IMPACT OF CONGENITAL UTERINE ANOMALIES ON OBSTETRIC AND PERINATAL OUTCOMES: SYSTEMATIC REVIEW AND META-ANALYSIS

Table SI. — Included studies.

Study	*Design and study period*	*Setting*	*Population of interest*	*Exclusion criteria*	*Müllerian abnormalities considered*	*Exposed patients (number and characteristics)*	*Non-exposed patients (number and characteristics)*	*Classification system applied*	*Method of diagnosis*	*Outcomes considered*	*Control for confounders*	*Sub-analyses*
Ben-Rafael 1991	Retrospective cohort study (study period not reported)	Tertiary hospital	Women who underwent HSG for history of primary or secondary infertility, or RPL	Arcuate and subseptate uterus	Unicornuate, bicornuate and dideplhys uterus	67 patients with mullerian anomalies: 58 bicornuate, 5 unicoruate and 4 didelphys uterus	130 patients with normal shaped uterus in HSG, quasi-randomly selected among patients with same indcations for HSG	AFS	HSG	Total pregnancies, spontaneous miscarriage, induced abortion, immature delivery (20-26 weeks), premature delivery, term birth, intrauterine fetal demise, bleeding during pregnancy, PPROM, postpartum haemorrhage, placental retention, type of presentation	Maternal age, parity	Indication for HSG (infertility or RPL)
Cooney 1998	Retrospective cohort study (study period not reported)	Tertiary hospital	Women with singleton ongoing pregnancies at 1st trimester US	Equivocal US images and a lack of independent confirmation	Septate or subseptate uterus	22 women in whom a uterine duplication abnormality (septate or subseptate uterus)	66 with patients with normal appearing uteri	AFS	US, HSG, hysteroscopy or laparotomy	Pregnancy loss, liveborn infants, delivery < 34 and ≥ 34 weeks, cesarean section, 1 minute Apgar <7, 5 minute Apgar <7	Maternal age, indication for US scan	None
Leible 1998	Prospective cohort study (1993-96)	Tertiary university hospital	Women with clinical pregnancies who delivered during study period	Not reported	Septate, bicornuate and didelphys uterus	CUA: 7 septate uterus, 7 bicornuate and 1 didelphys.	Pregnant women with a normal uterine cavity randomly selected from those attending for US (30)	AFS	Hysterography, US and surgical findings	Birth weight, gestational age at delivery, IUGR, preeclampsia, preterm birth, stillbirth	Gestational age	None

Erez 2007	Retrospective cohort study (1988-2002)	Tertiary university hospital	All patients with a previous cesarean section that attempted vaginal birth after cesarean section during the study period.	Patients with multiple pregnancies, more than 1 previous cesarean section or known congenital and/ or chromosomal fetal anomalies	Septate, arcuate, unicornuate, didelphys and bicornuate uterus	165 patients with müllerian anomalies (28 septated, 32 arcuate, 15 unicornis, 13 didelphys and 77 bicornuate uterus)	5406 patients with normal uterus	AFS	Diagnostic workout and surgical findings	Hydramnios, oligohyrdramnios, PROM, PPROM, preterm delivery, arrest of labor, placental abruption, severe preeclampsia, cord prolapse, caesarean section, 1 and 5 minute Apgar, birthweight, uterine rupture	Malpresentation, cord prolapse, arrest of labor, NRFHR, placental abruption, hydramnios, maternal age, preterm delivery, PPROM, maternal gestational diabetes, preeclampsia, LGA, SGA	Indication for primary CS according to specific type of Müllerian duct anomalies. Comparison of pregnancy outcome of the study groups according to fetal presentations
Zlopasa 2007	Retrospective cohort study (1997-2000)	Tertiary perinatal centre	General population of pregnant women	Twin gestations, chorioamnionitis, presence of submucosal myomas, fetal chromosomopathy, maternal diabetes, IVF pregnancies	Arcuate, bicornuate (partial and total), didelphys, unicornuate, subseptate and septate uterus	130 women with uterine anomalies (246 pregnancies): 13 arcuate, 78 partial bicornuate, 13 total bicornuate total, 43 didelphys, 8 unicornuate, 31subseptate and 60 septate uterus.	182 randomly selected women with a previously confirmed normally shaped uterus (379 pregnancies)	Modified AFS classification	Previous surgery findings, sonohysterography, laparoscopy with hysterography, or hysteroscopy	Bleeding during pregnancy, pregnancy, delivery, fetal asphyxia, placental abruption, Apgar score 1 min, Apgar score 5 min, miscarriage rate, term delivery, preterm delivery, birth weight, gestational age at delivery, fetal malposition, IUGR, cesarean section, mortality (fetal, early neonatal, perinatal).	Age, parity	Type of uterine abnormality
Ban-Frangez 2009	Retrospective cohort study (1993-2004)	Tertiary university hospital	Women who had conceived following an IVF/ICSI procedure during the period	Not reported explicitly	Subseptate and septate uterus	Pregnant women after IVF or ICSI prior to hysteroscopic resection of a large (n = 12) or small partial uterine septum (n = 19)	Women without uterine anomalies with a singleton intrauterine pregnancy and visible foetal heartbeat (n = 62)	AFS	2D vaginal US without intrauterine saline infusion, hysteroscopy	Miscarriage	Age, BMI, stimulation protocol, use of IVF or ICSI and infertility causes	None

Sugiura-Ogasawara 2010	Retrospective cohort study (referred by authors as case-control study) (1986-2007)	Tertiary university-affiliated hospital	Patients with a history of ≥ 2 consecutive miscarriages who became subsequently pregnant after a systematic assessment of RPL	Structural chromosomal abnormalities detected during study of causes of RPL	Septate and bicornuate uterus	5 patients with septate uterus and 37 patients with bicornuate uterus (53 pregnancies)	1528 women with normal uterus (3433 pregnancies)	Modified AFS classification and Tompkin's Index	Laparoscopy, laparotomy and/or MRI	Live birth rate per pregnancy Cumulative live birth rate	Maternal age, number of previous miscarriages, number of previous live births, number of previous live stillbirths	Type of uterine abnormality (septate and bicornuate)
Saravelos 2010	Retrospective cohort study (study period not reported)	Tertiary hospital	Women with recurrent RPL (three or more consecutive pregnancy losses prior to 24 weeks of gestation)	Pregnancies in which patients had received medical treatment (e.g. low molecular weight heparin, acetyl-salicylic acid, steroids) or surgery (e.g. septotomy, Strassman's metroplasty, cervical cerclage)		56 patients with a specific CUA (diagnosed by hysteroscopy/ laparoscopy) and no other identifiable cause of RM formed the study group	107 Women with normal investigations for identifiable causes of RPL (unexplained RM) formed the control group (n = 107)	Modified AFS classification	2D US , HSG and hysteroscopy/laparoscopy	Biochemical miscarriage, 1st and 2nd trimester miscarriage, ectopic pregnancy, live birth	Maternal age, height, weight, BMI and gravidity	Type of uterine abnormality
Tomazevic 2010	Retrospective cohort study (1993-2004)	Tertiary university hospital	Infertile patients treated with IVF/ICSI ET	Not reported	Septate/subseptate and arcuate uterus	113 ET in patients with septate-subseptate uterus and 176 ET in patients with arcuate uterus	578 ET in patients with normal uterus	Modified AFS classification	2D US	Pregnancy, live birth	Length of uterine septum, maternal age, classic IVF or ICSI, number and quality of embryos transferred.	Length of uterine septum (septate-subseptate or arcuate),
Hua 2011	Retrospective cohort study (1990-2008)	Tertiary care medical centre	Patients with singleton pregnancies undergoing routine anatomic survey	Multiple pregnancy, lack of information in database about exposure, outcomes or covariates	Bicornuate, didelphys, septum, unicornuate and other abnormal uteri.	203 patients with presence of a uterine anomaly diagnosed prior to pregnancy or at initial ultrasound evaluation of uterine anatomy	66753 patients with normal uterine morphology	Modified AFS classification	US	Spontaneous preterm birth (<34 and <37 weeks), PPROM, breech presentation, cesarean delivery IUGR	History of preeclampsia. maternal renal disease, chronic hypertension, gestational diabetes, stillbirth, preterm birth, race	None
Jayaprakasan 2011	Prospective cohort study (2005-2009)	Tertiary centre Fertility Unit	Infertile patients referred for treatment	Difficult delineation of the shapes of the uterus, or uterine cavity distortion by fibroids	Arcuatus,, septate, unicornuate, subseptate, bicornuate and T-shaped uterus	184 patients with abnormal uterus: 164 arcuatus, 7 septate, 6 unicornuate, 5 subseptate, 1 bicornuate, 1 T-shaped.	1201 patients with normal cavity uterus	AFS classification	2D and 3D US	First Trimester miscarriage and ongoing pregnancy (not defined)	Maternal age, basal FSH, AFC	Type of müllerian anomaly

