

**GRADE tables for review question: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour?**

**Table 4: Evidence profile for comparison 1: IV oxytocin vs IM oxytocin**

| Quality assessment   |                   |                         |                          |                         |                      |                      | No of patients     |                     | Effect                    |   | Quality  | Importance |
|--|-------------------|-------------------------|--------------------------|-------------------------|----------------------|----------------------|--------------------|---------------------|---------------------------|---|----------|------------|
| No of studies  | Design            | Risk of bias            | Inconsistency            | Indirectness            | Imprecision          | Other considerations | IV oxytocin        | IM oxytocin         | Relative (95% CI)         | Absolute  |          |            |
| <b>Maternal admission to intensive therapy unit (ITU) or high-dependency area - IV bolus injection</b>                   |                   |                         |                          |                         |                      |                      |                    |                     |                           |   |          |            |
| 1<br>(Adnan 2018)  | randomised trials | no serious risk of bias | no serious inconsistency | no serious indirectness | serious <sup>1</sup> | none                 | 9/517<br>(1.7%)    | 19/518<br>(3.7%)    | RR 0.47<br>(0.22 to 1.04) | 19 fewer per 1000<br>(from 29 fewer to 1 more)  | MODERATE | CRITICAL   |
| <b>Primary PPH (blood loss ≥ 500 mL)- overall estimate</b>   |                   |                         |                          |                         |                      |                      |                    |                     |                           |   |          |            |
| 6<br>(Adnan 2018, Charles 2019, Dagdeviren 2016, Durocher 2019, Oguz 2014, Sangkhomkhamh ang 2015)                       | randomised trials | serious <sup>2</sup>    | no serious inconsistency | no serious indirectness | serious <sup>1</sup> | none                 | 198/4218<br>(4.6%) | 242/3516<br>(6.9%)  | RR 0.78<br>(0.66 to 0.93) | 15 fewer per 1000<br>(from 5 fewer to 23 fewer) | LOW      | CRITICAL   |
| <b>Primary PPH (blood loss ≥ 500 mL) - IV slow infusion</b>  |                   |                         |                          |                         |                      |                      |                    |                     |                           |   |          |            |
| 3<br>(Charles 2019, Dagdeviren 2016, Durocher 2019)  | randomised trials | no serious risk of bias | no serious inconsistency | no serious indirectness | serious <sup>1</sup> | none                 | 75/2385<br>(3.1%)  | 93/2473<br>(3.8%)   | RR 0.82<br>(0.62 to 1.08) | 7 fewer per 1000<br>(from 14 fewer to 3 more)   | MODERATE | CRITICAL   |
| <b>Primary PPH (blood loss ≥ 500 mL) - IV bolus injection</b>  |                   |                         |                          |                         |                      |                      |                    |                     |                           |   |          |            |
| 4<br>(Adnan 2018, Charles 2019, Oguz 2014, Sangkhomkhamh ang 2015)   | randomised trials | serious <sup>2</sup>    | no serious inconsistency | no serious indirectness | serious <sup>1</sup> | none                 | 119/1743<br>(6.8%) | 170/3147<br>(14.3%) | RR 0.76<br>(0.61 to 0.95) | 13 fewer per 1000<br>(from 3 fewer to 21 fewer) | LOW      | CRITICAL   |
| <b>Primary PPH (blood loss ≥ 500 mL) - IV bolus injection (women who have had oxytocin in the first stage of labour)</b> |                   |                         |                          |                         |                      |                      |                    |                     |                           |   |          |            |

