Additional File 1 - Individual risk of bias assessments

The following assessments have been conducted with the use of previous Cochrane review assessments;
Althabe 2009

| Domain                                      | Review authors judgement | Support for judgement                                                                 |
|---------------------------------------------|---------------------------|---------------------------------------------------------------------------------------|
| Random sequence generation (selection bias) | Low risk                  | Sequence generated at the coordinating centre using computer-generated list of numbers with randomly permuted blocks of 4-6 in a 1:1 ratio |
| Allocation concealment (selection bias)     | Low risk                  | Use of sequentially numbered opaque sealed envelopes. When a woman is about to deliver, next numbered envelope was opened |
| Blinding of participants and personnel (performance bias) | High risk                | Participant: not blinded                                                              |
| All outcomes                                |                           | Clinician: not blinded                                                                 |
| Blinding of outcome assessment (detection bias) | High risk                | Outcome assessor: not blinded                                                        |
| All outcomes                                |                           |                                                                                        |
| Incomplete outcome data (attrition bias)    | Low risk                  | Only 5 women not included in analysis                                                 |
| All outcomes                                |                           |                                                                                        |
| Selective reporting (reporting bias)        | Low risk                  | No indication of selective reporting                                                   |

Hofmeyr GJ, Mshweshwe NT, Gülmezoglu AM. Controlled cord traction for the third stage of labour. Cochrane Database of Systematic Reviews 2015(1): Art. No.: CD008020. DOI: 10.1002/14651858.CD008020.pub.
Attilakos 2010

| Domain                                      | Review authors judgement | Support for judgement                                                                                                                                 |
|---------------------------------------------|--------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|
| Random sequence generation (selection bias)| Low risk                 | The randomisation sequence (1:1 ratio—blocks of 10, no stratification) was generated by computer.                                                        |
| Allocation concealment (selection bias)    | Low risk                 | The preparation of the ampoules was undertaken by DHP Ltd. (Powys, UK). All boxes and ampoules were identically labelled. The random allocation sequence was not known to the investigators until the study had finished and the analysis was started. |
| Blinding of participants and personnel (performance bias) | Low risk                 | Study participants and caregivers were blinded to treatment allocations.                                                                                   |
| Blinding of outcome assessment (detection bias) | Low risk                 | Assessors were blinded to treatment allocations.                                                                                                                                                              |
| Incomplete outcome data (attrition bias)   | Low risk                 | Data were collected completely from all randomised study participants.                                                                                                                                             |
| Selective reporting (reporting bias)       | Low risk                 | The study report matches the study protocol that was registered prospectively (EudraCT 2005-002812-94).                                                                                                          |

Gallos ID, Papadopoulou A, Man R, Athanasopoulos N, Tobias A, Price MJ, et al. Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. Cochrane Database of Systematic Reviews 2018(12): Art No.: CD011689. DOI: 10.1002/14651858.CD011689.pub3.

Su LL, Chong YS, Samuel M. Carbetocin for preventing postpartum haemorrhage. Cochrane Database of Systematic Reviews 2012(4): Art. No.: CD005457. DOI: 10.1002/14651858.CD005457.pub4.
| Domain                                      | Review authors judgement | Support for judgement                                                                 |
|---------------------------------------------|---------------------------|---------------------------------------------------------------------------------------|
| Random sequence generation (selection bias) | Low risk                  | Reported that a random number table was used to determine the sequence for randomisation |
| Allocation concealment (selection bias)     | Unclear risk              | The way women were allocated to groups at the point of randomisation was not clear. It was stated that women were divided into 2 “equal” groups and randomisation was at the point when delivery was imminent. |
| Blinding of participants and personnel      | High risk                 | Staff providing care and making clinical decisions about interventions would be aware of which intervention women received. The study protocol stated that there was no attempt to mask treatment from women and personnel. |
| (performance bias)                          |                           | All outcomes                                                                          |
| Blinding of outcome assessment (detection   | High risk                 | Outcomes would be recorded by staff aware of allocation, however, objective outcomes such as haemoglobin would have a lower risk of bias. |
| bias)                                       |                           | All outcomes                                                                          |
| Incomplete outcome data (attrition bias)    | Low risk                  | No loss to follow up                                                                  |
| (attrition bias)                            |                           | All outcomes                                                                          |
| Selective reporting (reporting bias)        | Low risk                  | This was a registered study and expected outcomes were reported. Incidence of prolonged 3rd stage not reported but duration was reported as a mean. |

