Clinical trial results:
An Open-Label Randomized-Controlled Trial of Early Screening Test For Pre-Eclampsia and Growth restriction : A Pilot Study (TEST Study)

Summary

EudraCT number	2013-004241-17
Trial protocol	IE
Global end of trial date	11 April 2016

Results information

Result version number	v1 (current)
This version publication date	20 February 2019
First version publication date	20 February 2019
Summary attachment (see zip file)	Trial of feasibility and acceptability of routine low-dose aspirin versus Early Screening Test indicated aspirin for pre-eclampsia prevention (TEST study): a multicentre randomised controlled trial (Mone et al. - 2018 - Trial of feasibility and acceptability of routine.pdf) An open-label randomized-controlled trial of low dose aspirin with an early screening test for pre-eclampsia and growth restriction (TEST): Trial protocol (Mone et al. - 2016 - An open-label randomized-controlled trial of low d.pdf)

Trial information

Trial identification

Sponsor protocol code	TEST_PILOT_V1

Additional study identifiers

ISRCTN number	ISRCTN15191778
ClinicalTrials.gov id (NCT number)	NCT03674606
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University College Dublin
Sponsor organisation address	Belfield, Dublin, Ireland,
Public contact	Clinical Research Centre, University College Dublin, 353 017164593, rabia.hussain@ucd.ie
Scientific contact	Clinical Research Centre, University College Dublin, 353 017164593, rabia.hussain@ucd.ie

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 April 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 April 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To Determine :
1. Proportion of eligible women who agree to participate in the pilot study of a three arm randomised controlled trial
2. Compliance with the study protocol
3. Proportion of women in whom it was possible to obtain trans- abdominal uterine artery Doppler at 14 weeks gestation
4. Proportion of women with completed screening test that are issued the screening result within one week of the test.
5. The acceptability of undergoing a screening test and or of taking aspirin to women in their first pregnancy

Protection of trial subjects:

Safety Assessment
The following safety evaluations will be performed during the study: adverse event monitoring, vital signs, physical examination, and laboratory assessments.

Vulnerable subjects
Our study will not include incapacitated adults or minors in line with inclusion criteria therefore this area in non-applicable.

Overdose of study treatment
Overdose of a study treatment must first be reported to the sponsor in the first instance as a potential serious adverse event and recorded on the case report form. If double the dose is taken a period of self-observation is adequate. If more than two tablets are taken medical attention must be sought, vital signs checked and fetal monitoring performed with the proceeding dose omitted.

Concomitant therapy
Any medications that are considered necessary for the participant’s welfare and will not interfere with the study medication or pregnancy will be given at the discretion of the Investigator. A record of all medication taken by research participants in the month before visit 1 and concomitant medication a research participant takes throughout the study will be recorded on the appropriate page of the Case Report Form. Participants cannot partake in any other studies when involved in TEST.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 January 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Ireland: 557
Worldwide total number of subjects	557
EEA total number of subjects	557

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	557
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects (pregnant women only) were recruited in the period between 08/05/2014 and 01/02/2016 from the National Maternity Hospital, Dublin, Ireland and the Rotunda Hospital, Dublin, Ireland. Prospective consent for study participation was obtained.

Pre-assignment

Screening details:

Inclusion criteria:
Nulliparous, English-speaking women with singleton pregnancy. Excluded were first-trimester foetal abnormalities, major risk group for pre-eclampsia or fetal growth restriction for which low-dose aspirin was indicated, <18 year olds, concurrently participating in other trials and subjects with contraindications to aspirin.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

This was an open label trial, both the research participants and the investigators were aware of the trial arm to which the research participant had been randomly allocated.

Arms

Are arms mutually exclusive?	Yes
Arm title	Low--dose aspirin (Group 1)

Arm description:

Subjects in the routine low-dose aspirin group were randomised to be having standard antenatal care as well as to be taking low dose aspirin from booking (11--13 + 6 weeks) until 36--week gestation orally once daily, as prescribed by the research clinician. All subjects had a recruitment visit involving the first-trimester fetal medicine foundation screening test for pre-eclampsia, the results of which were not revealed to the subjects.

