Prevention and treatment of postpartum haemorrhage

A. Metin Gülmezoglu

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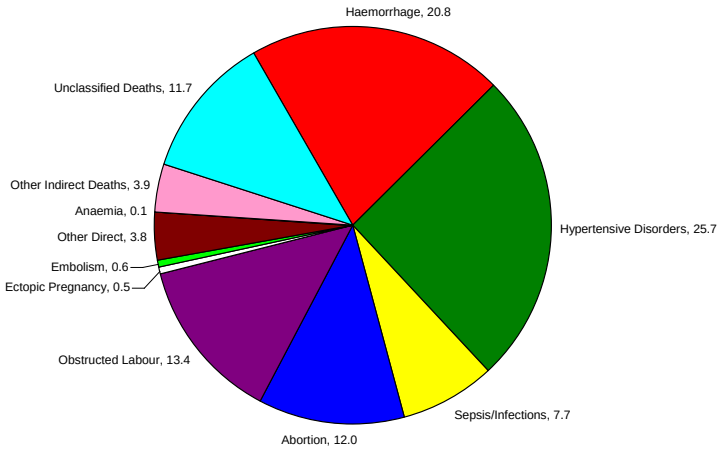
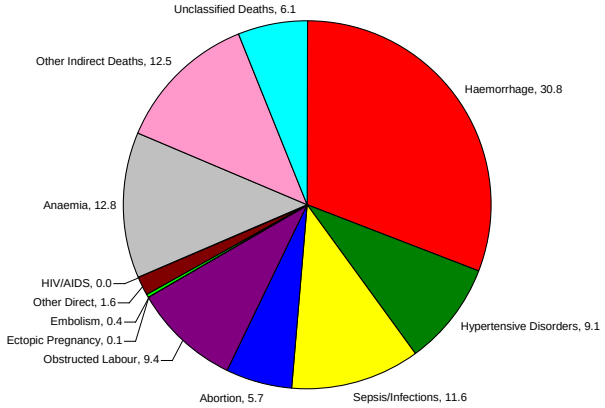
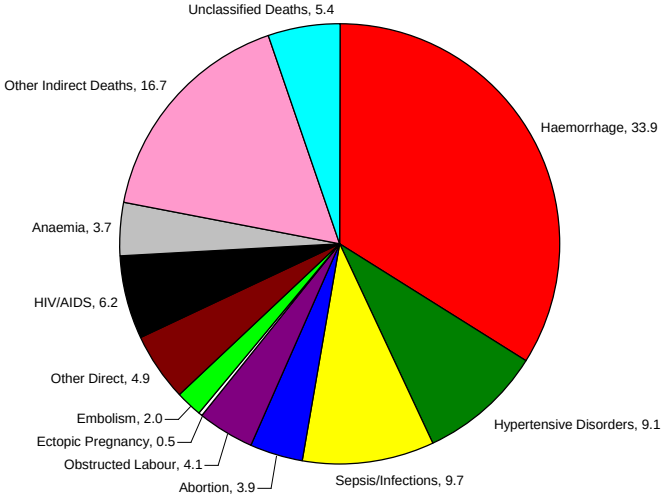
Latin America & The Caribbean



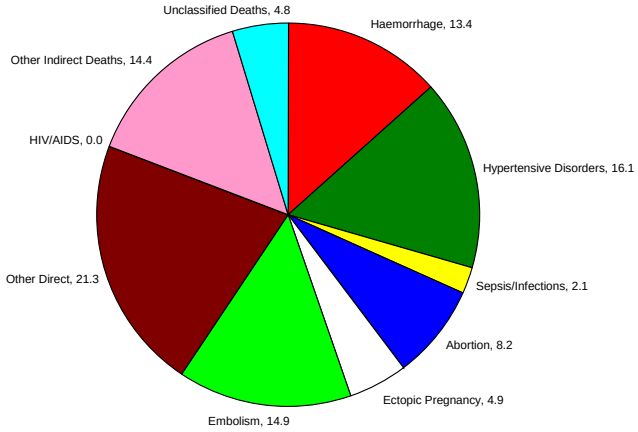
Asia



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						
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						
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						
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

