



Prevention and treatment of postpartum haemorrhage

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Postpartum haemorrhage is a leading cause of maternal morbidity and mortality

Primary Cause	N	%
❖ Antepartum haemorrhage	27	4.8
➤ Abruptio placentae	12	
➤ Abruptio placentae with hypertension	7	
➤ Placenta praevia	4	
➤ Other	4	
❖ Postpartum haemorrhage	48	8.5
➤ Retained placenta; placenta accreta, increta or percreta	12	
➤ Uterine atony - due to uterine over distension (multiple pregnancy, polyhydramnios)	4	
➤ Uterine atony due to prolonged labour	10	
➤ Ruptured uterus – with previous caesarean section	6	
➤ Ruptured uterus – without previous caesarean section	3	
➤ Inverted uterus	1	
➤ Other uterine trauma – specify	12	

SAVING MOTHERS. Report on Confidential Enquiries into Maternal Deaths in South Africa 1998.

Chairman: Prof. Jack Moodley, Editor of Report: Prof. Bob Pattinson



WHO morbidity review

Condition		Reference	No. women	Year	Population characteristics	WHO and other Data Banks	Available figures for developed countries
Severe PPH	All	PIS ²³	456 889	1985-1997	Hospital-based database in Latinamerica	5.3%	0.67% ²⁴
	≥1000 ml	MISO ^b	18 442	1998-1999	9 hospitals in all regions	3-4%	
		MOMA ¹⁴	20 326	1994-1996	Population based urban in 6 countries West Africa	1.7%	
		WHO / Indonesia ¹⁹	16 308	1998-1999	4 districts in Lombok island	3.3%	
	≥2000 ml	MISO ¹¹	18 530	1998-1999	9 hospitals in all regions	0.13-.0.17%	
Retained placenta		MISO ^b	18 453	1998-1999	9 hospitals in all regions	2.3-2.4%	
		WHO / Indonesia ¹⁹	16 308	1998-1999	4 districts in Lombok island	1.5%	



Assessment of blood loss after delivery

- Definition (500, 1000 ml)
- Visual estimation
 - Underestimates blood loss
 - More with increased blood loss
- Measurement
 - Several methods exist with varying precision and practicality
 - WHO protocol for measurement of blood loss used in the Misoprostol Trial



WHO protocol for measurement of blood loss

- Start immediately after cord cut
- Change dirty linen and receivers
- Put flat bedpan or bucket
- Collect all blood, clots, swabs soaked with blood
- Transfer all the contents to the measuring jar provided and measure



Strategies to reduce postpartum blood loss

- Active management
 - which uterotonic?
- Restrictive episiotomy
- Retained placenta
- Other measures

01 Active vs expectant management (all women)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 PPH clinically estimated blood loss greater than or equal to 500mls	4	6284	Relative Risk [Fixed] [95% CI]	0.38 [0.32, 0.46]
02 Severe PPH clinically estimated blood loss greater than or equal to 1000mls	4	6284	Relative Risk [Fixed] [95% CI]	0.33 [0.21, 0.51]
03 Mean blood loss (mls)	2	2941	WMD [Fixed] [95% CI]	-79.327 [-94.288, -64.367]
04 Maternal Hb < 9 g/dl 24 - 48 hours post partum	4	4255	Relative Risk [Fixed] [95% CI]	0.40 [0.29, 0.55]
05 Blood transfusion	5	6477	Relative Risk [Fixed] [95% CI]	0.34 [0.22, 0.53]
06 Iron tablets during the puerperium	1	1447	Relative Risk [Fixed] [95% CI]	0.60 [0.49, 0.74]
07 Therapeutic oxytocics	5	6477	Relative Risk [Fixed] [95% CI]	0.20 [0.17, 0.25]
08 Third stage > 20 minutes	3	4637	Relative Risk [Fixed] [95% CI]	0.15 [0.12, 0.19]
09 Third stage > 40 minutes	3	4636	Relative Risk [Fixed] [95% CI]	0.18 [0.14, 0.24]
10 Mean length of third stage (minutes)	3	4589	WMD [Fixed] [95% CI]	-9.766 [-10.004, -9.529]
11 Manual removal of placenta	5	6477	Relative Risk [Fixed] [95% CI]	1.21 [0.82, 1.78]
12 Subsequent surgical evacuation of retained products of conception	3	4636	Relative Risk [Fixed] [95% CI]	0.74 [0.43, 1.28]
13 Diastolic blood pressure > 100 mmHg between delivery of baby and discharge from labour ward	3	4636	Relative Risk [Fixed] [95% CI]	3.46 [1.68, 7.09]
14 Vomiting between delivery of baby and discharge from labour ward	3	3407	Relative Risk [Fixed] [95% CI]	2.19 [1.68, 2.86]
15 Nausea between delivery of baby and discharge from labour ward	3	3407	Relative Risk [Fixed] [95% CI]	1.83 [1.51, 2.23]
16 Headache between delivery of baby and discharge from labour ward	3	3405	Relative Risk [Fixed] [95% CI]	1.97 [1.01, 3.82]
17 Maternal pain during third stage of labour	2	391	Relative Risk [Fixed] [95% CI]	1.01 [0.55, 1.86]
18 Maternal dissatisfaction with third stage management	1	1466	Relative Risk [Fixed] [95% CI]	0.56 [0.35, 0.90]