Crane 2012	Retrospective cohort study (2000-08)	Three tertiary care centres	Pregnant women with singleton pregnancies who delivered	Multiple pregnancy, previous cervical cerclage or septum resection	Bicornuate, unicornuate, didelphys, and septate uterus,	52 uterine anomalies: 35 bicornuate uterus, 13 uterus didelphys, 2 septum, 2 unicornuate uterus)	Women without a uterine anomalies, and without a history of preterm delivery or treatment for cervical dysplasia, (122)	AFS	HSG, US, hysterosonography, CT, MRI, hysteroscopy/ laparoscopy or laparotomy	Preterm birth, gestational age at delivery, birth weight, Apgar score, neonatal intensive care unit admission, cord arterial pH, perinatal morbidity and mortality, type of delivery and need for induction.	Gestational age, cervical length	Type of müllerian anomaly
Takami 2014	Retrospective cohort study (2000-2012)	Tertiary care university centre	Women who delivered a live singleton baby after 22 gestational weeks	Pregnancies affected congenital abnormalities and prior uterine surgery	Arcuate, bicornuate, subseptate, septate and didelphic uterus	Patients with congenital uterine anomalies and without prior uterine surgery (n=80) including arcuate (n=4), unicornuate (n=3) bicornuate (n=25), subseptate (n=27), septate (n=6) and didelphic uterus (n=15)	5763 women with normal uterine morphology, who received prenatal care starting early in pregnancy and delivered a live singleton baby after 22 gestational weeks during the study period	AFS	2D US, MRI, hysteroscopy and surgical findings	Preterm birth, fetal malpresentation, caesarean delivery, placental abruption, SGA, LGA	Age, parity, gravidity	Number of cervical orifices (one vs two)

Hiersch 2016	Retrospective cohort study (2007-2014)	Tertiary university hospital	Women who delivered during study period	Women who underwent any surgical treatment of uterine anomalies, who delivered before 24 weeks of gestation and pregnancies with uncertain pregnancy dating or those complicated by stillbirth or major fetal anomalies	Bicornuate, septate, unicornuate and didelphyc uterus.	243 women with uterine congenital anomalies: 156 bicornuate uterus, 38 septate uterus, 27 unicornuate uterus and 22 didelphic uterus.	Women with normal uterus who delivered during study period matched by age (±2 years), number of fetuses and parity (total number of prior deliveries ≥24 weeks of gestation) in a 1:2 ratio (486)	AFS	HSG, US, hysterosonography, computed tomography, magnetic resonance imaging, hysteroscopy, laparoscopy or laparotomy	Oligohydramnios, PROM, PPROM, Preterm birth <37 weeks, <34 weeks and <32 weeks, Induction of labor, Elective caesarean section, operative vaginal delivery, Cesarean delivery, post-partum haemorrhage, retained placenta, post-partum fever, birthweight > 4000 g, mmall for GA, ppgar 5 min < 7, umbilical artery cord pH < 7.10, neonatal sepsis, neonatal death	Age, number of fetuses and parity	None
Li 2017	Retrospective cohort study (2012-2014)	Tertiary centre Fertility Unit	Infertile outpatients who successfully achieved pregnancy	Age > 40 years, BMI <18 or >28 kg/m2, missing one of the ovaries, donor oocytes, PGD/PGS, parental chromosomal abnormalities, embryo reduction (spontaneous or elective), triplet pregnancies, induced labour for fetal anomalies, uterine fibroids or polyps distorting the endometrial cavity	Unicornuate uterus	238 pregnant patients with unicornuate uterus from 455 who received IVF treatment	818 pregnant patients with normal uterus from 1484 who received IVF treatment	ESHRE/ESGE classification	US, HSG, hysteroscopy and/or laparoscopy	Clinical pregnancies, early pregnancy loss, late miscarriage, ectopic pregnancy, preterm delivery, very preterm birth, term delivery, live birth, stillbirth, perinatal mortality, LBW, VLBW	Maternal age, BMI, previous miscarriage, in- fertility type, insemination methods, transfer cycle, number of retrieved oocytes and endometrial thickness on transfer day, infertility duration, cause of infertility, FSH, number of transferred embryos and 14-day HCG.	Number of fetuses (all, single and twin pregnancies)

Ozgur, 2017	Retrospective cohort study (2009-2015)	Reproductive medicine centre	Infertile patients undergoing first IVF treatment with fresh or frozen embryo transfer.	Second or later attempts of IVF or FET	Unicornuate uterus	50 cycles as treatment of women with unicornuate uterus	100 matched cycles in women with normal uterus, randomly selected by embryo transfer strategy, woman's age, number of oocytes retrieved and antral follicular count	AFS	2D transvaginal US, HSG, saline-infused sonography or hysteroscopy or laparoscopy	Biochemical pregnancy, clinical pregnancy, ongoing pregnancy, pregnancy loss, implantation rate	Embryo transfer strategy age (fresh or frozen embryos), number of oocytes retrieved and antral follicular count	None
Mastrolia 2017	Retrospective cohort study (1988-2013)	Tertiary university hospital	Women carrying a singleton pregnancy who delivered during study period	Not reported	Bicornuate uterus	444 pregnancies in women with bicornuate uterus	279,662 pregnant women with normal uterus	Modified AFS classification	Not reported	Mild or severe preeclampsia, poly/ oligohydramnios, PROM, cervical insufficiency, vaginal bleeding, preterm contractions, macrosomia, placental abruption, placenta previa, non-progressive labor, cord prolapse, knots or laces, preterm delivery, postpartum haemorrhage, IUGR, abnormal presentation, mode of delivery, perinatal mortality. Apgar 1 min <7 and <5, Apgar 5 min <7 and <5, birth weight, gestational age at delivery, cord pH, base excess.	Maternal age, parity, grand multiparity, ethnicity, recurrent abortions (only for cervical insufficiency analysis)	None