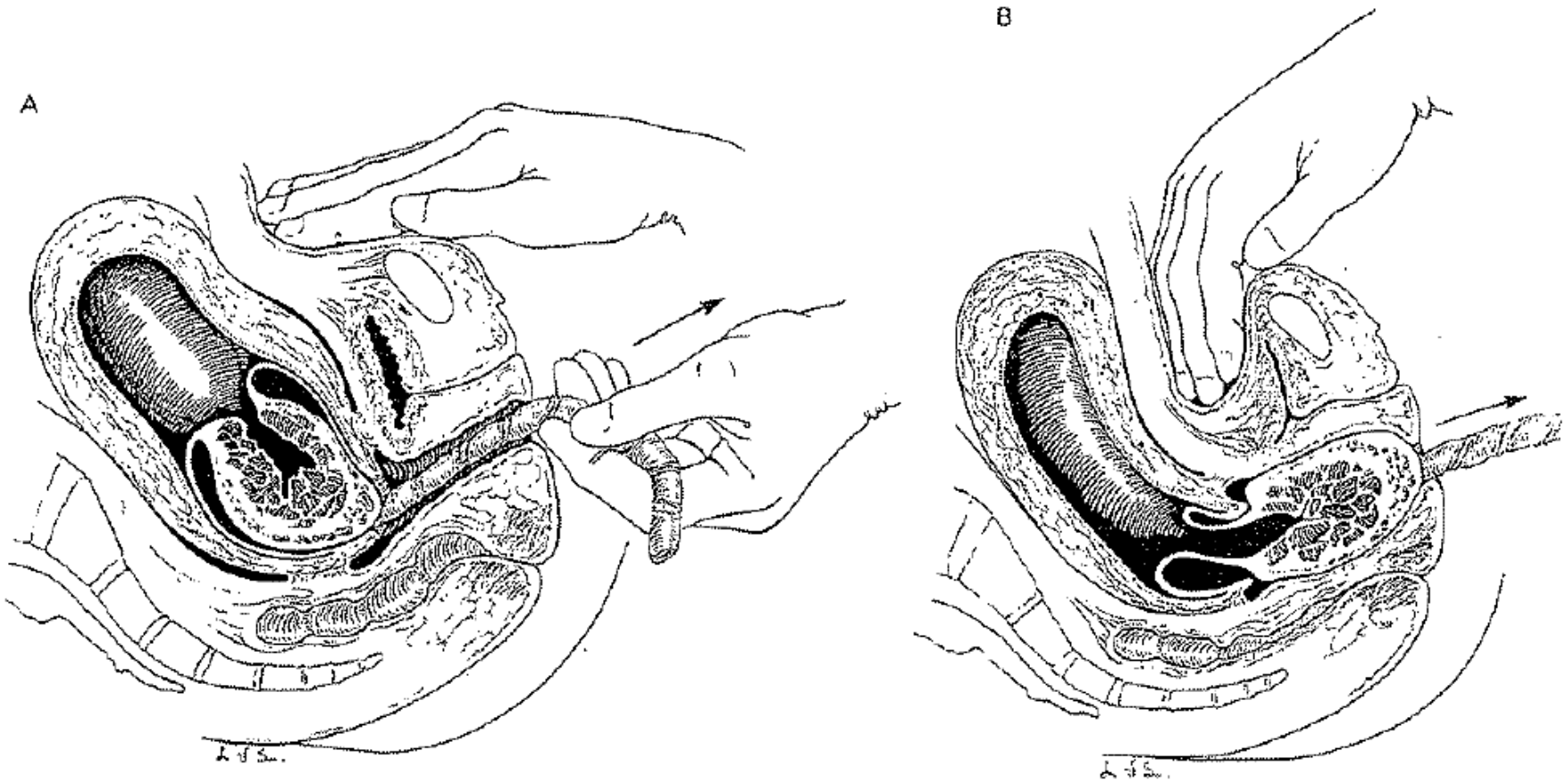


Figure 31–25. Brandt-Andrews maneuver. *A:* Traction is exerted on the cord as the uterus is gently elevated. *B:* Pressure is exerted between the symphysis and the uterine fundus, forcing the uterus upward and the placenta outward, as traction on the cord is continued.

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]

Active management versus expectant management: 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]

Which uterotonic?