Oxytocin vs. syntometrine

01 syntometrine vs oxytocin (any dose)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 blood loss >500 ml	6	10091	Peto OR [95% CI]	0.74 [0.65, 0.85]
02 blood loss > 1000ml	4	6963	Peto OR [95% CI]	0.79 [0.59, 1.06]
03 manual removal of the placenta	5	8341	Peto OR [95% CI]	1.04 [0.80, 1.34]
04 blood transfusion	3	6502	Peto OR [95% CI]	1.25 [0.77, 2.05]
05 elevation diastolic blood pressure	3	6495	Peto OR [95% CI]	2.81 [1.67, 4.74]
06 vomiting	3	6495	Peto OR [95% CI]	4.86 [3.99, 5.92]
07 apgar score <6 @ 5 min.	2	5511	Peto OR [95% CI]	1.01 [0.67, 1.51]
08 jaundice	2	5511	Peto OR [95% CI]	0.98 [0.85, 1.13]
09 not breastfed at discharge	1	3483	Peto OR [95% CI]	1.10 [0.91, 1.33]

02 syntometrine vs oxytocin (5iu)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 blood loss >500 ml	3	3089	Peto OR [95% CI]	0.36 [0.23, 0.55]
02 blood loss > 1000ml	1	461	Peto OR [95% CI]	0.14 [0.00, 6.85]
03 manual removal of the placenta	2	1839	Peto OR [95% CI]	1.54 [0.81, 2.92]
04 blood transfusion			No numerical data	
05 elevation of diastolic blood pressure			No numerical data	
06 vomiting			No numerical data	
07 apgar score <6 @ 5 min.			No numerical data	
08 jaundice			No numerical data	
09 not breastfed at discharge			No numerical data	

03 syntometrine vs oxytocin (10iu)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 blood loss >500 ml	4	8002	Peto OR [95% CI]	0.81 [0.70, 0.94]
02 blood loss > 1000ml	3	6502	Peto OR [95% CI]	0.80 [0.60, 1.07]
03 manual removal of the placenta	3	6502	Peto OR [95% CI]	0.96 [0.73, 1.27]
04 blood transfusion	3	6502	Peto OR [95% CI]	1.25 [0.77, 2.05]
05 elevation of diastolic blood pressure	3	6495	Peto OR [95% CI]	2.81 [1.67, 4.74]
06 vomiting	3	6495	Peto OR [95% CI]	4.86 [3.99, 5.92]
07 apgar < 6 @ 5 min	2	5511	Peto OR [95% CI]	1.00 [0.67, 1.50]
08 jaundice	2	5511	Peto OR [95% CI]	0.98 [0.85, 1.13]
09 not breastfed at discharge	1	3483	Peto OR [95% CI]	1.10 [0.91, 1.33]

WHO multicentre randomised trial of misoprostol in the management of the third stage of labour

*A Metin Gülmezoglu, José Villar, Nguyen Thi Nhu Ngoc, Gilda Piaggio, Guillermo Carroll, Lekan Adetoro, Hany Abdel-Aleem, Linan Cheng, G Justus Hofmeyr, Plisake Lumbiganon, Christian Unger, Walter Prendiville, Alain Pinol, Diana Elbourne, Hazem El-Refaey, Kenneth F Schulz, for the WHO Collaborative Group To Evaluate Misoprostol in the Management of the Third Stage of Labour**

Summary

Background Postpartum haemorrhage is a leading cause of maternal morbidity and mortality. Active management of the third stage of labour, including use of a uterotonic agent, has been shown to reduce blood loss. Misoprostol (a prostaglandin E1 analogue) has been suggested for this purpose because it has strong uterotonic effects, can be given orally, is inexpensive, and does not need refrigeration for storage. We did a multicentre, double-blind, randomised controlled trial to determine whether oral misoprostol is as effective as oxytocin during the third stage of labour.

Methods In hospitals in Argentina, China, Egypt, Ireland, Nigeria, South Africa, Switzerland, Thailand, and Vietnam, we randomly assigned women about to deliver vaginally to receive 600 µg misoprostol orally or 10 IU oxytocin intravenously or intramuscularly, according to routine practice, plus corresponding identical placebos. The medications were administered immediately after delivery as part of the active management of the third stage of labour. The primary outcomes were measured postpartum blood loss of 1000 mL or more, and the use of additional uterotonics without an unacceptable level of side-effects. We chose an upper limit of a 35% increase in the risk of

blood loss of 1000 mL or more as the margin of clinical equivalence, which was assessed by the confidence interval of the relative risk. Analysis was by intention to treat.

Findings 9264 women were assigned misoprostol and 9266 oxytocin. 37 women in the misoprostol group and 34 in the oxytocin group had emergency caesarean sections and were excluded. 366 (4%) of women on misoprostol had a measured blood loss of 1000 mL or more, compared with 263 (3%) of those on oxytocin (relative risk 1.39 [95% CI 1.19–1.63], $p < 0.0001$). 1398 (15%) women in the misoprostol group and 1002 (11%) in the oxytocin group required additional uterotonics (1.40 [1.29–1.51], $p < 0.0001$). Misoprostol use was also associated with a significantly higher incidence of shivering (3.48 [3.15–3.84]) and raised body temperature (7.17 [5.67–9.07]) in the first hour after delivery.

Interpretation 10 IU oxytocin (intravenous or intramuscular) is preferable to 600 µg oral misoprostol in the active management of the third stage of labour in hospital settings where active management is the norm.

Lancet 2001; **358**: 689–95

See Commentary page 682

*Other members listed at end of paper



Primary outcomes

- Measured blood loss \geq 1000 mls.
 - Additional uterotonic
-
- Secondary outcomes
 - Measured blood loss \geq 500 mls.
 - Blood transfusion
 - Manual removal of the placenta
 - Late haemorrhage (after 1st hour)
 - Treatments for severe haemorrhage (hysterectomy, bimanual compression, etc.)