Cahen-Peretz 2017	Popula-tion-based retrospec-tive cohort study (1991-2013)	Tertiary university hospital	Women who delivered during observation period	Multifetal pregnancies, unknown gestational age, gestational age of less than 24 weeks upon delivery, and fetal congenital malformations	Septate uterus, bicornuate uterus, unicornuate uterus, uterus didelphys, and arcuate uterus	Septate uterus, bicornuate uterus, unicornuate uterus, uterus didelphys, and arcuate uterus (n=1251)	Patients who were not diagnosed with Müllerian anomalies	Modified AFS clas-sification	US, HSG, hys-terosonography, MRI, hysteroscopy, laparoscopy, or laparotomy	Poly/oligo-hydramnios, placenta previa, retained placenta, placental abrup-tion, vasa previa, macrosomia, IUGR, chronic hypertension, preeclampsia, eclampsia, gestational diabetes, anemia, PROM, meconium stained amniotic fluid, postpartum haemorrhage, shoulder dystocia, uterine rupture, pathological presentation, breech presentation, vaginal birth, assisted birth, caesarean section, peripartum hysterectomy, low Apgar 1 min (<7), low Apgar 5 min (<7), birthweight (g), SGA, LBW, VLBW, perinatal mortality.	Maternal age, parity, gestational age at delivery, RPL, previous cesarean section, preeclampsia, gestational diabetes, fertility treatment, SGA, hypertensive disorders, gestational diabetes, previous cesarean section	Type of Müllerian anomalies: uterus didelphys/ other müllerian anomalies/ no anomalies

Mastrolia, 2018	Retrospective population-based cohortstudy (1988-2013)	Tertiary university hospital	General population who delivered during study period	Patients with multiple pregnancies or missing data were excluded from the study	Congenital uterine malformations	Women with congenital uterine malformations (n = 1099)	Women with anatomically normal uterus s (n = 279662).	AFS	Not specifically reported (workup for infertility or recurrent pregnancy loss, accidental finding during pregnancy, or noticed at the time of cesarean delivery).	Mild or severe preeclampsia, poly/oligohydramnios, PROM, cervical insufficiency, vaginal bleeding, preterm contractions, macrosomia, placental abruption, placenta previa, non-progressive labor, cord prolapse, knots or laces, preterm delivery, postpartum haemorrhage, IUGR, abnormal presentation, mode of delivery, perinatal mortality. Apgar 1 min <7 and <5, Apgar 5 min <7 and <5, birth weight, gestational age at delivery, cord pH, base excess.	Maternal age, parity, grand multiparity, ethnicity, recurrent abortions (only for cervical insufficiency analysis)	None
Ples, 2018	Retrospective cohort study (2016-17)	Tertiary university hospital	Infertile patients undergoing diagnostic workup and IVF treatment	Associated uterine pathology (one or more polyps, synechiae, or submucosa myomas) and ultrasound image not sufficient for a definitive diagnosis	Dysmorphic uterus (U1c), incompletely septate uterus (U2a), and completely septate uterus (U2b)	52 patients diagnosed with uterine congenital anomalies receiving IVF treatment: dysmorphic uterus (class U1c; 18 patients), incompletely septate uterus (class U2a; 17 patients), and completely septate uterus (classU2b; 10 patients)	148 patients with normal uterus receiving IVF treatment	ESHRE/ ESGE	2D and 3D US	Miscarriage, clinical pregnancy, ongoing pregnancy	Baseline characteristics of patients regarding infertility and IVF treatment	Type of Müllerian anomalies
Prior 2018	Prospective cohort study (2009-2015)	Reproductive medicine centre	Infertile patients recruited since initial assessment for subfertility and undergoing IVF treatment with fresh ET)	Impossibility of a definitive diagnosis caused by presence of fibroids, intrauterine device or polyps distorting the cavity, history of Asherman's syndrome or previous hysteroscopic surgery or poor quality of images	Arcuate, subseptate, septate, bicornuate, unicornuate and didelphys uterus	432 patients with congenital uterine abnormalities: 387 arcuate, 16 subseptate, 11 septate, 4 bicornuate, 13 unicornuate, 1 didelphys.	1943 patients with normal uterus	Modified AFS classification	3D US	Live birth rate, multiple live birth. clinical pregnancy, preterm birth (<37, < 34, and <32 weeks)	Covariates with significant differences between exposed and non-exposed patients: parity, BMI and number of embryos transferred	Type of abnormality regarding live birth, clinical pregnancy

Surrey 2018	Retrospective cohort study (2014)	Tertiary care assisted reproduction centre	Patients undergoing in vitro fertilization and euploid ET after chromosome screening	Use of donor oocytes or gestational carrier, evidence of other endometrial cavitary abnormalities, fundal indentation <4 mm.	Arcuate uterus	Arcuate uterus (83 FET cycles performed in 76 patients)	378 frozen-ET cycles performed in 354 patients without uterine abnormalities	Modified AFS classification	2D and 3D transvaginal US and hysteroscopy	Implantation rate, live birth rate, biochemical pregnancy rate, miscarriage rate	Maternal age, AMH, basal FSH, AFC, biopsied blastocysts, euploid blastocysts, transferred blastocysts	None
Chen 2018	Retrospective cohort study (2012-16)	University and university-affiliated reproductive medicine centres	Women who underwent first IVF/ICSI cycle in study centres.	Uterine malformations different than unicornuate uterus class IVb , endometrial lesions (polyps, endometrial hyperplasia, intrauterine adhesions), sonographic features of adenomyosis, parental chromosomal abnormality, donor oocytes, PGD/PGS, cancelled IVF cycle prior to ET	Unicornuate uterus class IVb (isolated hemi-uterus without functional rudimentary cavity)	Patients with unicornuate uterus (n=342)	1026 controls randomly selected, matched in a ratio of 1:3 by age, BMI, cause of infertility, and number of embryos transferred	ESHRE/ ESGE classification	3D transvaginal US, hysteroscopy with or without laparoscopy or MRI	Cumulative live birth rate, implantation rate, miscarriage rate, cumulative clinical pregnancy rate, clinical pregnancy per transfer cycle and live birth rate per transfer cycle	Maternal age, BMI, basal FSH, infertility duration, parity and main cause of infertility, GnRH analogue protocol, rate of ICSI procedure, total dose of gonadotropins, E2, LH and Progesterone on HCG day, number of collected oocytes and number of available embryos.	Reproductive outcomes calculated for fresh ET cycle: (cleavage day-3 or blastocyst) and for ET cycles (cleavage day-3 ET cycles or blastocyst). Cumulative reproductive outcomes from one complete ART cycle including fresh and frozen-thaw ETs
Chen 2019	Retrospective cohort study (2009-11)	University and university-affiliated reproductive medicine centres	Infertile patients treated with IVF or ICSI	Oocyte donor treatment cycles, abnormal uterine bleeding, endometrial fibroids or polyps, intrauterine adhesion, premature ovary insufficiency, polycystic ovary syndrome, and history of ≥ 3 consecutive spontaneous miscarriages.	Unicornuate uterus	160 patients with unicornuate uterus who underwent 329 IVF/ ICSI cycles	160 randomly selected controls with normal uterus (matched in a ratio of 1:1 by age, BMI, cause of infertility, and number of embryos transferred) who underwent 390 IVF/ ICSI cycles	Modified AFS classification	Transvaginal US, HSG and hysteroscopy/ laparoscopy	Endometrial thickness on HCG day, oocytes retrieved, biochemical pregnancy, clinical pregnancy, live birth, total pregnancy loss, early miscarriage (12 weeks), term delivery.	Maternal age, BMI, Primary infertility, History of spontaneous abortion (once or twice), Prior ectopic pregnancy, Indication for IVF/ICSI, Antral follicle count, basal FSH, basal LH, number of good quality embryos, fresh ET	Number of foetuses (singleton vs twin)