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

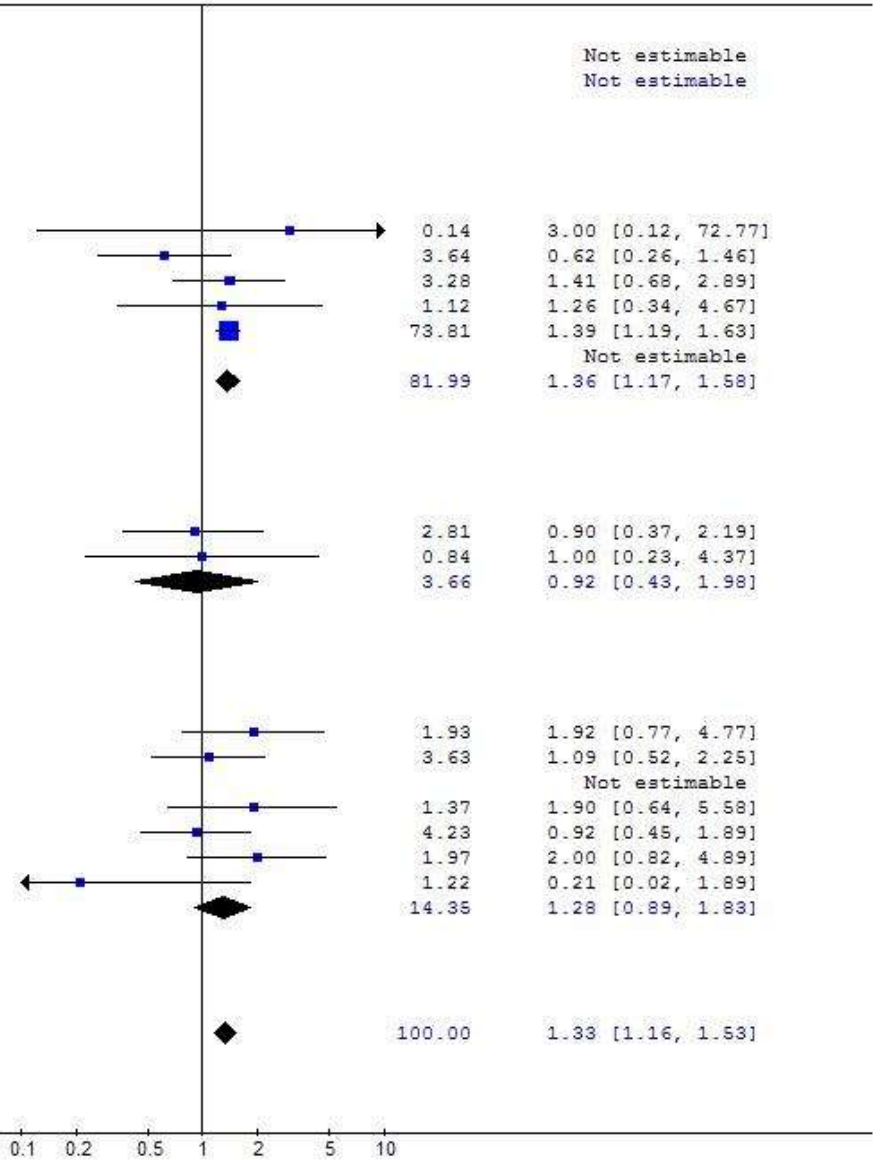
2 systematic reviews
- > 9,000 women
- Oxytocin vs. ergometrine vs. syntometrine
- Oxytocin dose (2-10 IU), IM/IV
- Only one trial with direct comparison (1049 women)

- 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

Review: Prostaglandins for preventing postpartum haemorrhage (MG edits (20FEB07))
Comparison: 03 Oral misoprostol versus injectable uterotonics
Outcome: 02 Severe postpartum haemorrhage (>= 1000 ml)