Arm type	Experimental
Investigational medicinal product name	Aspirin Acetylsalycylic Acid
Investigational medicinal product code	
Other name	Nu-Seals
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

75 mg taken once daily by oral ingestion from 1113 + 6 to 36 weeks gestation

Arm title	No aspirin (Group 2)

Arm description:

The no aspirin group were randomised to not be receiving aspirin but participation in all of the study ultrasound scans and blood tests were planned. All subjects had a recruitment visit involving the first-trimester fetal medicine foundation screening test for pre-eclampsia, the results of which were not revealed to the subjects.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Screen and treat (Group 3)

Arm description:

Subjects in the screen and treat arm were randomised to have the results from fetal medicine foundation screening test for pre-eclampsia prospectively revealed. Based upon the results of screening test components, the risk of developing any preeclampsia until 42--week gestation, set at a false positive rate of 5% was used to determine a subject at high risk. These subjects were subsequently

allocated to Group 3A if their risk >1:8 and were to commence a course of low-dose aspirin (75 mg taken once daily by oral ingestion from 1113 + 6 to 36 weeks gestation). Subjects allocated to Group 3B had a <1:8 risk of developing pre--eclampsia and were not to be taking aspirin.

Arm type	Experimental
Investigational medicinal product name	Aspirin Acetylsalycylic Acid
Investigational medicinal product code	
Other name	Nu-Seals
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

75 mg taken once daily by oral ingestion from 1113 + 6 to 36 weeks gestation

Number of subjects in period 1	Low--dose aspirin (Group 1)	No aspirin (Group 2)	Screen and treat (Group 3)
Started	185	187	185
Completed	179	183	184
Not completed	6	4	1
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	3	-	-
Protocol deviation	3	3	1

Period 2

Period 2 title	Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

This was an open label trial, both the research participants and the investigators were aware of the trial arm to which the research participant had been randomly allocated.

Arms

Are arms mutually exclusive?	Yes
Arm title	Low--dose aspirin (Group 1)

Arm description:

Subjects randomized to the routine low-dose aspirin group had standard antenatal care as well as taking low dose aspirin from booking (11--13 + 6 weeks) until 36--week gestation orally once daily, as prescribed by the research clinician. All subjects had a recruitment visit involving the first-trimester fetal medicine foundation screening test for pre-eclampsia, the results of which were not revealed to the subjects.

Arm type	Experimental
Investigational medicinal product name	Aspirin Acetylsalycylic Acid
Investigational medicinal product code	
Other name	Nu-Seals
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

75 mg taken once daily by oral ingestion from 1113 + 6 to 36 weeks gestation

Arm title	No aspirin (Group 2)

Arm description:

The no aspirin group did not receive aspirin but did participate in all of the study ultrasound scans and blood tests. All subjects had a recruitment visit involving the first-trimester fetal medicine foundation screening test for pre-eclampsia, the results of which were not revealed to the subjects.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	High-risk screen and treat (Group 3A)

Arm description:

This group contains subjects that were assessed to have a risk > 1:8 for pre-eclampsia on the scale of the fetal medicine foundation screening test. This subjects commenced a course of low-dose aspirin (75 mg taken once daily by oral ingestion from 1113 + 6 to 36 weeks gestation).

Arm type	Experimental
Investigational medicinal product name	Aspirin Acetylsalycylic Acid
Investigational medicinal product code	
Other name	Nu-Seals
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

75 mg taken once daily by oral ingestion from 1113 + 6 to 36 weeks gestation

Arm title	Low-risk screen and treat (Group 3B)

Arm description:

This group contains subjects assessed to have a risk < 1:8 for pre-eclampsia on the scale of the fetal medicine foundation screening test and were not given the IMP.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Low--dose aspirin (Group 1)	No aspirin (Group 2)	High-risk screen and treat (Group 3A)
Started	179	183	13
Completed	179	183	13

Number of subjects in period 2	Low-risk screen and treat (Group 3B)
Started	171
Completed	171

Baseline characteristics

Reporting groups	
Reporting group title	Low--dose aspirin (Group 1)

Reporting group description:

Subjects in the routine low-dose aspirin group were randomised to be having standard antenatal care as well as to be taking low dose aspirin from booking (11--13 + 6 weeks) until 36--week gestation orally once daily, as prescribed by the research clinician. All subjects had a recruitment visit involving the first-trimester fetal medicine foundation screening test for pre-eclampsia, the results of which were not revealed to the subjects.