Primary outcomes

Relative Risk

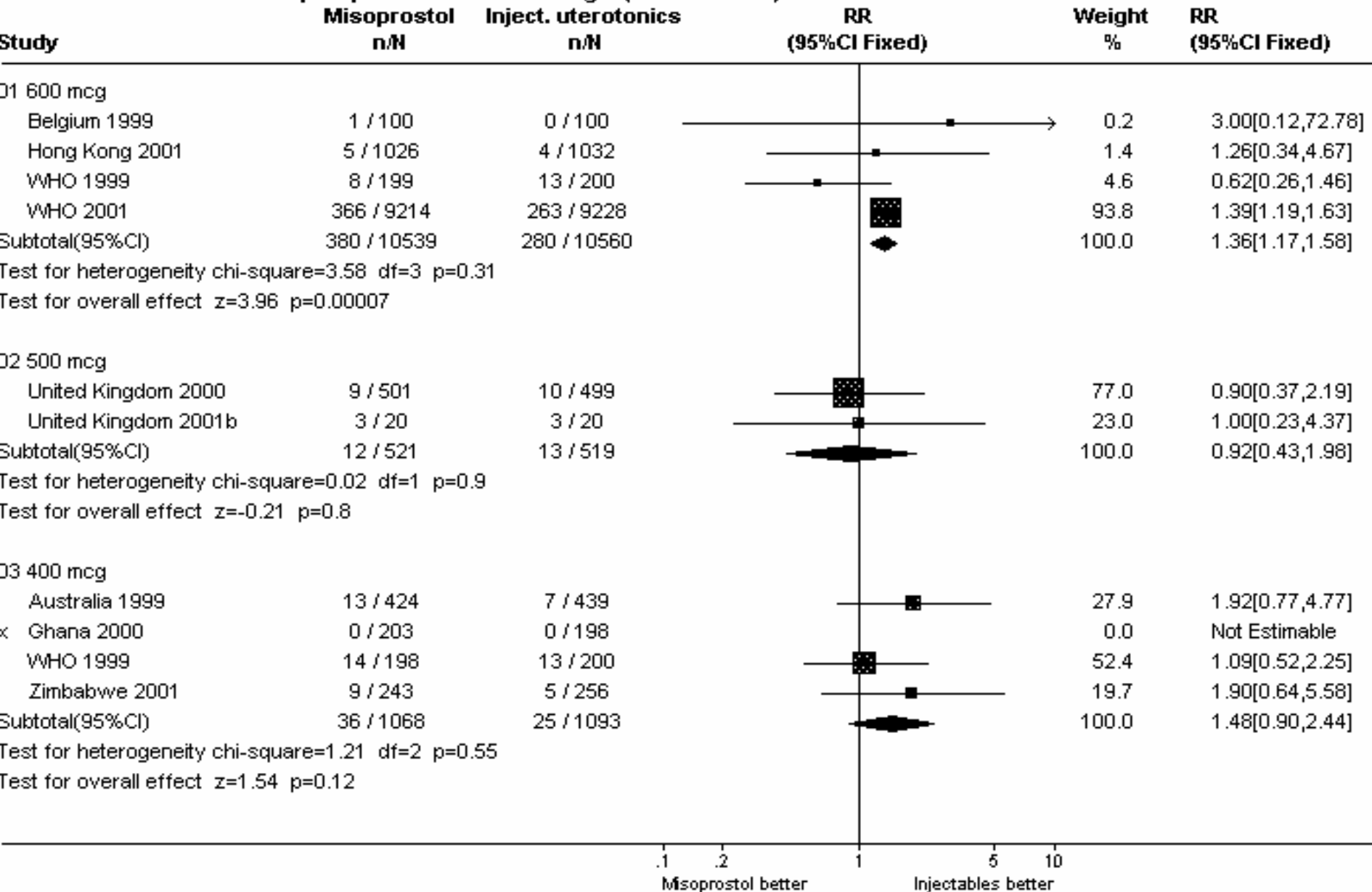
	Misoprostol n=9225 %	Oxytocin n=9228 %	RR	95% CI
Blood loss \geq 1000 mls*	4.0	2.9	1.39	1.19 to 1.63
Additional uterotonics	15.2	10.9	1.40	1.29 to 1.51

* n=9214

Misoprostol vs conventional injectable uterotonics

Comparison: 02 Oral misoprostol versus injectable uterotonics

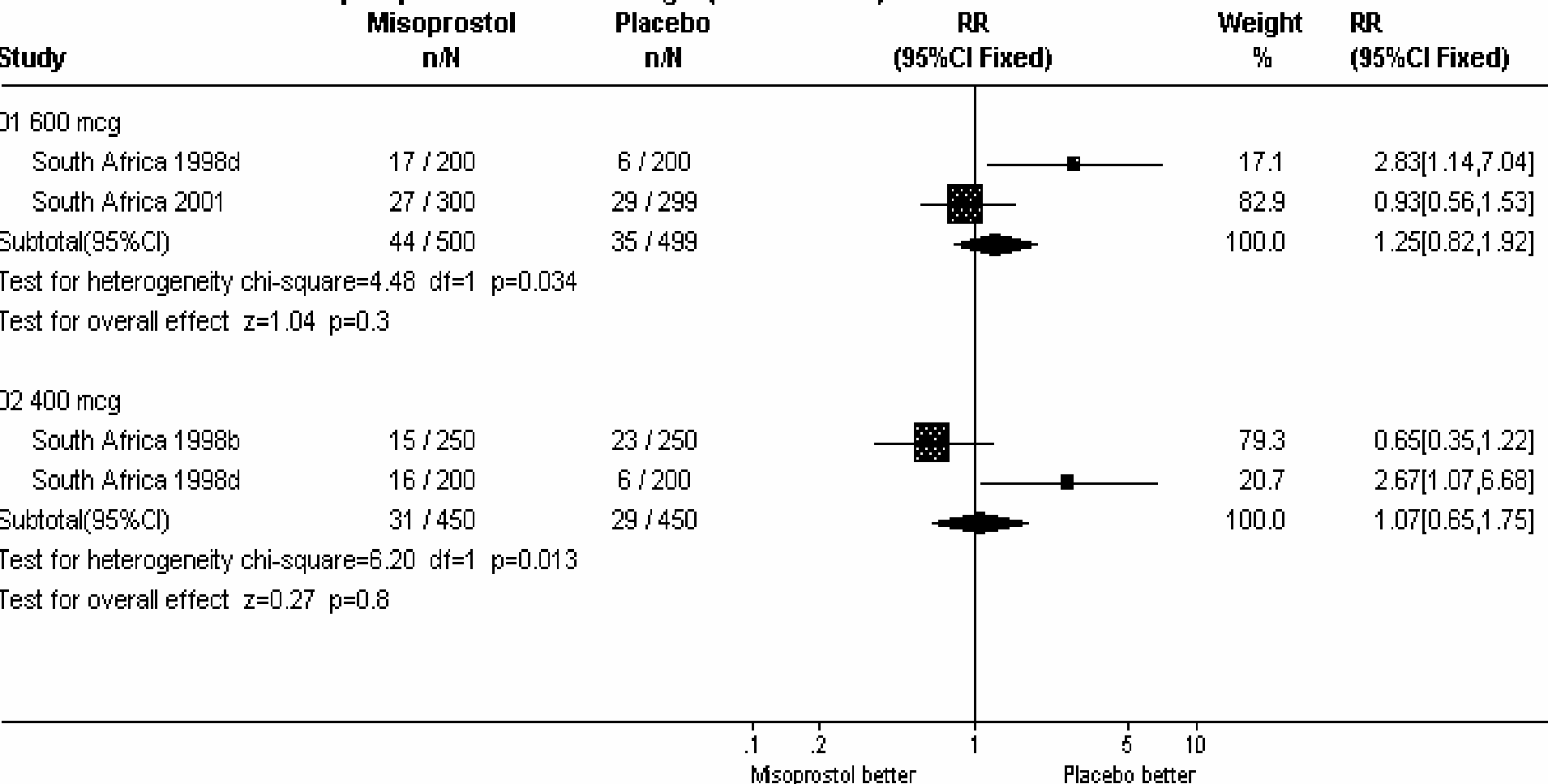
Outcome: 01 Severe postpartum haemorrhage (≥ 1000 mls)



