00	35.00	35.00
	SD	4.20	3.55	3.90
	MIN,MAX	0.0,41.5	0.0,53.0	0.0,53.0
	Q1,Q3	34.0,36.0	34.0,36.0	34.0,36.0
	n	164	152	316
	Nmiss	56	62	118
Baby Skinfold Triceps (mm)-V8	Mean	14.34	16.42	15.32
	Median	7.00	6.50	6.75
	SD	20.63	27.87	24.28
	MIN,MAX	0.0,90.0	0.0,162.0	0.0,162.0
	Q1,Q3	5.0,9.5	5.0,10.0	5.0,9.5
	n	111	99	210
	Nmiss	109	115	224

Section 7. Baby Anthropometry - Only Alive Births

7.2.1.4 Baby Skinfold Subscapular and fat at Visit 8 (Delivery)#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Baby Skinfold Subscapular (mm)- V8	Mean	13.46	15.69	14.49
	Median	6.00	6.15	6.00
	SD	20.44	27.96	24.19
	MIN,MAX	0.0,100.0	0.0,158.0	0.0,158.0
	Q1,Q3	5.0,9.5	5.0,9.0	5.0,9.5
	n	113	98	211
	Nmiss	107	116	223
BABY_FAT* (%)-V8	Mean	12.08	12.86	12.46
	Median	10.95	12.30	12.30
	SD	5.74	4.47	5.11
	MIN,MAX	1.0,24.3	5.7,20.6	1.0,24.3
	Q1,Q3	8.1,17.1	10.0,16.2	8.1,16.5
	n	22	21	43
	Nmiss	198	193	391

Section 7. Baby Anthropometry - Only Alive Births

7.2.1.5 Baby Fat Mass and Body mass at Visit 8 (Delivery)#

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
BABY_FatMass* (kg)-V8	Mean	0.43259	0.44833	0.44028
	Median	0.39545	0.44260	0.43290
	SD	0.24801	0.19505	0.22121
	MIN,MAX	0.0247,0.9767	0.1421,0.7902	0.0247,0.9767
	Q1,Q3	0.2703,0.6053	0.2933,0.5896	0.2703,0.6053
	n	22	21	43
	Nmiss	198	193	391
BABY_BodyMass* (kg)-V8	Mean	3.39626	3.37760	3.38715
	Median	3.38680	3.42610	3.41780
	SD	0.50097	0.41133	0.45403
	MIN,MAX	2.4244,4.4472	2.5026,3.9902	2.4244,4.4472
	Q1,Q3	3.0944,3.6853	3.1039,3.7412	3.0944,3.7141
	n	22	21	43
	Nmiss	198	193	391

Section 7. Baby Anthropometry - Only Alive Births

7.2.2.1 Baby Age and Weight at Visit 9 (Final 3 months postnatal)*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Neonatal Age (days)-V9	Mean	99.59	97.72	98.65
	Median	96.00	94.00	95.00
	SD	13.12	14.01	13.58
	MIN,MAX	59.0,143.0	53.0,172.0	53.0,172.0
	Q1,Q3	92.0,105.5	91.0,103.0	91.0,104.0
	n	128	129	257
	Nmiss	92	85	177
Baby Weight (g)-V9	Mean	6085.04	5971.97	6027.64
	Median	6205.50	6075.00	6156.60
	SD	1276.59	1724.20	1518.54
	MIN,MAX	666.0,8883.0	90.2,12500	90.2,12500
	Q1,Q3	5598.0,6845.0	5556.4,6735.0	5580.0,6795.0
	n	128	132	260
	Nmiss	87	77	164

Section 7. Baby Anthropometry - Only Alive Births

7.2.2.2 Baby Length and Ponderal Index at Visit 9 (Final 3 months postnatal)#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Baby Length (cm)-V9	Mean	66.47	61.69	64.08
	Median	62.00	62.00	62.00
	SD	48.75	6.33	34.77
	MIN,MAX	41.0,605.0	5.7,74.0	5.7,605.0
	Q1,Q3	60.0,64.5	60.0,64.0	60.0,64.3
	n	125	125	250
	Nmiss	90	84	174
Baby ponderal index* -V9	Mean	2.58	28.76	15.72
	Median	2.53	2.54	2.54
	SD	0.82	293.42	207.90
	MIN,MAX	0.0,8.9	0.0,3283.1	0.0,3283.1
	Q1,Q3	2.4,2.8	2.3,2.8	2.3,2.8
	n	124	125	249
	Nmiss	91	84	175

Section 7. Baby Anthropometry - Only Alive Births

7.2.2.3 Baby Head Circumference and Skinfold Triceps at Visit 9 (Final 3 months postnatal)*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Baby Head Circumfe (cm)-V9	Mean	41.30	41.02	41.16
	Median	41.00	41.00	41.00
	SD	2.87	4.42	3.72
	MIN,MAX	34.8,62.0	4.0,62.0	4.0,62.0
	Q1,Q3	40.0,42.6	39.8,42.5	40.0,42.5
	n	124	122	246
	Nmiss	91	87	178
BabySkinfoldTriceps (mm)-V9	Mean	22.05	24.61	23.32
	Median	10.40	11.00	11.00
	SD	33.17	34.59	33.82
	MIN,MAX	0.7,160.2	0.8,170.2	0.7,170.2
	Q1,Q3	8.0,15.0	9.0,15.0	9.0,15.0
	n	106	104	210
	Nmiss	109	105	214

Section 7. Baby Anthropometry - Only Alive Births

7.2.2.4 Baby Skinfold Subscapular and fat at Visit 9 (Final 3 months postnatal)#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
BabySkinfoldSubscapular (mm)-V9	Mean	17.00	23.11	20.05
	Median	8.65	10.00	9.00
	SD	23.95	31.33	27.99
	MIN,MAX	0.5,106.0	0.7,162.0	0.5,162.0
	Q1,Q3	7.0,11.0	7.4,14.9	7.0,13.0
	n	104	104	208
	Nmiss	111	105	216
BABY_FAT* (%) -V9	Mean	25.88	23.19	24.58
	Median	24.10	23.50	23.55
	SD	6.13	5.91	6.13
	MIN,MAX	15.1,41.6	12.0,32.3	12.0,41.6
	Q1,Q3	21.5,29.7	19.6,27.8	21.2,28.8
	n	31	29	60
	Nmiss	184	180	364

Section 7. Baby Anthropometry - Only Alive Births

7.2.2.5 Baby Fat Mass and Body mass at Visit 9 (Final 3 months postnatal)#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
BABY_FatMass* (kg)-V9	Mean	3.00671	1.41993	2.23977
	Median	1.53930	1.42560	1.49110
	SD	8.04716	0.50009	5.80390
	MIN,MAX	0.8625,46.309	0.5693,2.4550	0.5693,46.309
	Q1,Q3	1.1952,1.9387	1.0391,1.7338	1.1552,1.8330
	n	31	29	60
	Nmiss	184	180	364
BABY_BodyMass* (kg)-V9	Mean	9.68262	6.01111	7.91017
	Median	6.22815	6.10320	6.16140
	SD	19.4087	0.92006	13.9814
	MIN,MAX	4.8014,112.37	4.4105,8.0110	4.4105,112.37
	Q1,Q3	5.6061,6.5379	5.2742,6.5058	5.4949,6.5379
	n	30	28	58
	Nmiss	185	181	366

Section 7. Baby Anthropometry - Only Alive Births

7.2.3 Baby Ponderal Index at Visit 8 (Delivery) and Visit 9 (Final 3 months postnatal) #

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Baby ponderal index* -V8	Mean	2.60	2.67	2.63
	Median	2.53	2.61	2.56
	SD	0.41	0.50	0.46
	MIN,MAX	1.7,3.9	1.5,5.0	1.5,5.0
	Q1,Q3	2.3,2.8	2.4,2.9	2.3,2.9
	n	143	130	273
	Nmiss	77	84	161
Baby ponderal index* -V9	Mean	2.58	2.52	2.55
	Median	2.53	2.54	2.53
	SD	0.82	1.00	0.92
	MIN,MAX	0.0,8.9	0.0,9.8	0.0,9.8
	Q1,Q3	2.4,2.8	2.3,2.8	2.3,2.8
	n	124	124	248
	Nmiss	91	85	176

Section 7. Baby Anthropometry - Only Alive Births

7.2.4 Baby Weight at Visit 8 (Delivery) and Visit 9 (Final 3 months postnatal)#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Baby Weight* (g)-V8	Mean	3502.65	3455.18	3480.22
	Median	3510.00	3437.50	3460.00
	SD	561.32	545.08	553.32
	MIN,MAX	1490.0,5060.0	2110.0,4900.0	1490.0,5060.0
	Q1,Q3	3110.0,3860.0	3080.0,3820.0	3090.0,3850.0
	n	163	146	309
	Nmiss	57	68	125
Baby Weight (g)-V9	Mean	6085.04	5971.97	6027.64
	Median	6205.50	6075.00	6156.60
	SD	1276.59	1724.20	1518.54
	MIN,MAX	666.0,8883.0	90.2,12500	90.2,12500
	Q1,Q3	5598.0,6845.0	5556.4,6735.0	5580.0,6795.0
	n	128	132	260
	Nmiss	87	77	164

Section 7. Baby Anthropometry - Only Alive Births

7.2.5 Baby Length at Visit 8 (Delivery) and Visit 9 (Final 3 months postnatal)*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Baby Length (cm)-V8	Mean	51.24	50.73	50.99
	Median	51.90	50.50	51.00
	SD	4.01	3.26	3.67
	MIN,MAX	20.5,63.5	43.0,61.0	20.5,63.5
	Q1,Q3	49.5,53.0	48.0,53.0	49.0,53.0
	n	150	139	289
	Nmiss	70	75	145
Baby Length (cm)-V9	Mean	62.13	61.69	61.91
	Median	62.00	62.00	62.00
	SD	4.38	6.33	5.44
	MIN,MAX	41.0,73.0	5.7,74.0	5.7,74.0
	Q1,Q3	60.0,64.4	60.0,64.0	60.0,64.2
	n	124	125	249
	Nmiss	91	84	175

Section 8. Maternal inflammatory and metabolic variables (Secondary Outcome)

8.1 CRP - Visit 3 Randomisation (10-16 Weeks) and Visit 5 (28 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
CRP - V3 (mg/L)	Mean	11.11	10.70	10.90
	Median	9.00	9.00	9.00
	SD	7.39	6.85	7.12
	MIN,MAX	1.0,49.0	0.0,45.0	0.0,49.0
	Q1,Q3	6.0,15.0	5.0,14.0	5.5,15.0
	n	221	223	444
	Nmiss	2	3	5
CRP - V5 (mg/L)	Mean	10.65	9.78	10.23
	Median	9.00	8.00	8.00
	SD	7.41	6.54	7.01
	MIN,MAX	1.0,43.0	1.0,41.0	1.0,43.0
	Q1,Q3	5.0,14.0	5.0,13.0	5.0,13.1
	n	176	164	340
	Nmiss	47	62	109

Section 8. Maternal inflammatory and metabolic variables (Secondary Outcome)

8.1 CRP - Visit 6 (36 Weeks) (Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
CRP - V6 (mg/L)	Mean	9.20	7.47	8.36
	Median	7.00	6.00	6.30
	SD	7.10	4.62	6.08
	MIN,MAX	1.0,51.3	1.0,29.0	1.0,51.3
	Q1,Q3	5.0,12.0	4.3,10.0	5.0,11.0
	n	150	140	290
	Nmiss	73	86	159

Section 8. Maternal inflammatory and metabolic variables (Secondary Outcome)

8.2.1 Total Cholesterol - Visit 3 Randomisation (10-16 Weeks) and Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Total Cholesterol - V3 (mmol/L)	Mean	4.87	4.88	4.87
	Median	5.00	4.90	4.95
	SD	1.15	1.09	1.12
	MIN,MAX	2.0,8.3	1.8,8.2	1.8,8.3
	Q1,Q3	4.2,5.7	4.1,5.5	4.1,5.6
	n	216	214	430
	Nmiss	7	12	19
Total Cholesterol - V6 (mmol/L)	Mean	6.32	6.33	6.32
	Median	6.40	6.40	6.40
	SD	1.44	1.74	1.59
	MIN,MAX	2.5,10.5	2.6,12.7	2.5,12.7
	Q1,Q3	5.5,7.3	5.5,7.3	5.5,7.3
	n	144	139	283
	Nmiss	79	87	166

Section 8. Maternal inflammatory and metabolic variables (Secondary Outcome)

8.2.2 HDL - Visit 3 Randomisation (10-16 Weeks) and Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
HDL - V3 (mmol/L)	Mean	1.67	1.64	1.66
	Median	1.60	1.60	1.60
	SD	0.39	0.38	0.38
	MIN,MAX	0.9,3.6	0.0,3.2	0.0,3.6
	Q1,Q3	1.4,1.9	1.4,1.9	1.4,1.9
	n	215	214	429
	Nmiss	8	12	20
HDL - V6 (mmol/L)	Mean	1.70	1.76	1.73
	Median	1.70	1.71	1.70
	SD	0.38	0.43	0.41
	MIN,MAX	0.0,2.9	0.8,3.7	0.0,3.7
	Q1,Q3	1.4,1.9	1.5,2.0	1.4,2.0
	n	145	138	283
	Nmiss	78	88	166

Section 8. Maternal inflammatory and metabolic variables (Secondary Outcome)

8.2.3 LDL - Visit 3 Randomisation (10-16 Weeks) and Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
LDL - V3 (mmol/L)	Mean	2.91	2.89	2.90
	Median	2.84	2.81	2.81
	SD	0.78	0.86	0.82
	MIN,MAX	1.1,5.1	0.0,6.0	0.0,6.0
	Q1,Q3	2.3,3.5	2.3,3.4	2.3,3.4
	n	194	191	385
	Nmiss	29	35	64
LDL - V6 (mmol/L)	Mean	3.57	3.77	3.67
	Median	3.50	3.60	3.60
	SD	1.13	1.25	1.19
	MIN,MAX	0.0,6.8	1.8,9.2	0.0,9.2
	Q1,Q3	2.8,4.3	2.9,4.4	2.8,4.4
	n	126	118	244
	Nmiss	97	108	205

Section 8. Maternal inflammatory and metabolic variables (Secondary Outcome)

8.2.4 Triglycerides - Visit 3 Randomisation (10-16 Weeks) and Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Triglycerides - V3 (mmol/L)	Mean	1.51	1.43	1.47
	Median	1.40	1.30	1.40
	SD	0.53	0.56	0.55
	MIN,MAX	0.5,4.0	0.5,3.7	0.5,4.0
	Q1,Q3	1.1,1.8	1.0,1.6	1.1,1.8
	n	216	214	430
	Nmiss	7	12	19
Triglycerides - V6 (mmol/L)	Mean	2.79	2.76	2.77
	Median	2.70	2.69	2.70
	SD	0.84	0.88	0.86
	MIN,MAX	0.9,5.8	1.3,6.7	0.9,6.7
	Q1,Q3	2.1,3.3	2.1,3.2	2.1,3.2
	n	146	140	286
	Nmiss	77	86	163

Section 8. Maternal inflammatory and metabolic variables (Secondary Outcome)

8.3 CRP, Cholesterol, HDL, LDL and Triglycerides - Visit 6 (36 Weeks) - Statistical Analysis - POST-HOC

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
CRP_log_Visit6 - itt	2.023	0.0931	150	1.872	0.0879	140	-0.151	-0.297	-0.005	4.118	0.0434
Cholesterol_log_Visit6 - itt	1.780	0.0321	144	1.784	0.0302	139	0.004	-0.047	0.055	0.025	0.8751
HDL_Visit6# - itt	1.770	0.0576	145	1.821	0.0544	138	0.051	-0.040	0.142	1.206	0.2730
LDL_log_Visit6\$ - itt	1.160	0.0548	125	1.221	0.0508	118	0.062	-0.018	0.141	2.346	0.1270
Triglycerides_log_Visit6 - itt	0.968	0.0439	146	0.960	0.0413	140	-0.007	-0.077	0.062	0.045	0.8327

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 00:26

By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in tables 8.1 to 8.2 of this report

Outcome analysed using a linear regression model, adjusted by BMI band and centre. Significance level set at p<0.05

Estimated mean represents the adjusted mean of the non-transformed or log transformed variable by allocated treatment,

SE represents standard error of the estimated means or log transformed means and N represents number of observations

*Represents the difference between the estimated means or log transformed means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_5_4_other_labs_analysis_v6.lst'

#NOTE:HDL was not log transformed for the analysis

\$NOTE:LDL has a value of 0 for patient 16052, this values was set to missing in the log transformation of the parameter

All parameters shown normal or near-normal behavior

Section 9. Neonatal cord blood and placenta (Secondary Outcome)

9.1 Glucose and Insuling in the umbilical cord - Visit 8 (Delivery)

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Glucose Cord - V8 (mmol/L)	Mean	3.89	4.06	3.97
	Median	3.70	3.80	3.80
	SD	1.24	1.08	1.16
	MIN,MAX	1.4,7.6	1.6,7.0	1.4,7.6
	Q1,Q3	3.0,4.6	3.2,4.9	3.1,4.8
	n	79	74	153
	Nmiss	144	152	296
Insulin Cord - V8 (mIU/ml)	Mean	10.95	11.41	11.20
	Median	9.89	9.26	9.45
	SD	7.49	8.80	8.20
	MIN,MAX	2.0,32.7	2.0,42.9	2.0,42.9
	Q1,Q3	5.6,14.4	5.2,16.3	5.3,15.2
	n	47	57	104
	Nmiss	176	169	345

Section 9. Neonatal cord blood and placenta (Secondary Outcome)

9.2 HOMA-IR AND CRP in the umbilical cord - Visit 8 (Delivery)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
HOMA-IR Cord - V8 (mIU/ml)	Mean	1.92	1.91	1.91
	Median	1.81	1.48	1.59
	SD	1.39	2.00	1.72
	MIN,MAX	0.3,6.7	0.2,12.0	0.2,12.0
	Q1,Q3	0.9,2.3	0.7,2.6	0.7,2.5
	n	38	41	79
	Nmiss	185	185	370
CRP - V8 (mmol/L)	Mean	4.32	2.36	3.37
	Median	1.00	1.00	1.00
	SD	19.55	2.29	14.13
	MIN,MAX	0.1,173.8	0.2,11.0	0.1,173.8
	Q1,Q3	1.0,5.0	1.0,5.0	1.0,5.0
	n	78	73	151
	Nmiss	145	153	298

Section 9. Neonatal cord blood and placenta (Secondary Outcome)

9.3 Glucose, Insuling and HOMA-IR in the umbilical cord - Visit 8 (Delivery) - Statistical Analysis - POST-HOC

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
Glucose_cord_log_Visit_8* - itt	1.243	0.0550	79	1.308	0.0513	74	0.065	-0.027	0.157	1.961	0.1637
Insulin_cord_log_Visit_8* - itt	1.992	0.1884	47	2.050	0.1654	57	0.058	-0.265	0.381	0.127	0.7220
HOMA_cord_log_Visit_8* - itt	0.141	0.2009	38	0.154	0.1756	41	0.012	-0.355	0.380	0.004	0.9473

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 00:26

By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in tables 9.1 to 9.2 of this report

Outcome analysed using a linear regression model, adjusted by BMI band and centre. Significance level set at p<0.05

Estimated mean represents the adjusted means of the log transformed variable by allocated treatment,

SE represents standard error of the estimated log transformed means and N represents number of observations

*Represents the difference between the estimated log transformed means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_9_1_Neonatal_cord_blood.lst'

All parameters shown normal or near-normal behavior

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Section 9. Neonatal cord blood and placenta (Secondary Outcome)

9.4 CRP in the umbilical cord - Visit 8 (Delivery)* - Statistical Analysis - POST-HOC

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>P-value Wilcoxon Test (Two-sided)</i>	<i>P-value Wilcoxon t Approx (Two-sided)</i>	<i>P-value Kruskal-Wallis Test</i>
CRP_CORD_VISIT_8_itt	Non_parametric_test_metformin_vs_placebo*	0.7411	0.7416	0.7411

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 00:26

By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in table 9.2 of this report

*This variable was non-normal and the lack of normality could not be corrected. Therefore Non-parametric testing results are presented. Significance level set at $p < 0.05$

Calculations and detailed analysis are presented in study file 'Empowar_9_1_Neonatal_cord_blood.lst'

Section 10. Adverse Outcome

10.1.1 Maternal Complications - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Any SAE (n)#	Missing	1	4	5
	Yes	45 (20.3)	45 (20.3)	90 (20.3)
	No	177 (79.7)	177 (79.7)	354 (79.7)
Any Hypertension (n)	Missing	1	5	6
	Yes	14 (6.3)	21 (9.5)	35 (7.9)
	No	208 (93.7)	200 (90.5)	408 (92.1)
Any Preeclampsia (n)	Missing	1	5	6
	Yes	3 (1.4)	7 (3.2)	10 (2.3)
	No	219 (98.6)	214 (96.8)	433 (97.7)
Any Eclampsia (n)	Missing	1	5	6
	Yes	1 (0.5)	1 (0.5)	2 (0.5)
	No	221 (99.5)	220 (99.5)	441 (99.5)
Any Membrane Rupture (n)	Missing	1	5	6
	Yes	6 (2.7)	5 (2.3)	11 (2.5)
	No	216 (97.3)	216 (97.7)	432 (97.5)

Section 10. Adverse Outcome

10.1.1 Maternal Complications - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery) (Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Any Preterm Labour (n)#	Missing	1	5	6
	Yes	6 (2.7)	13 (5.9)	19 (4.3)
	No	216 (97.3)	208 (94.1)	424 (95.7)
Any Haemorrhage (n)	Missing	1	5	6
	Yes	12 (5.4)	8 (3.6)	20 (4.5)
	No	210 (94.6)	213 (96.4)	423 (95.5)
Any DVT (n)	Missing	1	5	6
	Yes	3 (1.4)	2 (0.9)	5 (1.1)
	No	219 (98.6)	219 (99.1)	438 (98.9)
Any Gestational Diabetes (n)	Missing	1	5	6
	Yes	29 (13.1)	22 (10.0)	51 (11.5)
	No	193 (86.9)	199 (90.0)	392 (88.5)

Section 10. Adverse Outcome

10.1.1 Maternal Complications - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery) (Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Any Other Mother Complication (n)	Missing	1	4	5
	Yes	62 (27.9)	65 (29.3)	127 (28.6)
	No	160 (72.1)	157 (70.7)	317 (71.4)
Any Other Mother Complication cat* (n)	Missing	0	1	1
	Infection	20	15	35
	Mood disturbance	4	6	10
	Musculoskeletal	12	16	28
	PV bleed <24 weeks gestation	5	5	10
	Obstetric cholestasis	9	5	14
	Miscellaneous	22	23	45
	Data captured elsewhere	43	38	81

Section 10. Adverse Outcome

10.1.2 Maternal Complications Details - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Other Maternal Complications (Y/N)	TimepointID	Other Maternal Complications Details
11136	METFORMIN	Yes	VISIT 8 (DELIVERY)	placental abruption
11315	METFORMIN	Yes	VISIT 8 (DELIVERY)	3rd degree tear
11317	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	cerebral venous sinus thrombosis
11317	METFORMIN	Yes	VISIT 8 (DELIVERY)	cerebral sinus thrombosis
11325	METFORMIN	Yes	VISIT 5 (28 WEEKS)	antenatal depression
11501	METFORMIN	Yes	VISIT 6 (36 WEEKS)	hospital admission with RUQ pain and deranged LFT, resolved spontaneously
11551	METFORMIN	Yes	VISIT 5 (28 WEEKS)	exacerbation of asthma requiring oral steroids
11657	METFORMIN	Yes	VISIT 5 (28 WEEKS)	UTI early pregnancy. Also just completed antibiotics and steroids for chest infection
11657	METFORMIN	Yes	VISIT 8 (DELIVERY)	Increased liquor volume
11686	METFORMIN	Yes	VISIT 8 (DELIVERY)	Breast cancer
11716	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Mild SPD
11748	METFORMIN	Yes	VISIT 6 (36 WEEKS)	UTI
11748	METFORMIN	Yes	VISIT 7 (TERM)	Sepsis secondary to mastitis
11748	METFORMIN	Yes	VISIT 8 (DELIVERY)	UTI SAE forms previously sent
11797	METFORMIN	Yes	VISIT 6 (36 WEEKS)	excessive vomiting in late pregnancy
11842	METFORMIN	Yes	VISIT 8 (DELIVERY)	Raised ALT
11881	METFORMIN	Yes	VISIT 8 (DELIVERY)	severe urosepsis
11916	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	contacted Lucy who reported she has been in hospital with kidney infection and was on abx. No note in electronic medical record.
12001	METFORMIN	Yes	VISIT 7 (TERM)	Swelling of hands and feet
12001	METFORMIN	Yes	VISIT 8 (DELIVERY)	oedema
12008	METFORMIN	Yes	VISIT 8 (DELIVERY)	Post Partum haemorrhage, 2000ml
12018	METFORMIN	Yes	VISIT 8 (DELIVERY)	EBL 600 mls
12099	METFORMIN	Yes	VISIT 8 (DELIVERY)	3rd degree tear,
13016	METFORMIN	Yes	VISIT 7 (TERM)	Seen in assessment room last week with headache and visual disturbances. Migrane diagnosed. Discharged home with paracetamol and codine.
13047	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	After a week of medication, reports severe vomiting and diarrhoea, lasting a week. Has been off work for a week, doesn't wish to recommence drugs.
13047	METFORMIN	Yes	VISIT 8 (DELIVERY)	IOL FOR FACTOR 5 LEIDENS
13082	METFORMIN	Yes	VISIT 8 (DELIVERY)	PYREXIA IN LABOUR
13111	METFORMIN	Yes	VISIT 8 (DELIVERY)	IOL FOR CHOLESTASIS ALSO HAD GESTATIONAL DIABETES, COMMENCED ON METFORMIN BY DIABETES TEAM AT 30WEEKS. TOOK METFORMIN 1,000MG BD UNTILL DELIVERY. ALSO COMMENCED ON INSULIN FROM 31WKS.
13147	METFORMIN	Yes	VISIT 6 (36 WEEKS)	cervical bleeds frequently throughout pregnancy. no admissions.
13209	METFORMIN	Yes	VISIT 6 (36 WEEKS)	HAD VIRAL INFECTION 2 WEEKS AGO LASTING A FORTNIGHT. RESULTED IN PRODUCTIVE COUGH, FOLLOWED MODERATE VOMITTING AND DIARRHOEA.
13248	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	ADMITTED TO WARD VIA EMERGENCY ROOM FOR ABDO PAIN, DISCHARGED AFTER 2DAYS, DIAGNOSIS - IBS.
13305	METFORMIN	Yes	VISIT 6 (36 WEEKS)	SPD PAIN. ON COCODAMOL.
13378	METFORMIN	Yes	VISIT 5 (28 WEEKS)	UTI CAUSED SEVERE HEADACHES. CLEARED AFTER COURSE OF ANTIBIOTICS.
13378	METFORMIN	Yes	VISIT 8 (DELIVERY)	Fatty deposits noted on placenta, samples taken for histology by delivery midwife, but enable to process as incorrectly sampled and stored
13493	METFORMIN	Yes	VISIT 5 (28 WEEKS)	Attended A+E for feeling dizzy, palpitations, breathless and tight chest. Reports ECG and all investigations found to be normal. No treatment or follow up required. Discussed with Dr Weeks and advised doesn't meet criteria of SAE, hospitalisation was for <12 hours

Section 10. Adverse Outcome

10.1.2 Maternal Complications Details - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Other Maternal Complications (Y/N)	TimepointID	Other Maternal Complications Details
1351	METFORMIN	Yes	VISIT 8 (DELIVERY)	PPH of 500ml followed by total hysterectomy
13780	METFORMIN	Yes	VISIT 8 (DELIVERY)	UNDIAGNOSED LOW LYING PLACENTA AT CS. BLOOD LOSS 1400MLS. NEEDED BLOOD TRANSFUSION AFTER CS.
14035	METFORMIN	Yes	VISIT 6 (36 WEEKS)	ALT result from today 95IU/L.No symptoms of PET/HELLP or Obstetric Cholestasis
14035	METFORMIN	Yes	VISIT 8 (DELIVERY)	Induced due to upper right abdominal and increased LFT's ? cause
14039	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Has had x1 episode of PV bleeding and mild abdominal pain @ 30+4. Admitted overnight. no further PV Loss. Also had viral illness 1 week ago, no treatment.
14039	METFORMIN	Yes	VISIT 7 (TERM)	B/P Slightly elevated. One episode of PV spotting
14039	METFORMIN	Yes	VISIT 8 (DELIVERY)	Pregnancy Induced Hypertension
14161	METFORMIN	Yes	VISIT 8 (DELIVERY)	PPH 1500ml
14303	METFORMIN	Yes	VISIT 8 (DELIVERY)	PPH 1200mls
14305	METFORMIN	Yes	VISIT 5 (28 WEEKS)	Maternal UTI
14417	METFORMIN	Yes	VISIT 5 (28 WEEKS)	Feeling faint on occasions when working
15012	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	has had small pv bleed as history of cervical polyps all well
15027	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Itching All blood tests NAD
16029	METFORMIN	Yes	VISIT 6 (36 WEEKS)	abdo pain ?SPD (admission) plus triage assessment for reduced fetal movements
16029	METFORMIN	Yes	VISIT 7 (TERM)	Abdo pain admission on 03.09.2012 (SAE) plus Raised ALT on 3 occasions ?obstetric cholestatis asymptomatic
16029	METFORMIN	Yes	VISIT 8 (DELIVERY)	Abdo pain (SAE) plus raised ALT, IOL for Obstetric Cholestasis
16054	METFORMIN	Yes	VISIT 5 (28 WEEKS)	Abdo pain and pinkish pv loss
16121	METFORMIN	Yes	VISIT 6 (36 WEEKS)	pyelonephritis
17138	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Palpitations, seen in hospital assessment unit but discharged home without admission. Normal ECG and Normal CTG.
21015	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Attended Day Unit 4/5/13 33+4 with brown pv discharge post coital.
21015	METFORMIN	Yes	VISIT 7 (TERM)	Questions asked in retrospect once delivered as unable to contact.Unsure when stopped tablets.
21015	METFORMIN	Yes	VISIT 8 (DELIVERY)	PPH following birth.Hb 63g/l.Had 2 units of blood.Hb 83g/l post transfusion.Didnt cause prolonged hospitalisation.
21034	METFORMIN	Yes	VISIT 5 (28 WEEKS)	Indigestion since 22 weeks resolved with use of gaviscon
21034	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Acupuncture for back/hip pain. Broke coccyx 5 years ago
21037	METFORMIN	Yes	VISIT 5 (28 WEEKS)	Sweating
21037	METFORMIN	Yes	VISIT 7 (TERM)	Green vaginal discharge today High vaginal swab obtained.
21039	METFORMIN	Yes	VISIT 8 (DELIVERY)	Maternal tachycardia post delivery. IV fluids & antibiotics given. Ragged membranes.
21042	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Heartburn. Using gaviscon. Awaiting prescription of ranitidine
21042	METFORMIN	Yes	VISIT 5 (28 WEEKS)	07/09/2013 self referral to maty ward feeling dizzy. 21/09/2013 ?SROM HVS showed Group B Strep. On last day of Amoxicillin treatment today.Gestational diabetes today. Attending for glucometer tomorrow
21042	METFORMIN	Yes	VISIT 7 (TERM)	Group B Strep diagnosed in pregnancy.
21042	METFORMIN	Yes	VISIT 8 (DELIVERY)	Induction of labour for gestational diabetes. Group B Strep identified in pregnancy.
21064	METFORMIN	Yes	VISIT 5 (28 WEEKS)	UTI 21/10/13 cephalaxin tds for 5 days taken.
21064	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Right sided abdo pain on 2 occasions 15 & 22/11/13 been fine since.
21064	METFORMIN	Yes	VISIT 8 (DELIVERY)	SPD
21070	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Lower backache has appt with physio on 8/10/13

Section 10. Adverse Outcome

10.1.2 Maternal Complications Details - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Other Maternal Complications (Y/N)	TimepointID	Other Maternal Complications Details
21070	METFORMIN	Yes	VISIT 5 (28 WEEKS)	Symphysis Pubis Disfunction-physio input
21070	METFORMIN	Yes	VISIT 6 (36 WEEKS)	SPD
21070	METFORMIN	Yes	VISIT 8 (DELIVERY)	SPD-S/B Physio & had acupuncture.
21074	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Backache 16+ weeks saw GP & resolved a few days later
21074	METFORMIN	Yes	VISIT 5 (28 WEEKS)	Wort on finger.
21074	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Itching on legs, had same prior to pregnancy. Wort on finger.
21074	METFORMIN	Yes	VISIT 7 (TERM)	03/02/14 headache for 24 hours.Started on antibiotics as ?UTI. Normal MSSU so stopped taking. Only took 1 tablet.
21074	METFORMIN	Yes	VISIT 8 (DELIVERY)	26/2/14 perineal infection flucloxylin commenced orally at home.
21081	METFORMIN	Yes	VISIT 7 (TERM)	Taking fluoxetine for depression.
21081	METFORMIN	Yes	VISIT 8 (DELIVERY)	On fluoxetine.
21082	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	20/10/13 attended primary care/gynae feeling unwell ?food poisoning/palpitations normal investigations.Some low mood/depression.
21082	METFORMIN	Yes	VISIT 6 (36 WEEKS)	3/1/14 29+4 episode of raised BP settled. 30/1/14 33+3 antibiotics for UTI.
21082	METFORMIN	Yes	VISIT 7 (TERM)	Some hypertension-settled now.
21082	METFORMIN	Yes	VISIT 8 (DELIVERY)	Pyrexial in labour/maternal tachycardia. IV paracetamol required.
21089	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Several symptoms feels were associated with tablet use, therefore stopped taking. Last dose taken 25/10/13.
21089	METFORMIN	Yes	VISIT 7 (TERM)	Admission to maternity Ward with hyperemesis for over 12 hours.
21089	METFORMIN	Yes	VISIT 8 (DELIVERY)	Anaemic post delivery. Taking ferrous sulphate tablets.
21095	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Started citalopram for depression on 04/11/13.
21095	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Lower back discomfort sees physio.
21095	METFORMIN	Yes	VISIT 8 (DELIVERY)	On citalopram for depression
21099	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Tooth abscess so had to reduce tablets one day.
21099	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Elevated BP today for close monitoring. Occasionally takes Co-dydramol for backache. Physio/acupuncture unsuccessful.
21099	METFORMIN	Yes	VISIT 8 (DELIVERY)	Raised blood pressure
21111	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Small pv bleed 08/12/13 19+ weeks. Investigations NAD. Not admitted to Gynae.
21111	METFORMIN	Yes	VISIT 5 (28 WEEKS)	Upper abdominal discomfort for 4-5 weeks on and off.
21111	METFORMIN	Yes	VISIT 7 (TERM)	Amoxycillin 500mgs TDS for suspected chest infection.
21125	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Occasional light headedness. Normal Hb.
21127	METFORMIN	Yes	VISIT 5 (28 WEEKS)	SPD on crutches seeing physio.
21127	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Seeing physio & having acupuncture for hip pain.
21127	METFORMIN	Yes	VISIT 8 (DELIVERY)	SPD/hip pain. Has seen physio/had crutches/acupuncture.
21128	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Backache & sciatica
21128	METFORMIN	Yes	VISIT 8 (DELIVERY)	Postpartum haemorrhage.
25180	METFORMIN	Yes	VISIT 5 (28 WEEKS)	Two separate overnight admissions mid June first time with ?pyelonephritis and second time with pain ?due to gall-stones found at time on ultrasound scan
25284	METFORMIN	Yes	VISIT 5 (28 WEEKS)	obstetric cholestasis
25382	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	diarrhoea

Section 10. Adverse Outcome

10.1.2 Maternal Complications Details - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Other Maternal Complications (Y/N)	TimepointID	Other Maternal Complications Details
25459	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Right Adrexal ovarian cyst
25459	METFORMIN	Yes	VISIT 8 (DELIVERY)	Induction of labour due to pain from known ovarian cyst
27317	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	stomach cramps & backache.
53059	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Had contact with nephew with chicken pox and does not have immunity. Therefore had to attend for immunoglobulin
11081	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	on going hyperemesis requiring antiemetic (predates trial)
11262	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Borderline raised ALT
11262	PLACEBO	Yes	VISIT 5 (28 WEEKS)	Raised ALT, probable obstetric cholestasis but advised to stop treatment for 2 weeks and then we will repeat ALT
11262	PLACEBO	Yes	VISIT 6 (36 WEEKS)	obstetric cholestasis
11262	PLACEBO	Yes	VISIT 8 (DELIVERY)	obstetric cholestasis
11263	PLACEBO	Yes	VISIT 6 (36 WEEKS)	APH-admitted for 24 hours at 34 weeks gestation following minimal PVB. No cause found
11263	PLACEBO	Yes	VISIT 8 (DELIVERY)	PPH
11323	PLACEBO	Yes	VISIT 8 (DELIVERY)	3rd degree tear (3a)
11397	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	occasional mild palpitations, experienced this in previous pregnancy
11411	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	aware of palpitations
11443	PLACEBO	Yes	VISIT 6 (36 WEEKS)	itch-possible obstetric cholestasis
11643	PLACEBO	Yes	VISIT 5 (28 WEEKS)	Hospitalised for abdominal pain at 25 weeks, found to have c. diff. Treated for this and then experienced very painful haemorrhoids. Stopped taking study medication, but happy to continue with GTT and other data collection.
11693	PLACEBO	Yes	VISIT 8 (DELIVERY)	Obstetric cholestasis
11725	PLACEBO	Yes	VISIT 7 (TERM)	SPD
11940	PLACEBO	Yes	VISIT 6 (36 WEEKS)	currently on prednisolone for chest infection
11940	PLACEBO	Yes	VISIT 8 (DELIVERY)	Hospitalised due to chest infection.
12019	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Thrush
12020	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Ear infection/vertigo
12020	PLACEBO	Yes	VISIT 5 (28 WEEKS)	vertigo
12020	PLACEBO	Yes	VISIT 8 (DELIVERY)	PPH 1500 - 2500 mls
12021	PLACEBO	Yes	VISIT 5 (28 WEEKS)	25/04/2012 In triage for UTI. Sent home with trimethoprim.
12065	PLACEBO	Yes	VISIT 8 (DELIVERY)	Diet controlled GDM
12074	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Admitted with pv bleed
12092	PLACEBO	Yes	VISIT 8 (DELIVERY)	Pyrexia. Treated with iv antibiotics.
13007	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Was weepy when increased dose to 4 tablets at week 4. Therefore has decreased to 2 tablets daily. Not having weepiness any longer, suggested trying to increase to TDS. - will try, but not willing to increase dose further. 4/3/11
13015	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	has had hyperemesis since randomisation until now and not commenced on study medication.
13015	PLACEBO	Yes	VISIT 5 (28 WEEKS)	Hyperemesis from 12-22wks. No hospital admission. Unable to take study drugs due to sickness.
13058	PLACEBO	Yes	VISIT 6 (36 WEEKS)	vomiting and feeling very unwell migraines increasingly worse
13144	PLACEBO	Yes	VISIT 5 (28 WEEKS)	SYMPHISIS PUBIS DISORDER
13144	PLACEBO	Yes	VISIT 7 (TERM)	Has had fainting episodes for past 6 weeks. Now has IOL booked for 38wks due to this. Reports has had several admissions with raised blood pressure and protein ura.
13144	PLACEBO	Yes	VISIT 8 (DELIVERY)	Reported frequent fainting episodes. not investigated, occasional episodes of raised BP. BP profile NAD. IOL on request in view of repeated fainting.

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Section 10. Adverse Outcome

10.1.2 Maternal Complications Details - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Other Maternal Complications (Y/N)	Timepoint/D	Other Maternal Complications Details
13217	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Hip pain due to looseness in joint. Under physio. Not on medication.
13217	PLACEBO	Yes	VISIT 8 (DELIVERY)	PPH, HAD OXYTOCIC DRUGS
13301	PLACEBO	Yes	VISIT 5 (28 WEEKS)	HAD COLLAPSE WHEN OUT SHOPPING. ADVISED TO STOP MEDICATION AS GLUCOSE LEVEL WAS REPORTED TO BE LOW WHEN CHECKED AT GP.
13301	PLACEBO	Yes	VISIT 8 (DELIVERY)	Intrapartum haemorrhage and postnatal haemorrhage total = 2000ml
13380	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	14mgs cetalopram seeing pysc assessment.Had already been on this dose before pregnancy, but may need to increase.
13504	PLACEBO	Yes	VISIT 8 (DELIVERY)	Prolonged rupture of membranes for 98 hours, sepsis
13591	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Fell on the bus when i stopped suddenly. Had small pv bleed, attended hospital for anti d, but was not admitted and not for any follow up. As reports fall was due to bus stopping suddenly and no episodes of dizziness or feeling faint not an SAE.
13667	PLACEBO	Yes	VISIT 8 (DELIVERY)	IOL FOR SPD PPH 1200ML
13712	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Obstetric Choleostasis
13712	PLACEBO	Yes	VISIT 8 (DELIVERY)	cholestasis
14036	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	PV spotting diagnosed as thrush by GP
14036	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Seen in Triage 11/10/11. C/O Tightenings, Abdominal pain, moderate Symphysis Pubis disfunction. Diagnosed with UTI and given analgesics and antibiotics.
14036	PLACEBO	Yes	VISIT 8 (DELIVERY)	Maternal Post Partum Haemorrhage
14037	PLACEBO	Yes	VISIT 5 (28 WEEKS)	Anaemia taking Ferrous Fumerate BD
14037	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Maternal Obstetric Cholestasis
14037	PLACEBO	Yes	VISIT 8 (DELIVERY)	Induced due to Maternal Obstetric Cholestasis
14061	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Viral illness
14061	PLACEBO	Yes	VISIT 8 (DELIVERY)	Maternal Intracranial Hypertension
14089	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Attended Triage 26.04.12 - Abdo pain, D&V. Not admitted. ?Viral gastroenteritis.
14145	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Admitted to Leeds General Infirmary. Reported on 07/09/12
14205	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Double vision. Currently under investigation by eye clinic.
14270	PLACEBO	Yes	VISIT 8 (DELIVERY)	suspected Chorioamnitis.
14272	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Severe headache requiring hospitalistaion and investigation 18.04.13
14336	PLACEBO	Yes	VISIT 5 (28 WEEKS)	Seen by SHO in Triage 13.09.13 re abdominal pain. Now resolved ?viral enteritis
14336	PLACEBO	Yes	VISIT 8 (DELIVERY)	see SAE
14354	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Ovarian cyst on right ovary diagnosed
14354	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Admitted with small APH and tightenings for 5 days - SAE completed 22.12.13
14413	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Abdominal pain 03.10.13 Seen in Early Pregnancy Assessment Centre
15010	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	metallic taste
15010	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Has some itching bile acids nad
15028	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Admitted to assessment centre and for PPRM on 140413 admitted for less than 12hours Seen by Mr Sirmm consultant who advised Research Midwife. For conservative management at the moment. For further scans on Thursday 18th April. Admitted as inpatient on Thursday 18th April with confirmed prom and oligohydramniotic.
15028	PLACEBO	Yes	VISIT 5 (28 WEEKS)	As stated earlier Prem rupture of Membranes
16052	PLACEBO	Yes	VISIT 8 (DELIVERY)	PPH 1800ml
17036	PLACEBO	Yes	VISIT 7 (TERM)	hospital admission as had flu
17036	PLACEBO	Yes	VISIT 8 (DELIVERY)	raised ALT liver scan

Section 10. Adverse Outcome

10.1.2 Maternal Complications Details - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Other Maternal Complications (Y/N)	TimepointID	Other Maternal Complications Details
17137	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Costochondritis
17137	PLACEBO	Yes	VISIT 8 (DELIVERY)	Costochondritis
21010	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Persistent glycosuria between 28+ and 35+ weeks gestation. Normal GTTs.
21018	PLACEBO	Yes	VISIT 5 (28 WEEKS)	pv bleed before 16 weeks gestation, prior to commencing tablets. Hospitalised for observation discharged within 12 hours.
21018	PLACEBO	Yes	VISIT 6 (36 WEEKS)	4/9/13 32+6 shortness of breath/palpitations. Investigations normal.
21018	PLACEBO	Yes	VISIT 7 (TERM)	Various episodes of reduced fetal movements see on MDCU had CTGs. H/o palpitations normal investigations.
21018	PLACEBO	Yes	VISIT 8 (DELIVERY)	Difficult caesarean section.
21038	PLACEBO	Yes	VISIT 8 (DELIVERY)	Readmitted via ambulance 29/12/13 pv bleed/abdo pain. Stayed in hospital for less than 12 hours. No SAE required.
21044	PLACEBO	Yes	VISIT 6 (36 WEEKS)	pyogenic granuloma on finger of left hand. Had x2 doses of flucloxacillin. UTI cephalixin for 1 week.
21047	PLACEBO	Yes	VISIT 5 (28 WEEKS)	20+4 (3-4/9/13) brief episode in A&E pain from gall stones settled after morphine discharged home after few hours.
21069	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Antibiotics for 1 week for ear infection 05/09/13
21069	PLACEBO	Yes	VISIT 5 (28 WEEKS)	UTI treated with cefalexin.
21069	PLACEBO	Yes	VISIT 8 (DELIVERY)	Sepsis in labour. SAE form completed as prolonged hospitalisation.
21077	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Attended A&E with abdo pain 29/9/13
21077	PLACEBO	Yes	VISIT 5 (28 WEEKS)	Headaches. Community Midwife advised to stop taking tablets on 23/9/13.
21077	PLACEBO	Yes	VISIT 6 (36 WEEKS)	5/12/13 29+2 GP referral clo headache/oedema/episode of palpitations/?fainting episode. Investigations NAD.
21077	PLACEBO	Yes	VISIT 7 (TERM)	Feeling generally unwell.
21078	PLACEBO	Yes	VISIT 5 (28 WEEKS)	Hb low for oral iron
21078	PLACEBO	Yes	VISIT 6 (36 WEEKS)	16/1/14 episode of reduced fetal movements. CTG NAD.
21078	PLACEBO	Yes	VISIT 7 (TERM)	On ferrous sulphate tablets as anaemic since last visit.
21093	PLACEBO	Yes	VISIT 5 (28 WEEKS)	Small antepartum haemorrhage. Overnight stay on maternity ward for over 12 hours.
21093	PLACEBO	Yes	VISIT 6 (36 WEEKS)	28/12/13 slight pv bleeding no admission. 24/1/14 Antibiotics for bacterial vaginosis & canestan for thrush. 3/2/14 brief isolated episode of raised BP settled on day unit no admission.
21093	PLACEBO	Yes	VISIT 8 (DELIVERY)	Raised BP in labour
21100	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	28/10/13 thrush detected. Prescription off GP.
21100	PLACEBO	Yes	VISIT 6 (36 WEEKS)	UTI on MSSU 17/01/14 treated with cefalexin.
21100	PLACEBO	Yes	VISIT 7 (TERM)	UTI-commenced Trimethoprim BD for 3 days on 31/3/14.
21100	PLACEBO	Yes	VISIT 8 (DELIVERY)	Antepartum haemorrhage 1200mls. Manual removal of placenta & postpartum haemorrhage of 800mls. Blood transfusion.
21109	PLACEBO	Yes	VISIT 5 (28 WEEKS)	Heartburn. Day Unit visit 16/12/13 abdo pain.
21109	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Admitted over 12 hours with UTI. Oral antibiotics/steroids/ferrous sulphate. SAE form completed & faxed to Sponsors.
21109	PLACEBO	Yes	VISIT 7 (TERM)	Admitted for 2 nights on 03/4/14 with lower abdo discomfort, braxton hicks, red pv loss, unstable lie.
21109	PLACEBO	Yes	VISIT 8 (DELIVERY)	Admitted with lower abdo discomfort, red pv loss, Braxton Hicks, unstable lie 03/4/14
21122	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Prolonged nausea.
21122	PLACEBO	Yes	VISIT 5 (28 WEEKS)	Prolonged nausea
21122	PLACEBO	Yes	VISIT 7 (TERM)	Musculoskeletal pain/SPD. Group B Strep positive.
21122	PLACEBO	Yes	VISIT 8 (DELIVERY)	SPD/musculoskeletal pain. Group B Strep positive.

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Section 10. Adverse Outcome

10.1.2 Maternal Complications Details - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Other Maternal Complications (Y/N)	Timepoint/D	Other Maternal Complications Details
21133	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Feels down.
21133	PLACEBO	Yes	VISIT 5 (28 WEEKS)	25/2/14 tonsillitis/viral infection treated with penecillin.
21133	PLACEBO	Yes	VISIT 6 (36 WEEKS)	11/4/14 & 23/5/14 admissions for likely costochondritis.
21133	PLACEBO	Yes	VISIT 7 (TERM)	Symphysis Pubis Dysfunction. Taking Co-Codamol.
21133	PLACEBO	Yes	VISIT 8 (DELIVERY)	SPD. Hypertension in labour.
24035	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	In last 48 hours has suffered with nausea and vomiting; high level stomach pains that radiate down her sides and into her back - above her bra strap; and headache. These symptoms she has had only for last 48 hours...?Viral
25100	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	severe headaches on the medication that the P.I. has reported as an SAE, headaches stopped when medication was suspended. P.I has recommended stopping medication completely
25100	PLACEBO	Yes	VISIT 6 (36 WEEKS)	symphius pubis dysfunction requiring a few days of bed rest in hospital
25100	PLACEBO	Yes	VISIT 7 (TERM)	depression, symphius pubis dysfunction
25165	PLACEBO	Yes	VISIT 8 (DELIVERY)	PPH 2.5L
25391	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	brown/green pv loss on 2.11.13. pv spotting on 12.11.13. HVS group B streptococcus.
25391	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Abdominal pain ?cause
25391	PLACEBO	Yes	VISIT 7 (TERM)	depression and musculoskeletal pain
53014	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	has had persistant cough since sept. Has seen own doctor (GP, had course of antibiotics. Also seen at general hospital advised re inhalers and improved with this (as is asthmatic)

Section 10. Adverse Outcome

10.1.3.1 Maternal Complications - Hypertension - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery) - Statistical Analysis - POST-HOC*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of ANY_HYPER by AllocatedTreatment</i>			
		<i>AllocatedTreatment(Allocated Treatment)</i>			
<i>ANY_HYPER</i>	<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>		
<i>Missing</i>	5	1	.		
<i>No</i>	200	208	408		
<i>Yes</i>	21	14	35		
<i>Total</i>	221	222	443		
<i>Frequency Missing = 6</i>					

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
ANY_HYPER_itt	AllocatedTreatment METFORMIN vs PLACEBO	1.560	0.772	3.152	0.2155	0.2232

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 00:26
 *Analised using logistic regression (binary logit), probability modeled is ANY_hyper='Yes'
 #Significance level set at p<0.05
 Detailed analysis in file 'Empowar_10_1_1_Npatients_hypertension_analysis.lst'

Section 10. Adverse Outcome

10.1.3.2 Maternal Complications - Preeclampsia - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery) - Statistical Analysis - POST-HOC*
 Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of ANY_Preecla by AllocatedTreatment</i>			
		<i>AllocatedTreatment(Allocated Treatment)</i>			
<i>ANY_Preecla</i>	<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>		
<i>Missing</i>	5	1	.		
<i>No</i>	214	219	433		
<i>Yes</i>	7	3	10		
<i>Total</i>	221	222	443		
<i>Frequency Missing = 6</i>					

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
ANY_Preecla_itt	AllocatedTreatment METFORMIN vs PLACEBO	2.388	0.609	9.355	0.2116	0.2207

Section 10. Adverse Outcome

10.2.1 Fetal Complications* - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Any Fetal Complication (n)	Missing	1	5	6
	Yes	47 (21.2)	43 (19.5)	90 (20.3)
	No	175 (78.8)	178 (80.5)	353 (79.7)
Fetal AC (n)	Missing	221	226	447
	No	2	0	2
Fetal Liquor (n)	Missing	158	173	331
	Yes	6	3	9
	No	59	50	109
Fetal Doppler (n)	Missing	159	174	333
	Yes	0	1	1
	No	64	51	115
Fetal Absent EDF (n)	Missing	160	175	335
	Yes	2	0	2
	No	61	51	112

Section 10. Adverse Outcome

10.2.1 Fetal Complications* - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)(Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Fetal Reverse EDF (n)	Missing	160	175	335
	No	63	51	114
Fetal Abnormal CTG (n)	Missing	157	175	332
	Yes	14	11	25
	No	52	40	92
Other Fetal Complication (n)	Missing	152	159	311
	Yes	32	35	67
	No	39	32	71
Other Fetal Complication cat#(n)	Data captured elsewhere	19	22	41
	Meconium stained liquor	4	5	9
	Miscellaneous	2	3	5
	Polyhydramnios	3	3	6
	Reduced fetal movements	7	10	17
	Shoulder dystocia	2	0	2

Section 10. Adverse Outcome
10.2.2 Fetal Complications Details - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)
 Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Fetal Complications Other (Y/N)	TimepointID	Fetal Complications Other Details
11078	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	abnormal anomaly scan - probable CCAM
11078	METFORMIN	Yes	VISIT 6 (36 WEEKS)	USS 26/10/11: large left sided CCAM with mediastinal shift.
11078	METFORMIN	Yes	VISIT 8 (DELIVERY)	baby known antenatally to have CCAM
11557	METFORMIN	Yes	VISIT 8 (DELIVERY)	reduced fetal movements and clinically felt to be small for dates although growth scan normal
11566	METFORMIN	Yes	VISIT 8 (DELIVERY)	Baby required resuscitation at delivery
11880	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	unknown cause of IUD detected at FAS
11880	METFORMIN	Yes	VISIT 8 (DELIVERY)	Fetal death diagnosed at 20 weeks
12001	METFORMIN	Yes	VISIT 8 (DELIVERY)	macrosomia
12006	METFORMIN	Yes	VISIT 8 (DELIVERY)	confirmed IUD on 10/02/2012
12018	METFORMIN	Yes	VISIT 6 (36 WEEKS)	scan at 36 weeks shows abdominal circumference static,attending further scan in one week
12034	METFORMIN	Yes	VISIT 8 (DELIVERY)	Premature delivery.
12055	METFORMIN	Yes	VISIT 8 (DELIVERY)	IUGR
12056	METFORMIN	Yes	VISIT 8 (DELIVERY)	fetal abnormality known fetal hydrops
13508	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	1840 spontaneous miscarriage
13551	METFORMIN	Yes	VISIT 8 (DELIVERY)	Low Cord Ph's on FBS
14131	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Renal pelvis Left kidney dilated
14162	METFORMIN	Yes	VISIT 8 (DELIVERY)	Reduced fetal Movements
14203	METFORMIN	Yes	VISIT 8 (DELIVERY)	Raised doppler on 07.01.13
14303	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Polyhydramnios
15003	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Breech presentation
16029	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Mesenterial Cyst
16029	METFORMIN	Yes	VISIT 8 (DELIVERY)	Reduced fetal movements
16064	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Reduced fetal movements x 2 days
16121	METFORMIN	Yes	VISIT 7 (TERM)	Persistent reduced fetal movements
16121	METFORMIN	Yes	VISIT 8 (DELIVERY)	Persistent reduced fetal movements
16133	METFORMIN	Yes	VISIT 7 (TERM)	polyhydramnios
16133	METFORMIN	Yes	VISIT 8 (DELIVERY)	polyhydramnios
17047	METFORMIN	Yes	VISIT 8 (DELIVERY)	Meconium liquor
21042	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Episodes of reduced fetal movements.
21070	METFORMIN	Yes	VISIT 8 (DELIVERY)	Thick meconium liquor on SROM.
21074	METFORMIN	Yes	VISIT 6 (36 WEEKS)	x1 episode of no fetal movements 25/11/13 28+5. Normal CTG.
21074	METFORMIN	Yes	VISIT 7 (TERM)	Reduced fetal movements 03/02/14. Normal scan.
21081	METFORMIN	Yes	VISIT 7 (TERM)	Episode of reduced fetal movements.
21082	METFORMIN	Yes	VISIT 5 (28 WEEKS)	Growth below lower centile.
21082	METFORMIN	Yes	VISIT 8 (DELIVERY)	Thick meconium liquor. Fetal tachycardia in labour.
21095	METFORMIN	Yes	VISIT 8 (DELIVERY)	Meconium liquor

Section 10. Adverse Outcome

10.2.2 Fetal Complications Details - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Fetal Complications Other (Y/N)	TimepointID	Fetal Complications Other Details
21125	METFORMIN	Yes	VISIT 8 (DELIVERY)	Lightly stained meconium liquor.
21127	METFORMIN	Yes	VISIT 8 (DELIVERY)	Growth on 10th centile.
21128	METFORMIN	Yes	VISIT 8 (DELIVERY)	IUGR, Growth on lower centile. Double knot in cord.
25180	METFORMIN	Yes	VISIT 8 (DELIVERY)	mildly dilated lateral ventricular horns on postnatal cephalic USS
25226	METFORMIN	Yes	VISIT 8 (DELIVERY)	Baby had IVABX as prev NND for Group B Strep and EColi.
25459	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Anomaly scan show right unilateral talipes
53059	METFORMIN	Yes	VISIT 6 (36 WEEKS)	HAD 2X GROWTH USS FOR ?IUGR. SECOND USS SHOWED NORMAL GROWTH.
11295	PLACEBO	Yes	VISIT 8 (DELIVERY)	cardiac abnormality as previously reported
11386	PLACEBO	Yes	VISIT 8 (DELIVERY)	shoulder dystocia, relieved with McRoberts and suprapubic pressure, Apgars 8 and 9
11564	PLACEBO	Yes	VISIT 8 (DELIVERY)	baby required resuscitation at delivery
11632	PLACEBO	Yes	VISIT 8 (DELIVERY)	Suspected IUGR
12020	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Reduced fetal movements
12021	PLACEBO	Yes	VISIT 5 (28 WEEKS)	Polyhydramnios
12021	PLACEBO	Yes	VISIT 6 (36 WEEKS)	polyhydramnios detected on scan at 28+4 weeks. Large for gestational age detected at 34+2 weeks.
12030	PLACEBO	Yes	VISIT 5 (28 WEEKS)	amniotic band noted at 20/40 repeat scan done NAD
12038	PLACEBO	Yes	VISIT 6 (36 WEEKS)	? iugr on uss
13301	PLACEBO	Yes	VISIT 8 (DELIVERY)	Undiagnosed oblique breech lie, intrapartum haemorrhage
13473	PLACEBO	Yes	VISIT 8 (DELIVERY)	Baby admitted to NICU for low BM's for 24 hours. No IV fluids required, baby tube fed only. Lowest BM 1.7mmol. Now maintaining BM's and back on postnatal ward with mum
13504	PLACEBO	Yes	VISIT 8 (DELIVERY)	Baby born in poor condition at birth, intubated and respiratory effort not achieved until 8 minutes of age, admitted to NICU for septic screen
13591	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Raised growth on USS, at 32/40 and 35/40 measurements >95th centile. EFW at 35/40 3456g
13591	PLACEBO	Yes	VISIT 8 (DELIVERY)	Suspected fetal macrosomia
14061	PLACEBO	Yes	VISIT 5 (28 WEEKS)	Reduced fetal movements. Growth scan performed AC on 5th centile shown. Repeat in 2 weeks. Scan 07/11/2011 Showed normal growth and normal fetal movements.
14061	PLACEBO	Yes	VISIT 8 (DELIVERY)	Maternal reporting of reduced fetal movements. FM's seen on USS
14145	PLACEBO	Yes	VISIT 5 (28 WEEKS)	On USS Fetus has transposition of the great arteries, a ventricular septal defect and ?coarctation of the aorta.
14145	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Fetal Abdominal Circumference on 97th centile. AFI increased (19cm)
14264	PLACEBO	Yes	VISIT 8 (DELIVERY)	intermittently absent EDF
15010	PLACEBO	Yes	VISIT 5 (28 WEEKS)	one episode of reduced fetal movements ctg monitoring normal
15026	PLACEBO	Yes	VISIT 5 (28 WEEKS)	oligohydramniotic
16053	PLACEBO	Yes	VISIT 8 (DELIVERY)	shoulder dystocia
16126	PLACEBO	Yes	VISIT 8 (DELIVERY)	Reduced fetal movements x3 episodes
18114	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Measuring Large for Dates. Head circumference and abdominal circumference above 95th centile.
21018	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Polyhydramniotic on uss 8/8/13 (29 weeks) & 21/8/13 (30+6 weeks) has since resolved. Reduced fetal movements had monitoring on x4 occasions & again today.
21038	PLACEBO	Yes	VISIT 5 (28 WEEKS)	Growth on lower centile today. Normal doppler
21069	PLACEBO	Yes	VISIT 8 (DELIVERY)	Thick meconium stained liquor during labour.
21077	PLACEBO	Yes	VISIT 8 (DELIVERY)	Meconium liquor
21093	PLACEBO	Yes	VISIT 6 (36 WEEKS)	27/1/14 growth on lower centile. 03/2/14 mild polyhydramniotic. 10/2/14 normal growth & liquor volume.