Ouyang, 2020	Retrospective cohort study (2012-2014)	Reproductive medicine centre	First clinical pregnancies from IVF-ET delivered at ≥ 22 gestational weeks (singleton, twins and embryo selective reduction)	Maternal age ≥ 40 years old; body mass index outside 18–28 kg/m2 range; only one ovary detected; uterine fibroids or polyps distorting the endometrial cavity; received donor oocytes; preimplantation genetic diagnosis/ preimplantation genetic screening; parental chromosomal abnormalities; spontaneous embryo reduction; monochorionic twin or triplet pregnancies; early or late miscarriage; ectopic pregnancy and induced labour	Unicornuate uterus	Pregnant patients with unicornuate uterus (n=206)	Outpatients with normal uterus (314)	AFS	3D transvaginal US	Live birth, preterm delivery, perinatal mortality, cesarean delivery, LBW, VLBW	Infertility type, number of transferred embryos, IVF method, maternal age, basal FSH	Number of fetuses (singleton, twin reduced to singleton and twins)
Cai 2021	Retrospective cohort study (2005-2018)	Tertiary perinatal hospital	Infertile patients who underwent IVF-ET and achieved clinical pregnancy	Asherman's syndrome, uterine fibroid or endometrioma distorting the uterine cavity, untreated hydrosalpinx, previous uterine surgery, cancellation of IVF cycle prior to ET, donor oocytes, PGT, selective/ spontaneous foetal reduction, induced labour for congenital abnormalities.	Uterus didelphys	83 infertile patients with uterus didelphys	249 patients presenting randomly selected and matched by number of gestational sacs (singleton or twin), maternal age (± 1 year), infertility type (primary or secondary), cause of infertility	Modified AFS classification	3D transvaginal US	Miscarriage, preterm delivery ectopic pregnancy, live birth, term birth, preterm birth (from 20 to 32 weeks of gestation), perinatal mortality, LBW, VLBW	Maternal age type of infertility (primary or secondary), cause of infertility, fertilization technique (classic IVF or ICSI), endometrial thickness one day before the day ET, number of embryos transferred	Per number of gestational sacs (singleton or twin)

Kong 2021	Retrospective cohort study (2009-2018)	University-affiliated centre of reproductive medicine	Patients treated with first cycle of IVF/ICSI and with subsequent FET cycles	Severe systemic disease, uterine or pelvic disease (severe intrauterine adhesions, uterine adenomyosis, or untreated hydrosalpinx), chromosomal abnormality in the male or female partner, donor oocytes, preimplantation genetic test treatment drop-out or no follow-up information availability	Bicornuate uterus	58 patients with bicornuate uterus	174 women with normal uterus who were randomly selected in accordance with three essential conditions (age, BMI and co-existing PCOS). Additional balancing criteria were applied with a 1:3 exposed/non-exposed ratio (four of six of following criteria: basal FSH, antral follicular count, cause of infertility, assisted reproduction treatment, controlled ovarian stimulation protocol; and number of embryos transferred).'	Modified AFS classification	Hysteroscopy combined with laparoscopy, surgery or caesarean section (12 patients), or pelvic MRI (1 patient), or 3D US (13 patients), or 2D US combined with hysteroscopy and/or HSG (32 patients).	Cumulative pregnancy rate and Cumulative live birth rate, Implantation rate, biochemical pregnancy, clinical pregnancy, multiple pregnancy (fresh ET cycles only), ectopic pregnancy; 1str and 2nd trimester miscarriage; live birth; preterm delivery; and (10) term delivery, caesarean section; neonatal birth weight; PPROM, placenta praevia, gestational diabetes and hypertensive disorders of pregnancy.	Maternal age, BMI, presence of PCOS (complete balancing) Basal FSH, AFC, cause of infertility, IVF technique, stimulation protocol and number of transferred embryos (relative balancing)	Reproductive outcomes calculated per fresh ET cycle Reproductive outcomes calculated per frozen ET cycle Cumulative reproduction outcomes considering fresh and frozen ET

Lü 2021	Retrospective cohort study (1999-2019)	Tertiary university hospital	Patients with singleton deliveries at ≥28 weeks	Multiple deliveries, singleton deliveries prior to 28 weeks	Unicornuate uterus	44 deliveries in 43 women with unicornuate uterus	367 randomly selected deliveries with normal uterus	Modified AFS classification	US or MRI, endoscopy for various indications, previous abdominal surgery	Preterm delivery rate, breech presentation, cesarean delivery	Multivariate adjustment by covariates which differs between exposed and non-exposed patients: gravidity, parity, nulliparity, IVF pregnancy rate, history of ectopic pregnancy, and incidence of preeclampsia)	Grade of preterm delivery (28 to <32 weeks or 32 to <37 weeks). Etiology of preterm birth (spontaneous or iatrogenic) and Indications of caesarean delivery
Zambrotta, 2021	Retrospective cohort study (2010-20)	Tertiary university hospital	Women with clinical pregnancies who delivered during study period	Women without ultrasonographically confirmed pregnancy, without confirmation or exclusion diagnosis of uterine malformations, who underwent ART cycles or who experienced at least one miscarriage	Didelphys, bicornuate, unicornuate, arcuate, complete septate and uncomplete septate uterus	Pregnant patients with history of one or more pregnancies or current pregnancy with diagnosis of uterine anomalies (n=29)	Women hospitalized for delivery with normal uterine morphology at ultrasound, recruited during the same period (100)	AFS	3D transvaginal US	Preterm birth, fetal malpresentation, and SGA fetus	Logistic regression (age, gestational week, ethnicity and smoking habit)	None

