MifeMiso

**Mifepristone and misoprostol versus misoprostol alone in the medical management of missed miscarriage: the MifeMiso randomised controlled trial**

**Appendix VII: Supplementary data tables**

**Table S1.** Concomitant medication post-randomisation

|  |  |  |
| --- | --- | --- |
|  | **Mifepristone + Misoprostol**(N=357) | **Placebo + Misoprostol** (N=354) |
| **Concomitant medication** |
| Analgesic | 172 (48%) | 163 (46%) |
| Anesthetics | 3 (1%) | 5 (1%) |
| Antibacterial | 54 (15%) | 46 (13%) |
| Anticonvulsant | 4 (1%) | 3 (1%) |
| Antidepressant | 2 (1%) | 3 (1%) |
| Antifungal | 1 (<1%) | 0 (-) |
| Anti-inflammatory agents | 2 (1%) | 5 (1%) |
| Anti-platelet | 1 (<1%) | 0 (-) |
| Antispacity agents | 3 (1%) | 0 (-) |
| Antivirals | 1 (<1%) | 0 (-) |
| Anxiolytics | 0 (-) | 1 (<1%) |
| Blood glucose regulators | 2 (1%) | 1 (<1%) |
| Blood Products/Modifiers/Volume Expanders | 21 (6%) | 18 (5%) |
| Cardiovascular agent | 1 (<1%) | 2 (1%) |
| Dermatological agent | 0 (-) | 1 (<1%) |
| Gastrointestinal agent | 11 (3%) | 10 (3%) |
| Hormonal Agents, Stimulant/Replacement/Modifying (Sex Hormones/Modifiers) | 6 (2%) | 5 (1%) |
| Hormonal Agents, Stimulant/Replacement/Modifying (Thyroid) | 4 (1%) | 3 (1%) |
| Hormonal Agents, Stimulant/Replacement/Modifying (Prostaglandins) | 2 (1%) | 1 (<1%) |
| Hormonal Agents, Suppressant (Sex Hormones/modifier) | 1 (<1%) | 0 (-) |
| Immunological agent | 0 (-) | 1 (<1%) |
| Migraine | 1 (<1%) | 1 (<1%) |
| Respiratory tract agent | 22 (6%) | 20 (6%) |
| Sedative/hypnotic | 1 (<1%) | 1 (<1%) |

**Table S2.** Adverse Events and Serious Adverse Events – total numbers

|  |  |  |
| --- | --- | --- |
|  | **Mifepristone + Misoprostol**(N=357) | **Placebo + Misoprostol** (N=354) |
| Total number of women experiencing at least one AE –n (%) | 26 (7%) | 24 (7%) |
| Total number of AEs | 30 | 26 |
| Total number of women experiencing at least one SAE –n (%) | 5 (1%) | 2 (1%) |
| Total number of SAEs | 5 | 2 |
| Total number of women experiencing at least one SUSAR –n (%) | 0 (-) | 0 (-) |
| Total number of SUSARs | 0 | 0 |

**Table S3.** Adverse events – further details by group

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | CTCAE category | Date of onset | Date resolved | Severity grade1 | Causality | Details of event |
| **Mifepristone + Misoprostol** (N=30) |  |  |  |
| 1 | 20 - Renal and urinary disorders | 11-Nov-17 | 13-Nov-17 | Grade 3 | Possibly related | Participant had a 2 unit blood transfusion due to a bleed at home after having her mifepristone or placebo lady had chronic kidney disease so it was advised that she go to theatre she was a risk of further bleeding |
| 2 | 25 - Surgical and medical procedures | 16-Dec-17 | 17-Dec-17 | Grade 3 | Unrelated | Heavy bleeding, came into ward 8, proceeded with an MVA, discharged on the 17/12/2017 |
| 3 | 18 - Pregnancy, puerperium and perinatal conditions | 30-Dec-17 | 30-Dec-17 | Grade 3 | Unrelated | Felt dizzy and faint just once at work, nil since, commenced on iron. |
| 4 | 11 – Infections and infestations | 03-Jan-18 | . | Grade 3 | Probably related | As the conception products are still remaining, she refers start to having offensive smell and discharge. She had some IVI antibiotics and she has been admitted for surgery |
| 5 | 25 - Surgical and medical procedures | 19-Jan-18 | . | Grade 3 | Probably related | Products of conception remaining and woman choose to have surgery as an option to remove them |
| 6 | 1 - Blood and lymphatic system disorders | 27-Mar-18 | 27-Mar-18 | Grade 3 | Unlikely to be related | Blood transfusion of 2 units RBC required as Hb 73g/l prior to surgical evacuation of uterus due to partial molar pregnancy & heavy bleeding |
| 7 | 25 - Surgical and medical procedures | 22-Feb-18 | 23-Feb-18 |  Not regulatory requirement – data missing and not mandated. |   Not regulatory requirement – data missing and not mandated. | Patient was admitted for heavy bleeding on 22/02/2018, she has a pelvic USS on 23/02/201 which showed retained products. Patient had an ERPC on 23/02/2018 |