Oladapo OT, Okusanya BO, Abalos E. Intramuscular versus intravenous prophylactic oxytocin for the third stage of labour. Cochrane Database of Systematic Reviews 2018(9): Art. No.: CD009332. DOI: 10.1002/14651858.CD009332.pub3
| Domain                                      | Review authors judgement | Support for judgement                                                                 |
|---------------------------------------------|---------------------------|----------------------------------------------------------------------------------------|
| Random sequence generation (selection bias) | Low risk                  | Randomisation was done through an automated web-based system, stratified by centre and balanced in blocks of four |
| Allocation concealment (selection bias)     | Low risk                  | Centrally through an automated web-based system, which ensured allocation concealment  |
| Blinding of participants and personnel (performance bias) All outcomes | High risk | Not possible to blind due to interventions                                                |
| Blinding of outcome assessment (detection bias) All outcomes | Low risk | Blinding not possible, but primary outcome objective measurement of blood loss          |
| Incomplete outcome data (attrition bias) All outcomes | Low risk | After randomisation and before delivery, 294 (6.8%) women became ineligible because an intrapartum caesarean was performed, and three others declined to participate. Women who underwent caesarean section were included in the analysis for outcomes where this was possible |
| Selective reporting (reporting bias)        | Low risk                  | No indication of selective reporting                                                    |

Hofmeyr GJ, Mshweshwe NT, Gülmezoglu AM. Controlled cord traction for the third stage of labour. Cochrane Database of Systematic Reviews 2015(1): Art. No.: CD008020. DOI: 10.1002/14651858.CD008020.pub.
### Domain

| Random sequence generation (selection bias) | Low risk | "Computer-generated randomization" was used |
|-------------------------------------------|----------|---------------------------------------------|
| Allocation concealment (selection bias)   | Low risk | A person uninvolved with the study prepared the study drugs. The labels on the ampoules (which were similar in size and colour) were removed and the ampoules were placed in opaque sealed envelopes. |
| Blinding of participants and personnel (performance bias) All outcomes | Low risk | "A person uninvolved with the study prepared the study drugs... The labels on the ampoules (which were similar in size and colour) were removed and the ampoules were placed in opaque sealed envelopes, such that only the computer-generated randomisation numbers on the envelopes were available to identify the study drug during unblinding." |
| Blinding of outcome assessment (detection bias) All outcomes | Low risk | Assessors were blinded to treatment allocations. |
| Incomplete outcome data (attrition bias) All outcomes | Low risk | Data were collected completely from all randomised study participants. |
| Selective reporting (reporting bias) | Low risk | The study protocol was registered (PACTR 201105000292708). |

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Gallos ID, Papadopoulou A, Man R, Athanasopoulos N, Tobias A, Price MJ, et al. Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. Cochrane Database of Systematic Reviews 2018(12): Art No.: CD011689. DOI: 10.1002/14651858.CD011689.pub3.
### Groot 1996

| Domain                                      | Review authors judgement | Support for judgement                                                                                                                                                                                                 |
|---------------------------------------------|--------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Random sequence generation (selection bias) | Low risk                 | Randomisation was achieved using a computer-generated random list.                                                                                                                                                   |
| Allocation concealment (selection bias)     | Low risk                 | Investigators used identical study boxes. Care was taken that no difference could be seen or heard between the packages of the ergometrine/placebo tablets and the oxytocin ampoules. |
| Blinding of participants and personnel (performance bias) All outcomes | High risk                | The study was "double-blind" with placebo to match ergometrine treatment, but "to allow comparison with a standard prophylactic regimen a third group receiving the standard intramuscular oxytocin was added, but for obvious reasons this could not be conducted in a blind manner." |
| Blinding of outcome assessment (detection bias) All outcomes | Unclear risk             | Assessor blinding was not reported, however, objective blood loss measurements were used.                                                                                                                            |
| Incomplete outcome data (attrition bias) All outcomes | Low risk                 | "4 women with exclusion criteria were entered erroneously. They are considered as non-participants."                                                                                                                     |
| Selective reporting (reporting bias)        | Low risk                 | It is clear that the published reports include all expected outcomes specified.                                                                                                                                     |

Gallos ID, Papadopoulou A, Man R, Athanasopoulos N, Tobias A, Price MJ, et al. Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. Cochrane Database of Systematic Reviews 2018(12): Art No.: CD011689. DOI: 10.1002/14651858.CD011689.pub3.

Liabsuetrakul T, Choobun T, Peeyananjarassri K, Islam QM. Prophylactic use of ergot alkaloids in the third stage of labour. Cochrane Database of Systematic Reviews 2018(6): Art. No.: CD005456. DOI: 10.1002/14651858.CD005456.pub3.