Zhang, 2021	Retrospective cohort study (2008-2019)	Tertiary university hospital	Women who underwent fresh and frozen-thawed cycles of in vitro fertilization/ intracytoplasmic sperm injection-embryo transfer (IVF/ ICSI-ET)	Other types of uterine malformations (mediastinal uterus, bicorne uterus, etc.); diminished ovarian reserve; endometrial lesions; uterine fibroids; adenomyosis; polycystic ovary syndrome; recurrent miscarriage; chromosomal abnormalities.	unicornuate	109 patients with unicornuate uterus Women who underwent fresh and frozen-thawed cycles of in vitro fertilization/ intracytoplasmic sperm injection-embryo transfer (IVF/ ICSI-ET)	2390 patients with normal uterine morphology	Not mentioned	Transvaginal ultrasound, HSG, and hysteroscopy/ laparoscopy	embryo implantation rate, clinical pregnancy rate, miscarriage rate, ectopic pregnancy rate, infant mortality rate, live birth rate, single live birth rate, twins live birth rate, reduction in twin pregnancy rate. Neonatal outcome: delivery method, newborn sex rate, premature birth rate, fetal birth weight, low birth weight infant (LBW) rate Macrosomia rate.	age, type of infertility, fertilization method, number of embryos transplanted, and uterine morphology	none
Marianna 2022	Hospital-based prospective cohort study	Tertiary university hospital	Patients 20−40 years old who underwent 3-dimensional ultrasound of uterine cavity before embryo transfer	Patients with uterine fibroids, uterine cavity deformities due to uterine surgery or synechiae or adenomyosis; with endometrial polyps, history of ovarian surgery, with genetic thrombophilia, hydrosalpinx, or significant obesity (BMI > 35 kg/m2).	U1a (T-shaped), intermediate (T borderline), U1b (infantilis), U2a (subseptate), U2B (septate), U3b (bicorporeal complete) and U5 uterus (aplastic)	Patients with U1a (T-shaped) (n = 27) intermediate (T borderline) uterus (n = 73), Other anomalies (U1b [infantilis], U2a [subseptate], U2b [septate], U3b [bicorporeal complete] and U5 uterus [aplastic]) (n = 22)	Patients with normal uterine cavity (n = 266)	ESHRE/ ESGE	3D transvaginal US	Term deliveries, preterm deliveries, miscarriage, ectopic pregnancy	Age, BMI, endometrial thickness on day of embryo transfer, previous pregnancies, deliveries, miscarriages, past failed IVF attempts, serum AMH and serum FSH.	Type of abnormality

Qiu 2022	Matched controls retrospective cohort study (2008-2019)	Tertiary university hospital	University-affiliated centre of reproductive medicine	Women undergoing their first FET cycles	Bicorporeal, septate and unicornuate uterus	92 bicorporeal uteri, 195 septate uteri and 124 unicornuate uteri.	Patients with normal uterus after routine infertility diagnosis workout, selected within the population-based cohort by mean of propensity score matching (900 controls for bicorporeal uterus group, 1496 controls for septate uterus group and 456 controls for hemi-uterus group	ESHRE/ ESGE and AFS	2D transvaginal US	Biochemical pregnancy, implantation, miscarriage, ectopic pregnancy, clinical pregnancy, live birth, diabetes mellitus, gestational hypertension, preeclampsia and eclampsia, nephritis gravidarum, gestational anaemia, intrahepatic cholestasis, placental abruption, placenta praevia, PROM, preterm birth, LBW, VLBW, ELBW, SGA, neonatal diseases	Age, BMI, duration of infertility, gravidity, parity, presence of different infertility causes, type of endometrial preparation (natural cycles, hormone therapy cycles and stimulated cycles), endometrial thickness on ET day, number of retrieved oocytes, number of frozen cleavage embryos, number of frozen blastocysts, number of embryos transferred and year of treatment	Type of abnormality

Abbreviations: AFC: antral follicular count; AFS: American Fertility Society; BMI: body mass index; ET: embryo transfer; HSG: HSG; IVF: in vitro fertilization; ICSI; intracytoplasmatic sperm injection; IUGR: intrauterine growth restriction; LGA: large for gestational age fetus; LBW: low birth weight (<2500 g); MRI: magnetic resonance imaging; PCOS: polycystic ovarian syndrome; PGD: preimplantational diagnosis; PGS: preimplantational screening; PGT: preimplantational testing; PPROM: preterm premature rupture of membranes; PROM: premature rupture of membranes; SGA: small for gestational age fetus; US: US; VLBW: very low birth weight (<1500 g); ELBW: extremely low birth weight (<1000 g)

Table SII. — Not included studies and reasons for exclusion.

Study	Design	Reasons for exclusion
Portuondo, 1986	Case-control study	Study design
Sorensen, 1987	Retrospective cohort study	Lack of control for potential confounders (not granted in comparability domain of NOS score and was considered not eligible following AHRQ standards)
Rogers, 1985	Descriptive study	Non-comparative study
Ben-Rafael, 1990	Retrospective cohort study	Double publication (same data analysed in Ben-Rafael, 1991)
Acien, 1993	Retrospective cohort study	Not normal controls (non-exposed patients have normal uterus but other congenital genitourinary abnormalities).
Fedele, 1995	Descriptive study	Non-comparative study
Maneschi, 1995	Retrospective cohort study	Lack of control for potential confounders (not granted in comparability domain of NOS score and was considered not eligible following AHRQ standards)
Lavergne, 1996	Retrospective cohort study	Lack of control for potential confounders (not granted in comparability domain of NOS score and was considered not eligible following AHRQ standards)
Colacurci, 1996	Retrospective cohort study	Studied population out of scope
Zupi, 1996	Descriptive study	Non-comparative study
Raga, 1997	Descriptive study	Non-comparative study
Ravasia, 1999	Retrospective cohort study	Lack of control for potential confounders
Grimbizis, 2001	Systematic review	Non-primary study
Woelfer, 2001	Prospective cohort study	Lack of control for potential confounders (not granted in comparability domain of NOS score and was considered not eligible following AHRQ standards)
Shuiqing, 2002	Prospective cohort study	Not normal controls (non-exposed patients have normal uterus but other congenital genitourinary abnormalities).
Salim, 2003	Case-control study	Study design
Akar, 2005	Descriptive study	Non-comparative study
Airoldi, 2005	Retrospective cohort study	Comparison out of scope
Tomazevic, 2007	Retrospective cohort study	Studied population out of scope
Sendag, 2010	Retrospective cohort study	Studied population out of scope
Liang, 2010	Retrospective cohort study	Lack of control for potential confounders (not granted in comparability domain of NOS score and was considered not eligible following AHRQ standards)
Zhang, 2010	Retrospective cohort study	Lack of control for potential confounders (not granted in comparability domain of NOS score and was considered not eligible following AHRQ standards)
Tonguc, 2011	Retrospective cohort study	Studied population out of scope
Ghi, 2012	Descriptive study	Non-comparative study
Chen, 2013	Retrospective cohort study	Studied population out of scope
Jaslow, 2013	Case-control study	Not included design
Acien, 2014	Retrospective cohort study	Studied population out of scope

Fox, 2014	Retrospective cohort study	Lack of control for potential confounders (cohorts differs in several baseline variables with could act as confounders; no adjustment was performed). The study was not granted in comparability domain of NOS score and was considered not eligible following AHRQ standards.
Tofoski, 2014	Retrospective cohort study	Studied population out of scope
Sugiura-Ogasawara, 2015	Retrospective cohort study	Studied population out of scope
Elsokkary, 2018	Retrospective cohort study	Studied population out of scope
Gabbai, 2018	Case-control study	Not included design
Ludwin, 2018	Letter to editor	Non suitable for analysis
Alonso-Pacheco, 2019	Retrospective cohort study	Studied population out of scope
Fox, 2019	Retrospective cohort study	Studied population out of scope
Neal, 2019	Retrospective cohort study	Lack of control for potential confounders (cohorts differs in several baseline variables with could act as confounders; no adjustment was performed). The study was not granted in comparability domain of NOS score and was considered not eligible following AHRQ standards.
Ridout, 2019	Retrospective cohort study	Comparison out of scope
Hynes, 2021	Descriptive study	Non-comparative study

Table SIII. — Summary of estimated effects of CUA on pregnancy and neonatal outcomes.