Misoprostol vs placebo

Comparison: 01 Oral misoprostol versus no uterotonic/placebo

Outcome: 01 Severe postpartum haemorrhage (≥ 1000 mls)



Restricted episiotomy

06 Severe vaginal/perineal trauma (primiparae)	3	2331	Relative Risk [Fixed] [95% CI]	1.15 [0.84, 1.58]
07 Severe vaginal/perineal trauma (multiparae)	3	1973	Relative Risk [Fixed] [95% CI]	1.14 [0.52, 2.48]
08 Severe perineal trauma	5	3850	Relative Risk [Fixed] [95% CI]	0.80 [0.55, 1.16]
09 Severe perineal trauma (primiparae)	5	2390	Relative Risk [Fixed] [95% CI]	0.84 [0.56, 1.25]
10 Severe perineal trauma (multiparae)	3	1460	Relative Risk [Fixed] [95% CI]	0.71 [0.28, 1.82]
11 Any posterior perineal trauma	4	2079	Relative Risk [Fixed] [95% CI]	0.88 [0.84, 0.92]
12 Any posterior perineal trauma (primiparae)	4	1157	Relative Risk [Fixed] [95% CI]	0.86 [0.82, 0.91]
13 Any posterior perineal trauma (multiparae)	2	922	Relative Risk [Fixed] [95% CI]	0.91 [0.83, 0.99]
14 Any anterior trauma	4	4342	Relative Risk [Fixed] [95% CI]	1.79 [1.55, 2.07]
15 Any anterior trauma (primiparae)	3	976	Relative Risk [Fixed] [95% CI]	1.24 [0.96, 1.60]
16 Any anterior trauma (multiparae)	2	922	Relative Risk [Fixed] [95% CI]	1.61 [1.19, 2.18]
17 Need for suturing perineal trauma	5	4133	Relative Risk [Fixed] [95% CI]	0.74 [0.71, 0.77]
18 Need for suturing perineal trauma (primiparae)	5	2441	Relative Risk [Fixed] [95% CI]	0.73 [0.70, 0.76]
19 Need for suturing perineal trauma (multiparae)	3	1692	Relative Risk [Fixed] [95% CI]	0.78 [0.72, 0.83]
20 Estimated blood loss at delivery	1	165	WMD [Fixed] [95% CI]	-58.000 [-107.575, -8.425]
21 Moderate/severe perineal pain at 3 days	1	165	Relative Risk [Fixed] [95% CI]	0.71 [0.48, 1.05]
22 Any perineal pain at discharge	1	2422	Relative Risk [Fixed] [95% CI]	0.72 [0.65, 0.81]
23 Any perineal pain at 10 days	1	885	Relative Risk [Fixed] [95% CI]	1.00 [0.78, 1.27]