Westhoff G, Cotter AM, Tolosa JE. Prophylactic oxytocin for the third stage of labour to prevent postpartum haemorrhage. Cochrane Database of Systematic Reviews 2013(10): Art. No.: CD001808. DOI: 10.1002/14651858.CD001808.pub2.
### Jackson 2001

| Domain                                      | Review authors judgement | Support for judgement                                                                                                                                 |
|---------------------------------------------|--------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|
| Random sequence generation (selection bias)| Low risk                 | "A computer-generated randomization was used to dictate which labeled vial in each pair would contain oxytocin and which would contain only normal saline. |
| Allocation concealment (selection bias)    | Low risk                 | Allocation was done sequentially, "each participant was assigned... on the basis of the order in which she was enrolled"                             |
| Blinding of participants and personnel (performance bias) All outcomes | Low risk | "Neither patients nor clinicians knew which infusion contained oxytocin"                                                                                           |
| Blinding of outcome assessment (detection bias) All outcomes | Low risk | As above                                                                                                                                                      |
| Incomplete outcome data (attrition bias) All outcomes | Low risk | Data was available for all participants, for all outcomes                                                                                                    |
| Selective reporting (reporting bias)       | Low risk                 | No specific reporting bias was identified.                                                                                                                                 |
Random sequence generation (selection bias) | Low risk | The ampoules were numbered by Sandoz using simple randomisation. There was no blocking or prognostic stratification. |
---|---|---|
Allocation concealment (selection bias) | Low risk | The ampoules were numbered by third party (Sandoz). |
Blinding of participants and personnel (performance bias) | Low risk | Delivery attendants were blinded to treatment allocations. |
Blinding of outcome assessment (detection bias) | Low risk | Assessors were blinded to treatment allocations. |
Incomplete outcome data (attrition bias) | Low risk | "All women allocated to receive a drug were included in that group, excluding only the 14 women for whom drug allocation was not recorded." |
Selective reporting (reporting bias) | Unclear risk | The protocol of the study was unavailable for verification. |

Gallos ID, Papadopoulou A, Man R, Athanasopoulos N, Tobias A, Price MJ, et al. Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. Cochrane Database of Systematic Reviews 2018(12): Art No.: CD011689. DOI: 10.1002/14651858.CD011689.pub3.
### Moeen 2011

| Domain                                              | Review authors judgement | Support for judgement                                                                                                                                 |
|-----------------------------------------------------|---------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|
| Random sequence generation (selection bias)         | Low risk                  | A computer-generated random code in blocks of 6 was maintained by Gynuity Health Projects in New York and not revealed until data collection and cleaning were completed. |
| Allocation concealment (selection bias)             | Low risk                  | Study medication was packed in numbered colour-coded boxes by Gynuity Health Projects in New York.                                                        |
| Blinding of participants and personnel (performance bias) All outcomes | Low risk                  | "Both women and TBAs were blinded to study assignment."                                                                                            |
| Blinding of outcome assessment (detection bias)     | Low risk                  | Assessors were blinded to treatment allocations.                                                                                                     |
| Incomplete outcome data (attrition bias) All outcomes | Low risk                  | "Invalid blood loss measures, which mainly occurred when monitoring visits were not possible because of poor weather conditions, were excluded from our analysis." |
| Selective reporting (reporting bias)                | Low risk                  | The study report matches the study protocol that was registered (ClinicalTrials.gov NCT00120237).                                                    |

Gallos ID, Papadopoulo A, Man R, Athanasopoulos N, Tobias A, Price MJ, et al. Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. Cochrane Database of Systematic Reviews 2018(12): Art No.: CD011689. DOI: 10.1002/14651858.CD011689.pub3.
| Domain                                             | Review authors judgement | Support for judgement                                                                                                                                 |
|---------------------------------------------------|--------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|
| Random sequence generation (selection bias)       | Low risk                 | Treatment was allocated by a computer-generated random allocation system created at the Statistics Unit of Assiut University Hospital.                |
| Allocation concealment (selection bias)           | Low risk                 | Allocation codes were placed in sealed, opaque, consecutively-numbered envelopes.                                                                    |
| Blinding of participants and personnel (performance bias) All outcomes | Low risk                 | The study was "double-blind": active treatments and placebo treatments were "identical-looking."                                                      |
| Blinding of outcome assessment (detection bias)    | Low risk                 | Assessors were blinded to treatment allocations.                                                                                                      |
| Incomplete outcome data (attrition bias)          | Low risk                 | Data were collected completely from all randomised study participants.                                                                                |
| Selective reporting (reporting bias)              | Unclear risk             | The protocol of the study was unavailable for verification.                                                                                           |

