RESULTS

A total of 385 pregnant women were screened for this study. Using block randomisation, 148 were assigned to the two arms, with 74 women in each arm.

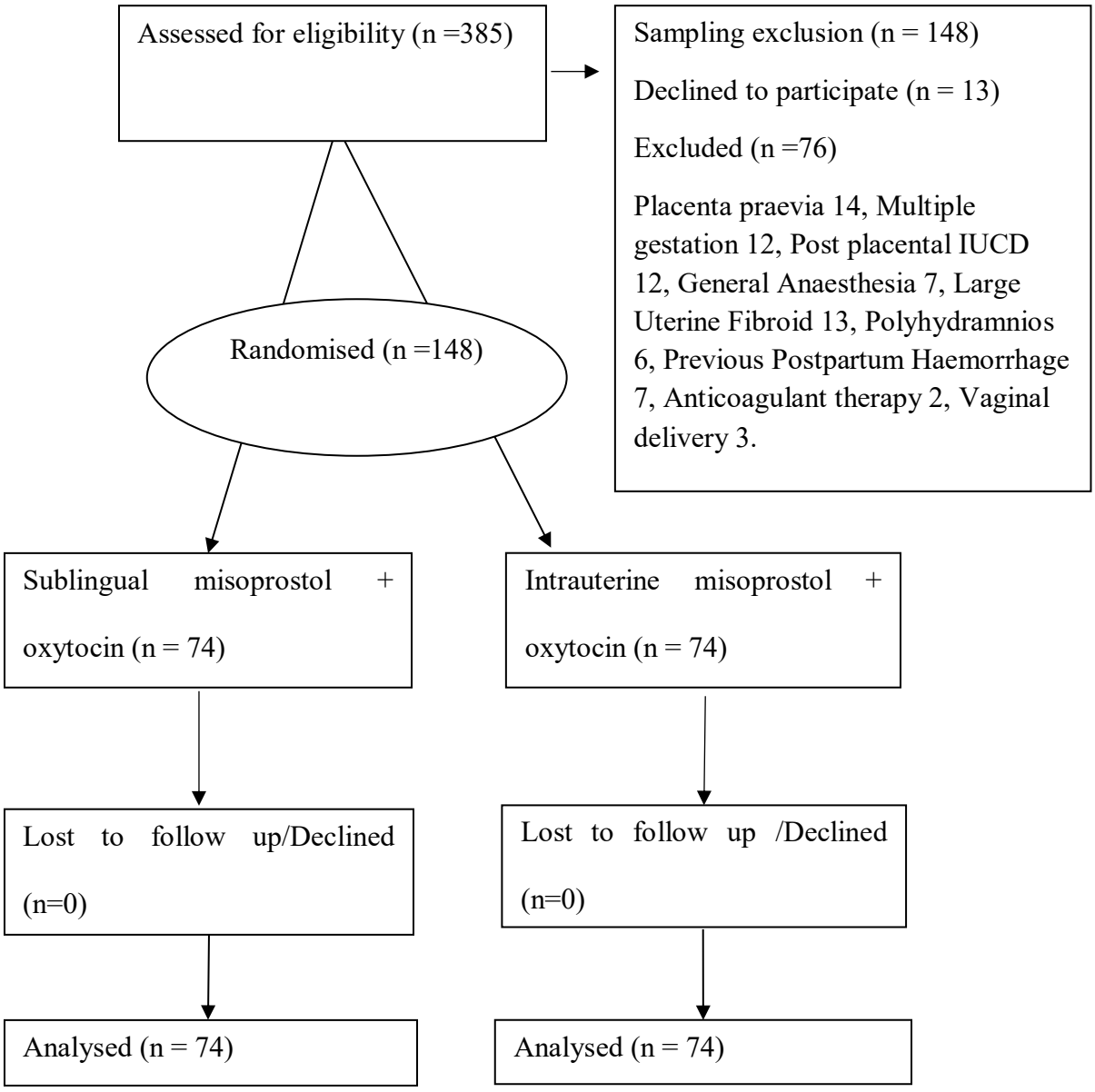

Figure 1: CONSORT Diagram of The Study Participants

SOCIODEMOGRAPHIC CHARACTERISTICS OF STUDY PARTICIPANTS (TABLE 1)

The age of the women ranged between 18 to 49 years. The mean age of women in the intrauterine misoprostol group (IUMO) was not statistically different from that of the sublingual group (SMO) (32.6 ± 4.9 vs 33.2 ± 5.0 years; p= 0.400). Women in the SMO group were significantly taller and heavier than those in the IUMO group (1.62 ± 0.06 vs 1.59 ± 0.08 m; p= 0.013 and 90.7 ± 20.6 vs 83.1 ± 17.2 kg, p= 0.017 respectively). However, there was no significant difference in the BMI between the two groups (34.5 ± 7.6 vs 32.8 ± 6.8 kg/m^2; p = 0.183). Most of the study participants 103 (87.2%) had a BMI ≥ 30.0 (69.6%).