Umbilical vein injection for retained placenta

02 SALINE SOLUTION PLUS OXYTOCIN VERSUS EXPECTANT MANAGEMENT				
Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Manual removal of the placenta	5	454	Relative Risk [Fixed] [95% CI]	0.86 [0.72, 1.01]
02 Postpartum haemorrhage	1	55	Relative Risk [Fixed] [95% CI]	1.12 [0.07, 16.95]
03 Blood loss = or > 500 ml after entry	1	130	Relative Risk [Fixed] [95% CI]	1.53 [0.88, 2.67]
04 Blood loss = or > 1000 ml after entry	1	130	Relative Risk [Fixed] [95% CI]	1.29 [0.38, 4.34]
05 Haemoglobin 24-48 hours postpartum	1	164	WMD [Fixed] [95% CI]	0.000 [-0.614, 0.614]
06 Haemoglobin 40-45 days postpartum	1	96	WMD [Fixed] [95% CI]	0.500 [-0.142, 1.142]
07 Blood transfusion	2	237	Relative Risk [Fixed] [95% CI]	0.89 [0.50, 1.58]
08 Curettage	1	182	Relative Risk [Fixed] [95% CI]	0.69 [0.44, 1.09]
09 Infection	1	179	Relative Risk [Fixed] [95% CI]	1.16 [0.32, 4.16]
10 Stay at hospital more than two days	1	180	Relative Risk [Fixed] [95% CI]	1.09 [0.60, 1.97]
03 SALINE SOLUTION PLUS OXYTOCIN VERSUS SALINE SOLUTION				
Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Manual removal of the placenta	10	649	Relative Risk [Fixed] [95% CI]	0.79 [0.69, 0.92]
02 Length of third stage of labour	1	30	WMD [Fixed] [95% CI]	16.200 [-15.223, 47.623]
03 Blood loss	2	48	WMD [Fixed] [95% CI]	21.605 [-49.728, 92.938]
04 Postpartum haemorrhage	1	52	Relative Risk [Fixed] [95% CI]	3.00 [0.13, 70.42]
05 Blood loss = or > 500 ml after entry	1	130	Relative Risk [Fixed] [95% CI]	1.43 [0.83, 2.45]
06 Blood loss = or > 1000 ml after entry	1	130	Relative Risk [Fixed] [95% CI]	1.71 [0.45, 6.56]
07 Haemoglobin 24-48 hours postpartum	1	167	WMD [Fixed] [95% CI]	-0.100 [-0.758, 0.558]
08 Haemoglobin 40-45 days postpartum	1	91	WMD [Fixed] [95% CI]	0.100 [-0.578, 0.778]
09 Blood transfusion	2	238	Relative Risk [Fixed]	1.17 [0.63, 2.19]



Summary

- Active management reduces blood loss
- Choice between oxytocin (10IU) and syntometrine involves trade-offs
- Routine episiotomy should be abandoned
- Retained placenta should be managed actively
 - Oxytocin +saline infusion is likely to reduce the likelihood of manual removal of the placenta



Management of postpartum haemorrhage

- Essential components
 - treat shock
 - ascertain the origin of bleeding and treat accordingly
 - control lower tract bleeding
 - ensure uterine contraction
 - remove placenta



Nonsurgical emergency measures

- Uterine massage
- Uterotonics
 - ergometrine IV, oxytocin infusion (20-40 IU)
 - PGF2alpha IM or intramyometrial, intrauterine gemeprost pessaries
 - rectal misoprostol
- Compression of aorta against the sacral promontory
- Bimanual uterine compression
- Stretching the uterine arteries by elevating the uterus



Nonsurgical emergency measures

- Intrauterine pressure
 - Packing
 - Sengstaken-Blakemore tube
 - Foley catheter with a large bulb
 - Silicone water-filled balloon
- *Uterine artery embolization*



Surgical measures

- Exploration under g/a
- Removal of retained products of conception
- Internal iliac artery ligation
- Stepwise uterine and ovarian artery ligation
- Uterine repair or hysterectomy
- Full-thickness uterine suture



Summary

- None of the therapeutic approaches have been evaluated systematically in RCTs.
- High dose (800-1200 mcg) rectal misoprostol that is being advocated should be evaluated in well-conducted trials with appropriate power.