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Section 10. Adverse Outcome

10.2.2 Fetal Complications Details - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Fetal Complications Other (Y/N)	TimepointID	Fetal Complications Other Details
21093	PLACEBO	Yes	VISIT 8 (DELIVERY)	Light, thin meconium liquor
21109	PLACEBO	Yes	VISIT 6 (36 WEEKS)	21/02/2014 uss normal growth. Liquor volume just above upper centile.
21119	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Fetal abnormality on anomaly ultrasound scan.
25034	PLACEBO	Yes	VISIT 8 (DELIVERY)	meconium stained liquor
25100	PLACEBO	Yes	VISIT 7 (TERM)	one episode of reduced fetal movement
25165	PLACEBO	Yes	VISIT 8 (DELIVERY)	PROM 66 hours
25320	PLACEBO	Yes	VISIT 8 (DELIVERY)	baby's scan on the 30/1/2014 continued to show baby had a full stomach, suspected Hirschsprungs disease in neonate.
25364	PLACEBO	Yes	VISIT 7 (TERM)	Large for dates on scan

Section 11. Neonatal Care - All Patients

11.1 Neonatal Care

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Care after delivery (n(%))	Missing	3	11	14
	Normal Care	185 (84.1)	196 (91.2)	381 (87.6)
	Special Care	14 (6.4)	7 (3.3)	21 (4.8)
	Level 2 intensive care (ie high dependency intensive care)	9 (4.1)	6 (2.8)	15 (3.4)
	Level 1 intensive care (maximal intensive care)	6 (2.7)	1 (0.5)	7 (1.6)
	Other	6 (2.7)	5 (2.3)	11 (2.5)
Any Congenital Abnormality (n(%))	Missing	5	15	20
	Yes	9 (4.1)	8 (3.8)	17 (4.0)
	No	209 (95.9)	203 (96.2)	412 (96.0)
Other Hospital Admission (n(%))	Missing	18	19	37
	Yes	3 (1.5)	2 (1.0)	5 (1.2)
	No	202 (98.5)	205 (99.0)	407 (98.8)

Section 11. Neonatal Care - Only Alive Births

11.2.1 Neonatal Care

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo</i>	<i>Metformin</i>	<i>Overall</i>
Care after delivery (n(%))	Missing	1	1	2
	Normal Care	185 (84.5)	196 (92.0)	381 (88.2)
	Special Care	14 (6.4)	7 (3.3)	21 (4.9)
	Level 2 intensive care (ie high dependency intensive care)	9 (4.1)	6 (2.8)	15 (3.5)
	Level 1 intensive care (maximal intensive care)	6 (2.7)	1 (0.5)	7 (1.6)
	Other	5 (2.3)	3 (1.4)	8 (1.9)
Any Congenital Abnormality (n(%))	Missing	3	5	8
	Yes	8 (3.7)	7 (3.3)	15 (3.5)
	No	209 (96.3)	202 (96.7)	411 (96.5)
Other Hospital Admission (n(%))	Missing	16	9	25
	Yes	3 (1.5)	2 (1.0)	5 (1.2)
	No	201 (98.5)	203 (99.0)	404 (98.8)

Section 11. Neonatal Care - Only Alive Births

11.2.2 Neonatal care after delivery - Statistical analysis - POST-HOC*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Frequency	Table of Care_Deliv by Allocated Treatment		
	Allocated Treatment (Allocated Treatment)		
Care_Deliv	METFORMIN	PLACEBO	Total
Missing	1	1	.
No	199	190	389
Yes	14	29	43
Total	213	219	432

Frequency Missing = 2

Parameter(s)	Studied effects	Odds Ratio Estimate	Lower 95% Confidence Limit for Odds Ratio	Upper 95% Confidence Limit for Odds Ratio	P-value#	Fisher exact P-value#
Care_Deliv_itt	Allocated Treatment METFORMIN vs PLACEBO	0.461	0.236	0.899	0.0231	0.0242

Section 11. Neonatal Care - Only Alive Births

11.2.3 Any Congenital Abnormality - Statistical analysis - POST-HOC*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Frequency	Table of Abnormal by AllocatedTreatment			
	AllocatedTreatment(Allocated Treatment)			
	Abnormal	METFORMIN	PLACEBO	Total
Missing		5	3	.
No		202	209	411
Yes		7	8	15
Total		209	217	426

Frequency Missing = 8

Parameter(s)	Studied effects	Odds Ratio Estimate	Lower	Upper	P-value#	Fisher exact P-value#
			95% Confidence Limit for Odds Ratio	95% Confidence Limit for Odds Ratio		
Abnormal_itt	AllocatedTreatment METFORMIN vs PLACEBO	0.905	0.322	2.543	0.8503	1.0000

Section 12. Maternal symptoms up to 36 weeks gestation

12.1.1 Taste Disturbance - from Visit 4 (18-20 Weeks) to Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
Any Taste Disturbance (n(%))	Missing	25	27	52
	Yes	32 (16.2)	25 (12.6)	57 (14.4)
	No	166 (83.8)	174 (87.4)	340 (85.6)
Taste Disturbance severity (n)	Mild	19	13	32
	Moderate	12	7	19
	Severe	1	5	6

Section 12. Maternal symptoms up to 36 weeks gestation

12.1.2 Taste Disturbance - Statistical analysis - POST-HOC*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of TasteDis_ana by AllocatedTreatment</i>			
<i>TasteDis_ana(Taste disturbance at least once from visit 4 to visit 7 (Y/N))</i>		<i>AllocatedTreatment(Allocated Treatment)</i>			
		<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>	
<i>Yes</i>		27	25	.	
<i>No</i>		174	166	340	
<i>Total</i>		199	198	397	
<i>Frequency Missing = 52</i>					

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
tastedis_itt	AllocatedTreatment METFORMIN vs PLACEBO	0.745	0.424	1.311	0.3077	0.3200

Section 12. Maternal symptoms up to 36 weeks gestation

12.2.1 Skin Reaction - from Visit 4 (18-20 Weeks) to Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=449
		Placebo N=223	Metformin N=226	
Any Skin Reaction (n(%))	Missing	25	27	52
	Yes	39 (19.7)	36 (18.1)	75 (18.9)
	No	159 (80.3)	163 (81.9)	322 (81.1)
Skin Reaction severity (n)	Mild	23	22	45
	Moderate	14	11	25
	Severe	2	3	5

Section 12. Maternal symptoms up to 36 weeks gestation

12.2.2 Skin Reaction - Statistical Analysis - POST-HOC*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of SkinReac_ana by AllocatedTreatment</i>		
<i>Frequency</i>	<i>SkinReac_ana(Skin Reaction at least once from visit 4 to visit 7 (Y/N))</i>	<i>AllocatedTreatment(Allocated Treatment)</i>		<i>Total</i>
		<i>METFORMIN</i>	<i>PLACEBO</i>	
		27	25	.
Yes		36	39	75
No		163	159	322
Total		199	198	397
<i>Frequency Missing = 52</i>				

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
skinreac_itt	AllocatedTreatment METFORMIN vs PLACEBO	0.900	0.545	1.489	0.6827	0.7022

Section 12. Maternal symptoms up to 36 weeks gestation

12.3.1 Abdominal Pain - from Visit 4 (18-20 Weeks) to Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
Any Abdominal Pain (n(%))	Missing	25	27	52
	Yes	42 (21.2)	49 (24.6)	91 (22.9)
	No	156 (78.8)	150 (75.4)	306 (77.1)
Abdominal Pain severity (n)	Mild	25	28	53
	Moderate	14	18	32
	Severe	3	3	6

Section 12. Maternal symptoms up to 36 weeks gestation

12.3.2 Abdominal Pain - Statistical Analysis - POST-HOC*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of AbdoPain_ana by AllocatedTreatment</i>				
<i>AbdoPain_ana</i> (Abdominal Pain at least once from visit 4 to visit 7 (Y/N))	<i>AllocatedTreatment</i> (Allocated Treatment)		<i>Total</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>Fisher exact P-value#</i>
	<i>METFORMIN</i>	<i>PLACEBO</i>				
	27	25	.			
<i>Yes</i>	49	42	91			
<i>No</i>	150	156	306			
<i>Total</i>	199	198	397			
<i>Frequency Missing = 52</i>						
<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
abdpain_itt	AllocatedTreatment METFORMIN vs PLACEBO	1.213	0.759	1.940	0.4192	0.4740

Section 12. Maternal symptoms up to 36 weeks gestation

12.4.1 Flatulence - from Visit 4 (18-20 Weeks) to Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Any Flatulence (n(%))	Missing	25	27	52
	Yes	44 (22.2)	51 (25.6)	95 (23.9)
	No	154 (77.8)	148 (74.4)	302 (76.1)
Flatulence severity (n)	Mild	27	19	46
	Moderate	14	23	37
	Severe	3	9	12

Section 12. Maternal symptoms up to 36 weeks gestation

12.4.2 Flatulence - Statistical Analysis - POST-HOC*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of Flatu_ana by AllocatedTreatment</i>				
	<i>Flatu_ana(Flatulence at least once from visit 4 to visit 7 (Y/N))</i>	<i>AllocatedTreatment(Allocated Treatment)</i>		<i>Total</i>		
		<i>METFORMIN</i>	<i>PLACEBO</i>			
		27	25	.		
Yes		51	44	95		
No		148	154	302		
Total		199	198	397		
<i>Frequency Missing = 52</i>						

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
flatu_itt	AllocatedTreatment METFORMIN vs PLACEBO	1.206	0.760	1.915	0.4268	0.4806

Section 12. Maternal symptoms up to 36 weeks gestation

12.5.1 Constipation - from Visit 4 (18-20 Weeks) to Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
Any Constipation (n(%))	Missing	25	27	52
	Yes	57 (28.8)	57 (28.6)	114 (28.7)
	No	141 (71.2)	142 (71.4)	283 (71.3)
Constipation severity (n)	Mild	33	32	65
	Moderate	21	17	38
	Severe	3	8	11

Section 12. Maternal symptoms up to 36 weeks gestation

12.5.2 Constipation - Statistical Analysis - POST-HOC*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Table of Consti_ana by AllocatedTreatment</i>			
<i>Consti_ana(Constipation at least once from visit 4 to visit 7 (Y/N))</i>	<i>AllocatedTreatment(Allocated Treatment)</i>		<i>Total</i>
	<i>METFORMIN</i>	<i>PLACEBO</i>	
	27	25	.
<i>Yes</i>	57	57	114
<i>No</i>	142	141	283
<i>Total</i>	199	198	397

Frequency Missing = 52

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
consti_itt	AllocatedTreatment METFORMIN vs PLACEBO	0.993	0.643	1.534	0.9746	1.0000

Section 12. Maternal symptoms up to 36 weeks gestation

12.6.1 Diarrhoea - from Visit 4 (18-20 Weeks) to Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Any Diarrhoea (n(%))	Missing	25	27	52
	Yes	37 (18.7)	83 (41.7)	120 (30.2)
	No	161 (81.3)	116 (58.3)	277 (69.8)
Diarrhoea severity (n)	Mild	21	49	70
	Moderate	14	24	38
	Severe	2	10	12

Section 12. Maternal symptoms up to 36 weeks gestation

12.6.2 Diarrhoea - Statistical Analysis - POST-HOC*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Table of Diarr_ana by AllocatedTreatment</i>			
<i>Frequency</i>			
<i>Diarr_ana(Diarrhoea at least once from visit 4 to visit 7 (Y/N))</i>	<i>AllocatedTreatment(Allocated Treatment)</i>		<i>Total</i>
	<i>METFORMIN</i>	<i>PLACEBO</i>	
	27	25	.
<i>Yes</i>	83	37	120
<i>No</i>	116	161	277
<i>Total</i>	199	198	397

Frequency Missing = 52

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
diarr_itt	AllocatedTreatment METFORMIN vs PLACEBO	3.113	1.975	4.908	<.0001	0.0000

Section 12. Maternal symptoms up to 36 weeks gestation

12.7.1 Nausea - from Visit 4 (18-20 Weeks) to Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
Any Nausea (n(%))	Missing	25	27	52
	Yes	79 (39.9)	97 (48.7)	176 (44.3)
	No	119 (60.1)	102 (51.3)	221 (55.7)
Nausea severity (n)	Missing	1	0	1
	Mild	48	50	98
	Moderate	25	38	63
	Severe	5	9	14

Section 12. Maternal symptoms up to 36 weeks gestation

12.7.2 Nausea - Statistical Analysis - POST-HOC*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of Nausea_ana by AllocatedTreatment</i>			
	<i>Nausea_ana(Nausea at least once from visit 4 to visit 7 (Y/N))</i>	<i>AllocatedTreatment(Allocated Treatment)</i>		<i>Total</i>	
		<i>METFORMIN</i>	<i>PLACEBO</i>		
		27	25	.	
Yes		97	79	176	
No		102	119	221	
Total		199	198	397	
<i>Frequency Missing = 52</i>					

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
nausea_itt	AllocatedTreatment METFORMIN vs PLACEBO	1.432	0.962	2.132	0.0765	0.0861

Section 12. Maternal symptoms up to 36 weeks gestation

12.8.1 Vomiting - from Visit 4 (18-20 Weeks) to Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
Any Vomiting (n(%))	Missing	25	27	52
	Yes	43 (21.7)	63 (31.7)	106 (26.7)
	No	155 (78.3)	136 (68.3)	291 (73.3)
Vomiting severity (n)	Missing	1	0	1
	Mild	25	31	56
	Moderate	13	26	39
	Severe	4	6	10

Section 12. Maternal symptoms up to 36 weeks gestation

12.8.2 Vomiting - Statistical Analysis - POST-HOC*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of Vomit_ana by AllocatedTreatment</i>		
<i>Vomit_ana(Vomit at least once from visit 4 to visit 7 (Y/N))</i>	<i>AllocatedTreatment(Allocated Treatment)</i>		<i>Total</i>	
	<i>METFORMIN</i>	<i>PLACEBO</i>		
	27	25	.	
Yes	63	43	106	
No	136	155	291	
<i>Total</i>	199	198	397	
<i>Frequency Missing = 52</i>				

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
			1.064	2.621		
vomit_itt	AllocatedTreatment METFORMIN vs PLACEBO	1.670	1.064	2.621	0.0259	0.0309

Section 12. Maternal symptoms up to 36 weeks gestation

12.9.1 Headache - from Visit 4 (18-20 Weeks) to Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=223	Metformin N=226	Overall N=449
Any Headache (n(%))	Missing	25	27	52
	Yes	66 (33.3)	65 (32.7)	131 (33.0)
	No	132 (66.7)	134 (67.3)	266 (67.0)
Headache severity (n)	Mild	37	38	75
	Moderate	19	19	38
	Severe	10	8	18

Section 12. Maternal symptoms up to 36 weeks gestation

12.9.2 Headache - Statistical Analysis - POST-HOC*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Table of Headache_ana by AllocatedTreatment</i>			
<i>Headache_ana(Headache at least once from visit 4 to visit 7 (Y/N))</i>	<i>AllocatedTreatment(Allocated Treatment)</i>		<i>Total</i>
	<i>METFORMIN</i>	<i>PLACEBO</i>	
	27	25	.
<i>Yes</i>	65	66	131
<i>No</i>	134	132	266
<i>Total</i>	199	198	397

Frequency Missing = 52

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
			0.638	1.474		
headache_itt	AllocatedTreatment METFORMIN vs PLACEBO	0.970	0.638	1.474	0.8871	0.9152

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Section 13. Serious Adverse Events

13.1.1.1 Mothers with at least one SAE

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
Number of Patient with a SAE (n)	OVERALL	41	37	78

Section 13. Serious Adverse Events

13.1.1.2 Mothers with at least one SAE - Statistical Analysis - POST-HOC*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Frequency	Table of ANY_SAE by AllocatedTreatment		
	AllocatedTreatment(Allocated Treatment)		
ANY_SAE	METFORMIN	PLACEBO	Total
Missing	1	1	.
No	188	181	369
Yes	37	41	78
Total	225	222	447

Frequency Missing = 2

Parameter(s)	Studied effects	Odds Ratio Estimate	Lower 95% Confidence Limit for Odds Ratio	Upper 95% Confidence Limit for Odds Ratio	P-value#	Fisher exact P-value#
pat_sae_itt	AllocatedTreatment METFORMIN vs PLACEBO	0.869	0.533	1.417	0.5731	0.6189

Section 13. Serious Adverse Events

13.1.1.3 SAE related to the mothers

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
Number of SAE (n)	OVERALL	47	42	89
Number of SAE by relationship (n)	Possibly	2	3	5
	Unrelated	45	39	84
Number of SAE by expectedness (n)	Yes	11	11	22
	No	34	29	63
	Unk	2	2	4

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Section 13. Serious Adverse Events

13.1.1.3 SAE related to the mothers (Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		
		<i>Placebo</i>	<i>Metformin</i>	<i>Overall</i>
Number of SAE by outcome (n)	Missing	1	0	1
	Completely recovered	43	33	76
	Condition improving	1	3	4
	Condition improving Completely recovered	1	0	1
	Condition improving Recovered with sequelae	0	1	1
	Condition still present and unchanged	0	1	1
	Recovered with sequelae	1	4	5

Section 13. Serious Adverse Events

13.1.2 SAE related to the mothers - Details

Population = Intention to treat (ITT) - Allocated/Treatment used for summarisation

Subject Number	Allocated Treatment	SAE - date of report	SAE - date of event	Description of SAE	Expedited Reporting Criteria	Relevant History	SAE_related_coded	SAE_expected_coded (Y/N)	SAE_outcome_coded	SAE - date of recovery
1136	METFORMIN	19JAN2012	14JAN2012	Diagnosis: Placental abruption. Description: Patient presented at 35+2 weeks gestation with a minor ante-partum haemorrhage. Clinical diagnosis of placental abruption was made, necessitating immediate delivery by caesarean section. Diagnosis was confirmed at delivery. Mother and baby are both well. Severity: Moderate	Involved or prolonged inpatient hospitalisation Life-threatening		Unrelated	No	Completely recovered	17JAN2012
11317	METFORMIN	05MAR2012	02MAR2012	Diagnosis: Venous sinus thrombosis Description: Developed headaches at 22 weeks gestation. MRI confirmed bilateral non-occlusive thrombi in the terminal transverse sinuses and the sigmoid sinus. Commenced on treatment with dalteparin. Outpatient management only, did not require admission to hospital. Diagnosis made on 02/03/12. PI only became aware 05/03/12. Follow-up 20/02/14: Venous sinus thrombosis provoked by pregnancy. Treated with 12 months of LMWH. Now completely resolved. Severity: Moderate	Life-threatening		Unrelated	No	Completely recovered	13MAR2013
11501	METFORMIN	14NOV2012	27OCT2012	Diagnosis: Unknown Description: Admitted with severe renal pain and vomiting. Noted to have deranged LFTs. Recent course of amoxicillin from GP for chest infection. Symptoms and LFTs resolved spontaneously. Severity: Mild	Involved or prolonged inpatient hospitalisation		Possibly	Yes	Completely recovered	31OCT2012
11686	METFORMIN	02APR2013	02APR2013	Diagnosis: Breast Cancer. Description: Has been attending the breast clinic for past 10 days. biopsy of a breast lump. Will require chemotherapy, early induction of labour, followed by surgery, radiotherapy and further chemotherapy. Follow-up 20/02/14: Developed breast cancer in second trimester of pregnancy. Commenced chemotherapy during pregnancy, elective delivery at 35 weeks gestation. completion of chemotherapy following delivery and then proceeded to mastectomy followed by postoperative radiotherapy. Continues to have oncology follow-up. Severity: Severe.	Other significant medical events (as defined in protocol) Life-threatening		Unrelated	No	Condition improving	
11748	METFORMIN	12DEC2013	11DEC2013	Diagnosis: Mastitis. Description: Sepsis secondary to Mastitis. Follow-up 20/02/14: Admitted 10 days postnatal with mastitis. Treated with IV then oral antibiotics. Severity: Moderate	Involved or prolonged inpatient hospitalisation	UTI 25/09/2013 - 27/09/2013. medication required.	Unrelated	No	Completely recovered	14DEC2013
11748	METFORMIN	27SEP2013	25SEP2013	Diagnosis: Pain and Vomiting. Description: Self presented with upper abdominal pain and vomiting. ?UTI. Severity: Moderate.	Involved or prolonged inpatient hospitalisation	Depression from 2009 to 2010. Urinary Tract Infection. April 5th 2013 to 6.4.2013.	Unrelated	No	Recovered with sequelae	27SEP2013
11748	METFORMIN	07OCT2013	06OCT2013	Diagnosis: Abdominal Pain ? Preterm Labour Description: Self presented with abdo pain. ?Preterm labour complicated by urinary tract infections. Severity: Moderate Follow-up 20/02/14: Diagnosis: UTI. Admitted at 32 weeks gestation with abdominal pain. Urine culture +ve for e.coli. Threatened pre-term labour excluded. Treated with antibiotics and resolved. Severity: Mild.	Involved or prolonged inpatient hospitalisation	Urinary Tract Infection. 02/04/13 - 05/04/2013 and 25/09/2013 - 26/09/2013. medication required for both infections.	Unrelated	No	Completely recovered	09OCT2014
11797	METFORMIN	18NOV2013	14NOV2013	Diagnosis: Vomiting in late pregnancy. Description: Self presented with excessive vomiting. Severity: Moderate.	Involved or prolonged inpatient hospitalisation	Hyperemesis. 20/05/13. ongoing medication required.	Possibly	Yes	Completely recovered	15NOV2013
11880	METFORMIN	28NOV2013	28NOV2013	Diagnosis: Intrauterine Death. Description: Patient attended for ultrasound scan for fetal anomaly at 20+1 weeks gestation. No fetal heartbeat seen. IUD performed. Follow-up 20/02/14: Diagnosis: Midtrimester fetal loss. Fetal death diagnosed on routine anomaly scan at 20+ weeks. Admitted for medical management of miscarriage on 30/11/2013. Home on 1/12/2013. Severity: Severe.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	01DEC2013
11881	METFORMIN	07JAN2014	30DEC2013	Diagnosis: Severe Sepsis. Description: Admitted at 30+4 weeks gestation with pyrexia, rigors and dysuria. Treated with multiple antibiotics for presumed urosepsis. Clinical deterioration over the course of a week. Decision made to deliver baby in maternal interest at 31+2 weeks gestation. Patient transferred to ITU for ventilatory support post delivery. Continues to improve. back in normal ward at present. Follow-up 14/01/14: Diagnosis: Probable urosepsis and atypical pneumonia necessitating preterm delivery in maternal interest. Description: Condition now resolved. patient recovered. Severity: Severe.	Life-threatening Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	13JAN2014

Section 13. Serious Adverse Events

13.1.2 SAE related to the mothers - Details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	SAE - date of report	SAE - date of event	Description of SAE	Expedited Reporting Criteria	Relevant History	SAE_related_coded	SAE_expected_coded (Y/N)	SAE_outcome_coded	SAE - date of recovery
11884	METFORMIN	03FEB2014	17DEC2013	Diagnosis: Probable preterm labour spontaneous rupture of membranes. Description: Initially presented at 21+ weeks gestation with vague history of possible SRM. Admitted to hospital for overnight observation and then reviewed weekly at DAU at St Johns Hospital Livingston. Diagnosis of SRM more probable at 23 weeks. Treated with 10 days erythromycin and prophylactic steroids at 24 weeks. Continues to be seen thrice weekly as an outpatient at St Johns. Patient did not inform research team. Did not attend for scheduled study visit today, which is when this came to our attention. Had discontinued study medication around 20 weeks gestation due to side effects. Severity: Mild.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Condition still present and unchanged	.
12008	METFORMIN	13FEB2012	09FEB2012	Atonic uterus resulting in massive obstetric haemorrhage. 2 litre loss. Severity: Severe	Life-threatening	N/a	Unrelated	No	Completely recovered	12FEB2012
12008	METFORMIN	16AUG2012	14FEB2012	Diagnosis: Chest Pain Description: Chest pain following LSCS 5/7 days after delivery. Severity: Moderate	Involved or prolonged inpatient hospitalisation		Unrelated	Yes	Completely recovered	16FEB2012
12041	METFORMIN	07NOV2012	07NOV2012	Diagnosis: Termination of pregnancy (TOP) Description: TOP due to confirmed Down's Syndrome by amniocentesis. Severity: severe	Involved or prolonged inpatient hospitalisation	No relevant medical history	Unrelated	No	Completely recovered	10NOV2012
12056	METFORMIN	16APR2013	30MAR2013	Diagnosis: Fetal Supraventricular Tachycardia Description: Patient attended on LW with a history of reduced fmf. CTL detected FHR of 200bpm. USS diagnosis fetal supraventricular tachycardia. Patient admitted and medicated with flecainide 100mg TDS. Follow-up 30/05/13. Diagnosis: Admitted with reduced fmf. Description: Admitted to antenatal ward with reduced fetal movements. On USS baby found to have cardiac abnormalities - SVT and hydrops. Severity: Moderate	Involved or prolonged inpatient hospitalisation		Unrelated	No	Recovered with sequelae	05APR2013
12060	METFORMIN	16SEP2013	03SEP2013	Diagnosis: Postpartum Haemorrhage. Description: Kwi delivery of male infant. PPH following delivery of 1.6 litres. Severity: Mild	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	05SEP2013
12076	METFORMIN	07NOV2013	04NOV2013	Diagnosis: ?Admitted DVT. Description: Client c/o groin and leg pain. ? DVT. Admitted to antenatal ward overnight. Dopplers normal. Follow-up 19/11/2013. Diagnosis: Right sided groin pain. Description: Complained of right sided groin pain and vulval swelling. Consultant review - admitted to ward for observation for ? pelvic thrombosis. XXX and anti-embolic treatment. Doppler of right leg 05/11/13 - no evidence of deep vein thrombosis. Discharged home 05/11/13. Severity: Mild.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	18NOV2013
12079	METFORMIN	20JAN2014	08DEC2013	Diagnosis: Suspected Urinary Tract Infection. Description: Self referred to labour ward triage with abdominal pain, back pain, diarrhoea (once only) and reduced fetal movements for one week. Antibiotics given for suspected urinary tract infection. Not admitted - discharged home after 2hrs 10 minutes. Severity: Mild	Other significant medical events (as defined in protocol)		Unrelated	No	Completely recovered	23DEC2013
12093	METFORMIN	03APR2014	30MAR2014	Diagnosis: Postpartum Haemorrhage. Description: Postpartum haemorrhage of 1500mls following IOL, prolonged labour and vaginal delivery. Postpartum syntocinon commenced. catheterised. Hb 100g/l. Discharged home 01/04/2014. Severity: Moderate.	Involved or prolonged inpatient hospitalisation		Unrelated	Yes	Completely recovered	01APR2014
12096	METFORMIN	06MAR2014	13FEB2014	Diagnosis: ? Preterm labour/Reduced Fetal Movements. Description: Admitted to antenatal ward with tightenings - speculum os closed. Reduced fetal movements for 1 week. Admitted for overnight observation. Tightenings settled. Discharged home 14/2/14 with routine follow-up in antenatal clinic. Severity: Mild.	Involved or prolonged inpatient hospitalisation		Unrelated	Yes	Completely recovered	14FEB2014
12099	METFORMIN	31DEC2013	30DEC2013	Diagnosis: Suspicion of pre-eclampsia. Description: Admitted with headaches, high blood pressure and proteinuria at 25+1. Remains an inpatient for observation. Not on any medication. Severity: Moderate	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	03JAN2014
13082	METFORMIN	07FEB2012	04FEB2012	Admitted for labile BP at 39 weeks. Commenced on labetalol 100mgs BD and IOL booked. Inpatient on Mat ward since 04/02/12. Completion of data 09/05/13: Participant delivered on 08.2.12 and was discharged on 11.2.12. On review of medical notes, hypertension resolved postnatally; was not discharged on any anti-hypertensives. Severity: Mild	Involved or prolonged inpatient hospitalisation	Has history of hypertension, was on irbesartan 75mgs daily in 2009. Not on treatment since	Unrelated	Yes	Completely recovered	11FEB2012
13147	METFORMIN	04MAY2012	28FEB2012	Diagnosis: Recurrent PV bleeds from cervical erosion Description: Has had recurrent PV bleeds of varying amounts throughout pregnancy. Diagnosed as cervical erosion. Not admitted at any stage. IOL booked at term due to this history. Severity: Moderate	Other significant medical events (as defined in protocol)		Unrelated	Yes	Completely recovered	15MAY2012
13209	METFORMIN	31AUG2012	24AUG2012	Diagnosis: Inpatient stay for over 24hrs for investigations. All negative. Description: Reported chest pain and calf pain at day 4 postnatal. Admitted to hospital for 2 days for chest x-ray and blood tests to rule out PE. Was commenced on Fragmin for 6/52 and attended for leg Doppler x 2. Severity: Moderate	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	04SEP2012

Section 13. Serious Adverse Events

13.1.2 SAE related to the mothers - Details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	SAE - date of report	SAE - date of event	Description of SAE	Expedited Reporting Criteria	Relevant History	SAE_related_coded	SAE_expected_coded (Y/N)	SAE_outcome_coded	SAE - date of recovery
13248	METFORMIN	24APR2012	22MAR2012	Diagnosis: Abdominal Pain due to IBS Description: Admitted to emergency room at 17:40 with abo pain 22/03/12. ? Renal cholic, admitted to ward and investigated. Treated with IV antiemetics as vomiting. USS normal. Discharged 24/03/12 with oral antiemetics. Discharge diagnosis IBS. Participant reported diarrhoea and abdominal cramps for several days before attending hospital, whilst on study medication. Severity: Moderate	Involved or prolonged inpatient hospitalisation		Possibly	Yes	Completely recovered	24MAR2012
13528	METFORMIN	19MAR2013	12MAR2013	Diagnosis: ?DVT Description: Patient admitted to antenatal ward on 12.3.13 with shortness of breath and chest pain ?DVT. Had all appropriate investigations including chest xray, leg Doppler and ECG. All investigations normal. Received fragmin 10.000iu BD until diagnosis. Discharged home the following day to normal care. for follow up in consultant clinic 22.3.13. Severity: Moderate	Involved or prolonged inpatient hospitalisation		Unrelated	Unk	Recovered with sequelae	19MAR2013
13551	METFORMIN	05MAR2013	02MAR2013	Diagnosis: Emcs for fetal distress, followed by 5000ml PPH and hysterectomy. Description: Background: NI has been having close monitoring in pregnancy for raised BP. She was commenced on labetalol on 2.1.13. Had subsequent admission for raised BP 6.2.13 (not an SAE according to protocol). Discharged back to community care the following day. Admitted to antenatal ward again with raised BP on 25.2.13. Remained an inpatient until IOL commenced 28.2.13 at 20.30 at 38 weeks gestation. Baby: EMCS for fetal distress (CTG and FBS) under GA. Baby delivered at 19.13, apgars 4 at 1 minute. 9 at 10 minutes. Cord P/bs 7.18, 7.24. Baby was admitted to NICU overnight due to NI being transferred to Whiston. Re-united with mum when returned to Liverpool Women's. NI: Following emcs NI suffered from major haemorrhage totalling 5000ml. A hysterectomy was undertaken. NI received a total of 7 units of blood (including 500ml cell salvaged blood) and 1 unit of FFP. She also had a dextrose infusion to correct transfusion-related hypo	Involved or prolonged inpatient hospitalisation Life-threatening	Raised BP, start 2.1.13, ongoing, medication required.	Unrelated	Yes	Condition improving Recovered with sequelae	07MAR2013
13553	METFORMIN	23JAN2013	21JAN2013	Diagnosis: Admitted for raised BP and proteinuria. Description: MR was admitted to the antenatal ward on 21/01/13 for raised BP and proteinuria at 26+3/40. She has been commenced on labetalol 200mg BD and is staying in for observation presently. F/up 25/01/13: Her BP dropped and the labetalol dose was reduced to 100mg BD. She was discharged home on 24.1.13 with an appointment at the day ward for a BP profile and CTG on Monday 28.1.13 with the plan to stop labetalol if BP normal. Severity: Mild	Involved or prolonged inpatient hospitalisation	Pregnancy induced hypertension with significant proteinuria, start 2008, not ongoing, medication required. Pregnancy induced hypertension, start 2010, not ongoing, medication required.	Unrelated	Yes	Completely recovered	24JAN2013
14035	METFORMIN	28NOV2011	28NOV2011	Had upper right quadrant pain since approx 28 weeks. Admitted to hospital on 26/11/2011 and discharged home on the 27/11/2011. No cause for this has been found. LFTs raised and pain now increasing admitted to hospital again today for urgent induction of labour planned. Her hospital consultant has recommended that the study drugs should be stopped.	Involved or prolonged inpatient hospitalisation	N/A	Unrelated	No	Recovered with sequelae	06DEC2011
14161	METFORMIN	24DEC2012	24DEC2012	Neville Barnes Forceps delivery on 24/12/2012 at 01.17am. Postpartum haemorrhage of 1500ml, thought to be in part due to a spurting blood vessel from episiotomy wound and vaginal tears. Transferred to high dependency unit. Hb 7.7g/dl at 07.16am. Patient offered blood transfusion, she is unsure at time of reporting SAE whether she wishes to accept this. Participant withdrew from the EMPOWaR study on 11/11/2012 at her request. She was taking one study tablet per day up until that date.	Involved or prolonged inpatient hospitalisation	N/A	Unrelated	No	Completely recovered	25DEC2012
14162	METFORMIN	12DEC2012	11DEC2012	Emergency L.S.C.S for failure to progress in labour. Post Partum Haemorrhage of 1200mls	Involved or prolonged inpatient hospitalisation	N/A	Unrelated	No	Completely recovered	14DEC2012
14303	METFORMIN	08AUG2013	08AUG2013	Post Partum Haemorrhage 1200mls.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	08AUG2013
16029	METFORMIN	09MAY2013	03SEP2012	Abdo pain and reduced fetal movements. Description: Abdo pain - intermittent - and reduced fetal movements. Admitted for observation. Contraction type pains 1:20 mins. Settled. Discharged 05/09/2012. Severity: Mild	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	05SEP2012
16121	METFORMIN	24JUN2013	30MAY2013	Diagnosis: Pyelonephritis Description: Pyelonephritis - ascending UTI involving pyelum, fever, tachycardia, abdo/back pain. Severity: Mild	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	04JUN2013
21089	METFORMIN	28MAR2014	17JAN2014	Diagnosis: Hyperemesis. Description: Admitted to maternity ward overnight with hyperemesis. Severity: Mild.	Involved or prolonged inpatient hospitalisation	Removal of brain hernia (Arnold-Chiari malformation), 18/01/2013.	Unrelated	No	Completely recovered	18JAN2014

Section 13. Serious Adverse Events

13.1.2 SAE related to the mothers - Details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	SAE - date of report	SAE - date of event	Description of SAE	Expedited Reporting Criteria	Relevant History	SAE_related_coded	SAE_expected_coded (Y/N)	SAE_outcome_coded	SAE - date of recovery
24010	METFORMIN	28SEP2013	16SEP2013	Diagnosis: Emergency Caesarean Section Post Partum Haemorrhage 1500mls. Description: Caesarean section for fetal distress at T+15 during induction of labour. Estimated blood loss at caesarean section 1500mls. Baby's birth weight 3868 - all normal. Severity: Moderate	Involved or prolonged inpatient hospitalisation	PCOS, ongoing, medication not required.	Unrelated	Unk	Completely recovered	18SEP2013
25180	METFORMIN	25JUN2013	14JUN2013	Diagnosis: Pain and ?Pyelonephritis. ?Cholelithiasis. Description: Admitted 14/06/13 overnight to Chesterfield Royal Hospital with dysuria, back pain, feeling unwell. Intravenous antibiotics overnight, discharged 15/06/13 on oral antibiotics. admitted Scunthorpe Hospital 17/06/13 overnight with severe right upper abdominal pain. Antibiotics changed. Ultrasound scan diagnosed cholelithiasis. Discharged 18/06/13 home with antibiotics and advice to see surgical review post pregnancy and low fat diet. Severity: Moderate	Involved or prolonged inpatient hospitalisation	Asthma, ongoing, medication required.	Unrelated	No	Condition improving	
25232	METFORMIN	17OCT2013	14OCT2013	Diagnosis: Preterm Labour Spontaneous Rupture of Membranes. Description: Spontaneous rupture of membranes occurred 14/10/2013 at 13.30. No uterine activity. On 15/10/2013 developed maternal tachycardia and increase of white blood cells. Decision made at 10:50 on 15/10/13 to induce labour. Labour augmented with syntocinon infusion. Live baby girl born on 16/10/2013 at 07.14hrs. Severity: Mild.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	16OCT2013
25264	METFORMIN	15AUG2013	08AUG2013	Diagnosis: benign Intracranial Hypertension. Description: Admitted to Hallamshire Hospital with headache due to this. Had lumbar puncture to drain some CSF. Symptoms resolved, had one night in hospital. Severity: Moderate.	Involved or prolonged inpatient hospitalisation	Benign Intracranial Hypertension, started in 2009, ongoing, medication not required.	Unrelated	No	Completely recovered	09AUG2013
25264	METFORMIN	01OCT2013	26SEP2013	Diagnosis: Raised intra-cranial pressure. Description: Admission to Chesterfield Royal Hospital with headache, blurred vision, tinnitus, nausea 26/09/13. Lumbar puncture eased symptoms but headache marked after procedure and thought to be related to same. Care continued with analgesic therapy and physio. Severity: Mild.	Involved or prolonged inpatient hospitalisation	Idiopathic Intracranial Hypertension, start spring 2009, end late 2011, and received medication between these dates. Diagnosed in 2009, ongoing and no medication required as contra-indicated in pregnancy.	Unrelated	Yes	Condition improving	
25459	METFORMIN	11APR2014	06APR2014	Diagnosis: Left Calf Pain ?Thrombosis. Description: Admitted with unilateral calf pain. No redness or swelling, x1 dose anti-coagulant and analgesia given. Severity: Mild.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	07APR2014
25459	METFORMIN	17JUN2014	16JUN2014	Diagnosis: Right ovarian cyst Admitted to birth centre with right sided abdominal pain on 16.06.14. C/section performed 17.06.14. Severity: Mild	Involved or prolonged inpatient hospitalisation	Right adnexal cyst (15/03/14)	Unrelated	No	Completely recovered	17JUN2014
11263	PLACEBO	29MAY2012	27MAY2012	Diagnosis: Post partum haemorrhage Description: Required delivery by caesarian section for failure to progress into labour. Had atonic post partum haemorrhage of 2000mls requiring examination under anaesthetic and use of Bakri balloon. Severity: Moderate	Life-threatening Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	30MAY2012
11323	PLACEBO	29MAY2012	20MAY2012	Diagnosis: Inconclusive Description: Admitted with shortness of breath and chest pain at 32 weeks gestation. Investigated thoroughly with CTPA, upperabdo ultrasound and blood tests but all investigation negative. Symptoms settled spontaneously. Severity: Moderate	Involved or prolonged inpatient hospitalisation	Asthma, ongoing, medication required Smoker, ongoing	Unrelated	No	Completely recovered	22MAY2012
11335	PLACEBO	21JUN2012	19JUN2012	Diagnosis: Post partum haemorrhage Description: Delivered by elective caesarian section on 19/06/12. Developed bleeding secondary to uterine atony following delivery while in recovery area. Rushed to theatre for EUA under GA. Haemorrhage managed with Bakri balloon. Estimated blood loss 2000mls. Severity: Moderate	Involved or prolonged inpatient hospitalisation Life-threatening		Unrelated	No	Completely recovered	21JUN2012
11643	PLACEBO	20MAR2013	13MAR2013	Diagnosis: Abdominal Pain. Description: Admitted with abdominal pain, originally thought to be ligamentous. Developed diarrhoea and vomiting Saturday 16/03/13. Stool sample result on 19/03/13 - c. diff. 20/03/13 well, no D + V since 18/3/13, commenced metronidazole. For discharge home today. Severity: Severe Follow-up 20/02/2014: Diagnosis: Clostridium Difficile Diarrhoea. Admitted with abdominal pain. Developed diarrhoea and vomiting during admission. Stool culture +ve for C.diff. Treated with IV fluids and oral metronidazole. Discharged home on 20/03/2013. Severity: Moderate.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	20MAR2013

Section 13. Serious Adverse Events

13.1.2 SAE related to the mothers - Details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	SAE - date of report	SAE - date of event	Description of SAE	Expedited Reporting Criteria	Relevant History	SAE_related_coded	SAE_expected_coded (Y/N)	SAE_outcome_coded	SAE - date of recovery
11714	PLACEBO	30SEP2013	27SEP2013	Diagnosis: Large Blood Loss - 1500ml. Description: Emergency c/s for failure to progress in labour. 1500ml blood loss at delivery. Follow-up 20/02/14. Diagnosis: Post Partum Haemorrhage. Atonic postpartum haemorrhage following emergency caesarean section for failure to progress in the 1st stage of labour. Estimated blood loss 1500ml. Severity: Moderate.	Life-threatening/ Involved or prolonged inpatient hospitalisation	Gestational Diabetes Mellitus. 09/07/13. ongoing, no medication required.	Unrelated	No	Completely recovered	03OCT2013
11786	PLACEBO	07OCT2013	04OCT2013	Diagnosis: Pre-term rupture of membranes. Description: Spontaneous pre-term. pre-labour rupture of membranes. Severity: Severe. Follow-up 20/02/14. Diagnosis: Spontaneous preterm rupture of membranes. Preterm SRM at 25+ weeks gestation. Managed as an outpatient until 28+ weeks when developed blood stained liquor. Admitted to hospital on 24/10/13. Managed conservatively as an inpatient until 4/11/13 when went into labour. Baby delivered on 4/11/13. Severity: Moderate.	Involved or prolonged inpatient hospitalisation	Nil of note.	Unrelated	No	Completely recovered	04NOV2013
11940	PLACEBO	04JUN2014	02JUN2014	Diagnosis: Respiratory Tract Infection. Presented with cough and feeling generally unwell at 37+ weeks gestation. Already taking amoxicillin and prednisolone prescribed by GP. Also complaining of reduced fetal movements. Admitted to hospital for optimisation of treatment and observation. Chest xray normal. Reviewed by respiratory physician and symptoms felt to be improving, likely viral origin. no further antibiotics or prednisolone required. advised to monitor PEFR and for GP to refer to outpatient respiratory clinic as necessary. Following Obstetric review. in view of persistently reduced fetal movements and recent diagnosis of gestational diabetes decision made for induction of labour. Severity: Mild.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	04JUN2014
12010	PLACEBO	28MAR2012	09MAR2012	Post partum haemorrhage - 500mls. At emergency section	Other significant medical events (as defined in protocol)		Unrelated	Yes	Completely recovered	11MAR2012
12013	PLACEBO	26MAR2012	26MAR2012	Post partum haemorrhage - 600ml following emergency section	Other significant medical events (as defined in protocol)		Unrelated	Yes	Completely recovered	26MAR2012
12043	PLACEBO	11MAR2013	07MAR2013	Diagnosis: Abdominal Pain Description: Client admitted at 35+6/40 with abdominal pain - ?UTI. ?Preterm labour ?D+V. Severity: Mild	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	09MAR2013
12059	PLACEBO	25JUL2013	27JUN2013	Diagnosis: EMCS. Description: EMCS at 33/40 for reduced fmf. reduced AFI. No EDF. Severity:	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	28JUN2013
12074	PLACEBO	04NOV2013	12OCT2013	Diagnosis: Small bleed per vaginum. Description: Patient self referred to labour ward triage with small bleed per vaginum and mild abdominal pain/ Speculum performed. cervical OS closed. Scan - no problems seen. Admitted to antenatal ward overnight for observation. Severity: Mild	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	13OCT2013
12077	PLACEBO	14NOV2013	13NOV2013	Diagnosis: Pre-term labour. Description: Preterm spontaneous vaginal delivery at 34+6 weeks of female infant. Severity: Mild.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	15NOV2013
12086	PLACEBO	02OCT2013	08SEP2013	Diagnosis: SRM @ 18+4 Medical TOP. Description: Medical termination of pregnancy due to SRM. Spontaneous vaginal delivery of foetus. Severity: Moderate.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	12SEP2013
12091	PLACEBO	26MAR2014	23MAR2014	Diagnosis: Baby admitted to SCBU with meconium aspirate. Description: Patient had emergency c/s for fetal distress. Baby had poor apgar and was admitted to SCBU - CTU. Ventilated. Baby improving and extubated 25/3/2014. Mum discharged home 26/05/14. Severity: Severe. Follow-up 19/05/14: Baby ventilated after delivery - poor apgars. Baby discharged home 06/04/14. No follow-up. Mum contacted baby doing well - no concerns.	Involved or prolonged inpatient hospitalisation		Unrelated	Yes	Completely recovered	16MAY2014
12104	PLACEBO	13MAR2014	11MAR2014	Diagnosis: ?UTI. Description: Admitted to triage via GP with history of pelvic pain. vomiting and feeling unwell. Pyrexia on admission. Admitted to antenatal ward for intravenous antibiotics and antiemetics. IV fluids. Discharged home with oral antibiotics 13/3/14. Apyrexial since admission. Severity:	Involved or prolonged inpatient hospitalisation		Unrelated	Yes	Completely recovered	13MAR2014
13007	PLACEBO	05AUG2011	28JUL2011	Diagnosis: prolonged hospital stay. Participant induced for suspected IUGR at 40 weeks+1day. Baby's BW below 9th centile. therefore needed blood sugar recordings (TBGs) pre and post feeds as per protocol. Baby BW 2.72kgs. These were completed within 24hrs. This resulted in a prolongation of hospital stay. 12/08/2011 IUGR is an Expected outcome and is being routinely collected as a secondary outcome of this study. Therefore. not a SUSAR but a SAR.	Involved or prolonged inpatient hospitalisation	2008 - normal vaginal delivery at term (41 weeks). 3100gms	Possibly	Yes	Completely recovered	28JUL2011
13144	PLACEBO	11MAY2012	31MAR2012	Diagnosis: Symphysis Pubis Pain. Physiological Faints in Pregnancy Description: Occasional fainting episodes and episodes of raised BP over past 6 weeks. 48hrs admission on ward for observation due to this. Also reports SPD. IOL at 36+7 booked for this reason. However on admission to IOL suite was found to be 36+6. reasons for IOL did not warrant delivery at this gestation. had been incorrectly calculated when IOL booked. therefore IOL rebooked and admission at 38+1 on 22/05/12. Severity: Moderate	Involved or prolonged inpatient hospitalisation		Unrelated	Yes	Completely recovered	22MAY2012

Section 13. Serious Adverse Events

13.1.2 SAE related to the mothers - Details

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13301	PLACEBO	19OCT2012	17OCT2012	Diagnosis: Intrapartum and postpartum haemorrhage of 2000mls Description: This lady was induced at 41+5 for postdates pregnancy. She received 2mg x 2 of Prostin gel. Prior to ARM she had fresh bleeding PV. Oligoic breech lie was diagnosed on USS. She was taken to theatre for emergency caesarean section. Intrapartum haemorrhage = 1000ml, postnatal haemorrhage = 1000ml. Total EBL = 2000ml. Baby born with Apgars 10 at 1 minute and 10 at 5 minutes. Cord pH's 7.26 and 7.28. Baby's weight = 4440g. AP well on demand. The lady was transfused 2 units of blood in theatre. Condition currently improving, today Hb 7.8g/dl, for further 2 units of blood. Follow-up 24/10/12: This lady was discharged home with baby from the postnatal ward on Sunday 20.10.12 at 14.00. Her HB was 8.7g/dl and she was prescribed ferrous sulphate 200mg TDS. Severity: Severe	Involved or prolonged inpatient hospitalisation Life-threatening	Previous PPH and subsequent blood transfusion in 2007, medication required, PCOS, ongoing, no medication required.	Unrelated	Unk	Completely recovered	20OCT2012
13473	PLACEBO	04JAN2013	03JAN2013	Diagnosis: Neonatal BM's low. Baby admitted to NICU. Lowest BM 1.7mmol Description: EP was delivered via emergency c/s. IOL at 36+3 for pre-eclampsia on 3.1.13. Baby was transferred to the neonatal unit for 24 hours post delivery for low BM's. Lowest BM 1.7mmol, baby tube fed only, no IV fluids required. Baby maintaining BM's and back on postnatal ward with mum after 24 hours. Discharged home 5.1.13, no follow-up anticipated. Severity: Mild	Involved or prolonged inpatient hospitalisation		Possibly	Yes	Completely recovered	04JAN2013
13591	PLACEBO	07MAY2013	30APR2013	Diagnosis: Hospital admission via ambulance with gall stones. Description: RB was admitted to Royal Liverpool Hospital on 30.04.13 via ambulance with chronic back pain. She is 3 weeks postnatal. Was kept nil by mouth for 24 hours and had a USS which diagnosed gall stones. Received antibiotics and analgesia whilst an inpatient and was discharged on 01.05.13. RB reports awaiting blood tests to see if presence of infection and has an appointment with a consultant at the Royal on 16.04.13. NB: Information obtained verbally from the patient only, no access to medical notes as attended a different hospital. Severity: Moderate	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	01MAY2013
13705	PLACEBO	02AUG2013	19JUL2013	Diagnosis: APH 31+2/40. Description: Patient admitted to antenatal ward with APH at 31+2/40. Had x 2 small PV bleeds at home. HVS sent. Speculum NAD. Discharged home after 24 hours as nil further PV bleeding. Taking ferrous sulphate. Severity: Mild.	Involved or prolonged inpatient hospitalisation		Unrelated	Yes	Completely recovered	20JUL2013
13712	PLACEBO	02AUG2013	23JUL2013	Diagnosis: Obstetric Cholelithiasis. Description: Patient presented at 31+5/40 with localised itching. Bile acids taken and indicate obstetric cholelithiasis. Patient prescribed Ursodeoxycholic acid 300mg TDS and Chlorphenamine 4mg. IOL booked for 05.09.2013. Having weekly bloods and CTG's. Information obtained from patient via telephone only. Severity: Moderate.	Other significant medical events (as defined in protocol)	Obstetric cholelithiasis in previous pregnancy in 2010. Start 27/01/2010, end 02/02/2010, medication required.	Unrelated	Yes	Completely recovered	06SEP2013
13914	PLACEBO	22JAN2014	15JAN2014	Diagnosis: Threatened Preterm Labour. Moderate rise in BP. Description: Threatened Preterm Labour. Admission to consultant unit following abdominal pains. Fibrinectin test positive. Steroids given to cover for potential preterm birth. BP moderately elevated whilst an inpatient. Discharged after approx. 48hrs and monitored on community. Severity: Mild	Involved or prolonged inpatient hospitalisation		Unrelated	Yes	Completely recovered	17JAN2014
14036	PLACEBO	23NOV2011	22NOV2011	Post-partum haemorrhage 1000mls - maternal collapse transferred to high dependency unit.	Involved or prolonged inpatient hospitalisation Other significant medical events (as defined in protocol)	N/A	Unrelated	No	Completely recovered	23NOV2011
14272	PLACEBO	29MAY2013	18APR2013	Sudden onset very severe headache 18.04.13. Admitted to neurological ward for treatment and lumbar puncture. 24 hour stay. Re-admitted 22.04.13 with re-occurrence of headache - diagnosis - this headache related to lumbar puncture. Resolved after 24 hours and discharged. No further headaches.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	23APR2013
14336	PLACEBO	27NOV2013	26NOV2013	Diagnosis: Post partum haemorrhage and pre-eclampsia. Description: Admitted to High Dependency Unit from theatre recovery after total PPH 700mls (at delivery 400mls) requiring prolonged IV syntocinon treatment. In addition had raised BP requiring medication after admission to HDU. Severity: Moderate.	Involved or prolonged inpatient hospitalisation	Gestational Diabetes, started 07/11/2013, ongoing, no medication required.	Unrelated	No	Recovered with sequelae	29NOV2013
14336	PLACEBO	23OCT2013	17SEP2013	Diagnosis: Abdominal pain cause unknown. Description: Admitted with abdominal pain for observation. Cause unknown. Possible UTI. Possible uterine stretching pain/. Routine blood and urine tests performed. Severity: Moderate.	Involved or prolonged inpatient hospitalisation		Unrelated	Yes	Completely recovered	23SEP2013
14336	PLACEBO	27NOV2013	20NOV2013	Diagnosis: Infective diarrhoea and vomiting. Description: Prolonged episode of diarrhoea and vomiting, followed by dehydration. IV fluid therapy required on admission to hospital on 23/11/2013. Admitted for 24 hours. Had one stat dose labetalol for raised BP whilst an inpatient. Stopped study medication. Severity: Moderate.	Involved or prolonged inpatient hospitalisation	Gestational diabetes, started 07/11/2013, ongoing, no medication required.	Unrelated	No	Completely recovered	24NOV2013

Section 13. Serious Adverse Events

13.1.2 SAE related to the mothers - Details

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Subject Number	Allocated Treatment	SAE - date of report	SAE - date of event	Description of SAE	Expedited Reporting Criteria	Relevant History	SAE_related_coded	SAE_expected_coded (Y/N)	SAE_outcome_coded	SAE - date of recovery
14354	PLACEBO	20DEC2013	17DEC2013	Diagnosis: Threatened pre term labour. Description: GS P2 33 weeks. admitted with PV bleed and irregular tightenings 17.12.13. Prescribed betamethasone and dalteparin. Hospitalised for observation. Severity: Mild	Involved or prolonged inpatient hospitalisation		Unrelated	No	Condition improving Completely recovered	20JAN2014
15031	PLACEBO	27NOV2013	29OCT2013	Diagnosis: Delivery. Description: Postpartum haemorrhage 1400mls. Severity: Moderate	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	30NOV2013
15034	PLACEBO	07NOV2013	24OCT2013	PPH 1600mls. Severity: Moderate	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	25OCT2013
16052	PLACEBO	05JAN2013	27DEC2012	PPH 1800mls Severity: Moderate	Life-threatening		Unrelated	No	Completely recovered	31DEC2012
17036	PLACEBO	12MAR2013	10MAR2013	Diagnosis: Influenza. Description: Inpatient hospitalisation due to influenza. Patient admitted on 10/03/13. Self discharged on 11/03/13 as feeling better. Study medication stopped whilst unwell, to recommence when well. Severity: Moderate. Follow-up 17/06/2014: Diagnosis: Influenza - resulting in raised ALTs requiring scan. Initial SAE reported due to hospitalisation due to influenza. Following this raised ALT levels were noted and a liver scan arranged. This showed an enlarged spleen (consistent with recent influenza. This patient has had raised ALT levels dating back to 2010. Discharged home following scan.	Involved or prolonged inpatient hospitalisation Other significant medical events (as defined in protocol)	Cholecystectomy. 2010 - 30/07/2010.	Unrelated	No	Completely recovered	17JUN2014
17137	PLACEBO	27DEC2013	25DEC2013	Diagnosis: Costochondritis. Description: Admitted with upper abdominal pain - bloods and USS all NAD. Presumed costochondritis. Discharged home 27/12/13. Severity:	Involved or prolonged inpatient hospitalisation	Previous episode of costochondritis	Unrelated	No	Completely recovered	27DEC2013
17137	PLACEBO	20JAN2014	17JAN2014	Admitted to antenatal ward with unstable lie. To remain inpatient until LSCS 24.1.14.	Involved or prolonged inpatient hospitalisation	Episode of costa chondritis	Unrelated	No	Completely recovered	21FEB2014
21033	PLACEBO	23MAY2014	27APR2014	Diagnosis: Abdominal Pain. Likely Costochondritis. Description: Admitted at 33+4 weeks gestation with abdominal pain. Severity: Mild.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	29APR2014
21033	PLACEBO	23MAY2014	11APR2014	Diagnosis: Likely Costochondritis. Description: Admitted at 31+2 weeks gestation for observation/monitoring for left sided chest pain. Investigations generally NAD. Severity: Mild.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Condition improving	
21033	PLACEBO	02APR2014	28DEC2013	Diagnosis: Non-specific chest pain. Description: Admitted via ambulance with suspected clinical suspicion of a pulmonary embolism. Had left pleuritic chest pain, with shortness of breath and collapse. Severity: Mild.	Involved or prolonged inpatient hospitalisation	Caesarean Section. 03/12/2013.	Unrelated	No	Completely recovered	30DEC2013
21069	PLACEBO	19MAR2014	18FEB2014	Diagnosis: Sepsis. Description: Pyrexial and tachycardic in labour. Raised CRP and white cell count, also platelets reduced. Had IV antibiotics, then oral. Went on septic pathway. Severity: Moderate.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	25FEB2014
21093	PLACEBO	23DEC2013	28NOV2013	Diagnosis: Small antepartum haemorrhage. Description: Admitted to maternity ward overnight for observation as PV bleed. Ectropion noted on cervix. Placenta not low-lying. No pain. 23 weeks gestation. Severity: Mild	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	29NOV2013
21100	PLACEBO	22APR2014	16APR2014	Diagnosis: Antepartum and Postpartum Haemorrhage. Description: Admitted via ambulance in advanced labour. Spontaneous rupture of membranes, then APH of 1200mls. Fetal bradycardia, so forceps delivery. Then required MROP and had PPH of 800mls. Total EBL: 2000mls. Returned to delivery suite for close monitoring and had 2 units of blood transfused. Severity: Severe.	Other significant medical events (as defined in protocol)		Unrelated	No	Completely recovered	18APR2014
21109	PLACEBO	09APR2014	03APR2014	Diagnosis: Small APH - nil on examination. Description: Admitted to maternity ward via maternity day unit with lower abdo discomfort/Braxton hicks/ted pv loss/unstable lie. Severity: Mild.	Involved or prolonged inpatient hospitalisation	Gestational Diabetes. 19/03/2014 - 08/04/2014.	Unrelated	No	Completely recovered	05APR2014
21109	PLACEBO	19MAR2014	14FEB2014	Diagnosis: Urinary Tract Infection. Description: Symptomatic of UTI and leukocytes in urine. Admitted for treatment and observation to maternity ward for over 12 hours. Severity: Mild.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	21FEB2014
25165	PLACEBO	07AUG2013	06AUG2013	Diagnosis: Post Partum Haemorrhage. Description: Following an instrumental vaginal delivery of live male infant, participant had a 2.5 litre blood loss per vagina. Oxytocin administered and norepinephrine. Blood loss stopped. HB dropped from 103g/L to 76.0g/L, and 2 units of blood administered. Participant stable and improving. Severity: Moderate.	Involved or prolonged inpatient hospitalisation		Unrelated	Unk	Completely recovered	07AUG2013

Section 13. Serious Adverse Events

13.1.2 SAE related to the mothers - Details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	SAE - date of report	SAE - date of event	Description of SAE	Expedited Reporting Criteria	Relevant History	SAE_related_coded	SAE_expected_coded (Y/N)	SAE_outcome_coded	SAE - date of recovery
25391	PLACEBO	12MAR2014	07MAR2014	Diagnosis: 1). Musculoskeletal Pain. 2). Depression. Description: Admitted to hospital for observation and analgesia for musculoskeletal pain and depression. Severity: Mild.	Involved or prolonged inpatient hospitalisation	Depression/Anxiety, started 2005, ongoing, medication required.	Unrelated	No	Missing	.
53072	PLACEBO	30JUN2014	27JUN2014	Diagnosis: Episode of fitting, unknown cause. Description: Singular episode of fitting 5 days postnatal, unknown cause. Admitted to hospital via ambulance. MRI, CT, Chest X ray and blood tests carried out. No abnormality found, declined inpatient stay overnight for observation and had same day discharge. For follow up at first fit clinic. Severity: moderate. UPDATE (01 Oct 2014): Diagnosis: Further reported 4-5 episodes of left sided numbness and tingling on upper body and face. Description: Reported 4 or 5 acute episodes of tingling commencing in left hand and ascending left side of body to face resulting in a heaviness and numb sensation. All occurred within 3 weeks of P/N fit episode and lasted around 5 minutes in duration. Nil since. Has had further ECG at neurology clinic which was normal. Still awaiting results of EEG and MRI.	Involved or prolonged inpatient hospitalisation Other significant medical events (as defined in protocol)		Unrelated	No	Completely recovered	27JUN2014

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Section 13. Serious Adverse Events

13.2.1 SAE related to the babies

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=449</i>
		<i>Placebo N=223</i>	<i>Metformin N=226</i>	
Number of Patient with a SAE (n)	OVERALL	21	14	35
Number of SAE (n)	OVERALL	21	15	36
Number of SAE by relationship (n)	Possibly	1	4	5
	Unrelated	20	11	31
Number of SAE by expectedness (n)	Yes	1	3	4
	No	20	12	32

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Section 13. Serious Adverse Events

13.2.1 SAE related to the babies (Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		
		<i>Placebo</i>	<i>Metformin</i>	<i>Overall</i>
Number of SAE by outcome (n)	Missing	0	1	1
	Completely recovered	12	5	17
	Condition still present and unchanged	5	4	9
	Condition still present and unchanged Death	0	1	1
	Death	3	2	5
	Recovered with sequelae	1	2	3

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Section 13. Serious Adverse Events

13.2.2 SAE related to the babies - Details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	SAE - date of report	SAE - date of event	Description of SAE	Expedited Reporting Criteria	Relevant History	SAE_related_coded	SAE_expected_coded (Y/N)	SAE_outcome_coded	SAE - date of recovery
11078	METFORMIN	22JUL2011	22JUL2011	Probable congenital cystic adenomatous malformation (CCAM) of fetal lung detected at routine fetal anomaly scan (can only be confirmed after delivery of the baby). Follow-up 20/02/2014. Diagnosis: Congenital cystic adenomatous malformation of lung in baby. CCAM detected on routine fetal anomaly scan at 23 weeks gestation. Subsequently confirmed when child was born. Child underwent uncomplicated thorascopic left lower lobectomy in May 2013. Subsequent follow-up appointment confirms he is well.	Congenital anomaly/birth defect	Obesity	Unrelated	No	Completely recovered	17MAY2013
12006	METFORMIN	13FEB2012	11FEB2012	Stillbirth at term. IUGR - 2610g	Patient died	Maternal Medical History - Osteogenesis imperfecta type 1	Unrelated	No	Death	.
12053	METFORMIN	02SEP2013	02JUN2013	Diagnosis: ?Stillbirth / Neonatal Death. Description: Patient admitted to LW in spontaneous labour. Proceeded to NBF of female infant. Apgars 0 1, 0 5, 0 10. ?Trisomy 21. ?stillbirth / NND. Severity: Severe	Patient died Congenital anomaly/birth defect		Unrelated	No	Condition still present and unchanged Death	.
12056	METFORMIN	30MAY2013	25APR2013	Stillbirth. Description: Cardiac abnormality noted on USS for fetus. SVD of female infant - stillbirth. Severity: Severe	Patient died Congenital anomaly/birth defect		Unrelated	No	Death	.
12083	METFORMIN	08MAY2014	12MAR2014	Diagnosis: Surgery to correct pyloric stenosis. Description: Baby self-referred by parents to A&E with vomiting and dehydration. H/O since 7 days old of vomiting post feeds. 13/3/14 surgery - Ramstedt's Pyloromyotomy. Discharged home 16/3/14. No flu . Seen 7/5/14 at visit 9. All well. Severity: Moderate.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	07MAY2014
12093	METFORMIN	03APR2014	30MAR2014	Diagnosis: Poor Apgars. ?infection. Description: Prolonged rupture of membranes - thick meconium at delivery. Poor Apgars commenced on IV antibiotics. Blood cultures negative after 36hrs. CRP < 3 on 01/04/2014. Baby discharged home 01/04/2014. Severity: Mild.	Involved or prolonged inpatient hospitalisation		Unrelated	Yes	Completely recovered	01APR2014
13147	METFORMIN	14AUG2012	22MAY2012	Diagnosis: Baby diagnosed with PKU Description: Baby diagnosed with PKU on routine blood screening at a week to ten days old. Severity: Severe	Congenital anomaly/birth defect		Unrelated	Yes	Recovered with sequelae	01JUN2012
13528	METFORMIN	05APR2013	24MAR2013	Neonatal hypospadias with chordee. Description: Normal vaginal delivery of male infant at 36+2 (ICL for APH) on 24.3.13. Neonatal hypospadias with chordee noted on paediatric examination. Baby otherwise well and PUing as normal. Referred to urology at Alder Hey for follow-up. Follow-up 04/04/2014. Baby diagnosed with hypospadias and referred to Children's hospital for urology follow-up. Severity: Moderate.	Congenital anomaly/birth defect Involved or prolonged inpatient hospitalisation		Unrelated	Yes	Missing	.
13670	METFORMIN	26JUL2013	21JUL2013	Diagnosis: Bilateral undescended testes. Description: Baby diagnosed with bilateral undescended testes. Baby born via normal vaginal delivery on 21/07/13. Undescended testes noted on 1st exam of the newborn, conducted by community midwife at home on 23/7/13. Baby otherwise well. referred to Alder Hey for follow-up. Severity: Moderate	Congenital anomaly/birth defect		Unrelated	No	Recovered with sequelae	26JUL2013
21095	METFORMIN	21MAR2014	20MAR2014	Diagnosis: No diagnosis yet. Description: Baby transferred to neonatal unit jittery/poor feeding/low BMS. Informed by paed. had significantly low BM's/hypoglycaemia. Raised lactate levels. Septic screen. Severity: Moderate.	Other significant medical events (as defined in protocol) Involved or prolonged inpatient hospitalisation	Depression (Parent) prior to pregnancy. ongoing medication required. Urine Infection (Parent). 17/03/2014. ongoing medication required.	Possibly	No	Completely recovered	23MAR2014
21099	METFORMIN	21MAR2014	15MAR2014	Diagnosis: Significant Neonatal Jaundice. Description: Baby admitted from home to paediatric ward with significant neonatal jaundice. Phototherapy treatment required. Severity: Severe.	Involved or prolonged inpatient hospitalisation Other significant medical events (as defined in protocol)	Raised BP (Parent). 06/03/2014 - 12/03/2014. no medication required.	Unrelated	No	Completely recovered	18MAR2014
25135	METFORMIN	09JUL2013	08JUL2013	Diagnosis: Congenital Malformation. Description: Circular thoracic lumbar spine lesion. Central 1 x 0.5cm vascular area. within 3 x 3 cm area of hypopigmentation. (No hair). ? vascular malformation / occult spinal dysraphism. Follow-up 12/11/13: Diagnosis of Aplasia Cutis Congenita made 11/09/13. Severity: Mild Follow-up 28/01/14: Dermatologist reports evidence of Livedo. more likely livedo racemosa. Investigating for systemic connective tissue disease and full lupus screen. Mother reported (09/11/14) clones in all 4 limbs of infant therefore referred to neurologist to investigate any central nervous system vasculopathy or abnormality. Severity: Moderate.	Congenital anomaly/birth defect		Possibly	No	Condition still present and unchanged	.