| Quality assessment   |                       |                         |                          |                         |                           |                      | No of patients  |                 | Effect                  |   | Quality  | Importance |
|--|-----------------------|-------------------------|--------------------------|-------------------------|---------------------------|----------------------|-----------------|-----------------|-------------------------|---|----------|------------|
| No of studies  | Design                | Risk of bias            | Inconsistency            | Indirectness            | Imprecision               | Other considerations | IV oxytocin     | IM oxytocin     | Relative (95% CI)       | Absolute                                      |          |            |
| 1 (Adnan 2018)   | randomised trials     | no serious risk of bias | no serious inconsistency | no serious indirectness | serious <sup>1</sup>      | none                 | 50/ 271 (18.5%) | 64/ 275 (23.3%) | RR 0.79 (0.57 to 1.1)   | 49 fewer per 1000 (from 100 fewer to 23 more) | MODERATE | CRITICAL   |
| <b>Primary PPH (blood loss ≥ 500 mL) - IV bolus injection (women who have not had oxytocin in the first stage of labour)</b> |                       |                         |                          |                         |                           |                      |                 |                 |                         |   |          |            |
| 2 (Adnan 2018, Charles 2019)   | randomised trials     | serious <sup>2</sup>    | no serious inconsistency | no serious indirectness | serious <sup>1</sup>      | none                 | 52/947 (5.5%)   | 77/2347 (3.3%)  | RR 0.81 (0.58 to 1.12)  | 6 fewer per 1000 (from 14 fewer to 4 more)    | LOW      | CRITICAL   |
| <b>Severe PPH (blood loss ≥ 1000 mL)- overall estimate</b>   |                       |                         |                          |                         |                           |                      |                 |                 |                         |   |          |            |
| 4 (Adnan 2018, Charles 2019, Dagdeviren 2016, Durocher 2019)   | observational studies | no serious risk of bias | serious <sup>3</sup>     | no serious indirectness | serious <sup>1</sup>      | none                 | 47/3693 (1.3%)  | 69/2991 (2.3%)  | POR 0.65 (0.44 to 0.94) | 8 fewer per 1000 (from 1 fewer to 13 fewer)   | LOW      | CRITICAL   |
| <b>Severe PPH (blood loss ≥ 1000 mL) - IV slow infusion</b>  |                       |                         |                          |                         |                           |                      |                 |                 |                         |   |          |            |
| 3 (Charles 2019, Dagdeviren 2016, Durocher 2019)   | randomised trials     | no serious risk of bias | serious <sup>3</sup>     | no serious indirectness | very serious <sup>4</sup> | none                 | 22/2385 (0.92%) | 27/2473 (1.1%)  | POR 0.82 (0.46 to 1.46) | 2 fewer per 1000 (from 6 fewer to 5 more)     | LOW      | CRITICAL   |
| <b>Severe PPH (≥ 1000 mL) - IV bolus injection</b>   |                       |                         |                          |                         |                           |                      |                 |                 |                         |   |          |            |
| 2 (Adnan 2018, Charles 2019)   | randomised trials     | no serious risk of bias | no serious inconsistency | no serious indirectness | serious <sup>1</sup>      | none                 | 24/517 (4.6%)   | 42/518 (8.1%)   | POR 0.55 (0.34 to 0.88) | 36 fewer per 1000 (from 6 fewer to 54 fewer)  | MODERATE | CRITICAL   |
| <b>Severe PPH (blood loss ≥ 1000 mL) - IV bolus injection (women who have had oxytocin in the first stage of labour)</b>     |                       |                         |                          |                         |                           |                      |                 |                 |                         |   |          |            |
| 1 (Adnan 2018)   | randomised trials     | no serious risk of bias | no serious inconsistency | no serious indirectness | no serious imprecision    | none                 | 10/253 (4%)     | 28/250 (11.2%)  | POR 0.35 (0.18 to 0.69) | 73 fewer per 1000 (from 35 fewer to 92 fewer) | HIGH     | CRITICAL   |
| <b>Severe PPH (blood loss ≥ 1000 mL) - IV bolus injection (women who have not had oxytocin in the first stage of labour)</b> |                       |                         |                          |                         |                           |                      |                 |                 |                         |   |          |            |
| 2 (Adnan 2018, Charles 2019)   | randomised trials     | no serious risk of bias | no serious inconsistency | no serious indirectness | very serious <sup>4</sup> | none                 | 15/954 (1.6%)   | 23/2354 (1%)    | POR 0.83 (0.42 to 1.63) | 2 fewer per 1000 (from 6 fewer to 6 more)     | LOW      | CRITICAL   |