Gallos ID, Papadopoulou A, Man R, Athanasopoulos N, Tobias A, Price MJ, et al. Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. Cochrane Database of Systematic Reviews 2018(12): Art No.: CD011689. DOI: 10.1002/14651858.CD011689.pub3.
Gallos ID, Papadopoulos A, Man R, Athanasopoulos N, Tobias A, Price MJ, et al. Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. Cochrane Database of Systematic Reviews 2018(12): Art No.: CD011689. DOI: 10.1002/14651858.CD011689.pub3.

| Domain | Review authors judgement | Support for judgement |
|--------|---------------------------|------------------------|
| Random sequence generation (selection bias) | Unclear risk | Randomisation sequence generation was not reported. |
| Allocation concealment (selection bias) | Unclear risk | Allocation was done by sealed sequentially-numbered envelopes. |
| Blinding of participants and personnel (performance bias) All outcomes | Unclear risk | Blinding (of study participants and caregivers) was not reported. |
| Blinding of outcome assessment (detection bias) All outcomes | Unclear risk | Assessor blinding was not reported. |
| Incomplete outcome data (attrition bias) All outcomes | Unclear risk | The study authors did not mention any incomplete outcome data. |
| Selective reporting (reporting bias) | Unclear risk | The protocol of the study was unavailable for verification, but not all of the outcomes projected by methodological descriptions were reported as results in the study report (cases of transfusion and PPH at least 1000 mL were omitted). |
### Poeschmann 1991

| Domain                                           | Review authors judgement | Support for judgement                                                                                           |
|--------------------------------------------------|--------------------------|-----------------------------------------------------------------------------------------------------------------|
| Random sequence generation (selection bias)      | Low risk                 | A random allocation list was set prior to the trial                                                            |
| Allocation concealment (selection bias)          | Low risk                 | "The hospital pharmacy supplied numbered boxes... allocation of the boxes was by order of entry" demonstrates adequate concealment |
| Blinding of participants and personnel (performance bias) | Low risk                 | Blinding was achieved by using "a nurse not working in the labour room" preparing the injection                 |
| Blinding of outcome assessment (detection bias)  | Low risk                 | As above                                                                                                          |
| Incomplete outcome data (attrition bias)         | Low risk                 | All outcomes are reported                                                                                         |
| Selective reporting (reporting bias)             | Low risk                 | All expected outcomes are reported                                                                                |
| Other bias                                       | High risk                | Trial was stopped early due to organisational issues                                                             |

Westhoff G, Cotter AM, Tolosa JE. Prophylactic oxytocin for the third stage of labour to prevent postpartum haemorrhage. Cochrane Database of Systematic Reviews 2013(10): Art. No.: CD001808. DOI: 10.1002/14651858.CD001808.pub2.
| Domain                                          | Review authors judgement | Support for judgement                                                                                                                                 |
|------------------------------------------------|--------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|
| Random sequence generation (selection bias)    | Unclear risk             | Randomisation sequence generation was not reported.                                                                                                                                                              |
| Allocation concealment (selection bias)        | Low risk                 | Investigators used sequentially-numbered, opaque, sealed envelopes.                                                                                                                                              |
| Blinding of participants and personnel         | High risk                | Study participants and caregivers were not blinded to treatment allocations.                                                                                                                                     |
| (performance bias) All outcomes                |                          |                                                                                                                                                                                                                 |
| Blinding of outcome assessment (detection bias)| Unclear risk             | Assessor blinding was not reported.                                                                                                                                                                               |
| All outcomes                                   |                          |                                                                                                                                                                                                                 |
| Incomplete outcome data (attrition bias)       | Low risk                 | Data were collected completely from all randomised study participants.                                                                                                                                             |
| All outcomes                                   |                          |                                                                                                                                                                                                                 |
| Selective reporting (reporting bias)           | Unclear risk             | The protocol of the study was unavailable for verification.                                                                                                                                                       |
| All outcomes                                   |                          |                                                                                                                                                                                                                 |
| Other bias                                     | High risk                | The protocol was modified after 5 months due to high blood loss in the expectant group but data from the initial 5 months were included in the analysis. Sample size was supposed to be 3900 but stopped at 1695. 30 women in the control group gave a late maternal refusal, whereas only 1 in the experimental group did so. The outcomes of these women are included in analysis. |

Begley CM, Gyte GML, Devane D, McGuire W, Weeks A. Active versus expectant management for women in the third stage of labour. Cochrane Database of Systematic Reviews 2015(3): Art No.: CD007412. DOI: 10.1002/14651858.CD007412.pub4.

Gallos ID, Papadopoulou A, Man R, Athanasopoulos N, Tobias A, Price MJ, et al. Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. Cochrane Database of Systematic Reviews 2018(12): Art No.: CD011689. DOI: 10.1002/14651858.CD011689.pub3.
Begley CM, Gyte GML, Devane D, McGuire W, Weeks A. Active versus expectant management for women in the third stage of labour. *Cochrane Database of Systematic Reviews* 2015(3): Art No.: CD007412. DOI: 10.1002/14651858.CD007412.pub4.