Study or sub-category	Misoprostol n/N	Inject. uterotonics n/N	RR (fixed) 95% CI	Weight %	RR (fixed) 95% CI
01 800 mcg					
Ghana 2006	0/225	0/225			Not estimable
Subtotal (95% CI)	225	225			Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 600 mcg					
Belgium 1999	1/100	0/100		0.14	3.00 [0.12, 72.77]
WHO 1999	8/199	13/200		3.64	0.62 [0.26, 1.46]
France 2001	16/186	12/196		3.28	1.41 [0.68, 2.89]
Hong Kong 2001	5/1026	4/1032		1.12	1.26 [0.34, 4.67]
WHO 2001	366/9214	263/9228		73.81	1.39 [1.19, 1.63]
Nigeria 2003	0/247	0/249			Not estimable
Subtotal (95% CI)	10972	11005		81.99	1.36 [1.17, 1.58]
Total events: 396 (Misoprostol), 292 (Inject. uterotonics)					
Test for heterogeneity: Chi² = 3.59, df = 4 (P = 0.46), I² = 0%					
Test for overall effect: Z = 4.07 (P < 0.0001)					
03 500 mcg					
United Kingdom 2000	9/501	10/499		2.81	0.90 [0.37, 2.19]
United Kingdom 2001b	3/20	3/20		0.84	1.00 [0.23, 4.37]
Subtotal (95% CI)	521	519		3.66	0.92 [0.43, 1.98]
Total events: 12 (Misoprostol), 13 (Inject. uterotonics)					
Test for heterogeneity: Chi² = 0.02, df = 1 (P = 0.90), I² = 0%					
Test for overall effect: Z = 0.21 (P = 0.83)					
04 400 mcg					
Australia 1999	13/424	7/439		1.93	1.92 [0.77, 4.77]
WHO 1999	14/198	13/200		3.63	1.09 [0.52, 2.25]
Ghana 2000	0/203	0/198			Not estimable
Zimbabwe 2001	9/243	5/256		1.37	1.90 [0.64, 5.58]
Turkey 2003	14/388	15/384		4.23	0.92 [0.45, 1.89]
Canada 2005	14/311	7/311		1.97	2.00 [0.82, 4.89]
India 2006b	1/730	4/617		1.22	0.21 [0.02, 1.89]
Subtotal (95% CI)	2497	2405		14.35	1.28 [0.89, 1.83]
Total events: 65 (Misoprostol), 51 (Inject. uterotonics)					
Test for heterogeneity: Chi² = 5.83, df = 5 (P = 0.32), I² = 14.3%					
Test for overall effect: Z = 1.35 (P = 0.18)					
Total (95% CI)	14215	14154		100.00	1.33 [1.16, 1.53]
Total events: 473 (Misoprostol), 356 (Inject. uterotonics)					
Test for heterogeneity: Chi² = 10.43, df = 12 (P = 0.58), I² = 0%					
Test for overall effect: Z = 4.18 (P < 0.0001)					



Misoprostol?

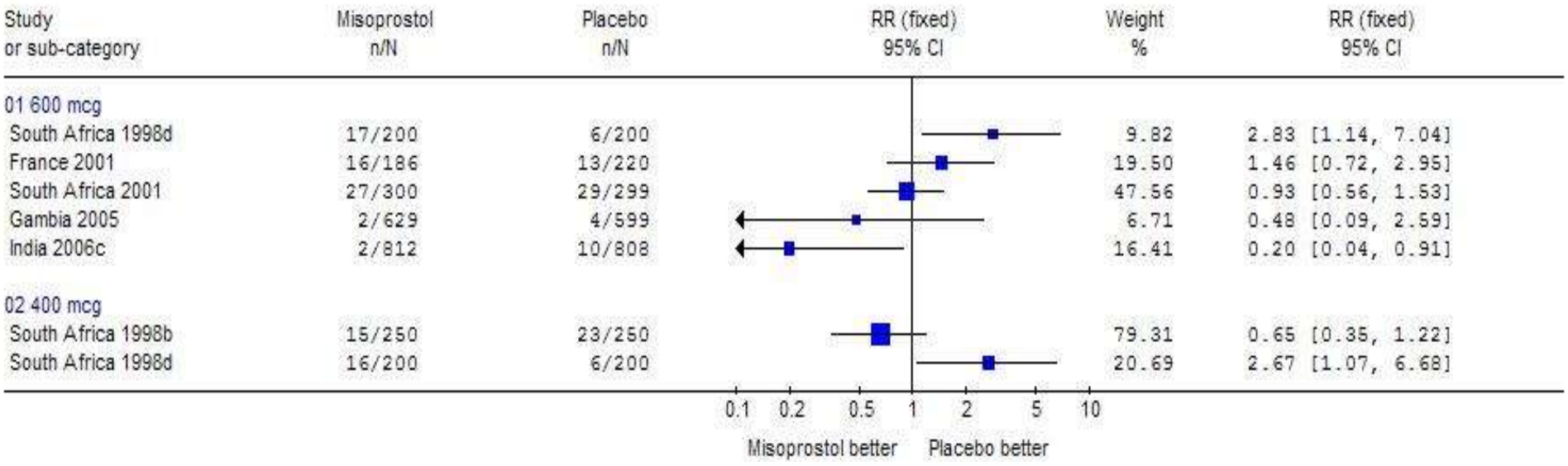
Should oral misoprostol (600 mcg) be offered instead of oxytocin (10 IU im) in active management?

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)



Uterotonics alone?

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*

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

Which uterotonics should be offered in the management of PPH due to uterine atony?