	Arcuate		Subseptate		Septate		Didelphys		Bicornuate		Unicornuate		T-shaped		Combined	
	OR (95% CI)	Studies I^2(%)	OR (95% CI)	Studies I^2(%)	OR (95% CI)	Studies I^2(%)	OR (95% CI)	Studies I^2(%)	OR (95% CI)	Studies I^2(%)	OR (95% CI)	Studies I^2(%)	OR (95% CI)	Studies I^2(%)	OR (95% CI)	Studies I^2(%)
First trimester miscarriage	1.21 (0.80-1.84)	3 0%	3.88 (0.86-17.54)	2 43%	1.95 (0.92-4.15)	3 63%	1.36 (0.77-2.40)	3 0%	1.56 (1.04-2.34)	4 0%	1.16 (0.56-2.39)	4 60%	N/A	--	1.62 (1.06-2.47)	7 76%
Second trimester miscarriage	0.84 (0.09-8.13)	2 58%	4.53 (1.37-15.00)	1 --	6.55 (2.66-16.16)	2 55%	1.48 (0.52-4.21)	3 0%	1.64 (0.25-10.54)	3 52%	2.07 (0.85-5.03)	4 0%	N/A	--	1.80 (1.19-2.73)	6 0%
First or second trimester miscarriage	1.14 (0.77-1.68)	4 0%	6.19 (2.30-16.66)	3 41%	2.93 (1.72-4.99)	7 49%	1.48 (0.91-2.39)	4 0%	2.09 (1.47-2.97)	6 16%	0.83 (0.45-1.56)	7 81%	5.22 (1.89-14.42)	2 0%	1.54 (1.14-2.07)	17 75%
Ectopic pregnancy	0.65 (0.15-2.83)	1 --	N/A	..	2.04 (1.03-4.04)	1 --	1.95 (0.35-10.79)	2 1%	0.65 (0.12-3.60)	3 0%	1.06 (0.32-3.51)	4 47%	5.08 (0.45-57.90)	1 --	1.30 (0.82-2.05)	6 0%
Placental abruption	15.32 (0.81-289.1)	1 --	17.45 (5.05-60.22)	1 --	10.61 (0.59-191.35)	1 --	4.45 (0.26-75.58)	1 --	12.11 (3.14-46.74)	2 81%	19.70 (1.00-387.39)	1 --	N/A	--	5.04 (3.60-7.04)	6 40%
PROM/PPROM	N/A	--	N/A	--	N/A	--	N/A	--	1.79 (1.37-2.33)	2 0%	0.46 (0.18-1.21)	1 --	N/A	--	1.71 (1.34-2.18)	9 65%
Malpresentation at delivery	11.38 (1.49-87.07)	2 41%	25.62 (10.79-60.85)	2 25%	45.48 (16.97-121.89)	2 0%	19.15 (15.16-24.18)	3 0%	17.96 (12.19-26.47)	3 27%	32.74 (6.21-172.67)	3 53%	N/A	--	21.04 (10.95-40.44)	7 97%
Preterm delivery	8.91 (3.10-25.63)	2 0%	5.24 (1.87-14.67)	2 58%	1.04* (0.51-2.01)	5 0%	4.62 (2.43-8.80)	7 74%	4.9* (3.93-6.11)	7 8%	3.85* (1.84, 8.16)	8 0%	4.45 (1.29-15.32)	1 --	4.34* (3.59-5.21)	19 56%
Premature delivery <34 weeks	N/A	--	N/A	--	16.2 (0.52-503.65)	1 --	53.78 (5.43-532.94)	1 --	11.34 (1.14-112.75)	1 --	16.20 (0.52-503.65)	1 --	N/A	--	5.36 (4.29-6.70)	6 12%
Premature delivery <32 weeks	N/A	--	N/A	--	16.2 (0.52-503.65)	1 --	6.65 (0.36-123.90)	2 81%	7.33 (0.64-83.39)	1 --	1.83 (1.00-3.35)	3 0%	N/A	--	1.64* (0.91-2,97)	6 0%
Cesarean delivery	6.44 (0.50-82.56)	2 70%	11.27 (3.01-42.23)	2 58%	5.07 (0.91-28.14)	4 82%	29.9* (8.24-126.4)	6 75%	23.8* (10.17-55.7)	6 46%	12.1* (5.64, 26.5)	6 0%	N/A	--	7.69* (4.17-14.29)	16 96%
IUGR/SGA	7.99 (0.16-405.90)	2 82%	2.54 (1.10-5.89)	2 0%	1.70 (0.43-6.78)	3 64%	3.82 (1.93-7.56)	3 36%	2.75 (1.96-3.86)	4 0%	2.74 (0.91-8.29)	4 42%	N/A	--	50* (6.11-424)	9 83%
Fetal mortality	0.93 (0.12-7.25)	2 0%	3.11 (0.35-27.44)	1 --	0.99 (0.18-5.52)	2 0%	2.67 (1.29-5.51)	3 0%	3.46 (2.00-5.99)	3 0%	2.36 (1.23-4.54)	3 0%	N/A	--	2.07 (1.56-2.73)	9 10%
Perinatal mortality	4.13 (0.47-36.57)	1 --	4.95 (0.97-25.37)	1 --	3.55 (0.83-15.08)	2 0%	6.69 (1.59-28.15)	2 25%	4.25 (1.56-11.60)	2 0%	3.05 (1.75-5.31)	3 0%	N/A	--	3.28 (2.01-5.36)	6 58%

*Adjusted OR | OR: Odds Ratio.

Index of results and figures

Ectopic pregnancy (all CUA)

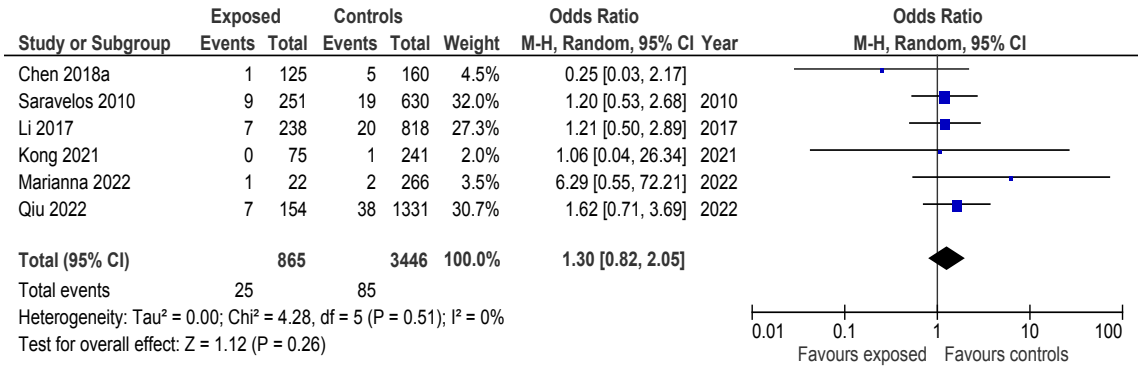


Figure S1: Forest plot of individual and pooled effects on ectopic pregnancy of all CUA