Reporting group title	No aspirin (Group 2)

Reporting group description:

The no aspirin group were randomised to not be receiving aspirin but participation in all of the study ultrasound scans and blood tests were planned. All subjects had a recruitment visit involving the first-trimester fetal medicine foundation screening test for pre-eclampsia, the results of which were not revealed to the subjects.

Reporting group title	Screen and treat (Group 3)

Reporting group description:

Subjects in the screen and treat arm were randomised to have the results from fetal medicine foundation screening test for pre-eclampsia prospectively revealed. Based upon the results of screening test components, the risk of developing any preeclampsia until 42--week gestation, set at a false positive rate of 5% was used to determine a subject at high risk. These subjects were subsequently allocated to Group 3A if their risk >1:8 and were to commence a course of low-dose aspirin (75 mg taken once daily by oral ingestion from 1113 + 6 to 36 weeks gestation). Subjects allocated to Group 3B had a <1:8 risk of developing pre--eclampsia and were not to be taking aspirin.

Reporting group values	Low--dose aspirin (Group 1)	No aspirin (Group 2)	Screen and treat (Group 3)
Number of subjects	185	187	185
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	185	187	185
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	33	34	33
full range (min-max)	19 to 44	18 to 43	19 to 44
Gender categorical Units: Subjects			
Female	185	187	185
Male	0	0	0
Race Units: Subjects			
White	181	179	180
Black	1	2	0

Asian	3	6	5
Other	0	0	0
University education			
Number of subjects with a university education			
Units: Subjects			
Yes	136	143	152
No	49	44	33
Smoking			
Units: Subjects			
Yes	17	11	7
No	168	176	178
Subject's mother had pre-eclampsia			
Number of subjects whose mother had pre-eclampsia			
Units: Subjects			
Yes	7	10	10
No	178	177	175
Previous miscarriage			
Number of subjects who had a previous miscarriage			
Units: Subjects			
Yes	20	31	31
No	165	156	154
Body mass index			
Units: kg/m^2			
arithmetic mean	25.2	22.9	23.8
full range (min-max)	17.4 to 39.4	17.7 to 41.4	18.1 to 45.2
Gestational age			
Units: weeks			
arithmetic mean	12.9	12.9	12.9
full range (min-max)	11.1 to 13.9	11.1 to 13.9	11.3 to 13.9

Reporting group values	Total		
Number of subjects	557		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	557		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
full range (min-max)	-		
Gender categorical			
Units: Subjects			
Female	557		

Male	0		

Race Units: Subjects			
White	540		
Black	3		
Asian	14		
Other	0		
University education			
Number of subjects with a university education			
Units: Subjects			
Yes	431		
No	126		
Smoking Units: Subjects			
Yes	35		
No	522		
Subject's mother had pre-eclampsia			
Number of subjects whose mother had pre-eclampsia			
Units: Subjects			
Yes	27		
No	530		
Previous miscarriage			
Number of subjects who had a previous miscarriage			
Units: Subjects			
Yes	82		
No	475		
Body mass index Units: kg/m^2 arithmetic mean full range (min-max)	--		
Gestational age Units: weeks arithmetic mean full range (min-max)	--		

End points

End points reporting groups

Reporting group title	Low--dose aspirin (Group 1)

Reporting group description:

Subjects in the routine low-dose aspirin group were randomised to be having standard antenatal care as well as to be taking low dose aspirin from booking (11--13 + 6 weeks) until 36--week gestation orally once daily, as prescribed by the research clinician. All subjects had a recruitment visit involving the first-trimester fetal medicine foundation screening test for pre-eclampsia, the results of which were not revealed to the subjects.

Reporting group title	No aspirin (Group 2)

Reporting group description:

The no aspirin group were randomised to not be receiving aspirin but participation in all of the study ultrasound scans and blood tests were planned. All subjects had a recruitment visit involving the first-trimester fetal medicine foundation screening test for pre-eclampsia, the results of which were not revealed to the subjects.

