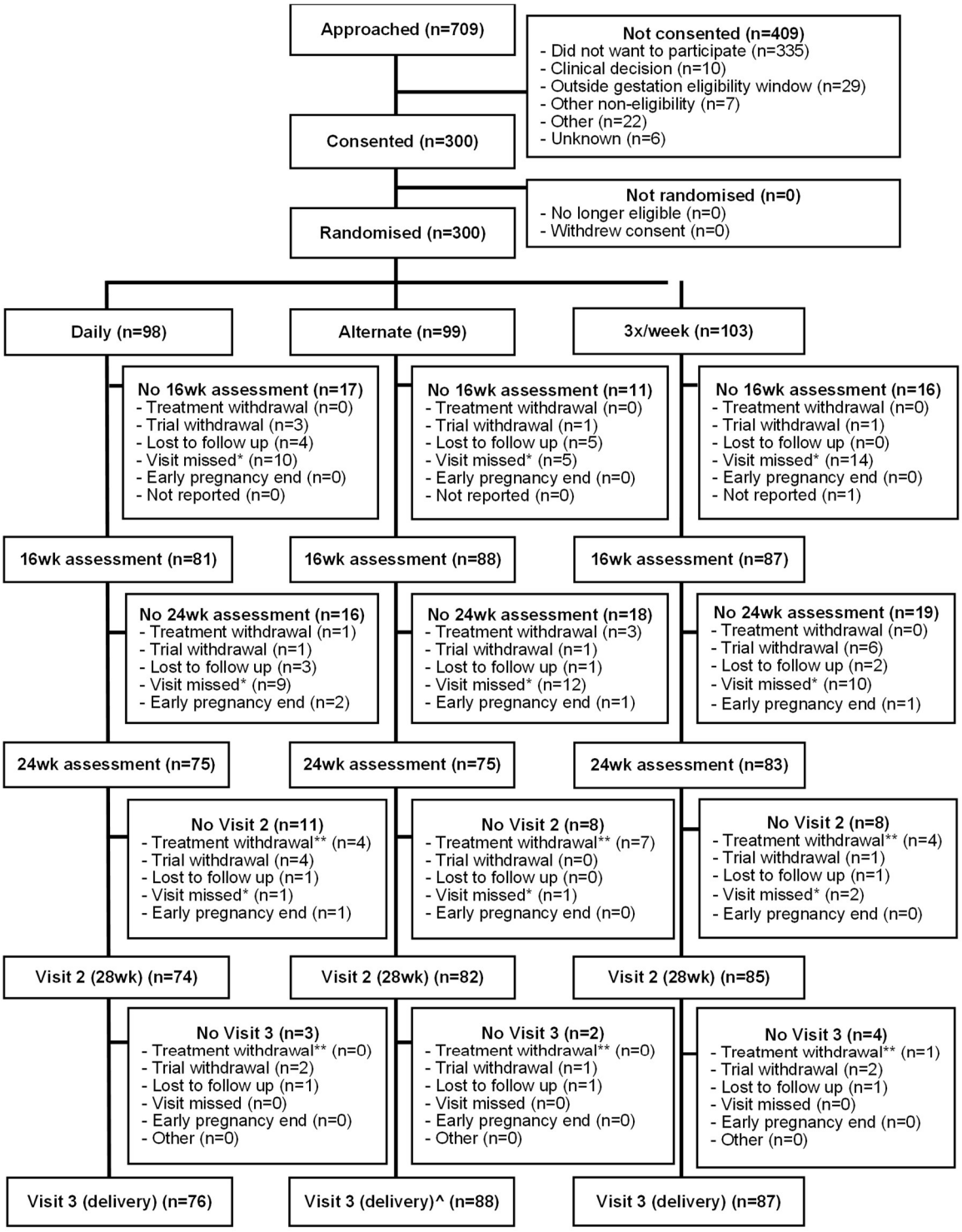
A pilot clinical trial to test the acceptability and feasibility of different doses of oral iron supplementation to prevent maternal anaemia

- **Participant Flow:**

Figure 1 Participant flow diagram



** Participants may miss visits and remain within the trial to attend other visits.*
*** If a participant withdraws from treatment, visit 2 and visit 3 are not considered as complete.*
^ One participant had a still birth at term and therefore is considered to have completed the trial.

- **Baseline Characteristics**:

Baseline Characteristics	**Total (n=300)**
Age (years)	**30.5 (27-34)**
Socioeconomic Status* (Quintile)	
1 (Most Deprived)	**54 (28.1)**
2	**57 (29.7)**
3	**25 (13.0)**
4	**31 (16.1)**
5 (Least Deprived)	**25 (13.0)**
Gestation (weeks)	**12.7 (12.3-13.1)**
Ethnicity	
White	**259 (86.3)**
Mixed	**4 (1.3)**
Asian OR Asian British	**27 (9.0)**
Black, African, Caribbean, Black British	**8 (2.7)**
Other	**2 (0.7)**
Smoker	**24 (8.0)**
Height (cm)	**164 (160-169)**
Weight (kg)	**70.5 (62-84)**
BMI (kg/m^2)	**26.5 (23.1-31.2)**
Parity	**1 (0-1)**
Hemoglobin (g/L)	**130 (125-136)**
Iron containing supplements being taken at baseline†	**63 (22.3)**
Known Haemoglobinopathy trait	**11 (3.7)**
Previous Anemia	
Outside of pregnancy	**30 (10.0)**
During pregnancy	**22 (7.3)**
Both	**2 (0.7)**
Comorbidity**	**38 (12.7)**
At least one previous termination	**39 (13.0)**
At least one previous miscarriage or still birth	**89 (29.7)**
At least one previous post-partum hemorrhage (>1/L)	**21 (7.0)**