Section 13. Serious Adverse Events

13.2.2 SAE related to the babies - Details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	SAE - date of report	SAE - date of event	Description of SAE	Expedited Reporting Criteria	Relevant History	SAE_related_coded	SAE_expected_coded (Y/N)	SAE_outcome_coded	SAE - date of recovery
25180	METFORMIN	25OCT2013	15OCT2013	Diagnosis: Aortic Stenosis. Description: Mother reported today that an ECG performed at Sheffield Children's Hospital on 15/10/13 had shown an abnormality. F.U. appointment today (25/10/13) in Sheffield. Mother reported she had been told Aortic Stenosis was evident. No actual hard copy reports yet seen by research staff. Will seek to obtain ASAP. Severity: Moderate Follow-up 05/11/13. Diagnosis (Mild to moderate aortic stenosis) confirmed by Echo. Severity: Mild Follow-up 28/01/14. Cardiology review by Dr JD Thomson at Sheffield Northern Hospital (working out of Children's Heart Unit in Leeds) in Dec 2013 concluded Aortic Stenosis more significant than previously presented and at 'Moderate Plus Range'. Likely to require intervention in first year of life. Severity: Moderate.	Congenital anomaly/birth defect		Unrelated	No	Condition still present and unchanged	.
25180	METFORMIN	11SEP2013	08SEP2013	Diagnosis: Mildly dilated lateral posterior ventricular horns seen on cephalic ultrasound scan of infant of participant on 10/09/13. Description: Postnatal scan performed to follow-up antenatal scans showing ventricular measurements at upper end of normal range. Severity: Mild.	Congenital anomaly/birth defect		Possibly	No	Condition still present and unchanged	.
25459	METFORMIN	29JAN2014	28JAN2014	Diagnosis: Left unilateral talipes. Description: Had anomaly scan at 20 weeks gestation - the baby was noted to have left unilateral talipes. Severity: Moderate. Follow-up 01/07/14. Diagnosis: Fixed Talipes left foot. Fixed talipes. Back/hips normal. Initial plaster applied. To be replaced weekly and continue correction programme. Detected on 20/40 anomaly scan. Severity: Moderate.	Congenital anomaly/birth defect	Mother: Right adrenal cyst. started 15/11/2013. ongoing.	Possibly	No	Condition still present and unchanged	.
11295	PLACEBO	01FEB2012	31JAN2012	Diagnosis: Congenital cardiac defect Description: Major complex cardiac defect diagnosed on fetal anomaly scan on 31/1/12 - double outlet right ventricle, VSD, transposition of the great arteries, likely pulmonary stenosis. Severity: Severe Follow-up 20/02/14. Diagnosis: Tetralogy of Fallot in fetus/baby. Tetralogy of Fallot detected on routine anomaly scan. Baby monitored after birth and continues to be followed up by the paediatric cardiology clinic. Corrective surgery is planned for Spring 2014.	Congenital anomaly/birth defect	Obesity	Unrelated	No	Condition still present and unchanged	.
11536	PLACEBO	17JUN2013	09MAR2013	Diagnosis: Infection. SVT. Description: baby admitted to RHSC, Edinburgh at 8 days old. diagnosed with an infection at that time. At 12 days old diagnosed with SVT. Severity: Moderate	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	23MAR2013
11786	PLACEBO	28APR2014	04NOV2013	Diagnosis: Premature Birth. Description: Born by spontaneous vaginal breech delivery at 30+1 weeks gestation following spontaneous rupture of membranes at 25 weeks gestation. Admitted to neonatal intensive care unit at RIE until 19/11/13 then transferred to Special Care baby Unit at St John's Hospital Livingston until 27/11/13 then transferred to the Royal Hospital for Sick Children, Edinburgh for surgery on inguinal herniae. Discharged on 19/01/14. Has had several readmissions to SJH for problems with feeding and suboptimal weight gain. Has a persistent patent ductus arteriosus and has recently been referred to Yorkhill Hospital Glasgow for surgical repair of this. This is a complication of prematurity, not a congenital anomaly. Severity: Moderate.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Condition still present and unchanged	.
11851	PLACEBO	08APR2014	03APR2014	Diagnosis: Right testicular hydrocoele, abnormal left testicle. Description: Right testicular hydrocoele, abnormal left testicle. Awaiting ultrasound scan and paediatric surgical review. Severity: Mild.	Congenital anomaly/birth defect		Unrelated	No	Condition still present and unchanged	.
12016	PLACEBO	10SEP2012	21APR2012	Diagnosis: Meconium Aspiration 1. Meconium Aspiration 2. Persistent Pulmonary Hypertension Severity: Severe	Involved or prolonged inpatient hospitalisation Life-threatening		Unrelated	No	Completely recovered	28APR2012
12039	PLACEBO	16APR2013	24MAR2013	Diagnosis: Respiratory Distress. Description: Baby admitted to SCBU following EMCS for respiratory distress and ? sepsis. Severity: Mild	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	28MAR2013
12059	PLACEBO	16SEP2013	28JUN2013	Diagnosis: IUGR. Description: Baby admitted to SCBU following C-section due to IUGR and absent EDF. Delivery at 33+3 weeks. Severity: Moderate.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	18JUL2013
12092	PLACEBO	23JUL2014	11JUN2014	Diagnosis: Upper respiratory infection. Viral gastroenteritis. Admitted to children's accident and emergency department with a history of pyrexia and being unsettled and decreased feeding. Lumbar puncture performed. IV antibiotics. IV fluids. Urine NAD. Blood cultures negative. Rhinovirus and enterovirus positive. No physiso needed. CSF negative. discharged home 14/06/2014. No follow-up. Severity: Moderate.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	23JUL2014
12111	PLACEBO	22AUG2014	02JUN2014	Diagnosis: weight loss and urinary tract infection Description: attended accident and emergency with vomiting after feeds and weight loss. Commenced on IV antibiotics as urine nitrite positive. treated for urinary tract infection. Allowed home on leave between IV antibiotic doses 04/06/14. Urine pure growth of e.coli. Discharged home 04/06/14 with 7 days of trimethoprim. No follow up needed Severity: moderate	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	19AUG2014

Section 13. Serious Adverse Events

13.2.2 SAE related to the babies - Details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	SAE - date of report	SAE - date of event	Description of SAE	Expedited Reporting Criteria	Relevant History	SAE_related_coded	SAE_expected_coded (Y/N)	SAE_outcome_coded	SAE - date of recovery
13496	PLACEBO	14FEB2013	11FEB2013	Diagnosis: Baby admitted to NICU for low blood glucose Description: EH diagnosed as gestational diabetic at 36 weeks. managed on diet control only. Had elective caesarian section on 11.02.13 at 11am. Baby cord blood 2.4mmol. was grunting and had low TBG's on ward. Was admitted to NICU at 22:35 hours 11.02.13. Discharged back to ward with mum at 14.15 the next day 12.02.13. Mum and baby discharged home 13.02.13 baby asymptomatic of hypoglycaemia and BF well on discharge. No anticipated follow up. Severity: Mild	Involved or prolonged inpatient hospitalisation		Possibly	Yes	Completely recovered	13FEB2013
13591	PLACEBO	26JUL2013	20APR2013	Date of onset: ?? 20/04/2013 (i.e. from 2 weeks old - see below). Diagnosis: Baby developed vascular malformation. Description: Baby diagnosed with a venous malformation on upper shoulder. The baby was born on 6th April and nil was noted at birth or on the first paediatric examination. At the 6 week postnatal check with the GP a birth mark was noted and thought to be a haemangioma of infancy. I saw mum at 3 month postnatal visit on 4th July, when I first became aware of the birth mark. but as it wasn't picked up until the baby was 6 weeks old, this was outside of the 28 day postnatal reporting period for EMPOWaR. Mum has since been in touch to say that the birth mark has now been diagnosed as a venous malformation as it is the blood vessels below the actual mark which are causing it to grow and cause a lump. On further questioning mum thinks that the mark may have been there since 2 weeks of life but initially very small. Baby has been referred to a specialist at Alder Hey for management and possible removal	Congenital anomaly/birth defect	See previous SAE dated 7.5.13: Mother had hospital admission for gall stones at 24 days post natal. Having follow up at Royal Liverpool Hospital.	Unrelated	No	Recovered with sequelae	26JUL2013
14145	PLACEBO	18JUN2012	18JUN2012	Date of onset: 18.06.12 (cardiac anomalies found on ultrasound). Initial: Fetus has transposition of the great arteries with a ventricular septal defect and suspected coarctation of the aorta. Fetal echocardiogram done at Leeds General Infirmary on 15.06.12. Follow-up: Baby was born at Leeds General Infirmary (LGI) as he was known to have a serious cardiac anomaly SSAE sent at the time. Baby died on 19th October 2012 at LGI. According to his mum (the study participant) this was due to infection following major cardiac surgery. I am awaiting confirmation of these details from the research midwives at LGI and will forward them to you asap.	Congenital anomaly/birth defect	Participant (mother) changed from the study drug (either Metformin or Placebo) to Metformin on 01.09.12. She had been admitted to hospital in threatened premature labour and had forgotten to take her study drugs with her. She was prescribed Metformin by t	Unrelated	No	Death	.
14413	PLACEBO	03MAR2014	03MAR2014	Diagnosis: Baby delivered with some abnormalities. Description: C/section at 3/3/14 at 12.30 - baby found to have abnormal toes, fingers and anteriorly placed anus. Left hand is normal. Right hand has a middle short finger with hypoplastic nail and is twisted. Index finger has an accessory digit. On the right foot the big toe has syndactyly and the 3rd toe is not formed. On the left foot, the big toe is syndactyly and the 3rd toe not formed. There is only one centimetre between the anus and the posterior forchette. Severity: Severe.	Congenital anomaly/birth defect		Unrelated	No	Condition still present and unchanged	.
15028	PLACEBO	17JUN2013	17JUN2013	Diagnosis: Neonatal Death on day 5. Male infant. Description: Neonatal death of infant on day 5 (born 13/06/2013). Baby born at 28+4 weeks of gestation. Premem rupture of membranes confirmed at 20+4 weeks gestation. Severity: Severe	Patient died	Gestational Diabetes 13/06/2013	Unrelated	No	Death	.
16212	PLACEBO	08JAN2014	04JAN2014	Diagnosis: VSD/ASD/PFO on echo. Description: Perimembranous ventricular septal defect with a L-R shunt. 2 x L-R shunt in the patent foramen ovale/PT cundum region of the atrial septum. Severity: Mild.	Congenital anomaly/birth defect		Unrelated	No	Condition still present and unchanged	.
21018	PLACEBO	05NOV2013	17OCT2013	Diagnosis: Presumed Sepsis/Pneumonia consolidation. Description: Admitted to neonatal unit shortly after birth for investigations for spreading vascular lesions on truck. grunting and tachypnoeic. Remained on neonatal unit 17 - 22/10/13. Severity: Moderate	Involved or prolonged inpatient hospitalisation	Vascular lesions. grunting. tachypnoeic. pneumonia. started 17/10/2013. ended 22/10/2013. medication required.	Unrelated	No	Completely recovered	24OCT2013
21038	PLACEBO	16JAN2014	31DEC2013	Diagnosis: Cyanotic episodes, likely vasomotor phenomenon. Description: Admitted to ward 8 via ambulance/A&E 7 days old with cyanotic episodes 10 times a day lasting 3 - 5 mins. Investigations all normal. Discharged home 02/01/2014. No further admissions. Severity: Moderate.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	02JAN2014

Section 13. Serious Adverse Events

13.2.2 SAE related to the babies - Details

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	SAE - date of report	SAE - date of event	Description of SAE	Expedited Reporting Criteria	Relevant History	SAE_related_coded	SAE_expected_coded (Y/N)	SAE_outcome_coded	SAE - date of recovery
21047	PLACEBO	22APR2014	22JAN2014	Diagnosis: RSV positive bronchiolitis. Description: Admitted to paediatric ward at 2 weeks old with cough and increased work of breathing. Required oxygen and help with NG feeds for a few days. Gradually recovered. Severity: Moderate.	Involved or prolonged inpatient hospitalisation	Gestational Diabetes (Mother). 17/12/2013 - 05/01/2014.	Unrelated	No	Completely recovered	30JAN2014
21069	PLACEBO	19MAR2014	18FEB2014	Diagnosis: Meningitis/Sepsis. Description: Admitted to Neonatal Unit shortly after birth jillary/maternal sepsis. Had dusky episodes/desaturations/agnoresis/jaundice/sepsis. Ventilated. Meningitis diagnosed. / Cerebral Haemorrhage. Severity: Severe.	Involved persistent or significant disability or incapacity Involved or prolonged inpatient hospitalisation	Sepsis in labour/maternal infection (Parent). 18/02/2014 - 25/02/2014. medication required.	Unrelated	No	Completely recovered	07MAR2014
21119	PLACEBO	06JAN2014	02JAN2014	Diagnosis: Congenital Anomaly. Description: Anomaly ultrasound scan showed structural abnormalities to hands and feet. Appearance suggestive of split hand and foot syndrome. Severity: Severe	Patient died Congenital anomaly/birth defect		Unrelated	No	Death	.
25320	PLACEBO	03FEB2014	31JAN2014	Diagnosis: ? Hirschsprungs in neonate. Description: Distended stomach on antenatal scans. At birth neonate admitted to NNU then transfer to tertiary centre same day (Nottingham Queen's Medical). Severity: Severe. Follow-up 27/02/2014. Subsequently resolved. no pathology. baby discharged. Severity: Severe.	Congenital anomaly/birth defect		Unrelated	No	Completely recovered	27FEB2014

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EMPOWaR: Efficacy of Metformin in Pregnant Obese Women, a Randomised Controlled Trial
Funding reference number: 08/246/09 (NIHR Efficacy and Mechanism Evaluation Programme)
EudraCT number 2009-017134-47

Statistical Report

Population = Per-Protocol (PP) - Allocated Treatment used for analysis
Report number: 02

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Data set analysed as it was on:

29 April 2015

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Section 1. Disposition / data checks

1.1 Patient disposition before randomisation - All Centres

		---Overall---
<i>Parameter(s)</i>	<i>Categories</i>	<i>Count (n(%))</i>
All patients in DB (n(%))	Yes	4867 (100)
Declined reason (n(%))	Subject participate has declined	2861 (58.8)
	Other Reason	57 (1.2)
	Failed Exclusion	100 (2.1)
	Failed Inclusion	626 (12.9)
	Failed both Exclu and Inclu	4 (0.1)
	Did not decline and pass IN_EX but not rand*	10 (0.2)
	Did not attend appointment	8 (0.2)
	Unable to contact	752 (15.5)
	Did not decline and pass IN_EX and rand	449 (9.2)

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 02:47

By: Aryelly Rodriguez - ECTU Statistician

n = number of observations

*These patients (13045 13053 13084 13102 13117 13121 13122 13123 13168 13189) were screened as eligible, but then they subsequently declined or were no longer contactable

NOTE: These patients (11562 11892 13047 13065) were randomised but also have a reason to decline

Section 1. Disposition / data checks

1.2.1.1 Patient disposition after randomisation - All Centres

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Consented/randomised (n(%))	Yes	118 (100)	109 (100)	227 (100)
Disposition in database (n(%))	Active	116 (98.3)	107 (98.2)	223 (98.2)
	Lost to follow up	1 (0.8)	0	1 (0.4)
	Participant withdrawn	1 (0.8)	2 (1.8)	3 (1.3)
Outcome (z score) available* (n(%))	Yes - Live Birth	117 (99.2)	108 (99.1)	225 (99.1)
	No - Termination of Pregnancy	1 (0.8)	0	1 (0.4)
	No - Not available	0	1 (0.9)	1 (0.4)
Outcome (Glucose test) available# (n(%))	Yes	103 (87.3)	92 (84.4)	195 (85.9)
	No	15 (12.7)	17 (15.6)	32 (14.1)

Section 1. Disposition / data checks

1.2.1.2 Patient disposition after randomisation - All Centres - Consort figures

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Treatment distributed(n(%))	Data available	118 (100)	109 (100)	227 (100)
Outcome (z score) available* (n(%))	Data available	117 (99.2)	108 (99.1)	225 (99.1)
	Withdrawn post treatment	0	1 (0.9)	1 (0.4)
	Termination of Pregnancy	1 (0.8)	0	1 (0.4)

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 02:47

By: Aryelly Rodriguez - ECTU Statistician

N = number of patients randomised, n = number of observations

*Available at visit 8 (Delivery)

IMPORTANT NOTES on manual identification:

Patients 12046 and 12047 withdrawn pre treatment

Patients 17063, 27317 and 18113 withdrawn post treatment

Patients 12041, 12086 and 21119 were identified as miscarriage but they were termination of pregnancies TOP

Section 1. Disposition / data checks

1.2.1.2 Patient disposition after randomisation - All Centres - Consort figures (Cont.)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	<i>Overall N=227</i>
Follow up Visit 9 data available* (n(%))	Data available	90 (76.3)	91 (83.5)	181 (79.7)
	Did not attend the visit	25 (21.2)	16 (14.7)	41 (18.1)
	Decline to further participate	1 (0.8)	1 (0.9)	2 (0.9)
	Lost to follow up	1 (0.8)	0	1 (0.4)
	Withdrawn post treatment	0	1 (0.9)	1 (0.4)
	Termination of Pregnancy	1 (0.8)	0	1 (0.4)

Section 1. Disposition / data checks

1.2.2 Study Populations - All Centres

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo</i>	<i>Metformin</i>	<i>Overall</i>
Randomised - ITT population (n(%))*	Yes	223 (100)	226 (100)	449 (100)
IMP at least once (n(%))#	Missing	46	59	105
	No	8 (4.5)	9 (5.4)	17 (4.9)
	Yes	169 (95.5)	158 (94.6)	327 (95.1)
Compliant - PP population (n(%))\$	Missing	46	59	105
	No	59 (33.3)	58 (34.7)	117 (34.0)
	Yes	118 (66.7)	109 (65.3)	227 (66.0)

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N = number of patients randomised, n = number of observations

*The intention to treat (ITT) population will comprise all randomised subjects

#Members of the ITT population who took IMP at least once

\$The per-protocol (PP) population will comprise those members of the ITT population who completed the study without a major protocol violation and who complied adequately with the randomised treatment, further details of treatment compliance are in table 3.2.2 of this report

By: Aryelly Rodriguez - ECTU Statistician

Section 1. Disposition / data checks

1.3 Patient disposition - Minimisation variables

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Centres (n(%))	Royal Infirmary of Edinburgh	32 (27.1)	36 (33.0)	68 (30.0)
	Coventry	14 (11.9)	8 (7.3)	22 (9.7)
	Liverpool Womens Hospital	26 (22.0)	19 (17.4)	45 (19.8)
	Sheffield	11 (9.3)	7 (6.4)	18 (7.9)
	Notts City	3 (2.5)	4 (3.7)	7 (3.1)
	Notts QMC	5 (4.2)	5 (4.6)	10 (4.4)
	Bradford	3 (2.5)	3 (2.8)	6 (2.6)
	St Helens	1 (0.8)	2 (1.8)	3 (1.3)
	Chelsea and Westminster	0	1 (0.9)	1 (0.4)
	Preston	15 (12.7)	15 (13.8)	30 (13.2)
	Arrow Park Wirral	0	1 (0.9)	1 (0.4)
	Chesterfield	8 (6.8)	8 (7.3)	16 (7.0)
BMI band at randomisation*(n(%))	30-39 Kg/m ²	80 (67.8)	73 (67.0)	153 (67.4)
	>40 Kg/m ²	38 (32.2)	36 (33.0)	74 (32.6)

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Section 1. Disposition / data checks

1.4 Data Completeness by time point

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Patients CRF Completeness by CRF SECTIONS</i>	<i>Allocated Regimen</i>			
	<i>METFORMIN</i>		<i>PLACEBO</i>	
	<i>Visit attended</i>		<i>Visit attended</i>	
	<i>Yes</i>	<i>No</i>	<i>Yes</i>	<i>No</i>
<i>VISIT 1 (SCREENING)</i>	109	0	118	0
<i>VISIT 2 (BASELINE)</i>	109	0	118	0
<i>VISIT 3 (RANDOMISATION)</i>	109	0	118	0
<i>VISIT 4 (18 TO 20 WEEKS)</i>	108	1	115	3
<i>VISIT 5 (28 WEEKS)</i>	109	0	117	1
<i>VISIT 6 (36 WEEKS)</i>	96	13	107	11
<i>VISIT 7 (TERM)</i>	52	57	55	63
<i>VISIT 8 (DELIVERY)</i>	106	3	115	3
<i>VISIT 9 (FINAL)</i>	91	18	90	28

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Section 1. Disposition / data checks

1.4 Data Completeness by time point

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Patients CRF Completeness by CRF SECTIONS</i>	<i>Allocated Regimen</i>	
	<i>OVERALL</i>	
	<i>Visit attended</i>	
	<i>Yes</i>	<i>No</i>
<i>VISIT 1 (SCREENING)</i>	227	0
<i>VISIT 2 (BASELINE)</i>	227	0
<i>VISIT 3 (RANDOMISATION)</i>	227	0
<i>VISIT 4 (18 TO 20 WEEKS)</i>	223	4
<i>VISIT 5 (28 WEEKS)</i>	226	1
<i>VISIT 6 (36 WEEKS)</i>	203	24
<i>VISIT 7 (TERM)</i>	107	120
<i>VISIT 8 (DELIVERY)</i>	221	6
<i>VISIT 9 (FINAL)</i>	181	46

Section 2. Baseline - Visit 2 (10-16 Weeks) - Demographics and Lifestyle

2.1.1 Maternal Age

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=227</i>
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	
Maternal Age at consent (years)	Mean	29.6	29.8	29.7
	Median	29.0	30.0	30.0
	SD	5.0	5.6	5.3
	MIN,MAX	20,43	19,42	19,43
	Q1,Q3	26,33	25,34	25,34
	n	118	109	227
	Nmiss	0	0	0

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Section 2. Baseline - Visit 2 (10-16 Weeks) - Demographics and Lifestyle

2.1.2 Maternal Life Style Status

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=227</i>
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	
Smoking Status (n(%))	ACTIVE	13 (11.0)	13 (11.9)	26 (11.5)
	PREVIOUSLY	6 (5.1)	6 (5.5)	12 (5.3)
	NOT SMOKING	99 (83.9)	90 (82.6)	189 (83.3)
Alcohol During Pregnancy (n(%))	Yes	6 (5.1)	0	6 (2.6)
	No	112 (94.9)	109 (100)	221 (97.4)
Illicit Drug Status (n(%))	NOT USING	118 (100)	109 (100)	227 (100)

Section 2. Baseline - Visit 2 (10-16 Weeks) - Demographics and Lifestyle

2.1.3 Maternal Education

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Educational Qualifications (n(%))	No formal qualifications	8 (6.8)	3 (2.8)	11 (4.8)
	Entry level certification/foundation diploma	2 (1.7)	5 (4.6)	7 (3.1)
	GCSE, Standard grade, "O" grades	27 (22.9)	18 (16.5)	45 (19.8)
	A level, A/S level, Highers or BTEC Dip/Cert.	21 (17.8)	15 (13.8)	36 (15.9)
	Cert. higher Education, City & Guilds	9 (7.6)	9 (8.3)	18 (7.9)
	Diploma HE/FE or HND/HNC	19 (16.1)	14 (12.8)	33 (14.5)
	Graduate certificate or Diploma	2 (1.7)	5 (4.6)	7 (3.1)
	Degree	20 (16.9)	35 (32.1)	55 (24.2)
	Professional Qualification	2 (1.7)	2 (1.8)	4 (1.8)
	PGCE/Postgraduate certificate or Diploma, Masters. Doctorate	8 (6.8)	3 (2.8)	11 (4.8)
Educational Qualifications coded (n(%))	None	8 (6.8)	3 (2.8)	11 (4.8)
	School up to 16 years	29 (24.6)	23 (21.1)	52 (22.9)
	School 16 to 18 years	30 (25.4)	24 (22.0)	54 (23.8)
	College or Uni degree or Higher	51 (43.2)	59 (54.1)	110 (48.5)

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Section 2. Baseline - Visit 2 (10-16 Weeks) - Demographics and Lifestyle

2.1.4.1 Previous pregnancy status* PARITY 1

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=227</i>
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	
PARITY1 (n(%))	0	44 (37.3)	54 (49.5)	98 (43.2)
	=>1	74 (62.7)	55 (50.5)	129 (56.8)

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N = number of patients randomised, n = number of observations

*Only pregnancies lasting at least 24 weeks or more were considered

By: Aryelly Rodriguez - ECTU Statistician

Section 2. Baseline - Visit 2 (10-16 Weeks) - Demographics and Lifestyle

2.1.4.2 Previous pregnancy status*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Number of Previous Pregnancies (n(%))	0	31 (26.3)	41 (37.6)	72 (31.7)
	1	41 (34.7)	28 (25.7)	69 (30.4)
	2	22 (18.6)	18 (16.5)	40 (17.6)
	3	10 (8.5)	12 (11.0)	22 (9.7)
	4	6 (5.1)	5 (4.6)	11 (4.8)
	5	6 (5.1)	1 (0.9)	7 (3.1)
	6	1 (0.8)	1 (0.9)	2 (0.9)
	7	1 (0.8)	2 (1.8)	3 (1.3)
	8	0	1 (0.9)	1 (0.4)
At least one Prev Preg* (n(%))	Yes	87 (73.7)	68 (62.4)	155 (68.3)
	No	31 (26.3)	41 (37.6)	72 (31.7)

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Section 2. Baseline - Visit 2 (10-16 Weeks) - Demographics and Lifestyle

2.1.4.3 Previous Pregnancy details*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Multiple Pregnancy#(%)	Yes	2 (2.3)	1 (1.5)	3 (1.9)
	No	85 (97.7)	67 (98.5)	152 (98.1)
Gestation of Pregnancy#(weeks)(n(%))	<12	21 (24.1)	19 (27.9)	40 (25.8)
	12<22	0	3 (4.4)	3 (1.9)
	>22	66 (75.9)	46 (67.6)	112 (72.3)
Last Pregnancy Outcome#(%)	Miscarriage	15 (17.2)	18 (26.5)	33 (21.3)
	Ectopic	1 (1.1)	1 (1.5)	2 (1.3)
	Termination of Pregnancy	5 (5.7)	3 (4.4)	8 (5.2)
	Live Birth	66 (75.9)	46 (67.6)	112 (72.3)
Pre term Birth#(n(%))	Missing	13	16	29
	Yes	3 (4.1)	2 (3.8)	5 (4.0)
	No	71 (95.9)	50 (96.2)	121 (96.0)

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N = number of patients randomised, n = number of observations

*Only pregnancies lasting at least 12 weeks or more were considered regardless of outcome and if a patient had more than one previous pregnancy, only her latest pregnancy was counted

#Only summarised for patients who has a previous pregnancy in the previous table

By: Aryelly Rodriguez - ECTU Statistician

Section 2. Baseline - Visit 2 (10-16 Weeks) - Demographics and Lifestyle

2.1.5 Maternal Blood Pressure at baseline

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Maternal Systolic BP (mmHg)	Mean	119.3	117.1	118.3
	Median	120.0	118.0	119.0
	SD	11.2	11.3	11.3
	MIN,MAX	100,142	91,148	91,148
	Q1,Q3	110,129	110,124	110,127
	n	118	109	227
	Nmiss	0	0	0
Maternal Diastolic BP (mmHg)	Mean	69.0	68.5	68.8
	Median	69.5	70.0	70.0
	SD	7.7	7.9	7.8
	MIN,MAX	54,90	49,86	49,90
	Q1,Q3	64,74	60,74	61,74
	n	118	109	227
	Nmiss	0	0	0

Section 2. Baseline - Visit 2 (10-16 Weeks) - Demographics and Lifestyle

2.1.6 Current pregnancy details

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Ultrasound Confirmation (n(%))	Yes	117 (99.2)	109 (100)	226 (99.6)
	No	1 (0.8)	0	1 (0.4)
Gestation at baseline* (days)	Mean	98.9	100.0	99.4
	Median	100.0	100.0	100.0
	SD	9.0	7.9	8.5
	MIN,MAX	71,112	74,112	71,112
	Q1,Q3	92,106	95,107	94,107
	n	118	109	227
	Nmiss	0	0	0

Section 2. Baseline - Visit 2 (10-16 Weeks) - Putative father

2.2.1 Putative father Age

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall N=227</i>
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	
Paternal age (years)	Mean	32.3	32.0	32.2
	Median	32.0	32.0	32.0
	SD	6.2	6.0	6.1
	MIN,MAX	15,50	21,46	15,50
	Q1,Q3	28,36	27,37	28,36
	n	117	108	225
	Nmiss	1	1	2

Section 2. Baseline - Visit 2 (10-16 Weeks) - Putative father

2.2.2 Putative father Height and Weight

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Paternal height (cm)	Mean	178.5	177.9	178.2
	Median	178.0	178.0	178.0
	SD	7.8	13.2	10.7
	MIN,MAX	156,200	76,196	76,200
	Q1,Q3	173,183	174,185	174,183
	n	107	100	207
	Nmiss	11	9	20
Paternal weight (Kg)	Mean	92.1	94.6	93.3
	Median	89.7	89.0	89.1
	SD	21.9	27.7	24.8
	MIN,MAX	57,148	57,196	57,196
	Q1,Q3	74,105	77,108	76,107
	n	102	95	197
	Nmiss	16	14	30

Section 2. Baseline - Visit 2 (10-16 Weeks) - Putative father

2.2.3 Putative father Ethnicity

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=227</i>
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	
Ethnic Origin (n(%))	White	114 (96.6)	101 (92.7)	215 (94.7)
	Non-White	4 (3.4)	8 (7.3)	12 (5.3)
Ethnic Origin-More detail (n(%))	White	114 (96.6)	101 (92.7)	215 (94.7)
	Mixed	1 (0.8)	2 (1.8)	3 (1.3)
	Asian	0	2 (1.8)	2 (0.9)
	Black	2 (1.7)	3 (2.8)	5 (2.2)
	Othe Ethnic group	1 (0.8)	1 (0.9)	2 (0.9)

Section 2. Baseline - Visit 2 (10-16 Weeks) - Mother Medical history

2.3.1 Preeclampsia or Hypertension / Hypertension Requiring Treatment

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Preeclampsia or Hypertension (n(%))	Yes	3 (2.5)	6 (5.5)	9 (4.0)
	No	115 (97.5)	103 (94.5)	218 (96.0)
Currently taking Medication (n)	No	3	6	9
Hypertension Require Treatment (n(%))	Yes	1 (0.8)	1 (0.9)	2 (0.9)
	No	117 (99.2)	108 (99.1)	225 (99.1)
Currently taking Medication (n)	No	1	1	2

Section 2. Baseline - Visit 2 (10-16 Weeks) - Mother Medical history

2.3.2 Polycystic Ovarian Syndrome / Depression Requiring Treatment

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Polycystic Ovarian Syndrome (n(%))	Yes	14 (11.9)	16 (14.7)	30 (13.2)
	No	103 (87.3)	92 (84.4)	195 (85.9)
	Unk	1 (0.8)	1 (0.9)	2 (0.9)
Currently taking Medication (n)	No	14	16	30
Depression Require Treatment (n(%))	Yes	33 (28.0)	24 (22.0)	57 (25.1)
	No	85 (72.0)	85 (78.0)	170 (74.9)
Currently taking Medication (n)	Yes	5	4	9
	No	28	20	48

Section 2. Baseline - Visit 2 (10-16 Weeks) - Mother Medical history

2.3.3 Anxiety Requiring Treatment / Use of Steroids

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Anxiety Require Treatment (n(%))	Yes	7 (5.9)	7 (6.4)	14 (6.2)
	No	111 (94.1)	102 (93.6)	213 (93.8)
Currently taking Medication (n)	Yes	2	1	3
	No	5	6	11
Use of Steroids (n(%))	Yes	12 (10.2)	7 (6.4)	19 (8.4)
	No	106 (89.8)	102 (93.6)	208 (91.6)
Currently taking Medication (n)	Yes	12	7	19

Section 2. Baseline - Visit 2 (10-16 Weeks) - Mother Family history

2.4 Any family history for the following conditions

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Any Medical History* (n(%))	Yes	73 (61.9)	76 (69.7)	149 (65.6)
	No	42 (35.6)	32 (29.4)	74 (32.6)
	Unk	3 (2.5)	1 (0.9)	4 (1.8)
Cardiovascular disease (n(%))	Yes	41 (34.7)	31 (28.4)	72 (31.7)
	No	74 (62.7)	77 (70.6)	151 (66.5)
	Unk	3 (2.5)	1 (0.9)	4 (1.8)
Diabetes(n(%))	Yes	54 (45.8)	47 (43.1)	101 (44.5)
	No	62 (52.5)	61 (56.0)	123 (54.2)
	Unk	2 (1.7)	1 (0.9)	3 (1.3)
Preeclampsia(n(%))	Yes	8 (6.8)	4 (3.7)	12 (5.3)
	No	107 (90.7)	102 (93.6)	209 (92.1)
	Unk	3 (2.5)	3 (2.8)	6 (2.6)
Any other medical history(n(%))	Yes	58 (49.2)	57 (52.3)	115 (50.7)
	No	60 (50.8)	52 (47.7)	112 (49.3)

Section 2. Baseline - Visit 2 (10-16 Weeks) - Mother details

2.5.1 Mother Anthropometry / Height and Weight*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Maternal Height (cm)	Mean	166.1	165.8	166.0
	Median	166.2	165.5	166.0
	SD	6.0	5.7	5.9
	MIN,MAX	152,184	153,180	152,184
	Q1,Q3	162,170	162,170	162,170
	n	118	109	227
	Nmiss	0	0	0
Maternal Weight (kg)	Mean	103.74	104.04	103.88
	Median	98.33	104.00	101.30
	SD	16.95	15.22	16.10
	MIN,MAX	75.6,154.0	74.0,140.3	74.0,154.0
	Q1,Q3	90.6,114.6	93.3,115.0	92.0,115.0
	n	118	109	227
	Nmiss	0	0	0

Section 2. Baseline - Visit 2 (10-16 Weeks) - Mother details

2.5.2 Mother Anthropometry / BMI_c and Waist*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Maternal BMI Calculated (kg/m ²)	Mean	37.549	37.782	37.661
	Median	36.583	37.494	37.036
	SD	5.462	4.708	5.104
	MIN,MAX	30.23,52.79	30.08,47.87	30.08,52.79
	Q1,Q3	33.14,41.25	34.27,41.45	33.56,41.28
	n	118	109	227
	Nmiss	0	0	0
Maternal Waist (cm)	Mean	108.32	108.57	108.44
	Median	106.00	108.60	107.00
	SD	12.58	11.20	11.91
	MIN,MAX	85.0,148.0	84.0,134.0	84.0,148.0
	Q1,Q3	98.5,118.0	100.5,117.0	100.0,117.0
	n	118	109	227
	Nmiss	0	0	0

Section 2. Baseline - Visit 2 (10-16 Weeks) - Mother details

2.5.3 Mother Anthropometry / Hip and MidArm*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Maternal Hip (cm)	Mean	126.80	127.50	127.14
	Median	125.00	126.00	125.00
	SD	11.58	12.22	11.87
	MIN,MAX	103.5,155.0	100.0,155.0	100.0,155.0
	Q1,Q3	118.0,133.5	119.0,136.0	118.5,134.0
	n	118	109	227
	Nmiss	0	0	0
Maternal Mid Arm (cm)	Mean	36.63	37.05	36.83
	Median	36.00	37.00	36.00
	SD	4.75	4.42	4.59
	MIN,MAX	22.0,48.0	28.0,52.0	22.0,52.0
	Q1,Q3	34.0,39.0	34.0,39.4	34.0,39.0
	n	117	106	223
	Nmiss	1	3	4

Section 2. Baseline - Visit 2 (10-16 Weeks) - Mother details

2.5.4 Mother Anthropometry / Mid Thigh and Tricep Skinfold*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Maternal Mid Thigh (cm)	Mean	64.22	65.34	64.75
	Median	64.25	64.00	64.00
	SD	7.31	7.00	7.17
	MIN,MAX	25.0,84.0	50.0,86.0	25.0,86.0
	Q1,Q3	60.0,68.8	61.0,69.0	60.0,69.0
	n	116	106	222
	Nmiss	2	3	5
Maternal Tricep Skinfold (mm)	Mean	33.326	32.564	32.960
	Median	31.200	31.500	31.200
	SD	9.379	9.659	9.501
	MIN,MAX	15.00,62.00	10.00,66.00	10.00,66.00
	Q1,Q3	27.00,40.00	26.00,38.70	26.50,39.00
	n	117	108	225
	Nmiss	1	1	2

Section 2. Baseline - Visit 2 (10-16 Weeks) - Mother details

2.5.5 Mother Anthropometry / Bicep Skinfold and Subscapular Skinfold*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Maternal Bicep Skinfold (mm)	Mean	27.362	27.824	27.584
	Median	25.000	26.000	25.500
	SD	10.087	10.707	10.369
	MIN,MAX	8.50,60.00	9.00,61.00	8.50,61.00
	Q1,Q3	21.00,32.00	20.00,33.00	20.80,32.40
	n	117	108	225
	Nmiss	1	1	2
Maternal Subscapular Skinfold (mm)	Mean	35.313	34.784	35.059
	Median	34.000	33.000	34.000
	SD	11.026	11.730	11.346
	MIN,MAX	12.00,67.80	9.90,67.00	9.90,67.80
	Q1,Q3	28.00,40.60	26.50,40.00	27.00,40.00
	n	117	108	225
	Nmiss	1	1	2

Section 3. Compliance

3.1 Gestation by timepoint - Visit 1 Screening (10-16 Weeks), Visit 2 Consent/Baseline (10-16 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Calculated* Gestation - Visit 1 (days)	Mean	86.2	86.3	86.3
	Median	87.5	88.0	88.0
	SD	14.1	13.6	13.9
	MIN,MAX	51,112	52,112	51,112
	Q1,Q3	76,97	79,95	79,96
	n	118	109	227
	Nmiss	0	0	0
Recorded# Gestation - Visit 2 (days)	Mean	98.9	100.0	99.4
	Median	100.0	100.0	100.0
	SD	9.0	7.9	8.5
	MIN,MAX	71,112	74,112	71,112
	Q1,Q3	92,106	95,107	94,107
	n	118	109	227
	Nmiss	0	0	0

Section 3. Compliance

3.1 Gestation by timepoint - Visit 3 Randomisation (10-16 Weeks), Visit 4 (18-20 Weeks) (Cont.)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Calculated* Gestation - Visit 3 (days)	Mean	101.4	101.6	101.5
	Median	103.0	102.0	102.0
	SD	8.2	7.2	7.7
	MIN,MAX	84,118	85,113	84,118
	Q1,Q3	95,108	97,108	96,108
	n	118	109	227
	Nmiss	0	0	0
Calculated* Gestation - Visit 4 (days)	Mean	141.6	139.8	140.7
	Median	140.0	140.0	140.0
	SD	11.4	7.6	9.7
	MIN,MAX	108,198	124,166	108,198
	Q1,Q3	136,146	134,143	135,145
	n	116	108	224
	Nmiss	2	1	3

Section 3. Compliance

3.1 Gestation by timepoint - Visit 5 (28 Weeks), Visit 6 (36 Weeks) (Cont.)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Calculated* Gestation - Visit 5 (days)	Mean	196.9	197.3	197.1
	Median	197.0	197.0	197.0
	SD	6.7	6.3	6.5
	MIN,MAX	155,224	167,226	155,226
	Q1,Q3	194,200	195,200	194,200
	n	118	109	227
	Nmiss	0	0	0
Calculated* Gestation - Visit 6 (days)	Mean	252.2	253.6	252.9
	Median	253.0	253.5	253.0
	SD	10.3	4.9	8.2
	MIN,MAX	155,263	234,266	155,266
	Q1,Q3	250,256	251,256	251,256
	n	109	102	211
	Nmiss	9	7	16

Section 3. Compliance

3.1 Gestation by timepoint - Visit 7 Term (Cont.)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Calculated* Gestation - Visit 7 (days)	Mean	285.7	277.9	281.8
	Median	276.5	277.0	277.0
	SD	90.8	16.7	65.4
	MIN,MAX	155,1011	250,393	155,1011
	Q1,Q3	273,282	273,281	273,281
	n	68	67	135
	Nmiss	50	42	92
Calculated* Gestation - Visit 8 (days)	Mean	279.9	278.0	279.0
	Median	281.0	278.0	280.0
	SD	21.2	13.2	17.8
	MIN,MAX	155,375	216,337	155,375
	Q1,Q3	273,289	271,285	271,287
	n	118	108	226
	Nmiss	0	1	1

Section 3. Compliance

3.1 Gestation by timepoint - Visit 8 Delivery (Cont.)

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Recorded* Gestation - Visit 8 (days)	Mean	276.6	276.6	276.6
	Median	277.5	278.0	278.0
	SD	17.1	11.5	14.7
	MIN,MAX	152,297	219,297	152,297
	Q1,Q3	271,287	271,284	271,285
	n	118	108	226
	Nmiss	0	1	1
Coded R_gestation - Visit 8 (n(%))	Missing	0	1	1
	<= 24 WEEKS	1 (0.8)	0	1 (0.4)
	>24 and <=37 WEEKS	4 (3.4)	8 (7.4)	12 (5.3)
	>37 WEEKS	113 (95.8)	100 (92.6)	213 (94.2)

Section 3. Compliance

3.2.1 Treatment compliance / Tablets returned by study visit

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	<i>Overall N=227</i>
Tablets Returned Visit 5 (28 Weeks) (n(%))	Missing	20	11	31
	Yes	9 (9.2)	6 (6.1)	15 (7.7)
	No	89 (90.8)	92 (93.9)	181 (92.3)
Tablets Returned Visit 8 (Delivery) (n(%))	Missing	19	9	28
	Yes	53 (53.5)	57 (57.0)	110 (55.3)
	No	46 (46.5)	43 (43.0)	89 (44.7)

Section 3. Compliance

3.2.2 Treatment compliance Calculated using the patient diary (as per SAP)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Calculated Compliance* (n(%))	Yes	118 (100)	109 (100)	227 (100)

N = number of patients randomised, n = number of observations

*The number of weeks that a patient was pregnant within the study period was calculated using the gestation at baseline and the gestation at delivery, this value was then halved and compared to the number of weeks recorded in the diary, if a patient has less week diary entries than the halved total weeks then she is non-compliant straight away. If a patient had equal or more week diary entries than halved total weeks then it was required that she taken at least one pill for 4 days in order to declare a compliant week. Finally for being treatment compliant the patient should have equal or more than 50% of compliant weeks out of all available weeks

Section 3. Compliance

3.2.3.1 Cross Check* of Treatment compliance Calculated# vs tablets returned - Visit 5 (28 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Compliance by tablets returned at visit 5</i>	<i>Allocated Regimen</i>			
	<i>METFORMIN</i>		<i>PLACEBO</i>	
	<i>Tablets returned</i>		<i>Tablets returned</i>	
	<i>Yes</i>	<i>No</i>	<i>Yes</i>	<i>No</i>
<i>Compliance</i>				
<i>Yes</i>	6	92	9	89

<i>Compliance by tablets returned at visit 5</i>	<i>Allocated Regimen</i>	
	<i>OVERALL</i>	
	<i>Tablets returned</i>	
	<i>Yes</i>	<i>No</i>
<i>Compliance</i>		
<i>Yes</i>	15	181

Section 3. Compliance

3.2.3.2 Cross Check* of Treatment compliance Calculated# vs tablets returned - Visit 8 Delivery

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Compliance by tablets returned at visit 8</i>	<i>Allocated Regimen</i>			
	<i>METFORMIN</i>		<i>PLACEBO</i>	
	<i>Tablets returned</i>		<i>Tablets returned</i>	
	<i>Yes</i>	<i>No</i>	<i>Yes</i>	<i>No</i>
<u><i>Compliance</i></u>				
<i>Yes</i>	57	43	53	46

<i>Compliance by tablets returned at visit 8</i>	<i>Allocated Regimen</i>	
	<i>OVERALL</i>	
	<i>Tablets returned</i>	
	<i>Yes</i>	<i>No</i>
<u><i>Compliance</i></u>		
<i>Yes</i>	110	89

Section 3. Compliance

3.3 Treatment compliance / Metformin level in blood samples at Visit 6 (36 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Metformin level (ng/mL)	Mean	1.5	90.8	43.6
	Median	0.0	28.5	0.0
	SD	11.6	210.5	151.1
	MIN,MAX	0,110	0,1611	0,1611
	Q1,Q3	0,0	1,75	0,27
	n	93	83	176
	Nmiss	25	26	51
Any Metformin level coded (n(%))	Missing	25	26	51
	Yes	7 (7.5)	63 (75.9)	70 (39.8)
	No	86 (92.5)	20 (24.1)	106 (60.2)

Section 3. Compliance

3.4 Cross Check* of Treatment compliance Calculated# vs Metformin level in blood samples at Visit 6 (36 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Compliance by metformin level at visit 6	Allocated Regimen			
	METFORMIN		PLACEBO	
	Any Metformin		Any Metformin	
	Yes	No	Yes	No
<u>Compliance</u>				
Yes	63	20	7	86

Compliance by metformin level at visit 6	Allocated Regimen	
	OVERALL	
	Any Metformin	
	Yes	No
<u>Compliance</u>		
Yes	70	106

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Section 4. Secondary Outcome - All Patients

4.1.1.1.1.1 Delivery Details

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Delivery Method (n(%))	Missing	0	1	1
	Spontaneous vaginal delivery	64 (54.2)	65 (60.2)	129 (57.1)
	LSCS in labour	18 (15.3)	14 (13.0)	32 (14.2)
	LSCS pre labour	25 (21.2)	17 (15.7)	42 (18.6)
	Forceps/ventouse	11 (9.3)	12 (11.1)	23 (10.2)
C-SECTION index pregnancy (n(%))	Missing	0	1	1
	Yes	43 (36.4)	31 (28.7)	74 (32.7)
	No	75 (63.6)	77 (71.3)	152 (67.3)
Primary C-SECTION in index pregnancy (n(%))	Missing	0	1	1
	Yes	25 (21.2)	22 (20.4)	47 (20.8)
	No	93 (78.8)	86 (79.6)	179 (79.2)

Section 4. Secondary Outcome - All Patients

4.1.1.1.2 Birth Outcome - C-SECTION current pregnancy - Statistical analysis - POST-HOC*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Table of CSECTIONYN by AllocatedTreatment</i>			
<i>CSECTIONYN(C-section coded (Y/N))</i>	<i>AllocatedTreatment(Allocated Treatment)</i>		<i>Total</i>
	<i>METFORMIN</i>	<i>PLACEBO</i>	
<i>Missing</i>	1	0	.
<i>Yes</i>	31	43	74
<i>No</i>	77	75	152
<i>Total</i>	108	118	226

Frequency Missing = 1

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower</i>	<i>Upper</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
			<i>95% Confidence Limit for Odds Ratio</i>	<i>95% Confidence Limit for Odds Ratio</i>		
c_section_pp	AllocatedTreatment METFORMIN vs PLACEBO	0.702	0.401	1.230	0.2165	0.2566

Section 4. Secondary Outcome - All Patients

4.1.1.1.1.3 Birth Outcome - First ever C-SECTION - Statistical analysis - POST-HOC*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Table of first_c_section by AllocatedTreatment</i>			
<i>first_c_section(First ever c-section in current pregnancy (Y/N))</i>	<i>AllocatedTreatment(Allocated Treatment)</i>		<i>Total</i>
	<i>METFORMIN</i>	<i>PLACEBO</i>	
<i>Missing</i>	1	0	.
<i>Yes</i>	22	25	47
<i>No</i>	86	93	179
<i>Total</i>	108	118	226

Frequency Missing = 1

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
first_csec_pp	AllocatedTreatment METFORMIN vs PLACEBO	0.952	0.500	1.811	0.8800	1.0000

Section 4. Secondary Outcome - All Patients

4.1.1.1.2.1 Delivery Details

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Delivery Blood Loss (mL)	Mean	519.2	500.0	510.0
	Median	400.0	400.0	400.0
	SD	407.7	550.8	480.9
	MIN,MAX	100,2000	50,5000	50,5000
	Q1,Q3	250,600	250,600	250,600
	n	114	106	220
	Nmiss	4	3	7
Hemorrhage* (n(%))	Missing	4	3	7
	Yes	13 (11.4)	9 (8.5)	22 (10.0)
	No	101 (88.6)	97 (91.5)	198 (90.0)
SAE recorded due to Hemorrhage# (n(%))	Missing	0	1	1
	Yes	5	4	9
	No	8	4	12

Section 4. Secondary Outcome - All Patients

4.1.1.1.2.2 Birth Outcome - Hemorrhage - Statistical analysis - POST-HOC*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Frequency</i>		<i>Table of HEMORRHAGE by Allocated Treatment</i>			
<i>HEMORRHAGE (Heamorrhage (Y/N))</i>		<i>Allocated Treatment (Allocated Treatment)</i>			
		<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>	
<i>Missing</i>		3	4	.	
<i>Yes</i>		9	13	22	
<i>No</i>		97	101	198	
<i>Total</i>		106	114	220	
<i>Frequency Missing = 7</i>					

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
HEMORRHAGE_pp	Allocated Treatment METFORMIN vs PLACEBO	0.721	0.295	1.763	0.4732	0.5079

Section 4. Secondary Outcome - All Patients

4.1.1.1.3 Delivery Details

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Labour Type (n(%))	Missing	0	1	1
	Spontaneous	45 (38.1)	44 (40.7)	89 (39.4)
	Induced	51 (43.2)	47 (43.5)	98 (43.4)
	C-section	22 (18.6)	17 (15.7)	39 (17.3)
Non Spontaneous Reason* (n(%))	Missing	0	1	1
	Post dates	15 (20.5)	8 (12.5)	23 (16.8)
	Pre-eclampsia	3 (4.1)	2 (3.1)	5 (3.6)
	Abruption	0	1 (1.6)	1 (0.7)
	Other maternal condition	21 (28.8)	28 (43.8)	49 (35.8)
	Previous C-section	14 (19.2)	4 (6.3)	18 (13.1)
	Previous obstetric history (other)	3 (4.1)	2 (3.1)	5 (3.6)
	Maternal request	5 (6.8)	3 (4.7)	8 (5.8)
	Suspected fetal compromise	4 (5.5)	8 (12.5)	12 (8.8)
	Malpresentation	3 (4.1)	4 (6.3)	7 (5.1)
	Suspected IUGR	3 (4.1)	0	3 (2.2)
	Suspected Macrosomia	2 (2.7)	4 (6.3)	6 (4.4)

Section 4. Secondary Outcome - All Patients

4.1.1.1.4 Delivery Details

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Gesta_coded by method* (n(%))	Missing	0	1	1
	Sponta_vaginal_delivery_<=37 WEEKS	1 (0.8)	2 (1.9)	3 (1.3)
	Sponta_vaginal_delivery_>37 WEEKS	62 (52.5)	63 (58.3)	125 (55.3)
	LSCS in labour_<=37 WEEKS	1 (0.8)	1 (0.9)	2 (0.9)
	LSCS in labour_>37 WEEKS	17 (14.4)	13 (12.0)	30 (13.3)
	LSCS pre labour_<=37 WEEKS	2 (1.7)	4 (3.7)	6 (2.7)
	LSCS pre labour_>37 WEEKS	23 (19.5)	13 (12.0)	36 (15.9)
	Forceps/ventouse_<=37 WEEKS	0	1 (0.9)	1 (0.4)
	Forceps/ventouse_>37 WEEKS	11 (9.3)	11 (10.2)	22 (9.7)
	TOP_Stillbirth_Miscarriage	1 (0.8)	0	1 (0.4)

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Section 4. Secondary Outcome - All Patients

4.1.1.1.5 Delivery Details

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	<i>Overall N=227</i>
Gesta_coded by labour* (n(%))	Missing	0	1	1
	Spontaneous_<=37 WEEKS	1 (0.8)	1 (0.9)	2 (0.9)
	Spontaneous_>37 WEEKS	44 (37.3)	43 (39.8)	87 (38.5)
	Induced_<=37 WEEKS	2 (1.7)	3 (2.8)	5 (2.2)
	Induced_>37 WEEKS	48 (40.7)	44 (40.7)	92 (40.7)
	C-section_<=37 WEEKS	1 (0.8)	4 (3.7)	5 (2.2)
	C-section_>37 WEEKS	21 (17.8)	13 (12.0)	34 (15.0)
	TOP_Stillbirth_Miscarriage	1 (0.8)	0	1 (0.4)

Section 4. Secondary Outcome - All Patients

4.1.1.1.6 Delivery Details

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Labour by method* <=37 Weeks (n(%))	Spontaneous_vaginal_deliv	1 (20.0)	1 (12.5)	2 (15.4)
	Induced_vaginal_deliv	0	1 (12.5)	1 (7.7)
	Induced_LSCS in labour	1 (20.0)	1 (12.5)	2 (15.4)
	Induced_LSCS pre labour	1 (20.0)	0	1 (7.7)
	Induced_Forceps/ventouse	0	1 (12.5)	1 (7.7)
	C-section_LSCS pre labour	1 (20.0)	4 (50.0)	5 (38.5)
	TOP_Stillbirth_Miscarriage	1 (20.0)	0	1 (7.7)

Section 4. Secondary Outcome - All Patients

4.1.1.1.7 Delivery Details

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo</i>	<i>Metformin</i>	<i>Overall</i>
Labour by method* >37 Weeks (n(%))	Spontaneous_vaginal_deliv	34 (30.1)	33 (33.0)	67 (31.5)
	Spontaneous_LSCS in labour	3 (2.7)	3 (3.0)	6 (2.8)
	Spontaneous_Forceps/ventouse	7 (6.2)	7 (7.0)	14 (6.6)
	Induced_vaginal_deliv	28 (24.8)	30 (30.0)	58 (27.2)
	Induced_LSCS in labour	14 (12.4)	10 (10.0)	24 (11.3)
	Induced_LSCS pre labour	2 (1.8)	0	2 (0.9)
	Induced_Forceps/ventouse	4 (3.5)	4 (4.0)	8 (3.8)
	C-section_LSCS pre labour	21 (18.6)	13 (13.0)	34 (16.0)

Section 4. Secondary Outcome - All Patients

4.1.1.2.1.1 Delivery Outcome

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Baby Gestational age (Days)*	Mean	276.6	276.6	276.6
	Median	277.5	278.0	278.0
	SD	17.1	11.5	14.7
	MIN,MAX	152,297	219,297	152,297
	Q1,Q3	271,287	271,284	271,285
	n	118	108	226
	Nmiss	0	1	1
Baby Gestational age coded (n(%))*	Missing	0	1	1
	<= 24 WEEKS	1 (0.8)	0	1 (0.4)
	>24 and <=37 WEEKS	4 (3.4)	8 (7.4)	12 (5.3)
	>37 WEEKS	113 (95.8)	100 (92.6)	213 (94.2)

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Section 4. Secondary Outcome - All Patients

4.1.1.2.1.1 Delivery Outcome (Cont.)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Baby Gender (n(%))	NA	0	1	1
	Male	58 (49.2)	54 (50.0)	112 (49.6)
	Female	60 (50.8)	54 (50.0)	114 (50.4)
Birth Outcome (n(%))	NA	0	1	1
	Live Birth	117 (99.2)	108 (100)	225 (99.6)
	Termination of Pregnancy	1 (0.8)	0	1 (0.4)