Reporting group title	Screen and treat (Group 3)

Reporting group description:

Subjects in the screen and treat arm were randomised to have the results from fetal medicine foundation screening test for pre-eclampsia prospectively revealed. Based upon the results of screening test components, the risk of developing any preeclampsia until 42--week gestation, set at a false positive rate of 5% was used to determine a subject at high risk. These subjects were subsequently allocated to Group 3A if their risk >1:8 and were to commence a course of low-dose aspirin (75 mg taken once daily by oral ingestion from 1113 + 6 to 36 weeks gestation). Subjects allocated to Group 3B had a <1:8 risk of developing pre--eclampsia and were not to be taking aspirin.

Reporting group title	Low--dose aspirin (Group 1)

Reporting group description:

Subjects randomized to the routine low-dose aspirin group had standard antenatal care as well as taking low dose aspirin from booking (11--13 + 6 weeks) until 36--week gestation orally once daily, as prescribed by the research clinician. All subjects had a recruitment visit involving the first-trimester fetal medicine foundation screening test for pre-eclampsia, the results of which were not revealed to the subjects.

Reporting group title	No aspirin (Group 2)

Reporting group description:

The no aspirin group did not receive aspirin but did participate in all of the study ultrasound scans and blood tests. All subjects had a recruitment visit involving the first-trimester fetal medicine foundation screening test for pre-eclampsia, the results of which were not revealed to the subjects.

Reporting group title	High-risk screen and treat (Group 3A)

Reporting group description:

This group contains subjects that were assessed to have a risk > 1:8 for pre-eclampsia on the scale of the fetal medicine foundation screening test. This subjects commenced a course of low-dose aspirin (75 mg taken once daily by oral ingestion from 1113 + 6 to 36 weeks gestation).

Reporting group title	Low-risk screen and treat (Group 3B)

Reporting group description:

This group contains subjects assessed to have a risk < 1:8 for pre-eclampsia on the scale of the fetal medicine foundation screening test and were not given the IMP.

Primary: Eligible women that agree to participate in the study

End point title	Eligible women that agree to participate in the study[1]

End point description:

The proportion of eligible women that agree to participate in the study – this is reflected as a proportion of the number of women approached at the screening stage (feasibility).

End point type	Primary

End point timeframe:

1 year and 11 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No hypothesis tests were performed as the goals of this pilot trial were to provide estimates of feasibility and acceptability.

Statistical analyses

No statistical analyses for this end point

Primary: Adherence to aspirin based on diary cards

End point title	Adherence to aspirin based on diary cards[2]

End point description:

The number of subjects on low-dose aspirin that adhere to the intervention based on diary cards

End point type	Primary

End point timeframe:

1 year and 11 months

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No hypothesis tests were performed as the goals of this pilot trial were to provide estimates of feasibility and acceptability.

End point values	Low--dose aspirin (Group 1)	High-risk screen and treat (Group 3A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	13		
Units: subjects				
0% adherence	7	0		
<10% adherence	3	0		
50 - <70% adherence	5	1		
70 - <80% adherence	6	0		
80 - <90% adherence	21	2		
90 - <100% adherence	87	6		
100% adherence	45	4		
Unknown	5	0		

Statistical analyses

No statistical analyses for this end point

Primary: Adherence to aspirin based on tablet counts

End point title	Adherence to aspirin based on tablet counts[3]

End point description:

The number of subjects on low-dose aspirin that adhere to the intervention based on diary cards

End point type	Primary

End point timeframe:

1 year and 11 months

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No hypothesis tests were performed as the goals of this pilot trial were to provide estimates of feasibility and acceptability.

End point values	Low--dose aspirin (Group 1)	High-risk screen and treat (Group 3A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	13		
Units: subjects				
0% adherence	7	0		
<10% adherence	2	0		
50 - <70% adherence	3	0		
70 - <80% adherence	14	0		
80 - <90% adherence	26	0		
90 - <100% adherence	105	12		
100% adherence	18	1		
Unknown	4	0		

Statistical analyses

No statistical analyses for this end point

Primary: Attendance at study visits

End point title	Attendance at study visits[4]

End point description:

Number of subjects included in the trial that attend all study visits

End point type	Primary

End point timeframe:

1 year and 11 months

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No hypothesis tests were performed as the goals of this pilot trial were to provide estimates of feasibility and acceptability.