| 8 | 25 - Surgical and medical procedures | 07-Mar-18 | . | Grade 4 | Probably related | Started heavy bleeding at home 07/03/2018 few hours after administering Misoprostol PV that morning. Invited into Gyne emergency. Retained products removed from Os however bleeding still heavy. Taken to theatre for surgical management .Retained products products visualised under ultrasound suction evacuation of products of conception. Total blood loss estimated 2400mls.2 unit blood transfusion |
| 9 | 18 - Pregnancy, puerperium and perinatal conditions | 23-Mar-18 | 30-Mar-18 | Grade 3 | Unlikely to be related | Was started on prophylactic antibiotics on 23/03/2018 for 7 days, patient says loss was a bit offensive, nothing detected. No infection. |
| 10 | 25 - Surgical and medical procedures | 08-May-18 | 09-May-18 | Grade 3 | Definitely related | still had gestation scan in uterus after day 21 |
| 11 | 25 - Surgical and medical procedures | 07-Jun-18 | 07-Jun-18 | Grade 3 | Possibly related | Randomised on the 04/05/2018. had fainted positive pregnancy test result on the 25/05/2018 as she was still bleeding. Stopped eventually on the 30/05/2018 and recommenced on the 03/06/2018. As bleeding continued, she had a new scan on the 05/06/2018 and ? RPOC/old blood. Deciding to have surgery as PV bleed continued on the 07/06/02018. Day surgery without night admission . |
| 12 | 21 - Reproductive system and breast disorders | 22-May-18 | 23-May-18 | Grade 4 | Unlikely to be related | Participant was entered into the trial on Monday 21/05/18 and was due to have her second part of mifemiso on Wednesday 23/05/18. However, due to heavy bleeding yesterday (22//5/18) she was admitted to the gynaecology ward and was given misoprostol yesterday (22/05/18) |
| 13 | 25 - Surgical and medical procedures | 29-Jun-18 | 29-Jun-18 | Grade 3 | Definitely related | Patient attended today for second part of medical treatment for miscarriage on the mifemiso trial. Patient reported pv bleeding on assessment. Was examined by SHO in ER, advised to continue with medical management as planned. Patient received 800mcg misoprostol this morning as per trial protocol taken orally and escorted home by her mother. Patient has since experienced heavy vaginal bleeding and pain, passing clots and query pregnancy tissue and fainted at home. Ambulance was called and patient was brought to Liverpool women's emergency room for assessment. Patient brought in what appears to be complete pregnancy tissue yet continues to experience pain and moderate vaginal bleeding. Patient currently being monitored by emergency room staff. Patient was examined by SR2 Twist, cervical OS remained open with minimal blood loss on examination. Plan to prvie analgesia and monitor blood loss over next hour Patient was reviewed again 1 hour later, pain and vaginal bleeding now settling. Plan for patient to go home |
| 14 | 25 - Surgical and medical procedures | 28-Sep-18 | 30-Sep-18 | Grade 3 | Possibly related | started bleeding, attended A&E transferred to ward. Had an ERPC the next day. Bleeding settled, sent home later that day, with ferrous sulphate tablets for anemia. |
| 15 | 21 - Reproductive system and breast disorders | 21-Nov-18 | . | Grade 3 | Unrelated | seen on EPU for scan on 21.11.18 following failed medical and surgical management with continued pain and bleeding? RPC's. Thickened endometrium. Fibroid uterus- MRI arranged as ? some abnormality seen on scan. MRI on 27.11.18. Radiology review with Senior Gynae consultant- degenerative fibroid with some vascular malformation- likely to cause further bleeding. Notes review by Study PI and senior Gynae consultant.Possible implantation on fibroid suggested by study PI on review of history but MRI suggests no RPC's. Senior Consultant to decide on management plan as BHCG still +VE as of 27.11.18 (308). Will continue to monitor |
| 16 | 21 - Reproductive system and breast disorders | 03-Jan-19 | 09-Jan-19 | Grade 3 | Unrelated | seen on gynae ward as emergency admission 3/1/19. Bleeding PV++. Known fibroaid and AV malformation of fibroid. HCG still positive (M/C diagnosed 26.10.18). Had hysteroscopy, suction evacuation of clots, and insertion of balloon tamponade. referred for embolisation of uterine artery. Had 6 night stay |
| 17 | 25 - Surgical and medical procedures | 30-Nov-18 | 01-Dec-18 | Grade 3 | Possibly related | On the 7th day scan, MSD 29.9mm and CRL 3.7mm. Participant did not pass the sac and offered treatment options. Surgical procedure took place as pregnancy tissue remaining. |
| 18 | 25 - Surgical and medical procedures | 08-Dec-18 | 10-Dec-18 | Grade 4 | Possibly related | Commenced to have bleeding after the misoprostol was given and then she collapsed. An ambulance took her to Hillingdon hospital and they performed a surgery on her as she bleed extensively. |
| 19 | 25 - Surgical and medical procedures | 02-Feb-19 | 03-Feb-19 | Grade 3 | Possibly related | Patient attended A&E 02/02/2019 with heavy pv bleeding and feeling faint. Misoprostal 800mcg given 01/02/2019. Due to patients presenting symptoms she was admitted for surgical management of miscarriage. The patient was admitted for one night post surgery and was discharged home on the following day - 03/02/2019. |
| 20 | 18 - Pregnancy, puerperium and perinatal conditions | 04-May-19 | 05-May-19 | Grade 3 | Unrelated | participant was diagnosed with suspected ectopic pregnancy and treatment with Methotrexate was commenced. Ruptured ectopic pregnancy subsequently diagnosed and participant underwent laparoscopic right salpinjectomy |
| 21 | 25 - Surgical and medical procedures | 03-May-19 | 03-May-19 | Grade 3 | Possibly related | Patient attended A&E with heavy pv bleeding the early hours of 03/05/2019. Admitted for surgery as patient bleeding heavily. Surgical management of miscarriage completed and patient was discharged home later that day without any complications. Surgical management of miscarriage performed under GA |
| 22 | 11 - Infections and infestations | 15-May-19 | 19-May-19 | Grade 3 | Possibly related | Developed rash a few days after taking IMP. |
| 23 | 5 - Endocrine disorders | 22-May-19 | 22-May-19 | Grade 3 | Unrelated | Patient is type 1 diabetic and attended A & E with high blood sugars and a concern that she may have DKA. Blood gas ruled out DKA. Patient left A & E department before full assessment, G.P letter sent to update and no further follow up at present. |
| 24 | 11 - Infections and infestations | 30-May-19 | . | Grade 3 | Possibly related | Patient attended EPAS for repeat scan post 14 days since randomisation scheduled by EPAS team. Patient has felt symptomatic with P.V foul odour, nausea and vomited x 1 episode. Reviewed by Registrar and prescribed co-amoxiclav and discharged home. To return to EPAS in one week for repeat bloods. Low vaginal swab obtained showed no growth, but suggestive of bacterial vaginosis, CRP and lactate bloods normal, low Hb, currently on iron therapy. To be reviewed in EPAS on the 6/6/19. |
| 25 | 25 - Surgical and medical procedures | 23-May-19 | 24-May-19 | Grade 3 | Definitely related | On the day she inserted the misoprostol, she commenced to bleed heavily and feeling dizzy. Went to A& E as the bleeding wont settled. She needed emergency surgical procedure. HB on admission was 111, but after procedure, the hemocute marked 64. She was transfused 2 units of blood. |
| 26 | 25 - Surgical and medical procedures | 14-Jun-19 | 15-Jun-19 | Grade 3 | Possibly related | Patient attended A&E with heavy blood loss and pain. Had u/s scan, showed retained products. Patient requested surgical intervention. |
| 27 | 25 - Surgical and medical procedures | 05-Jul-19 | 06-Jul-19 | Grade 3 | Possibly related | Patient attended A&E late evening 05/07/2019 with heavy pv bleeding and severe lower abdominal pain. Admitted overnight for observation and seen in EPU 06/07/2019 for further assessment. Participant was due to attend EPU on 06/07/2019 for misoprostal insertion. USS confirmed that the sac had passed - no need for misoprostal. Bleeding had settled when the participant was seen in clinic and was discharged from hospital. Hb recorded as 94 05/07/2019 sent home with oral ferrous sulphate. |
| 28 | 18 - Pregnancy, puerperium and perinatal conditions | 13-Jul-19 | 15-Jul-19 | Grade 3 | Possibly related | During the day 4/5 phone call on the 13th July 2019, the participant informed research staff that she had had heavy bleeding on Saturday, passed clots and fainted twice. Her husband had called an ambulance to attend. The paramedics assessed the participant's wellbeing and in conjunction with advice from the Gynae ward, the plan was for her to be invited in to the ward for assessment. The participant felt that her bleeding had settled and was feeling better and wished to remain at home. The paramedics contacted the ward to inform them that she would not be attending hospital. She was provided safety bnetting advice by Cotswold ward and has been documented on the telephone preforms. On the 14th July, the participant fainted whilst on the toilet, fell and sustained a cut to her head which her husband cleaned and dressed. She reports passing the gestational sac on this day too. Today, she feels better, has lighter bleeding and has had no further fainting episodes. The participant will be attending for her USS o |
| 29 | 18 - Pregnancy, puerperium and perinatal conditions | 18-Jul-19 | 19-Jul-19 | Grade 3 | Possibly related | 18/7/19 Seen in EPC. USS showed gestational sac has been passed, but there are still retained products. She was offered surgical, conservative or medical management (this would be the first dose of Misoprostol) and she chose conservative. Her Hb was taken as she was symptomatic of anaemia and she didn’t wait for the result. She was later contacted by the on call doctor to tell her that the HB result was 51g/dl and she needed admission. He managed to persuade her to return to the hospital. 18/7/19 at 20:30hrs she was seen on the gynae ward and Hb repeated=49g/dl. At 23:30hrs she received 2 units of blood transfused overnight. Reviewed this afternoon and clinically deemed fit for discharge. Hb repeated prior to discharge. Result=77g/dl. Prescribed Ferrous sulphate. |
| 30 | 25 - Surgical and medical procedures | 13-Jul-19 | 14-Jul-19 | Grade 3 | Unlikely to be related | Patient admited from clinic post misoprostal due to severe onset of pain. Admitted from clinic to ward via A&E and seen by Gynae doctor, products passed. Patient was found to be pyrexial and started on antibiotics. Kept overnight for observations and discharged the following day as fever and pain resolved.. |
| **Placebo + Misoprostol** (N=26) |  |  |  |
| 1 | 25 - Surgical and medical procedures | 17-Nov-17 | 21-Nov-17 |  Not regulatory requirement – data missing and not mandated. |   Not regulatory requirement – data missing and not mandated. | Patient had elective surgical intervention for RPOC. the surgery was uncomplicated and patient is doing well post surgery. |
| 2 | 25 - Surgical and medical procedures | 24-Nov-17 | 25-Nov-17 | Grade 4 | Possibly related | Patient attended EPAU with heavy bleeding . Required surgical management for retained products of conception. HB 7.5 transfused 2 units of blood. |
| 3 | 25 - Surgical and medical procedures | 29-Dec-17 | 05-Jan-18 |  Not regulatory requirement – data missing and not mandated. |   Not regulatory requirement – data missing and not mandated. | Patient came in for surgical intervention for ERPC. She called on 05/01/2018 to let EPU nurse know her pregnancy result is still negative. |
| 4 | 18 - Pregnancy, puerperium and perinatal conditions | 29-Nov-17 | 29-Nov-17 | Grade 3 | Probably related | Patient bled very heavy at home and passed out. ambulance was called and patient brought into hospital. clots removed, bleeding settled. patient discharged home. |
| 5 | 7 - Gastrointestinal disorders | 27-Nov-17 | 27-Nov-17 | Grade 3 | Unlikely to be related | Vomited 2 hours after taking mife/placebo |
| 6 | 1 - Blood and lymphatic system disorders | 06-Dec-17 | 06-Dec-17 | Grade 3 | Definitely related | Attended A&E with heavy PV loss and passing clots. Changed 4 pads in one hour and experiencing worsening abdominal pain. Given pain relief and fluids prior to discharge. Was not admitted to a ward and was discharged from A&E. |
| 7 | 11 - Infections and infestations | 02-Dec-17 | 03-Dec-17 | Grade 3 | Unrelated | heavy bleeding, severe pain |
| 8 | 18 - Pregnancy, puerperium and perinatal conditions | 06-Dec-17 | 08-Dec-17 | Grade 3 | Unrelated | feeling dizzy, light headed. Low haemoglobin level On ferrous sulphate 600mgs daily. |
| 9 | 1 - Blood and lymphatic system disorders | 07-Dec-17 | . | Grade 3 | Unrelated | Antibiotics commenced on 07/12/2017 for prevention of infection. No infection diagnosed |
| 10 | 18 - Pregnancy, puerperium and perinatal conditions | 14-Dec-17 | 15-Dec-17 | Grade 3 | Unrelated | Heavy bleeding, pregnancy sac removed from cervix, bleeding became minimal, discharged 15/12/2017 |
| 11 | 18 - Pregnancy, puerperium and perinatal conditions | 17-Dec-17 | 18-Dec-17 | Grade 4 | Unlikely to be related | Started bleeding at home became unwell feeling faint. Call 999 attended by a paramedic. BP 96/62 89/30. Admitted to A&E pre-syncopal. Transferred to Bramshaw and had an ERPC. Large blood loss Hb dropped from 117 to 85 and transfused 2 units of blood. discharged from hospital on the 18th Dec Hb100 . |
| 12 | 25 - Surgical and medical procedures | 05-Feb-18 | 05-Feb-18 |  Not regulatory requirement – data missing and not mandated. |  Not regulatory requirement – data missing and not mandated. | Patient was scanned on 22/01/2018 as her day 7 follow-up and found she did not pass the gestational sac. She was re-scanned on 31/01/2018 and was diagnosed with an incomplete miscarriage, she opted to have surgical management to resolve. She had surgical management on 05/02/2018 |
| 13 | 18 - Pregnancy, puerperium and perinatal conditions | 21-Jan-18 | 22-Jan-18 | Grade 3 | Probably related | admitted to D47 with bleeding at 2100hrs 21/01/18 2100hrs and discharged Monday 22/01/18 at around 1230hrs |
| 14 | 25 - Surgical and medical procedures | 25-Jan-18 | 29-Jan-18 |  Not regulatory requirement – data missing and not mandated. | Not regulatory requirement – data missing and not mandated.  | Patient had an emergency ERPC on 25/01/2018. |
| 15 | 11 – Infections and infestations | 27-Feb-18 | 01-Mar-18 | Grade 3 | Probably related | The 2nd dose of misoprostol was given on day 7th after the scan and the confirmation that the some products are still remaining in place, though not the sac. She came to A&E with symptoms of infection; fever, offensive smell. As she stabilized, the surgery |
| 16 | 25 - Surgical and medical procedures | 18-Feb-18 | 19-Feb-18 | Grade 3 | Probably related | heavy bleeding and clots pv Suction evacuatation of POC in uterine cavity |
| 17 | 2 - Cardiac disorders | 22-Feb-18 | 22-Feb-18 | Grade 3 | Unlikely to be related | Participant was seen by medical staff after administration of misoprostol due to vomiting. Bradycardia noted 32. ECG carried out and vaginal examination performed. Impression was that it was cervical shock.Anti emetic given and symptoms improved. intravenous access given. |
| 18 | 25 - Surgical and medical procedures | 23-Mar-18 | 25-Mar-18 | Grade 3 | Possibly related | She refer to start to bleed excessively hours she took the first trial tablet (Mifepristone/Placebo) She went to A & E and was admitted as per excessive bleeding, as she started to be haemodinamicaly compromised, she required emergency surgery. Her Hb dropped 81 g/L. She did not have the misoprostol tablets, neither the scan on the 7th day. |
| 19 | 18 - Pregnancy, puerperium and perinatal conditions | 07-Aug-18 | 08-Aug-18 | Grade 3 | Unrelated | patient had surgical management and had complications that included blood transfusion, overnight stay. ?Molar pregnancy tissue sent for analysis |
| 20 | 18 - Pregnancy, puerperium and perinatal conditions | 30-Sep-18 | 01-Oct-18 | Grade 3 | Unlikely to be related | Patient was readmitted 10 Hours after the 800mg PV dose of misoprostol with bleeding PV. She was admitted in the hospital overnight and received 1 further dose of 400 mcg Misoprostol and her bleeding settled down after that. |
| 21 | 25 - Surgical and medical procedures | 24-Nov-18 | 24-Nov-18 | Grade 3 | Possibly related | Initial treatment with the randomised drug and misoprostol failed and sac reaming in, on the 7th day scan. Woman opting to have surgical procedure against repeating 2nd dose of misoprostol. Surgery happening on the 24/11/2018 and discharged on the same day. |
| 22 | 25 - Surgical and medical procedures | 15-Jan-19 | 15-Jan-19 | Grade 3 | Unlikely to be related | After failed on the medical management and the UPT at her 21st day was still positive probably due to her bleeding. She has a scan on the 11/01/2019 with a diagnose of having still RPOC. Therefore, surgical management was adviced |
| 23 | 21 - Reproductive system and breast disorders | 23-Dec-18 | 28-Dec-18 | Grade 4 | Probably related | Participant was admitted to Sunderland Royal Hospital ward D47 on 23/12/18 following Misoprostol administration Pv that morning , she was kept overnight and discharged 24/12/18. Participant was then visiting her relative in Durham 26/12/18 and she started to bleed heavily PV therefore relative called for an ambulance and participant was taken to A&E from this department she went for surgery and then admitted to ward 9 Durham Hospital, and will be home later today. |
| 24 | 21 - Reproductive system and breast disorders | 20-Jan-19 | 21-Jan-19 | Grade 3 | Possibly related | Participant admitted to D47 with vaginal bleeding following day 2 administration of Misoprostol 800mcg Pv. Participant admitted around 18:00hrs 20/01/19 and discharged the next day 21/01/19 after review. |
| 25 | 25 - Surgical and medical procedures | 08-May-19 | 09-May-19 | Grade 3 | Possibly related | Patient attended A&E with heavy bleeding and lower abdo pain. Seen and bleeding monitored for a few hours in A&E as came in late at night. Analgesia given and discharged home. Observations were stable and Hb 125. |
| 26 | 25 - Surgical and medical procedures | 03-Jul-19 | 08-Jul-19 | Grade 3 | Unrelated | Patient took study drug 1.7.19 nil issues noted. Patient then took Misoprostol as directed on 3.7.19. Bleeding became increasingly heavy and patient called the ambulance. Patient was taken to local hospital Accident and Emergency where she underwent an emergency evacuation of retained products of conception in the early hours of 4.7.19. Patient was admitted to ITU after and reports receiving 5 units of blood transfused. Patient informs me her HB was 81 and therefore moved to the ward on 6.7.19. She was observed for 2 nights before being discharged from hospital on 8.7.19 where I contacted her at home to ensure she was now recovering and safe. |

**Table S4.** Serious Adverse Events – further details by group

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | CTCAE category | Date of onset | Date resolved | Related to the intervention | Severity | Details of event |
| **Mifepristone + Misoprostol** (N=5) |  |  |  |
| 1 | Renal and urinary disorders | 11/11/17 | 12/11/17 | Possibly related | Grade 3 | Chronic renal disease stage 3 |
| 2 | Surgical and medical procedures | 07/03/18 | 08/03/18 | Possibly related | Grade 4 | Significant blood loss |
| 3 | Reproductive system and breast disorders | 03/01/19 | 09/01/19 | Unrelated | Grade 3 | BPV++ due to AV malformation of fibroid |
| 4 | Pregnancy, puerperium and perinatal conditions/Reproductive system and breast disorders/Surgical and medical procedures | 04/05/19 | 05/05/19 | Unrelated | Grade 3 | Ruptured ectopic pregnancy |
| 5 | Pregnancy, puerperium and perinatal conditions | 18/07/19 | 19/07/19 | Possibly related | Grade 3 | Anaemia secondary to bleeding from miscarriage |
| **Placebo + Misoprostol** (N=2) |  |  |  |
| 1 | Pregnancy, puerperium and perinatal conditions | 17/12/17 | 18/12/17 | Unlikely to be related | Grade 4 | Discharged from hospital with Hb of 100, ERPC, Bleeding settled |
| 2 | Pregnancy, puerperium and perinatal conditions/ Surgical and medical procedures | 03/07/19 | 08/07/19 | Unrelated | Grade 3 | Heavy vaginal bleeding leading to hypovolaemic shock, need for admission to I.T.U and blood transfusion |

**Table S5.** Results of the deterministic sensitivity analyses for the cost-effectiveness analysis

|  |  |  |  |
| --- | --- | --- | --- |
| Management Strategy | Average cost (£)per woman | Effectiveness | ICER (£) |
| *1. Proportion of women undergoing a second stage of expectant management decreased by 50%*  |
| Medical management with mifepristone + misoprostol  | 761 | 0.830 | - |
| Surgical management | 1658 | 0.959  | 6969 |
| Current medical management | 876 | 0.717 | Dominated |
| Expectant management  | 1216 | 0.289 | Dominated |
|  |  |  |  |
| *2. Proportion of women undergoing a second stage of expectant management increased by 50%*  |
| Medical management with mifepristone + misoprostol  | 761 | 0.830 | - |
| Surgical management | 1658 | 0.959  | 6969 |
| Current medical management | 876 | 0.717 | Dominated |
| Expectant management  | 1125 | 0.289 | Dominated |
|  |  |  |  |
| *3. All surgeries performed using MVA*  |  |  |  |
| Medical management with mifepristone + misoprostol  | 7212 | 0.830 | - |
| Surgical management | 1519 | 0.959  | 6193 |
| Current medical management | 830 | 0.717 | Dominated |
| Expectant management  | 1086 | 0.289 | Dominated |
|  |  |  |  |
| *5. All surgeries performed using D&E* |  |  |  |
| Medical management with mifepristone + misoprostol  | 772 | 0.830 | - |
| Surgical management | 1700 | 0.959  | 7205 |
| Current medical management | 889 | 0.717 | Dominated |
| Expectant management  | 1204 | 0.289 | Dominated |
|  |  |  |  |
| *6. 50% of surgeries performed using MVA/50% of surgeries performed using D&E* |
| Medical management with mifepristone + misoprostol  | 747 | 0.830 | - |
| Surgical management | 1609 | 0.959  | 6699 |
| Current medical management | 859 | 0.717 | Dominated |
| Expectant management  | 1145 | 0.289 | Dominated |
|  |  |  |  |
| *7. Effectiveness of stage 2 medical management (expectant management branch) increased by 10%* |
| Medical management with mifepristone + misoprostol  | 761 | 0.830 | - |
| Surgical management | 1658 | 0.959  | 6969 |
| Current medical management | 876 | 0.717 | Dominated |
| Expectant management  | 1216 | 0.289 | Dominated |
|  |  |  |  |
| *8. Effectiveness of stage 2 medical management (expectant management branch) decreased by 10%* |
| Medical management with mifepristone + misoprostol  | 761 | 0.830 | - |
| Surgical management | 1658 | 0.959  | 6969 |
| Current medical management | 876 | 0.717 | Dominated |
| Expectant management  | 1137 | 0.289 | Dominated |
|  |  |  |  |
| *8. Nights of inpatient admission decreased by 50% in all strategies populated by secondary source data* |
| Medical management with mifepristone + misoprostol  | 761 | 0.830 | - |
| Surgical management | 1633 | 0.959  | 6773 |
| Current medical management | 833 | 0.717 | Dominated |
| Expectant management  | 1137 | 0.289 | Dominated |
| Note: Costs and ICERs are reported to the nearest pound |  |  |  |