Ectopic pregnancy by type of CUA

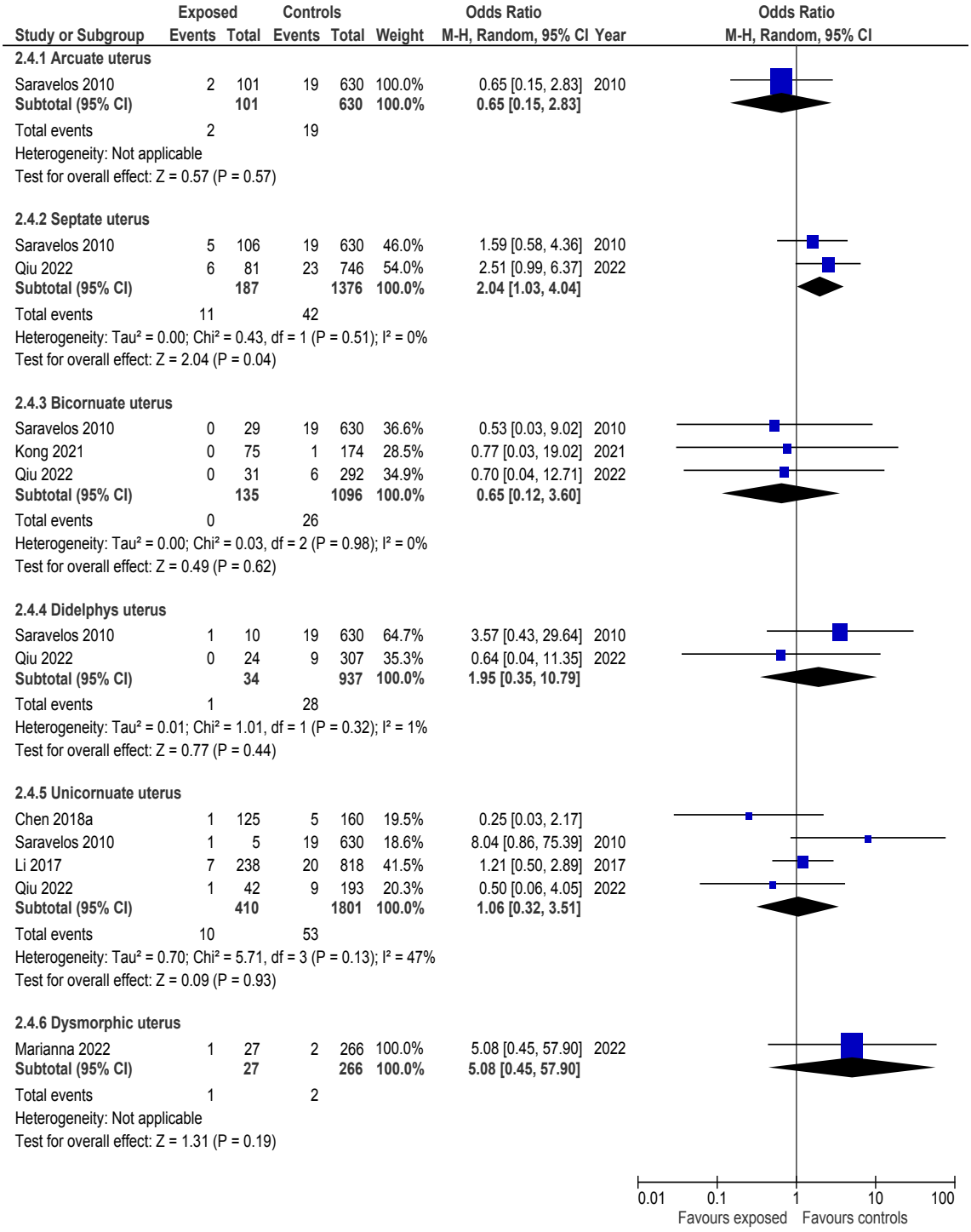


Figure S2: Forest plots of individual and pooled effects on ectopic pregnancy by type of CUA.

Placental abruption (all CUA)

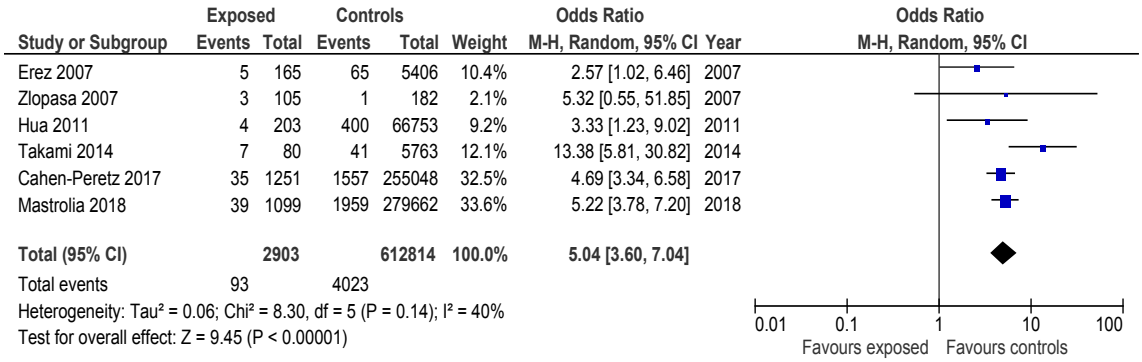


Figure S3: Forest plot of individual and pooled effects on placental abruption of all CUA (combined).