Statistical analyses

No statistical analyses for this end point

Primary: Satisfactory collection of all endpoints and variables

End point title	Satisfactory collection of all endpoints and variables[5]

End point description:

Number of subjects from whom all endpoints and variables were collected

End point type	Primary

End point timeframe:

1 year and 11 months

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No hypothesis tests were performed as the goals of this pilot trial were to provide estimates of feasibility and acceptability.

Statistical analyses

No statistical analyses for this end point

Primary: Study protocol violations

End point title	Study protocol violations[6]

End point description:

The number of protocol violations recorded

End point type	Primary

End point timeframe:

1 year and 11 months

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No hypothesis tests were performed as the goals of this pilot trial were to provide estimates of feasibility and acceptability.

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects from whom it was possible to obtain trans--abdominal uterine artery Doppler at 14 weeks gestation.

End point title	Number of subjects from whom it was possible to obtain trans--abdominal uterine artery Doppler at 14 weeks gestation.[7]

End point description:

End point type	Primary

End point timeframe:

1 year and 11 months

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No hypothesis tests were performed as the goals of this pilot trial were to provide estimates of feasibility and acceptability.

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of women with a completed fetal medicine foundation screening test who are issued the screening result within one week of having the test performed

End point title	Proportion of women with a completed fetal medicine foundation screening test who are issued the screening result within one week of having the test performed[8][9]

End point description:

End point type	Primary

End point timeframe:

1 year and 11 months

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No hypothesis tests were performed as the goals of this pilot trial were to provide estimates of feasibility and acceptability.
[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No hypothesis tests were performed as the goals of this pilot trial were to provide estimates of feasibility and acceptability.

End point values	Screen and treat (Group 3)			
Subject group type	Reporting group			
Number of subjects analysed	184			
Units: subjects				
Issued within one week	106			
Not issued within one week	78			

Statistical analyses

No statistical analyses for this end point

Secondary: The rate of pre-eclampsia as defined by the International Society for the Study of Pre-eclampsia in Pregnancy.

End point title	The rate of pre-eclampsia as defined by the International Society for the Study of Pre-eclampsia in Pregnancy.

End point description:

End point type	Secondary

End point timeframe:

1 year and 11 months

End point values	Low--dose aspirin (Group 1)	No aspirin (Group 2)	Screen and treat (Group 3)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	179	183	184	
Units: subjects				
Pre-eclampsia	8	7	7	

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of foetal growth restriction

End point title	Rate of foetal growth restriction

End point description:

End point type	Secondary

End point timeframe:

1 year and 11 months

End point values	Low--dose aspirin (Group 1)	No aspirin (Group 2)	Screen and treat (Group 3)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	179	183	184	
Units: cases				
Birthweight <10th centile	14	18	25	

Statistical analyses

No statistical analyses for this end point

Secondary: Spontaneous or iatrogenic delivery prior to 34 and 37 completed weeks gestation.

End point title	Spontaneous or iatrogenic delivery prior to 34 and 37 completed weeks gestation.

End point description:

End point type	Secondary

End point timeframe:

1 year and 11 months

End point values	Low--dose aspirin (Group 1)	No aspirin (Group 2)	Screen and treat (Group 3)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	179	183	184	
Units: cases				
Pre-term delivery <34 weeks	1	3	2	

Statistical analyses

No statistical analyses for this end point

Secondary: The rate of admission to the neonatal intensive care unit.

End point title	The rate of admission to the neonatal intensive care unit.

End point description:

End point type	Secondary

End point timeframe:

1 year and 11 months

End point values	Low--dose aspirin (Group 1)	No aspirin (Group 2)	Screen and treat (Group 3)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	179	183	184	
Units: admissions				
NICU admission	9	7	9	

Statistical analyses

No statistical analyses for this end point

Secondary: The rate of placental abruption, any reported death (stillbirth, neonatal or infant death) and small for gestational age infants.

End point title	The rate of placental abruption, any reported death (stillbirth, neonatal or infant death) and small for gestational age infants.

