Prevention and treatment of postpartum haemorrhage

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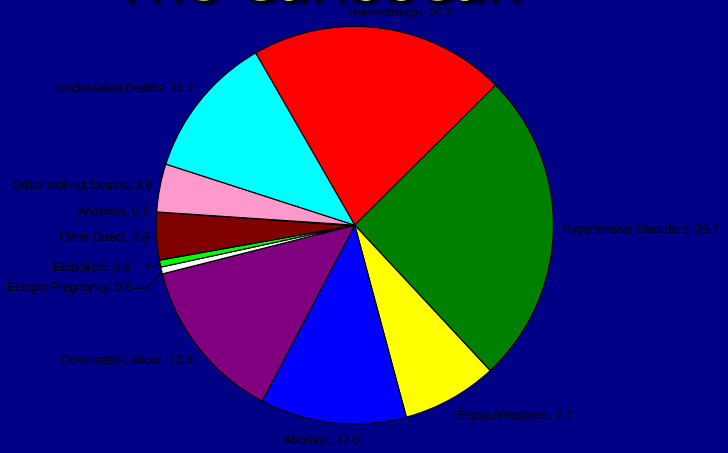
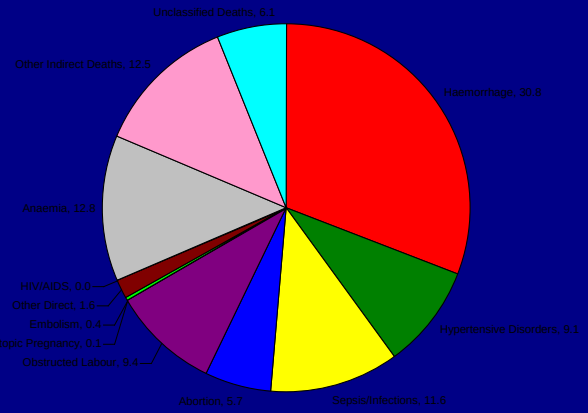
Training Course in Reproductive Health Research 2008