Gallos ID, Papadopoulou A, Man R, Athanasopoulos N, Tobias A, Price MJ, et al. Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. *Cochrane Database of Systematic Reviews* 2018(12): Art No.: CD011689. DOI: 10.1002/14651858.CD011689.pub3.

| Domain                                         | Review authors judgement | Support for judgement                                                                 |
|------------------------------------------------|--------------------------|----------------------------------------------------------------------------------------|
| Random sequence generation (selection bias)   | Low risk                 | Variable sized balanced blocks “...randomisation envelopes were prepared in advance...” in an external academic unit - National Perinatal Epidemiology Unit, Oxford. |
| Allocation concealment (selection bias)       | Low risk                 | Sequentially numbered, opaque, sealed envelopes stored on the ward. Entry to the trial occurred when an envelope was opened. |
| Blinding of participants and personnel (performance bias) All outcomes | High risk                 | Not possible to blind participants and personnel.                                       |
| Blinding of outcome assessment (detection bias) All outcomes | Unclear risk             | Partly blinded. The technicians who did antenatal and postnatal blood tests were unaware of allocation. |
| Incomplete outcome data (attrition bias) All outcomes | Low risk                 | Data available on 1507 out of 1512 at discharge (less than 0.5% attrition, approximately equal losses in both groups). At 6 weeks follow-up less than 5% attrition. |
| Selective reporting (reporting bias)          | Unclear risk             | Both significant and non-significant results presented but we have not been able to check the trial protocol. Most as above reported plus others. Only a few neonatal outcomes reported. |
| Other bias                                     | High risk                | Sample size was supposed to be 2000 but interim analysis showed a higher postpartum haemorrhage rate than expected so it was stopped early at 1500. |
| Domain                                      | Review authors judgement | Support for judgement                                                                                                                                 |
|--------------------------------------------|---------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------|
| Random sequence generation (selection bias)| Low risk                  | The 52 CHOs were randomly allocated equally to either the intervention or the control group; this allocation was stratified by both district and distance (at least 10 km, or less than 10 km) to emergency obstetric care. The randomisation sequence was determined using Stata (version 12). |
| Allocation concealment (selection bias)    | Unclear risk              | Allocation concealment was not reported.                                                                                                               |
| Blinding of participants and personnel (performance bias) | High risk                  | "The random allocation was not masked."                                                                                                              |
| All outcomes                               |                           |                                                                                                                                                      |
| Blinding of outcome assessment (detection bias) | High risk                  | Assessors were not blinded to treatment allocations.                                                                                                     |
| All outcomes                               |                           |                                                                                                                                                      |
| Incomplete outcome data (attrition bias)   | Low risk                  | "7 and 9 enrolled women in the oxytocin and control arms, respectively, lacked a blood-loss measure."                                                      |
| All outcomes                               |                           |                                                                                                                                                      |
| Selective reporting (reporting bias)       | Low risk                  | The study report matches the study protocol that was registered (ClinicalTrials.gov NCT01108289).                                                       |

Gallos ID, Papadopoulou A, Man R, Athanasopoulos N, Tobias A, Price MJ, et al. Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. Cochrane Database of Systematic Reviews 2018(12): Art No.: CD011689. DOI: 10.1002/14651858.CD011689.pub3.

Pantoja T, Abalos E, Chapman E, Vera C, Serrano VP. Oxytocin for preventing postpartum haemorrhage (PPH) in non-facility birth settings. Cochrane Database of Systematic Reviews 2016(4): Art. No.: CD011491. DOI: 10.1002/14651858.CD011491.pub2.
| Domain                                      | Review authors judgement | Support for judgement                                                                 |
|--------------------------------------------|--------------------------|---------------------------------------------------------------------------------------|
| Random sequence generation (selection bias)| Low risk                 | Treatment was allocated by a computer-generated random number.                        |
| Allocation concealment (selection bias)    | Unclear risk             | Allocation concealment was not reported.                                               |
| Blinding of participants and personnel (performance bias) All outcomes | Unclear risk             | Blinding (of study participants and caregivers) was unclear.                           |
| Blinding of outcome assessment (detection bias) All outcomes | Unclear risk             | Assessor blinding was not reported.                                                    |
| Incomplete outcome data (attrition bias) All outcomes | Low risk                 | Data were collected completely from all randomised study participants.                 |
| Selective reporting (reporting bias)       | Unclear risk             | The protocol of the study was unavailable for verification.                           |

Gallos ID, Papadopoulou A, Man R, Athanasopoulos N, Tobias A, Price MJ, et al. Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. Cochrane Database of Systematic Reviews 2018(12): Art No.: CD011689. DOI: 10.1002/14651858.CD011689.pub3.
The following assessments have been conducted by LH, and have been checked by AW;

Davies 2005

| Domain                                         | Review authors judgement | Support for judgement                                                                 |
|------------------------------------------------|--------------------------|----------------------------------------------------------------------------------------|
| Random sequence generation (selection bias)    | Low risk                 | Randomisation was carried out using a random numbers table                              |
| Allocation concealment (selection bias)        | Low risk                 | "sealed, numbered packages"                                                             |
| Blinding of participants and personnel (performance bias) | Low risk                 | A placebo was used which looked the same as the intervention used in the opposite arm, so both personnel and participants were blinded |
| Blinding of outcome assessment (detection bias) | Low risk                 | As above                                                                               |
| Incomplete outcome data (attrition bias)       | Low risk                 | No attrition                                                                           |
| Selective reporting (reporting bias)           | Unclear risk             | Protocol not seen                                                                       |
| Domain                                      | Review authors judgement | Support for judgement                                                                                                                                                                                                 |
|---------------------------------------------|--------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Random sequence generation (selection bias) | Low risk                 | "Maternity huts with auxiliary midwives located 3–21 km from the closest referral centre were randomly assigned (1:1) by staff at Gynuity Health Projects"                                                                 |
| Allocation concealment (selection bias)     | High risk                | As a cluster randomised trial, allocation would be known in advance.                                                                                                                                                   |
| Blinding of participants and personnel      | High risk                | Blinding was not possible due to differences in administration                                                                                                                                                        |
| Blinding of outcome assessment (detection   | High risk                | As above. Assessors would not have been blinded                                                                                                                                                                        |
| bias)                                       |                          |                                                                                                                                                                                                                        |
| Incomplete outcome data (attrition bias)    | Unclear risk             | After randomisation, there was an attrition rate of 27.5% in the misoprostol group and 22.5% in the oxytocin group. However, all women given the interventions were followed up and data was analysed |
| Selective reporting (reporting bias)        | Low risk                 | All outcomes were previously discussed and are the same as the published registration (NCT01713153)                                                                                                                     |
| Other bias                                  | High risk                | Selected huts in the oxytocin and misoprostol groups were changed after initiation of the trial                                                                                                                       |
| Domain                                                                 | Review authors judgement | Support for judgement                                                                 |
|-----------------------------------------------------------------------|--------------------------|----------------------------------------------------------------------------------------|
| Random sequence generation (selection bias)                           | Low risk                 | Random number table was used                                                           |
| Allocation concealment (selection bias)                               | Low risk                 | "Infusion bags were prepared in accordance with randomization and labeled as bag A (oxytocin group), which contained 20 international units oxytocin diluted with 26 mL of saline, and bag B (placebo group)" |
| Blinding of participants and personnel (performance bias)             | Low risk                 | "Providers and patients were blinded to the contents of the bags" as the bags were labelled generically by pharmacists not involved further in the trial. However, labelling A and B would have indicated different interventions. |
| Blinding of outcome assessment (detection bias)                       | Low risk                 | As above                                                                               |
| Incomplete outcome data (attrition bias)                              | Low risk                 | Loss to follow up equated to less than 10% on those allocated to an intervention       |
| Selective reporting (reporting bias)                                  | Low risk                 | Outcomes reported as per protocol                                                      |
| Domain                                                   | Review authors judgement | Support for judgement                                                                 |
|----------------------------------------------------------|---------------------------|---------------------------------------------------------------------------------------|
| Random sequence generation (selection bias)              | Low risk                  | "The random allocation sequence was generated by using computer-generated random numbers and was stratified by country in blocks of 6–8" |
| Allocation concealment (selection bias)                  | Low risk                  | Study packs were selected sequentially as each woman was enrolled and "the study drug packs were prepared, by Gynuity Health Projects. The packs were identical in shape, color, weight, and feel" |
| Blinding of participants and personnel (performance bias) | Low risk                  | Packs containing tablets identical in appearance were prepared at a different site, maintaining blinding of personnel and participants |
| Blinding of outcome assessment (detection bias)          | Low risk                  | As above                                                                             |
| Incomplete outcome data (attrition bias)                 | Low risk                  | Less than 0.5% loss to follow up. Primary outcome data relevant to this review was available for all participants followed up. |
| Selective reporting (reporting bias)                     | High risk                 | Secondary outcome data for blood transfusion and haemoglobin level <8 g/dL 24 hours after delivery was not reported as described in the published registration (NCT00124540) |
| Domain                                      | Review authors judgement | Support for judgement                                                                 |
|--------------------------------------------|---------------------------|---------------------------------------------------------------------------------------|
| Random sequence generation (selection bias) | Unclear risk              | There is no specific description of the randomisation methods used.                    |
| Allocation concealment (selection bias)    | Low risk                  | "opaque sealed envelope"                                                               |
| Blinding of participants and personnel (performance bias) | Low risk                  | "by the hospital pharmacist who alone was aware of the content of the ampoules"     |
| Blinding of outcome assessment (detection bias) | Low risk                  | As above                                                                               |
| Incomplete outcome data (attrition bias)   | Low risk                  | No attrition after randomisation                                                       |
| Selective reporting (reporting bias)       | Low risk                  | Although no protocol was available, all the expected outcomes have been reported.     |
| Domain                                      | Review authors judgement | Support for judgement                                                                 |
|---------------------------------------------|--------------------------|---------------------------------------------------------------------------------------|
| Random sequence generation (selection bias) | Unclear risk             | The authors state that participants were randomly allocated to an arm but do not explain the randomisation process in full, however, we believe that randomisation was likely adequate |
| Allocation concealment (selection bias)     | Low risk                 | "randomisation slips were contained in enveloped opened by a person not involved in the trial... who resealed the envelope" |
| Blinding of participants and personnel (performance bias) | Low risk | Blinding was achieved through preparation of the drug by an independent person not involved in further care of participants or assessments |
| Blinding of outcome assessment (detection bias) | Low risk | As above.                                                                            |
| Incomplete outcome data (attrition bias)    | Low risk                 | No attrition                                                                         |
| Selective reporting (reporting bias)        | High risk                | Not all expected outcomes for this trial have been reported – such as additional surgery and transfusion rates |
Masuzawa 2017