End point description:

End point type	Secondary

End point timeframe:

1 year and 11 months

End point values	Low--dose aspirin (Group 1)	No aspirin (Group 2)	Screen and treat (Group 3)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	179	183	184	
Units: cases				
Alive at 6 weeks	177	181	182	
Stillbirth	2	1	0	
Neonatal death	0	1	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Acceptability questionnaire: Aspirin was easy to swallow

End point title	Acceptability questionnaire: Aspirin was easy to swallow

End point description:

End point type	Secondary

End point timeframe:

1 year and 11 months

End point values	Low--dose aspirin (Group 1)	High-risk screen and treat (Group 3A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	11		
Units: subjects				
Strongly agree	151	10		
Agree	23	1		
Neither agree/Disagree	2	0		

Disagree	1	0		
Strongly disagree	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Acceptability questionnaire: With regards the screening test I found it

End point title	Acceptability questionnaire: With regards the screening test I found it

End point description:

End point type	Secondary

End point timeframe:

1 year and 11 months

End point values	Low--dose aspirin (Group 1)	No aspirin (Group 2)	High-risk screen and treat (Group 3A)	Low-risk screen and treat (Group 3B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	179	177	11	165
Units: subjects				
Useful	172	175	9	160
Neither useful/inconvenient	4	0	0	1
Inconvenient	3	2	2	4

Statistical analyses

No statistical analyses for this end point

Secondary: Acceptability questionnaire: Reason aspirin missed.

End point title	Acceptability questionnaire: Reason aspirin missed.

End point description:

End point type	Secondary

End point timeframe:

1 year and 11 months

End point values	Low--dose aspirin (Group 1)	High-risk screen and treat (Group 3A)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	7		
Units: subjects				
Reservations of taking aspirin	8	0		
Bleeding	5	0		
It caused stomach upset	7	0		
I forgot	108	7		
Other	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Acceptability questionnaire: In a future pregnancy I would

End point title	Acceptability questionnaire: In a future pregnancy I would

End point description:

End point type	Secondary

End point timeframe:

1 year and 11 months

End point values	Low--dose aspirin (Group 1)	No aspirin (Group 2)	High-risk screen and treat (Group 3A)	Low-risk screen and treat (Group 3B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	176	177	11	166
Units: subjects				
Take aspirin routinely	92	13	2	2
Take aspirin only if I was at risk	72	145	9	154
Neither	12	19	0	10

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From study enrollment until 28-days post-delivery.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Low--dose aspirin (Group 1)

Reporting group description:

Subjects randomized to the routine low-dose aspirin group had standard antenatal care as well as taking low dose aspirin from booking (11--13 + 6 weeks) until 36--week gestation orally once daily, as prescribed by the research clinician. All subjects had a recruitment visit involving the first-trimester fetal medicine foundation screening test for pre-eclampsia, the results of which were not revealed to the subjects.

Reporting group title	No aspirin (Group 2)

Reporting group description:

The no aspirin group did not receive aspirin but did participate in all of the study ultrasound scans and blood tests. All subjects had a recruitment visit involving the first-trimester fetal medicine foundation screening test for pre-eclampsia, the results of which were not revealed to the subjects.

Reporting group title	Screen and treat (Group 3)

Reporting group description:

For this arm the results from fetal medicine foundation screening test for pre-eclampsia were prospectively revealed. Based upon the results of screening test components, the risk of developing any preeclampsia until 42--week gestation, set at a false positive rate of 5% was used to determine a subject at high risk. These subjects were subsequently allocated to Group 3A if their risk >1:8 and commenced a course of low-dose aspirin (75 mg taken once daily by oral ingestion from 1113 + 6 to 36 weeks gestation). Subjects allocated to Group 3B had a <1:8 risk of developing pre--eclampsia and did not take aspirin.

Serious adverse events	Low--dose aspirin (Group 1)	No aspirin (Group 2)	Screen and treat (Group 3)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 179 (1.68%)	2 / 183 (1.09%)	2 / 184 (1.09%)
number of deaths (all causes)	2	2	2
number of deaths resulting from adverse events			
Pregnancy, puerperium and perinatal conditions			
Perinatal death	Additional description: Foetal death		
subjects affected / exposed	2 / 179 (1.12%)	2 / 183 (1.09%)	2 / 184 (1.09%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 2	0 / 2
Psychiatric disorders			
Suspected Pre-eclampsia			