Section 4. Secondary Outcome - All Patients

4.1.1.2.1.2 Birth Outcome - Statistical analysis - POST-HOC*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of Birth_Out_Ana by AllocatedTreatment</i>				
<i>Birth_Out_Ana(Birth Outcome categorised for analysis)</i>	<i>AllocatedTreatment(Allocated Treatment)</i>		<i>Total</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>Fisher exact P-value#</i>
	<i>METFORMIN</i>	<i>PLACEBO</i>				
<i>NA</i>	1	0	.			
<i>Live Birth</i>	108	117	225			
<i>TOP_Stillbirth_Miscarriage</i>	0	1	1			
<i>Total</i>	108	118	226			
<i>Frequency Missing = 1</i>						
<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
BirthOut_pp	AllocatedTreatment METFORMIN vs PLACEBO	<0.001	<0.001	>999.999	0.9604	1.0000

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Section 4. Secondary Outcome - All Patients

4.1.1.2.2.1 Delivery Outcome - birth weight

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=227</i>
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	
Birth weight (g)	Mean	3512.4	3503.6	3508.2
	Median	3570.0	3525.0	3550.0
	SD	622.7	562.8	593.5
	MIN,MAX	400,4800	1800,4900	400,4900
	Q1,Q3	3190,3860	3110,3838	3140,3850
	n	118	108	226
	Nmiss	0	1	1

Section 4. Secondary Outcome - All Patients

4.1.1.2.2.2 Delivery Outcome - birth weight split by gender

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight Males (g)	Mean	3603.5	3568.3	3586.5
	Median	3670.0	3540.0	3590.0
	SD	642.1	571.0	606.4
	MIN,MAX	400,4800	2330,4900	400,4900
	Q1,Q3	3308,3970	3135,3880	3273,3908
	n	58	54	112
	Nmiss	0	0	0
Birth weight Females(g)	Mean	3424.3	3438.9	3431.2
	Median	3450.0	3515.0	3485.0
	SD	595.4	552.2	572.9
	MIN,MAX	690,4550	1800,4530	690,4550
	Q1,Q3	3090,3728	3110,3780	3110,3760
	n	60	54	114
	Nmiss	0	0	0

Section 4. Secondary Outcome - All Patients

4.1.1.2.2.3 Delivery Outcome - birth weight split by gestation

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight <=24 WEEKS (g)	Mean		400.0	400.0
	Median		400.0	400.0
	SD		.	.
	MIN,MAX		400,400	400,400
	Q1,Q3		400,400	400,400
	n		1	1
	Nmiss		0	0
Birth weight >24 and <=37 WEEKS (g)	Mean	2721.3	2823.1	2789.2
	Median	2697.5	2737.5	2737.5
	SD	1695.6	629.9	1019.4
	MIN,MAX	690,4800	1800,3740	690,4800
	Q1,Q3	1545,3898	2465,3320	2365,3320
	n	4	8	12
	Nmiss	0	0	0

Section 4. Secondary Outcome - All Patients

4.1.1.2.2.3 Delivery Outcome - birth weight split by gestation (Cont.)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight >37 WEEKS (g)	Mean	3567.9	3558.1	3563.3
	Median	3580.0	3550.0	3570.0
	SD	464.8	523.3	492.0
	MIN,MAX	2600,4700	2110,4900	2110,4900
	Q1,Q3	3240,3860	3200,3890	3220,3860
	n	113	100	213
	Nmiss	0	0	0

Section 4. Secondary Outcome - All Patients

4.1.1.2.2.4 Delivery Outcome - birth weight split by parity

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight parity=0 (g)	Mean	3361.0	3471.7	3421.5
	Median	3380.0	3480.0	3410.0
	SD	597.7	580.8	588.1
	MIN,MAX	690,4450	1800,4900	690,4900
	Q1,Q3	3054,3710	3110,3836	3060,3730
	n	44	53	97
	Nmiss	0	1	1
<hr/>				
Birth weight parity=>1 (g)	Mean	3602.4	3534.4	3573.4
	Median	3665.0	3580.0	3640.0
	SD	623.7	548.5	591.5
	MIN,MAX	400,4800	2110,4790	400,4800
	Q1,Q3	3260,3920	3110,3840	3240,3905
	n	74	55	129
	Nmiss	0	0	0

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Section 4. Secondary Outcome - All Patients

4.1.1.3 Delivery Outcome - Low birth weights

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Gestation (days) at delivery	Delivery date	Labour Type	Birth Outcome categorised as per CRF	Baby death date	Baby gender	Birth weight corrected from kg to g (g)
21119	PLACEBO	152	10JAN2014	Induced	Termination of Pregnancy	10JAN2014	Male	400
14264	PLACEBO	191	12JAN2013	C-section	Live Birth	.	Female	690
11881	METFORMIN	219	04JAN2014	C-section	Live Birth	.	Female	1800

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Section 4. Secondary Outcome - All Patients

4.1.1.4 Delivery Outcome - births before 24 weeks

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Subject Number	Allocated Treatment	Gestation (days) at delivery	Delivery date	LabourType	Birth Outcome categorised as per CRF	Baby death date	Baby gender
21119	PLACEBO	152	10JAN2014	Induced	Termination of Pregnancy	10JAN2014	Male

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Section 4. Secondary Outcome - Only Alive Births

4.1.2.1.1 Delivery Details

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Delivery Method(n(%))	Spontaneous vaginal delivery	63 (53.8)	65 (60.2)	128 (56.9)
	LSCS in labour	18 (15.4)	14 (13.0)	32 (14.2)
	LSCS pre labour	25 (21.4)	17 (15.7)	42 (18.7)
	Forceps/ventouse	11 (9.4)	12 (11.1)	23 (10.2)
C-SECTION index pregnancy(n(%))	Yes	43 (36.8)	31 (28.7)	74 (32.9)
	No	74 (63.2)	77 (71.3)	151 (67.1)
Primary C-SECTION in index pregnancy(n(%))	Yes	25 (21.4)	22 (20.4)	47 (20.9)
	No	92 (78.6)	86 (79.6)	178 (79.1)

Section 4. Secondary Outcome - Only Alive Births

4.1.2.1.2 Delivery Details

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Delivery Blood Loss (mL)	Mean	522.9	500.0	511.8
	Median	400.0	400.0	400.0
	SD	407.6	550.8	481.2
	MIN,MAX	100,2000	50,5000	50,5000
	Q1,Q3	250,600	250,600	250,600
	n	113	106	219
	Nmiss	4	2	6
<hr/>				
Hemorrhage* (n(%))	Missing	4	2	6
	Yes	13 (11.5)	9 (8.5)	22 (10.0)
	No	100 (88.5)	97 (91.5)	197 (90.0)
<hr/>				
SAE recorded due to Hemorrhage# (n(%))	Missing	0	1	1
	Yes	5	4	9
	No	8	4	12

Section 4. Secondary Outcome - Only Alive Births

4.1.2.1.3 Delivery Details

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo	Metformin	Overall
Labour Type (n(%))	Spontaneous	45 (38.5)	44 (40.7)	89 (39.6)
	Induced	50 (42.7)	47 (43.5)	97 (43.1)
	C-section	22 (18.8)	17 (15.7)	39 (17.3)
Non Spontaneous Reason* (n(%))	Post dates	15 (20.8)	8 (12.5)	23 (16.9)
	Pre-eclampsia	3 (4.2)	2 (3.1)	5 (3.7)
	Abruption	0	1 (1.6)	1 (0.7)
	Other maternal condition	21 (29.2)	28 (43.8)	49 (36.0)
	Previous C-section	14 (19.4)	4 (6.3)	18 (13.2)
	Previous obstetric history (other)	3 (4.2)	2 (3.1)	5 (3.7)
	Maternal request	5 (6.9)	3 (4.7)	8 (5.9)
	Suspected fetal compromise	3 (4.2)	8 (12.5)	11 (8.1)
	Malpresentation	3 (4.2)	4 (6.3)	7 (5.1)
	Suspected IUGR	3 (4.2)	0	3 (2.2)
	Suspected Macrosomia	2 (2.8)	4 (6.3)	6 (4.4)

Section 4. Secondary Outcome - Only Alive Births

4.1.2.1.4.1 Delivery Details

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo	Metformin	Overall
Gesta_coded by method* (n(%))	Sponta_vaginal_delivery_<=37 WEEKS	1 (0.9)	2 (1.9)	3 (1.3)
	Sponta_vaginal_delivery_>37 WEEKS	62 (53.0)	63 (58.3)	125 (55.6)
	LSCS in labour_<=37 WEEKS	1 (0.9)	1 (0.9)	2 (0.9)
	LSCS in labour_>37 WEEKS	17 (14.5)	13 (12.0)	30 (13.3)
	LSCS pre labour_<=37 WEEKS	2 (1.7)	4 (3.7)	6 (2.7)
	LSCS pre labour_>37 WEEKS	23 (19.7)	13 (12.0)	36 (16.0)
	Forceps/ventouse_<=37 WEEKS	0	1 (0.9)	1 (0.4)
	Forceps/ventouse_>37 WEEKS	11 (9.4)	11 (10.2)	22 (9.8)
Gesta_coded by labour# (n(%))	Spontaneous_<=37 WEEKS	1 (0.9)	1 (0.9)	2 (0.9)
	Spontaneous_>37 WEEKS	44 (37.6)	43 (39.8)	87 (38.7)
	Induced_<=37 WEEKS	2 (1.7)	3 (2.8)	5 (2.2)
	Induced_>37 WEEKS	48 (41.0)	44 (40.7)	92 (40.9)
	C-section_<=37 WEEKS	1 (0.9)	4 (3.7)	5 (2.2)
	C-section_>37 WEEKS	21 (17.9)	13 (12.0)	34 (15.1)

Section 4. Secondary Outcome - Only Alive Births

4.1.2.1.4.2 Delivery Details (Cont.)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo</i>	<i>Metformin</i>	<i>Overall</i>
Labour by method* <=37 Weeks (n(%))	Spontaneous_vaginal_deliv	1 (25.0)	1 (12.5)	2 (16.7)
	Induced_vaginal_deliv	0	1 (12.5)	1 (8.3)
	Induced_LSCS in labour	1 (25.0)	1 (12.5)	2 (16.7)
	Induced_LSCS pre labour	1 (25.0)	0	1 (8.3)
	Induced_Forceps/ventouse	0	1 (12.5)	1 (8.3)
	C-section_LSCS pre labour	1 (25.0)	4 (50.0)	5 (41.7)
Labour by method* >37 Weeks (n(%))	Spontaneous_vaginal_deliv	34 (30.1)	33 (33.0)	67 (31.5)
	Spontaneous_LSCS in labour	3 (2.7)	3 (3.0)	6 (2.8)
	Spontaneous_Forceps/ventouse	7 (6.2)	7 (7.0)	14 (6.6)
	Induced_vaginal_deliv	28 (24.8)	30 (30.0)	58 (27.2)
	Induced_LSCS in labour	14 (12.4)	10 (10.0)	24 (11.3)
	Induced_LSCS pre labour	2 (1.8)	0	2 (0.9)
	Induced_Forceps/ventouse	4 (3.5)	4 (4.0)	8 (3.8)
	C-section_LSCS pre labour	21 (18.6)	13 (13.0)	34 (16.0)

Section 4. Secondary Outcome - Only Alive Births

4.1.2.1.4.3 Delivery Details - Preterm Birth - Statistical analysis - POST-HOC*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of GESTA_2CODE by AllocatedTreatment</i>			
<i>GESTA_2CODE(Gestation Code 2)</i>		<i>AllocatedTreatment(Allocated Treatment)</i>			
		<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>	
<i>>24 and <=37 WEEKS</i>		8	4	12	
<i>>37 WEEKS</i>		100	113	213	
<i>Total</i>		108	117	225	

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
PRETERM_pp	AllocatedTreatment METFORMIN vs PLACEBO	2.260	0.661	7.732	0.1939	0.2392

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Section 4. Secondary Outcome - Only Alive Births

4.1.2.2.1.1 Delivery Outcome

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth Outcome (n(%))	Live Birth	117 (100)	108 (100)	225 (100)
Baby Gender (n(%))	Male	57 (48.7)	54 (50.0)	111 (49.3)
	Female	60 (51.3)	54 (50.0)	114 (50.7)

Section 4. Secondary Outcome - Only Alive Births

4.1.2.2.1.2 Delivery Outcome - Birth Outcome-Neonatal Death after delivery - Statistical analysis - POST-HOC*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of BirthOutcome by AllocatedTreatment</i>				
		<i>AllocatedTreatment(Allocated Treatment)</i>				
<i>BirthOutcome(Birth Outcome categorised as per CRF)</i>		<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>		
<i>Live Birth</i>		108	117	225		
<i>Total</i>		108	117	225		

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
NEO_DEATH_pp	AllocatedTreatment METFORMIN vs PLACEBO	<0.001	<0.001	>999.999	0.9603	1.0000

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Section 4. Secondary Outcome - Only Alive Births

4.1.2.2.1.3 Delivery Outcome(Cont.)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Baby Gestational age (Days)*	Mean	277.6	276.6	277.1
	Median	278.0	278.0	278.0
	SD	12.7	11.5	12.1
	MIN,MAX	191,297	219,297	191,297
	Q1,Q3	271,287	271,284	271,285
	n	117	108	225
	Nmiss	0	0	0
Baby Gestational age coded (n(%))*	>24 and <=37 WEEKS	4 (3.4)	8 (7.4)	12 (5.3)
	>37 WEEKS	113 (96.6)	100 (92.6)	213 (94.7)

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Section 4. Secondary Outcome - Only Alive Births

4.1.2.2.2.1 Delivery Outcome - birth weight

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight (g)	Mean	3539.0	3503.6	3522.0
	Median	3570.0	3525.0	3550.0
	SD	553.9	562.8	557.2
	MIN,MAX	690,4800	1800,4900	690,4900
	Q1,Q3	3200,3860	3110,3838	3150,3850
	n	117	108	225
	Nmiss	0	0	0

Section 4. Secondary Outcome - Only Alive Births

4.1.2.2.2.2 Delivery Outcome - birth weight split by gender

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight Males (g)	Mean	3659.7	3568.3	3615.2
	Median	3670.0	3540.0	3600.0
	SD	482.9	571.0	527.1
	MIN,MAX	2720,4800	2330,4900	2330,4900
	Q1,Q3	3310,3970	3135,3880	3285,3910
	n	57	54	111
	Nmiss	0	0	0
Birth weight Females(g)	Mean	3424.3	3438.9	3431.2
	Median	3450.0	3515.0	3485.0
	SD	595.4	552.2	572.9
	MIN,MAX	690,4550	1800,4530	690,4550
	Q1,Q3	3090,3728	3110,3780	3110,3760
	n	60	54	114
	Nmiss	0	0	0

Section 4. Secondary Outcome - Only Alive Births

4.1.2.2.2.3 Delivery Outcome - birth weight split by gestation

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight >24 and <=37 WEEKS (g)	Mean	2721.3	2823.1	2789.2
	Median	2697.5	2737.5	2737.5
	SD	1695.6	629.9	1019.4
	MIN,MAX	690,4800	1800,3740	690,4800
	Q1,Q3	1545,3898	2465,3320	2365,3320
	n	4	8	12
	Nmiss	0	0	0
Birth weight >37 WEEKS (g)	Mean	3567.9	3558.1	3563.3
	Median	3580.0	3550.0	3570.0
	SD	464.8	523.3	492.0
	MIN,MAX	2600,4700	2110,4900	2110,4900
	Q1,Q3	3240,3860	3200,3890	3220,3860
	n	113	100	213
	Nmiss	0	0	0

Section 4. Secondary Outcome - Only Alive Births

4.1.2.2.2.4 Delivery Outcome - birth weight split by parity

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Birth weight parity=0 (g)	Mean	3361.0	3471.7	3421.5
	Median	3380.0	3480.0	3410.0
	SD	597.7	580.8	588.1
	MIN,MAX	690,4450	1800,4900	690,4900
	Q1,Q3	3054,3710	3110,3836	3060,3730
	n	44	53	97
	Nmiss	0	0	0
Birth weight parity=>1 (g)	Mean	3646.2	3534.4	3598.2
	Median	3670.0	3580.0	3645.0
	SD	500.0	548.5	522.2
	MIN,MAX	2600,4800	2110,4790	2110,4800
	Q1,Q3	3290,3920	3110,3840	3240,3908
	n	73	55	128
	Nmiss	0	0	0

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Section 4. Secondary Outcome - Only Alive Births

4.1.2.3 Delivery Outcome - Low birth weights

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Gestation (days) at delivery	Delivery date	Labour Type	Birth Outcome categorised as per CRF	Baby death date	Baby gender	Birth weight corrected from kg to g (g)
14264	PLACEBO	191	12JAN2013	C-section	Live Birth	.	Female	690
11881	METFORMIN	219	04JAN2014	C-section	Live Birth	.	Female	1800

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Section 4. Outcomes - Only Alive Births

4.2.1.1 PRIMARY EFFICACY: Birth weight centile

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight centile	Mean	58.527	59.894	59.183
	Median	59.685	64.530	63.585
	SD	27.690	28.273	27.917
	MIN,MAX	1.58,99.95	0.03,99.83	0.03,99.95
	Q1,Q3	34.33,82.48	34.95,83.13	34.53,82.77
	n	117	108	225
	Nmiss	0	0	0

Section 4. Outcomes - Only Alive Births

4.2.1.2 PRIMARY EFFICACY: Birth weight centile split by gender

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight centile Males	Mean	59.594	57.029	58.346
	Median	62.022	62.261	62.022
	SD	27.780	28.811	28.186
	MIN,MAX	1.58,99.95	3.91,99.76	1.58,99.95
	Q1,Q3	35.73,82.48	33.65,79.74	33.69,79.89
	n	57	54	111
	Nmiss	0	0	0
Birth weight centile Females	Mean	57.513	62.759	59.998
	Median	57.154	66.501	64.268
	SD	27.800	27.695	27.752
	MIN,MAX	3.75,99.34	0.03,99.83	0.03,99.83
	Q1,Q3	34.31,82.72	38.90,87.36	35.35,86.16
	n	60	54	114
	Nmiss	0	0	0

Section 4. Outcomes - Only Alive Births

4.2.1.3 PRIMARY EFFICACY: Birth weight centile split by gestation

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight centile >24 and <=37 WEEKS	Mean	55.075	70.181	65.146
	Median	50.782	80.241	76.141
	SD	37.927	28.695	31.171
	MIN,MAX	18.78,99.95	20.03,97.13	18.78,99.95
	Q1,Q3	23.90,86.25	50.45,91.45	31.14,91.45
	n	4	8	12
	Nmiss	0	0	0
Birth weight centile >37 WEEKS (g)	Mean	58.649	59.071	58.847
	Median	59.685	63.906	62.996
	SD	27.480	28.222	27.766
	MIN,MAX	1.58,99.34	0.03,99.83	0.03,99.83
	Q1,Q3	35.17,82.48	34.95,82.77	35.17,82.60
	n	113	100	213
	Nmiss	0	0	0

Section 4. Outcomes - Only Alive Births

4.2.1.4 PRIMARY EFFICACY: Birth weight centile split by parity

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight centile parity=0 (g)	Mean	54.041	59.862	57.222
	Median	50.234	66.310	56.322
	SD	27.729	29.505	28.713
	MIN,MAX	3.34,97.52	3.91,99.83	3.34,99.83
	Q1,Q3	30.56,78.50	33.69,84.14	32.13,83.49
	n	44	53	97
	Nmiss	0	0	0
Birth weight centile parity=>1 (g)	Mean	61.230	59.924	60.669
	Median	65.879	64.228	64.490
	SD	27.502	27.306	27.318
	MIN,MAX	1.58,99.95	0.03,99.28	0.03,99.95
	Q1,Q3	39.95,82.60	38.37,82.77	39.10,82.69
	n	73	55	128
	Nmiss	0	0	0

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Section 4. Outcomes - Only Alive Births

4.2.2.1.1 PRIMARY EFFICACY: Birth weight centile categorised

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Split Birth weight Centile (n(%))	<=3rd	1 (0.9)	1 (0.9)	2 (0.9)
	>3rd and <=5th	2 (1.7)	2 (1.9)	4 (1.8)
	>5th and <=10th	3 (2.6)	3 (2.8)	6 (2.7)
	>10th and <=90th	90 (76.9)	81 (75.0)	171 (76.0)
	>90th and <=95th	9 (7.7)	9 (8.3)	18 (8.0)
	>95th and <=97th	5 (4.3)	4 (3.7)	9 (4.0)
	>97th	7 (6.0)	8 (7.4)	15 (6.7)

Section 4. Secondary Outcome - Only Alive Births

4.2.2.1.2 PRIMARY EFFICACY: Birth weight centile categorised - Statistical analysis - POST-HOC*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of centile_03b by AllocatedTreatment</i>					
		<i>AllocatedTreatment(Allocated Treatment)</i>					
<i>centile_03b</i>	<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>				
<i>No</i>	107	116	223				
<i>Yes</i>	1	1	2				
<i>Total</i>	108	117	225				

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
centile_03b_pp	AllocatedTreatment METFORMIN vs PLACEBO	1.084	0.067	17.549	0.9547	1.0000

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 *Analysed using logistic regression (binary logit), probability modeled is centile_03b='Yes'
 #Significance level set at p<0.05
 Fisher's exact test should be used for reporting due to low cell count
 Detailed analysis in file 'Empowar_4_2_2_1_weight_centile.lst'

Section 4. Secondary Outcome - Only Alive Births

4.2.2.1.3 PRIMARY EFFICACY: Birth weight centile categorised - Statistical analysis - POST-HOC*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of centile_10b by AllocatedTreatment</i>			
		<i>AllocatedTreatment(Allocated Treatment)</i>			
<i>centile_10b</i>	<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>		
<i>No</i>	102	111	213		
<i>Yes</i>	6	6	12		
<i>Total</i>	108	117	225		

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
centile_10b_pp	AllocatedTreatment METFORMIN vs PLACEBO	1.088	0.340	3.482	0.8867	1.0000

Section 4. Outcomes - Only Alive Births

4.2.2.2 PRIMARY EFFICACY: Birth weight centile categorised split by gender

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Split Birth weight Centile Males(n(%))	<=3rd	1 (1.8)	0	1 (0.9)
	>3rd and <=5th	1 (1.8)	2 (3.7)	3 (2.7)
	>5th and <=10th	2 (3.5)	2 (3.7)	4 (3.6)
	>10th and <=90th	42 (73.7)	41 (75.9)	83 (74.8)
	>90th and <=95th	5 (8.8)	2 (3.7)	7 (6.3)
	>95th and <=97th	3 (5.3)	3 (5.6)	6 (5.4)
	>97th	3 (5.3)	4 (7.4)	7 (6.3)
Split Birth weight Centile Females(n(%))	<=3rd	0	1 (1.9)	1 (0.9)
	>3rd and <=5th	1 (1.7)	0	1 (0.9)
	>5th and <=10th	1 (1.7)	1 (1.9)	2 (1.8)
	>10th and <=90th	48 (80.0)	40 (74.1)	88 (77.2)
	>90th and <=95th	4 (6.7)	7 (13.0)	11 (9.6)
	>95th and <=97th	2 (3.3)	1 (1.9)	3 (2.6)
	>97th	4 (6.7)	4 (7.4)	8 (7.0)

Section 4. Outcomes - Only Alive Births

4.2.2.3 PRIMARY EFFICACY: Birth weight centile categorised split by gestation

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Split Birth weight Centile >24 and <=37 WEEKS(n(%))	>10th and <=90th	3 (75.0)	6 (75.0)	9 (75.0)
	>95th and <=97th	0	1 (12.5)	1 (8.3)
	>97th	1 (25.0)	1 (12.5)	2 (16.7)
Split Birth weight Centile >37 WEEKS(n(%))	<=3rd	1 (0.9)	1 (1.0)	2 (0.9)
	>3rd and <=5th	2 (1.8)	2 (2.0)	4 (1.9)
	>5th and <=10th	3 (2.7)	3 (3.0)	6 (2.8)
	>10th and <=90th	87 (77.0)	75 (75.0)	162 (76.1)
	>90th and <=95th	9 (8.0)	9 (9.0)	18 (8.5)
	>95th and <=97th	5 (4.4)	3 (3.0)	8 (3.8)
	>97th	6 (5.3)	7 (7.0)	13 (6.1)

Section 4. Outcomes - Only Alive Births

4.2.2.4 PRIMARY EFFICACY: Birth weight centile categorised split by parity

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Split Birth weight Centile parity=0 (n(%))	>3rd and <=5th	1 (2.3)	2 (3.8)	3 (3.1)
	>5th and <=10th	1 (2.3)	1 (1.9)	2 (2.1)
	>10th and <=90th	37 (84.1)	39 (73.6)	76 (78.4)
	>90th and <=95th	1 (2.3)	6 (11.3)	7 (7.2)
	>95th and <=97th	3 (6.8)	0	3 (3.1)
	>97th	1 (2.3)	5 (9.4)	6 (6.2)
Split Birth weight Centile parity=>1 (n(%))	<=3rd	1 (1.4)	1 (1.8)	2 (1.6)
	>3rd and <=5th	1 (1.4)	0	1 (0.8)
	>5th and <=10th	2 (2.7)	2 (3.6)	4 (3.1)
	>10th and <=90th	53 (72.6)	42 (76.4)	95 (74.2)
	>90th and <=95th	8 (11.0)	3 (5.5)	11 (8.6)
	>95th and <=97th	2 (2.7)	4 (7.3)	6 (4.7)
	>97th	6 (8.2)	3 (5.5)	9 (7.0)

Section 4. Outcomes - Only Alive Births

4.3.1 PRIMARY EFFICACY: Calculated Z score

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall N=227</i>
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	
Z-score for birth weight centile	Mean	0.3130	0.3604	0.3358
	Median	0.2452	0.3727	0.3474
	SD	0.9781	1.0580	1.0152
	MIN,MAX	-2.150,3.299	-3.428,2.929	-3.428,3.299
	Q1,Q3	-0.404,0.934	-0.387,0.959	-0.398,0.945
	n	117	108	225
	Nmiss	0	0	0

Section 4. Outcomes - Only Alive Births

4.3.2 PRIMARY EFFICACY: Calculated Z score - Statistical Analysis

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
z-score - pp	0.270	0.1584	117	0.338	0.1506	108	0.068	-0.188	0.324	0.276	0.6001

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By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in table 4.3.1 of this report

Outcome analysed using a linear regression model, adjusted by BMI band and centre. Significance level set at p<0.05

Estimated mean represents the adjusted means for the z score by allocated treatment,

SE represents standard error of the estimated mean and N represents number of observations

*Represents the difference between the estimated means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_4_3_2_primary_outcome_z_analysis.lst'

Parameter shown normal behavior

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.1 Fasted Glucose - Visit 3 Randomisation (12-16 Weeks)*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
GTT - V3 - base (mmol/L)	Mean	4.42	4.41	4.41
	Median	4.40	4.40	4.40
	SD	0.36	0.37	0.36
	MIN,MAX	3.5,5.6	3.5,5.4	3.5,5.6
	Q1,Q3	4.2,4.6	4.1,4.7	4.1,4.7
	n	118	109	227
	Nmiss	0	0	0
GTT - V3 - 2 hr (mmol/L)	Mean	5.45	5.17	5.31
	Median	5.45	5.10	5.30
	SD	1.18	1.10	1.15
	MIN,MAX	2.6,7.8	2.2,7.7	2.2,7.8
	Q1,Q3	4.6,6.4	4.6,5.9	4.6,6.1
	n	118	109	227
	Nmiss	0	0	0

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.2 Fasted Glucose - Visit 5 (28 Weeks)

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
GTT - V5 - base (mmol/L)	Mean	4.49	4.34	4.42
	Median	4.45	4.30	4.40
	SD	0.43	0.38	0.41
	MIN,MAX	3.7,5.6	3.4,5.2	3.4,5.6
	Q1,Q3	4.2,4.8	4.1,4.6	4.2,4.7
	n	116	109	225
	Nmiss	2	0	2
GTT - V5 - 2 hr (mmol/L)	Mean	5.90	5.56	5.74
	Median	5.85	5.50	5.60
	SD	1.18	1.20	1.20
	MIN,MAX	2.4,8.3	3.1,10.0	2.4,10.0
	Q1,Q3	5.1,6.7	4.9,6.1	5.0,6.5
	n	116	108	224
	Nmiss	2	1	3

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.3 Fasted Glucose - Visit 6 (36 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
GTT - V6 - base (mmol/L)	Mean	4.43	4.34	4.39
	Median	4.40	4.20	4.30
	SD	0.51	0.45	0.48
	MIN,MAX	2.7,5.8	3.4,5.9	2.7,5.9
	Q1,Q3	4.0,4.8	4.0,4.6	4.0,4.7
	n	104	93	197
	Nmiss	14	16	30
GTT - V6 - 2 hr (mmol/L)	Mean	6.04	5.79	5.92
	Median	5.90	5.70	5.80
	SD	1.53	1.34	1.44
	MIN,MAX	3.0,10.3	2.7,9.1	2.7,10.3
	Q1,Q3	4.9,7.2	5.0,6.5	4.9,6.8
	n	103	92	195
	Nmiss	15	17	32

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.4.1 Fasted Glucose - Visit 6 (36 Weeks) - Statistical Analysis

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
Glucose_V6_Baseline - pp	4.458	0.0767	104	4.367	0.0735	93	-0.091	-0.221	0.040	1.875	0.1726
Glucose_V6_Two_Hour - pp	6.052	0.2315	103	5.804	0.2217	92	-0.248	-0.643	0.148	1.529	0.2179

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By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in table 5.1.3 of this report

Outcome analysed using a linear regression model. Significance level set at p<0.05

Estimated mean represents the adjusted means for the glucose in blood by allocated treatment,

SE represents standard error of the estimated mean and N represents number of observations

*Represents the difference between the estimated means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_5_1_4_glucose_outcome_analysis.lst'

Parameters shown normal or near-normal behavior

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.4.2 Fasted Glucose - Visit 5 (28 Weeks) - Statistical Analysis - POST-HOC

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Lower CI*	Estimated Mean Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
Glucose_V5_Baseline - pp	4.454	0.0650	116	4.313	0.0613	109	-0.141	-0.246	-0.036	7.044	0.0086
Glucose_V5_Two_Hour - pp	5.766	0.1908	116	5.454	0.1801	108	-0.312	-0.620	-0.004	3.989	0.0471

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 02:47

By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in table 5.1.2 of this report

Outcome analysed using a linear regression model. Significance level set at p<0.05

Estimated mean represents the adjusted means for the glucose in blood by allocated treatment,

SE represents standard error of the estimated mean and N represents number of observations

*Represents the difference between the estimated means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_5_1_4_glucose_outcome_analysis_v5.lst'

Parameters shown normal or near-normal behavior

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.1 Fasted Glucose - Visit 5 (28 Weeks) split by C-section

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Yes C-section - GTT - V5 - base (mmol/L)	Mean	4.58	4.37	4.49
	Median	4.60	4.40	4.50
	SD	0.48	0.37	0.45
	MIN,MAX	3.7,5.5	3.5,5.0	3.5,5.5
	Q1,Q3	4.2,5.0	4.2,4.7	4.2,4.8
	n	43	31	74
	Nmiss	0	0	0
Yes C-section - GTT - V5 - 2 hr (mmol/L)	Mean	6.26	5.90	6.11
	Median	6.30	5.60	6.00
	SD	1.46	1.24	1.37
	MIN,MAX	2.4,8.3	4.2,8.9	2.4,8.9
	Q1,Q3	5.3,7.5	5.1,6.5	5.1,7.3
	n	43	31	74
	Nmiss	0	0	0

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.1 Fasted Glucose - Visit 5 (28 Weeks) split by C-section

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
No C-section - GTT - V5 - base (mmol/L)	Mean	4.44	4.33	4.38
	Median	4.40	4.30	4.40
	SD	0.39	0.39	0.39
	MIN,MAX	3.7,5.6	3.4,5.2	3.4,5.6
	Q1,Q3	4.2,4.7	4.1,4.6	4.1,4.6
	n	73	77	150
	Nmiss	2	0	2
No C-section - GTT - V5 - 2 hr (mmol/L)	Mean	5.68	5.44	5.56
	Median	5.60	5.45	5.50
	SD	0.93	1.17	1.06
	MIN,MAX	3.5,8.3	3.1,10.0	3.1,10.0
	Q1,Q3	5.0,6.3	4.8,6.0	4.9,6.2
	n	73	76	149
	Nmiss	2	1	3

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.2 Fasted Glucose - Visit 6 (36 Weeks) split by C-section

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Yes C-section - GTT - V6 - base (mmol/L)	Mean	4.42	4.34	4.39
	Median	4.50	4.30	4.40
	SD	0.53	0.44	0.49
	MIN,MAX	2.7,5.6	3.6,5.5	2.7,5.6
	Q1,Q3	4.0,4.8	4.0,4.5	4.0,4.7
	n	38	25	63
	Nmiss	5	4	9
Yes C-section - GTT - V6 - 2 hr (mmol/L)	Mean	6.32	5.85	6.13
	Median	6.30	5.80	6.10
	SD	1.65	1.20	1.49
	MIN,MAX	3.0,10.3	2.7,8.0	2.7,10.3
	Q1,Q3	5.1,7.4	5.5,6.5	5.2,7.2
	n	38	25	63
	Nmiss	5	4	9

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.2 Fasted Glucose - Visit 6 (36 Weeks) split by C-section

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
No C-section - GTT - V6 - base (mmol/L)	Mean	4.43	4.34	4.38
	Median	4.30	4.20	4.30
	SD	0.50	0.46	0.48
	MIN,MAX	3.4,5.8	3.4,5.9	3.4,5.9
	Q1,Q3	4.1,4.7	4.0,4.6	4.0,4.6
	n	66	68	134
	Nmiss	9	9	18
No C-section - GTT - V6 - 2 hr (mmol/L)	Mean	5.88	5.76	5.82
	Median	5.70	5.70	5.70
	SD	1.44	1.39	1.41
	MIN,MAX	3.5,9.8	3.2,9.1	3.2,9.8
	Q1,Q3	4.9,6.8	4.9,6.4	4.9,6.5
	n	65	67	132
	Nmiss	10	10	20

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.3 Fasted Glucose - Visit 5 (28 Weeks) split by birth centile

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
3%<=_GTT_V5_base (mmol/L)	Mean	4.00	4.00	4.00
	Median	4.00	4.00	4.00
	SD	.	.	0.00
	MIN,MAX	4.0,4.0	4.0,4.0	4.0,4.0
	Q1,Q3	4.0,4.0	4.0,4.0	4.0,4.0
	n	1	1	2
	Nmiss	0	0	0
3%<=_GTT_V5_2 hr (mmol/L)	Mean	4.80	5.10	4.95
	Median	4.80	5.10	4.95
	SD	.	.	0.21
	MIN,MAX	4.8,4.8	5.1,5.1	4.8,5.1
	Q1,Q3	4.8,4.8	5.1,5.1	4.8,5.1
	n	1	1	2
	Nmiss	0	0	0

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.3 Fasted Glucose - Visit 5 (28 Weeks) split by birth centile

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
5%<=_GTT_V5_base (mmol/L)	Mean	4.03	4.00	4.02
	Median	4.00	4.00	4.00
	SD	0.06	0.40	0.26
	MIN,MAX	4.0,4.1	3.6,4.4	3.6,4.4
	Q1,Q3	4.0,4.1	3.6,4.4	4.0,4.1
	n	3	3	6
	Nmiss	0	0	0
5%<=_GTT_V5_2 hr (mmol/L)	Mean	4.07	4.93	4.50
	Median	4.80	5.10	4.90
	SD	1.45	1.06	1.23
	MIN,MAX	2.4,5.0	3.8,5.9	2.4,5.9
	Q1,Q3	2.4,5.0	3.8,5.9	3.8,5.1
	n	3	3	6
	Nmiss	0	0	0

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.3 Fasted Glucose - Visit 5 (28 Weeks) split by birth centile

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
10%<=_GTT_V5_base (mmol/L)	Mean	4.38	4.15	4.27
	Median	4.25	4.20	4.25
	SD	0.43	0.34	0.39
	MIN,MAX	4.0,5.0	3.6,4.5	3.6,5.0
	Q1,Q3	4.0,4.8	4.0,4.4	4.0,4.5
	n	6	6	12
	Nmiss	0	0	0
10%<=_GTT_V5_2 hr (mmol/L)	Mean	4.63	4.72	4.68
	Median	4.90	4.75	4.90
	SD	1.27	0.89	1.05
	MIN,MAX	2.4,6.2	3.7,5.9	2.4,6.2
	Q1,Q3	4.2,5.2	3.8,5.4	4.0,5.3
	n	6	6	12
	Nmiss	0	0	0

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.3 Fasted Glucose - Visit 5 (28 Weeks) split by birth centile

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
10%> AND 90%<=_GTT_V5_base (mmol/L)	Mean	4.47	4.34	4.41
	Median	4.40	4.30	4.40
	SD	0.42	0.40	0.41
	MIN,MAX	3.7,5.5	3.4,5.2	3.4,5.5
	Q1,Q3	4.2,4.7	4.1,4.6	4.2,4.7
	n	89	81	170
	Nmiss	1	0	1
10%> AND 90%<=_GTT_V5_2 hr (mmol/L)	Mean	5.86	5.64	5.76
	Median	5.80	5.60	5.70
	SD	1.13	1.25	1.19
	MIN,MAX	3.5,8.3	3.1,10.0	3.1,10.0
	Q1,Q3	5.1,6.7	4.9,6.4	5.0,6.5
	n	89	80	169
	Nmiss	1	1	2

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.3 Fasted Glucose - Visit 5 (28 Weeks) split by birth centile

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
90%>_GTT_V5_base (mmol/L)	Mean	4.60	4.41	4.50
	Median	4.70	4.40	4.55
	SD	0.48	0.33	0.42
	MIN,MAX	3.7,5.6	3.7,5.0	3.7,5.6
	Q1,Q3	4.4,4.9	4.3,4.7	4.3,4.7
	n	21	21	42
	Nmiss	0	0	0
90%>_GTT_V5_2 hr (mmol/L)	Mean	6.40	5.58	5.99
	Median	6.30	5.50	5.90
	SD	1.14	1.03	1.15
	MIN,MAX	4.4,8.3	3.6,8.4	3.6,8.4
	Q1,Q3	5.4,7.4	5.1,6.0	5.2,6.9
	n	21	21	42
	Nmiss	0	0	0

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.3 Fasted Glucose - Visit 5 (28 Weeks) split by birth centile

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
95%>_GTT_V5_base (mmol/L)	Mean	4.60	4.46	4.53
	Median	4.55	4.45	4.55
	SD	0.49	0.25	0.39
	MIN,MAX	4.0,5.6	4.0,4.8	4.0,5.6
	Q1,Q3	4.3,4.9	4.3,4.7	4.3,4.7
	n	12	12	24
	Nmiss	0	0	0
95%>_GTT_V5_2 hr (mmol/L)	Mean	6.30	5.58	5.94
	Median	6.15	5.70	5.95
	SD	0.97	1.21	1.13
	MIN,MAX	5.2,8.3	3.6,8.4	3.6,8.4
	Q1,Q3	5.4,7.0	4.9,6.1	5.3,6.4
	n	12	12	24
	Nmiss	0	0	0

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.3 Fasted Glucose - Visit 5 (28 Weeks) split by birth centile

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
97%>_GTT_V5_base (mmol/L)	Mean	4.71	4.45	4.57
	Median	4.70	4.45	4.60
	SD	0.48	0.29	0.40
	MIN,MAX	4.1,5.6	4.0,4.8	4.0,5.6
	Q1,Q3	4.4,5.0	4.3,4.7	4.3,4.7
	n	7	8	15
	Nmiss	0	0	0
97%>_GTT_V5_2 hr (mmol/L)	Mean	5.93	5.45	5.67
	Median	5.90	5.95	5.90
	SD	0.71	1.00	0.88
	MIN,MAX	5.2,7.1	3.6,6.3	3.6,7.1
	Q1,Q3	5.3,6.4	4.9,6.1	5.3,6.3
	n	7	8	15
	Nmiss	0	0	0

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.4 Fasted Glucose - Visit 6 (36 Weeks) split by birth centile

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
3%<=_GTT_V6_base (mmol/L)	Mean	3.40	.	3.40
	Median	3.40	.	3.40
	SD	.	.	.
	MIN,MAX	3.4,3.4	..	3.4,3.4
	Q1,Q3	3.4,3.4	..	3.4,3.4
	n	1	0	1
	Nmiss	0	1	1
3%<=_GTT_V6_2 hr (mmol/L)	Mean	7.40	.	7.40
	Median	7.40	.	7.40
	SD	.	.	.
	MIN,MAX	7.4,7.4	..	7.4,7.4
	Q1,Q3	7.4,7.4	..	7.4,7.4
	n	1	0	1
	Nmiss	0	1	1

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.4 Fasted Glucose - Visit 6 (36 Weeks) split by birth centile

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
5%<=_GTT_V6_base (mmol/L)	Mean	3.73	3.90	3.80
	Median	3.90	3.90	3.90
	SD	0.29	0.42	0.31
	MIN,MAX	3.4,3.9	3.6,4.2	3.4,4.2
	Q1,Q3	3.4,3.9	3.6,4.2	3.6,3.9
	n	3	2	5
	Nmiss	0	1	1
5%<=_GTT_V6_2 hr (mmol/L)	Mean	5.30	5.40	5.34
	Median	5.50	5.40	5.50
	SD	2.21	1.13	1.66
	MIN,MAX	3.0,7.4	4.6,6.2	3.0,7.4
	Q1,Q3	3.0,7.4	4.6,6.2	4.6,6.2
	n	3	2	5
	Nmiss	0	1	1

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.4 Fasted Glucose - Visit 6 (36 Weeks) split by birth centile

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
10%<=_GTT_V6_base (mmol/L)	Mean	4.13	4.38	4.25
	Median	4.10	4.60	4.30
	SD	0.49	0.49	0.48
	MIN,MAX	3,4,4.7	3,6,4.8	3,4,4.8
	Q1,Q3	3,9,4.6	4,2,4.7	3,9,4.7
	n	6	5	11
	Nmiss	0	1	1
10%<=_GTT_V6_2 hr (mmol/L)	Mean	5.92	4.92	5.46
	Median	5.85	5.20	5.80
	SD	1.72	1.39	1.59
	MIN,MAX	3,0,7.9	2,7,6.2	2,7,7.9
	Q1,Q3	5,5,7.4	4,6,5.9	4,6,6.2
	n	6	5	11
	Nmiss	0	1	1

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.4 Fasted Glucose - Visit 6 (36 Weeks) split by birth centile

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall
		Placebo	Metformin	
10%> AND 90%<=_GTT_V6_base (mmol/L)	Mean	4.41	4.31	4.37
	Median	4.40	4.20	4.30
	SD	0.50	0.46	0.48
	MIN,MAX	2.7,5.8	3.4,5.9	2.7,5.9
	Q1,Q3	4.0,4.7	4.0,4.6	4.0,4.7
	n	80	69	149
	Nmiss	10	11	21
10%> AND 90%<=_GTT_V6_2 hr (mmol/L)	Mean	5.84	5.88	5.86
	Median	5.70	5.70	5.70
	SD	1.46	1.43	1.44
	MIN,MAX	3.2,9.5	3.2,9.1	3.2,9.5
	Q1,Q3	4.6,6.8	4.9,6.5	4.8,6.7
	n	79	69	148
	Nmiss	11	11	22

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.4 Fasted Glucose - Visit 6 (36 Weeks) split by birth centile

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
90%>_GTT_V6_base (mmol/L)	Mean	4.61	4.41	4.51
	Median	4.40	4.40	4.40
	SD	0.54	0.43	0.49
	MIN,MAX	3.8,5.6	3.9,5.5	3.8,5.6
	Q1,Q3	4.3,5.0	4.1,4.6	4.2,4.8
	n	18	19	37
	Nmiss	3	1	4
90%>_GTT_V6_2 hr (mmol/L)	Mean	6.94	5.67	6.30
	Median	6.80	5.75	6.00
	SD	1.52	0.84	1.37
	MIN,MAX	5.1,10.3	3.6,7.2	3.6,10.3
	Q1,Q3	5.8,7.5	5.0,6.1	5.3,7.1
	n	18	18	36
	Nmiss	3	2	5

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.4 Fasted Glucose - Visit 6 (36 Weeks) split by birth centile

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
95%>_GTT_V6_base (mmol/L)	Mean	4.88	4.31	4.58
	Median	4.80	4.30	4.40
	SD	0.53	0.34	0.52
	MIN,MAX	4.2,5.6	3.9,5.1	3.9,5.6
	Q1,Q3	4.4,5.3	4.0,4.4	4.2,5.0
	n	9	10	19
	Nmiss	3	1	4
95%>_GTT_V6_2 hr (mmol/L)	Mean	7.06	5.90	6.48
	Median	7.20	5.90	6.05
	SD	1.40	0.77	1.25
	MIN,MAX	5.1,9.8	5.0,7.2	5.0,9.8
	Q1,Q3	6.1,7.5	5.3,6.0	5.8,7.2
	n	9	9	18
	Nmiss	3	2	5

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.5.4 Fasted Glucose - Visit 6 (36 Weeks) split by birth centile

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
97%>_GTT_V6_base (mmol/L)	Mean	5.08	4.31	4.59
	Median	5.15	4.30	4.40
	SD	0.51	0.39	0.56
	MIN,MAX	4.4,5.6	3.9,5.1	3.9,5.6
	Q1,Q3	4.7,5.5	4.0,4.4	4.2,5.1
	n	4	7	11
	Nmiss	3	0	3
97%>_GTT_V6_2 hr (mmol/L)	Mean	7.83	5.88	6.66
	Median	7.85	5.60	6.40
	SD	1.66	0.97	1.56
	MIN,MAX	5.8,9.8	5.0,7.2	5.0,9.8
	Q1,Q3	6.7,9.0	5.0,6.9	5.3,7.5
	n	4	6	10
	Nmiss	3	1	4

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.6.1 Gestational diabetes mellitus (GDM) - OGTT Test*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
GDM WHO CRITERIA*# (n(%))	Missing	15	16	31
	No	84 (81.6)	80 (86.0)	164 (83.7)
	Yes	19 (18.4)	13 (14.0)	32 (16.3)
GDM WHO CRITERIA CODED# (n(%))	Missing	15	16	31
	GDM first at visit 5 (28 weeks)	8 (7.8)	6 (6.5)	14 (7.1)
	GDM first at visit 6 (36 weeks)	11 (10.7)	7 (7.5)	18 (9.2)
	NO GDM	84 (81.6)	80 (86.0)	164 (83.7)
GDM IADPSG CRITERIA*\$ (n(%))	Missing	14	17	31
	No	82 (78.8)	77 (83.7)	159 (81.1)
	Yes	22 (21.2)	15 (16.3)	37 (18.9)
GDM IADPSG CRITERIA CODED\$ (n(%))	Missing	14	17	31
	GDM first at visit 5 (28 weeks)	14 (13.5)	5 (5.4)	19 (9.7)
	GDM first at visit 6 (36 weeks)	8 (7.7)	10 (10.9)	18 (9.2)
	NO GDM	82 (78.8)	77 (83.7)	159 (81.1)

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N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*Once GDM is present in visit 5 then it will stay present in visit 6

#WHO criteria: Fasting glucose \geq 7.0 mmol/l or 2hr glucose \geq 7.8 mmol/l\$IADPSG criteria: Fasting glucose \geq 5.1 mmol/l or 2hr glucose \geq 8.5 mmol/l

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.6.2 Gestational diabetes mellitus (GDM) IADPSG\$ - OGTT Test* - Statistical Analysis - POST-HOC*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Frequency</i>			
<i>Table of GDM_IAD by Allocated Treatment</i>			
<i>GDM_IAD(GDM calculated using IADPSG criteria (Y/N))</i>	<i>Allocated Treatment(Allocated Treatment)</i>		<i>Total</i>
	<i>METFORMIN</i>	<i>PLACEBO</i>	
<i>Missing</i>	17	14	.
<i>No</i>	77	82	159
<i>Yes</i>	15	22	37
<i>Total</i>	92	104	196

Frequency Missing = 31

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
GDMIAD_pp	Allocated Treatment METFORMIN vs PLACEBO	0.726	0.351	1.501	0.3877	0.4655

Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.6.3 Gestational diabetes mellitus (GDM) IADPSG\$ - OGTT Test* - Statistical Analysis - POST-HOC*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Frequency</i>	<i>Table of GDM_CODE_IAD by AllocatedTreatment</i>		
	<i>GDM_CODE_IAD(GDM calculated using IADPSG criteria by visit)</i>	<i>AllocatedTreatment(Allocated Treatment)</i>	
	<i>METFORMIN</i>	<i>PLACEBO</i>	
<i>Missing</i>	17	14	.
<i>GDM first at visit 5 (28 weeks)</i>	5	14	19
<i>GDM first at visit 6 (36 weeks)</i>	10	8	18
<i>NO GDM</i>	77	82	159
<i>Total</i>	92	104	196

Frequency Missing = 31

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Section 5. Maternal insulin resistance (Secondary Outcome)

5.1.6.3 Gestational diabetes mellitus (GDM) IADPSG\$ - OGTT Test* - Statistical Analysis - POST-HOC*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Statistics for Table of GDM_CODE_IAD by Allocated Treatment

Statistic	DF	Value	Prob
Chi-Square	2	3.9226	0.1407
Likelihood Ratio Chi-Square	2	4.0837	0.1298
Mantel-Haenszel Chi-Square	1	2.0234	0.1549
Phi Coefficient		0.1415	
Contingency Coefficient		0.1401	
Cramer's V		0.1415	

Effective Sample Size = 196

Frequency Missing = 31

WARNING: 14 % of the data are missing.

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Summary statistics are presented in table 5.1.6.1 of this report

*Analysed using The Mantel-Haenszel chi-square statistic tests

#Significance level set at $p < 0.05$. Detailed analysis in file 'Empowar_5_1_6_glucose_GDM_analysis.lst'

\$IADPSG criteria: Fasting glucose ≥ 5.1 mmol/l or 2hr glucose ≥ 8.5 mmol/l

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Section 5. Maternal insulin resistance (Secondary Outcome)

5.2.1 Insulin - Visit 2 Consent/Baseline (10-16 Weeks), Visit 5 (28 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Insulin - Visit 2 (mIU/ml)	Mean	22.963	21.915	22.464
	Median	20.823	20.557	20.773
	SD	10.462	8.996	9.779
	MIN,MAX	7.43,71.22	2.00,45.46	2.00,71.22
	Q1,Q3	16.50,27.27	15.64,26.94	15.81,27.27
	n	101	92	193
	Nmiss	17	17	34
Insulin - Visit 5 (mIU/ml)	Mean	28.073	24.539	26.371
	Median	24.360	22.995	23.810
	SD	13.285	12.181	12.854
	MIN,MAX	9.82,89.98	6.82,91.05	6.82,91.05
	Q1,Q3	19.74,31.85	16.95,29.19	18.05,30.73
	n	99	92	191
	Nmiss	19	17	36

Section 5. Maternal insulin resistance (Secondary Outcome)

5.2.1 Insulin - Visit 6 (36 Weeks) (Cont.)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Insulin - Visit 6 (mIU/ml)	Mean	31.886	32.588	32.218
	Median	29.134	27.088	28.632
	SD	13.402	26.065	20.334
	MIN,MAX	10.10,91.87	9.78,204.26	9.78,204.26
	Q1,Q3	22.44,37.46	17.65,37.34	20.83,37.34
	n	88	79	167
	Nmiss	30	30	60

Section 5. Maternal insulin resistance (Secondary Outcome)

5.2.2.1 Fasted Insulin - Visit 6 (36 Weeks) - Statistical Analysis - POST-HOC

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
Insulin_log_visit_6 - pp	3.502	0.0860	88	3.438	0.0831	79	-0.063	-0.199	0.072	0.851	0.3576

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By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in table 5.2.1 of this report

Outcome analysed using a linear regression model. Significance level set at p<0.05

Estimated mean represents the adjusted means of the log transformed insulin in blood by allocated treatment,

SE represents standard error of the estimated log transformed mean and N represents number of observations

*Represents the difference between the estimated log transformed mean and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_5_2_2_INSULIN_RES_outcome_analysis.lst'

Parameter shown normal or near-normal behavior

Section 5. Maternal insulin resistance (Secondary Outcome)

5.2.2.2 Fasted Insulin - Visit 5 (28 Weeks) - Statistical Analysis - POST-HOC

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Lower CI*	Estimated Mean Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
Insulin_log_visit_5 - pp	3.323	0.0737	99	3.185	0.0696	92	-0.138	-0.251	-0.025	5.772	0.0173

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 02:47

By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in table 5.2.1 of this report

Outcome analysed using a linear regression model. Significance level set at p<0.05

Estimated mean represents the adjusted means of the log transformed insulin in blood by allocated treatment,

SE represents standard error of the estimated log transformed mean and N represents number of observations

*Represents the difference between the estimated log transformed mean and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_5_2_2_INSULIN_RES_outcome_analysis_v5'.lst

Parameter shown normal or near-normal behavior

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.1 HOMA-IR - Visit 2 Consent/Baseline (10-16 Weeks) and Visit 5 (28 Weeks)

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
HOMA - visit 2 - base	Mean	4.592	4.338	4.471
	Median	3.954	3.966	3.961
	SD	2.322	1.824	2.098
	MIN,MAX	1.16,14.24	0.34,8.93	0.34,14.24
	Q1,Q3	3.09,5.54	3.10,5.44	3.09,5.53
	n	101	92	193
	Nmiss	17	17	34
HOMA - visit 5 - base	Mean	5.683	4.812	5.261
	Median	4.902	4.650	4.754
	SD	2.986	2.544	2.808
	MIN,MAX	1.83,18.99	1.23,19.42	1.23,19.42
	Q1,Q3	3.82,6.56	3.09,6.01	3.37,6.23
	n	98	92	190
	Nmiss	20	17	37

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.2 HOMA-IR - Visit 6 (36 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
HOMA - visit 6 - base	Mean	6.362	6.222	6.297
	Median	5.809	5.056	5.358
	SD	2.963	4.904	3.976
	MIN,MAX	1.62,16.74	1.74,34.50	1.62,34.50
	Q1,Q3	4.40,7.42	3.40,7.16	3.71,7.31
	n	88	77	165
	Nmiss	30	32	62

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.3.1 HOMA_IR - VISIT 6 (36 WEEKS) - Statistical Analysis

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
HOMA-IR_log_visit_6 - pp	1.876	0.0947	88	1.784	0.0920	77	-0.092	-0.243	0.059	1.459	0.2290

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 02:47

By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in table 5.3.2 of this report

Outcome analysed using a linear regression model. Significance level set at p<0.05

Estimated mean represents the adjusted means of the log transformed HOMA-IR in blood by allocated treatment,

SE represents standard error of the estimated log transformed means and N represents number of observations

*Represents the difference between the estimated log transformed means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_5_3_4_glucose_outcome_analysis.lst'

Parameter shown normal or near-normal behavior

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.3.2 HOMA_IR - VISIT 5 (28 WEEKS) - Statistical Analysis - POST-HOC

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Lower CI*	Estimated Mean Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
HOMA-IR_log_visit_5 - pp	1.692	0.0816	98	1.527	0.0770	92	-0.165	-0.290	-0.039	6.726	0.0103

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 02:47

By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in table 5.3.1 of this report

Outcome analysed using a linear regression model. Significance level set at p<0.05

Estimated mean represents the adjusted means of the log transformed HOMA-IR in blood by allocated treatment,

SE represents standard error of the estimated log transformed mean and N represents number of observations

*Represents the difference between the estimated log transformed means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_5_3_4_glucose_outcome_analysis_5v.lst'

Parameter shown normal or near-normal behavior

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.4.1 HOMA-IR - Visit 5 (28 Weeks) split by C-section

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Yes C-section - HOMA_IR - V5 - base	Mean	5.85	5.39	5.64
	Median	5.37	5.25	5.25
	SD	2.61	3.19	2.87
	MIN,MAX	2.6,13.4	1.9,19.4	1.9,19.4
	Q1,Q3	3.8,7.1	3.3,6.2	3.7,6.8
	n	35	29	64
	Nmiss	8	2	10
No C-section - HOMA_IR - V5 - base	Mean	5.59	4.54	5.07
	Median	4.69	4.30	4.59
	SD	3.19	2.18	2.78
	MIN,MAX	1.8,19.0	1.2,11.3	1.2,19.0
	Q1,Q3	3.5,6.3	3.0,5.7	3.2,5.8
	n	63	62	125
	Nmiss	12	15	27

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.4.2 HOMA-IR - Visit 6 (36 Weeks) split by C-section

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Yes C-section - HOMA_IR - V6 - base	Mean	6.79	5.10	6.11
	Median	6.23	5.06	5.40
	SD	3.06	2.03	2.80
	MIN,MAX	2.7,13.8	1.7,9.5	1.7,13.8
	Q1,Q3	4.7,8.0	3.3,6.7	4.1,7.2
	n	33	22	55
	Nmiss	10	7	17
No C-section - HOMA_IR - V6 - base	Mean	6.10	6.67	6.39
	Median	5.60	4.99	5.32
	SD	2.90	5.61	4.46
	MIN,MAX	1.6,16.7	1.9,34.5	1.6,34.5
	Q1,Q3	4.1,7.4	3.4,7.9	3.6,7.5
	n	55	55	110
	Nmiss	20	22	42

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.4.3 HOMA-IR - Visit 5 (28 Weeks) split by birth centile

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
3%<=_HOMA_IR_V5_base	Mean	4.04	2.34	3.19
	Median	4.04	2.34	3.19
	SD	.	.	1.20
	MIN,MAX	4.0,4.0	2.3,2.3	2.3,4.0
	Q1,Q3	4.0,4.0	2.3,2.3	2.3,4.0
	n	1	1	2
	Nmiss	0	0	0
5%<=_HOMA_IR_V5_base	Mean	3.85	2.88	3.36
	Median	4.04	2.83	3.14
	SD	0.94	0.56	0.88
	MIN,MAX	2.8,4.7	2.3,3.5	2.3,4.7
	Q1,Q3	2.8,4.7	2.3,3.5	2.8,4.0
	n	3	3	6
	Nmiss	0	0	0

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.4.3 HOMA-IR - Visit 5 (28 Weeks) split by birth centile

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
10%<=_HOMA_IR_V5_base	Mean	4.72	3.77	4.29
	Median	4.81	3.44	4.04
	SD	1.23	1.75	1.49
	MIN,MAX	2.8,6.5	2.3,6.8	2.3,6.8
	Q1,Q3	4.0,5.4	2.8,3.5	2.8,5.4
	n	6	5	11
	Nmiss	0	1	1
10%> AND 90%<=_HOMA_IR_V5_base	Mean	5.53	4.65	5.11
	Median	4.62	4.65	4.64
	SD	2.98	2.09	2.62
	MIN,MAX	1.8,19.0	1.2,11.3	1.2,19.0
	Q1,Q3	3.7,6.4	3.1,5.6	3.3,6.1
	n	75	68	143
	Nmiss	15	13	28

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.4.3 HOMA-IR - Visit 5 (28 Weeks) split by birth centile

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
90%>_HOMA_IR_V5_base	Mean	6.72	5.71	6.20
	Median	5.78	5.56	5.77
	SD	3.31	3.92	3.62
	MIN,MAX	2.7,14.8	1.5,19.4	1.5,19.4
	Q1,Q3	4.9,7.0	3.1,6.9	4.3,6.9
	n	17	18	35
	Nmiss	4	3	7
95%>_HOMA_IR_V5_base	Mean	5.37	5.82	5.64
	Median	5.74	4.94	5.53
	SD	1.34	4.68	3.66
	MIN,MAX	2.7,7.0	1.5,19.4	1.5,19.4
	Q1,Q3	4.7,6.2	3.0,6.9	3.9,6.7
	n	8	12	20
	Nmiss	4	0	4

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.4.3 HOMA-IR - Visit 5 (28 Weeks) split by birth centile

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
97%>_HOMA_IR_V5_base	Mean	5.74	6.54	6.27
	Median	5.74	5.15	5.73
	SD	0.67	5.54	4.45
	MIN,MAX	4.9,6.6	1.5,19.4	1.5,19.4
	Q1,Q3	5.3,6.2	3.6,6.9	4.5,6.7
	n	4	8	12
	Nmiss	3	0	3

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.4.4 HOMA-IR - Visit 6 (36 Weeks) split by birth centile

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
3%<=_HOMA_IR_V6_base	Mean	2.14	.	2.14
	Median	2.14	.	2.14
	SD	.	.	.
	MIN,MAX	2.1,2.1	..	2.1,2.1
	Q1,Q3	2.1,2.1	..	2.1,2.1
	n	1	0	1
	Nmiss	0	1	1
5%<=_HOMA_IR_V6_base	Mean	3.07	3.64	3.30
	Median	3.51	3.64	3.51
	SD	0.81	0.92	0.80
	MIN,MAX	2.1,3.6	3.0,4.3	2.1,4.3
	Q1,Q3	2.1,3.6	3.0,4.3	3.0,3.6
	n	3	2	5
	Nmiss	0	1	1