Most of the women 129 (87.2%), were married and close to half of them, 66 (44.6%) had attained a tertiary level of education. Christianity was the predominant religion (116, 78.4%) of study participants followed by Islam (32, 21.6%). There were no statistically significant differences in the marital status, level of education, religion, or occupation of participants in the two groups. (Table 1).

Table 1: Sociodemographic characteristics of the study population

Variable	Intervention group		Total N=148	P-value
	IUMO N=74	SMO N=74		
Age (years) Mean ± SD	32.6 ±4.9	33.2 ±5.0	32.9 ±5.0	0.400*
Age group (years)				0.610
<25	4 (5.4)	6 (8.1)	10 (6.8)	
25-29	11 (14.9)	9 (12.2)	20 (13.5)	
30-34	32 (43.2)	26 (35.1)	58 (39.2)	
35+	27 (36.5)	33 (44.6)	60 (40.5)	
Height (m) Mean ± SD	1.59 ±0.08	1.62 ±0.06	1.61 ±0.07	0.013*
Weight (kg) Mean ± SD	83.1 ±17.2	90.7 ±20.6	86.9 ±19.3	0.017*
BMI (kg/m^2)	32.8 ± 6.8	34.5 ± 7.6	33.7 ± 7.2	0.183

BMI Group				0.654
Normal	7 (9.5)	5 (6.8)	12 (8.1)	
Overweight	18 (24.3)	15 (20.3)	33 (22.3)	
Obese	49 (66.2)	54 (73.0)	103 (69.6)	
Marital status				0.741
Single	3 (4.1)	5 (6.8)	8 (5.4)	
Married	65 (87.8)	64 (86.5)	129 (87.2)	
Co-habiting	6 (8.1)	5 (6.8)	11 (7.4)	
Educational level				0.597
No formal education	3 (4.1)	1 (1.4)	4 (2.7)	
Primary	3 (4.1)	1 (1.4)	4 (2.7)	
JHS	15 (20.3)	12 (16.2)	27 (18.2)	
SHS	22 (29.7)	25 (33.8)	47 (31.8)	
Tertiary	31 (41.9)	35 (47.3)	66 (44.6)	
Religion				0.318
Christian	55 (74.3)	61 (82.4)	116 (78.4)	
Muslim	19 (25.7)	13 (17.6)	32 (21.6)	
Occupation				0.116
Professional	9 (12.2)	21 (28.4)	30 (20.3)	
Semi-professional	11 (14.9)	10 (13.5)	21 (14.2)	
Artisan	20 (27.0)	13 (17.6)	33 (22.3)	
Trader	30 (40.5)	24 (32.4)	54 (36.5)	
Unemployed	4 (5.4)	6 (8.1)	10 (6.8)	
Partner's Occupation				0.428
Professional	18 (24.3)	15 (20.3)	33 (22.3)	
Semi-professional	11 (14.9)	18 (24.3)	29 (19.6)	
Artisan	21 (28.4)	22 (29.7)	43 (29.1)	
Trader	24 (32.4)	18 (24.3)	42 (28.4)	
Unemployed	0 (0.0)	1 (1.4)	1 (0.7)	

Independent t-test, the rest are chi-squared tests

OBSTETRIC HISTORY OF STUDY PARTICIPANTS (TABLE 2)

The obstetric history of participants was comparable in both groups. Almost all the study participants, 146 (98.6%), were booked patients and attended antenatal clinics in registered facilities in Ghana, with only two, 1.4% unbooked. There was no significant difference in the booking status of participants in the two groups.

There were no significant differences between the two groups in median gravidity and parity or in the proportion of nulliparous women; a majority of study participants, 125 (84.5%), were multiparous. There was no significant difference between the two groups in the number of previous abortions. The mean gestational age at delivery in the IUMO group, 38.0 ± 1.0 weeks, was not significantly different from that of the SMO group, 38.1 ± 1.0 weeks (p = 0.417). The most identified indication for elective caesarean section in both groups was a history of previous caesarean section, which occurred in identical proportions (i.e. 56, 75.7% of participants) in each group, with the number of previous caesarean sections in the two groups also not being significantly different. There were no significant differences in the occurrence of important indications such as hypertensive disorders in pregnancy, gestational diabetes, previous myomectomy, sickle cell disease and HIV infection.