| Domain                                      | Review authors judgement | Support for judgement                                                                 |
|--------------------------------------------|--------------------------|---------------------------------------------------------------------------------------|
| Random sequence generation (selection bias) | Low risk                 | "Participants were randomly assigned... by use of a web-based randomisation system, with permuted blocks of six and stratified by parity" |
| Allocation concealment (selection bias)    | Low risk                 | The investigator did not know allocation until the time of placental delivery thus had no prior knowledge |
| Blinding of participants and personnel (performance bias) | High risk                | Blinding not possible due to nature of the intervention                                 |
| Blinding of outcome assessment (detection bias) | High risk                | As above                                                                              |
| Incomplete outcome data (attrition bias)   | Low risk                 | Although some women did not receive or discontinued the intervention, all data from randomised participants was analysed |
| Selective reporting (reporting bias)       | Low risk                 | Outcomes reported as per protocol (UMIN000019834)                                      |
## Table: Bias Assessment

| Domain                                           | Review authors judgement | Support for judgement                                                                                                                                 |
|--------------------------------------------------|--------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------|
| Random sequence generation (selection bias)      | Low risk                 | "To ensure balanced randomization and to conceal treatment assignment, a computer-generated randomization list with a random block size for each hospital was used. The data coordinating center generated a randomization list stratified by hospital" |
| Allocation concealment (selection bias)          | Low risk                 | "sequentially numbered sealed opaque envelope out of a locked cabinet in the delivery room"                                                             |
| Blinding of participants and personnel (performance bias) | Low risk                 | Envelopes were prepared by a member of the research team not involved in patient care. As misoprostol and ZB11 are administered at different times, a placebo was used alongside the allocated intervention to avoid knowledge of the intervention by the clinician or participant |
| Blinding of outcome assessment (detection bias)  | Low risk                 | Blinding of assessor as above, with objective measurement of the primary outcome (postpartum haemorrhage) used                                            |
| Incomplete outcome data (attrition bias)         | Low risk                 | Attrition was low as data was available for 960/967 women who had been randomised to the trial (less than 1% attrition)                               |
| Selective reporting (reporting bias)             | Low risk                 | Outcomes reported as per protocol (NCT00147420)                                                                                                          |
| Domain                                           | Review authors judgement | Support for judgement                                                                 |
|--------------------------------------------------|---------------------------|---------------------------------------------------------------------------------------|
| Random sequence generation (selection bias)      | Low risk                  | "...block randomisation, stratified according to number of births (first and second and more childbirths) with block sizes of 4 and 6 and allocation ratio of 1:1." |
| Allocation concealment (selection bias)          | Low risk                  | "...opaque sequentially numbered sealed packages"                                     |
| Blinding of participants and personnel (performance bias) | High risk                | A nurse not involved directly with participant prepared the drugs so "the data assessor and participants had no knowledge of the study medication." However, it is likely that blinding could have been broken. |
| Blinding of outcome assessment (detection bias)  | High risk                 | As above                                                                              |
| Incomplete outcome data (attrition bias)         | Low risk                  | No attrition                                                                          |
| Selective reporting (reporting bias)             | Unclear risk              | Protocol not seen.                                                                    |
| Domain                                      | Review authors judgement | Support for judgement                                      |
|--------------------------------------------|--------------------------|------------------------------------------------------------|
| Random sequence generation (selection bias)| Low risk                 | "They were randomized using computer-generated numbers"   |
| Allocation concealment (selection bias)    | Unclear risk             | There is no specific description of allocation concealment methods |
| Blinding of participants and personnel (performance bias) | High risk               | Blinding not possible due to differences in administration |
| Blinding of outcome assessment (detection bias) | High risk               | As above                                                  |
| Incomplete outcome data (attrition bias)   | Low risk                 | No attrition                                              |
| Selective reporting (reporting bias)       | Low risk                 | All expected outcomes for this trial type were reported    |
| Domain                                               | Review authors judgement | Support for judgement                                                                 |
|------------------------------------------------------|---------------------------|---------------------------------------------------------------------------------------|
| Random sequence generation (selection bias)          | Low risk                  | "An independent, centralized computer-generated randomization sequence... based on a randomization list established by an independent statistician" |
| Allocation concealment (selection bias)              | Low risk                  | "To conceal allocation, treatment boxes were sealed and numbered sequentially"         |
| Blinding of participants and personnel (performance bias) | High risk                 | "The treatment was administered by a research midwife who did not otherwise participate in this trial". However, it is likely that blinding could have been broken. |
| Blinding of outcome assessment (detection bias)      | High risk                 | As above                                                              |
| Incomplete outcome data (attrition bias)             | Low risk                  | There was no loss to follow up                                                     |
| Selective reporting (reporting bias)                 | Low risk                  | As per protocol with an additional post hoc analysis (NCT01113229)               |
| Domain                                      | Review authors judgement | Support for judgement                                                                 |
|--------------------------------------------|--------------------------|---------------------------------------------------------------------------------------|
| Random sequence generation (selection bias) | Low risk                 | "Randomisation was performed by Gynuity Health Projects using a computer-generated random sequence within each stratum. |
| Allocation concealment (selection bias)    | High risk                | This was a cluster randomised trial, so allocation will have been known in advance.   |
| Blinding of participants and personnel (performance bias) | High risk                | Blinding was not possible                                                              |
| Blinding of outcome assessment (detection bias) | High risk                | As above                                                                              |
|Incomplete outcome data (attrition bias)    | Low risk                 | Less than 1.5% of participants were lost to follow up, and primary outcome data was unavailable for a further 1.6% |
| Selective reporting (reporting bias)       | Low risk                 | Outcomes reported as per protocol (NCT01462422)                                        |
| Domain                                                      | Review authors judgement | Support for judgement                                      |
|-------------------------------------------------------------|---------------------------|-----------------------------------------------------------|
| Random sequence generation (selection bias)                  | Low risk                  | A computer-generated randomisation table was used         |
| Allocation concealment (selection bias)                      | Low risk                  | Allocation data was placed in "serially numbered closed opaque envelopes" |
| Blinding of participants and personnel (performance bias)    | High risk                 | This was an open label trial, so blinding would not be possible. |
| Blinding of outcome assessment (detection bias)              | High risk                 | As above                                                 |
| Incomplete outcome data (attrition bias)                     | Low risk                  | All data from randomised participants were analysed and reported |
| Selective reporting (reporting bias)                         | Unclear risk              | There is an unclear definition of postpartum haemorrhage. |
| Domain                                           | Support for judgement                                      |
|--------------------------------------------------|-----------------------------------------------------------|
| Random sequence generation (selection bias)      | "Women were randomized to one of the three study arms according to a confidential computer-generated block randomization algorithm. The algorithm randomly allocated three women to each study dose in blocks of nine, thus ensuring equal allocation among the study arms" |
| Allocation concealment (selection bias)          | Preparation of the oxytocin was done prior to the randomisation process and by research members who had "no role in patient enrolment or outcome ascertainment" |
| Blinding of participants and personnel (performance bias) | Participants and personnel (who had patient contact) were blinding to the concentration of oxytocin in the numbered bags |
| Blinding of outcome assessment (detection bias)   | "Only the investigational pharmacist and one statistician, who had no role in patient enrolment or outcome ascertainment" |
| Incomplete outcome data (attrition bias)         | Data was analysed for all participants who had been randomised |
| Selective reporting (reporting bias)             | All outcomes reported had been previously described in the published registration (NCT00790062) |