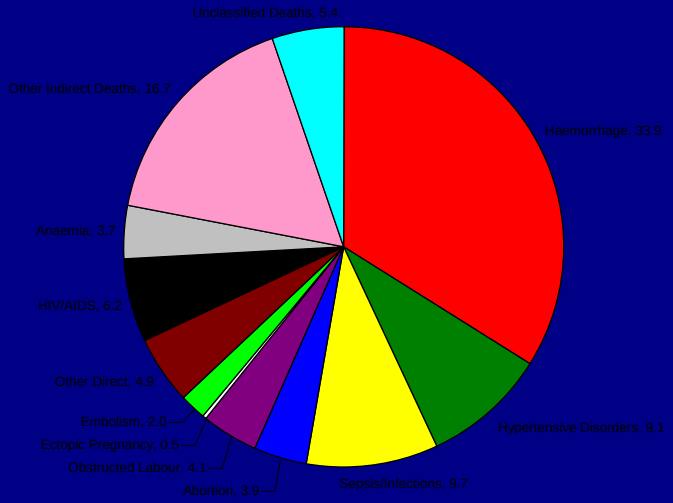
Latin America & The Caribbean



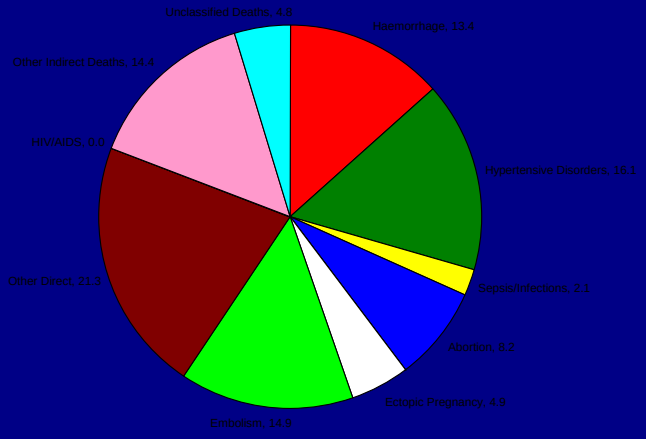
Asia



Africa



Developed Countries



Severe PPH prevalence

SPPH (BLOOD LOSS ≥ 1000 ML)						
	% (CI 95%)	# articles	# datasets	# women	% Min	%Max
Overall	1.86 (1.82 – 1.90)	25	70	505 379	0.00	16.92
By Method of Assessment of Blood Loss						
Group/Subgroup	% (CI 95%)	# articles	# datasets	# women	% Min	%Max
Objectively Assessed	3.04 (2.90 – 3.17)	14	48	60 086	0.17	16.92
Subjectively Assessed	1.68 (1.64 – 1.72)	9	17	440 564	0.00	12.80
Unspecified	3.83 (3.28 – 4.37)	2	5	4 729	0.38	7.57
By Place Studied						
Group/Subgroup	% (CI 95%)	# articles	# datasets	# women	% Min	%Max
National/Province/Region/City	1.67 (1.64 – 1.71)	4	8	73 973	0.32	12.80
Medical Facilities	2.95 (2.83 – 3.07)	21	62	431 406	0.00	16.92
By Study Design						
Group/Subgroup	% (CI 95%)	# articles	# datasets	# women	% Min	%Max
Observational Study	1.69 (1.65 – 1.73)	9	15	448 047	0.51	12.80
Clinical Trial	3.18 (3.04 – 3.33)	16	55	57 332	0.00	16.92

Severe PPH prevalence

By Type of Delivery							
Group/Subgroup		% (CI 95%)	# articles	# datasets	# women	% Min	%Max
Vaginal		2.94 (2.82-3.07)	21	61	72 662	0.00	16.92
Parity	Nulliparous	4.18 (3.52-4.85)	1	1	3 464	4.18	4.18
	Multiparous	0.45 (0.23-0.69)	2	4	3 286	0.32	0.67
	Unspecified	3.00 (2.87-3.13)	18	56	65 912	0.00	16.92
Gestation	Singleton	3.01 (2.54-3.48)	5	11	5 150	0.39	8.83
	Multiple	--	--	--	--	--	--
	Unspecified	2.94 (2.81-3.07)	16	50	67 512	0.00	16.92
Management of Labour	Expectant Management	3.84 (3.31-4.37)	6	6	4 999	0.51	16.92
	Active Management	2.99 (2.80-3.18)	10	21	30 608	0.00	4.73
	Oxytocic before placenta delivery- NO or NOT specified cord management	2.47 (2.06-2.88)	7	11	5 585	0.25	11.21
	Oxytocic after placenta delivery	2.08 (1.39-2.77)	2	2	1 635	0.98	3.17
	Unspecified	2.88 (2.69-3.07)	4	21	29 835	0.18	9.83
Cesarean		6.38 (5.45-7.31)	1	3	2 647	4.32	7.57
Unspecified		1.65 (1.61-1.69)	3	6	430 070	0.38	12.80

Strategies to reduce postpartum blood loss

- Routine management of 3rd stage of labour
- Management of complications
  - Uterine atony
  - Retained placenta management

Prevention of PPH

Clinical

- Active management
  - Uterotonic
    - Drug/dose/route (oxytocin/syntometrine /ergometrine/misoprostol)
    - Timing (anterior shoulder / baby/placenta)
  - Controlled cord traction
  - Cord clamping – timing
  - Uterine massage – duration, procedure
- Expectant management

System / environment

- Manual skills
- Injection safety
- Storage conditions
- Pharmaceutical commodity management

Cost

- Purchase cost
- Indirect costs

Active management of the third stage of labour

- Administration of a uterotonic after delivery of the baby, early cord clamping and cutting, and controlled cord traction
- Cochrane review, ICM/FIGO and WHO MCPC guidelines differ slightly
- ICM/FIGO and WHO guidelines do not mention 'early' cord clamping

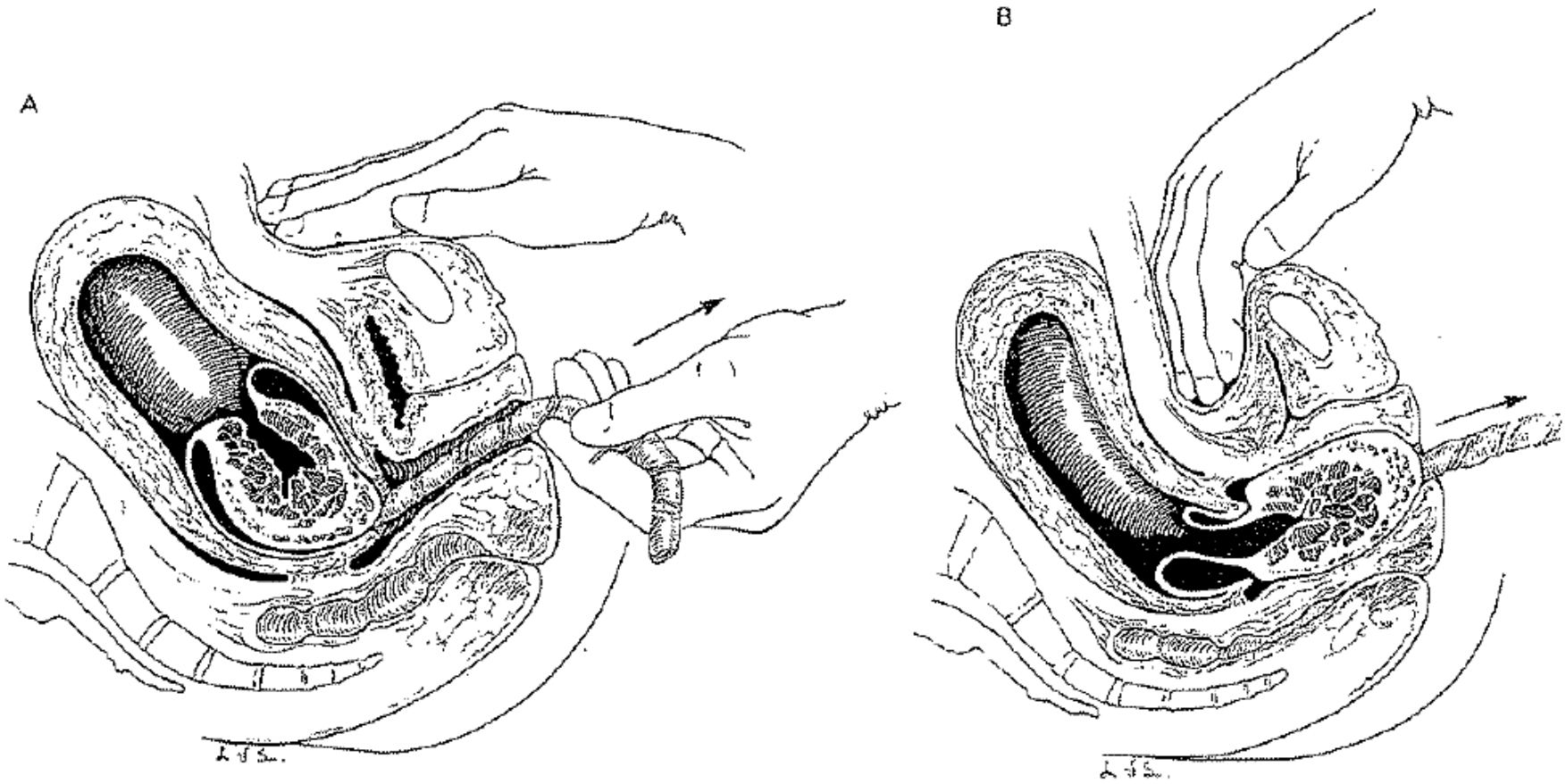
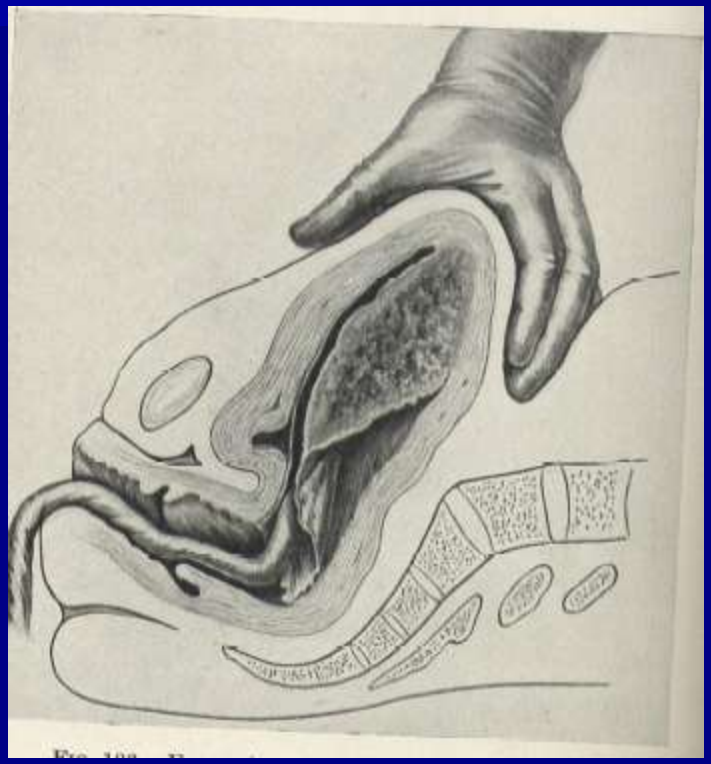


Figure 31–25. Brandt-Andrews maneuver. *A:* Traction is exerted on the cord as the uterus is gently elevated. *B:* Pressure is exerted between the symphysis and the uterine fundus, forcing the uterus upward and the placenta outward, as traction on the cord is continued.

Crede manoeuvre



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]

Should active management of 3rd stage be offered by skilled attendants?

1 systematic review
- 5 trials
- UK, Ireland, UAE
- Different combinations of the components

- Active management should be offered to all women delivering with skilled attendants
- Recommendation: STRONG
- Quality of evidence: MODERATE
- Active management by non-skilled attendants is not recommended
  - *The group placed high value on the potential risk of uterine inversion that may result from pulling the cord inadvertently although there was no evidence for or against the use of active management by nonskilled providers*

Oxytocin vs. syntometrine

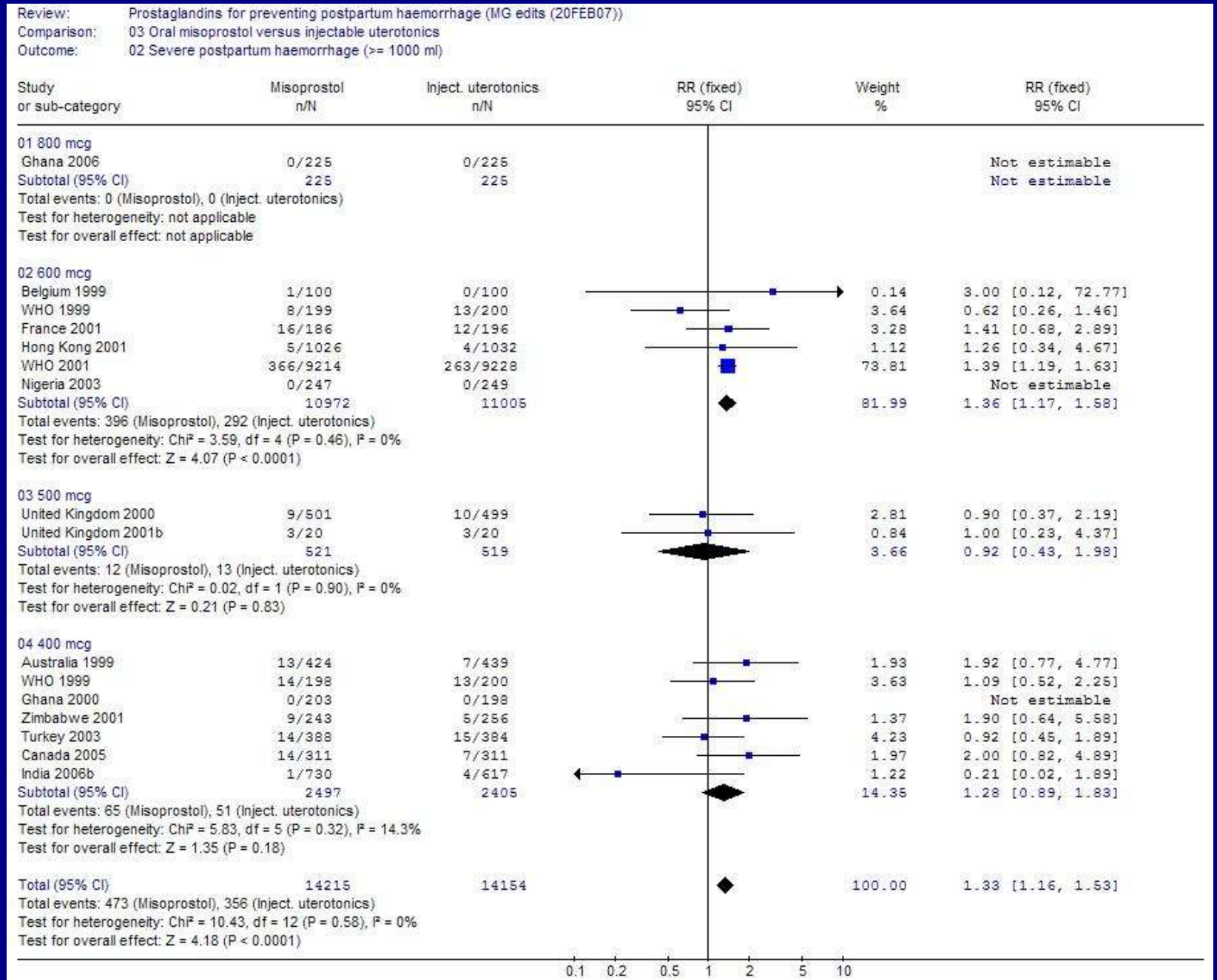
01 syntometrine vs oxytocin (any dose)				
Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 blood loss >500 ml	6	10091	Peto OR [95% CI]	0.74 [0.65, 0.85]
02 blood loss > 1000ml	4	6963	Peto OR [95% CI]	0.79 [0.59, 1.06]
03 manual removal of the placenta	5	8341	Peto OR [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]

Should oxytocin (10IU im/iv) or ergometrine (0.25 mg im) be offered in active management?

2 systematic reviews
- > 9,000 women
- Oxytocin vs. ergometrine vs. syntometrine
- Oxytocin dose (2-10 IU), IM/IV
- Only one trial with direct comparison (1049 women)

- Oxytocin 10 IU im/iv should be offered to all women in preference to ergometrine
- If oxytocin is not available ergo/methylergo or syntometrine to women without hypertension and heart disease
- Recommendation: STRONG
- Quality of evidence: LOW
  - *The recommendation places a high value on avoiding the adverse effects of ergometrine, and assumes similar benefit for oxytocin and ergometrine*

Misoprostol vs conventional injectable uterotonics



Should oral misoprostol (600 mcg) be offered instead of oxytocin (10 IU im) in active management?

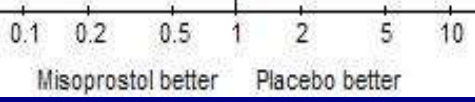
One systematic review
- 7 trials with direct comparison
- Largest trial > 18,000 women

- In the context of active management of the third stage of labour skilled attendants should offer oxytocin in preference to misoprostol
- Recommendation: STRONG
- Quality of evidence: HIGH
  - *The recommendation places a high value on the relative benefits of oxytocin in preventing blood loss as well as increased side-effects with misoprostol*

Misoprostol vs placebo

Review: Prostaglandins for preventing postpartum haemorrhage (MG edits (20FEB07))
Comparison: 02 Oral misoprostol versus no uterotonic/placebo
Outcome: 03 Severe postpartum haemorrhage (>= 1000 ml)

Study or sub-category	Misoprostol n/N	Placebo n/N	RR (fixed) 95% CI	Weight %	RR (fixed) 95% CI
01 600 mcg					
South Africa 1998d	17/200	6/200		9.82	2.83 [1.14, 7.04]
France 2001	16/186	13/220		19.50	1.46 [0.72, 2.95]
South Africa 2001	27/300	29/299		47.56	0.93 [0.56, 1.53]
Gambia 2005	2/629	4/599		6.71	0.48 [0.09, 2.59]
India 2006c	2/812	10/808		16.41	0.20 [0.04, 0.91]
02 400 mcg					
South Africa 1998b	15/250	23/250		79.31	0.65 [0.35, 1.22]
South Africa 1998d	16/200	6/200		20.69	2.67 [1.07, 6.68]



In the absence of active management, should uterotonics be used alone for PPH prevention?

Two systematic reviews

Two oxytocin trials (one with 5 IU the other 10IU, 1221 women in total)

One misoprostol trial (1620 women, auxiliary nurse-midwives)

- In the absence of active management a uterotonic drug (oxytocin or misoprostol) should be offered by a health worker trained in its use for PPH prevention
- Recommendation: STRONG
- Quality of evidence: MODERATE
  - *For misoprostol this recommendation places a high value on potential benefits of avoiding PPH. Ease of oral administration of an oral drug, but notes there is one study*
  - *The only trial relevant to this recommendation used 600 mcg. There is uncertainty about the lowest effective dose and administration route*

When should the cord be clamped to maximise benefits for mother and baby?

One systematic review
- three additional trials
- varying definitions of early clamping (10 sec – 1 min) and delayed (2 min – stopping pulsation)
- no priority outcomes reported, but newborn anemia as an important outcome
- unclear whether timing of cord clamping has an effect on PPH

- Because of the benefits for the baby, the cord should not be clamped earlier than is necessary for applying cord traction in active management of the third stage of labour
- Recommendation: WEAK
- Quality of evidence: LOW
  - *For the sake of clarity, it is estimated that this will take approximately 3 minutes*
  - *Early clamping may be required if the baby requires immediate resuscitation*

Should the placenta be delivered by controlled traction in all women?

No direct evidence found

studies have compared cord drainage with none, cord traction and drainage with uterotonic (given in various ways)

- Given the current evidence for active management includes cord traction, no change to the current practice is recommended
- Recommendation: STRONG
- Quality of evidence: VERY LOW
  - *Further research into the effects of individual components of active management is needed*

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 pospartum	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]

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

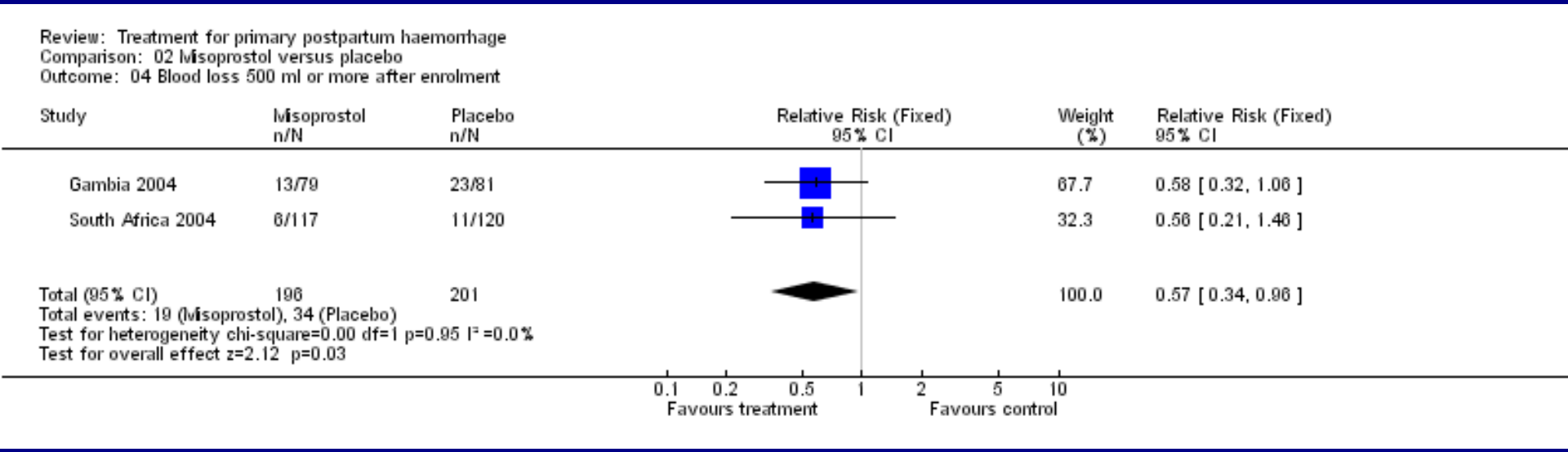
- Uterine massage
- Uterotonics
  - ergometrine IV, oxytocin infusion (20-40 IU)
  - PGF2alpha IM or intramyometrial, intrauterine gemeprost pessaries
  - misoprostol
- Compression of aorta against the sacral promontory
- Bimanual uterine compression
- Stretching the uterine arteries by elevating the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

Nonsurgical emergency measures

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

- *Uterine artery embolization*

Misoprostol for PPH treatment



Surgical measures

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

Summary

- Misoprostol is promising but should be evaluated in well-conducted trials with appropriate power
- Other methods have not been evaluated rigorously