- *Recommendations:*
  - For management of PPH, oxytocin should be preferred over ergometrine alone, fixed-dose combination of ergometrine and oxytocin, carbetocin, and prostaglandins. **(Quality of evidence: very low–low; strength of recommendation: strong)**
  - If oxytocin is not available, or if bleeding has not responded to oxytocin, ergometrine and fixed-dose combination of ergometrine and oxytocin should be offered as second-line treatments. **(Quality of evidence: very low–low; strength of recommendation: strong)**
  - If the above second-line treatments are not available, or if the bleeding has not responded to the second-line treatments, a prostaglandin should be offered as the third line of treatment. **(Quality of evidence: very low–low; strength of recommendation: strong)**

Should misoprostol be offered for the management of PPH in women who have received prophylactic oxytocin during the third stage of labour?

- *Recommendation:*
  - There is no added benefit of offering misoprostol as adjunct treatment for PPH in women who have received oxytocin during the third stage of labour. In settings where oxytocin is available, and is used in the management of the third stage of labour, oxytocin alone should be used in preference to adjunct misoprostol for the management of PPH in women who have received prophylactic oxytocin during the third stage of labour.
  - **(Quality of evidence: moderate–high; strength of recommendation: strong)**

Should tranexamic acid be offered in the treatment of PPH due to uterine atony?

- *Recommendation:*
  - Tranexamic acid may be offered as a treatment for PPH if:
    - administration of oxytocin, followed by second-line treatment options and prostaglandins, have failed to stop the bleeding; or
    - it is thought that the bleeding may be partly due to trauma. **(Quality of evidence: very low; strength of recommendation: weak)**

Should uterine massage be offered to treat PPH?

- *Recommendation:*
  - Uterine massage should be started once PPH is diagnosed. **(Quality of evidence: very low; strength of recommendation: strong)**

Should bimanual uterine compression be offered to treat PPH?

- *Recommendation:*
  - Bimanual uterine compression may be offered as a temporizing measure in the treatment of PPH due to uterine atony after vaginal delivery. **(Quality of evidence: very low; strength of recommendation: weak)**

Should uterine packing be offered to treat PPH?

- *Recommendation:*
  - Uterine packing is not recommended for the treatment of PPH due to uterine atony after vaginal delivery **(Quality of evidence: very low; strength of recommendation: weak)**

Should intrauterine balloon/condom tamponade be offered to treat PPH?

- *Recommendation:*
  - In women who have not responded to treatment with uterotonics, or if uterotonics are not available, intrauterine balloon/condom tamponade may be offered to treat PPH due to uterine atony **(Quality of evidence: low; strength of recommendation: weak)**

Should surgical interventions be employed in the treatment of PPH?

- *Recommendation:*
  - If bleeding does not stop in spite of treatment with uterotonics, other conservative interventions (e.g. uterine massage) and external or internal pressure on the uterus, surgical interventions should be initiated.
    - The order of surgical interventions should be from conservative approaches to more invasive procedures. For example, compression sutures may be attempted first and if that intervention fails, uterine, utero-ovarian and hypogastric vessel ligation may be tried. If life threatening bleeding continues even after ligation, subtotal hysterectomy (also called supracervical hysterectomy) should be performed. **(Quality of evidence: No formal scientific evidence of benefit or harm; strength of recommendation: strong)**

Surgical measures

- Internal iliac artery ligation
- Stepwise uterine and ovarian artery ligation
- Vaginal uterine artery ligation
- Compression sutures
- Uterine repair or hysterectomy

Should uterotonics be offered as treatment for retained placenta?

- *Recommendations:*
  - If the placenta is not expelled spontaneously, clinicians may offer oxytocin 10 IU combined with controlled cord traction. **(No formal scientific evidence of benefit or harm; strength of recommendation: weak)**
  - Ergometrine is not recommended as it may cause tetanic uterine contractions, which may delay expulsion of the placenta. **(Quality of evidence: very low; strength of recommendation: weak)**
  - The use of prostaglandin E2 (dinoprostone and sulprostone) is not recommended. **(Quality of evidence: very low; strength of recommendation: strong)**

Should intra-umbilical vein injection of oxytocin with or without saline be offered to treat retained placenta?

- *Recommendations:*
  - Intraumbilical vein injection of oxytocin with saline may be offered for the management of retained placenta.**(Quality of evidence: moderate; strength of recommendation: weak)**
  - If in spite of controlled cord traction, administration of uterotonics and intraumbilical vein oxytocin plus saline injection, the placenta is not delivered, manual extraction of the placenta should be offered as the definitive treatment. **(No formal assessment of quality of evidence; strength of recommendation: strong)**