Table 2: Obstetric history of study participants

Variable	Intervention group		Total N=148	P-value
	IUMO N=74	SMO N=74		
Booking status				0.497
Booked	72 (97.3)	74 (100.0)	146 (98.6)	
Unbooked	2 (2.7)	0 (0.0)	2 (1.4)	
Gravidity: Median (interquartile range)	3 (2-4)	3 (2-4)	3 (2-5)	0.992#

Parity: Median (interquartile range)	1 (1-2)	1 (1-2)	1 (1-2)	0.609#
Parity				0.651
Nulliparous	10 (13.5)	13 (17.6)	23 (15.5)	
Multiparous	64 (86.5)	61 (82.4)	125 (84.5)	
Number of previous abortions				0.839
1	14 (50.0)	19 (57.6)	33 (54.1)	
2	9 (32.1)	9 (27.3)	18 (29.5)	
3+	5 (17.9)	5 (15.2)	10 (16.4)	
Gestational age at Caesarean delivery (weeks), mean ± SD	38.0 ±1.0	38.1 ±1.0	38.1 ±1.0	0.417*
Indication for Elective Caesarean Section≈				
Hypertensive disorders	9 (12.2)	14 (18.9)	23 (15.5)	0.364
Gestational diabetes	19 (25.7)	20 (27.0)	39 (26.4)	0.999
Uterine fibroids	6 (8.1)	12 (16.2)	18 (12.2)	0.208
Sickle cell disease	3 (4.1)	3 (4.1)	6 (4.1)	0.999
Previous Myomectomy	6 (8.1)	7 (9.5)	13 (8.8)	0.999
Previous Caesarean Section	56 (75.7)	56 (75.7)	112 (75.7)	0.999
Malpresentation	8 (10.8)	2 (2.7)	10 (6.8)	0.097
Others	7 (9.5)	5 (6.8)	12 (8.1)	0.765
Number of previous Caesarean deliveries				0.115
1	33 (58.9)	28 (50.0)	61 (54.5)	
2	13 (23.2)	22 (39.3)	35 (31.3)	
3+	10 (17.9)	6 (10.7)	16 (14.3)	

Independent t-test, #Mann-Whitney U test, the rest are chi-squared tests, ≈some had multiple indications for elective caesarean section

INTRAOPERATIVE EVENTS OF STUDY PARTICIPANTS (TABLE 3)

There was no statistically significant difference in the intraoperative characteristics of both groups. The mean temperature before misoprostol administration was 36.3 ± 0.3 vs 36.4 ± 0.3, p 0.589 in IUMO and SMO groups, respectively. Spinal anaesthesia was the most common form of anaesthesia used (100% in IUMO group and 97.3% in SMO group, p =0.497). Two participants in the SMO group received a combined spinal epidural for post-operative pain management.

Pfannenstiel incision was the most common skin incision performed in both groups (72, 97.3% in IUMO vs 71, 95.9% in SMO, p = 0.999). Transverse lower uterine segment incision was performed for all the participants in the IUMO group, while one participant in the SMO group had an inverted "T" uterine incision on account of dense adhesions in a previous myomectomy.

There was no significant difference in the mean birth weights (3223.9 ± 520.7 vs 3221.1 ± 586.1 grams, p = 0.976), duration of surgery (50.5 (40 - 65) vs 54.0 (42 - 75) mins, p = 0.274) and rank of surgeon between the two groups.

Table 3: Intraoperative events of participants in the two groups

Variable	Intervention group		χ^2/t/Z	P-value
	IUMO N=74	SMO N=74		
Pre-misoprostol temperature (ºC), mean ± SD	36.3±0.3	36.4±0.3	-0.541	0.589*
Type of Anaesthesia			2.027	0.497
Spinal	74 (100.0)	72 (97.3)		
Combined spinal-epidural	0 (0.0)	2 (2.7)		
Skin incision			0.207	0.999
Pfannenstiel	72 (97.3)	71 (95.9)		
Sub umbilical midline	2 (2.7)	3 (4.1)		
Type of uterine incision			1.007	0.999
Transverse lower uterine segment	74 (100.0)	73 (98.6)		
Inverted "T"	0 (0.0)	1 (1.4)		
Birthweight (grams) Mean ± SD	3223.9 ±520.7	3221.1 ±586.1	0.031	0.976*