subjects affected / exposed	1 / 179 (0.56%)	0 / 183 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Low--dose aspirin (Group 1)	No aspirin (Group 2)	Screen and treat (Group 3)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	85 / 179 (47.49%)	55 / 183 (30.05%)	61 / 184 (33.15%)
Congenital, familial and genetic disorders			
Congenital anomaly			
subjects affected / exposed	6 / 179 (3.35%)	5 / 183 (2.73%)	5 / 184 (2.72%)
occurrences (all)	6	5	5
Vaginal bleed			
subjects affected / exposed	27 / 179 (15.08%)	18 / 183 (9.84%)	12 / 184 (6.52%)
occurrences (all)	27	18	12
Surgical and medical procedures			
In-patient admission			
subjects affected / exposed	3 / 179 (1.68%)	5 / 183 (2.73%)	8 / 184 (4.35%)
occurrences (all)	3	5	8
Neonatal Unit Admission			
subjects affected / exposed	12 / 179 (6.70%)	7 / 183 (3.83%)	10 / 184 (5.43%)
occurrences (all)	12	7	10
Pregnancy, puerperium and perinatal conditions			
Abruption			
subjects affected / exposed	0 / 179 (0.00%)	0 / 183 (0.00%)	1 / 184 (0.54%)
occurrences (all)	0	0	1
Labour complication			
subjects affected / exposed	8 / 179 (4.47%)	3 / 183 (1.64%)	5 / 184 (2.72%)
occurrences (all)	8	3	5
Pregnancy induced hypertension			
subjects affected / exposed	6 / 179 (3.35%)	7 / 183 (3.83%)	7 / 184 (3.80%)
occurrences (all)	6	7	7
Post-partum bleeding			

subjects affected / exposed	21 / 179 (11.73%)	8 / 183 (4.37%)	11 / 184 (5.98%)
occurrences (all)	21	8	11
Small for gestational age			
subjects affected / exposed	4 / 179 (2.23%)	4 / 183 (2.19%)	2 / 184 (1.09%)
occurrences (all)	4	4	2
Threatened pre-term labour			
subjects affected / exposed	3 / 179 (1.68%)	2 / 183 (1.09%)	0 / 184 (0.00%)
occurrences (all)	3	2	0
Blood and lymphatic system disorders			
Haematoma			
subjects affected / exposed	1 / 179 (0.56%)	0 / 183 (0.00%)	0 / 184 (0.00%)
occurrences (all)	1	0	0
Anemia			
subjects affected / exposed	0 / 179 (0.00%)	3 / 183 (1.64%)	0 / 184 (0.00%)
occurrences (all)	0	3	0
Bruising			
subjects affected / exposed	2 / 179 (1.12%)	0 / 183 (0.00%)	0 / 184 (0.00%)
occurrences (all)	2	0	0
Epistaxis			
subjects affected / exposed	2 / 179 (1.12%)	0 / 183 (0.00%)	0 / 184 (0.00%)
occurrences (all)	2	0	0
General disorders and administration site conditions			
Trauma			
subjects affected / exposed	3 / 179 (1.68%)	0 / 183 (0.00%)	0 / 184 (0.00%)
occurrences (all)	3	0	0
Eye disorders			
Neonatal eye haematoma			
subjects affected / exposed	1 / 179 (0.56%)	1 / 183 (0.55%)	0 / 184 (0.00%)
occurrences (all)	1	1	0
Subconjunctival haemorrhage			
subjects affected / exposed	0 / 179 (0.00%)	1 / 183 (0.55%)	0 / 184 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Rectal bleed			
subjects affected / exposed	1 / 179 (0.56%)	0 / 183 (0.00%)	1 / 184 (0.54%)
occurrences (all)	1	0	1

Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	 3 / 179 (1.68%) 3	 0 / 183 (0.00%) 0	 2 / 184 (1.09%) 2
Endocrine disorders Gestational diabetes subjects affected / exposed occurrences (all)	 2 / 179 (1.12%) 2	 0 / 183 (0.00%) 0	 3 / 184 (1.63%) 3
Infections and infestations Infection subjects affected / exposed occurrences (all)	 7 / 179 (3.91%) 7	 6 / 183 (3.28%) 6	 10 / 184 (5.43%) 10

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported