

Appendix 2. Detailed list of all included studies

Name study	Study population	Tested intervention	Comparison 1	Comparison 2	Publication	Funding in euros
Studies with recruitment failure						
Obstetrics						
APOSTEL-IV	Women with preterm pre-labour rupture of membranes without contractions 24-34 weeks	Drugs	Nifedipine	Placebo	EJOG Repr Biology 2016	0
APOSTEL VIII	Women with threatened preterm birth (gestational age 30-34 weeks)	Obstetrical treatments	Treatment with atosiban for 48 hours	Placebo	Not yet (analyzing data)	1 400 000
DIGITAT	Women with intra-uterine growth restriction beyond 36 weeks gestation	Obstetrical treatments	Induction of labour	Expectant management	BMJ 2010	400 000
GLUCOMOMS	Pregnant women with type 1 or 2 diabetes undergoing insulin therapy <16 or > 30 weeks	Obstetrical treatments	Intermittent use of retrospective continuous glucose monitoring	Standard treatment	Diabetes Obes Metab 2018	300 000
HighLow	Pregnant women with a history of venous thromboembolism	Drugs	Weigh-adjusted intermediate-dose heparin	Fixed low-dose low-molecular-weight heparin	Lancet 2022	1 600 000
HYPITAT-II	Women with non-severe hypertensive disorders of pregnancy 34-37 weeks gestation	Obstetrical treatments	Immediate delivery (induction of labour or caesarean section)	Expectant management until 37 weeks of gestation	Lancet 2015	355 432
INDEX	Low risk women with an uncomplicated singleton pregnancy at 41 weeks	Obstetrical treatments	Induction of labour	Expectant management until 42 weeks	BMJ 2019	670 870
IUPC	Women in whom induced or augmented labour was required	Obstetrical treatments	Internal tocodynamometry	External monitoring	NEJM 2010	0

PPROMEXIL-3	Women with a singleton pregnancy and preterm pre-labour rupture of the membranes 16-24 weeks gestation with oligohydramnios	Obstetrical treatments	Transabdominal amnion infusion	No intervention	Obstetrics & Gynecology 2019	No funding
QP singletons	Women with a short cervix < 35mm in a singleton and < 38 mm in a multiple pregnancy	Obstetrical treatments	Cervical pessary	Progesterone	Submitted	No funding
SIMPLE-III	Term nulliparous women with a singleton pregnancy and a child in cephalic presentation and the Freidman partogram action line is crossed after regular interventions	Obstetrical treatments	Caesarean section	Expectant management waiting until the simple partogram line is crossed	Unpublished	397 220
STOPORGO	Pregnant women gestational age < 16 weeks who use SSRIs without clinically relevant depressive symptoms	Drugs	Preventive cognitive therapy with gradual guided discontinuation of SSRIs under medical management	Continue use of SSRIs	J Clin Psychiatry 2020	500 000
Sugardip	Women with GDM who do not reach target glycaemic control with modification of diet 16-34 weeks gestation	Drugs	Oral glucose lowering drugs	Insulin	Submitted	437 148
TOTEM	Women with severe preeclampsia 28-34 weeks	Obstetrical treatments	Induction of labour	Expectant management	Acta Obstetricia et Gynecologica Scandinavica 2020	0
TRIPLE P	Women with a singleton pregnancy without a history of preterm birth and a cervix length ≤ 30 mm	Drugs	Progesterone	Placebo	Am J Perinatol 2015	1 000 000

WOMB	Women with acute anaemia 12-24 hours postpartum without severe anaemic symptoms or comorbidities	Obstetrical treatments	Red blood cell transfusion	Expectant management	BJOG 2014	214 450
Reproductive medicine						
AID	Women who were eligible for donor sperm treatment with cryopreserved donor semen	Fertility treatments	Intracervical insemination with cryopreserved donor sperm	Intrauterine insemination	Human Reproduction 2021	276 000
ALIFE	Women with a history of unexplained recurrent pregnancy loss	Drugs	Aspirin*	Placebo	NEJM 2010	112 500
ALIFE2	Women with recurrent pregnancy loss and inherited thrombophilia	Drugs	Low-molecular-weight heparin + standard treatment	Standard treatment	Lancet 2023	1 200 000
COSY	Heterosexual couples diagnosed with (relatively) unexplained subfertility and a good prognosis	Fertility treatments	6 month web-based interactive educational programme of sex counselling	Expectant management	Submitted	300 000
DESH	Women aged 18-41 years with uni- or bilateral ultrasound visible hydrosalpinges who were scheduled for an IVF/ICSI treatment	Fertility treatment	Hysteroscopic proximal occlusion by intratubal device placement	Laparoscopic salpingectomy	Human Reproduction 2016	0
ESEP	Women with a laparoscopically confirmed tubal pregnancy and a healthy contralateral tube	Surgery	Salpingotomy	Salpingectomy	Lancet 2014	63 000
EX-IUI	Heterosexual couples with unexplained subfertility and a poor	Fertility treatments	6 months IUI with ovarian stimulation	6 months expectant management	Human Reproduction 2022	423 827

FOAM	prognosis for natural conception Infertile women who were scheduled for tubal patency testing during fertility work-up	Diagnostic strategies	Hysterosalpingo-foam sonography	Hysterosalpingography	Human Reproduction 2022	214 340
H2OLIE	Infertile women who were undergoing hysterosalpingography	Diagnostic strategies	Oil-based contrast	Water-based contrast	NEJM 2017	0
IVF38	Subfertile couples diagnosed with unexplained or mild male subfertility in which the women are 38-42 years old	Fertility treatments	IVF treatment	Expectant management	Manuscript in preparation	365 000
M-OVIN	Women with normogonadotropic anovulation not pregnant after six ovulatory cycles of clomiphene citrate	Drugs	Six cycles of gondadotrophines***	Six cycles of clomiphene citrate**	Lancet 2019	305 000
MASTER 1	Subfertile couples with male subfertility pre-wash total motile sperm count 3-10 x 10 ⁶	Fertility treatments	IUI	Expectant management	Manuscript in preparation	388 208
MASTER 2	Subfertile couples with male subfertility pre-was total motile sperm count < 3 x 10 ⁶	Fertility treatments	ICSI	IVF	Manuscript in preparation	388 208
MEDIUM2	Subfertile couples undergoing an IVF/ICSI treatment	Fertility treatments	Culture medium G5 to culture all oocytes and resulting embryos of each patient	Culture medium CSCM	Manuscript in preparation	0
MISOREST	Women who had primary misoprostol treatment for miscarriage with sonographic evidence of incomplete evacuation of	Obstetrical treatment	Curettage	Expectant management	Human Reproduction 2016	216 000

SCRATCH OFO	the uterus Women with unexplained infertility and a good prognosis for spontaneous conception	Fertility treatment	Endometrial scratching in the luteal phase of the natural cycle	Expectant management	Manuscript in preparation	349 732
SOMA	Premenopausal women with pain and an ovarian endometrioma	Surgery	Medication	Surgery	Not yet	393 000
STIM	Women 18-43 years with breast cancer who opted for banking of oocytes or embryos	Drugs	Ovarian stimulation**** plus tamoxifen	Standard ovarian stimulation	Human Reproduction 2022	300 000
T4life	Women who were TPO-Ab positive 2 or more pregnancy losses and TSH normal range	Drugs	Levothyroxine	Placebo	Lancet Diabetes Endocrinol 2022	205 983
TRUST	Women with a septate uterus and a wish to conceive	Surgery	Uterine septum resection	Expectant management	Human reproduction 2021	322 430
Oncology						
LAPOVCA	Patients with suspected advanced-stage ovarian cancer who qualified for primary cytoreductive surgery	Surgery	Laparoscopy	Primary cytoreductive surgery	J Clin Oncol 2016	322 430
PARIS	Women undergoing pelvic radiotherapy	Diagnostic strategies	Chondroitin sulphate solution	Placebo	Unpublished	3 000
SOCCER	Women with recurrent platinum-sensitive epithelial ovarian cancer	Surgery	Secondary cytoreductive surgery + chemotherapy	Chemotherapy alone	Unpublished	0
(Uro)gynaecology						
CUPIDO-II	Women with a prolapse and occult stress incontinence	Surgery	Prolapse and concomitant anti-incontinence surgery	Prolapse surgery	Int Urogynecol J 2016	24 000