APGAR 1min: <7 ≥7	4 (5.4) 70 (94.6)	7 (9.5) 67 (90.5)	0.884	0.533
APGAR 5min: <7 ≥7	1 (1.4) 73 (98.6)	2 (2.7) 72 (97.3)	0.340	0.999
Duration of surgery (mins) Median (interquartile range)	50.5 (40-65)	54.0 (42-75)	51	0.274#
Rank of surgeon				0.961
Junior resident	24 (32.4)	25 (33.8)	49 (33.1)	
Senior resident	41 (55.4)	41 (55.4)	82 (55.4)	
Consultant	9 (12.2)	8 (10.8)	17 (11.5)	

Independent t-test, #Mann-Whitney U test, the rest are chi-squared tests

The intraoperative, post-operative and overall blood loss were not normally distributed. There was no statistically significant difference in the median intraoperative blood loss (722.5 vs 610.5ml, p = 0.861), 3-hour postoperative blood loss (50.0 vs 57.5ml, p = 0.112) and overall blood loss in both groups. (787.5 vs 772.0ml, p = 0.687) (Table 4).

Table 4: Blood loss of study participants

Variable	Intervention group		Z	P-value
	IUMO N=74	SMO N=74		
Blood Loss, ml				
Intraoperative blood loss, Median (interquartile range)	722.5 (450-907)	610.5 (465-946)	-0.174	0.861#
3 hours post-operative blood loss, Median (interquartile range)	50.0 (20-90)	57.5 (35-124.0)	-1.590	0.112#
Overall blood loss (Intraoperative + 3hours post-operative), Median (interquartile range)	787.5 (512-981.0)	772.0 (552-1070.9)	-0.403	0.687#

#Mann-Whitney U test

PREOPERATIVE AND POSTOPERATIVE HAEMATOCRIT LEVELS OF STUDY PARTICIPANTS (TABLE 5)

There was no significant difference in the mean pre-operative haematocrit levels (34.0 ± 3.4 vs 34.2 ± 3.7 %; p= 0.795) and mean post-operative haematocrit levels (31.2 ±3.7 vs 30.9 ±4.0 %; p= 0.694) of both groups. There was also no significant difference in the mean change in pre-operative and post-operative haematocrit of both groups (2.8 ±2.7 vs 3.2 ±2.5 %; p= 0.349). (Table 5)

Table 5: Preoperative and Postoperative haematocrit level of participants

Variable	Intervention group		Total N=148	t	P-value
	IUMO N=74	SMO N=74			
Pre-operative haematocrit (%)	34.0 ±3.4	34.2 ±3.7	34.1 ±3.5	-0.260	0.795*
Post-operative haematocrit (%)	31.2 ±3.7	30.9 ±4.0	31.1 ±3.9	-0.394	0.694*
Mean Change in haematocrit (%)	2.8 ±2.7	3.2 ±2.5	3.0 ±2.6	-0.939	0.349*

Independent t-test

Primary postpartum haemorrhage was defined as blood loss of more than 1000ml within the first 24 hours of delivery, which was calculated using the modified Gross formula occurred in 8 (10.8%) intrauterine misoprostol participants and 12 (16.2%) sublingual participants; the difference was however, not statistically significant (RR 0.78, 95% CI 0.44 – 1.37, p = 0.471). (Table 6)

Table 6: Incidence of Primary Postpartum Haemorrhage

Variable	Intervention group		Total N=148	P-value
	IUMO N=74	SMO N=74		
Primary PPH *				
Actual Blood Loss in 24 hours >1000ml (%)	8 (10.8%)	12 (16.2%)	20 (13.5)	0.471
Relative Risk (RR) of PPH	0.78 (95% CI 0.44 – 1.37)			

** Primary Postpartum haemorrhage calculated using the Gross formula*

POSTPARTUM HAEMORRHAGE INTERVENTIONS IN THE STUDY PARTICIPANTS (TABLE 7)

There was no statistically significant difference in PPH interventions in the two groups. Almost all the study participants (95.9% vs 97.3%, p = 0.999) received additional PPH intervention, with oxytocin infusion given to 91.9% of participants in each group (p = 0.999). Blood transfusion was given to more participants in the sublingual group than in the intrauterine group; this difference was, however, not statistically significant (5 vs 2, p= 0.442). A caesarean hysterectomy was performed on one participant in the sublingual group who had a morbidly adherent placenta.