| Quality assessment  |                   |                         |                          |                         |                      |                      | No of patients  |                 | Effect                  |  | Quality  | Importance |
|---|-------------------|-------------------------|--------------------------|-------------------------|----------------------|----------------------|-----------------|-----------------|-------------------------|--|----------|------------|
| No of studies   | Design            | Risk of bias            | Inconsistency            | Indirectness            | Imprecision          | Other considerations | IV oxytocin     | IM oxytocin     | Relative (95% CI)       | Absolute                                     |          |            |
| <b>Need for manual removal of placenta- overall estimate</b>  |                   |                         |                          |                         |                      |                      |                 |                 |                         |  |          |            |
| 4<br>(Charles 2019, Dagdeviren 2016, Durocher 2019, Oguz 2014)  | randomised trials | serious <sup>2</sup>    | no serious inconsistency | no serious indirectness | serious <sup>1</sup> | none                 | 63/3476 (1.8%)  | 67/4877 (2.4%)  | POR 0.71 (0.50 to 1.01) | 7 fewer per 1000 (from 12 fewer to 0 more)   | LOW      | IMPORTANT  |
| <b>Need for manual removal of placenta - IV slow infusion</b>   |                   |                         |                          |                         |                      |                      |                 |                 |                         |  |          |            |
| 3<br>(Charles 2019, Dagdeviren 2016, Durocher 2019)   | randomised trials | no serious risk of bias | no serious inconsistency | no serious indirectness | serious <sup>1</sup> | none                 | 52/2475 (2.1%)  | 65/2473 (2.6%)  | POR 0.79 (0.55 to 1.15) | 6 fewer per 1000 (from 12 fewer to 4 more)   | MODERATE | IMPORTANT  |
| <b>Need for manual removal of placenta - IV bolus injection</b>   |                   |                         |                          |                         |                      |                      |                 |                 |                         |  |          |            |
| 2<br>(Charles 2019, Oguz 2014)  | randomised trials | serious <sup>2</sup>    | no serious inconsistency | no serious indirectness | serious <sup>1</sup> | none                 | 11/1001 (1.1%)  | 62/2404 (2.6%)  | POR 0.55 (0.32 to 0.93) | 12 fewer per 1000 (from 2 fewer to 18 fewer) | LOW      | IMPORTANT  |
| <b>Need for additional uterotonics during the third stage or within the first 48 hours- overall estimate</b>                                  |                   |                         |                          |                         |                      |                      |                 |                 |                         |  |          |            |
| 6 (Adnan 2018, Charles 2019, Dagdeviren 2016, Durocher 2019, Neri-Mejia 2016, Oguz 2014)  | randomised trials | serious <sup>2</sup>    | no serious inconsistency | no serious indirectness | serious <sup>1</sup> | none                 | 179/4174 (4.3%) | 230/3463 (6.6%) | POR 0.79 (0.63 to 0.99) | 14 fewer per 1000 (from 1 fewer to 25 fewer) | LOW      | IMPORTANT  |
| <b>Need for additional uterotonics during the third stage or within the first 48 hours - IV slow infusion</b>                                 |                   |                         |                          |                         |                      |                      |                 |                 |                         |  |          |            |
| 3<br>(Charles 2019, Dagdeviren 2016, Durocher 2019)   | randomised trials | no serious risk of bias | serious <sup>3</sup>     | no serious indirectness | serious <sup>1</sup> | none                 | 38/2475 (1.5%)  | 56/2473 (2.3%)  | POR 0.67 (0.44 to 1.01) | 7 fewer per 1000 (from 13 fewer to 0 MORE)   | HIGH     | IMPORTANT  |
| <b>Need for additional uterotonics during the third stage or within the first 48 hours - IV bolus injection</b>                               |                   |                         |                          |                         |                      |                      |                 |                 |                         |  |          |            |
| 4 (Adnan 2018, Charles 2019, Neri-Mejia 2016, Oguz 2014)  | randomised trials | serious <sup>2</sup>    | no serious inconsistency | no serious indirectness | serious <sup>1</sup> | none                 | 141/1539 (9.2%) | 174/2944 (5.9%) | POR 0.86 (0.67 to 1.11) | 8 fewer per 1000 (from 20 fewer to 7 more)   | LOW      | IMPORTANT  |
| <b>Need for additional uterotonics during the third stage or within the first 48 hours - Combined IV bolus injection and IV slow infusion</b> |                   |                         |                          |                         |                      |                      |                 |                 |                         |  |          |            |

| Quality assessment                       |                   |                         |                          |                         |                           |                      | No of patients |              | Effect                  |   | Quality | Importance |
|--|-------------------|-------------------------|--------------------------|-------------------------|---------------------------|----------------------|----------------|--------------|-------------------------|---|---------|------------|
| No of studies                            | Design            | Risk of bias            | Inconsistency            | Indirectness            | Imprecision               | Other considerations | IV oxytocin    | IM oxytocin  | Relative (95% CI)       | Absolute                                    |         |            |
| 1 (Biradar 2021)                         | randomised trials | no serious risk of bias | no serious inconsistency | no serious indirectness | very serious <sup>4</sup> | none                 | 0/160 (0%)     | 3/160 (1.9%) | POR 0.13 (0.01 to 1.29) | 16 fewer per 1000 (from 19 fewer to 5 more) | LOW     | IMPORTANT  |
| <b>Side effects - IV bolus injection</b> |                   |                         |                          |                         |                           |                      |                |              |                         |   |         |            |
| 2 (Adnan 2018, Neri-Mejia 2016)          | randomised trials | serious <sup>2</sup>    | no serious inconsistency | no serious indirectness | very serious <sup>4</sup> | none                 | 22/538 (4.1%)  | 27/540 (5%)  | POR 0.81 (0.46 to 1.44) | 9 fewer per 1000 (from 27 fewer to 22 more) | LOW     | IMPORTANT  |

IM: intramuscular; ITU: intensive therapy unit; IV: intravenous; mL: millimetres; POR: peto odds ratio; PPH: postpartum haemorrhage

1 95% CI crosses 1 MID

2 Serious concerns of risk of bias in the evidence contributing to the outcomes as per RoB 2.0

3 Serious heterogeneity

4 95% CI crosses 2 MIDs