HYSNICHE	Women with postmenstrual spotting after a cesarean section and a niche with a residual myometrium of at least 3 mm during sonohysterography	Surgery	Hysteroscopic resection of the niche	Expectant management	BJOG 2017	250 000
PEOPLE	Treatment naïve women with pelvic organ prolapse who present with moderate to severe symptoms	Surgery	Pessary therapy	Vaginal pelvic organ prolapse surgery	JAMA 2022	387 000
POMPOEN	Women with postmenopausal bleeding an endometrial thickness > 4 mm and benign result from endometrial sampling	Diagnostic	Further diagnostic workup by hysteroscopy (preceded by saline infusion sonography)	Expectant management	BJOG 2016	0
PROSECCO	Women with a maximum of 3 symptomatic type 0 or 1 submucosal fibroids with maximum 3.5 cm diameter	Surgery	Hysteroscopic myomectomy procedural sedation and analgesia with propofol in outpatient setting	General anaesthesia in operating theatre	Submitted	337 747
SALTO	Women with a history of hysterectomy presenting with symptomatic vaginal vault prolapse with or without concomitant cystocele and rectocele who chose to undergo surgery	Surgery	Laparoscopic sacrocolpopexy	Open abdominal sacrocolpopexy	Int Urogynaecol J 2017	350 000
VUSIS-I	Women with symptomatic stress urinary incontinence in whom conservative measures failed and in whom surgical treatment is considered	Diagnostic strategies	Stress urinary incontinence therapy based on history clinical examination pad test and 48h voiding diary	Therapy based on the same parameters AND urodynamic findings	Neurourol Urodyn 2012	151 000

WOMAN	Women with a symptomatic cyst or abscess of the Bartholin gland	Gynaecological treatment	Treatment with Word catheter	Marsupialisation	BJOG 2016	0
Studies without recruitment failure						
<i>Obstetrics</i>						
2CLOSE	Caesarean section	Surgery	Single layer uterine closure	Double layer uterine closure	BJOG 2021	359 143
ALLO	Women in labour at term with clinical indices of foetal hypoxia prompting immediate delivery	Drugs	Allopurinol	Placebo	Arch Dis Child Fetal Neonatal Ed 2015	124 576
AMPHIA	Women with a multiple pregnancy	Drugs	Progesterone injections	Placebo	Obstetrics & Gynecology 2011	400 000
APOSTEL-I	Women with symptoms of preterm labour 24-34 weeks negative fibronectin test	Drugs	Nifedipine	Placebo	Am J Perinatol 2015	286 413
APOSTEL-II	Women with threatened preterm labour 26-32 weeks after tocolysis and corticosteroids 48 hours	Drugs	Nifedipine for 12 days	Placebo	JAMA 2013	316 168
APOSTEL-III	Women with threatened preterm birth 25-34 weeks	Drugs	Nifidipine	Atosiban	Lancet 2016	320 000
APRIL	Women with a singleton pregnancy and history of spontaneous preterm birth of singleton between 22 and 37 weeks	Drugs	Low dose aspirin	Placebo	PLOS Med 2022	351 898
HYPITAT	Women with a singleton pregnancy 36-41 weeks with gestational hypertension or mild pre-eclampsia	Obstetrical treatments	Induction of labour	Expectant management	Lancet 2009	380 000

MOTHER	Women with hyperemesis gravidarum	Obstetrical treatments	Enteral tube feeding	Standard care	Am J Clin Nutr 2017	1 000
PPROMEXIL	Non-labouring women with > 24h preterm pre-labour rupture of membranes 34-37 weeks gestation	Obstetrical treatments	Induction of labour	Expectant management	PLos medicine 2012	600 000
PPROMEXIL-2	Non-labouring women with preterm pre-labour rupture of membranes	Obstetrical treatments	Induction of labour	Expectant management	Am J Obstet Gynecol 2012	600 000
PROBAAT	Women with an unfavourable cervix	Obstetrical treatments	Foley catheter	Vaginal prostaglandin E2 gel	Lancet 2011	0
PROBAAT-II	Women with a term singleton pregnancy and an unfavourable cervix	Obstetrical treatments	Foley catheter	Misoprostol	Lancet 2016	80 000
PROTWIN	Women with a multiple pregnancy 12-20 weeks gestation	Obstetrical treatments	Cervical pessary	Control group	Lancet 2013	313 399
RAVEL	Women with an intermediate to high obstetric risk with an intention to deliver vaginally	Obstetrical treatment	Pain relief strategy with patient controlled remifentanyl	Epidural analgesia	BMJ 2015	450 000
STAN	Labouring women with a high-risk singleton pregnancy in cephalic presentation beyond 36 weeks of gestation	Obstetrical treatments	Monitoring by cardiotocography with ST analysis	Cardiotocography only	Obstetrics & Gynecology 2010	400 000
Reproductive medicine						
Antarctica2	Timing frozen embryo transfers	Fertility treatments	Home-based monitoring of ovulation	Hospital-controlled monitoring	Lancet 2023	599 375
BEDREST	Women having intrauterine insemination	Fertility treatments	15 minutes of immobilisation after insemination	Immediate immobilisation	BMJ 2009	0
INES	Couples seeking fertility treatment unexplained	Fertility treatments	Three cycles of in vitro fertilisation with	Six cycles of in vitro fertilisation in a	BMJ 2015	374 116

	or mild male subfertility		single embryo transfer	modified natural cycle**		
INSIGHT	Women with a normal transvaginal ultrasound of the uterine cavity who were scheduled for their first IVF treatment	Surgery	Hysteroscopy with treatment of detected intra-cavity abnormalities before start IVF	Immediate start of IVF	Lancet 2016	474 147
LIFESTYLE	Infertile women with a BMI of 29 or higher who did not conceive naturally	Fertility treatments	6 month lifestyle-intervention program preceding 18 months of infertility treatment	Prompt infertility treatment	NEJM 2016	766 000
OPTIMIST	Women initiating IVF/ICSI	Drugs	Dose adjustment according to AFC	Standard dose	Human reproduction 2017	480 000
SCRATCH	Women with one previous failed IVF/ICSI treatment and planning a second fresh IVF/ICSI treatment	Surgery	Endometrium scratching	Standard treatment	Human reproduction 2021	550 899
SelecTimo	Couples undergoing in-vitro fertilisation or intracytoplasmic sperm injection	Fertility treatments	Time-lapse routine or early embryo viability assessment	Standard treatment	Lancet 2023	650 000
SUPER	Couples diagnosed with unexplained subfertility and scheduled for a maximum of four cycles of IUI with ovarian stimulation	Drugs	FSH	Clomiphene citrate	Human Reproduction 2018	314 310
TOF	Women under 43 years receiving a IVF/ICSI treatment	Fertility treatments	Blastocyst stage (day 5) embryo transfer	Cleavage stage (day 3) embryo transfer	Submitted	700 000
Oncology						
TLH	Women with stage I endometrioid adenocarcinoma or	Surgery	Total laparoscopic hysterectomy	Total abdominal hysterectomy	Lancet 2010	400 000

Vaccin	complex atypical hyperplasia Adult female patients diagnosed with (histologically proven) CIN II-III and treated with LEEP and no prior vaccination for HPV	Drugs	HPV vaccination	Placebo	Awaiting follow-up	Unknown
(Uro)gynaecology						
CUPIDO-I	Women with a prolapse and evident stress incontinence	Surgery	Prolapse and concomitant anti-incontinence surgery	Prolapse surgery	BJOG 2015	0
EVA	Postmenopausal women undergoing primary pelvic organ prolapse surgery POP-Q stage > 2	Drugs	Vaginal oestrogen cream	Placebo	Manuscript in preparation	250 000
MIRA1	Women with heavy menstrual bleeding without intracavitary pathology	Gynaecological treatments	Levonorgestrel releasing intrauterine system (Mirena)	Bipolar radiofrequency endometrial ablation (Novasure)	Am J Obstet Gynecol 2021	409 270
MIRA2	Women with heavy menstrual bleeding who opt for treatment with endometrial ablation	Surgery	Endometrial ablation plus LNG-IUS	Endometrial ablation	Manuscript in preparation	473 852
PORTRET	Women with stress urinary incontinence	Surgery	Physiotherapy	Midurethral-sling surgery	NEJM 2013	400 000
SAM	Women with symptomatic POP in any stage uterine descent and POP point D < minus 1 cm	Surgery	Sacrospinous hysteropexy	Modified Manchester surgery	JAMA 2023	489 891
SAVE U	Women with uterine prolapse stage 2 or higher requiring surgery and no history of pelvic floor surgery	Surgery	Sacrospinous hysteropexy	Vaginal hysterectomy with suspension of the uterosacral ligaments	BMJ 2015	Unknown

VUSIS-II	Women with symptomatic stress urinary incontinence in whom conservative measures failed and in whom surgical treatment is considered	Surgery/diagnostic strategy	Surgical therapy	Any other therapy (surgical therapy or conservative treatments) as based on individual findings	Neurourol Urodyn 2012	151 000
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*with or without nadroparin **or six cycles of intrauterine insemination with ovarian hyper stimulation ***with intrauterine insemination or intercourse ****plus tamoxifen or letrozol