** Estimated using the participant's postcode to determine their Index of Multiple Deprivation (2019). IMD data were not recorded for 108 participants due to consent not being obtained to collect their postcode.*
† There were 17 participants where baseline medication was indicated but it is unknown whether it contained iron. In total, of those taking iron supplements at baseline, 41 (65%) were still taking them at the end of study.
*** including hypertension, cardiac disease, thyroid disorders, renal disease, pre-existing diabetes, clotting disorders and anticoagulant therapy*
There were 2 missing haemoglobin values from participants at baseline assessment.
Data are number (%) for categorical variables, and median (Q1-Q3) for continuous variables

- **Outcome Measures:**

Summary of main outcomes of interest		
	Total (n=300)	
Adherence based on tablet count		
Number (%) of participants considered to be adherent	**130/228 (57.0)**	
Mean (SD) proportion of tablets taken as expected per participant	**82.5 (40.5)**	
Recruitment and protocol compliance		
	n/N (%)	**95% CI for %**
Approached women consented	300/709 (42.3)	(38.6-46.0)
Enrolled participants who completed all trial visits and data collection- n/N	**186/300**	
Maintenance of maternal haemoglobin		
Change in haemoglobin between randomisation and 28 weeks:		
n/N(%)	**230/268 (85.8)**	
Mean (SD)	**12 (8.0)**	
Proportion of participants maintaining haemoglobin above diagnostic thresholds, according to trimester at 28 weeks		
n/N (%)	**217/230 (94.3)**	
Side effects		
Black stools reported – n/N (%)		
Randomisation	**6/300 (2.0)**	
16 weeks	**105/256 (41.0)**	
24 weeks	**96/233 (41.2)**	
28 weeks	**100/249 (40.2)**	
Frequency and median* severity of side effects reported		
	N (%)	**Median**
Nausea		
Randomisation	**199 (66.6)**	**2**
16 weeks	**104 (40.9)**	**2**
24 weeks	**57 (24.6)**	**2**
28 weeks	**51 (20.6)**	**2**
Heartburn		
Randomisation	**76 (25.4)**	**2**
16 weeks	**82 (32.4)**	**2**
24 weeks	**107 (46.5)**	**2**
28 weeks	**123 (49.8)**	**2**

Summary of main outcomes of interest		
	Total (n=300)	
Vomiting		
Randomisation	**109 (36.5)**	**2**
16 weeks	**68 (26.8)**	**2**
24 weeks	**42 (18.2)**	**2**
28 weeks	**35 (14.2)**	**2**
Indigestion		
Randomisation	**53 (17.9)**	**2**
16 weeks	**48 (19.0)**	**2**
24 weeks	**55 (23.8)**	**2**
28 weeks	**66 (26.7)**	**2**
Constipation		
Randomisation	**91 (30.5)**	**2**
16 weeks	**102 (40.2)**	**2**
24 weeks	**92 (39.8)**	**2**
28 weeks	**109 (44.0)**	**2**
**Median of symptom scale (2=mild, 5=severe)*		

- **Adverse Events:**

Serious Adverse Events Summary		
Event	**Causality**	**Severity**
Abdominal pain, PV bleed and reduced fetal movements.	Not related	Other important medical events
Reduced fetal movements.	Not related	Requires hospitalisation or prolongs existing hospitalisation
Intra-uterine fetal death.	Not related	Requires hospitalisation or prolongs existing hospitalisation
Abdominal Pain	Not related	Requires hospitalisation or prolongs existing hospitalisation
Distal hypospadias.	Not related	Congenital abnormality or birth defect
Unilateral posterior horn ventriculomegaly.	Not related	Congenital abnormality or birth defect
Fetal ventriculomegaly.	Not related	Congenital abnormality or birth defect
Anhydramnios and Bilateral renal dysplasia.	Not related	Congenital abnormality or birth defect

Serious Adverse Events Summary

Event	Causality	Severity
Cleft palate.	Not related	Congenital abnormality or birth defect
Sustained Supraventricular tachycardia (SVT).	Not related	Requires hospitalisation or prolongs existing hospitalisation
Left ureteric stone.	Not related	Requires hospitalisation or prolongs existing hospitalisation
Admitted following a loss of consciousness, vomiting and possible cerebral event.	Not related	Requires hospitalisation or prolongs existing hospitalisation
Hydronephrosis.	Not related	Requires hospitalisation or prolongs existing hospitalisation
Pyelonephritis.	Not related	Requires hospitalisation or prolongs existing hospitalisation
Acute appendicitis.	Not related	Requires hospitalisation or prolongs existing hospitalisation
Hyperemesis.	Not related	Requires hospitalisation or prolongs existing hospitalisation
Pregnancy induced hypertension (PIH)	Not related	Requires hospitalisation or prolongs existing hospitalisation
Idiopathic Intracranial Hypertension and cardiomegaly and enlarged pulmonary vasculature.	Not related	Other important medical events
Down's Syndrome (Trisomy 21).	Not related	Congenital abnormality or birth defect
Pulmonary Embolism	Not related	Requires hospitalisation or prolongs existing hospitalisation
Mid-muscular Ventricular Septal Defect	Not related	Congenital abnormality or birth defect
Hypothyroidism.	Not related	Congenital abnormality or birth defect
Hyperemesis gravidarum.	Not related	Requires hospitalisation or prolongs existing hospitalisation
Double Aortic Arch found on scan at 20 weeks.	Not related	Congenital abnormality or birth defect