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.4.4 HOMA-IR - Visit 6 (36 Weeks) split by birth centile

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
10%<=_HOMA_IR_V6_base	Mean	5.50	4.56	5.08
	Median	3.57	4.00	3.72
	SD	3.61	1.87	2.84
	MIN,MAX	2.1,11.0	3.0,7.3	2.1,11.0
	Q1,Q3	3.5,7.3	3.4,5.8	3.5,7.3
	n	5	4	9
	Nmiss	1	2	3
10%> AND 90%<=_HOMA_IR_V6_base	Mean	6.00	6.58	6.27
	Median	5.60	5.11	5.34
	SD	2.57	5.44	4.13
	MIN,MAX	1.6,14.0	1.9,34.5	1.6,34.5
	Q1,Q3	4.4,6.8	3.3,7.4	3.7,7.2
	n	69	58	127
	Nmiss	21	22	43

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.4.4 HOMA-IR - Visit 6 (36 Weeks) split by birth centile

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall
		Placebo	Metformin	
90%>_HOMA_IR_V6_base	Mean	8.44	5.26	6.80
	Median	7.57	4.63	6.30
	SD	3.81	2.61	3.57
	MIN,MAX	3.6,16.7	1.7,10.0	1.7,16.7
	Q1,Q3	5.0,11.9	3.5,6.5	4.1,8.3
	n	14	15	29
	Nmiss	7	5	12
95%>_HOMA_IR_V6_base	Mean	8.25	4.71	6.13
	Median	7.57	4.11	6.05
	SD	3.34	2.73	3.39
	MIN,MAX	4.8,12.7	1.7,10.0	1.7,12.7
	Q1,Q3	5.0,11.9	2.3,6.3	3.5,7.8
	n	6	9	15
	Nmiss	6	2	8

Section 5. Maternal insulin resistance (Secondary Outcome)

5.3.4.4 HOMA-IR - Visit 6 (36 Weeks) split by birth centile

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
97%>_HOMA_IR_V6_base	Mean	8.44	5.15	5.98
	Median	8.44	5.20	5.66
	SD	4.84	3.09	3.53
	MIN,MAX	5.0,11.9	1.7,10.0	1.7,11.9
	Q1,Q3	5.0,11.9	2.3,6.5	3.2,8.3
	n	2	6	8
	Nmiss	5	1	6

Section 5. Laboratory results (Secondary Outcome)

5.4.1 NEFA by study visit

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall N=227</i>
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	
NEFA - visit 2* (mmol/L)	Mean	0.544	0.468	0.508
	Median	0.520	0.440	0.480
	SD	0.202	0.161	0.187
	MIN,MAX	0.16,1.35	0.13,0.82	0.13,1.35
	Q1,Q3	0.40,0.66	0.35,0.59	0.37,0.63
	n	101	92	193
	Nmiss	17	17	34
NEFA - visit 5* (mmol/L)	Mean	0.428	0.441	0.434
	Median	0.440	0.410	0.440
	SD	0.135	0.165	0.150
	MIN,MAX	0.11,0.78	0.12,0.86	0.11,0.86
	Q1,Q3	0.31,0.52	0.33,0.54	0.32,0.53
	n	99	92	191
	Nmiss	19	17	36

Section 5. Laboratory results (Secondary Outcome)

5.4.1 NEFA by study visit (Cont.)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
NEFA - visit 6* (mmol/L)	Mean	0.465	0.481	0.472
	Median	0.445	0.470	0.460
	SD	0.194	0.207	0.200
	MIN,MAX	0.13,0.97	0.11,1.00	0.11,1.00
	Q1,Q3	0.31,0.60	0.31,0.62	0.31,0.60
	n	88	79	167
	Nmiss	30	30	60

Section 5. Laboratory results (Secondary Outcome)

5.4.2 IL_6 by study visit

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
IL_6 - visit 2* (pg/ml)	Mean	2.304	2.031	2.174
	Median	2.020	1.823	1.911
	SD	1.120	1.108	1.120
	MIN,MAX	0.80,7.21	0.62,8.14	0.62,8.14
	Q1,Q3	1.50,2.88	1.39,2.31	1.45,2.55
	n	101	92	193
	Nmiss	17	17	34
IL_6 - visit 5* (pg/ml)	Mean	2.456	2.288	2.375
	Median	2.093	2.087	2.093
	SD	1.261	1.192	1.228
	MIN,MAX	0.80,7.72	0.88,8.76	0.80,8.76
	Q1,Q3	1.62,3.08	1.60,2.69	1.62,2.86
	n	99	92	191
	Nmiss	19	17	36

Section 5. Laboratory results (Secondary Outcome)

5.4.2 IL_6 by study visit (Cont.)

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
IL_6 - visit 6* (pg/ml)	Mean	3.659	2.774	3.240
	Median	2.753	2.291	2.567
	SD	3.733	1.264	2.872
	MIN,MAX	1.19,29.94	1.11,7.35	1.11,29.94
	Q1,Q3	2.14,3.73	1.91,3.38	2.01,3.64
	n	88	79	167
	Nmiss	30	30	60

Section 5. Laboratory results (Secondary Outcome)

5.4.3 Leptin by study visit

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Leptin - visit 2* (ng/ml)	Mean	90.659	99.787	95.010
	Median	82.244	91.700	87.270
	SD	46.173	39.236	43.139
	MIN,MAX	24.19,305.25	33.04,250.68	24.19,305.25
	Q1,Q3	58.41,105.04	74.23,115.62	66.74,112.67
	n	101	92	193
	Nmiss	17	17	34
Leptin - visit 5* (ng/ml)	Mean	100.761	98.464	99.654
	Median	93.404	87.486	91.854
	SD	49.942	40.053	45.345
	MIN,MAX	25.94,376.10	27.14,212.98	25.94,376.10
	Q1,Q3	66.81,117.12	69.59,125.97	68.27,124.41
	n	99	92	191
	Nmiss	19	17	36

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Section 5. Laboratory results (Secondary Outcome)

5.4.3 Leptin by study visit (Cont.)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=227</i>
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	
Leptin - visit 6* (ng/ml)	Mean	103.798	101.257	102.596
	Median	92.129	88.806	91.308
	SD	55.337	47.019	51.433
	MIN,MAX	22.67,397.20	33.78,255.00	22.67,397.20
	Q1,Q3	69.61,128.54	66.98,122.46	68.78,127.27
	n	88	79	167
	Nmiss	30	30	60

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By: Aryelly Rodriguez - ECTU Statistician

N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*Visit 6 (36 Weeks)

Section 5. Laboratory results (Secondary Outcome)

5.4.4 Cortisol by study visit

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Cortisol - visit 2* (nmol/l)	Mean	384.760	438.183	410.226
	Median	369.660	409.711	375.366
	SD	135.506	186.538	163.619
	MIN,MAX	164.06,733.26	150.26,1197.1	150.26,1197.1
	Q1,Q3	279.72,476.13	292.00,546.21	288.03,506.95
	n	101	92	193
	Nmiss	17	17	34
Cortisol - visit 5* (nmol/l)	Mean	708.183	802.516	753.621
	Median	627.150	751.033	702.800
	SD	230.255	263.424	250.628
	MIN,MAX	395.60,1922.5	234.30,1826.3	234.30,1922.5
	Q1,Q3	547.84,809.18	654.20,930.33	594.08,893.09
	n	99	92	191
	Nmiss	19	17	36

Section 5. Laboratory results (Secondary Outcome)

5.4.4 Cortisol by study visit (Cont.)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=227</i>
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	
Cortisol - visit 6* (nmol/l)	Mean	806.477	888.378	845.220
	Median	778.645	842.706	800.754
	SD	225.004	250.727	240.321
	MIN,MAX	432.38,1903.3	432.71,1859.6	432.38,1903.3
	Q1,Q3	659.11,884.97	694.70,1022.1	675.39,967.38
	n	88	79	167
	Nmiss	30	30	60

Section 5. Laboratory results (Secondary Outcome)

5.4.5 PAI1/PAI2 ratio by study visit

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
PAI_ratio - visit 2*	Mean	1.550	2.158	1.838
	Median	1.084	0.986	1.044
	SD	1.563	6.493	4.607
	MIN,MAX	0.28,11.89	0.33,57.63	0.28,57.63
	Q1,Q3	0.78,1.73	0.74,1.47	0.76,1.58
	n	91	82	173
	Nmiss	27	27	54
PAI_ratio - visit 6*	Mean	3.396	3.314	3.357
	Median	2.637	1.864	2.296
	SD	2.651	3.090	2.859
	MIN,MAX	0.64,13.98	0.68,16.41	0.64,16.41
	Q1,Q3	1.44,4.70	1.24,4.23	1.34,4.52
	n	91	82	173
	Nmiss	27	27	54

Section 5. Laboratory results (Secondary Outcome)

5.4.6 NEFA, IL-6, Leptin, Cortisol, PAI1/PAI2 ratio Visit 6 (36 Weeks) - Statistical Analysis - POST-HOC

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Lower CI*	Estimated Mean Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
IL_6_log_Visit6 - pp	1.056	0.0892	88	0.903	0.0861	79	-0.153	-0.294	-0.012	4.613	0.0333
Leptin_log_Visit6 - pp	4.521	0.0812	88	4.528	0.0784	79	0.007	-0.121	0.135	0.011	0.9152
Cortisol_nmol_l_log_Visit6 - pp	6.639	0.0497	88	6.727	0.0480	79	0.088	0.010	0.167	4.913	0.0281
NEFA_log_Visit6 - pp	-0.776	0.0790	88	-0.736	0.0763	79	0.040	-0.085	0.165	0.406	0.5249
PAI_ratio_log_Visit6 - pp	1.009	0.1442	91	0.899	0.1339	82	-0.110	-0.328	0.107	1.009	0.3167

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By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in tables 5.4.1 to 5.4.5 of this report

Outcome analysed using a linear regression model, adjusted by BMI band and centre. Significance level set at p<0.05

Estimated mean represents the adjusted means of the log transformed variable by allocated treatment,

SE represents standard error of the estimated log transformed means and N represents number of observations

*Represents the difference between estimated log transformed means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_5_4_other_labs_analysis_v6.lst'

All parameters shown normal or near-normal behavior

Section 5. Laboratory results (Secondary Outcome)

5.5.1 B12# - Visit 2 Consent/Baseline (10-16 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
B12 (ng/l) - visit 2	Mean	256.6	259.4	257.9
	Median	240.5	246.0	245.0
	SD	108.1	71.6	92.3
	MIN,MAX	55,760	80,404	55,760
	Q1,Q3	191,324	214,306	205,314
	n	90	82	172
	Nmiss	28	27	55
B12 below 95th - visit 2 (n(%))*	Missing	28	27	55
	Yes	82 (91.1)	78 (95.1)	160 (93.0)
	No	8 (8.9)	4 (4.9)	12 (7.0)
B12 below 5th - visit 2 (n(%))*	Missing	28	27	55
	Yes	6 (6.7)	4 (4.9)	10 (5.8)
	No	84 (93.3)	78 (95.1)	162 (94.2)

Section 5. Laboratory results (Secondary Outcome)

5.5.1 B12# - Visit 6 (36 Weeks)(Cont.)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
B12 (ng/l) - visit 6	Mean	226.1	205.5	216.1
	Median	224.5	198.0	206.0
	SD	75.4	68.6	72.7
	MIN,MAX	60,482	47,417	47,482
	Q1,Q3	176,275	162,244	168,253
	n	88	83	171
	Nmiss	30	26	56
B12 below 95th - visit 6 (n(%))*	Missing	30	26	56
	Yes	85 (96.6)	82 (98.8)	167 (97.7)
	No	3 (3.4)	1 (1.2)	4 (2.3)
B12 below 5th - visit 6 (n(%))*	Missing	30	26	56
	Yes	5 (5.7)	6 (7.2)	11 (6.4)
	No	83 (94.3)	77 (92.8)	160 (93.6)

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N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*5th centile was set at 117 ng/l and 95th centile was set at 389 ng/l

#Reference range 200-940 ng/l

Section 5. Laboratory results (Secondary Outcome)

5.5.2 Serum folate# - Visit 2 Consent/Baseline (10-16 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Serum Folate (ug/l) - visit 2	Mean	13.93	14.48	14.19
	Median	17.00	16.85	16.85
	SD	4.56	4.37	4.46
	MIN,MAX	4.3,17.5	2.4,21.0	2.4,21.0
	Q1,Q3	10.5,17.5	12.2,17.5	11.2,17.5
	n	90	82	172
	Nmiss	28	27	55
Serum Folate below 95th - visit 2 (n(%))*	Missing	28	27	55
	Yes	45 (50.0)	46 (56.1)	91 (52.9)
	No	45 (50.0)	36 (43.9)	81 (47.1)
Serum Folate below 5th - visit 2 (n(%))*	Missing	28	27	55
	Yes	0	1 (1.2)	1 (0.6)
	No	90 (100)	81 (98.8)	171 (99.4)

Section 5. Laboratory results (Secondary Outcome)

5.5.2 Serum folate# - Visit 6 (36 Weeks) (Cont.)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Serum Folate (ug/l) - visit 6	Mean	9.15	9.46	9.30
	Median	6.95	7.40	7.30
	SD	6.01	5.72	5.86
	MIN,MAX	1.3,17.5	1.2,21.0	1.2,21.0
	Q1,Q3	3.8,16.3	4.2,15.2	4.1,16.1
	n	90	83	173
	Nmiss	28	26	54
Serum Folate below 95th - visit 6 (n(%))*	Missing	28	26	54
	Yes	70 (77.8)	66 (79.5)	136 (78.6)
	No	20 (22.2)	17 (20.5)	37 (21.4)
Serum Folate below 5th - visit 6 (n(%))*	Missing	28	26	54
	Yes	7 (7.8)	5 (6.0)	12 (6.9)
	No	83 (92.2)	78 (94.0)	161 (93.1)

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N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*5th centile was set at 2.6 ug/l and 95th centile was set at 17.5 ug/l

#Reference range 3.1-17.5 ug/l, if Serum folate value was reported as greater than 17.5 ug/l, then the value was imputed at 17.5 ug/l for summarisation

Section 5. Laboratory results (Secondary Outcome)

5.5.3 B12 and Serum Folate Visit 6 (36 Weeks) - Statistical Analysis - POST-HOC

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
B12_log_99_Visit6 - pp	5.401	0.0669	88	5.284	0.0619	83	-0.117	-0.218	-0.015	5.134	0.0248
SFOLATE_log_99_Visit6 - pp	1.946	0.1428	90	2.054	0.1327	83	0.108	-0.109	0.325	0.970	0.3263

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Summary statistics are presented in tables 5.5.2 and 5.6.2 of this report

Outcome analysed using a linear regression model, adjusted by BMI band and centre. Significance level set at $p < 0.05$

Estimated mean represents the adjusted means of the log transformed variable by allocated treatment,

SE represents standard error of the estimated log transformed means and N represents number of observations

*Represents the difference between the estimated log transformed means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_5_5_B12_folate_continuo_analysis_v6.lst'

All parameters shown normal or near-normal behavior

Section 5. Laboratory results (Secondary Outcome)

5.5.4.1 B12* - Patients below 5th centile - Visit 6 (36 Weeks) - Statistical Analysis - POST-HOC

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of B12_N5TH by AllocatedTreatment</i>				
<i>B12_N5TH(Patients with B12 below 5th centile (Y/N))</i>	<i>AllocatedTreatment(Allocated Treatment)</i>		<i>Total</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>Fisher exact P-value#</i>
	<i>METFORMIN</i>	<i>PLACEBO</i>				
<i>Missing</i>	26	30	.			
<i>Yes</i>	6	5	11			
<i>No</i>	77	83	160			
<i>Total</i>	83	88	171			
<i>Frequency Missing = 56</i>						
<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
b12_n5th_pp	AllocatedTreatment METFORMIN vs PLACEBO	1.294	0.379	4.411	0.6809	0.7614

Section 5. Laboratory results (Secondary Outcome)

5.5.4.2 Serum Folate* - Patients below 5th centile - Visit 6 (36 Weeks) - Statistical Analysis - POST-HOC

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of SFOL_N5TH by AllocatedTreatment</i>			
	<i>SFOL_N5TH(Patients with Serum Folate below 5th centile (Y/N))</i>	<i>AllocatedTreatment(Allocated Treatment)</i>			<i>Total</i>
		<i>METFORMIN</i>	<i>PLACEBO</i>		
<i>Missing</i>		26	28		.
<i>Yes</i>		5	7		12
<i>No</i>		78	83		161
<i>Total</i>		83	90		173
<i>Frequency Missing = 54</i>					

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
			0.232	2.495		
<i>sfol_n5th_pp</i>	<i>AllocatedTreatment METFORMIN vs PLACEBO</i>	0.760	0.232	2.495	0.6510	0.7686

Section 6. Mother Anthropometry

6.1.1 Maternal Height at Visit 2 Consent/Baseline (10-16 Weeks)*#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Height (cm) at Visit 2	Mean	166.1	165.8	166.0
	Median	166.2	165.5	166.0
	SD	6.0	5.7	5.9
	MIN,MAX	152,184	153,180	152,184
	Q1,Q3	162,170	162,170	162,170
	n	118	109	227
	Nmiss	0	0	0

Section 6. Mother Anthropometry

6.1.2 Maternal Height at Visit 6 (36 Weeks) and its change from baseline*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Height (cm) at Visit 6	Mean	166.2	166.4	166.3
	Median	166.0	166.5	166.5
	SD	6.1	5.7	5.9
	MIN,MAX	152,184	155,183	152,184
	Q1,Q3	162,170	163,170	162,170
	n	105	94	199
	Nmiss	13	15	28
Height (cm) change V6 baseline	Mean	0.2	0.1	0.2
	Median	0.0	0.0	0.0
	SD	0.8	0.8	0.8
	MIN,MAX	-2,2	-3,3	-3,3
	Q1,Q3	0,0	0,0	0,0
	n	105	94	199
	Nmiss	13	15	28

Section 6. Mother Anthropometry

6.1.3 Maternal Height at Visit 9 (Final 3 months postnatal) and its change from baseline*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Height (cm) at Visit 9	Mean	165.6	166.2	165.9
	Median	166.0	166.0	166.0
	SD	6.0	5.7	5.8
	MIN,MAX	152,184	155,180	152,184
	Q1,Q3	162,169	162,170	162,170
	n	89	89	178
	Nmiss	29	20	49
Height (cm) change V9 baseline	Mean	-0.2	-0.1	-0.1
	Median	0.0	0.0	0.0
	SD	0.7	0.7	0.7
	MIN,MAX	-3,2	-2,3	-3,3
	Q1,Q3	0,0	0,0	0,0
	n	89	89	178
	Nmiss	29	20	49

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Section 6. Mother Anthropometry

6.2.1 Maternal Weight at Visit 2 Consent/Baseline (10-16 Weeks)*#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	<i>Overall N=227</i>
Weight (kg) at Visit 2	Mean	103.74	104.04	103.88
	Median	98.33	104.00	101.30
	SD	16.95	15.22	16.10
	MIN,MAX	75.6,154.0	74.0,140.3	74.0,154.0
	Q1,Q3	90.6,114.6	93.3,115.0	92.0,115.0
	n	118	109	227
	Nmiss	0	0	0

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N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is a repeat from section 2.5 in this report

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

Section 6. Mother Anthropometry

6.2.2.1 Maternal Weight at Visit 6 (36 Weeks) and its change from baseline*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Weight (kg) at Visit 6	Mean	111.32	111.97	111.62
	Median	106.45	111.00	109.70
	SD	17.51	15.75	16.67
	MIN,MAX	79.8,159.0	79.1,165.7	79.1,165.7
	Q1,Q3	98.2,123.0	103.9,120.0	100.0,121.0
	n	106	93	199
	Nmiss	12	16	28
Weight (kg) change V6 baseline	Mean	7.40	6.85	7.14
	Median	6.95	6.50	6.80
	SD	4.56	6.11	5.34
	MIN,MAX	-4.5,18.8	-5.7,35.7	-5.7,35.7
	Q1,Q3	4.8,9.5	3.2,10.0	3.9,9.7
	n	106	93	199
	Nmiss	12	16	28

Section 6. Mother Anthropometry

6.2.2.2 Maternal Weight at Visit 6 (36 Weeks) change from baseline - Statistical Analysis - POST-HOC

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			-- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
Weight-DIFF-Visit_6 - pp	6.932	0.8458	106	6.593	0.8087	93	-0.339	-1.769	1.091	0.218	0.6408

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Summary statistics are presented in table 6.2.2.1 of this report

Outcome analysed using a linear regression model. Significance level set at $p < 0.05$

Estimated mean represents the means for the Weight Difference by allocated treatment,

SE represents standard error of the estimated means and N represents number of observations

*Represents the difference between the estimated means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_6_2_2_Mother Anthropometry_weight_gain_v6.lst'

Parameter shown normal or near-normal behavior

Section 6. Mother Anthropometry

6.2.3 Maternal Weight at Visit 9 (Final 3 months postnatal) and its change from baseline*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Weight (kg) at Visit 9	Mean	102.04	105.07	103.54
	Median	98.20	104.57	101.20
	SD	15.69	18.53	17.17
	MIN,MAX	72.7,143.0	73.8,193.0	72.7,193.0
	Q1,Q3	92.0,112.0	94.5,112.2	92.3,112.1
	n	89	87	176
	Nmiss	29	22	51
Weight (kg) change V9 baseline	Mean	0.05	0.83	0.44
	Median	0.00	-0.80	-0.30
	SD	6.08	10.95	8.81
	MIN,MAX	-13.6,18.2	-19.2,79.5	-19.2,79.5
	Q1,Q3	-3.5,3.7	-4.0,2.7	-3.6,3.2
	n	89	87	176
	Nmiss	29	22	51

Section 6. Mother Anthropometry

6.3.1 Maternal Waist at Visit 2 Consent/Baseline (10-16 Weeks)*#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=227</i>
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	
Waist (cm) at Visit 2	Mean	108.3	108.6	108.4
	Median	106.0	108.6	107.0
	SD	12.6	11.2	11.9
	MIN,MAX	85,148	84,134	84,148
	Q1,Q3	99,118	101,117	100,117
	n	118	109	227
	Nmiss	0	0	0

Section 6. Mother Anthropometry

6.3.2 Maternal Waist at Visit 6 (36 Weeks) and its change from baseline*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Waist (cm) at Visit 6	Mean	119.0	117.4	118.3
	Median	117.3	117.0	117.0
	SD	12.6	10.9	11.9
	MIN,MAX	95,161	88,140	88,161
	Q1,Q3	108,127	109,126	109,126
	n	106	93	199
	Nmiss	12	16	28
Waist (cm) change V6 baseline	Mean	10.3	9.0	9.7
	Median	10.0	9.0	9.0
	SD	7.4	8.2	7.8
	MIN,MAX	-10,29	-22,28	-22,29
	Q1,Q3	5,15	4,13	5,14
	n	106	93	199
	Nmiss	12	16	28

Section 6. Mother Anthropometry

6.3.3 Maternal Waist at Visit 9 (Final 3 months postnatal) and its change from baseline*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Waist (cm) at Visit 9	Mean	108.4	109.3	108.9
	Median	106.0	109.0	107.0
	SD	13.0	13.2	13.0
	MIN,MAX	80,142	79,141	79,142
	Q1,Q3	99,115	100,117	100,117
	n	88	89	177
	Nmiss	30	20	50
Waist (cm) change V9 baseline	Mean	0.9	1.0	0.9
	Median	0.3	1.0	0.5
	SD	7.6	8.2	7.8
	MIN,MAX	-21,22	-25,23	-25,23
	Q1,Q3	-4,5	-4,5	-4,5
	n	88	89	177
	Nmiss	30	20	50

Section 6. Mother Anthropometry

6.4.1 Maternal Hip at Visit 2 Consent/Baseline (10-16 Weeks)*#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Hip (cm) at Visit 2	Mean	126.8	127.5	127.1
	Median	125.0	126.0	125.0
	SD	11.6	12.2	11.9
	MIN,MAX	104,155	100,155	100,155
	Q1,Q3	118,134	119,136	119,134
	n	118	109	227
	Nmiss	0	0	0

Section 6. Mother Anthropometry

6.4.2 Maternal Hip at Visit 6 (36 Weeks) and its change from baseline*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Hip (cm) at Visit 6	Mean	129.8	131.1	130.4
	Median	128.3	130.0	129.5
	SD	11.9	11.8	11.8
	MIN,MAX	108,158	107,174	107,174
	Q1,Q3	122,139	123,140	122,139
	n	106	93	199
	Nmiss	12	16	28
Hip (cm) change V6 baseline	Mean	2.9	3.0	2.9
	Median	2.8	2.5	2.5
	SD	6.0	6.5	6.2
	MIN,MAX	-11,18	-12,20	-12,20
	Q1,Q3	-1,6	-1,7	-1,7
	n	106	93	199
	Nmiss	12	16	28

Section 6. Mother Anthropometry

6.4.3 Maternal Hip at Visit 9 (Final 3 months postnatal) and its change from baseline*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Hip (cm) at Visit 9	Mean	127.1	127.7	127.4
	Median	126.0	127.0	126.0
	SD	12.0	13.4	12.7
	MIN,MAX	99,154	79,167	79,167
	Q1,Q3	121,135	121,133	121,134
	n	88	89	177
	Nmiss	30	20	50
Hip (cm) change V9 baseline	Mean	0.9	-0.3	0.3
	Median	1.0	0.0	1.0
	SD	6.9	8.1	7.5
	MIN,MAX	-19,17	-41,16	-41,17
	Q1,Q3	-3,6	-5,5	-4,6
	n	88	89	177
	Nmiss	30	20	50

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Section 6. Mother Anthropometry

6.5.1 Maternal Mid Arm at Visit 2 Consent/Baseline (10-16 Weeks)*#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	<i>Overall N=227</i>
Mid Arm (cm) at Visit 2	Mean	36.6	37.0	36.8
	Median	36.0	37.0	36.0
	SD	4.8	4.4	4.6
	MIN,MAX	22,48	28,52	22,52
	Q1,Q3	34,39	34,39	34,39
	n	117	106	223
	Nmiss	1	3	4

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N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is a repeat from section 2.5 in this report

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

Section 6. Mother Anthropometry

6.5.2 Maternal Mid Arm at Visit 6 (36 Weeks) and its change from baseline*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Mid Arm (cm) at Visit 6	Mean	36.4	36.4	36.4
	Median	36.0	36.0	36.0
	SD	4.7	4.4	4.6
	MIN,MAX	22,48	22,52	22,52
	Q1,Q3	34,39	34,39	34,39
	n	105	93	198
	Nmiss	13	16	29
Mid Arm (cm) change V6 baseline	Mean	-0.3	-1.1	-0.7
	Median	-0.4	-1.0	-0.5
	SD	3.6	4.0	3.8
	MIN,MAX	-10,12	-20,9	-20,12
	Q1,Q3	-2,1	-2,1	-2,1
	n	104	92	196
	Nmiss	14	17	31

Section 6. Mother Anthropometry

6.5.3 Maternal Mid Arm at Visit 9 (Final 3 months postnatal) and its change from baseline*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Mid Arm (cm) at Visit 9	Mean	37.2	37.0	37.1
	Median	36.8	37.0	37.0
	SD	4.6	4.2	4.4
	MIN,MAX	28,52	28,54	28,54
	Q1,Q3	35,40	34,40	34,40
	n	87	89	176
	Nmiss	31	20	51
Mid Arm (cm) change V9 baseline	Mean	0.8	-0.2	0.3
	Median	0.5	0.0	0.0
	SD	4.5	3.6	4.1
	MIN,MAX	-7,25	-9,7	-9,25
	Q1,Q3	-2,3	-3,2	-2,3
	n	86	87	173
	Nmiss	32	22	54

Section 6. Mother Anthropometry

6.6.1 Maternal Mid Thigh at Visit 2 Consent/Baseline (10-16 Weeks)*#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Mid Thigh (cm) at Visit 2	Mean	64.2	65.3	64.8
	Median	64.3	64.0	64.0
	SD	7.3	7.0	7.2
	MIN,MAX	25,84	50,86	25,86
	Q1,Q3	60,69	61,69	60,69
	n	116	106	222
	Nmiss	2	3	5

Section 6. Mother Anthropometry

6.6.2 Maternal Mid Thigh at Visit 6 (36 Weeks) and its change from baseline*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Mid Thigh (cm) at Visit 6	Mean	64.8	65.7	65.2
	Median	65.0	65.0	65.0
	SD	7.2	6.6	6.9
	MIN,MAX	29,80	53,83	29,83
	Q1,Q3	60,70	60,70	60,70
	n	105	93	198
	Nmiss	13	16	29
Mid Thigh (cm) change V6 baseline	Mean	0.5	0.1	0.3
	Median	0.0	1.0	0.5
	SD	4.5	5.1	4.8
	MIN,MAX	-10,14	-16,14	-16,14
	Q1,Q3	-3,4	-4,3	-3,3
	n	103	91	194
	Nmiss	15	18	33

Section 6. Mother Anthropometry

6.6.3 Maternal Mid Thigh at Visit 9 (Final 3 months postnatal) and its change from baseline*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Mid Thigh (cm) at Visit 9	Mean	64.7	65.7	65.2
	Median	64.8	65.0	65.0
	SD	6.3	6.7	6.5
	MIN,MAX	51,84	52,84	51,84
	Q1,Q3	60,68	61,70	61,70
	n	86	88	174
	Nmiss	32	21	53
Mid Thigh (cm) change V9 baseline	Mean	1.1	0.5	0.8
	Median	0.5	1.0	1.0
	SD	7.0	5.7	6.4
	MIN,MAX	-10,47	-19,21	-19,47
	Q1,Q3	-2,4	-3,4	-3,4
	n	84	86	170
	Nmiss	34	23	57

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Section 6. Mother Anthropometry

6.7.1 Maternal Tricep Skinfold at Visit 2 Consent/Baseline (10-16 Weeks)*#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	<i>Overall N=227</i>
Tricep Skinfold (mm) at Visit 2	Mean	33.3	32.6	33.0
	Median	31.2	31.5	31.2
	SD	9.4	9.7	9.5
	MIN,MAX	15,62	10,66	10,66
	Q1,Q3	27,40	26,39	27,39
	n	117	108	225
	Nmiss	1	1	2

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N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is a repeat from section 2.5 in this report

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

Section 6. Mother Anthropometry

6.7.2 Maternal Tricep Skinfold at Visit 6 (36 Weeks) and its change from baseline*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Tricep Skinfold (mm) at Visit 6	Mean	31.4	33.4	32.3
	Median	32.0	31.5	32.0
	SD	9.4	11.5	10.4
	MIN,MAX	11,65	11,80	11,80
	Q1,Q3	24,36	26,39	25,38
	n	106	94	200
	Nmiss	12	15	27
Tricep Skinfold (mm) change V6 baseline	Mean	-1.9	0.4	-0.8
	Median	-1.0	0.0	-0.4
	SD	9.1	12.3	10.7
	MIN,MAX	-31,24	-44,34	-44,34
	Q1,Q3	-6,3	-6,6	-6,4
	n	105	93	198
	Nmiss	13	16	29

Section 6. Mother Anthropometry

6.7.3 Maternal Tricep Skinfold at Visit 9 (Final 3 months postnatal) and its change from baseline*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Tricep Skinfold (mm) at Visit 9	Mean	33.1	33.8	33.5
	Median	32.6	31.0	32.3
	SD	11.0	12.6	11.8
	MIN,MAX	8,77	13,110	8,110
	Q1,Q3	27,39	27,40	27,39
	n	87	89	176
	Nmiss	31	20	51
Tricep Skinfold (mm) change V9 baseline	Mean	0.4	1.1	0.8
	Median	0.0	0.0	0.0
	SD	10.4	12.1	11.3
	MIN,MAX	-32,37	-26,64	-32,64
	Q1,Q3	-6,4	-6,6	-6,5
	n	86	88	174
	Nmiss	32	21	53

Section 6. Mother Anthropometry

6.8.1 Maternal Bicep Skinfold at Visit 2 Consent/Baseline (10-16 Weeks)*#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Bicep Skinfold (mm) at Visit 2	Mean	27.4	27.8	27.6
	Median	25.0	26.0	25.5
	SD	10.1	10.7	10.4
	MIN,MAX	9,60	9,61	9,61
	Q1,Q3	21,32	20,33	21,32
	n	117	108	225
	Nmiss	1	1	2

Section 6. Mother Anthropometry

6.8.2 Maternal Bicep Skinfold at Visit 6 (36 Weeks) and its change from baseline*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Bicep Skinfold (mm) at Visit 6	Mean	26.7	28.4	27.5
	Median	26.1	25.0	26.0
	SD	10.3	12.2	11.2
	MIN,MAX	8,66	11,71	8,71
	Q1,Q3	19,33	20,34	20,33
	n	106	94	200
	Nmiss	12	15	27
Bicep Skinfold (mm) change V6 baseline	Mean	-0.9	0.0	-0.5
	Median	-1.0	0.0	-0.6
	SD	10.3	10.0	10.1
	MIN,MAX	-42,24	-21,33	-42,33
	Q1,Q3	-6,4	-5,4	-6,4
	n	105	93	198
	Nmiss	13	16	29

Section 6. Mother Anthropometry

6.8.3 Maternal Bicep Skinfold at Visit 9 (Final 3 months postnatal) and its change from baseline*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Bicep Skinfold (mm) at Visit 9	Mean	27.5	29.5	28.6
	Median	24.0	26.0	25.0
	SD	12.5	16.5	14.6
	MIN,MAX	9,70	8,120	8,120
	Q1,Q3	20,32	20,34	20,34
	n	87	89	176
	Nmiss	31	20	51
Bicep Skinfold (mm) change V9 baseline	Mean	-0.1	2.0	1.0
	Median	-0.2	1.1	0.0
	SD	10.8	13.8	12.4
	MIN,MAX	-35,38	-20,76	-35,76
	Q1,Q3	-5,8	-5,7	-5,7
	n	86	88	174
	Nmiss	32	21	53

Section 6. Mother Anthropometry

6.9.1 Maternal Subscapular Skinfold at Visit 2 Consent/Baseline (10-16 Weeks)*#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Subscapular Skinfold (mm) at Visit 2	Mean	35.3	34.8	35.1
	Median	34.0	33.0	34.0
	SD	11.0	11.7	11.3
	MIN,MAX	12,68	10,67	10,68
	Q1,Q3	28,41	27,40	27,40
	n	117	108	225
	Nmiss	1	1	2

Section 6. Mother Anthropometry

6.9.2 Maternal Subscapular Skinfold at Visit 6 (36 Weeks) and its change from baseline*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Subscapular Skinfold (mm) at Visit 6	Mean	34.9	36.3	35.5
	Median	33.0	35.0	34.0
	SD	13.1	12.6	12.9
	MIN,MAX	6,71	5,71	5,71
	Q1,Q3	26,44	28,43	27,44
	n	105	92	197
	Nmiss	13	17	30
Subscapular Skinfold (mm) change V6 base	Mean	-0.7	1.1	0.1
	Median	-1.8	0.8	0.0
	SD	10.6	10.6	10.6
	MIN,MAX	-23,39	-23,25	-23,39
	Q1,Q3	-7,4	-5,7	-6,6
	n	104	91	195
	Nmiss	14	18	32

Section 6. Mother Anthropometry

6.9.3 Maternal Subscapular Skinfold at Visit 9 (Final 3 months postnatal) and its change from baseline*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Subscapular Skinfold (mm) at Visit 9	Mean	35.1	36.4	35.8
	Median	32.0	34.0	33.8
	SD	13.3	12.8	13.0
	MIN,MAX	15,83	9,80	9,83
	Q1,Q3	25,42	28,45	27,44
	n	87	89	176
	Nmiss	31	20	51
Subscapular Skinfold (mm) change V9 base	Mean	0.5	1.0	0.7
	Median	-0.5	1.0	0.0
	SD	10.5	13.2	11.9
	MIN,MAX	-20,47	-31,56	-31,56
	Q1,Q3	-6,5	-8,9	-7,7
	n	86	88	174
	Nmiss	32	21	53

Section 6. Mother Anthropometry

6.10.1 Maternal Calculated BMI at Visit 2 Consent/Baseline (10-16 Weeks)*#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Calculated BMI (kg/m ²) at Visit 2	Mean	37.5	37.8	37.7
	Median	36.6	37.5	37.0
	SD	5.5	4.7	5.1
	MIN,MAX	30,53	30,48	30,53
	Q1,Q3	33,41	34,41	34,41
	n	118	109	227
	Nmiss	0	0	0

Section 6. Mother Anthropometry

6.10.2 Maternal Calculated BMI at Visit 6 (36 Weeks) and its change from baseline*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Calculated BMI (kg/m ²) at Visit 6	Mean	40.2	40.4	40.3
	Median	39.6	39.7	39.6
	SD	5.4	4.7	5.1
	MIN,MAX	31,54	32,55	31,55
	Q1,Q3	36,43	37,43	36,43
	n	105	93	198
	Nmiss	13	16	29
Calculated BMI (kg/m ²) change V6 baseli	Mean	2.6	2.4	2.5
	Median	2.4	2.5	2.4
	SD	1.7	2.1	1.9
	MIN,MAX	-3,7	-2,12	-3,12
	Q1,Q3	2,4	1,3	1,3
	n	105	93	198
	Nmiss	13	16	29

Section 6. Mother Anthropometry

6.10.3 Maternal Calculated BMI at Visit 9 (Final 3 months postnatal) and ist change from baseline*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Calculated BMI (kg/m ²) at Visit 9	Mean	37.1	38.0	37.6
	Median	36.6	37.5	37.1
	SD	4.9	5.5	5.2
	MIN,MAX	28,52	29,61	28,61
	Q1,Q3	34,40	34,41	34,41
	n	89	87	176
	Nmiss	29	22	51
Calculated BMI (kg/m ²) change V9 baseli	Mean	0.1	0.3	0.2
	Median	0.0	-0.3	-0.0
	SD	2.2	3.7	3.0
	MIN,MAX	-5,5	-7,25	-7,25
	Q1,Q3	-1,1	-1,1	-1,1
	n	89	87	176
	Nmiss	29	22	51

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Section 6. Mother Anthropometry

6.11 Maternal body percentage fat (Edinburgh)*#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Fat (%) Visit 1	Mean	46.21	48.56	47.51
	Median	46.00	48.50	47.45
	SD	5.17	5.01	5.17
	MIN,MAX	36.0,57.3	38.5,58.7	36.0,58.7
	Q1,Q3	42.1,49.5	45.2,51.7	44.7,50.8
	n	27	33	60
	Nmiss	5	3	8
<hr/>				
Fat (%) Visit 6	Mean	45.55	47.44	46.63
	Median	46.80	47.60	47.10
	SD	4.69	4.71	4.75
	MIN,MAX	34.3,53.5	39.1,56.3	34.3,56.3
	Q1,Q3	42.8,47.6	43.9,51.2	42.8,50.1
	n	22	29	51
	Nmiss	10	7	17

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N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is only applicable to Edinburgh patients

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

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Section 6. Mother Anthropometry

6.11 Maternal body percentage fat (Edinburgh) (Cont.)*#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Fat (%) Visit 9	Mean	46.78	48.49	47.74
	Median	48.10	47.60	47.85
	SD	5.00	4.80	4.91
	MIN,MAX	36.6,54.1	37.9,56.7	36.6,56.7
	Q1,Q3	42.7,49.2	44.8,53.1	44.7,51.8
	n	21	27	48
	Nmiss	11	9	20

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By: Aryelly Rodriguez - ECTU Statistician

N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is only applicable to Edinburgh patients

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

Section 6. Mother Anthropometry

6.12 Maternal Body fat mass (Edinburgh)*#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
FatMass (kg) Visit 1	Mean	46.684	52.117	49.672
	Median	46.260	52.569	49.378
	SD	9.209	12.214	11.212
	MIN,MAX	31.05,72.84	28.30,76.17	28.30,76.17
	Q1,Q3	42.45,52.44	42.32,61.25	42.39,56.81
	n	27	33	60
	Nmiss	5	3	8
FatMass (kg) Visit 6	Mean	48.983	54.150	51.921
	Median	49.642	54.452	50.430
	SD	8.073	12.325	10.914
	MIN,MAX	27.38,61.62	30.52,76.38	27.38,76.38
	Q1,Q3	47.52,54.42	46.75,65.08	46.78,57.24
	n	22	29	51
	Nmiss	10	7	17

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Section 6. Mother Anthropometry

6.12 Maternal Body fat mass (Edinburgh) (Cont.)*#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
FatMass (kg) Visit 9	Mean	48.390	50.474	49.562
	Median	50.731	48.980	50.128
	SD	9.522	13.385	11.780
	MIN,MAX	26.64,63.25	13.56,75.76	13.56,75.76
	Q1,Q3	43.26,55.43	45.45,59.07	45.27,55.88
	n	21	27	48
	Nmiss	11	9	20

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N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is only applicable to Edinburgh patients

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

Section 6. Mother Anthropometry

6.13 Maternal Body mass (Edinburgh)*#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
BodyMass (kg) Visit 1	Mean	100.525	106.227	103.661
	Median	97.810	105.137	102.230
	SD	12.742	16.966	15.357
	MIN,MAX	74.97,127.06	73.54,140.37	73.54,140.37
	Q1,Q3	90.23,111.61	96.70,116.33	92.28,113.94
	n	27	33	60
	Nmiss	5	3	8
BodyMass (kg) Visit 6	Mean	106.923	112.954	110.352
	Median	105.156	111.208	108.272
	SD	10.713	16.881	14.727
	MIN,MAX	79.82,123.78	78.11,147.87	78.11,147.87
	Q1,Q3	100.00,116.18	104.43,121.06	102.35,118.56
	n	22	29	51
	Nmiss	10	7	17

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Section 6. Mother Anthropometry

6.13 Maternal Body mass (Edinburgh) (Cont.)*#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
BodyMass (kg) Visit 9	Mean	102.723	107.627	105.481
	Median	102.540	106.227	104.381
	SD	13.705	16.223	15.217
	MIN,MAX	72.74,126.73	73.76,146.86	72.74,146.86
	Q1,Q3	96.36,114.25	98.65,115.30	97.22,114.78
	n	21	27	48
	Nmiss	11	9	20

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N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is only applicable to Edinburgh patients

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

Section 6. Mother Anthropometry

6.2.2.2.extra Maternal Weight at Visit 6 (36 Weeks) - Statistical Analysis - POST-HOC

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
Weight-Visit_6 - pp	111.358	0.8478	106	110.983	0.8165	93	-0.375	-1.806	1.056	0.267	0.6060

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Summary statistics are presented in table 6.2.2.1 of this report

Outcome analysed using a linear regression model, adjusted by weight_V2, BMI band and centre.

Significance level set at p<0.05. Estimated mean represents the means for the Weight by allocated treatment,

SE represents standard error of the estimated means and N represents number of observations

*Represents the difference between the estimated means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_6_2_2_Mother_Anthropometry_weight_v6.lst'

Parameter shown normal or near-normal behavior

Section 7. Baby Anthropometry - All Patients

7.1.1.1 Baby Age and Weight at Visit 8 (Delivery)#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Neonatal Age (days)-V8	Mean	1.34	1.12	1.24
	Median	1.00	1.00	1.00
	SD	3.00	2.63	2.82
	MIN,MAX	0.0,26.0	0.0,23.0	0.0,26.0
	Q1,Q3	0.0,2.0	0.0,1.0	0.0,1.0
	n	97	89	186
	Nmiss	21	20	41
Baby Weight* (g)-V8	Mean	3532.66	3492.74	3514.12
	Median	3575.00	3480.00	3528.00
	SD	602.66	578.47	590.27
	MIN,MAX	400.0,5060.0	2110.0,4900.0	400.0,5060.0
	Q1,Q3	3140.0,3870.0	3075.0,3880.0	3110.0,3880.0
	n	98	85	183
	Nmiss	20	24	44

Section 7. Baby Anthropometry - All Patients

7.1.1.2 Baby Length and Ponderal Index at Visit 8 (Delivery)#

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Baby Length (cm)-V8	Mean	51.44	50.48	50.99
	Median	52.00	51.00	51.25
	SD	3.03	6.47	4.97
	MIN,MAX	43.0,63.5	0.0,61.0	0.0,63.5
	Q1,Q3	50.0,53.0	49.0,53.0	49.0,53.0
	n	94	84	178
	Nmiss	24	25	49
Baby ponderal index* -V8	Mean	2.64	2.63	2.64
	Median	2.54	2.60	2.57
	SD	0.42	0.46	0.43
	MIN,MAX	1.7,3.9	1.7,3.8	1.7,3.9
	Q1,Q3	2.4,2.9	2.3,2.9	2.4,2.9
	n	90	79	169
	Nmiss	28	30	58

Section 7. Baby Anthropometry - All Patients

7.1.1.3 Baby Head Circumference and Skinfold Triceps at Visit 8 (Delivery)*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Baby Head Circumfe (cm)-V8	Mean	35.32	34.88	35.11
	Median	35.00	35.00	35.00
	SD	1.78	4.54	3.38
	MIN,MAX	32.0,41.5	0.0,53.0	0.0,53.0
	Q1,Q3	34.0,36.3	34.0,36.0	34.0,36.0
	n	99	89	188
	Nmiss	19	20	39
Baby Skinfold Triceps (mm)-V8	Mean	16.26	17.29	16.76
	Median	7.00	7.00	7.00
	SD	22.04	30.05	26.14
	MIN,MAX	0.0,90.0	0.0,162.0	0.0,162.0
	Q1,Q3	5.5,11.0	5.2,10.0	5.5,10.0
	n	79	74	153
	Nmiss	39	35	74

Section 7. Baby Anthropometry - All Patients

7.1.1.4 Baby Skinfold Subscapular and fat at Visit 8 (Delivery)#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Baby Skinfold Subscapular (mm)- V8	Mean	14.84	15.88	15.33
	Median	7.00	6.50	7.00
	SD	21.08	29.49	25.36
	MIN,MAX	0.0,100.0	0.0,158.0	0.0,158.0
	Q1,Q3	5.0,11.0	5.4,9.0	5.0,10.0
	n	80	73	153
	Nmiss	38	36	74
BABY_FAT* (%)-V8	Mean	13.45	12.78	13.07
	Median	13.50	12.30	12.30
	SD	5.78	4.56	5.05
	MIN,MAX	2.1,24.3	5.7,20.6	2.1,24.3
	Q1,Q3	8.8,17.7	8.8,16.4	8.8,17.1
	n	15	20	35
	Nmiss	103	89	192

Section 7. Baby Anthropometry - All Patients

7.1.1.5 Baby Fat Mass and Body mass at Visit 8 (Delivery)#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
BABY_FatMass* (kg)-V8	Mean	0.49107	0.44587	0.46524
	Median	0.43600	0.43775	0.43600
	SD	0.25963	0.19978	0.22489
	MIN,MAX	0.0583,0.9767	0.1421,0.7902	0.0583,0.9767
	Q1,Q3	0.2703,0.6536	0.2772,0.6041	0.2703,0.6186
	n	15	20	35
	Nmiss	103	89	192
BABY_BodyMass* (kg)-V8	Mean	3.49751	3.37595	3.42805
	Median	3.41780	3.44520	3.42610
	SD	0.50496	0.42194	0.45630
	MIN,MAX	2.7571,4.4472	2.5026,3.9902	2.5026,4.4472
	Q1,Q3	3.0992,3.8997	3.0842,3.7430	3.0992,3.7448
	n	15	20	35
	Nmiss	103	89	192

Section 7. Baby Anthropometry - All Patients

7.1.2.1 Baby Age and Weight at Visit 9 (Final 3 months postnatal)*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Neonatal Age (days)-V9	Mean	99.95	96.84	98.40
	Median	97.00	93.50	95.00
	SD	11.91	13.87	12.98
	MIN,MAX	59.0,143.0	53.0,172.0	53.0,172.0
	Q1,Q3	92.0,105.0	91.0,101.0	92.0,103.0
	n	91	90	181
	Nmiss	27	19	46
Baby Weight (g)-V9	Mean	6075.67	6108.76	6092.31
	Median	6265.00	6111.60	6200.00
	SD	1362.04	1664.00	1517.23
	MIN,MAX	666.0,8727.0	524.0,12500	524.0,12500
	Q1,Q3	5606.0,6890.0	5433.0,6900.0	5564.0,6890.0
	n	90	91	181
	Nmiss	28	18	46

Section 7. Baby Anthropometry - All Patients

7.1.2.2 Baby Length and Ponderal Index at Visit 9 (Final 3 months postnatal)#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Baby Length (cm)-V9	Mean	68.44	61.51	64.97
	Median	62.45	62.10	62.25
	SD	57.33	7.15	40.88
	MIN,MAX	42.1,605.0	5.7,74.0	5.7,605.0
	Q1,Q3	60.1,64.5	60.7,64.0	60.4,64.0
	n	90	90	180
	Nmiss	28	19	47
Baby ponderal index* -V9	Mean	2.48	39.04	20.86
	Median	2.53	2.57	2.55
	SD	0.62	345.79	245.20
	MIN,MAX	0.0,3.7	0.3,3283.1	0.0,3283.1
	Q1,Q3	2.3,2.8	2.3,2.8	2.3,2.8
	n	89	90	179
	Nmiss	29	19	48

Section 7. Baby Anthropometry - All Patients

7.1.2.3 Baby Head Circumference and Skinfold Triceps at Visit 9 (Final 3 months postnatal)*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Baby Head Circumfe (cm)-V9	Mean	41.08	41.11	41.09
	Median	41.00	41.50	41.00
	SD	1.95	5.07	3.82
	MIN,MAX	34.8,46.0	4.0,62.0	4.0,62.0
	Q1,Q3	40.0,42.0	40.0,42.4	40.0,42.2
	n	89	88	177
	Nmiss	29	21	50
BabySkinfoldTriceps (mm)-V9	Mean	23.98	25.67	24.82
	Median	11.00	11.00	11.00
	SD	35.62	35.98	35.70
	MIN,MAX	0.7,160.2	0.8,170.2	0.7,170.2
	Q1,Q3	9.0,16.0	9.0,15.2	9.0,15.2
	n	83	83	166
	Nmiss	35	26	61

Section 7. Baby Anthropometry - All Patients

7.1.2.4 Baby Skinfold Subscapular and fat at Visit 9 (Final 3 months postnatal)#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
BabySkinfoldSubscapular (mm)-V9	Mean	17.80	24.70	21.27
	Median	8.65	10.00	9.20
	SD	25.09	33.06	29.49
	MIN,MAX	0.5,106.0	0.7,162.0	0.5,162.0
	Q1,Q3	7.0,11.0	8.0,18.0	7.0,13.0
	n	82	83	165
	Nmiss	36	26	62
BABY_FAT* (%) -V9	Mean	25.80	23.33	24.46
	Median	25.75	23.55	23.90
	SD	5.94	5.66	5.86
	MIN,MAX	15.1,41.6	12.1,32.3	12.1,41.6
	Q1,Q3	22.2,29.0	19.6,27.8	20.6,28.8
	n	22	26	48
	Nmiss	96	83	179

Section 7. Baby Anthropometry - All Patients

7.1.2.5 Baby Fat Mass and Body mass at Visit 9 (Final 3 months postnatal)#

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
BABY_FatMass* (kg)-V9	Mean	1.61385	1.43933	1.51932
	Median	1.68260	1.44345	1.53335
	SD	0.44937	0.49073	0.47544
	MIN,MAX	0.8625,2.6138	0.6259,2.4550	0.6259,2.6138
	Q1,Q3	1.1920,1.9387	1.0391,1.7338	1.1096,1.8044
	n	22	26	48
	Nmiss	96	83	179
BABY_BodyMass* (kg)-V9	Mean	6.24116	6.07335	6.15190
	Median	6.30410	6.11160	6.21560
	SD	0.82294	0.92984	0.87603
	MIN,MAX	4.8014,7.7721	4.4105,8.0110	4.4105,8.0110
	Q1,Q3	5.6061,6.7473	5.3395,6.6500	5.5427,6.7473
	n	22	25	47
	Nmiss	96	84	180

Section 7. Baby Anthropometry - Only Alive Births

7.2.1.1 Baby Age and Weight at Visit 8 (Delivery)#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Neonatal Age (days)-V8	Mean	1.34	1.12	1.24
	Median	1.00	1.00	1.00
	SD	3.00	2.63	2.82
	MIN,MAX	0.0,26.0	0.0,23.0	0.0,26.0
	Q1,Q3	0.0,2.0	0.0,1.0	0.0,1.0
	n	97	89	186
	Nmiss	20	19	39
Baby Weight* (g)-V8	Mean	3564.96	3492.74	3531.23
	Median	3580.00	3480.00	3530.00
	SD	513.52	578.47	544.49
	MIN,MAX	2400.0,5060.0	2110.0,4900.0	2110.0,5060.0
	Q1,Q3	3175.0,3870.0	3075.0,3880.0	3120.0,3880.0
	n	97	85	182
	Nmiss	20	23	43

Section 7. Baby Anthropometry - Only Alive Births

7.2.1.2.1 Baby Lenght and Ponderal Index at Visit 8 (Delivery)#

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Baby Length (cm)-V8	Mean	51.44	50.48	50.99
	Median	52.00	51.00	51.25
	SD	3.03	6.47	4.97
	MIN,MAX	43.0,63.5	0.0,61.0	0.0,63.5
	Q1,Q3	50.0,53.0	49.0,53.0	49.0,53.0
	n	94	84	178
	Nmiss	23	24	47
Baby ponderal index* -V8	Mean	2.64	2.63	2.64
	Median	2.54	2.60	2.57
	SD	0.42	0.46	0.43
	MIN,MAX	1.7,3.9	1.7,3.8	1.7,3.9
	Q1,Q3	2.4,2.9	2.3,2.9	2.4,2.9
	n	90	79	169
	Nmiss	27	29	56

Section 7. Baby Anthropometry - Only Alive Births

7.2.1.2.2 Ponderal index #,\$ - Statistical Analysis - POST-HOC

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
baby_ponderal_alive_log - pp	0.969	0.0245	90	0.973	0.0253	79	0.004	-0.040	0.048	0.038	0.8460

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 02:47

By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in table 7.2.1.2.1 of this report

Outcome analysed using a linear regression model, adjusted by BMI band and centre. Significance level set at $p < 0.05$. Estimated mean represents the mean of the log transformed variable by allocated treatment, Parameter shown normal or near-normal behavior

SE represents standard error of the estimated log transformed mean and N represents number of observations

*Represents the difference between the estimated log means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_7_2_2_Baby_Ponderal_delivery.lst'

#Ponderal index was calculated using the following formula: $(100 * (\text{baby_weight_in_g})) / ((\text{baby_length_in_cm})^3)$,

\$Data have been checked, inaccuracies happened at time and point of recording and there are not other sources

for further checks, outliers outside +/- 6SD were removed to exclude extreme errors in data entry

Section 7. Baby Anthropometry - Only Alive Births

7.2.1.3 Baby Head Circumference and Skinfold Triceps at Visit 8 (Delivery)*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Baby Head Circumfe (cm)-V8	Mean	35.32	34.88	35.11
	Median	35.00	35.00	35.00
	SD	1.78	4.54	3.38
	MIN,MAX	32.0,41.5	0.0,53.0	0.0,53.0
	Q1,Q3	34.0,36.3	34.0,36.0	34.0,36.0
	n	99	89	188
	Nmiss	18	19	37
Baby Skinfold Triceps (mm)-V8	Mean	16.26	17.29	16.76
	Median	7.00	7.00	7.00
	SD	22.04	30.05	26.14
	MIN,MAX	0.0,90.0	0.0,162.0	0.0,162.0
	Q1,Q3	5.5,11.0	5.2,10.0	5.5,10.0
	n	79	74	153
	Nmiss	38	34	72

Section 7. Baby Anthropometry - Only Alive Births

7.2.1.4 Baby Skinfold Subscapular and fat at Visit 8 (Delivery)#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Baby Skinfold Subscapular (mm)- V8	Mean	14.84	15.88	15.33
	Median	7.00	6.50	7.00
	SD	21.08	29.49	25.36
	MIN,MAX	0.0,100.0	0.0,158.0	0.0,158.0
	Q1,Q3	5.0,11.0	5.4,9.0	5.0,10.0
	n	80	73	153
	Nmiss	37	35	72
BABY_FAT* (%)-V8	Mean	13.45	12.78	13.07
	Median	13.50	12.30	12.30
	SD	5.78	4.56	5.05
	MIN,MAX	2.1,24.3	5.7,20.6	2.1,24.3
	Q1,Q3	8.8,17.7	8.8,16.4	8.8,17.1
	n	15	20	35
	Nmiss	102	88	190

Section 7. Baby Anthropometry - Only Alive Births

7.2.1.5 Baby Fat Mass and Body mass at Visit 8 (Delivery)#

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
BABY_FatMass* (kg)-V8	Mean	0.49107	0.44587	0.46524
	Median	0.43600	0.43775	0.43600
	SD	0.25963	0.19978	0.22489
	MIN,MAX	0.0583,0.9767	0.1421,0.7902	0.0583,0.9767
	Q1,Q3	0.2703,0.6536	0.2772,0.6041	0.2703,0.6186
	n	15	20	35
	Nmiss	102	88	190
BABY_BodyMass* (kg)-V8	Mean	3.49751	3.37595	3.42805
	Median	3.41780	3.44520	3.42610
	SD	0.50496	0.42194	0.45630
	MIN,MAX	2.7571,4.4472	2.5026,3.9902	2.5026,4.4472
	Q1,Q3	3.0992,3.8997	3.0842,3.7430	3.0992,3.7448
	n	15	20	35
	Nmiss	102	88	190

Section 7. Baby Anthropometry - Only Alive Births

7.2.2.1 Baby Age and Weight at Visit 9 (Final 3 months postnatal)*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Neonatal Age (days)-V9	Mean	99.95	96.84	98.40
	Median	97.00	93.50	95.00
	SD	11.91	13.87	12.98
	MIN,MAX	59.0,143.0	53.0,172.0	53.0,172.0
	Q1,Q3	92.0,105.0	91.0,101.0	92.0,103.0
	n	91	90	181
	Nmiss	26	18	44
Baby Weight (g)-V9	Mean	6075.67	6108.76	6092.31
	Median	6265.00	6111.60	6200.00
	SD	1362.04	1664.00	1517.23
	MIN,MAX	666.0,8727.0	524.0,12500	524.0,12500
	Q1,Q3	5606.0,6890.0	5433.0,6900.0	5564.0,6890.0
	n	90	91	181
	Nmiss	26	16	42

Section 7. Baby Anthropometry - Only Alive Births

7.2.2.2 Baby Length and Ponderal Index at Visit 9 (Final 3 months postnatal)#

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Baby Length (cm)-V9	Mean	68.44	61.51	64.97
	Median	62.45	62.10	62.25
	SD	57.33	7.15	40.88
	MIN,MAX	42.1,605.0	5.7,74.0	5.7,605.0
	Q1,Q3	60.1,64.5	60.7,64.0	60.4,64.0
	n	90	90	180
	Nmiss	26	17	43
Baby ponderal index* -V9	Mean	2.48	39.04	20.86
	Median	2.53	2.57	2.55
	SD	0.62	345.79	245.20
	MIN,MAX	0.0,3.7	0.3,3283.1	0.0,3283.1
	Q1,Q3	2.3,2.8	2.3,2.8	2.3,2.8
	n	89	90	179
	Nmiss	27	17	44

Section 7. Baby Anthropometry - Only Alive Births

7.2.2.3 Baby Head Circumference and Skinfold Triceps at Visit 9 (Final 3 months postnatal)*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Baby Head Circumfe (cm)-V9	Mean	41.08	41.11	41.09
	Median	41.00	41.50	41.00
	SD	1.95	5.07	3.82
	MIN,MAX	34.8,46.0	4.0,62.0	4.0,62.0
	Q1,Q3	40.0,42.0	40.0,42.4	40.0,42.2
	n	89	88	177
	Nmiss	27	19	46
BabySkinfoldTriceps (mm)-V9	Mean	23.98	25.67	24.82
	Median	11.00	11.00	11.00
	SD	35.62	35.98	35.70
	MIN,MAX	0.7,160.2	0.8,170.2	0.7,170.2
	Q1,Q3	9.0,16.0	9.0,15.2	9.0,15.2
	n	83	83	166
	Nmiss	33	24	57

Section 7. Baby Anthropometry - Only Alive Births

7.2.2.4 Baby Skinfold Subscapular and fat at Visit 9 (Final 3 months postnatal)#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
BabySkinfoldSubscapular (mm)-V9	Mean	17.80	24.70	21.27
	Median	8.65	10.00	9.20
	SD	25.09	33.06	29.49
	MIN,MAX	0.5,106.0	0.7,162.0	0.5,162.0
	Q1,Q3	7.0,11.0	8.0,18.0	7.0,13.0
	n	82	83	165
	Nmiss	34	24	58
BABY_FAT* (%) -V9	Mean	25.80	23.33	24.46
	Median	25.75	23.55	23.90
	SD	5.94	5.66	5.86
	MIN,MAX	15.1,41.6	12.1,32.3	12.1,41.6
	Q1,Q3	22.2,29.0	19.6,27.8	20.6,28.8
	n	22	26	48
	Nmiss	94	81	175

Section 7. Baby Anthropometry - Only Alive Births

7.2.2.5 Baby Fat Mass and Body mass at Visit 9 (Final 3 months postnatal)#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
BABY_FatMass* (kg)-V9	Mean	1.61385	1.43933	1.51932
	Median	1.68260	1.44345	1.53335
	SD	0.44937	0.49073	0.47544
	MIN,MAX	0.8625,2.6138	0.6259,2.4550	0.6259,2.6138
	Q1,Q3	1.1920,1.9387	1.0391,1.7338	1.1096,1.8044
	n	22	26	48
	Nmiss	94	81	175
BABY_BodyMass* (kg)-V9	Mean	6.24116	6.07335	6.15190
	Median	6.30410	6.11160	6.21560
	SD	0.82294	0.92984	0.87603
	MIN,MAX	4.8014,7.7721	4.4105,8.0110	4.4105,8.0110
	Q1,Q3	5.6061,6.7473	5.3395,6.6500	5.5427,6.7473
	n	22	25	47
	Nmiss	94	82	176

Section 7. Baby Anthropometry - Only Alive Births

7.2.3 Baby Ponderal Index at Visit 8 (Delivery) and Visit 9 (Final 3 months postnatal) #

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Baby ponderal index* -V8	Mean	2.64	2.63	2.64
	Median	2.54	2.60	2.57
	SD	0.42	0.46	0.43
	MIN,MAX	1.7,3.9	1.7,3.8	1.7,3.9
	Q1,Q3	2.4,2.9	2.3,2.9	2.4,2.9
	n	90	79	169
	Nmiss	27	29	56
Baby ponderal index* -V9	Mean	2.48	2.59	2.54
	Median	2.53	2.56	2.54
	SD	0.62	1.05	0.86
	MIN,MAX	0.0,3.7	0.3,9.8	0.0,9.8
	Q1,Q3	2.3,2.8	2.3,2.8	2.3,2.8
	n	89	89	178
	Nmiss	27	18	45

Section 7. Baby Anthropometry - Only Alive Births

7.2.4 Baby Weight at Visit 8 (Delivery) and Visit 9 (Final 3 months postnatal)#

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Baby Weight* (g)-V8	Mean	3564.96	3492.74	3531.23
	Median	3580.00	3480.00	3530.00
	SD	513.52	578.47	544.49
	MIN,MAX	2400.0,5060.0	2110.0,4900.0	2110.0,5060.0
	Q1,Q3	3175.0,3870.0	3075.0,3880.0	3120.0,3880.0
	n	97	85	182
	Nmiss	20	23	43
Baby Weight (g)-V9	Mean	6075.67	6108.76	6092.31
	Median	6265.00	6111.60	6200.00
	SD	1362.04	1664.00	1517.23
	MIN,MAX	666.0,8727.0	524.0,12500	524.0,12500
	Q1,Q3	5606.0,6890.0	5433.0,6900.0	5564.0,6890.0
	n	90	91	181
	Nmiss	26	16	42

Section 7. Baby Anthropometry - Only Alive Births

7.2.5 Baby Length at Visit 8 (Delivery) and Visit 9 (Final 3 months postnatal)*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Baby Length (cm)-V8	Mean	51.44	51.09	51.28
	Median	52.00	51.00	51.50
	SD	3.03	3.31	3.16
	MIN,MAX	43.0,63.5	43.0,61.0	43.0,63.5
	Q1,Q3	50.0,53.0	49.0,53.0	49.0,53.0
	n	94	83	177
	Nmiss	23	25	48
Baby Length (cm)-V9	Mean	62.41	61.51	61.96
	Median	62.40	62.10	62.20
	SD	3.92	7.15	5.78
	MIN,MAX	42.1,73.0	5.7,74.0	5.7,74.0
	Q1,Q3	60.1,64.3	60.7,64.0	60.2,64.0
	n	89	90	179
	Nmiss	27	17	44

Section 8. Maternal inflammatory and metabolic variables (Secondary Outcome)

8.1 CRP - Visit 3 Randomisation (10-16 Weeks) and Visit 5 (28 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
CRP - V3 (mg/L)	Mean	11.41	10.04	10.75
	Median	9.05	9.00	9.00
	SD	7.94	6.30	7.21
	MIN,MAX	1.0,49.0	1.0,34.0	1.0,49.0
	Q1,Q3	5.0,15.5	5.0,14.0	5.0,15.0
	n	118	109	227
	Nmiss	0	0	0
CRP - V5 (mg/L)	Mean	10.55	9.56	10.07
	Median	8.00	7.65	8.00
	SD	7.56	6.76	7.19
	MIN,MAX	2.0,43.0	1.0,41.0	1.0,43.0
	Q1,Q3	5.0,14.0	5.0,12.0	5.0,13.0
	n	115	106	221
	Nmiss	3	3	6

Section 8. Maternal inflammatory and metabolic variables (Secondary Outcome)

8.1 CRP - Visit 6 (36 Weeks) (Cont.)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=227</i>
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	
CRP - V6 (mg/L)	Mean	8.91	7.48	8.23
	Median	6.80	6.00	6.00
	SD	6.39	4.58	5.64
	MIN,MAX	1.0,43.3	1.4,29.0	1.0,43.3
	Q1,Q3	5.0,12.0	5.0,9.8	5.0,10.8
	n	104	93	197
	Nmiss	14	16	30

Section 8. Maternal inflammatory and metabolic variables (Secondary Outcome)

8.2.1 Total Cholesterol - Visit 3 Randomisation (10-16 Weeks) and Visit 6 (36 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Total Cholesterol - V3 (mmol/L)	Mean	4.86	4.82	4.84
	Median	5.00	4.90	4.90
	SD	1.16	1.13	1.15
	MIN,MAX	2.1,8.3	2.2,8.2	2.1,8.3
	Q1,Q3	4.0,5.7	4.1,5.5	4.0,5.6
	n	117	108	225
	Nmiss	1	1	2
Total Cholesterol - V6 (mmol/L)	Mean	6.29	6.16	6.23
	Median	6.40	6.40	6.40
	SD	1.54	1.88	1.71
	MIN,MAX	2.5,10.5	2.6,12.7	2.5,12.7
	Q1,Q3	5.6,7.2	5.1,7.3	5.2,7.2
	n	100	91	191
	Nmiss	18	18	36

Section 8. Maternal inflammatory and metabolic variables (Secondary Outcome)

8.2.2 HDL - Visit 3 Randomisation (10-16 Weeks) and Visit 6 (36 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
HDL - V3 (mmol/L)	Mean	1.67	1.64	1.65
	Median	1.60	1.60	1.60
	SD	0.38	0.39	0.39
	MIN,MAX	0.9,3.6	0.0,3.2	0.0,3.6
	Q1,Q3	1.4,1.9	1.4,1.9	1.4,1.9
	n	117	108	225
	Nmiss	1	1	2
HDL - V6 (mmol/L)	Mean	1.71	1.76	1.73
	Median	1.70	1.70	1.70
	SD	0.37	0.38	0.38
	MIN,MAX	0.9,2.9	0.9,2.7	0.9,2.9
	Q1,Q3	1.4,1.9	1.5,2.0	1.5,2.0
	n	100	91	191
	Nmiss	18	18	36

Section 8. Maternal inflammatory and metabolic variables (Secondary Outcome)

8.2.3 LDL - Visit 3 Randomisation (10-16 Weeks) and Visit 6 (36 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
LDL - V3 (mmol/L)	Mean	2.98	2.90	2.94
	Median	2.90	2.84	2.90
	SD	0.75	0.90	0.83
	MIN,MAX	1.6,5.1	0.0,6.0	0.0,6.0
	Q1,Q3	2.5,3.5	2.3,3.4	2.4,3.4
	n	106	101	207
	Nmiss	12	8	20
LDL - V6 (mmol/L)	Mean	3.67	3.71	3.69
	Median	3.60	3.55	3.60
	SD	1.09	1.22	1.15
	MIN,MAX	1.1,6.8	1.8,9.2	1.1,9.2
	Q1,Q3	3.0,4.4	2.8,4.4	2.9,4.4
	n	89	80	169
	Nmiss	29	29	58

Section 8. Maternal inflammatory and metabolic variables (Secondary Outcome)

8.2.4 Triglycerides - Visit 3 Randomisation (10-16 Weeks) and Visit 6 (36 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Triglycerides - V3 (mmol/L)	Mean	1.51	1.45	1.48
	Median	1.41	1.30	1.40
	SD	0.54	0.58	0.56
	MIN,MAX	0.5,3.6	0.5,3.7	0.5,3.7
	Q1,Q3	1.1,1.8	1.1,1.6	1.1,1.7
	n	117	108	225
	Nmiss	1	1	2
Triglycerides - V6 (mmol/L)	Mean	2.79	2.84	2.81
	Median	2.70	2.69	2.70
	SD	0.90	0.96	0.93
	MIN,MAX	0.9,5.8	1.3,6.7	0.9,6.7
	Q1,Q3	2.1,3.3	2.2,3.3	2.1,3.3
	n	101	92	193
	Nmiss	17	17	34

Section 8. Maternal inflammatory and metabolic variables (Secondary Outcome)

8.3 CRP, Cholesterol, HDL, LDL and Triglycerides - Visit 6 (36 Weeks) - Statistical Analysis - POST-HOC

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Lower CI*	Estimated Mean Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
CRP_log_Visit6 - pp	1.962	0.1008	104	1.858	0.0963	93	-0.104	-0.275	0.067	1.433	0.2329
Cholesterol_log_Visit6 - pp	1.794	0.0379	100	1.768	0.0360	91	-0.026	-0.091	0.038	0.645	0.4230
HDL_Visit6# - pp	1.767	0.0590	100	1.822	0.0561	91	0.055	-0.046	0.155	1.142	0.2866
LDL_log_Visit6\$ - pp	1.208	0.0560	89	1.221	0.0527	80	0.013	-0.081	0.107	0.079	0.7793
Triglycerides_log_Visit6 - pp	0.947	0.0525	101	0.977	0.0500	92	0.030	-0.059	0.120	0.441	0.5073

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 02:47

By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in tables 8.1 to 8.2 of this report

Outcome analysed using a linear regression model, adjusted by BMI band and centre. Significance level set at p<0.05

Estimated mean represents the adjusted mean of the non-transformed or log transformed variable by allocated treatment,

SE represents standard error of the estimated means or log transformed means and N represents number of observations

*Represents the difference between the estimated means or log transformed means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_5_4_other_labs_analysis_v6.lst'

#NOTE:HDL was not log transformed for the analysis

\$NOTE:LDL has a value of 0 for patient 16052, this values was set to missing in the log transformation of the parameter

All parameters shown normal or near-normal behavior

Section 9. Neonatal cord blood and placenta (Secondary Outcome)

9.1 Glucose and Insulin in the umbilical cord - Visit 8 (Delivery)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Glucose Cord - V8 (mmol/L)	Mean	3.94	4.02	3.97
	Median	3.65	3.80	3.80
	SD	1.25	1.05	1.16
	MIN,MAX	1.9,7.6	1.6,6.3	1.6,7.6
	Q1,Q3	3.0,4.6	3.1,4.9	3.1,4.8
	n	62	54	116
	Nmiss	56	55	111
Insulin Cord - V8 (mIU/ml)	Mean	11.14	12.04	11.63
	Median	9.91	10.57	10.03
	SD	7.48	9.21	8.44
	MIN,MAX	2.0,32.7	2.0,42.9	2.0,42.9
	Q1,Q3	6.4,14.3	5.2,17.0	5.5,16.3
	n	37	45	82
	Nmiss	81	64	145

Section 9. Neonatal cord blood and placenta (Secondary Outcome)

9.2 HOMA-IR AND CRP in the umbilical cord - Visit 8 (Delivery)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
HOMA-IR Cord - V8 (mIU/ml)	Mean	1.83	1.93	1.88
	Median	1.81	1.50	1.62
	SD	1.36	2.19	1.80
	MIN,MAX	0.3,6.7	0.2,12.0	0.2,12.0
	Q1,Q3	0.8,2.3	0.6,2.7	0.6,2.4
	n	32	30	62
	Nmiss	86	79	165
CRP - V8 (mmol/L)	Mean	4.85	2.15	3.60
	Median	1.00	1.00	1.00
	SD	21.89	1.82	16.11
	MIN,MAX	0.3,173.8	0.2,5.0	0.2,173.8
	Q1,Q3	1.0,5.0	1.0,5.0	1.0,5.0
	n	62	53	115
	Nmiss	56	56	112

Section 9. Neonatal cord blood and placenta (Secondary Outcome)

9.3 Glucose, Insuling and HOMA-IR in the umbilical cord - Visit 8 (Delivery) - Statistical Analysis - POST-HOC

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Lower CI*	Estimated Mean Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
Glucose_cord_log_Visit_8* - pp	1.262	0.0592	62	1.322	0.0552	54	0.060	-0.046	0.166	1.269	0.2626
Insulin_cord_log_Visit_8* - pp	2.042	0.1885	37	2.170	0.1705	45	0.129	-0.217	0.475	0.551	0.4602
HOMA_cord_log_Visit_8* - pp	0.151	0.1999	32	0.215	0.1823	30	0.064	-0.328	0.457	0.108	0.7436

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 02:47

By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in tables 9.1 to 9.2 of this report

Outcome analysed using a linear regression model, adjusted by BMI band and centre. Significance level set at p<0.05

Estimated mean represents the adjusted means of the log transformed variable by allocated treatment,

SE represents standard error of the estimated log transformed means and N represents number of observations

*Represents the difference between the estimated log transformed means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_9_1_Neonatal_cord_blood.lst'

All parameters shown normal or near-normal behavior

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Section 9. Neonatal cord blood and placenta (Secondary Outcome)

9.4 CRP in the umbilical cord - Visit 8 (Delivery)* - Statistical Analysis - POST-HOC

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>P-value Wilcoxon Test (Two-sided)</i>	<i>P-value Wilcoxon t Approx (Two-sided)</i>	<i>P-value Kruskal-Wallis Test</i>
CRP_CORD_VISIT_8_pp	Non_parametric_test_metformin_vs_placebo*	0.7987	0.7992	0.7987

EMPOWaR Statistical Analysis Report - Final 02 - tables run on: 05MAR2016 at 02:47

By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in table 9.2 of this report

*This variable was non-normal and the lack of normality could not be corrected. Therefore Non-parametric testing results are presented. Significance level set at $p < 0.05$

Calculations and detailed analysis are presented in study file 'Empowar_9_1_Neonatal_cord_blood.lst'

Section 10. Adverse Outcome

10.1.1 Maternal Complications - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Any SAE (n)#	Yes	22 (18.6)	19 (17.4)	41 (18.1)
	No	96 (81.4)	90 (82.6)	186 (81.9)
Any Hypertension (n)	Yes	11 (9.3)	11 (10.1)	22 (9.7)
	No	107 (90.7)	98 (89.9)	205 (90.3)
Any Preeclampsia (n)	Yes	3 (2.5)	3 (2.8)	6 (2.6)
	No	115 (97.5)	106 (97.2)	221 (97.4)
Any Eclampsia (n)	Yes	0	1 (0.9)	1 (0.4)
	No	118 (100)	108 (99.1)	226 (99.6)
Any Membrane Rupture (n)	Yes	0	2 (1.8)	2 (0.9)
	No	118 (100)	107 (98.2)	225 (99.1)

Section 10. Adverse Outcome

10.1.1 Maternal Complications - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery) (Cont.)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Any Preterm Labour (n)#	Yes	2 (1.7)	6 (5.5)	8 (3.5)
	No	116 (98.3)	103 (94.5)	219 (96.5)
Any Haemorrhage (n)	Yes	4 (3.4)	4 (3.7)	8 (3.5)
	No	114 (96.6)	105 (96.3)	219 (96.5)
Any DVT (n)	Yes	2 (1.7)	0	2 (0.9)
	No	116 (98.3)	109 (100)	225 (99.1)
Any Gestational Diabetes (n)	Yes	19 (16.1)	14 (12.8)	33 (14.5)
	No	99 (83.9)	95 (87.2)	194 (85.5)

Section 10. Adverse Outcome

10.1.1 Maternal Complications - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery) (Cont.)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Any Other Mother Complication (n)	Yes	37 (31.4)	44 (40.4)	81 (35.7)
	No	81 (68.6)	65 (59.6)	146 (64.3)
Any Other Mother Complication cat* (n)	Missing	0	1	1
	Infection	10	12	22
	Mood disturbance	1	4	5
	Musculoskeletal	8	14	22
	PV bleed <24 weeks gestation	3	3	6
	Obstetric cholestasis	4	1	5
	Miscellaneous	13	18	31
	Data captured elsewhere	28	24	52

Section 10. Adverse Outcome

10.1.2 Maternal Complications Details - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Other Maternal Complications (Y/N)	TimepointID	Other Maternal Complications Details
11136	METFORMIN	Yes	VISIT 8 (DELIVERY)	placental abruption
11315	METFORMIN	Yes	VISIT 8 (DELIVERY)	3rd degree tear
11325	METFORMIN	Yes	VISIT 5 (28 WEEKS)	antenatal depression
11501	METFORMIN	Yes	VISIT 6 (36 WEEKS)	hospital admission with RUQ pain and deranged LFT, resolved spontaneously
11551	METFORMIN	Yes	VISIT 5 (28 WEEKS)	exacerbation of asthma requiring oral steroids
11716	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Mild SPD
11748	METFORMIN	Yes	VISIT 6 (36 WEEKS)	UTI
11748	METFORMIN	Yes	VISIT 7 (TERM)	Sepsis secondary to mastitis
11748	METFORMIN	Yes	VISIT 8 (DELIVERY)	UTI SAE forms previously sent
11797	METFORMIN	Yes	VISIT 6 (36 WEEKS)	excessive vomiting in late pregnancy
11842	METFORMIN	Yes	VISIT 8 (DELIVERY)	Raised ALT
11881	METFORMIN	Yes	VISIT 8 (DELIVERY)	severe urosepsis
12001	METFORMIN	Yes	VISIT 7 (TERM)	Swelling of hands and feet
12001	METFORMIN	Yes	VISIT 8 (DELIVERY)	oedema
12006	METFORMIN	Yes	VISIT 8 (DELIVERY)	Post Partum haemorrhage, 2000ml
12018	METFORMIN	Yes	VISIT 8 (DELIVERY)	EBL 600 mls
13016	METFORMIN	Yes	VISIT 7 (TERM)	Seen in assessment room last week with headache and visual disturbances. Migrane diagnosed. Discharged home with paracetamol and codine.
13082	METFORMIN	Yes	VISIT 8 (DELIVERY)	PYREXIA IN LABOUR
13209	METFORMIN	Yes	VISIT 6 (36 WEEKS)	HAD VIRAL INFECTION 2 WEEKS AGO LASTING A FORTNIGHT. RESULTED IN PRODUCTIVE COUGH, FOLLOWED MODERATE VOMITTING AND DIARRHOEA.
13378	METFORMIN	Yes	VISIT 5 (28 WEEKS)	UTI CAUSED SEVERE HEADACHES. CLEARED AFTER COURSE OF ANTIBIOTICS.
13378	METFORMIN	Yes	VISIT 8 (DELIVERY)	Fatty deposits noted on placenta, samples taken for histology by delivery midwife, but unable to process as incorrectly sampled and stored
13551	METFORMIN	Yes	VISIT 8 (DELIVERY)	PPH of 5000ml followed by total hysterectomy
13780	METFORMIN	Yes	VISIT 8 (DELIVERY)	UNDIAGNOSED LOW LYING PLACENTA AT CS. BLOOD LOSS 1400MLS. NEEDED BLOOD TRANSFUSION AFTER CS.
14303	METFORMIN	Yes	VISIT 8 (DELIVERY)	PPH 1200mls
14417	METFORMIN	Yes	VISIT 5 (28 WEEKS)	Feeling faint on occasions when working
15012	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	has had small pv bleed as history of cervical polyps all well
15027	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Itching All blood tests NAD
16054	METFORMIN	Yes	VISIT 5 (28 WEEKS)	Abdo pain and pinkish pv loss
16121	METFORMIN	Yes	VISIT 6 (36 WEEKS)	pyelonephritis
17138	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Palpitations, seen in hospital assessment unit but discharged home without admission. Normal ECG and Normal CTG.
21015	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Attended Day Unit 4/9/13 33+4 with brown pv discharge post coital.
21015	METFORMIN	Yes	VISIT 7 (TERM)	Questions asked in retrospect once delivered as unable to contact.Unsure when stopped tablets.
21015	METFORMIN	Yes	VISIT 8 (DELIVERY)	PPH following birth.Hb 63g/l.Had 2 units of blood.Hb 83g/l post transfusion.Didnt cause prolonged hospitalisation.
21034	METFORMIN	Yes	VISIT 5 (28 WEEKS)	Indigestion since 22 weeks resolved with use of gaviscon
21034	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Acupuncture for back/hip pain. Broke coccyx 5 years ago

Section 10. Adverse Outcome

10.1.2 Maternal Complications Details - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Other Maternal Complications (Y/N)	TimepointID	Other Maternal Complications Details
21037	METFORMIN	Yes	VISIT 5 (28 WEEKS)	Sweating
21037	METFORMIN	Yes	VISIT 7 (TERM)	Green vaginal discharge today High vaginal swab obtained.
21039	METFORMIN	Yes	VISIT 8 (DELIVERY)	Maternal tachycardia post delivery. IV fluids & antibiotics given. Ragged membranes.
21042	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Hearburn. Using gaviscon. Awaiting prescription of ranitidine
21042	METFORMIN	Yes	VISIT 5 (28 WEEKS)	07/09/2013 self referral to maty ward feeling dizzy. 21/09/2013 ?SROM HVS showed Group B Strep. On last day of Amoxycillin treatment today. Gestational diabetes today. Attending for glucometer tomorrow
21042	METFORMIN	Yes	VISIT 7 (TERM)	Group B Strep diagnosed in pregnancy.
21042	METFORMIN	Yes	VISIT 8 (DELIVERY)	Induction of labour for gestational diabetes. Group B Strep identified in pregnancy.
21064	METFORMIN	Yes	VISIT 5 (28 WEEKS)	UTI 21/10/13 cephalixin tds for 5 days taken.
21064	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Right sided abdo pain on 2 occasions 15 & 22/11/13 been fine since.
21064	METFORMIN	Yes	VISIT 8 (DELIVERY)	SPD
21070	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Lower backache has appt with physio on 8/10/13
21070	METFORMIN	Yes	VISIT 5 (28 WEEKS)	Symphysis Pubis Dysfunction-physio input
21070	METFORMIN	Yes	VISIT 6 (36 WEEKS)	SPD
21070	METFORMIN	Yes	VISIT 8 (DELIVERY)	SPD-S/B Physio & had acupuncture.
21074	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Backache 16+ weeks saw GP & resolved a few days later
21074	METFORMIN	Yes	VISIT 5 (28 WEEKS)	Wort on finger.
21074	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Itching on legs, had same prior to pregnancy. Wort on finger.
21074	METFORMIN	Yes	VISIT 7 (TERM)	03/02/14 headache for 24 hours. Started on antibiotics as ?UTI. Normal MSSU so stopped taking. Only took 1 tablet.
21074	METFORMIN	Yes	VISIT 8 (DELIVERY)	26/2/14 perineal infection flucloxyllin commenced orally at home.
21082	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	20/10/13 attended primary care/gynae feeling unwell ?food poisoning/palpitations normal investigations. Some low mood/depression.
21082	METFORMIN	Yes	VISIT 6 (36 WEEKS)	3/1/14 29+4 episode of raised BP settled. 30/1/14 33+3 antibiotics for UTI.
21082	METFORMIN	Yes	VISIT 7 (TERM)	Some hypertension-settled now.
21082	METFORMIN	Yes	VISIT 8 (DELIVERY)	Pyrexial in labour/maternal tachycardia. IV paracetamol required.
21095	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Started citalopram for depression on 04/11/13.
21095	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Lower back discomfort sees physio.
21095	METFORMIN	Yes	VISIT 8 (DELIVERY)	On citalopram for depression
21099	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Tooth abcess so had to reduce tablets one day.
21099	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Elevated BP today for close monitoring. Occasionally takes Co-dydramol for backache. Physio/acupuncture unsuccessful.
21099	METFORMIN	Yes	VISIT 8 (DELIVERY)	Raised blood pressure
21111	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Small pv bleed 08/12/13 19+ weeks. Investigations NAD. Not admitted to Gynae.
21111	METFORMIN	Yes	VISIT 5 (28 WEEKS)	Upper abdominal discomfort for 4-5 weeks on and off.
21111	METFORMIN	Yes	VISIT 7 (TERM)	Amoxycillin 500mgs TDS for suspected chest infection.
21127	METFORMIN	Yes	VISIT 5 (28 WEEKS)	SPD on crutches seeing physio.
21127	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Seeing physio & having acupuncture for hip pain.
21127	METFORMIN	Yes	VISIT 8 (DELIVERY)	SPD/Hip pain. Has seen physio/had crutches/acupuncture.

Section 10. Adverse Outcome

10.1.2 Maternal Complications Details - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Other Maternal Complications (Y/N)	Timepoint/D	Other Maternal Complications Details
21128	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Backache & sciatica
21128	METFORMIN	Yes	VISIT 8 (DELIVERY)	Postpartum haemorrhage.
25264	METFORMIN	Yes	VISIT 5 (28 WEEKS)	obstetric cholestasis
25382	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	diarrhoea
25459	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Right Adrexal ovarian cyst
25459	METFORMIN	Yes	VISIT 8 (DELIVERY)	Induction of labour due to pain from known ovarian cyst
53059	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Had contact with nephew with chicken pox and does not have immunity. Therefore had to attend for immunoglobulin
11081	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	on going hyperemesis requiring antiemetic (predates trial)
11323	PLACEBO	Yes	VISIT 8 (DELIVERY)	3rd degree tear (3a)
11443	PLACEBO	Yes	VISIT 6 (36 WEEKS)	itch-possible obstetric cholestasis
11693	PLACEBO	Yes	VISIT 8 (DELIVERY)	Obstetric cholestasis
11725	PLACEBO	Yes	VISIT 7 (TERM)	SPD
11940	PLACEBO	Yes	VISIT 6 (36 WEEKS)	currently on prednisolone for chest infection
11940	PLACEBO	Yes	VISIT 8 (DELIVERY)	Hospitalised due to chest infection.
12019	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Thrush
12020	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Ear infection/vertigo
12020	PLACEBO	Yes	VISIT 5 (28 WEEKS)	vertigo
12020	PLACEBO	Yes	VISIT 8 (DELIVERY)	PPH 1500 - 2500 mls
12021	PLACEBO	Yes	VISIT 5 (28 WEEKS)	25/04/2012 In triage for UTI. Sent home with trimethoprim.
12065	PLACEBO	Yes	VISIT 8 (DELIVERY)	Diet controlled GDM
13007	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Was weepy when increased dose to 4 tablets at week 4. Therefore has decreased to 2 tablets daily. Not having weepiness any longer, suggested trying to increase to TDS, - will try, but not willing to increase dose further. 4/3/11
13058	PLACEBO	Yes	VISIT 6 (36 WEEKS)	vomiting and feeling very unwell migraines increasingly worse
13144	PLACEBO	Yes	VISIT 5 (28 WEEKS)	SYMPHISIS PUBIS DISORDER
13144	PLACEBO	Yes	VISIT 7 (TERM)	Has had fainting episodes for past 6 weeks. Now has IOL booked for 38wks due to this. Reports has had several admissions with raised blood pressure and protein ura.
13144	PLACEBO	Yes	VISIT 8 (DELIVERY)	Reported frequent fainting episodes. not investigated, occasional episodes of raised BP. BP profile NAD. IOL on request in view of repeated fainting.
13217	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Hip pain due to looseness in joint. Under physio. Not on medication.
13217	PLACEBO	Yes	VISIT 8 (DELIVERY)	PPH, HAD OXYTOCIC DRUGS
13301	PLACEBO	Yes	VISIT 5 (28 WEEKS)	HAD COLLAPSE WHEN OUT SHOPPING. ADVISED TO STOP MEDICATION AS GLUCOSE LEVEL WAS REPORTED TO BE LOW WHEN CHECKED AT GP.
13301	PLACEBO	Yes	VISIT 8 (DELIVERY)	Intrapartum haemorrhage and postnatal haemorrhage total = 2000ml
13591	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Fell on the bus when it stopped suddenly. Had small pv bleed, attended hospital for anti d, but was not admitted and not for any follow up. As reports fall was due to bus stopping suddenly and no episodes of dizziness or feeling faint not an SAE.
13667	PLACEBO	Yes	VISIT 8 (DELIVERY)	IOL FOR SPD PPH 1200ML
13712	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Obstetric Cholestasis
13712	PLACEBO	Yes	VISIT 8 (DELIVERY)	cholestasis
14205	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Double vision. Currently under investigation by eye clinic.
14336	PLACEBO	Yes	VISIT 5 (28 WEEKS)	Seen by SHO in Triage 13.09.13 re abdominal pain. Now resolved ?viral enteritis

Section 10. Adverse Outcome

10.1.2 Maternal Complications Details - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Other Maternal Complications (Y/N)	TimepointID	Other Maternal Complications Details
14336	PLACEBO	Yes	VISIT 8 (DELIVERY)	see SAE
14354	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Ovarian cyst on right ovary diagnosed
14354	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Admitted with small APH and tightenings for 5 days - SAE completed 22.12.13
14413	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Abdominal pain 03.10.13 Seen in Early Pregnancy Assessment Centre
15010	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	metallic taste
15010	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Has some itching bile acids nad
17036	PLACEBO	Yes	VISIT 7 (TERM)	hospital admission as had flu
17036	PLACEBO	Yes	VISIT 8 (DELIVERY)	raised ALT liver scan
17137	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Costochondritis
17137	PLACEBO	Yes	VISIT 8 (DELIVERY)	Costochondritis
21010	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Persistent glycosuria between 28+ and 35+ weeks gestation. Normal GTTs.
21018	PLACEBO	Yes	VISIT 5 (28 WEEKS)	pv bleed before 16 weeks gestation, prior to commencing tablets.Hospitalised for observation discharged within 12 hours.
21018	PLACEBO	Yes	VISIT 6 (36 WEEKS)	4/9/13 32+6 shortness of breath/palpitations. Investigations normal.
21018	PLACEBO	Yes	VISIT 7 (TERM)	Various episodes of reduced fetal movements see on MDCU had CTGs. H/o palpitations normal investigations.
21018	PLACEBO	Yes	VISIT 8 (DELIVERY)	Difficult caesarean section.
21038	PLACEBO	Yes	VISIT 8 (DELIVERY)	Readmitted via ambulance 29/12/13 pv bleed/abdo pain. Stayed in hospital for less than 12 hours. No SAE required.
21044	PLACEBO	Yes	VISIT 6 (36 WEEKS)	pyogenic granuloma on finger of left hand.Had x2 doses of flucloxyllin.UTI cephalixin for 1 week.
21047	PLACEBO	Yes	VISIT 5 (28 WEEKS)	20+4 (3-4/9/13) brief episode in A&E pain from gall stones settled after morphine discharged home after few hours.
21069	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Antibiotics for 1 week for ear infection 05/09/13
21069	PLACEBO	Yes	VISIT 5 (28 WEEKS)	UTI treated with cefalexin.
21069	PLACEBO	Yes	VISIT 8 (DELIVERY)	Sepsis in labour.SAE form completed as prolonged hospitalisation.
21078	PLACEBO	Yes	VISIT 5 (28 WEEKS)	Hb low for oral iron
21078	PLACEBO	Yes	VISIT 6 (36 WEEKS)	16/1/14 episode of reduced fetal movements. CTG NAD.
21078	PLACEBO	Yes	VISIT 7 (TERM)	On ferrous sulphate tablets as anaemic since last visit.
21093	PLACEBO	Yes	VISIT 5 (28 WEEKS)	Small antepartum haemorrhage. Overnight stay on maternity ward for over 12 hours.
21093	PLACEBO	Yes	VISIT 6 (36 WEEKS)	28/12/13 slight pv bleeding no admission. 24/1/14 Antibiotics for bacterial vaginosis & canestan for thrush. 3/2/14 brief isolated episode of raised BP settled on day unit no admission.
21093	PLACEBO	Yes	VISIT 8 (DELIVERY)	Raised BP in labour
21109	PLACEBO	Yes	VISIT 5 (28 WEEKS)	Heartburn. Day Unit visit 16/12/13 abdo pain.
21109	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Admitted over 12 hours with UTI. Oral antibiotics/steroids/ferrous sulphate.SAE form completed & faxed to Sponsors.
21109	PLACEBO	Yes	VISIT 7 (TERM)	Admitted for 2 nights on 03/4/14 with lower abdo discomfort, braxton hicks, red pv loss, unstable lie.
21109	PLACEBO	Yes	VISIT 8 (DELIVERY)	Admitted with lower abdo discomfort, red pv loss, Braxton Hicks,unstable lie 03/4/14
21122	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Prolonged nausea.
21122	PLACEBO	Yes	VISIT 5 (28 WEEKS)	Prolonged nausea
21122	PLACEBO	Yes	VISIT 7 (TERM)	Musculoskeletal pain/SPD. Group B Strep positive.
21122	PLACEBO	Yes	VISIT 8 (DELIVERY)	SPD/musculoskeletal pain. Group B Strep positive.

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Section 10. Adverse Outcome

10.1.2 Maternal Complications Details - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Other Maternal Complications (Y/N)	Timepoint/D	Other Maternal Complications Details
25391	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	brown/green pv loss on 2.11.13. pv spotting on 12.11.13. HVS group B streptococcus.
25391	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Abdominal pain ?cause
25391	PLACEBO	Yes	VISIT 7 (TERM)	depression and musculoskeletal pain
53014	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	has had persistant cough since sept. Has seen own doctor (GP, had course of antibiotics. Also seen at general hospital advised re inhalers and improved with this (as is asthmatic)

Section 10. Adverse Outcome

10.1.3.1 Maternal Complications - Hypertension - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery) - Statistical Analysis - POST-HOC*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of ANY_HYPER by AllocatedTreatment</i>								
		<i>AllocatedTreatment(Allocated Treatment)</i>								
<i>ANY_HYPER</i>	<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>							
<i>No</i>	98	107	205							
<i>Yes</i>	11	11	22							
<i>Total</i>	109	118	227							

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
ANY_HYPER_pp	AllocatedTreatment METFORMIN vs PLACEBO	1.092	0.453	2.631	0.8448	1.0000

Section 10. Adverse Outcome

10.1.3.2 Maternal Complications - Preeclampsia - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery) - Statistical Analysis - POST-HOC*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of ANY_Preecla by AllocatedTreatment</i>			
		<i>AllocatedTreatment(Allocated Treatment)</i>			
<i>ANY_Preecla</i>	<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>		
<i>No</i>	106	115	221		
<i>Yes</i>	3	3	6		
<i>Total</i>	109	118	227		

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
ANY_Preecla_pp	AllocatedTreatment METFORMIN vs PLACEBO	1.085	0.214	5.493	0.9216	1.0000

Section 10. Adverse Outcome

10.2.1 Fetal Complications* - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Any Fetal Complication (n)	Yes	28 (23.7)	26 (23.9)	54 (23.8)
	No	90 (76.3)	83 (76.1)	173 (76.2)
Fetal AC (n)	Missing	118	109	227
Fetal Liquor (n)	Missing	77	76	153
	Yes	2	3	5
	No	39	30	69
Fetal Doppler (n)	Missing	77	77	154
	No	41	32	73
Fetal Absent EDF (n)	Missing	78	77	155
	Yes	1	0	1
	No	39	32	71

Section 10. Adverse Outcome

10.2.1 Fetal Complications* - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)(Cont.)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall N=227
		Placebo N=118	Metformin N=109	
Fetal Reverse EDF (n)	Missing	78	77	155
	No	40	32	72
Fetal Abnormal CTG (n)	Missing	77	77	154
	Yes	8	8	16
	No	33	24	57
Other Fetal Complication (n)	Missing	70	69	139
	Yes	21	21	42
	No	27	19	46
Other Fetal Complication cat#(n)	Data captured elsewhere	12	10	22
	Meconium stained liquor	3	4	7
	Miscellaneous	1	1	2
	Polyhydramnios	3	3	6
	Reduced fetal movements	3	7	10
	Shoulder dystocia	2	0	2

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Section 10. Adverse Outcome
 10.2.2 Fetal Complications Details - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)
 Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Fetal Complications Other (Y/N)	TimepointID	Fetal Complications Other Details
11557	METFORMIN	Yes	VISIT 8 (DELIVERY)	reduced fetal movements and clinically felt to be small for dates although growth scan normal
12001	METFORMIN	Yes	VISIT 8 (DELIVERY)	macrosomia
12018	METFORMIN	Yes	VISIT 6 (36 WEEKS)	scan at 36 weeks shows abdominal circumference static, attending further scan in one week
12034	METFORMIN	Yes	VISIT 8 (DELIVERY)	Premature delivery.
13551	METFORMIN	Yes	VISIT 8 (DELIVERY)	Low Cord Ph's on FBS
14303	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Polyhydramnios
15003	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Breech presentation
16064	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Reduced fetal movements x 2 days
16121	METFORMIN	Yes	VISIT 7 (TERM)	Persistent reduced fetal movements
16121	METFORMIN	Yes	VISIT 8 (DELIVERY)	Persistent reduced fetal movements
16133	METFORMIN	Yes	VISIT 7 (TERM)	polyhydramnios
16133	METFORMIN	Yes	VISIT 8 (DELIVERY)	polyhydramnios
17047	METFORMIN	Yes	VISIT 8 (DELIVERY)	Meconium liquor
21042	METFORMIN	Yes	VISIT 6 (36 WEEKS)	Episodes of reduced fetal movements.
21070	METFORMIN	Yes	VISIT 8 (DELIVERY)	Thick meconium liquor on SROM.
21074	METFORMIN	Yes	VISIT 6 (36 WEEKS)	x1 episode of no fetal movements 25/11/13 28+5. Normal CTG.
21074	METFORMIN	Yes	VISIT 7 (TERM)	Reduced fetal movements 03/02/14. Normal scan.
21082	METFORMIN	Yes	VISIT 5 (28 WEEKS)	Growth below lower centile.
21082	METFORMIN	Yes	VISIT 8 (DELIVERY)	Thick meconium liquor. Fetal lachycardia in labour.
21095	METFORMIN	Yes	VISIT 8 (DELIVERY)	Meconium liquor
21127	METFORMIN	Yes	VISIT 8 (DELIVERY)	Growth on 10th centile.
21128	METFORMIN	Yes	VISIT 8 (DELIVERY)	IUGR. Growth on lower centile. Double knot in cord.
25226	METFORMIN	Yes	VISIT 8 (DELIVERY)	Baby had NABX as prev NND for Group B Strep and EColi.
25459	METFORMIN	Yes	VISIT 4 (18 TO 20 WEEKS)	Anomaly scan show right unilateral talipes
53059	METFORMIN	Yes	VISIT 6 (36 WEEKS)	HAD 2X GROWTH USS FOR ?IUGR. SECOND USS SHOWED NORMAL GROWTH.
11386	PLACEBO	Yes	VISIT 8 (DELIVERY)	shoulder dystocia, relieved with McRoberts and suprapubic pressure, Apgars 8 and 9
11564	PLACEBO	Yes	VISIT 8 (DELIVERY)	baby required resuscitation at delivery
11632	PLACEBO	Yes	VISIT 8 (DELIVERY)	Suspected IUGR
12020	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Reduced fetal movements
12021	PLACEBO	Yes	VISIT 5 (28 WEEKS)	Polyhydramnios
12021	PLACEBO	Yes	VISIT 6 (36 WEEKS)	polyhydramnios detected on scan at 28+4 weeks. Large for gestational age detected at 34+2 weeks.
13301	PLACEBO	Yes	VISIT 8 (DELIVERY)	Undiagnosed oblique breech lie, intrapartum haemorrhage
13473	PLACEBO	Yes	VISIT 8 (DELIVERY)	Baby admitted to NICU for low BM's for 24 hours. No IV fluids required, baby tube fed only. Lowest BM 1.7mmol. Now maintaining BM's and back on postnatal ward with mum
13591	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Raised growth on USS, at 32/40 and 35/40 measurements >95th centile. EPW at 35/40 3456g
13591	PLACEBO	Yes	VISIT 8 (DELIVERY)	Suspected fetal macrosomia
14264	PLACEBO	Yes	VISIT 8 (DELIVERY)	Intermittently absent EDF

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Section 10. Adverse Outcome

10.2.2 Fetal Complications Details - from Visit 4 (18-20 Weeks) to Visit 8 (Delivery)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	Fetal Complications Other (Y/N)	TimepointID	Fetal Complications Other Details
15010	PLACEBO	Yes	VISIT 5 (28 WEEKS)	one episode of reduced fetal movements ctg monitoring normal
16053	PLACEBO	Yes	VISIT 8 (DELIVERY)	shoulder dystocia
18114	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Measuring Large for Dates. Head circumference and abdominal circumference above 95th centile.
21018	PLACEBO	Yes	VISIT 6 (36 WEEKS)	Polyhydramniotic on uss 8/8/13 (29 weeks) & 21/8/13 (30+6 weeks) has since resolved. Reduced fetal movements had monitoring on x4 occasions & again today.
21038	PLACEBO	Yes	VISIT 5 (28 WEEKS)	Growth on lower centile today. Normal doppler
21069	PLACEBO	Yes	VISIT 8 (DELIVERY)	Thick meconium stained liquor during labour.
21093	PLACEBO	Yes	VISIT 6 (36 WEEKS)	27/1/14 growth on lower centile. 03/2/14 mild polyhydramniotic. 10/2/14 normal growth & liquor volume.
21093	PLACEBO	Yes	VISIT 8 (DELIVERY)	Light, thin meconium liquor
21109	PLACEBO	Yes	VISIT 6 (36 WEEKS)	21/02/2014 uss normal growth. Liquor volume just above upper centile.
21119	PLACEBO	Yes	VISIT 4 (18 TO 20 WEEKS)	Fetal abnormality on anomaly ultrasound scan.
25034	PLACEBO	Yes	VISIT 8 (DELIVERY)	meconium stained liquor
25320	PLACEBO	Yes	VISIT 8 (DELIVERY)	baby's scan on the 30/1/2014 continued to show baby had a full stomach. suspected Hirschsprungs disease in neonate.
25364	PLACEBO	Yes	VISIT 7 (TERM)	Large for dates on scan

Section 11. Neonatal Care - All Patients

11.1 Neonatal Care

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Care after delivery (n(%))	Missing	1	1	2
	Normal Care	100 (85.5)	98 (90.7)	198 (88.0)
	Special Care	6 (5.1)	4 (3.7)	10 (4.4)
	Level 2 intensive care (ie high dependency intensive care)	6 (5.1)	3 (2.8)	9 (4.0)
	Level 1 intensive care (maximal intensive care)	1 (0.9)	1 (0.9)	2 (0.9)
	Other	4 (3.4)	2 (1.9)	6 (2.7)
Any Congenital Abnormality (n(%))	Missing	2	2	4
	Yes	5 (4.3)	4 (3.7)	9 (4.0)
	No	111 (95.7)	103 (96.3)	214 (96.0)
Other Hospital Admission (n(%))	Missing	9	7	16
	Yes	2 (1.8)	1 (1.0)	3 (1.4)
	No	107 (98.2)	101 (99.0)	208 (98.6)

Section 11. Neonatal Care - Only Alive Births

11.2.1 Neonatal Care

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo</i>	<i>Metformin</i>	<i>Overall</i>
Care after delivery (n(%))	Missing	1	0	1
	Normal Care	100 (86.2)	98 (90.7)	198 (88.4)
	Special Care	6 (5.2)	4 (3.7)	10 (4.5)
	Level 2 intensive care (ie high dependency intensive care)	6 (5.2)	3 (2.8)	9 (4.0)
	Level 1 intensive care (maximal intensive care)	1 (0.9)	1 (0.9)	2 (0.9)
	Other	3 (2.6)	2 (1.9)	5 (2.2)
Any Congenital Abnormality (n(%))	Missing	2	1	3
	Yes	4 (3.5)	4 (3.7)	8 (3.6)
	No	111 (96.5)	103 (96.3)	214 (96.4)
Other Hospital Admission (n(%))	Missing	9	6	15
	Yes	2 (1.9)	1 (1.0)	3 (1.4)
	No	106 (98.1)	101 (99.0)	207 (98.6)

Section 11. Neonatal Care - Only Alive Births

11.2.2 Neonatal care after delivery - Statistical analysis - POST-HOC*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of Care_Deliv by AllocatedTreatment</i>						
		<i>AllocatedTreatment(Allocated Treatment)</i>						
<i>Care_Deliv</i>	<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>					
<i>Missing</i>	0	1	.					
<i>No</i>	100	103	203					
<i>Yes</i>	8	13	21					
<i>Total</i>	108	116	224					
<i>Frequency Missing = 1</i>								

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
Care_Deliv_pp	AllocatedTreatment METFORMIN vs PLACEBO	0.634	0.252	1.595	0.3329	0.3667

Section 11. Neonatal Care - Only Alive Births

11.2.3 Any Congenital Abnormality - Statistical analysis - POST-HOC*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of Abnormal by AllocatedTreatment</i>			
		<i>AllocatedTreatment(Allocated Treatment)</i>			
<i>Abnormal</i>	<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>		
<i>Missing</i>	1	2	.		
<i>No</i>	103	111	214		
<i>Yes</i>	4	4	8		
<i>Total</i>	107	115	222		
<i>Frequency Missing = 3</i>					

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
Abnormal_pp	AllocatedTreatment METFORMIN vs PLACEBO	1.078	0.263	4.421	0.9173	1.0000

Section 12. Maternal symptoms up to 36 weeks gestation

12.1.1 Taste Disturbance - from Visit 4 (18-20 Weeks) to Visit 6 (36 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=227</i>
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	
Any Taste Disturbance (n(%))	Yes	20 (16.9)	17 (15.6)	37 (16.3)
	No	98 (83.1)	92 (84.4)	190 (83.7)
Taste Disturbance severity (n)	Mild	11	10	21
	Moderate	9	3	12
	Severe	0	4	4

Section 12. Maternal symptoms up to 36 weeks gestation

12.1.2 Taste Disturbance - Statistical analysis - POST-HOC*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of TasteDis_ana by AllocatedTreatment</i>				
<i>TasteDis_ana(Taste disturbance at least once from visit 4 to visit 7 (Y/N))</i>		<i>AllocatedTreatment(Allocated Treatment)</i>				
		<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>		
<i>Yes</i>		17	20	37		
<i>No</i>		92	98	190		
<i>Total</i>		109	118	227		

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
tastedis_pp	AllocatedTreatment METFORMIN vs PLACEBO	0.905	0.447	1.835	0.7828	0.8581

Section 12. Maternal symptoms up to 36 weeks gestation

12.2.1 Skin Reaction - from Visit 4 (18-20 Weeks) to Visit 6 (36 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Any Skin Reaction (n(%))	Yes	23 (19.5)	21 (19.3)	44 (19.4)
	No	95 (80.5)	88 (80.7)	183 (80.6)
Skin Reaction severity (n)	Mild	13	12	25
	Moderate	8	7	15
	Severe	2	2	4

Section 12. Maternal symptoms up to 36 weeks gestation

12.2.2 Skin Reaction - Statistical Analysis - POST-HOC*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Frequency</i>		<i>Table of SkinReac_ana by AllocatedTreatment</i>					
	<i>SkinReac_ana(Skin Reaction at least once from visit 4 to visit 7 (Y/N))</i>	<i>AllocatedTreatment(Allocated Treatment)</i>			<i>Total</i>		
		<i>METFORMIN</i>	<i>PLACEBO</i>				
<i>Yes</i>		21	23		44		
<i>No</i>		88	95		183		
<i>Total</i>		109	118		227		

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
skinreac_pp	AllocatedTreatment METFORMIN vs PLACEBO	0.986	0.510	1.905	0.9658	1.0000

Section 12. Maternal symptoms up to 36 weeks gestation

12.3.1 Abdominal Pain - from Visit 4 (18-20 Weeks) to Visit 6 (36 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	<i>Overall N=227</i>
Any Abdominal Pain (n(%))	Yes	26 (22.0)	32 (29.4)	58 (25.6)
	No	92 (78.0)	77 (70.6)	169 (74.4)
Abdominal Pain severity (n)	Mild	16	21	37
	Moderate	8	10	18
	Severe	2	1	3

Section 12. Maternal symptoms up to 36 weeks gestation

12.3.2 Abdominal Pain - Statistical Analysis - POST-HOC*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of AbdoPain_ana by AllocatedTreatment</i>				
	<i>AbdoPain_ana(Abdominal Pain at least once from visit 4 to visit 7 (Y/N))</i>	<i>AllocatedTreatment(Allocated Treatment)</i>		<i>Total</i>		
		<i>METFORMIN</i>	<i>PLACEBO</i>			
	<i>Yes</i>	32	26	58		
	<i>No</i>	77	92	169		
	<i>Total</i>	109	118	227		

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
abdopain_pp	AllocatedTreatment METFORMIN vs PLACEBO	1.471	0.807	2.678	0.2074	0.2255

Section 12. Maternal symptoms up to 36 weeks gestation

12.4.1 Flatulence - from Visit 4 (18-20 Weeks) to Visit 6 (36 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	<i>Overall N=227</i>
Any Flatulence (n(%))	Yes	28 (23.7)	38 (34.9)	66 (29.1)
	No	90 (76.3)	71 (65.1)	161 (70.9)
Flatulence severity (n)	Mild	16	16	32
	Moderate	9	16	25
	Severe	3	6	9

Section 12. Maternal symptoms up to 36 weeks gestation

12.4.2 Flatulence - Statistical Analysis - POST-HOC*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Frequency</i>		<i>Table of Flatu_ana by AllocatedTreatment</i>					
<i>Flatu_ana(Flatulence at least once from visit 4 to visit 7 (Y/N))</i>	<i>AllocatedTreatment(Allocated Treatment)</i>			<i>Total</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>Fisher exact P-value#</i>
	<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>				
<i>Yes</i>	38	28	66				
<i>No</i>	71	90	161				
<i>Total</i>	109	118	227				

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
flatu_pp	AllocatedTreatment METFORMIN vs PLACEBO	1.720	0.964	3.069	0.0662	0.0793

Section 12. Maternal symptoms up to 36 weeks gestation

12.5.1 Constipation - from Visit 4 (18-20 Weeks) to Visit 6 (36 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=227</i>
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	
Any Constipation (n(%))	Yes	38 (32.2)	37 (33.9)	75 (33.0)
	No	80 (67.8)	72 (66.1)	152 (67.0)
Constipation severity (n)	Mild	19	21	40
	Moderate	17	11	28
	Severe	2	5	7

Section 12. Maternal symptoms up to 36 weeks gestation

12.5.2 Constipation - Statistical Analysis - POST-HOC*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of Consti_ana by AllocatedTreatment</i>				
<i>Consti_ana(Constipation at least once from visit 4 to visit 7 (Y/N))</i>	<i>AllocatedTreatment(Allocated Treatment)</i>		<i>Total</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>Fisher exact P-value#</i>
	<i>METFORMIN</i>	<i>PLACEBO</i>				
<i>Yes</i>	37	38	75			
<i>No</i>	72	80	152			
<i>Total</i>	109	118	227			

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
consti_pp	AllocatedTreatment METFORMIN vs PLACEBO	1.082	0.622	1.882	0.7805	0.8878

Section 12. Maternal symptoms up to 36 weeks gestation

12.6.1 Diarrhoea - from Visit 4 (18-20 Weeks) to Visit 6 (36 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	<i>Overall N=227</i>
Any Diarrhoea (n(%))	Yes	24 (20.3)	60 (55.0)	84 (37.0)
	No	94 (79.7)	49 (45.0)	143 (63.0)
Diarrhoea severity (n)	Mild	14	34	48
	Moderate	8	21	29
	Severe	2	5	7

Section 12. Maternal symptoms up to 36 weeks gestation

12.6.2 Diarrhoea - Statistical Analysis - POST-HOC*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of Diarrh_ana by AllocatedTreatment</i>				
<i>Diarrh_ana(Diarrhoea at least once from visit 4 to visit 7 (Y/N))</i>	<i>AllocatedTreatment(Allocated Treatment)</i>		<i>Total</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>Fisher exact P-value#</i>
	<i>METFORMIN</i>	<i>PLACEBO</i>				
<i>Yes</i>	60	24	84			
<i>No</i>	49	94	143			
<i>Total</i>	109	118	227			

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
diarrh_pp	AllocatedTreatment METFORMIN vs PLACEBO	4.796	2.669	8.617	<.0001	0.0000

Section 12. Maternal symptoms up to 36 weeks gestation

12.7.1 Nausea - from Visit 4 (18-20 Weeks) to Visit 6 (36 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=227</i>
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	
Any Nausea (n(%))	Yes	46 (39.0)	49 (45.0)	95 (41.9)
	No	72 (61.0)	60 (55.0)	132 (58.1)
Nausea severity (n)	Mild	31	27	58
	Moderate	13	19	32
	Severe	2	3	5

Section 12. Maternal symptoms up to 36 weeks gestation

12.7.2 Nausea - Statistical Analysis - POST-HOC*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of Nausea_ana by AllocatedTreatment</i>				
<i>Nausea_ana(Nausea at least once from visit 4 to visit 7 (Y/N))</i>		<i>AllocatedTreatment(Allocated Treatment)</i>				
		<i>METFORMIN</i>	<i>PLACEBO</i>	<i>Total</i>		
<i>Yes</i>		49	46	95		
<i>No</i>		60	72	132		
<i>Total</i>		109	118	227		

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
nausea_pp	AllocatedTreatment METFORMIN vs PLACEBO	1.278	0.754	2.168	0.3626	0.4194

Section 12. Maternal symptoms up to 36 weeks gestation

12.8.1 Vomiting - from Visit 4 (18-20 Weeks) to Visit 6 (36 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	<i>Overall N=227</i>
Any Vomiting (n(%))	Yes	24 (20.3)	34 (31.2)	58 (25.6)
	No	94 (79.7)	75 (68.8)	169 (74.4)
Vomiting severity (n)	Mild	14	20	34
	Moderate	7	13	20
	Severe	3	1	4

Section 12. Maternal symptoms up to 36 weeks gestation

12.8.2 Vomiting - Statistical Analysis - POST-HOC*

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Frequency</i>		<i>Table of Vomit_ana by AllocatedTreatment</i>					
	<i>Vomit_ana(Vomit at least once from visit 4 to visit 7 (Y/N))</i>	<i>AllocatedTreatment(Allocated Treatment)</i>		<i>Total</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>Fisher exact P-value#</i>
		<i>METFORMIN</i>	<i>PLACEBO</i>				
	<i>Yes</i>	34	24	58			
	<i>No</i>	75	94	169			
	<i>Total</i>	109	118	227			
<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>	
vomit_pp	AllocatedTreatment METFORMIN vs PLACEBO	1.775	0.970	3.249	0.0626	0.0687	

Section 12. Maternal symptoms up to 36 weeks gestation

12.9.1 Headache - from Visit 4 (18-20 Weeks) to Visit 6 (36 Weeks)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		
		Placebo N=118	Metformin N=109	Overall N=227
Any Headache (n(%))	Yes	40 (33.9)	37 (33.9)	77 (33.9)
	No	78 (66.1)	72 (66.1)	150 (66.1)
Headache severity (n)	Mild	21	24	45
	Moderate	13	9	22
	Severe	6	4	10

Section 12. Maternal symptoms up to 36 weeks gestation

12.9.2 Headache - Statistical Analysis - POST-HOC*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

<i>Frequency</i>		<i>Table of Headache_ana by AllocatedTreatment</i>				
	<i>Headache_ana(Headache at least once from visit 4 to visit 7 (Y/N))</i>	<i>AllocatedTreatment(Allocated Treatment)</i>		<i>Total</i>		
		<i>METFORMIN</i>	<i>PLACEBO</i>			
	<i>Yes</i>	37	40	77		
	<i>No</i>	72	78	150		
	<i>Total</i>	109	118	227		

<i>Parameter(s)</i>	<i>Studied effects</i>	<i>Odds Ratio Estimate</i>	<i>Lower 95% Confidence Limit for Odds Ratio</i>	<i>Upper 95% Confidence Limit for Odds Ratio</i>	<i>P-value#</i>	<i>Fisher exact P-value#</i>
headache_pp	AllocatedTreatment METFORMIN vs PLACEBO	1.002	0.578	1.737	0.9941	1.0000

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Section 13. Serious Adverse Events

13.1.1.1 Mothers with at least one SAE

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=227</i>
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	
Number of Patient with a SAE (n)	OVERALL	22	14	36

Section 13. Serious Adverse Events

13.1.1.2 Mothers with at least one SAE - Statistical Analysis - POST-HOC*

Population = Per-Protocol (PP) - AllocatedTreatment used for summarisation

Frequency	Table of ANY_SAE by AllocatedTreatment			
	AllocatedTreatment(Allocated Treatment)			
	ANY_SAE	METFORMIN	PLACEBO	Total
No		95	96	191
Yes		14	22	36
Total		109	118	227

Parameter(s)	Studied effects	Odds Ratio Estimate	Lower 95% Confidence Limit for Odds Ratio	Upper 95% Confidence Limit for Odds Ratio	P-value#	Fisher exact P-value#
			0.311	1.331		
pat_sae_pp	AllocatedTreatment METFORMIN vs PLACEBO	0.643	0.311	1.331	0.2344	0.2767

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Section 13. Serious Adverse Events

13.1.1.3 SAE related to the mothers

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall N=227</i>
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	
Number of SAE (n)	OVERALL	28	19	47
Number of SAE by relationship (n)	Possibly	2	2	4
	Unrelated	26	17	43
Number of SAE by expectedness (n)	Yes	6	6	12
	No	21	13	34
	Unk	1	0	1

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Section 13. Serious Adverse Events

13.1.1.3 SAE related to the mothers (Cont.)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo</i>	<i>Metformin</i>	<i>Overall</i>
Number of SAE by outcome (n)	Missing	1	0	1
	Completely recovered	24	16	40
	Condition improving	1	1	2
	Condition improving Completely recovered	1	0	1
	Condition improving Recovered with sequelae	0	1	1
	Recovered with sequelae	1	1	2

Section 13. Serious Adverse Events

13.1.2 SAE related to the mothers - Details

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	SAE - date of report	SAE - date of event	Description of SAE	Expedited Reporting Criteria	Relevant History	SAE_related_coded	SAE_expected_coded (Y/N)	SAE_outcome_coded	SAE - date of recovery
11136	METFORMIN	19JAN2012	14JAN2012	Diagnosis: Placental abruption. Description: Patient presented at 35+2 weeks gestation with a minor ante-partum haemorrhage. Clinical diagnosis of placental abruption was made, necessitating immediate delivery by caesarean section. Diagnosis was confirmed at delivery. Mother and baby are both well. Severity: Moderate	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	17JAN2012
11501	METFORMIN	14NOV2012	27OCT2012	Diagnosis: Unknown Description: Admitted with severe renal pain and vomiting. Noted to have deranged LFTs. Recent course of amoxicillin from GP for chest infection. Symptoms and LFTs resolved spontaneously. Severity: Mild	Involved or prolonged inpatient hospitalisation		Possibly	Yes	Completely recovered	31OCT2012
11748	METFORMIN	12DEC2013	11DEC2013	Diagnosis: Mastitis. Description: Sepsis secondary to Mastitis. Follow-up 20/02/14: Admitted 10 days postnatal with mastitis. Treated with IV then oral antibiotics. Severity: Moderate	Involved or prolonged inpatient hospitalisation	UTI. 25/09/2013 - 27/09/2013, medication required.	Unrelated	No	Completely recovered	14DEC2013
11748	METFORMIN	27SEP2013	25SEP2013	Diagnosis: Pain and Vomiting. Description: Self presented with upper abdominal pain and vomiting. ?UTI. Severity: Moderate.	Involved or prolonged inpatient hospitalisation	Depression from 2009 to 2010. Urinary Tract Infection. April 9th 2013 to 6.4.2013.	Unrelated	No	Recovered with sequelae	27SEP2013
11748	METFORMIN	07OCT2013	06OCT2013	Diagnosis: Abdominal Pain ? Preterm Labour Description: Self presented with abdo pain. ?Preterm labour complicated by urinary tract infections. Severity: Moderate Follow-up 20/02/14: Diagnosis: UTI. Admitted at 32 weeks gestation with abdominal pain. Urine culture +ve for e.coli. Threatened pre-term labour excluded. Treated with antibiotics and resolved. Severity: Mild.	Involved or prolonged inpatient hospitalisation	Urinary Tract Infection. 02/04/13 - 05/04/2013 and 25/09/2013 - 26/09/2013, medication required for both infections.	Unrelated	No	Completely recovered	09OCT2014
11797	METFORMIN	18NOV2013	14NOV2013	Diagnosis: Vomiting in late pregnancy. Description: Self presented with excessive vomiting. Severity: Moderate.	Involved or prolonged inpatient hospitalisation	Hyperemesis. 20/05/13, ongoing, medication required.	Possibly	Yes	Completely recovered	15NOV2013
11881	METFORMIN	07JAN2014	30DEC2013	Diagnosis: Severe Sepsis. Description: Admitted at 30+4 weeks gestation with pyrexia, rigors and dysuria. Treated with multiple antibiotics for presumed urosepsis. Clinical deterioration over the course of a week. Decision made to deliver baby in maternal interest at 31+2 weeks gestation. Patient transferred to ITU for ventilatory support post delivery. Continue to improve, back in normal ward at present. Follow-up 14/01/14: Diagnosis: Probable urosepsis and atypical pneumonia necessitating preterm delivery in maternal interest. Description: Condition now resolved, patient recovered. Severity: Severe.	Life-threatening Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	13JAN2014
12008	METFORMIN	13FEB2012	09FEB2012	Atonic uterus resulting in massive obstetric haemorrhage. 2 litre loss. Severity: Severe	Life-threatening	N/a	Unrelated	No	Completely recovered	12FEB2012
12008	METFORMIN	16AUG2012	14FEB2012	Diagnosis: Chest Pain Description: Chest pain following LSCS 5/7 days after delivery. Severity: Moderate	Involved or prolonged inpatient hospitalisation		Unrelated	Yes	Completely recovered	16FEB2012
13082	METFORMIN	07FEB2012	04FEB2012	Admitted for labile BP at 39 weeks. Commenced on labetalol 100mgs BD and IOL booked. Inpatient on Mat ward since 04/02/12. Completion of data 09/05/13: Participant delivered on 08.2.12 and was discharged on 11.2.12. On review of medical notes, hypertension resolved postnatally, was not discharged on any anti-hypertensives. Severity: Mild	Involved or prolonged inpatient hospitalisation	Has history of hypertension, was on lisinartan 75mgs daily in 2009. Not on treatment since	Unrelated	Yes	Completely recovered	11FEB2012
13209	METFORMIN	31AUG2012	24AUG2012	Diagnosis: Inpatient stay for over 24hrs for investigations. All negative. Description: Reported chest pain and calf pain at day 4 postnatal. Admitted to hospital for 2 days for chest x-ray and blood tests to rule out PE. Was commenced on Fragmin for 6/52 and attended for leg Doppler x 2. Severity: Moderate	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	04SEP2012

Section 13. Serious Adverse Events

13.1.2 SAE related to the mothers - Details

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	SAE - date of report	SAE - date of event	Description of SAE	Expedited Reporting Criteria	Relevant History	SAE_related_coded	SAE_expected_coded (Y/N)	SAE_outcome_coded	SAE - date of recovery
13551	METFORMIN	05MAR2013	02MAR2013	Diagnosis: Emcs for fetal distress, followed by 5000ml PPH and hysterectomy. Description: Background: NI has been having close monitoring in pregnancy for raised BP. She was commenced on labetalol on 2.1.13. Had subsequent admission for raised BP 6.2.13 (not an SAE according to protocol). Discharged back to community care the following day. Admitted to antenatal ward again with raised BP on 25.2.13. Remained an inpatient until IOL commenced 28.2.13 at 20.30 at 38 weeks gestation. Baby: EMCS for fetal distress (CTG and FBS) under GA. Baby delivered at 1913, appears 4 at 1 minute. 9 at 10 minutes. Cord PH's 7.16. 7.24. Baby was admitted to NICU overnight due to NI being transferred to Whiston. Re-united with mum when returned to Liverpool Women's. NI: Following emcs NI suffered from major haemorrhage totalling 5000ml. A hysterectomy was undertaken. NI received a total of 7 units of blood (including 500ml cell salvaged blood) and 1 unit of FFP. She also had a dextrose infusion to correct transfusion-related hypo	Involved or prolonged inpatient hospitalisation] Life-threatening	Raised BP, start 2.1.13, ongoing, medication required.	Unrelated	Yes	Condition improving Recovered with sequelae	07MAR2013
14303	METFORMIN	08AUG2013	08AUG2013	Post Partum Haemorrhage 1200mls.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	08AUG2013
16121	METFORMIN	24JUN2013	30MAY2013	Diagnosis: Pyelonephritis Description: Pyelonephritis - ascending UTI involving pyelum, fever, tachycardia, abdo/back pain. Severity: Mild	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	04JUN2013
25232	METFORMIN	17OCT2013	14OCT2013	Diagnosis: Preterm Labour Spontaneous Rupture of Membranes. Description: Spontaneous rupture of membranes occurred 14/10/2013 at 13.30. No uterine activity. On 15/10/2013 developed maternal tachycardia and increase of white blood cells. Decision made at 10.50 on 15/10/13 to induce labour. Labour augmented with syntocinon infusion. Live baby girl born on 16/10/2013 at 07.14hrs. Severity: Mild.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	16OCT2013
25264	METFORMIN	15AUG2013	08AUG2013	Diagnosis: benign Intracranial Hypertension. Description: Admitted to Hallamshire Hospital with headache due to this. Had lumbar puncture to drain some CSF. Symptoms resolved. had one night in hospital. Severity: Moderate.	Involved or prolonged inpatient hospitalisation	Benign Intracranial Hypertension. started in 2009, ongoing, medication not required.	Unrelated	No	Completely recovered	09AUG2013
25264	METFORMIN	01OCT2013	26SEP2013	Diagnosis: Raised intra-cranial pressure. Description: Admission to Chesterfield Royal Hospital with headache, blurred vision, tinnitus, nausea 26/09/13. Lumbar puncture eased symptoms but backache marked after procedure and thought to be related to same. Care continued with analgesic therapy and physio. Severity: Mild.	Involved or prolonged inpatient hospitalisation	Idiopathic Intracranial Hypertension, start spring 2009, end late 2011, and received medication between these dates. Diagnosed in 2009, ongoing and no medication required as contra-indicated in pregnancy.	Unrelated	Yes	Condition improving	
25459	METFORMIN	11APR2014	06APR2014	Diagnosis: Left Calf Pain ?Thrombosis. Description: Admitted with unilateral calf pain. No redness or swelling, x1 dose anti-coagulant and analgesia given. Severity: Mild.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	07APR2014
25459	METFORMIN	17JUN2014	16JUN2014	Diagnosis: Right ovarian cyst Admitted to birth centre with right sided abdominal pain on 16.06.14. C/section performed 17.06.14. Severity: Mild	Involved or prolonged inpatient hospitalisation	Right adnexal cyst (15/03/14)	Unrelated	No	Completely recovered	17JUN2014
11323	PLACEBO	29MAY2012	20MAY2012	Diagnosis: Inconclusive Description: Admitted with shortness of breath and chest pain at 32 weeks gestation. Investigated thoroughly with CTPA, upperabdo ultrasound and blood tests but all investigation negative. Symptoms settled spontaneously. Severity: Moderate	Involved or prolonged inpatient hospitalisation	Asthma, ongoing, medication required Smoker, ongoing	Unrelated	No	Completely recovered	22MAY2012
11335	PLACEBO	21JUN2012	19JUN2012	Diagnosis: Post partum haemorrhage Description: Delivered by elective caesarian section on 19/06/12. Developed bleeding secondary to uterine atony following delivery while in recovery area. Rushed to theatre for EUA under GA. Haemorrhage managed with Bakri balloon. Estimated blood loss 2000mls. Severity: Moderate	Involved or prolonged inpatient hospitalisation] Life-threatening		Unrelated	No	Completely recovered	21JUN2012
11714	PLACEBO	30SEP2013	27SEP2013	Diagnosis: Large Blood Loss - 1500ml. Description: Emergency c/s for failure to progress in labour, 1500ml blood loss at delivery. Follow-up 20/02/14: Diagnosis: Post Partum Haemorrhage. Atonic postpartum haemorrhage following emergency caesarean section for failure to progress in the 1st stage of labour. Estimated blood loss 1500ml. Severity: Moderate.	Life-threatening] Involved or prolonged inpatient hospitalisation	Gestational Diabetes Mellitus. 09/07/13, ongoing, no medication required.	Unrelated	No	Completely recovered	03OCT2013

Section 13. Serious Adverse Events

13.1.2 SAE related to the mothers - Details

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	SAE - date of report	SAE - date of event	Description of SAE	Expedited Reporting Criteria	Relevant History	SAE_related_coded	SAE_expected_coded (Y/N)	SAE_outcome_coded	SAE - date of recovery
11940	PLACEBO	04JUN2014	02JUN2014	Diagnosis: Respiratory Tract Infection. Presented with cough and feeling generally unwell at 37+ weeks gestation. Already taking amoxicillin and prednisolone prescribed by GP. Also complaining of reduced fetal movements. Admitted to hospital for optimisation of treatment and observation. Chest xray normal. Reviewed by respiratory physician and symptoms felt to be improving. likely viral origin. no further antibiotics or prednisolone required. advised to monitor PEFR and for GP to refer to outpatient respiratory clinic as necessary. Following Obstetric review. in view of persistently reduced fetal movements and recent diagnosis of gestational diabetes decision made for induction of labour. Severity: Mild.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	04JUN2014
13007	PLACEBO	05AUG2011	28JUL2011	Diagnosis: prolonged hospital stay. Participant induced for suspected IUGR at 40 weeks+1day. Baby's BW below 9th centile. therefore needed blood sugar recordings (TBGs) pre and post feeds as per protocol. Baby BW 2.72kgs. These were completed within 24hrs. This resulted in a prolongation of hospital stay. 12/08/2011 IUGR is an Expected outcome and is being routinely collected as a secondary outcome of this study. Therefore. not a SUSAR but a SAR.	Involved or prolonged inpatient hospitalisation	2008 - normal vaginal delivery at term (41 weeks). 3100gms	Possibly	Yes	Completely recovered	28JUL2011
13144	PLACEBO	11MAY2012	31MAR2012	Diagnosis: Symphysis Pubis Pain. Physiological Faints in Pregnancy Description: Occasional fainting episodes and episodes of raised BP over past 6 weeks. 48hrs admission on ward for observation due to this. Also reports SPD. IOL at 36+7 booked for this reason. However on admission to IOL suite was found to be 36+6. reasons for IOL did not warrant delivery at this gestation. had been incorrectly calculated when IOL booked. therefore IOL rebooked and performed at 36+1 on 22/05/12. Severity: Moderate	Involved or prolonged inpatient hospitalisation		Unrelated	Yes	Completely recovered	22MAY2012
13301	PLACEBO	19OCT2012	17OCT2012	Diagnosis: Intrapartum and postpartum haemorrhage of 2000mls Description: This lady was induced at 41+5 for postdates pregnancy. She received 2mg x 2 of Prostin gel. Prior to ARM she had fresh bleeding PV. Oblique breech lie was diagnosed on USS. She was taken to theatre for emergency caesarean section. Intrapartum haemorrhage = 1000ml. postnatal haemorrhage = 1000ml. Total EBL = 2000ml. Baby born with Apgars 10 at 1 minute and 10 at 5 minutes. Cord pH's 7.26 and 7.28. Baby's weight = 4440g. AP well on demand. The lady was transfused 2 units of blood in theatre. Condition currently improving. today Hb 7.8g/dl. for further 2 units of blood. Follow-up 24/10/12. This lady was discharged home with baby from the postnatal ward on Sunday 20.10.12 at 14.00. Her HB was 8.7g/dl and she was prescribed ferrous sulphate 200mg TDS. Severity: Severe	Involved or prolonged inpatient hospitalisation Life-threatening	Previous PPH and subsequent blood transfusion in 2007. medication required. PCOS. ongoing. no medication required.	Unrelated	Unk	Completely recovered	20OCT2012
13473	PLACEBO	04JAN2013	03JAN2013	Diagnosis: Neonatal BM's low. Baby admitted to NICU. lowest BM 1.7mmol Description: EP was delivered via emergency cis. IOL at 36+3 for pre-eclampsia on 3.1.13. Baby was transferred to the neonatal unit for 24 hours post delivery for low BM's. Lowest BM 1.7mmol. baby tube fed only. no IV fluids required. Baby maintaining BM's and back on postnatal ward with mum after 24 hours. Discharged home 5.1.13. no follow-up anticipated. Severity: Mild	Involved or prolonged inpatient hospitalisation		Possibly	Yes	Completely recovered	04JAN2013
13591	PLACEBO	07MAY2013	30APR2013	Diagnosis: Hospital admission via ambulance with gall stones. Description: RB was admitted to Royal Liverpool Hospital on 30.04.13 via ambulance with chronic back pain. She is 3 weeks postnatal. Was kept nil by mouth for 24 hours and had a USS which diagnosed gall stones. Received antibiotics and analgesia whilst an inpatient and was discharged on 01.05.13. RB reports awaiting blood tests to see if presence of infection and has an appointment with a consultant at the Royal on 16.04.13. NB. Information obtained verbally from the patient only. no access to medical notes as attended a different hospital. Severity: Moderate	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	01MAY2013
13705	PLACEBO	02AUG2013	19JUL2013	Diagnosis: APH 31+2/40. Description: Patient admitted to antenatal ward with APH at 31+2/40. Had x 2 small PV bleeds at home. HVS smel. Speculum NAD. Discharged home after 24 hours as nil further PV bleeding. Taking ferrous sulphate. Severity: Mild.	Involved or prolonged inpatient hospitalisation		Unrelated	Yes	Completely recovered	20JUL2013
13712	PLACEBO	02AUG2013	23JUL2013	Diagnosis: Obstetric Cholestasis. Description: Patient presented at 31+5/40 with localised itching. Bile acids taken and indicate obstetric cholestasis. Patient prescribed Ursodeoxycholic acid 300mg TDS and Chlorphenamine 4mg. IOL booked for 05.09.2013. Having weekly bloods and CTG's. Information obtained from patient via telephone only. Severity: Moderate.	Other significant medical events (as defined in protocol)	Obstetric cholestasis in previous pregnancy in 2010. Start 27/01/2010. and 02/02/2010. medication required.	Unrelated	Yes	Completely recovered	06SEP2013
14336	PLACEBO	27NOV2013	26NOV2013	Diagnosis: Post partum haemorrhage and pre-eclampsia. Description: Admitted to High Dependency Unit from theatre recovery after total PPH 700mls (at delivery 400mls) requiring prolonged IV syntocinon treatment. In addition had raised BP requiring medication after admission to HDU. Severity: Moderate.	Involved or prolonged inpatient hospitalisation	Gestational Diabetes. started 07/11/2013. ongoing. no medication required.	Unrelated	No	Recovered with sequelae	29NOV2013

Section 13. Serious Adverse Events

13.1.2 SAE related to the mothers - Details

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	SAE - date of report	SAE - date of event	Description of SAE	Expedited Reporting Criteria	Relevant History	SAE_related_coded	SAE_expected_coded (Y/N)	SAE_outcome_coded	SAE - date of recovery
14336	PLACEBO	23OCT2013	17SEP2013	Diagnosis: Abdominal pain cause unknown. Description: Admitted with abdominal pain for observation. Cause unknown. Possible UTI. Possible 'uterine stretching pain'. Routine blood and urine tests performed. Severity: Moderate.	Involved or prolonged inpatient hospitalisation		Unrelated	Yes	Completely recovered	23SEP2013
14336	PLACEBO	27NOV2013	20NOV2013	Diagnosis: Infective diarrhoea and vomiting. Description: Prolonged episode of diarrhoea and vomiting causing dehydration. IV fluid rehydration required on admission to hospital on 23/11/2013. Admitted for 24 hours. Had one stat dose labetalol for raised BP whilst an inpatient. Stopped study medication. Severity: Moderate.	Involved or prolonged inpatient hospitalisation	Gestational diabetes, started 07/11/2013, ongoing, no medication required.	Unrelated	No	Completely recovered	24NOV2013
14354	PLACEBO	20DEC2013	17DEC2013	Diagnosis: Threatened pre term labour. Description: GS P2 33 weeks, admitted with PV bleed and irregular lightening 17.12.13. Prescribed betamethasone and dalteparin. Hospitalised for observation. Severity: Mild	Involved or prolonged inpatient hospitalisation		Unrelated	No	Condition improving Completely recovered	20JAN2014
15034	PLACEBO	07NOV2013	24OCT2013	PPH 1600mls. Severity: Moderate	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	25OCT2013
17036	PLACEBO	12MAR2013	10MAR2013	Diagnosis: Influenza. Description: Inpatient hospitalisation due to influenza. Patient admitted on 10/03/13. Self discharged on 11/03/13 as feeling better. Study medication stopped whilst unwell, to recommence when well. Severity: Moderate. Follow-up 17/06/2014: Diagnosis: Influenza - resulting in raised ALTs requiring scan. Initial SAE reported due to hospitalisation due to influenza. Following this raised ALT levels were noted and a liver scan arranged. This showed an enlarged spleen consistent with recent influenza. This patient has had raised ALT levels dating back to 2010. Discharged home following scan.	Involved or prolonged inpatient hospitalisation Other significant medical events (as defined in protocol)	Cholecystectomy, 2010 - 30/07/2010.	Unrelated	No	Completely recovered	17JUN2014
17137	PLACEBO	27DEC2013	25DEC2013	Diagnosis: Costochondritis. Description: Admitted with upper abdominal pain - bloods and USS all NAD. Presumed costochondritis. Discharged home 27/12/13. Severity:	Involved or prolonged inpatient hospitalisation	Previous episode of costochondritis	Unrelated	No	Completely recovered	27DEC2013
17137	PLACEBO	20JAN2014	17JAN2014	Admitted to antenatal ward with unstable lie. To remain inpatient until LSCS 24.1.14.	Involved or prolonged inpatient hospitalisation	Episode of costochondritis	Unrelated	No	Completely recovered	21FEB2014
21033	PLACEBO	23MAY2014	27APR2014	Diagnosis: Abdominal Pain. Likely Costochondritis. Description: Admitted at 33+4 weeks gestation with abdominal pain. Severity: Mild.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	29APR2014
21033	PLACEBO	23MAY2014	11APR2014	Diagnosis: Likely Costochondritis. Description: Admitted at 31+2 weeks gestation for observation/monitoring for left sided chest pain. Investigations generally NAD. Severity: Mild.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Condition improving	
21033	PLACEBO	02APR2014	28DEC2013	Diagnosis: Non-specific chest pain. Description: Admitted via ambulance with suspected clinical suspicion of a pulmonary embolism. Had left pleuritic chest pain, with shortness of breath and collapse. Severity: Mild.	Involved or prolonged inpatient hospitalisation	Caesarean Section, 03/12/2013.	Unrelated	No	Completely recovered	30DEC2013
21069	PLACEBO	19MAR2014	18FEB2014	Diagnosis: Sepsis. Description: Pyrexial and tachycardic in labour. Raised CRP and white cell count, also platelets reduced. Had IV antibiotics, then oral. Went on septic pathway. Severity: Moderate.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	25FEB2014
21063	PLACEBO	23DEC2013	28NOV2013	Diagnosis: Small antepartum haemorrhage. Description: Admitted to maternity ward overnight for observation as PV bleed. Ectropion noted on cervix. Placenta not low-lying. No pain. 23 weeks gestation. Severity: Mild	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	29NOV2013
21109	PLACEBO	09APR2014	03APR2014	Diagnosis: Small APH - nil on examination. Description: Admitted to maternity ward via maternity day unit with lower abdo discomfort/Braxton hicks/red pv loss/unstable lie. Severity: Mild.	Involved or prolonged inpatient hospitalisation	Gestational Diabetes, 19/03/2014 - 08/04/2014.	Unrelated	No	Completely recovered	05APR2014
21109	PLACEBO	19MAR2014	14FEB2014	Diagnosis: Urinary Tract Infection. Description: Symptomatic of UTI and leucocytes in urine. Admitted for treatment and observation to maternity ward for over 12 hours. Severity: Mild.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	21FEB2014

Section 13. Serious Adverse Events

13.1.2 SAE related to the mothers - Details

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	SAE - date of report	SAE - date of event	Description of SAE	Expedited Reporting Criteria	Relevant History	SAE_related_coded	SAE_expected_coded (Y/N)	SAE_outcome_coded	SAE - date of recovery
25391	PLACEBO	12MAR2014	07MAR2014	Diagnosis: 1). Musculoskeletal Pain. 2). Depression. Description: Admitted to hospital for observation and analgesia for musculoskeletal pain and depression. Severity: Mild.	Involved or prolonged inpatient hospitalisation	Depression/Anxiety, started 2005, ongoing, medication required.	Unrelated	No	Missing	.
53072	PLACEBO	30JUN2014	27JUN2014	Diagnosis: Episode of fitting, unknown cause. Description: Singular episode of fitting 5 days postnatal, unknown cause. Admitted to hospital via ambulance. MRI, CT, Chest X ray and blood tests carried out. No abnormality found, declined inpatient stay overnight for observation and had same day discharge. For follow up at first fit clinic. Severity: moderate. UPDATE (01 Oct 2014): Diagnosis: Further reported 4-5 episodes of left sided numbness and tingling on upper body and face. Description: Reported 4 or 5 acute episodes of tingling commencing in left hand and ascending left side of body to face resulting in a heaviness and numb sensation. All occurred within 3 weeks of P/N fit episode and lasted around 5 minutes in duration. Nil since. Has had further ECG at neurology clinic which was normal. Still awaiting results of EEG and MRI.	Involved or prolonged inpatient hospitalisation Other significant medical events (as defined in protocol)		Unrelated	No	Completely recovered	27JUN2014

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Section 13. Serious Adverse Events

13.2.1 SAE related to the babies

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo N=118</i>	<i>Metformin N=109</i>	<i>Overall N=227</i>
Number of Patient with a SAE (n)	OVERALL	12	5	17
Number of SAE (n)	OVERALL	12	5	17
Number of SAE by relationship (n)	Possibly	1	3	4
	Unrelated	11	2	13
Number of SAE by expectedness (n)	Yes	1	0	1
	No	11	5	16

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Section 13. Serious Adverse Events

13.2.1 SAE related to the babies (Cont.)

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Number of SAE by outcome (n)	Completely recovered	8	2	10
	Condition still present and unchanged	2	2	4
	Death	1	0	1
	Recovered with sequelae	1	1	2

Section 13. Serious Adverse Events

13.2.2 SAE related to the babies - Details

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	SAE - date of report	SAE - date of event	Description of SAE	Expedited Reporting Criteria	Relevant History	SAE_related_coded	SAE_expected_coded (Y/N)	SAE_outcome_coded	SAE - date of recovery
13670	METFORMIN	26JUL2013	21JUL2013	Diagnosis: Bilateral undescended testes. Description: Baby diagnosed with bilateral undescended testes. Baby born via normal vaginal delivery on 21/07/13. Undescended testes noted on 1st exam of the newborn, conducted by community midwife at home on 23/7/13. Baby otherwise well, referred to Alder Hey for follow-up. Severity: Moderate	Congenital anomaly/birth defect		Unrelated	No	Recovered with sequelae	26JUL2013
21095	METFORMIN	21MAR2014	20MAR2014	Diagnosis: No diagnosis yet. Description: Baby transferred to neonatal unit jittery/poor feeding/low BMS. Informed by paed. had significantly low BM's/hypoglycaemia. Raised lactate levels. Septic screen. Severity: Moderate.	Other significant medical events (as defined in protocol) Involved or prolonged inpatient hospitalisation	Depression (Parent) prior to pregnancy, ongoing, medication required. Urine infection (Parent). 17/03/2014, ongoing, medication required.	Possibly	No	Completely recovered	23MAR2014
21099	METFORMIN	21MAR2014	15MAR2014	Diagnosis: Significant Neonatal Jaundice. Description: Baby admitted from home to paediatric ward with significant neonatal jaundice. Phototherapy treatment required. Severity: Severe.	Involved or prolonged inpatient hospitalisation] Other significant medical events (as defined in protocol)	Raised BP (Parent). 09/03/2014 - 12/03/2014, no medication required.	Unrelated	No	Completely recovered	18MAR2014
25135	METFORMIN	09JUL2013	08JUL2013	Diagnosis: Congenital Malformation. Description: Circular thoracic lumbar spine lesion. Central 1 x 0.5cm vascular area, within 3 x 1cm area of hypopigmentation. (No hair). ? vascular malformation / occult spinal dysraphism. Follow-up 12/11/13. Diagnosis of Aplasia Cutis Congenita made 11/09/13. Severity: Mild Follow-up 28/01/14. Dermatologist reports evidence of Livedo, more likely livedo racemosa. Investigating for systemic connective tissue disease and full lupus screen. Mother reported (09/01/14) clonus in all 4 limbs of infant therefore referred to neurologist to investigate any central nervous system vasculopathy or abnormality. Severity: Moderate.	Congenital anomaly/birth defect		Possibly	No	Condition still present and unchanged	.
25459	METFORMIN	29JAN2014	26JAN2014	Diagnosis: Left unilateral talipes. Description: Had anomaly scan at 20 weeks gestation - the baby was noted to have left unilateral talipes. Severity: Moderate. Follow-up 01/07/14. Diagnosis: Fixed Talipes left foot. Fixed talipes. Back/hips normal. Initial ponseti plaster applied. To be replaced weekly and continue correction programme. Detected on 20/40 anomaly scan. Severity: Moderate.	Congenital anomaly/birth defect	Mother: Right adrenal cyst started 15/11/2013, ongoing.	Possibly	No	Condition still present and unchanged	.
11536	PLACEBO	17JUN2013	09MAR2013	Diagnosis: Infection. SVT. Description: baby admitted to RHSC, Edinburgh at 8 days old, diagnosed with an infection at that time. At 12 days old diagnosed with SVT. Severity: Moderate	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	23MAR2013
11851	PLACEBO	08APR2014	03APR2014	Diagnosis: Right testicular hydrocele, abnormal left testicle. Description: Right testicular hydrocele, abnormal left testicle. Awaiting ultrasound scan and paediatric surgical review. Severity: Mild.	Congenital anomaly/birth defect		Unrelated	No	Condition still present and unchanged	.
12016	PLACEBO	10SEP2012	21APR2012	Diagnosis: Meconium Aspiration 1, Meconium Aspiration 2, Persistent Pulmonary Hypertension Severity: Severe	Involved or prolonged inpatient hospitalisation] Life-threatening		Unrelated	No	Completely recovered	28APR2012
13496	PLACEBO	14FEB2013	11FEB2013	Diagnosis: Baby admitted to NICU for low blood glucose Description: EH diagnosed as gestational diabetic at 36 weeks, managed on diet control only. Had elective caesarian section on 11.02.13 at 11am. Baby cord blood 2.4mmol, was grunting and had low TBG's on ward. Was admitted to NICU at 22.35 hours 11.02.13. Discharged back to ward with mum at 14.15 the next day 12.02.13. Mum and baby discharged home 13.02.13 baby asymptomatic of hypoglycaemia and BF well on discharge. No anticipated follow up. Severity: Mild	Involved or prolonged inpatient hospitalisation		Possibly	Yes	Completely recovered	13FEB2013
13591	PLACEBO	26JUL2013	20APR2013	Date of onset: ?? 20/04/2013 (i.e. from 2 weeks old - see below). Diagnosis: Baby developed vascular malformation. Description: Baby diagnosed with a venous malformation on upper shoulder. The baby was born on 6th April and nil was noted at birth or on the first paediatric examination. At the 6 week postnatal check with the GP a birth mark was noted and thought to be a haemangioma of infancy. I saw mum at 3 month postnatal visit on 4th July, when I first became aware of the birth mark, but as it wasn't picked up until the baby was 6 weeks old, this was outside of the 28 day postnatal reporting period for EMPOWaR. Mum has since been in touch to say that the birth mark has now been diagnosed as a venous malformation as it is the blood vessels below the actual mark which are causing it to grow and cause a lump. On further questioning mum thinks that the mark may have been there since 2 weeks of life but initially very small. Baby has been referred to a specialist at Alder Hey for management and possible removal	Congenital anomaly/birth defect	See previous SAE dated 7.5.13. Mother had hospital admission for gall stones at 24 days post natal. Having follow up at Royal Liverpool Hospital.	Unrelated	No	Recovered with sequelae	26JUL2013

Section 13. Serious Adverse Events

13.2.2 SAE related to the babies - Details

Population = Per-Protocol (PP) - Allocated Treatment used for summarisation

Subject Number	Allocated Treatment	SAE - date of report	SAE - date of event	Description of SAE	Expedited Reporting Criteria	Relevant History	SAE_related_coded	SAE_expected_coded (Y/N)	SAE_outcome_coded	SAE - date of recovery
14413	PLACEBO	03MAR2014	03MAR2014	Diagnosis: Baby delivered with some abnormalities. Description: C/section at 3/3/14 at 12.30 - baby found to have abnormal toes, fingers and anteriorly placed anus. Left hand is normal. Right hand has a middle short finger with hypoplastic nail and is twisted. Index finger has an accessory digit. On the right foot the big toe has syndactyly and the 3rd toe is not formed. On the left foot, the big toe is syndactyly and the 3rd toe not formed. There is only one centimetre between the anus and the posterior forchette. Severity: Severe.	Congenital anomaly/birth defect		Unrelated	No	Condition still present and unchanged	.
21018	PLACEBO	05NOV2013	17OCT2013	Diagnosis: Presumed Sepsis/Pneumonia consolidation. Description: Admitted to neonatal unit shortly after birth for investigations for spreading vascular lesions on trunk, grunting and tachypnoeic. Remained on neonatal unit 17 - 22/10/13. Severity: Moderate	Involved or prolonged inpatient hospitalisation	Vascular lesions, grunting, tachypnoeic, pneumonia, started 17/10/2013, ended 22/10/2013, medication required.	Unrelated	No	Completely recovered	24OCT2013
21038	PLACEBO	16JAN2014	31DEC2013	Diagnosis: Cyanotic episodes, likely vasomotor phenomenon. Description: Admitted to ward 8 via ambulance/A&E 7 days old with cyanotic episodes 10 times a day lasting 3 - 5 mins. Investigations all normal. Discharged home 02/01/2014. No further admissions. Severity: Moderate.	Involved or prolonged inpatient hospitalisation		Unrelated	No	Completely recovered	02JAN2014
21047	PLACEBO	22APR2014	22JAN2014	Diagnosis: RSV positive bronchiolitis. Description: Admitted to paediatric ward at 2 weeks old with cough and increased work of breathing. Required oxygen and help with NG feeds for a few days. Gradually recovered. Severity: Moderate.	Involved or prolonged inpatient hospitalisation	Gestational Diabetes (Mother), 17/12/2013 - 08/01/2014.	Unrelated	No	Completely recovered	30JAN2014
21069	PLACEBO	19MAR2014	18FEB2014	Diagnosis: Meningitis/Sepsis. Description: Admitted to Neonatal Unit shortly after birth jittery/maternal sepsis. Had dusky episodes/desaturations/apnoeas/jaundice/sepsis. Ventilated. Meningitis diagnosed. / Cerebral Haemorrhage. Severity: Severe.	Involved persistent or significant disability or incapacity Involved or prolonged inpatient hospitalisation	Sepsis in labour/maternal infection (Parent), 18/02/2014 - 25/02/2014, medication required.	Unrelated	No	Completely recovered	07MAR2014
21119	PLACEBO	06JAN2014	02JAN2014	Diagnosis: Congenital Anomaly. Description: Anomaly ultrasound scan showed structural abnormalities to hands and feet. Appearance suggestive of split hand and foot syndrome. Severity: Severe	Patient died Congenital anomaly/birth defect		Unrelated	No	Death	.
25320	PLACEBO	03FEB2014	31JAN2014	Diagnosis: ? Hirschsprungs in neonate. Description: Distended stomach on antenatal scans. At birth neonate admitted to NNU then transfer to tertiary centre same day (Nottingham Queen's Medical). Severity: Severe. Follow-up 27/02/2014. Subsequently resolved, no pathology, baby discharged. Severity: Severe.	Congenital anomaly/birth defect		Unrelated	No	Completely recovered	27FEB2014

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EMPOWaR: Efficacy of Metformin in Pregnant Obese Women, a Randomised Controlled Trial
Funding reference number: 08/246/09 (NIHR Efficacy and Mechanism Evaluation Programme)
EudraCT number 2009-017134-47

Statistical Report - Mechanistic paper (MP) - Final

Population = Intention to treat (ITT) - Allocated Treatment used for analysis
Report number: 02

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Data set analysed as it was on:

29 April 2015

Section 1. Maternal body fat

1.1.1 Maternal Body mass (Edinburgh)*# - ALL AVAILABLE OBSERVATIONS

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
BodyMass (kg) Visit 2	Mean	101.388	103.322	102.413
	Median	97.810	104.018	100.077
	SD	16.190	15.961	16.017
	MIN,MAX	74.97,170.25	73.54,140.37	73.54,170.25
	Q1,Q3	89.72,111.83	92.19,112.90	90.53,112.40
	n	47	53	100
	Nmiss	13	7	20
BodyMass (kg) Visit 6	Mean	108.794	113.366	111.043
	Median	105.046	111.525	108.272
	SD	14.871	16.740	15.853
	MIN,MAX	79.82,165.47	78.11,147.87	78.11,165.47
	Q1,Q3	100.32,117.60	104.43,124.68	102.65,118.64
	n	31	30	61
	Nmiss	29	30	59

Section 1. Maternal body fat

1.1.1 Maternal Body mass (Edinburgh) (Cont.)*# - ALL AVAILABLE OBSERVATIONS

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
BodyMass (kg) Visit 9	Mean	102.821	106.471	104.677
	Median	102.540	105.399	104.190
	SD	12.759	16.507	14.772
	MIN,MAX	72.74,126.73	73.76,146.86	72.74,146.86
	Q1,Q3	96.36,112.37	98.50,115.30	96.80,114.25
	n	29	30	59
	Nmiss	31	30	61

Section 1. Maternal body fat

1.1.2.1 Maternal Body fat mass (Edinburgh)*# - ALL AVAILABLE OBSERVATIONS

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
FatMass (kg) Visit 2	Mean	47.93	50.32	49.19
	Median	45.85	49.38	47.51
	SD	12.05	11.79	11.92
	MIN,MAX	29.9,96.8	26.8,76.2	26.8,96.8
	Q1,Q3	38.6,54.4	42.2,59.5	41.2,55.5
	n	48	53	101
	Nmiss	12	7	19
FatMass (kg) Visit 6	Mean	50.83	54.37	52.57
	Median	50.28	54.58	50.69
	SD	10.94	12.17	11.61
	MIN,MAX	27.4,89.2	30.5,76.4	27.4,89.2
	Q1,Q3	46.9,55.4	46.8,65.1	46.9,57.9
	n	31	30	61
	Nmiss	29	30	59

Section 1. Maternal body fat

1.1.2.1 Maternal Body fat mass (Edinburgh) (Cont.)*# - ALL AVAILABLE OBSERVATIONS

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
FatMass (kg) Visit 9	Mean	49.06	50.09	49.58
	Median	51.27	48.55	50.26
	SD	9.01	13.73	11.56
	MIN,MAX	26.6,63.2	13.6,75.8	13.6,75.8
	Q1,Q3	46.3,55.4	45.1,59.1	45.1,56.3
	n	29	30	59
	Nmiss	31	30	61

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N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is only applicable to Edinburgh patients

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

By: Aryelly Rodriguez - ECTU Statistician

Section 1. Maternal body fat

1.1.2.2 Fat mass (kg) - Statistical Analysis - ALL AVAILABLE OBSERVATIONS

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
MOTHER_FATMASS_V2_ALL_OBS - itt	51.623	1.2656	48	52.835	1.1788	53	1.212	-2.111	4.535	0.524	0.4708
MOTHER_FATMASS_V6_ALL_OBS - itt	53.538	1.6104	31	55.390	1.5907	30	1.852	-2.623	6.327	0.686	0.4108
MOTHER_FATMASS_V9_ALL_OBS - itt	50.860	1.8982	29	50.858	1.8299	30	-0.002	-5.227	5.223	0.000	0.9994

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By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in table 1.1.2.1 of this report

Outcome analysed using a linear regression model, adjusted by BMI band and c-section delivery. Significance level set at p<0.05

Estimated mean represents the adjusted means of the non-transformed variable by allocated treatment for V9,

SE represents standard error of the non-transformed estimated means and N represents number of observations for V9

*Represents the difference between non-transformed estimated means and CI Represents the 95% confidence interval for V9

Calculations and detailed analysis are presented in study file 'Empowar_1_1_2_BODPOD_fat_percent_ANALYSIS.lst'

All parameters shown normal or near-normal behavior

Section 1. Maternal body fat

1.1.2.3 Maternal Body fat mass(Edinburgh)*# - V2 and V6 data must be present (paired observations)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
FatMass (kg) Visit 2	Mean	48.75	52.70	50.72
	Median	47.57	53.50	50.10
	SD	13.23	11.72	12.55
	MIN,MAX	31.1,96.8	28.3,76.2	28.3,96.8
	Q1,Q3	40.5,54.9	42.5,61.8	42.4,58.7
	n	28	28	56
	Nmiss	0	0	0
FatMass (kg) Visit 6	Mean	50.92	53.91	52.41
	Median	49.99	52.80	50.51
	SD	11.49	12.37	11.93
	MIN,MAX	27.4,89.2	30.5,76.4	27.4,89.2
	Q1,Q3	47.2,56.2	45.8,62.9	46.8,58.4
	n	28	28	56
	Nmiss	0	0	0

EMPOWaR Statistical Analysis Report MECHANISTIC PAPER - Final 02 - tables run on: 05MAR2016 at 03:54

N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is only applicable to Edinburgh patients

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

By: Aryelly Rodriguez - ECTU Statistician

Section 1. Maternal body fat

1.1.2.3 Maternal Body fat mass (Edinburgh)(Cont.)*# - V2 and V6 data must be present (paired observations)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Change FatMass (%) V6 from V2\$	Mean	5.66	2.47	4.06
	Median	3.79	0.74	1.21
	SD	10.34	7.31	9.02
	MIN,MAX	-11.8,32.9	-8.9,17.1	-11.8,32.9
	Q1,Q3	-1.5,12.1	-2.9,8.2	-1.9,10.2
	n	28	28	56
	Nmiss	0	0	0

EMPOWaR Statistical Analysis Report MECHANISTIC PAPER - Final 02 - tables run on: 05MAR2016 at 03:54

N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is only applicable to Edinburgh patients

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

\$Change calculated as: $((\text{FatMass_V6} - \text{FatMass_V2}) / \text{FatMass_V2}) * 100$

By: Aryelly Rodriguez - ECTU Statistician

Section 1. Maternal body fat

1.1.2.4 Maternal Body fat mass (Edinburgh)*# - V2 and V9 data must be present (paired observations)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
FatMass (kg) Visit 2	Mean	48.98	54.52	51.85
	Median	50.10	54.85	51.95
	SD	9.68	11.16	10.74
	MIN,MAX	31.1,72.8	34.9,76.2	31.1,76.2
	Q1,Q3	42.7,54.4	44.9,63.1	42.9,58.2
	n	26	28	54
	Nmiss	0	0	0
FatMass (kg) Visit 9	Mean	48.48	50.81	49.69
	Median	50.58	49.49	50.13
	SD	9.30	13.75	11.77
	MIN,MAX	26.6,63.2	13.6,75.8	13.6,75.8
	Q1,Q3	43.3,55.4	45.3,59.9	45.1,56.3
	n	26	28	54
	Nmiss	0	0	0

EMPOWaR Statistical Analysis Report MECHANISTIC PAPER - Final 02 - tables run on: 05MAR2016 at 03:54

N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is only applicable to Edinburgh patients

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

By: Aryelly Rodriguez - ECTU Statistician

Section 1. Maternal body fat

1.1.2.4 Maternal Body fat mass (Edinburgh)(Cont.)*# - V2 and V9 data must be present (paired observations)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Change FatMass (%) V9 from V2\$	Mean	-0.38	-6.16	-3.38
	Median	-2.50	-2.63	-2.63
	SD	12.42	17.13	15.19
	MIN,MAX	-16.5,35.3	-80.1,12.0	-80.1,35.3
	Q1,Q3	-10.7,7.9	-11.9,3.1	-11.8,3.3
	n	26	28	54
	Nmiss	0	0	0

EMPOWaR Statistical Analysis Report MECHANISTIC PAPER - Final 02 - tables run on: 05MAR2016 at 03:54

N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is only applicable to Edinburgh patients

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

\$Change calculated as: ((FatMass_V9-FatMass_V2)/FatMass_V2)*100

By: Aryelly Rodriguez - ECTU Statistician

Section 1. Maternal body fat

1.1.2.5 Fat mass (kg) (paired observations) and Change FatMass (%) V6 from V2 and V9 from V2\$ - Statistical Analysis

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Lower CI*	Estimated Mean Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
MOTHER_FATMASS_V2_PAISED_OBS - itt	52.105	1.6120	28	53.373	1.5617	28	1.268	-3.204	5.740	0.323	0.5720
MOTHER_FATMASS_V6_PAISED_OBS - itt	53.907	1.6579	28	54.508	1.6062	28	0.601	-3.998	5.200	0.069	0.7942
MOTHER_FATMASS_V9_PAISED_OBS - itt	50.320	2.0138	26	51.241	1.8984	28	0.921	-4.604	6.446	0.112	0.7392
MOTHER_FATMASS_PRCENT_CHNG_V2_V6 - itt	4.747	1.6482	28	2.285	1.5968	28	-2.461	-7.034	2.111	1.166	0.2852
MOTHER_FATMASS_PRCENT_CHNG_V2_V9 - itt	-1.298	2.9065	26	-6.376	2.7399	28	-5.078	-13.052	2.896	1.635	0.2069

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By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in tables 1.1.2.3 to 1.1.2.4 of this report

Outcome analysed using a linear regression model, adjusted by BMI band. Significance level set at p<0.05

Estimated mean represents the adjusted means of the non-transformed variable by allocated treatment

SE represents standard error of the non-transformed estimated means and N represents number of observations

*Represents the difference between non-transformed estimated means and CI Represents the 95% confidence interval for V9

Calculations and detailed analysis are presented in study file 'Empower_1_1_2_BODPOD_fat_percent_ANALYSIS.lst'

All parameters shown normal or near-normal behavior

\$Change calculated as: ((FatMass_V6-FatMass_V2)/FatMass_V2)*100 and ((FatMass_V9-FatMass_V2)/FatMass_V2)*100

Section 1. Maternal body fat

1.1.3 Maternal body percentage fat (Edinburgh)*# - ALL AVAILABLE OBSERVATIONS

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Fat (%) Visit 2	Mean	46.82	48.19	47.54
	Median	46.85	48.00	47.50
	SD	5.62	5.18	5.41
	MIN,MAX	33.9,59.0	34.3,58.7	33.9,59.0
	Q1,Q3	42.6,50.4	45.3,51.7	44.8,51.1
	n	48	53	101
	Nmiss	12	7	19
Fat (%) Visit 6	Mean	46.30	47.48	46.88
	Median	47.10	47.65	47.30
	SD	4.84	4.63	4.74
	MIN,MAX	34.3,53.9	39.1,56.3	34.3,56.3
	Q1,Q3	43.9,48.8	43.9,51.2	43.9,50.2
	n	31	30	61
	Nmiss	29	30	59

Section 1. Maternal body fat

1.1.3 Maternal body percentage fat (Edinburgh) (Cont.)*# - ALL AVAILABLE OBSERVATIONS

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Fat (%) Visit 9	Mean	47.45	48.35	47.91
	Median	48.10	47.30	48.00
	SD	4.97	5.31	5.12
	MIN,MAX	36.6,54.6	37.9,58.6	36.6,58.6
	Q1,Q3	43.6,51.9	44.6,53.1	44.4,52.0
	n	29	30	59
	Nmiss	31	30	61

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N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is only applicable to Edinburgh patients

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

By: Aryelly Rodriguez - ECTU Statistician

Section 1.2 Neonatal body fat - Only Alive Births

1.2.1 Baby Body mass at Visit 8 (delivery) and Visit 9 (Final 3 months postnatal)# - ALL AVAILABLE OBSERVATIONS

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall
		Placebo	Metformin	
BABY_BodyMass* (kg)-V8	Mean	3.396	3.378	3.387
	Median	3.387	3.426	3.418
	SD	0.501	0.411	0.454
	MIN,MAX	2.42,4.45	2.50,3.99	2.42,4.45
	Q1,Q3	3.09,3.69	3.10,3.74	3.09,3.71
	n	22	21	43
	Nmiss	36	37	73
BABY_BodyMass* (kg)-V9	Mean	9.683	6.011	7.910
	Median	6.228	6.103	6.161
	SD	19.409	0.920	13.981
	MIN,MAX	4.80,112.37	4.41,8.01	4.41,112.37
	Q1,Q3	5.61,6.54	5.27,6.51	5.49,6.54
	n	30	28	58
	Nmiss	28	30	58

Section 1.2 Neonatal body fat - Only Alive Births

1.2.2.1 Baby Fat Mass at Visit 8 (delivery) and Visit 9 (Final 3 months postnatal)** - ALL AVAILABLE OBSERVATIONS

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall
		Placebo	Metformin	
BABY_FatMass* (kg)-V8	Mean	0.43	0.45	0.44
	Median	0.40	0.44	0.43
	SD	0.25	0.20	0.22
	MIN,MAX	0.0,1.0	0.1,0.8	0.0,1.0
	Q1,Q3	0.3,0.6	0.3,0.6	0.3,0.6
	n	22	21	43
	Nmiss	36	37	73
BABY_FatMass* (kg)-V9	Mean	3.01	1.42	2.24
	Median	1.54	1.43	1.49
	SD	8.05	0.50	5.80
	MIN,MAX	0.9,46.3	0.6,2.5	0.6,46.3
	Q1,Q3	1.2,1.9	1.0,1.7	1.2,1.8
	n	31	29	60
	Nmiss	27	29	56

Section 1.2 Neonatal body fat - Only Alive Births - V8 and V9 data must be present (paired observations)

1.2.2.2 Baby Fat Mass at Visit 8 (delivery) and Visit 9 (Final 3 months postnatal)##

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
BABY_FatMass* (kg)-V8	Mean	0.40	0.45	0.42
	Median	0.40	0.44	0.42
	SD	0.21	0.20	0.20
	MIN,MAX	0.0,0.8	0.1,0.8	0.0,0.8
	Q1,Q3	0.3,0.6	0.3,0.6	0.3,0.6
	n	16	15	31
	Nmiss	0	0	0
BABY_FatMass* (kg)-V9	Mean	4.35	1.47	2.95
	Median	1.53	1.46	1.52
	SD	11.20	0.50	8.06
	MIN,MAX	1.0,46.3	0.6,2.3	0.6,46.3
	Q1,Q3	1.3,1.8	1.0,1.8	1.2,1.8
	n	16	15	31
	Nmiss	0	0	0

Section 1.2 Neonatal body fat - Only Alive Births - V8 and V9 data must be present (paired observations)

1.2.2.3 Baby Fat Mass percentage change\$ from Visit 8 (delivery) to Visit 9 (Final 3 months postnatal)##

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
BABY_FatMass change\$ V8 to V9 (%)	Mean	1466.00	325.17	913.99
	Median	337.48	230.16	269.91
	SD	3183.06	311.85	2333.92
	MIN,MAX	63.0,12546	13.8,1139.8	13.8,12546
	Q1,Q3	165.4,571.0	106.2,433.7	158.7,515.8
	n	16	15	31
	Nmiss	0	0	0

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N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*Baby Fat Mass was only measured at the Edinburgh site

#Data have been checked, inaccuracies happened at time and point

of recording and there are not other sources for further checks

\$Percentage change calculated as ((B_FatMass_V9-B_FatMass_V8)/B_FatMass_V8)*100

By: Aryelly Rodriguez - ECTU Statistician

Section 1.2 Neonatal body fat - Only Alive Births

1.2.2.4 Baby Fat Mass - Statistical Analysis

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Lower CI*	Estimated Mean Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
BABY_FATMASS_V8_PAISED_OBS -	0.422	0.0545	16	0.445	0.0503	15	0.023	-0.130	0.177	0.098	0.7566
BABY_FATMASS_V9_PAISED_OBS -	1.665	0.1279	15	1.456	0.1094	15	-0.208	-0.559	0.142	1.491	0.2326
BABY_FATMASS_CHANGE_V8_TO_V9#	1.232	0.1408	15	1.012	0.1205	15	-0.220	-0.606	0.165	1.376	0.2511
BABY_FATMASS_V8_ALL_OBS - itt	0.456	0.0517	22	0.447	0.0472	21	-0.010	-0.152	0.133	0.019	0.8905
BABY_FATMASS_V9_ALL_OBS - itt	1.599	0.0848	30	1.435	0.0833	29	-0.164	-0.398	0.070	1.970	0.1660

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By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in tables 1.2.2.1 to 1.2.2.3 of this report

Outcome analysed using a linear regression model, adjusted by BMI band. Significance level set at p<0.05. Estimated mean represents the mean of the non-transformed variable by allocated treatment, Parameter shown normal or near-normal behavior SE represents standard error of the estimated non-transformed mean and N represents number of observations

*Represents the difference between the estimated log means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file '1_2_2_PEAPOD_fat_percent_ANALYSIS.lst'

NOTE: Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks, outliers outside +/- 6SD were removed to exclude extreme errors in data entry

#Percentage change calculated as ((B_FatMass_V9-B_FatMass_V8)/B_FatMass_V8)*100

Section 1.2 Neonatal body fat - Only Alive Births - ALL AVAILABLE OBSERVATIONS

1.2.3 Baby Fat % at Visit 8 (delivery) and Visit 9 (Final 3 months postnatal)**

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
BABY_Fat* (%) - V8	Mean	12.08	12.86	12.46
	Median	10.95	12.30	12.30
	SD	5.74	4.47	5.11
	MIN,MAX	1.0,24.3	5.7,20.6	1.0,24.3
	Q1,Q3	8.1,17.1	10.0,16.2	8.1,16.5
	n	22	21	43
	Nmiss	36	37	73
BABY_Fat* (%) - V9	Mean	25.88	23.19	24.58
	Median	24.10	23.50	23.55
	SD	6.13	5.91	6.13
	MIN,MAX	15.1,41.6	12.0,32.3	12.0,41.6
	Q1,Q3	21.5,29.7	19.6,27.8	21.2,28.8
	n	31	29	60
	Nmiss	27	29	56

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N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*Baby Fat % was only measured at the Edinburgh site

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

By: Aryelly Rodriguez - ECTU Statistician

Section 2. Hyperinsulinaemic euglycaemic clamp study

2.1 Maternal Age at Baseline - Visit 2 (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Number of patients in substudy-CLAMP (n)	Yes	11	9	20
Maternal Age at consent (years)	Mean	29.6	32.6	31.0
	Median	29.0	32.0	31.0
	SD	3.6	3.7	3.8
	MIN,MAX	25,37	25,38	25,38
	Q1,Q3	27,31	31,35	28,34
	n	11	9	20
	Nmiss	0	0	0

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Section 2. Hyperinsulinaemic euglycaemic clamp study

2.2 Previous pregnancy status* PARITY 1 at Baseline - Visit 2 (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
PARITY1 (n(%))	0	5 (45.5)	3 (33.3)	8 (40.0)
	=>1	6 (54.5)	6 (66.7)	12 (60.0)

Section 2. Hyperinsulinaemic euglycaemic clamp study

2.3.1 Maternal Calculated BMI at Baseline - Visit 2 (10-16 Weeks)*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Calculated BMI (kg/m ²) at Visit 2	Mean	35.7	37.9	36.7
	Median	36.1	38.2	36.4
	SD	3.5	4.4	4.0
	MIN,MAX	30,42	31,47	30,47
	Q1,Q3	32,39	36,39	34,39
	n	11	9	20
	Nmiss	0	0	0

Section 2. Hyperinsulinaemic euglycaemic clamp study

2.3.2 Maternal Calculated BMI at Visit 6 (36 Weeks) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Calculated BMI (kg/m ²) at Visit 6	Mean	38.7	39.4	39.0
	Median	40.1	39.3	39.4
	SD	3.5	2.6	3.1
	MIN,MAX	33,43	36,43	33,43
	Q1,Q3	35,42	38,41	37,42
	n	11	8	19
	Nmiss	0	1	1
Calculated BMI (kg/m ²) change V6 baseli	Mean	3.0	2.6	2.8
	Median	2.4	2.3	2.4
	SD	2.1	1.8	1.9
	MIN,MAX	-0,7	0,6	-0,7
	Q1,Q3	1,5	1,4	1,4
	n	11	8	19
	Nmiss	0	1	1

Section 2. Hyperinsulinaemic euglycaemic clamp study

2.3.3 Maternal Calculated BMI at Visit 9 (Final 3 months postnatal) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated BMI (kg/m ²) at Visit 9	Mean	35.7	37.9	36.6
	Median	36.7	37.4	37.2
	SD	4.0	4.1	4.1
	MIN,MAX	29,40	33,46	29,46
	Q1,Q3	31,39	35,40	35,39
	n	10	8	18
	Nmiss	1	1	2
Calculated BMI (kg/m ²) change V9 baseli	Mean	-0.1	-0.6	-0.3
	Median	-0.5	-0.7	-0.5
	SD	1.5	2.1	1.8
	MIN,MAX	-3,2	-5,2	-5,2
	Q1,Q3	-1,1	-1,1	-1,1
	n	10	8	18
	Nmiss	1	1	2

Section 2. Hyperinsulinaemic euglycaemic clamp study

2.3.4 Maternal body percentage fat (Edinburgh)*#

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Fat (%) Visit 1	Mean	46.14	49.31	47.45
	Median	47.10	49.70	48.20
	SD	4.46	5.78	5.13
	MIN,MAX	39.6,52.4	41.6,57.1	39.6,57.1
	Q1,Q3	41.4,48.8	44.0,55.2	44.0,51.1
	n	10	7	17
	Nmiss	1	2	3
Fat (%) Visit 6	Mean	46.20	48.19	47.10
	Median	47.30	49.30	47.45
	SD	5.28	4.53	4.94
	MIN,MAX	34.3,53.5	41.1,55.8	34.3,55.8
	Q1,Q3	43.9,48.8	44.7,51.0	44.6,50.6
	n	11	9	20
	Nmiss	0	0	0

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N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations

*This summary is only applicable to Edinburgh patients

#Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

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Section 2. Hyperinsulinaemic euglycaemic clamp study

2.3.4 Maternal body percentage fat (Edinburgh) (Cont.)*#

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Fat (%) Visit 9	Mean	46.89	49.50	47.96
	Median	48.10	48.90	48.10
	SD	5.51	5.07	5.34
	MIN,MAX	36.6,52.4	42.2,56.7	36.6,56.7
	Q1,Q3	45.4,51.9	46.0,53.2	46.0,52.0
	n	10	7	17
	Nmiss	1	2	3

Section 2. Hyperinsulinaemic euglycaemic clamp study

2.4.1 Gestation by timepoint - Visit 1 Screening (10-16 Weeks), Visit 2 Consent/Baseline (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 1 (days)	Mean	85.5	93.8	89.3
	Median	84.0	94.0	90.5
	SD	10.8	8.1	10.4
	MIN,MAX	72,102	82,106	72,106
	Q1,Q3	76,96	89,99	83,99
	n	11	9	20
	Nmiss	0	0	0
Recorded# Gestation - Visit 2 (days)	Mean	96.5	101.0	98.5
	Median	94.0	101.0	99.0
	SD	9.2	7.3	8.5
	MIN,MAX	84,111	89,111	84,111
	Q1,Q3	89,102	97,107	93,105
	n	11	9	20
	Nmiss	0	0	0

Section 2. Hyperinsulinaemic euglycaemic clamp study

2.4.2 Gestation by timepoint - Visit 3 Randomisation (10-16 Weeks), Visit 4 (18-20 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 3 (days)	Mean	98.7	101.9	100.2
	Median	100.0	102.0	100.5
	SD	8.4	7.1	7.8
	MIN,MAX	87,113	89,111	87,113
	Q1,Q3	90,102	98,107	95,107
	n	11	9	20
	Nmiss	0	0	0
Calculated* Gestation - Visit 4 (days)	Mean	150.5	141.7	146.6
	Median	149.0	141.0	145.5
	SD	7.3	4.5	7.5
	MIN,MAX	142,164	137,151	137,164
	Q1,Q3	145,154	139,141	141,151
	n	11	9	20
	Nmiss	0	0	0

Section 2. Hyperinsulinaemic euglycaemic clamp study

2.4.3 Gestation by timepoint - Visit 5 (28 Weeks), Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Calculated* Gestation - Visit 5 (days)	Mean	196.9	198.6	197.7
	Median	198.0	198.0	198.0
	SD	5.2	4.3	4.7
	MIN,MAX	190,207	193,205	190,207
	Q1,Q3	192,200	195,201	194,201
	n	11	9	20
	Nmiss	0	0	0
Calculated* Gestation - Visit 6 (days)	Mean	255.3	255.0	255.2
	Median	256.0	254.0	255.5
	SD	4.6	3.7	4.1
	MIN,MAX	245,263	251,263	245,263
	Q1,Q3	253,258	253,256	253,257
	n	11	9	20
	Nmiss	0	0	0

Section 2. Hyperinsulinaemic euglycaemic clamp study

2.4.4 Gestation by timepoint - Visit 7 Term, Visit 8 Delivery

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 7 (days)	Mean	282.0	282.0	282.0
	Median	282.0	283.0	282.0
	SD	4.5	3.6	4.0
	MIN,MAX	275,289	278,285	275,289
	Q1,Q3	281,283	278,285	281,283
	n	6	3	9
	Nmiss	5	6	11
Calculated* Gestation - Visit 8 (days)	Mean	282.1	280.9	281.6
	Median	283.0	278.0	283.0
	SD	9.9	8.3	9.0
	MIN,MAX	260,292	267,293	260,293
	Q1,Q3	281,289	277,285	278,288
	n	11	9	20
	Nmiss	0	0	0

Section 2. Hyperinsulinaemic euglycaemic clamp study

2.4.5 Gestation by timepoint - Visit 8 Delivery

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Recorded* Gestation - Visit 8 (days)	Mean	280.5	280.6	280.6
	Median	282.0	278.0	282.0
	SD	8.5	8.2	8.1
	MIN,MAX	260,290	267,292	260,292
	Q1,Q3	277,287	276,285	277,287
	n	11	9	20
	Nmiss	0	0	0
Coded R_gestation - Visit 8 (n%)	>37 WEEKS	11 (100)	9 (100)	20 (100)

Section 2. Hyperinsulinaemic euglycaemic clamp study

2.5.1 HOMA-IR - Visit 2 Consent/Baseline (10-16 Weeks) and Visit 5 (28 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
HOMA - visit 2	Mean	3.797	4.052	3.912
	Median	3.542	3.907	3.723
	SD	1.167	1.550	1.321
	MIN,MAX	2.37,6.51	2.21,6.55	2.21,6.55
	Q1,Q3	2.94,4.49	2.68,5.06	2.87,4.53
	n	11	9	20
	Nmiss	0	0	0
HOMA - visit 5	Mean	3.797	4.052	3.912
	Median	3.542	3.907	3.723
	SD	1.167	1.550	1.321
	MIN,MAX	2.37,6.51	2.21,6.55	2.21,6.55
	Q1,Q3	2.94,4.49	2.68,5.06	2.87,4.53
	n	11	9	20
	Nmiss	0	0	0

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Section 2. Hyperinsulinaemic euglycaemic clamp study

2.5.2 HOMA-IR - Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
HOMA - visit 6	Mean	3.797	4.052	3.912
	Median	3.542	3.907	3.723
	SD	1.167	1.550	1.321
	MIN,MAX	2.37,6.51	2.21,6.55	2.21,6.55
	Q1,Q3	2.94,4.49	2.68,5.06	2.87,4.53
	n	11	9	20
	Nmiss	0	0	0

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Section 2. Hyperinsulinaemic euglycaemic clamp study

2.6.1 Calculated Z score (*)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Number of patients in substudy-CLAMP (n)	Yes	11	9	20
Z-score for birth weight centile_CLAMP	Mean	0.0123	1.2038	0.5140
	Median	0.1565	1.2843	0.3786
	SD	0.9957	1.0711	1.1672
	MIN,MAX	-1.834,1.815	-0.742,2.711	-1.834,2.711
	Q1,Q3	-0.370,0.501	0.662,1.885	0.044,1.624
	n	11	8	19
	Nmiss	0	0	0

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N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations
(*) Patient 11551 has been excluded from the summary

By: Aryelly Rodriguez - ECTU Statistician

Section 2. Hyperinsulinaemic euglycaemic clamp study

2.6.2 Calculated Z score - Statistical Analysis

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Lower CI*	Estimated Mean Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
z-score_CLAMP - itt	0.012	0.2930	11	1.204	0.3436	8	1.192	0.239	2.144	6.962	0.0172

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 Summary statistics are presented in table 2.6.1 of this report. Patient 11551 has been excluded from the analysis
 Outcome analysed using a linear regression model. Significance level set at p<0.05

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Estimated mean represents the means for the z score by allocated treatment,

SE represents standard error of the estimated mean and N represents number of observations

*Represents the difference between the estimated means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empower_2_6_primary_outcome_z_analysis_CLAMP.lst'

Parameter shown normal behavior

Section 3. Endothelial function Effect of metformin on flow-mediated dilatation

3.1.1 Maternal Age at Baseline - Visit 2 (10-16 Weeks)

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Number of patients in substudy-Endothe (n)	Yes	15	16	31
Maternal Age at consent (years)	Mean	31.5	27.3	29.3
	Median	32.0	26.0	31.0
	SD	4.4	6.1	5.7
	MIN,MAX	22,38	19,38	19,38
	Q1,Q3	29,34	22,32	25,34
	n	15	16	31
	Nmiss	0	0	0

Section 3. Endothelial function Effect of metformin on flow-mediated dilatation

3.1.2 Maternal smoking Status at Baseline - Visit 2 (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Smoking Status (n(%))	ACTIVE	1 (6.7)	3 (18.8)	4 (12.9)
	NOT SMOKING	14 (93.3)	13 (81.3)	27 (87.1)

Section 3. Endothelial function Effect of metformin on flow-mediated dilatation

3.1.3 Maternal Blood Pressure at Baseline - Visit 2 (10-16 Weeks)

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Maternal Systolic BP (mmHg)	Mean	121.7	117.3	119.4
	Median	120.0	120.0	120.0
	SD	10.8	9.7	10.3
	MIN,MAX	108,140	100,134	100,140
	Q1,Q3	110,130	110,125	110,126
	n	15	16	31
	Nmiss	0	0	0
Maternal Diastolic BP (mmHg)	Mean	69.1	69.1	69.1
	Median	68.0	70.0	70.0
	SD	7.3	9.5	8.3
	MIN,MAX	60,80	54,84	54,84
	Q1,Q3	64,76	60,78	60,78
	n	15	16	31
	Nmiss	0	0	0

Section 3. Endothelial function Effect of metformin on flow-mediated dilatation

3.2 Previous pregnancy status* PARITY 1 at Baseline - Visit 2 (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
PARITY1 (n(%))	0	7 (46.7)	11 (68.8)	18 (58.1)
	=>1	8 (53.3)	5 (31.3)	13 (41.9)

Section 3. Endothelial function Effect of metformin on flow-mediated dilatation

3.3.1 Maternal Calculated BMI at Visit 2 Consent/Baseline (10-16 Weeks)*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Calculated BMI (kg/m ²) at Visit 2	Mean	38.4	37.7	38.1
	Median	38.5	35.1	37.5
	SD	4.9	5.7	5.2
	MIN,MAX	30,48	30,47	30,48
	Q1,Q3	35,42	34,44	34,42
	n	15	16	31
	Nmiss	0	0	0

Section 3. Endothelial function Effect of metformin on flow-mediated dilatation

3.3.2 Maternal Calculated BMI at Visit 6 (36 Weeks) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated BMI (kg/m ²) at Visit 6	Mean	40.9	40.1	40.5
	Median	41.1	39.4	40.4
	SD	4.5	5.5	4.9
	MIN,MAX	33,51	32,48	32,51
	Q1,Q3	38,44	36,45	37,44
	n	15	13	28
	Nmiss	0	3	3
Calculated BMI (kg/m ²) change V6 baseli	Mean	2.5	1.7	2.1
	Median	2.2	1.6	1.9
	SD	1.6	2.0	1.8
	MIN,MAX	0,5	-2,6	-2,6
	Q1,Q3	1,4	1,3	1,3
	n	15	13	28
	Nmiss	0	3	3

Section 3. Endothelial function Effect of metformin on flow-mediated dilatation

3.3.3 Maternal Calculated BMI at Visit 9 (Final 3 months postnatal) and ist change from baseline*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Calculated BMI (kg/m ²) at Visit 9	Mean	38.4	37.1	37.8
	Median	39.6	36.2	38.7
	SD	3.6	6.2	4.9
	MIN,MAX	29,43	29,47	29,47
	Q1,Q3	36,40	32,43	36,40
	n	13	11	24
	Nmiss	2	5	7
Calculated BMI (kg/m ²) change V9 baseli	Mean	-0.1	-1.4	-0.7
	Median	-0.8	-1.3	-0.9
	SD	2.5	2.6	2.6
	MIN,MAX	-5,5	-7,1	-7,5
	Q1,Q3	-1,1	-3,1	-2,1
	n	13	11	24
	Nmiss	2	5	7

Section 3. Endothelial function Effect of metformin on flow-mediated dilatation

3.4.1 Gestation by timepoint - Visit 1 Screening (10-16 Weeks), Visit 2 Consent/Baseline (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 1 (days)	Mean	88.0	86.7	87.3
	Median	87.0	88.5	88.0
	SD	11.2	14.9	13.0
	MIN,MAX	72,105	60,109	60,109
	Q1,Q3	78,99	77,98	78,99
	n	15	16	31
	Nmiss	0	0	0
Recorded# Gestation - Visit 2 (days)	Mean	99.1	99.1	99.1
	Median	98.0	99.5	99.0
	SD	7.4	8.1	7.6
	MIN,MAX	91,111	86,111	86,111
	Q1,Q3	92,104	93,107	92,106
	n	15	16	31
	Nmiss	0	0	0

Section 3. Endothelial function Effect of metformin on flow-mediated dilatation
 3.4.2 Gestation by timepoint - Visit 3 Randomisation (10-16 Weeks), Visit 4 (18-20 Weeks)
 Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 3 (days)	Mean	100.5	99.9	100.2
	Median	100.0	100.0	100.0
	SD	7.2	7.8	7.4
	MIN,MAX	92,112	86,111	86,112
	Q1,Q3	93,108	95,108	93,108
	n	15	16	31
	Nmiss	0	0	0
Calculated* Gestation - Visit 4 (days)	Mean	152.9	142.9	147.7
	Median	144.5	141.0	143.0
	SD	29.1	8.0	21.2
	MIN,MAX	137,252	134,166	134,252
	Q1,Q3	142,149	138,145	141,145
	n	14	15	29
	Nmiss	1	1	2

Section 3. Endothelial function Effect of metformin on flow-mediated dilatation

3.4.3 Gestation by timepoint - Visit 5 (28 Weeks), Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 5 (days)	Mean	197.4	196.2	196.8
	Median	198.0	195.5	196.5
	SD	4.8	4.4	4.6
	MIN,MAX	189,204	190,206	189,206
	Q1,Q3	195,202	193,198	194,201
	n	14	14	28
	Nmiss	1	2	3
Calculated* Gestation - Visit 6 (days)	Mean	253.1	253.0	253.1
	Median	252.0	254.0	253.5
	SD	3.4	5.9	4.6
	MIN,MAX	248,259	240,260	240,260
	Q1,Q3	251,255	251,256	251,256
	n	15	13	28
	Nmiss	0	3	3

Section 3. Endothelial function Effect of metformin on flow-mediated dilatation

3.4.4 Gestation by timepoint - Visit 7 Term, Visit 8 Delivery

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 7 (days)	Mean	281.6	279.0	280.3
	Median	281.0	279.0	280.0
	SD	5.4	2.4	4.2
	MIN,MAX	275,288	275,281	275,288
	Q1,Q3	278,286	279,281	278,281
	n	5	5	10
	Nmiss	10	11	21
Calculated* Gestation - Visit 8 (days)	Mean	278.2	277.0	277.6
	Median	281.0	280.5	281.0
	SD	10.5	17.7	14.5
	MIN,MAX	260,291	216,294	216,294
	Q1,Q3	273,287	274,287	273,287
	n	15	16	31
	Nmiss	0	0	0

Section 3. Endothelial function Effect of metformin on flow-mediated dilatation

3.4.5 Gestation by timepoint - Visit 8 Delivery

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall
		Placebo	Metformin	
Recorded* Gestation - Visit 8 (days)	Mean	277.4	276.1	276.7
	Median	277.0	278.0	277.0
	SD	10.2	16.5	13.6
	MIN,MAX	260,291	219,290	219,291
	Q1,Q3	272,286	274,286	272,286
	n	15	16	31
	Nmiss	0	0	0
Coded R_gestation - Visit 8 (n(%))	>24 and <=37 WEEKS	0	1 (6.3)	1 (3.2)
	>37 WEEKS	15 (100)	15 (93.8)	30 (96.8)

Section 4. Magnetic resonance studies

4.1 Maternal Age at Baseline - Visit 2 (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Number of patients in substudy-MRI (n)	Yes	30	27	57
Maternal Age at consent (years)	Mean	29.4	30.1	29.7
	Median	29.0	31.0	30.0
	SD	4.5	5.5	5.0
	MIN,MAX	21,37	19,39	19,39
	Q1,Q3	26,33	26,35	26,33
	n	30	27	57
	Nmiss	0	0	0

Section 4. Magnetic resonance studies

4.2 Previous pregnancy status* PARITY 1 at Baseline - Visit 2 (10-16 Weeks) - Demographics and Lifestyle

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
PARITY1 (n(%))	0	11 (36.7)	11 (40.7)	22 (38.6)
	=>1	19 (63.3)	16 (59.3)	35 (61.4)

Section 4. Magnetic resonance studies

4.3.1 Maternal Calculated BMI at Visit 2 Consent/Baseline (10-16 Weeks)*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Calculated BMI (kg/m ²) at Visit 2	Mean	38.2	39.4	38.7
	Median	37.5	38.7	38.2
	SD	5.6	4.7	5.2
	MIN,MAX	30,56	31,47	30,56
	Q1,Q3	35,41	36,44	36,42
	n	30	27	57
	Nmiss	0	0	0

Section 3. Endothelial function Effect of metformin on flow-mediated dilatation

4.3.2 Maternal Calculated BMI at Visit 6 (36 Weeks) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated BMI (kg/m ²) at Visit 6	Mean	40.3	41.4	40.8
	Median	40.6	40.2	40.4
	SD	5.4	4.3	4.9
	MIN,MAX	32,56	35,48	32,56
	Q1,Q3	37,43	38,45	37,43
	n	29	23	52
	Nmiss	1	4	5
Calculated BMI (kg/m ²) change V6 baseli	Mean	2.1	1.8	2.0
	Median	1.8	1.7	1.8
	SD	1.7	1.7	1.7
	MIN,MAX	-0,7	-2,6	-2,7
	Q1,Q3	1,3	1,3	1,3
	n	29	23	52
	Nmiss	1	4	5

Section 3. Endothelial function Effect of metformin on flow-mediated dilatation

4.3.3 Maternal Calculated BMI at Visit 9 (Final 3 months postnatal) and ist change from baseline*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Calculated BMI (kg/m ²) at Visit 9	Mean	38.0	39.0	38.5
	Median	39.0	38.0	38.8
	SD	4.0	4.6	4.3
	MIN,MAX	29,44	33,49	29,49
	Q1,Q3	35,40	36,40	36,40
	n	23	21	44
	Nmiss	7	6	13
Calculated BMI (kg/m ²) change V9 baseli	Mean	-0.6	-1.0	-0.8
	Median	-0.8	-1.1	-0.9
	SD	2.0	2.3	2.1
	MIN,MAX	-5,3	-7,4	-7,4
	Q1,Q3	-2,1	-2,0	-2,1
	n	23	21	44
	Nmiss	7	6	13

Section 4. Magnetic resonance studies

4.4.1 Gestation by timepoint - Visit 1 Screening (10-16 Weeks), Visit 2 Consent/Baseline (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 1 (days)	Mean	89.8	89.1	89.5
	Median	89.0	89.0	89.0
	SD	13.4	11.9	12.6
	MIN,MAX	69,111	60,109	60,111
	Q1,Q3	77,102	84,98	81,99
	n	30	27	57
	Nmiss	0	0	0
Recorded# Gestation - Visit 2 (days)	Mean	100.5	99.3	99.9
	Median	103.0	100.0	100.0
	SD	10.2	7.9	9.2
	MIN,MAX	78,112	85,111	78,112
	Q1,Q3	91,110	93,107	92,109
	n	30	27	57
	Nmiss	0	0	0

Section 4. Magnetic resonance studies

4.4.2 Gestation by timepoint - Visit 3 Randomisation (10-16 Weeks), Visit 4 (18-20 Weeks)

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 3 (days)	Mean	102.6	100.1	101.4
	Median	103.5	100.0	102.0
	SD	8.5	7.7	8.2
	MIN,MAX	87,113	85,112	85,113
	Q1,Q3	93,111	96,109	96,109
	n	30	27	57
	Nmiss	0	0	0
Calculated* Gestation - Visit 4 (days)	Mean	146.7	144.0	145.4
	Median	145.0	141.0	143.5
	SD	7.8	8.5	8.2
	MIN,MAX	133,164	134,166	133,166
	Q1,Q3	142,151	139,149	140,151
	n	29	27	56
	Nmiss	1	0	1

Section 4. Magnetic resonance studies

4.4.3 Gestation by timepoint - Visit 5 (28 Weeks), Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 5 (days)	Mean	196.5	198.1	197.2
	Median	197.5	198.0	198.0
	SD	4.0	4.0	4.0
	MIN,MAX	189,202	190,206	189,206
	Q1,Q3	193,200	195,201	195,200
	n	30	27	57
	Nmiss	0	0	0
Calculated* Gestation - Visit 6 (days)	Mean	253.3	254.7	253.9
	Median	254.0	254.0	254.0
	SD	3.8	4.5	4.1
	MIN,MAX	244,259	243,264	243,264
	Q1,Q3	251,256	252,256	251,256
	n	29	26	55
	Nmiss	1	1	2

Section 4. Magnetic resonance studies

4.4.4 Gestation by timepoint - Visit 7 Term, Visit 8 Delivery

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 7 (days)	Mean	282.2	280.6	281.5
	Median	282.0	281.0	281.0
	SD	3.4	2.7	3.2
	MIN,MAX	275,288	275,285	275,288
	Q1,Q3	281,285	280,282	280,283
	n	13	10	23
	Nmiss	17	17	34
Calculated* Gestation - Visit 8 (days)	Mean	282.0	279.3	280.7
	Median	283.0	280.0	283.0
	SD	9.7	9.6	9.7
	MIN,MAX	257,294	250,294	250,294
	Q1,Q3	275,289	274,285	275,287
	n	30	27	57
	Nmiss	0	0	0

Section 4. Magnetic resonance studies

4.4.5 Gestation by timepoint - Visit 8 Delivery

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall
		Placebo	Metformin	
Recorded* Gestation - Visit 8 (days)	Mean	280.8	278.4	279.7
	Median	281.5	278.0	280.0
	SD	9.4	9.6	9.5
	MIN,MAX	256,294	247,293	247,294
	Q1,Q3	275,287	274,285	275,286
	n	30	27	57
	Nmiss	0	0	0
Coded R_gestation - Visit 8 (n(%))	>24 and <=37 WEEKS	1 (3.3)	1 (3.7)	2 (3.5)
	>37 WEEKS	29 (96.7)	26 (96.3)	55 (96.5)

Section 4. Magnetic resonance studies

4.5.1 Demographic characteristics of neonate

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Baby Gender (n(%))	Male	14 (46.7)	11 (40.7)	25 (43.9)
	Female	16 (53.3)	16 (59.3)	32 (56.1)
Birth weight (g)	Mean	3493.0	3596.1	3541.8
	Median	3450.0	3660.0	3500.0
	SD	512.4	494.7	502.3
	MIN,MAX	2400,4520	2730,4490	2400,4520
	Q1,Q3	3020,3850	3260,3820	3190,3850
	n	30	27	57
	Nmiss	0	0	0

Section 4. Magnetic resonance studies

4.5.2 Demographic characteristics of neonate (Cont.)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth weight centile	Mean	51.724	63.415	57.262
	Median	52.903	66.692	57.844
	SD	29.619	25.839	28.266
	MIN,MAX	3.34,98.13	8.88,98.51	3.34,98.51
	Q1,Q3	28.70,78.37	39.55,84.52	35.36,82.48
	n	30	27	57
	Nmiss	0	0	0
Split Birth weight Centile (n(%))	>3rd and <=5th	1 (3.3)	0	1 (1.8)
	>5th and <=10th	3 (10.0)	1 (3.7)	4 (7.0)
	>10th and <=90th	22 (73.3)	20 (74.1)	42 (73.7)
	>90th and <=95th	1 (3.3)	3 (11.1)	4 (7.0)
	>95th and <=97th	2 (6.7)	1 (3.7)	3 (5.3)
	>97th	1 (3.3)	2 (7.4)	3 (5.3)

Section 4. Magnetic resonance studies

4.6.1 Anthropometry of neonate - Ponderal index#

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall
		Placebo	Metformin	
Baby ponderal index*-V8	Mean	3.44	2.60	3.04
	Median	2.42	2.57	2.54
	SD	4.59	0.32	3.32
	MIN,MAX	2.1,24.9	1.9,3.2	1.9,24.9
	Q1,Q3	2.3,2.6	2.5,2.8	2.4,2.8
	n	24	22	46
	Nmiss	6	5	11
Baby ponderal index*-V9	Mean	2.61	2.56	2.59
	Median	2.53	2.60	2.56
	SD	0.26	0.26	0.26
	MIN,MAX	2.1,3.2	2.2,2.9	2.1,3.2
	Q1,Q3	2.4,2.8	2.3,2.8	2.4,2.8
	n	24	22	46
	Nmiss	6	5	11

EMPOWaR Statistical Analysis Report MECHANISTIC PAPER - Final 02 - tables run on: 05MAR2016 at 03:54
 N = number of patients randomised, n = the number of observations, Nmiss = number of missing observations
 *Ponderal index was calculated using the following formula: $(100 * (\text{baby_weight_in_g})) / ((\text{baby_length_in_cm})^3)$
 #Data have been checked, inaccuracies happened at time and point of recording and there are not other sources for further checks

By: Aryelly Rodriguez - ECTU Statistician

Section 4. Magnetic resonance studies

4.6.2 Anthropometry of neonate - Baby Skinfold Triceps*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Baby Skinfold Triceps(mm)-V8	Mean	11.38	8.30	9.84
	Median	8.00	8.00	8.00
	SD	18.08	2.46	12.84
	MIN,MAX	4.5,90.0	5.2,14.0	4.5,90.0
	Q1,Q3	6.0,9.0	6.5,10.0	6.0,9.0
	n	21	21	42
	Nmiss	9	6	15
Baby Skinfold Triceps(mm)-V9	Mean	12.87	11.00	12.00
	Median	12.00	10.70	11.00
	SD	3.92	3.68	3.88
	MIN,MAX	7.5,19.0	6.0,24.0	6.0,24.0
	Q1,Q3	9.5,17.0	10.0,12.0	10.0,14.0
	n	23	20	43
	Nmiss	7	7	14

Section 4. Magnetic resonance studies

4.6.3 Anthropometry of neonate - Baby Skinfold Subscapular*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Baby Skinfold Subscapular(mm)-V8	Mean	10.06	7.11	8.59
	Median	7.00	7.00	7.00
	SD	13.94	2.33	9.98
	MIN,MAX	4.5,70.0	4.0,12.0	4.0,70.0
	Q1,Q3	5.0,8.0	6.0,8.0	5.0,8.0
	n	21	21	42
	Nmiss	9	6	15
Baby Skinfold Subscapular(mm)-V9	Mean	9.80	9.68	9.74
	Median	9.00	9.00	9.00
	SD	3.18	2.89	3.01
	MIN,MAX	6.0,19.0	7.0,20.0	6.0,20.0
	Q1,Q3	7.5,11.5	8.0,11.0	8.0,11.0
	n	22	20	42
	Nmiss	8	7	15

Section 4. Magnetic resonance studies

4.6.4 Anthropometry of neonate - Baby Fat %*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
BABY FAT (%) - V8	Mean	12.53	12.63	12.58
	Median	10.90	12.30	12.30
	SD	5.68	4.27	4.90
	MIN,MAX	2.1,24.3	5.7,19.6	2.1,24.3
	Q1,Q3	8.1,17.1	10.0,15.9	8.5,16.1
	n	15	17	32
	Nmiss	15	10	25
BABY FAT (%) - V9	Mean	25.80	23.73	24.85
	Median	25.70	24.50	25.30
	SD	6.02	6.01	6.02
	MIN,MAX	15.1,41.6	12.1,32.3	12.1,41.6
	Q1,Q3	22.2,29.0	19.6,27.9	20.9,29.0
	n	21	18	39
	Nmiss	9	9	18

Section 5. Saliva Samples

5.1.1 Maternal Age at Baseline - Visit 2 (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
number of patients in substudy-SALIVA (n)	Yes	121	114	235
Maternal Age at consent (years)	Mean	29.9	29.1	29.5
	Median	30.0	29.0	29.0
	SD	5.0	5.6	5.3
	MIN,MAX	20,41	18,42	18,42
	Q1,Q3	26,34	25,33	25,33
	n	121	114	235
	Nmiss	0	0	0

Section 5. Saliva Samples

5.1.2 Maternal smoking Status at Baseline - Visit 2 (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Smoking Status (n(%))	ACTIVE	9 (7.4)	15 (13.2)	24 (10.2)
	PREVIOUSLY	6 (5.0)	5 (4.4)	11 (4.7)
	NOT SMOKING	106 (87.6)	94 (82.5)	200 (85.1)

Section 5. Saliva Samples

5.1.3 Maternal Education

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo</i>	<i>Metformin</i>	<i>Overall</i>
Educational Qualifications (n(%))	No formal qualifications	7 (5.8)	5 (4.4)	12 (5.1)
	Entry level certification/foundation diploma	3 (2.5)	6 (5.3)	9 (3.8)
	GCSE, Standard grade, "O" grades	31 (25.6)	20 (17.5)	51 (21.7)
	A level, A/S level, Highers or BTEC Dip/Cert.	29 (24.0)	15 (13.2)	44 (18.7)
	Cert. higher Education, City & Guilds	9 (7.4)	9 (7.9)	18 (7.7)
	Diploma HE/FE or HND/HNC	11 (9.1)	18 (15.8)	29 (12.3)
	Graduate certificate or Diploma	3 (2.5)	7 (6.1)	10 (4.3)
	Degree	18 (14.9)	27 (23.7)	45 (19.1)
	Professional Qualification	3 (2.5)	2 (1.8)	5 (2.1)
	PGCE/Postgraduate certificate or Diploma, Masters. Doctorate	7 (5.8)	5 (4.4)	12 (5.1)
Educational Qualifications coded (n(%))	None	7 (5.8)	5 (4.4)	12 (5.1)
	School up to 16 years	34 (28.1)	26 (22.8)	60 (25.5)
	School 16 to 18 years	38 (31.4)	24 (21.1)	62 (26.4)
	College or Uni degree or Higher	42 (34.7)	59 (51.8)	101 (43.0)

Section 5. Saliva Samples

5.2 Previous pregnancy status* PARITY 1 at Baseline - Visit 2 (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
PARITY1 (n(%))	0	50 (41.3)	52 (45.6)	102 (43.4)
	=>1	71 (58.7)	62 (54.4)	133 (56.6)

Section 5. Saliva Samples

5.3.1 Maternal Calculated BMI at Visit 2 Consent/Baseline (10-16 Weeks)*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Calculated BMI (kg/m ²) at Visit 2	Mean	36.9	37.5	37.2
	Median	36.1	36.8	36.3
	SD	5.0	5.2	5.1
	MIN,MAX	30,53	30,57	30,57
	Q1,Q3	33,40	34,41	33,40
	n	121	114	235
	Nmiss	0	0	0

Section 5. Saliva Samples

5.3.2 Maternal Calculated BMI at Visit 6 (36 Weeks) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Calculated BMI (kg/m ²) at Visit 6	Mean	39.5	40.1	39.8
	Median	38.7	39.2	38.8
	SD	5.2	5.1	5.2
	MIN,MAX	32,54	32,55	32,55
	Q1,Q3	35,42	36,43	36,43
	n	101	86	187
	Nmiss	20	28	48
Calculated BMI (kg/m ²) change V6 baseli	Mean	2.8	2.3	2.5
	Median	2.6	2.2	2.5
	SD	1.9	2.1	2.0
	MIN,MAX	-3,7	-2,12	-3,12
	Q1,Q3	2,4	1,3	1,3
	n	101	86	187
	Nmiss	20	28	48

Section 5. Saliva Samples

5.3.3 Maternal Calculated BMI at Visit 9 (Final 3 months postnatal) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated BMI (kg/m ²) at Visit 9	Mean	36.7	38.1	37.4
	Median	36.4	37.4	36.9
	SD	4.5	5.8	5.2
	MIN,MAX	29,52	29,61	29,61
	Q1,Q3	34,40	33,42	33,40
	n	83	84	167
	Nmiss	38	30	68
Calculated BMI (kg/m ²) change V9 baseli	Mean	0.3	0.2	0.2
	Median	-0.0	-0.2	-0.1
	SD	2.1	3.5	2.9
	MIN,MAX	-5,5	-5,25	-5,25
	Q1,Q3	-1,2	-1,1	-1,1
	n	83	84	167
	Nmiss	38	30	68

Section 5. Saliva Samples

5.4.1 Gestation by timepoint - Visit 1 Screening (10-16 Weeks), Visit 2 Consent/Baseline (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 1 (days)	Mean	86.7	86.4	86.5
	Median	86.0	88.0	88.0
	SD	13.3	13.7	13.5
	MIN,MAX	51,111	51,110	51,111
	Q1,Q3	80,96	82,95	80,96
	n	121	114	235
	Nmiss	0	0	0
Recorded# Gestation - Visit 2 (days)	Mean	99.7	99.9	99.8
	Median	102.0	100.0	101.0
	SD	8.8	7.7	8.2
	MIN,MAX	74,112	75,112	74,112
	Q1,Q3	93,107	94,107	93,107
	n	121	114	235
	Nmiss	0	0	0

Section 5. Saliva Samples

5.4.2 Gestation by timepoint - Visit 3 Randomisation (10-16 Weeks), Visit 4 (18-20 Weeks)

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 3 (days)	Mean	101.5	101.4	101.5
	Median	103.0	102.0	102.0
	SD	8.3	6.9	7.6
	MIN,MAX	84,118	85,112	84,118
	Q1,Q3	95,108	97,108	96,108
	n	121	114	235
	Nmiss	0	0	0
Calculated* Gestation - Visit 4 (days)	Mean	142.5	140.2	141.4
	Median	141.0	140.0	141.0
	SD	11.0	10.0	10.6
	MIN,MAX	125,198	114,200	114,200
	Q1,Q3	137,146	134,143	137,145
	n	116	111	227
	Nmiss	5	3	8

Section 5. Saliva Samples

5.4.3 Gestation by timepoint - Visit 5 (28 Weeks), Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 5 (days)	Mean	197.6	197.7	197.6
	Median	198.0	198.0	198.0
	SD	4.8	5.5	5.1
	MIN,MAX	185,217	167,217	167,217
	Q1,Q3	195,200	196,201	195,200
	n	117	106	223
	Nmiss	4	8	12
Calculated* Gestation - Visit 6 (days)	Mean	253.1	253.0	253.1
	Median	253.0	253.0	253.0
	SD	4.3	5.0	4.6
	MIN,MAX	241,263	234,264	234,264
	Q1,Q3	251,256	250,256	251,256
	n	104	93	197
	Nmiss	17	21	38

Section 5. Saliva Samples

5.4.4 Gestation by timepoint - Visit 7 Term, Visit 8 Delivery

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 7 (days)	Mean	279.1	280.2	279.6
	Median	276.0	278.0	278.0
	SD	17.9	23.2	20.6
	MIN,MAX	262,414	250,419	250,419
	Q1,Q3	273,281	274,280	274,280
	n	71	68	139
	Nmiss	50	46	96
Calculated* Gestation - Visit 8 (days)	Mean	281.9	276.1	279.1
	Median	281.0	280.0	281.0
	SD	16.8	21.2	19.2
	MIN,MAX	209,375	143,306	143,375
	Q1,Q3	274,289	271,286	273,287
	n	120	112	232
	Nmiss	1	2	3

Section 5. Saliva Samples

5.4.5 Gestation by timepoint - Visit 8 Delivery

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall
		Placebo	Metformin	
Recorded* Gestation - Visit 8 (days)	Mean	277.6	275.0	276.4
	Median	278.0	278.0	278.0
	SD	11.8	18.1	15.2
	MIN,MAX	211,298	143,297	143,298
	Q1,Q3	272,287	271,285	271,286
	n	121	111	232
	Nmiss	0	3	3
Coded R_gestation - Visit 8 (n(%))	Missing	0	3	3
	<= 24 WEEKS	0	1 (0.9)	1 (0.4)
	>24 and <=37 WEEKS	5 (4.1)	10 (9.0)	15 (6.5)
	>37 WEEKS	116 (95.9)	100 (90.1)	216 (93.1)

Section 5. Saliva Samples

5.5.1.1 Saliva Free Cortisol (SFC) at Visit 2 Consent/Baseline (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
SFC V2 BEDTIME	Mean	2.2314	1.9952	2.1167
	Median	0.9690	1.1340	1.0750
	SD	8.0296	2.3755	5.9796
	MIN,MAX	0.358,77.820	0.338,12.481	0.338,77.820
	Q1,Q3	0.680,1,320	0.784,1,983	0.732,1,570
	n	107	101	208
	Nmiss	0	0	0
SFC V2 WAKING	Mean	9.0267	6.3600	7.7318
	Median	5.8280	5.6950	5.7775
	SD	24.5826	3.8566	17.8443
	MIN,MAX	0.638,258.56	0.714,19,996	0.638,258.56
	Q1,Q3	4.605,8,363	3.731,9,012	4.160,8,657
	n	107	101	208
	Nmiss	0	0	0

Section 5. Saliva Samples

5.5.1.2 Saliva Free Cortisol (SFC) at Visit 2 Consent/Baseline (10-16 Weeks) - Difference Bedtime-Awake

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
SFC V2 DIFF bedtime to awake	Mean	-6.7953	-4.3649	-5.6151
	Median	-4.8610	-4.5830	-4.6875
	SD	22.4869	5.1146	16.5244
	MIN,MAX	-227.2,53.343	-17.27,11.642	-227.2,53.343
	Q1,Q3	-7.169,-3.321	-7.489,-2.450	-7.181,-2.953
	n	107	101	208
	Nmiss	0	0	0

Section 5. Saliva Samples

5.5.2.1 Saliva Free Cortisol (SFC) at Visit 5 (28 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
SFC V5 BEDTIME	Mean	3.1661	2.0399	2.5805
	Median	1.9545	1.7570	1.8555
	SD	3.9816	1.5810	3.0222
	MIN,MAX	1.120,23.885	0.838,12.126	0.838,23.885
	Q1,Q3	1.645,2.835	1.457,2.082	1.531,2.353
	n	48	52	100
	Nmiss	0	1	1
SFC V5 WAKING	Mean	8.6792	9.2571	8.9797
	Median	8.7065	8.4330	8.5250
	SD	6.9342	4.2930	5.6926
	MIN,MAX	0.986,47.022	2.401,26.293	0.986,47.022
	Q1,Q3	4.221,10.426	6.325,11.388	6.023,11.271
	n	48	52	100
	Nmiss	0	1	1

Section 5. Saliva Samples

5.5.2.2 Saliva Free Cortisol (SFC) at Visit 5 (28 Weeks)- Difference Bedtime-Awake

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
SFC V5 DIFF bedtime to awake	Mean	-5.5131	-7.2172	-6.3992
	Median	-6.2640	-6.6210	-6.4945
	SD	7.8224	3.7307	6.0788
	MIN,MAX	-43.79,14.895	-18.29,-0.540	-43.79,14.895
	Q1,Q3	-8.158,-2.400	-9.697,-4.488	-8.984,-4.175
	n	48	52	100
	Nmiss	0	1	1

Section 5. Saliva Samples

5.5.3.1 Saliva Free Cortisol (SFC) at Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
SFC V6 BEDTIME	Mean	3.3966	2.9771	3.1732
	Median	2.5890	2.3480	2.3720
	SD	3.1531	1.8249	2.5250
	MIN,MAX	1.562,20.063	1.500,8.688	1.500,20.063
	Q1,Q3	2.084,3.361	2.071,2.975	2.078,3.163
	n	36	41	77
	Nmiss	0	0	0
SFC V6 WAKING	Mean	8.8989	8.7360	8.8122
	Median	8.2175	7.9910	8.2100
	SD	4.1708	4.8077	4.4926
	MIN,MAX	2.948,21.496	1.918,32.084	1.918,32.084
	Q1,Q3	5.940,10.071	6.011,10.407	6.008,10.283
	n	36	41	77
	Nmiss	0	0	0

Section 5. Saliva Samples

5.5.3.2 Saliva Free Cortisol (SFC) at Visit 6 (36 Weeks)- Difference Bedtime-Awake

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
SFC V6 DIFF bedtime to awake	Mean	-5.5023	-5.7590	-5.6390
	Median	-4.8690	-5.5540	-5.3730
	SD	3.6587	5.6015	4.7640
	MIN,MAX	-14.23,0.373	-29.06,6.770	-29.06,6.770
	Q1,Q3	-7.566,-2.889	-7.568,-3.665	-7.568,-3.300
	n	36	41	77
	Nmiss	0	0	0

Section 5. Saliva Samples

5.5.4 Saliva Free Cortisol (SFC) Differences Bedtime-Awake Statistical Analysis by timepoint

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Difference Lower CI*	Estimated Mean Difference Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
SA_2V_DIF_log - itt	5.484	0.0170	107	5.507	0.0173	101	0.023	-0.022	0.069	1.031	0.3111
SA_5V_DIF_log - itt	5.495	0.0040	48	5.489	0.0037	52	-0.006	-0.016	0.004	1.509	0.2223
SA_6V_DIF_log - itt	5.499	0.0036	36	5.498	0.0032	41	-0.001	-0.010	0.008	0.080	0.7780

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By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in tables 5.5.1 to 5.5.3 of this report

Outcome analysed using a linear regression model, adjusted by BMI band. Significance level set at p<0.05

Estimated mean represents the adjusted means of the log transformed variable by allocated treatment,

SE represents standard error of the estimated log transformed means and N represents number of observations

*Represents the difference between estimated log transformed means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_5_5_SALIVA_LABS_ANALYSIS.lst'

All parameters shown normal or near-normal behavior

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Section 6. Placental biopsies

6.1.1 Maternal Age at Baseline - Visit 2 (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Number of patients in substudy-PLACENTATISSUE (n)	Yes	64	61	125
Maternal Age at consent (years)	Mean	29.2	29.7	29.4
	Median	29.0	30.0	29.0
	SD	5.5	5.3	5.4
	MIN,MAX	21,41	19,40	19,41
	Q1,Q3	24,33	25,34	25,34
	n	64	61	125
	Nmiss	0	0	0

Section 6. Placental biopsies

6.1.2 Maternal smoking Status at Baseline - Visit 2 (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Smoking Status (n(%))	ACTIVE	7 (10.9)	10 (16.4)	17 (13.6)
	PREVIOUSLY	2 (3.1)	2 (3.3)	4 (3.2)
	NOT SMOKING	55 (85.9)	49 (80.3)	104 (83.2)

Section 6. Placental biopsies

6.1.3 Maternal Education

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		
		<i>Placebo</i>	<i>Metformin</i>	<i>Overall</i>
Educational Qualifications (n(%))	No formal qualifications	4 (6.3)	4 (6.6)	8 (6.4)
	Entry level certification/foundation diploma	1 (1.6)	3 (4.9)	4 (3.2)
	GCSE, Standard grade, "O" grades	15 (23.4)	6 (9.8)	21 (16.8)
	A level, A/S level, Highers or BTEC Dip/Cert.	13 (20.3)	7 (11.5)	20 (16.0)
	Cert. higher Education, City & Guilds	5 (7.8)	6 (9.8)	11 (8.8)
	Diploma HE/FE or HND/HNC	9 (14.1)	11 (18.0)	20 (16.0)
	Graduate certificate or Diploma	2 (3.1)	4 (6.6)	6 (4.8)
	Degree	12 (18.8)	19 (31.1)	31 (24.8)
	PGCE/Postgraduate certificate or Diploma, Masters. Doctorate	3 (4.7)	1 (1.6)	4 (3.2)
Educational Qualifications coded (n(%))	None	4 (6.3)	4 (6.6)	8 (6.4)
	School up to 16 years	16 (25.0)	9 (14.8)	25 (20.0)
	School 16 to 18 years	18 (28.1)	13 (21.3)	31 (24.8)
	College or Uni degree or Higher	26 (40.6)	35 (57.4)	61 (48.8)

Section 6. Placental biopsies

6.2 Previous pregnancy status* PARITY 1 at Baseline - Visit 2 (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
PARITY1 (n(%))	0	22 (34.4)	27 (44.3)	49 (39.2)
	=>1	42 (65.6)	34 (55.7)	76 (60.8)

Section 6. Placental biopsies

6.3.1 Maternal Calculated BMI at Visit 2 Consent/Baseline (10-16 Weeks)*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Calculated BMI (kg/m ²) at Visit 2	Mean	37.0	38.3	37.6
	Median	36.1	38.2	36.7
	SD	5.2	5.3	5.2
	MIN,MAX	30,53	30,51	30,53
	Q1,Q3	33,41	34,42	33,41
	n	64	61	125
	Nmiss	0	0	0

Section 6. Placental biopsies

6.3.2 Maternal Calculated BMI at Visit 6 (36 Weeks) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Calculated BMI (kg/m ²) at Visit 6	Mean	39.1	40.3	39.7
	Median	37.8	39.4	38.9
	SD	4.8	5.1	5.0
	MIN,MAX	31,53	32,51	31,53
	Q1,Q3	36,42	37,45	36,43
	n	55	55	110
	Nmiss	9	6	15
Calculated BMI (kg/m ²) change V6 baseli	Mean	2.2	2.0	2.1
	Median	2.2	2.0	2.1
	SD	1.6	1.8	1.7
	MIN,MAX	-3,6	-2,7	-3,7
	Q1,Q3	2,3	1,3	1,3
	n	55	55	110
	Nmiss	9	6	15

Section 6. Placental biopsies

6.3.3 Maternal Calculated BMI at Visit 9 (Final 3 months postnatal) and ist change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Calculated BMI (kg/m ²) at Visit 9	Mean	36.9	38.0	37.5
	Median	36.1	37.3	37.0
	SD	4.6	6.2	5.5
	MIN,MAX	28,48	29,61	28,61
	Q1,Q3	34,40	33,42	34,40
	n	48	53	101
	Nmiss	16	8	24
Calculated BMI (kg/m ²) change V9 baseli	Mean	-0.3	-0.1	-0.2
	Median	-0.6	-0.7	-0.6
	SD	2.3	4.2	3.4
	MIN,MAX	-5,5	-7,25	-7,25
	Q1,Q3	-2,1	-2,1	-2,1
	n	48	53	101
	Nmiss	16	8	24

Section 6. Placental biopsies

6.4.1 Gestation by timepoint - Visit 1 Screening (10-16 Weeks), Visit 2 Consent/Baseline (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 1 (days)	Mean	83.8	84.5	84.1
	Median	84.0	85.0	85.0
	SD	13.9	14.4	14.1
	MIN,MAX	51,109	51,109	51,109
	Q1,Q3	74,95	76,94	74,94
	n	64	61	125
	Nmiss	0	0	0
Recorded# Gestation - Visit 2 (days)	Mean	100.1	100.0	100.0
	Median	103.5	100.0	102.0
	SD	9.6	7.7	8.7
	MIN,MAX	71,112	82,111	71,112
	Q1,Q3	95,108	94,107	94,108
	n	64	61	125
	Nmiss	0	0	0

Section 6. Placental biopsies

6.4.2 Gestation by timepoint - Visit 3 Randomisation (10-16 Weeks), Visit 4 (18-20 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 3 (days)	Mean	102.2	101.6	101.9
	Median	105.5	103.0	104.0
	SD	8.1	7.1	7.6
	MIN,MAX	84,112	85,112	84,112
	Q1,Q3	97,108	96,108	97,108
	n	64	61	125
	Nmiss	0	0	0
Calculated* Gestation - Visit 4 (days)	Mean	142.8	138.9	140.8
	Median	140.0	140.0	140.0
	SD	19.7	6.7	14.8
	MIN,MAX	108,252	126,166	108,252
	Q1,Q3	133,145	134,142	133,144
	n	61	61	122
	Nmiss	3	0	3

Section 6. Placental biopsies

6.4.3 Gestation by timepoint - Visit 5 (28 Weeks), Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 5 (days)	Mean	198.2	197.6	197.9
	Median	198.0	197.0	197.0
	SD	10.6	5.5	8.5
	MIN,MAX	189,275	167,208	167,275
	Q1,Q3	195,200	196,201	196,200
	n	63	60	123
	Nmiss	1	1	2
Calculated* Gestation - Visit 6 (days)	Mean	253.9	252.8	253.3
	Median	254.0	253.0	253.0
	SD	3.6	3.8	3.7
	MIN,MAX	246,263	240,261	240,263
	Q1,Q3	252,256	251,254	251,256
	n	58	57	115
	Nmiss	6	4	10

Section 6. Placental biopsies

6.4.4 Gestation by timepoint - Visit 7 Term, Visit 8 Delivery

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 7 (days)	Mean	277.2	279.4	278.3
	Median	276.0	276.5	276.0
	SD	7.2	19.6	14.6
	MIN,MAX	256,298	263,393	256,393
	Q1,Q3	273,282	273,280	273,281
	n	39	38	77
	Nmiss	25	23	48
Calculated* Gestation - Visit 8 (days)	Mean	279.3	278.7	279.0
	Median	279.5	280.0	280.0
	SD	10.7	9.6	10.1
	MIN,MAX	257,305	254,298	254,305
	Q1,Q3	273,288	271,285	272,287
	n	64	61	125
	Nmiss	0	0	0

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Section 6. Placental biopsies

6.4.5 Gestation by timepoint - Visit 8 Delivery

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall
		Placebo	Metformin	
Recorded* Gestation - Visit 8 (days)	Mean	277.5	277.6	277.6
	Median	277.0	278.0	277.0
	SD	9.4	9.6	9.5
	MIN,MAX	256,294	253,297	253,297
	Q1,Q3	272,285	271,284	271,284
	n	64	61	125
	Nmiss	0	0	0
Coded R_gestation - Visit 8 (n(%))	>24 and <=37 WEEKS	2 (3.1)	3 (4.9)	5 (4.0)
	>37 WEEKS	62 (96.9)	58 (95.1)	120 (96.0)

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Section 6. Placental biopsies

6.5.1 Delivery Details - alive births

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Delivery Method (n(%))	Spontaneous vaginal delivery	34 (53.1)	34 (55.7)	68 (54.4)
	LSCS in labour	10 (15.6)	7 (11.5)	17 (13.6)
	LSCS pre labour	17 (26.6)	13 (21.3)	30 (24.0)
	Forceps/ventouse	3 (4.7)	7 (11.5)	10 (8.0)
C-SECTION index pregnancy (n(%))	Yes	27 (42.2)	20 (32.8)	47 (37.6)
	No	37 (57.8)	41 (67.2)	78 (62.4)
Primary C-SECTION in index pregnancy (n(%))	Yes	15 (23.4)	10 (16.4)	25 (20.0)
	No	49 (76.6)	51 (83.6)	100 (80.0)

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Section 6. Placental biopsies

6.5.2 Delivery Outcome

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Birth Outcome (n(%))	Live Birth	64 (100)	61 (100)	125 (100)
Baby Gender (n(%))	Male	31 (48.4)	34 (55.7)	65 (52.0)
	Female	33 (51.6)	27 (44.3)	60 (48.0)

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Section 6. Placental biopsies

6.6.1 GR_NR3C

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
GR_NR3C1	Mean	0.8404	0.8088	0.8250
	Median	0.7729	0.7208	0.7628
	SD	0.4924	0.4367	0.4644
	MIN,MAX	0.110,2.887	0.109,2.452	0.109,2.887
	Q1,Q3	0.527,0.979	0.529,1.055	0.529,0.995
	n	64	61	125
	Nmiss	0	0	0

Section 6. Placental biopsies

6.6.2 HSD1 and HSD2

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
HSD1	Mean	2.2783	2.4612	2.3675
	Median	1.0648	1.3578	1.3066
	SD	3.0948	3.2035	3.1369
	MIN,MAX	0.037,18.376	0.067,17.556	0.037,18.376
	Q1,Q3	0.531,2.866	0.597,3.057	0.562,2.911
	n	64	61	125
	Nmiss	0	0	0
HSD2	Mean	4.2637	3.3163	3.8014
	Median	1.4368	1.7528	1.6229
	SD	7.2764	5.3983	6.4208
	MIN,MAX	0.234,43.101	0.145,29.653	0.145,43.101
	Q1,Q3	0.873,4.040	0.915,2.775	0.878,3.050
	n	64	61	125
	Nmiss	0	0	0

Section 6. Placental biopsies

6.6.3 gr_nr3c1, hsd2 and hsd2 Statistical Analysis

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	--- Placebo ---			--- Metformin ---			Estimated Mean Difference*	Estimated Mean Lower CI*	Estimated Mean Upper CI*	Statistic (t-test)	p-value
	Estimated Mean	SE	n	Estimated Mean	SE	n					
gr_nr3c1_log - itt	-0.299	0.0775	64	-0.324	0.0792	61	-0.025	-0.236	0.187	0.053	0.8176
hsd1_log - itt	0.056	0.1666	64	0.189	0.1705	61	0.133	-0.322	0.589	0.336	0.5633
hsd2_log - itt	0.590	0.1367	64	0.433	0.1398	61	-0.157	-0.531	0.216	0.696	0.4059

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By: Aryelly Rodriguez - ECTU Statistician

Summary statistics are presented in tables 6.6.1 to 6.6.2 of this report

Outcome analysed using a linear regression model, adjusted by BMI band and c-section index pregnancy (6.5.1). Significance level set at p<0.05

Estimated mean represents the adjusted means of the log transformed variable by allocated treatment,

SE represents standard error of the estimated log transformed means and N represents number of observations

*Represents the difference between estimated log transformed means and CI Represents the 95% confidence interval

Calculations and detailed analysis are presented in study file 'Empowar_6_6_PLACENTA_LABS_ANALYSIS.lst'

All parameters shown normal or near-normal behavior

Section 7. Myometrial biopsies - Myometrial contractility

7.1.1 Maternal Age at Baseline - Visit 2 (10-16 Weeks)

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Number of patients in substudy-Myo_cont (n)	Yes	2	6	8
Maternal Age at consent (years)	Mean	34.5	27.7	29.4
	Median	34.5	28.0	29.5
	SD	7.8	4.3	5.6
	MIN,MAX	29,40	23,33	23,40
	Q1,Q3	29,40	23,31	25,32
	n	2	6	8
	Nmiss	0	0	0

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Section 7. Myometrial biopsies - Myometrial contractility

7.1.2 Previous pregnancy status* PARITY 1 at Baseline - Visit 2 (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
PARITY1 (n(%))	0	0	4 (66.7)	4 (50.0)
	=>1	2 (100)	2 (33.3)	4 (50.0)

Section 7. Myometrial biopsies - Myometrial contractility
7.1.3.1 Maternal Calculated BMI at Visit 2 Consent/Baseline (10-16 Weeks)*#
 Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Calculated BMI (kg/m ²) at Visit 2	Mean	37.6	38.1	38.0
	Median	37.6	38.2	38.2
	SD	7.1	3.7	4.1
	MIN,MAX	33,43	32,43	32,43
	Q1,Q3	33,43	36,41	34,42
	n	2	6	8
	Nmiss	0	0	0

Section 7. Myometrial biopsies - Myometrial contractility

7.1.3.2 Maternal Calculated BMI at Visit 6 (36 Weeks) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated BMI (kg/m ²) at Visit 6	Mean	37.5	41.0	40.5
	Median	37.5	41.4	40.4
	SD	.	3.7	3.6
	MIN,MAX	37,37	35,45	35,45
	Q1,Q3	37,37	40,44	37,44
	n	1	6	7
	Nmiss	1	0	1
Calculated BMI (kg/m ²) change V6 baseli	Mean	4.8	3.0	3.2
	Median	4.8	2.2	2.2
	SD	.	3.1	2.9
	MIN,MAX	5,5	-1,7	-1,7
	Q1,Q3	5,5	1,6	1,6
	n	1	6	7
	Nmiss	1	0	1

Section 7. Myometrial biopsies - Myometrial contractility

7.1.3.3 Maternal Calculated BMI at Visit 9 (Final 3 months postnatal) and ist change from baseline*

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall
		Placebo	Metformin	
Calculated BMI (kg/m ²) at Visit 9	Mean	39.1	39.3	39.3
	Median	39.1	41.6	41.6
	SD	6.8	5.5	5.3
	MIN,MAX	34,44	30,44	30,44
	Q1,Q3	34,44	38,43	34,44
	n	2	5	7
	Nmiss	0	1	1
Calculated BMI (kg/m ²) change V9 baseli	Mean	1.4	1.5	1.5
	Median	1.4	-1.1	1.2
	SD	0.3	5.2	4.2
	MIN,MAX	1,2	-3,8	-3,8
	Q1,Q3	1,2	-2,6	-2,6
	n	2	5	7
	Nmiss	0	1	1

Section 7. Myometrial biopsies - Myometrial contractility

7.1.4.1 Gestation by timepoint - Visit 1 Screening (10-16 Weeks), Visit 2 Consent/Baseline (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 1 (days)	Mean	62.0	79.0	74.8
	Median	62.0	78.5	74.5
	SD	15.6	10.7	13.4
	MIN,MAX	51,73	68,97	51,97
	Q1,Q3	51,73	69,83	69,82
	n	2	6	8
	Nmiss	0	0	0
Recorded# Gestation - Visit 2 (days)	Mean	90.5	92.5	92.0
	Median	90.5	95.5	95.0
	SD	6.4	5.9	5.6
	MIN,MAX	86,95	82,97	82,97
	Q1,Q3	86,95	89,96	88,96
	n	2	6	8
	Nmiss	0	0	0

Section 7. Myometrial biopsies - Myometrial contractility

7.1.4.2 Gestation by timepoint - Visit 3 Randomisation (10-16 Weeks), Visit 4 (18-20 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 3 (days)	Mean	93.5	100.0	98.4
	Median	93.5	98.0	97.5
	SD	4.9	8.4	7.9
	MIN,MAX	90,97	89,113	89,113
	Q1,Q3	90,97	96,106	93,102
	n	2	6	8
	Nmiss	0	0	0
Calculated* Gestation - Visit 4 (days)	Mean	138.0	137.0	137.3
	Median	138.0	135.0	135.0
	SD	17.0	9.4	10.2
	MIN,MAX	126,150	126,148	126,150
	Q1,Q3	126,150	130,148	128,148
	n	2	6	8
	Nmiss	0	0	0

Section 7. Myometrial biopsies - Myometrial contractility

7.1.4.3 Gestation by timepoint - Visit 5 (28 Weeks), Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 5 (days)	Mean	195.0	193.3	193.8
	Median	195.0	196.0	195.5
	SD	0.0	14.1	12.0
	MIN,MAX	195,195	167,210	167,210
	Q1,Q3	195,195	194,197	195,197
	n	2	6	8
	Nmiss	0	0	0
Calculated* Gestation - Visit 6 (days)	Mean	254.0	255.7	255.4
	Median	254.0	252.5	253.0
	SD	.	6.0	5.5
	MIN,MAX	254,254	251,266	251,266
	Q1,Q3	254,254	252,260	252,260
	n	1	6	7
	Nmiss	1	0	1

Section 7. Myometrial biopsies - Myometrial contractility

7.1.4.4 Gestation by timepoint - Visit 7 Term, Visit 8 Delivery

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 7 (days)	Mean	275.0	393.0	334.0
	Median	275.0	393.0	334.0
	SD	.	.	83.4
	MIN,MAX	275,275	393,393	275,393
	Q1,Q3	275,275	393,393	275,393
	n	1	1	2
	Nmiss	1	5	6
Calculated* Gestation - Visit 8 (days)	Mean	274.5	275.8	275.5
	Median	274.5	272.5	273.5
	SD	0.7	7.9	6.7
	MIN,MAX	274,275	270,291	270,291
	Q1,Q3	274,275	271,278	272,277
	n	2	6	8
	Nmiss	0	0	0

Section 7. Myometrial biopsies - Myometrial contractility

7.1.4.5 Gestation by timepoint - Visit 8 Delivery

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Recorded* Gestation - Visit 8 (days)	Mean	274.0	272.5	272.9
	Median	274.0	271.0	272.5
	SD	1.4	3.7	3.2
	MIN,MAX	273,275	269,278	269,278
	Q1,Q3	273,275	270,276	270,276
	n	2	6	8
	Nmiss	0	0	0
Coded R_gestation - Visit 8 (n(%))	>37 WEEKS	2 (100)	6 (100)	8 (100)

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Section 7. Myometrial biopsies - Myometrial contractility

7.1.5 Delivery Details - alive births

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Delivery Method (n(%))	Spontaneous vaginal delivery	0	1 (16.7)	1 (12.5)
	LSCS in labour	0	1 (16.7)	1 (12.5)
	LSCS pre labour	2 (100)	3 (50.0)	5 (62.5)
	Forceps/ventouse	0	1 (16.7)	1 (12.5)
C-SECTION index pregnancy (n(%))	Yes	2 (100)	4 (66.7)	6 (75.0)
	No	0	2 (33.3)	2 (25.0)
Primary C-SECTION in index pregnancy (n(%))	Yes	0	3 (50.0)	3 (37.5)
	No	2 (100)	3 (50.0)	5 (62.5)

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Section 7. Myometrial biopsies - Glycogen storage

7.2.1 Maternal Age at Baseline - Visit 2 (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Number of patients in substudy-Gly_sto (n)	Yes	17	11	28
Maternal Age at consent (years)	Mean	29.8	30.0	29.9
	Median	30.0	30.0	30.0
	SD	5.8	4.7	5.3
	MIN,MAX	20,40	23,36	20,40
	Q1,Q3	26,34	27,35	27,35
	n	17	11	28
	Nmiss	0	0	0

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Section 7. Myometrial biopsies - Glycogen storage

7.2.2 Previous pregnancy status* PARITY 1 at Baseline - Visit 2 (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
PARITY1 (n(%))	0	6 (35.3)	4 (36.4)	10 (35.7)
	=>1	11 (64.7)	7 (63.6)	18 (64.3)

Section 7. Myometrial biopsies - Glycogen storage

7.2.3.1 Maternal Calculated BMI at Visit 2 Consent/Baseline (10-16 Weeks)*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated_Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Calculated BMI (kg/m ²) at Visit 2	Mean	37.5	40.6	38.7
	Median	37.5	41.1	39.2
	SD	4.6	4.2	4.6
	MIN,MAX	31,45	32,47	31,47
	Q1,Q3	33,42	37,44	34,43
	n	17	11	28
	Nmiss	0	0	0

Section 7. Myometrial biopsies - Glycogen storage

7.2.3.2 Maternal Calculated BMI at Visit 6 (36 Weeks) and its change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated BMI (kg/m ²) at Visit 6	Mean	39.4	42.7	40.6
	Median	38.1	42.5	39.8
	SD	4.2	4.8	4.6
	MIN,MAX	34,47	35,51	34,51
	Q1,Q3	36,43	40,45	37,44
	n	16	9	25
	Nmiss	1	2	3
Calculated BMI (kg/m ²) change V6 baseli	Mean	2.1	2.1	2.1
	Median	2.0	2.0	2.0
	SD	1.9	2.5	2.1
	MIN,MAX	-3,5	-2,6	-3,6
	Q1,Q3	2,3	1,2	1,3
	n	16	9	25
	Nmiss	1	2	3

Section 7. Myometrial biopsies - Glycogen storage

7.2.3.3 Maternal Calculated BMI at Visit 9 (Final 3 months postnatal) and ist change from baseline*

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Calculated BMI (kg/m ²) at Visit 9	Mean	37.5	39.2	38.1
	Median	37.7	40.1	38.5
	SD	5.0	4.0	4.7
	MIN,MAX	29,47	30,44	29,47
	Q1,Q3	34,41	38,42	34,41
	n	17	8	25
	Nmiss	0	3	3
Calculated BMI (kg/m ²) change V9 baseli	Mean	0.0	-1.6	-0.5
	Median	-0.4	-1.2	-0.5
	SD	2.3	2.7	2.5
	MIN,MAX	-4,5	-7,1	-7,5
	Q1,Q3	-2,1	-3,0	-2,1
	n	17	8	25
	Nmiss	0	3	3

Section 7. Myometrial biopsies - Glycogen storage

7.2.4.1 Gestation by timepoint - Visit 1 Screening (10-16 Weeks), Visit 2 Consent/Baseline (10-16 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 1 (days)	Mean	81.1	86.5	83.3
	Median	83.0	87.0	84.0
	SD	14.0	13.1	13.7
	MIN,MAX	51,107	68,109	51,109
	Q1,Q3	72,88	76,96	73,94
	n	17	11	28
	Nmiss	0	0	0
Recorded# Gestation - Visit 2 (days)	Mean	97.9	99.5	98.5
	Median	95.0	101.0	98.5
	SD	9.2	9.4	9.1
	MIN,MAX	84,112	82,111	82,112
	Q1,Q3	92,105	92,108	92,107
	n	17	11	28
	Nmiss	0	0	0

Section 7. Myometrial biopsies - Glycogen storage

7.2.4.2 Gestation by timepoint - Visit 3 Randomisation (10-16 Weeks), Visit 4 (18-20 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 3 (days)	Mean	99.8	102.1	100.7
	Median	101.0	103.0	102.0
	SD	8.7	7.1	8.0
	MIN,MAX	84,112	89,111	84,112
	Q1,Q3	93,106	98,108	95,107
	n	17	11	28
	Nmiss	0	0	0
Calculated* Gestation - Visit 4 (days)	Mean	145.5	143.5	144.7
	Median	141.0	141.0	141.0
	SD	29.5	9.6	23.5
	MIN,MAX	125,252	126,166	125,252
	Q1,Q3	127,146	140,148	136,146
	n	17	11	28
	Nmiss	0	0	0

Section 7. Myometrial biopsies - Glycogen storage

7.2.4.3 Gestation by timepoint - Visit 5 (28 Weeks), Visit 6 (36 Weeks)

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 5 (days)	Mean	195.8	193.7	195.0
	Median	195.5	196.0	196.0
	SD	5.4	9.6	7.2
	MIN,MAX	182,207	167,201	167,207
	Q1,Q3	194,199	196,197	194,198
	n	16	10	26
	Nmiss	1	1	2
Calculated* Gestation - Visit 6 (days)	Mean	255.3	252.3	254.2
	Median	255.5	252.0	253.5
	SD	3.8	4.6	4.3
	MIN,MAX	248,263	245,260	245,263
	Q1,Q3	253,258	251,256	252,258
	n	16	10	26
	Nmiss	1	1	2

Section 7. Myometrial biopsies - Glycogen storage

7.2.4.4 Gestation by timepoint - Visit 7 Term, Visit 8 Delivery

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

Parameter(s)	Categories	-----Allocated Intervention-----		Overall
		Placebo	Metformin	
Calculated* Gestation - Visit 7 (days)	Mean	276.4	273.6	275.5
	Median	275.0	273.0	274.0
	SD	5.4	1.5	4.6
	MIN,MAX	271,289	272,276	271,289
	Q1,Q3	273,277	273,274	273,276
	n	10	5	15
	Nmiss	7	6	13
Calculated* Gestation - Visit 8 (days)	Mean	276.0	276.1	276.0
	Median	275.0	274.0	274.5
	SD	8.8	10.8	9.4
	MIN,MAX	257,292	263,306	257,306
	Q1,Q3	273,280	271,278	273,280
	n	17	11	28
	Nmiss	0	0	0

Section 7. Myometrial biopsies - Glycogen storage

7.2.4.5 Gestation by timepoint - Visit 8 Delivery

Population = Intention to treat (ITT) - AllocatedTreatment used for summarisation

Parameter(s)	Categories	-----Allocated_Intervention-----		Overall
		Placebo	Metformin	
Recorded* Gestation - Visit 8 (days)	Mean	274.9	272.5	273.9
	Median	274.0	273.0	273.0
	SD	7.7	4.2	6.6
	MIN,MAX	256,290	263,280	256,290
	Q1,Q3	273,280	270,274	272,277
	n	17	11	28
	Nmiss	0	0	0
Coded R_gestation - Visit 8 (n(%))	>24 and <=37 WEEKS	1 (5.9)	0	1 (3.6)
	>37 WEEKS	16 (94.1)	11 (100)	27 (96.4)

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Section 7. Myometrial biopsies - Glycogen storage

7.2.5 Delivery Details - alive births

Population = Intention to treat (ITT) - Allocated Treatment used for summarisation

<i>Parameter(s)</i>	<i>Categories</i>	<i>-----Allocated Intervention-----</i>		<i>Overall</i>
		<i>Placebo</i>	<i>Metformin</i>	
Delivery Method (n(%))	LSCS in labour	4 (23.5)	1 (9.1)	5 (17.9)
	LSCS pre labour	13 (76.5)	10 (90.9)	23 (82.1)
C-SECTION index pregnancy (n(%))	Yes	17 (100)	11 (100)	28 (100)
Primary C-SECTION in index pregnancy (n(%))	Yes	8 (47.1)	4 (36.4)	12 (42.9)
	No	9 (52.9)	7 (63.6)	16 (57.1)