Table 7: Postpartum Haemorrhage Interventions between the two groups

Variable	Intervention group		Total N=148	P-value
	IUMO N=74 (%)	SMO N=74 (%)		
PPH Intervention	71 (95.9)	72 (97.3)	143 (96.6)	0.999
Oxytocin infusion*	68 (91.9)	68 (91.9)	136 (91.9)	0.999
Ergometrine	7 (9.5)	5 (6.8)	12 (8.1)	0.765
Carbetocin	3 (4.1)	3 (4.1)	6 (4.1)	0.999
Tranexamic acid*	59 (79.7)	60 (81.1)	119 (80.4)	0.999
Compression sutures	2 (2.7)	1 (1.4)	3 (2.0)	0.999
Hysterectomy at primary surgery	0 (0.0)	1 (1.4)	1 (0.7)	0.999
Blood transfusion	2 (2.7)	5 (6.8)	7 (4.7)	0.442
Others	2 (2.7)	0 (0.0)	2 (1.4)	0.497
≤ 2(*) PPH interventions	63 (88.7)	64 (88.9)	127 (88.8)	0.999
> 2(*) PPH interventions	8 (11.3)	8 (11.1)	16 (11.2)	

Some received multiple PPH interventions

SIDE EFFECTS PROFILE OF THE STUDY PARTICIPANTS (TABLE 8)

The incidence of fever was significantly lower in the intrauterine group compared to the sublingual group (5, 6.8% vs 52, 70.3%, RR 0.12 [955 CI 0.05 – 0.27], p = <0.001). The mean temperatures at 30, 60, 90, 120 and 180 minutes were significantly higher in the sublingual group (p<0.001), and the highest temperatures occurred 2 hours after sublingual misoprostol administration.

The proportion and the duration of shivering were significantly lower in the intrauterine group compared to the sublingual group (36.3 vs 91.9%, RR 0.32 [95% CI 0.23 – 0.45], p <0.001, 30.0 vs 61.5 minutes; p = <0.001, respectively). Shivering women in the SMO group were significantly more likely to require an additional device, the Bair Hugger, in the management of their shivering (24.5% vs 3.8%, p =0.035).

Although the proportion of women who had vomiting in the SMO group was higher than in the IUMO group, the difference was not statistically significant (20.3% vs 10.8%; p 0.173). In addition, there was no significant difference in the frequency of vomiting episodes between the two groups (p 0.866).

Table 8: Side effects profile of study participants

Variable	Intervention group		Total N=148	χ^2	P-value
	IUMO N=74	SMO N=74			
Fever	5 (6.8%)	52 (70.3%)	57 (38.5%)	63.029	**<0.001**
Relative Risk (RR) of Fever	0.12 95% CI (0.05 – 0.27)				
Immediate Post-operative Temperatures (°c), Mean ± SD					
at 30 mins	35.5 ±0.7	36.2 ±1.1	35.9 ±1.0		**<0.001**
at 60 mins	36.0 ±0.6	37.3 ±1.1	36.6 ±1.1		**<0.001**
at 90 mins	36.2 ±0.7	37.8 ±1.0	37.0 ±1.2		**<0.001**
at 120 mins	36.5 ±0.7	**38.0 ±0.8**	37.3 ±1.1		**<0.001**
at 180 mins	36.7 ±0.8	37.7 ±1.0	37.2 ±1.0		**<0.001**

Number experiencing shivering	27 (36.5%)	68 (91.9%)	95 (64.2%)	49.412	**<0.001**
Relative Risk (RR) of shivering	0.32 95% CI (0.23-0.45)				
Duration of shivering, minutes. Median (interquartile range)	30.0 (20-45)	61.5 (40-81.5)	50 (30-80)	-3.931	**<0.001**
Number needing treatment For Shivering	26 (96.3%)	66 (97.1%)	92 (96.8%)		0.999
Blanket	25 (96.2%)	48 (72.7%)	73 (79.3%)	6.247	**0.011**
Bair hugger	0 (0.0%)	2 (3.0%)	2 (2.2%)	0.805	0.999
Both Blanket and Bair Hugger	1 (3.8%)	16 (24.5%)	17 (18.5%)	5.151	**0.034**
Vomiting	8 (10.8%)	15 (20.3%)	23 (15.5%)	2.522	0.173
Relative Risk (RR) of vomiting	0.66 95% CI (0.37 – 1.18)				
No. of times vomited, n (interquartile range)	1 (1-1.5)	1 (1-2)	1 (1-2)	-0.169	0.866#