Placental abruption by type of CUA

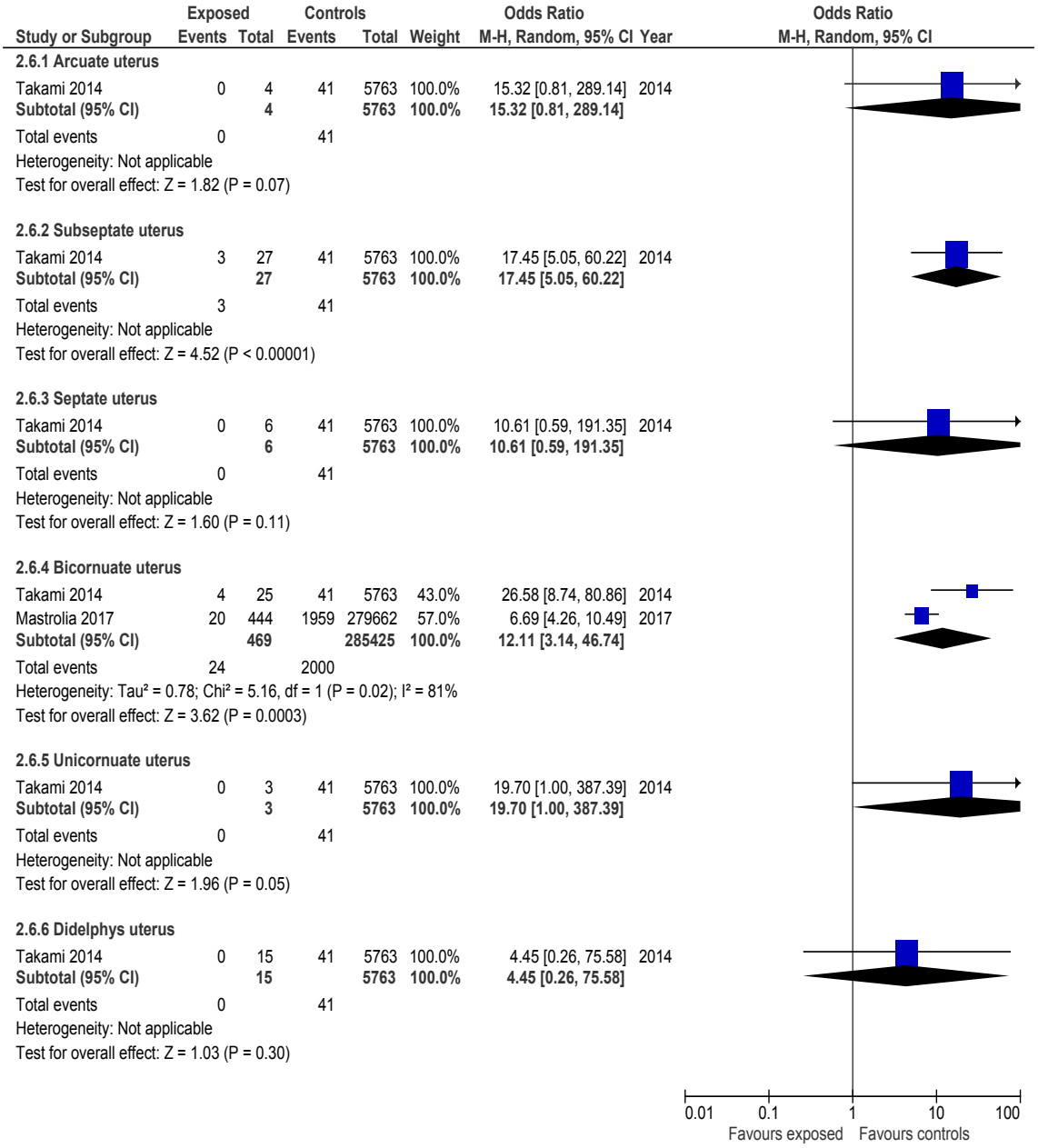


Figure S4: Forest plots of individual and pooled effects on placental abruption by type of CUA.

PROM/PPROM (all CUA)

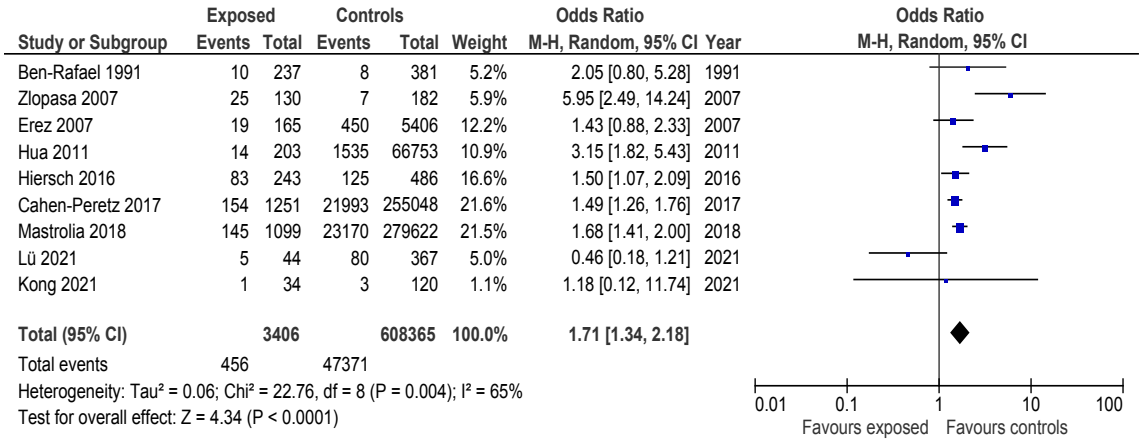


Figure S5: Forest plot of individual and pooled effects on PROM/PPROM of all CUA (combined).

PROM/PPROM by type of CUA

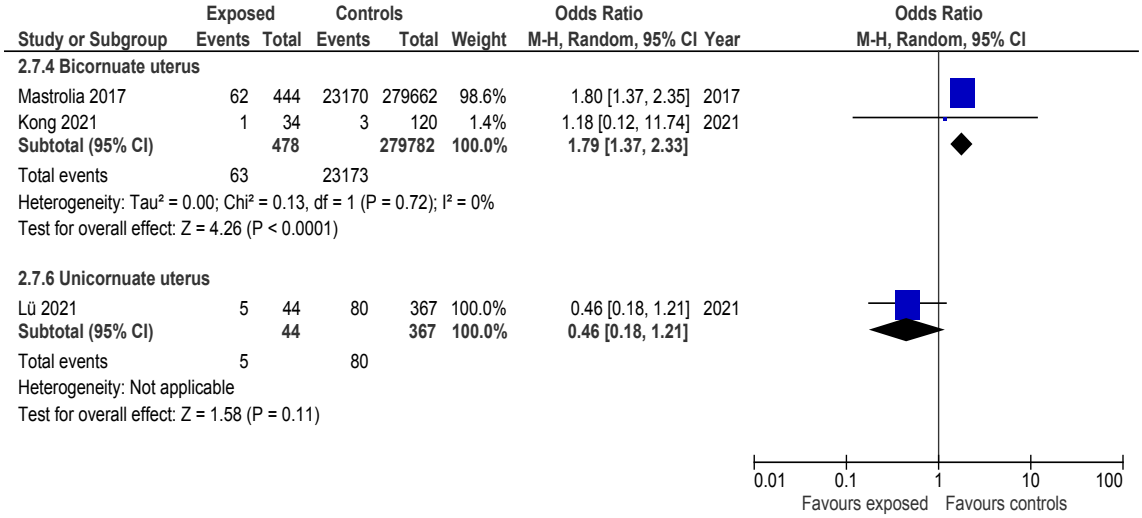


Figure S6: Forest plots of individual and pooled effects on PROM/PPROM by type of CUA.

Fetal malpresentation at delivery (all CUA)

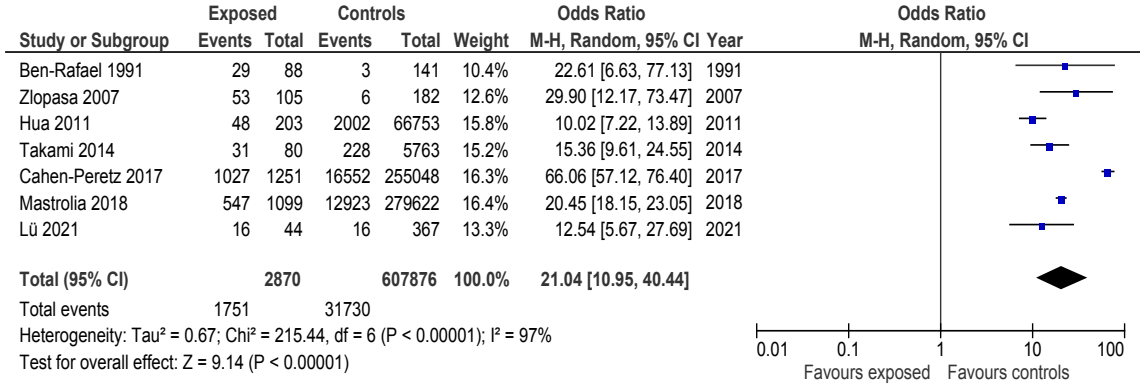


Figure S7: Forest plot of individual and pooled effects on fetal malpresentation at delivery of all CUA (combined).

Fetal malpresentation at delivery by type of CUA

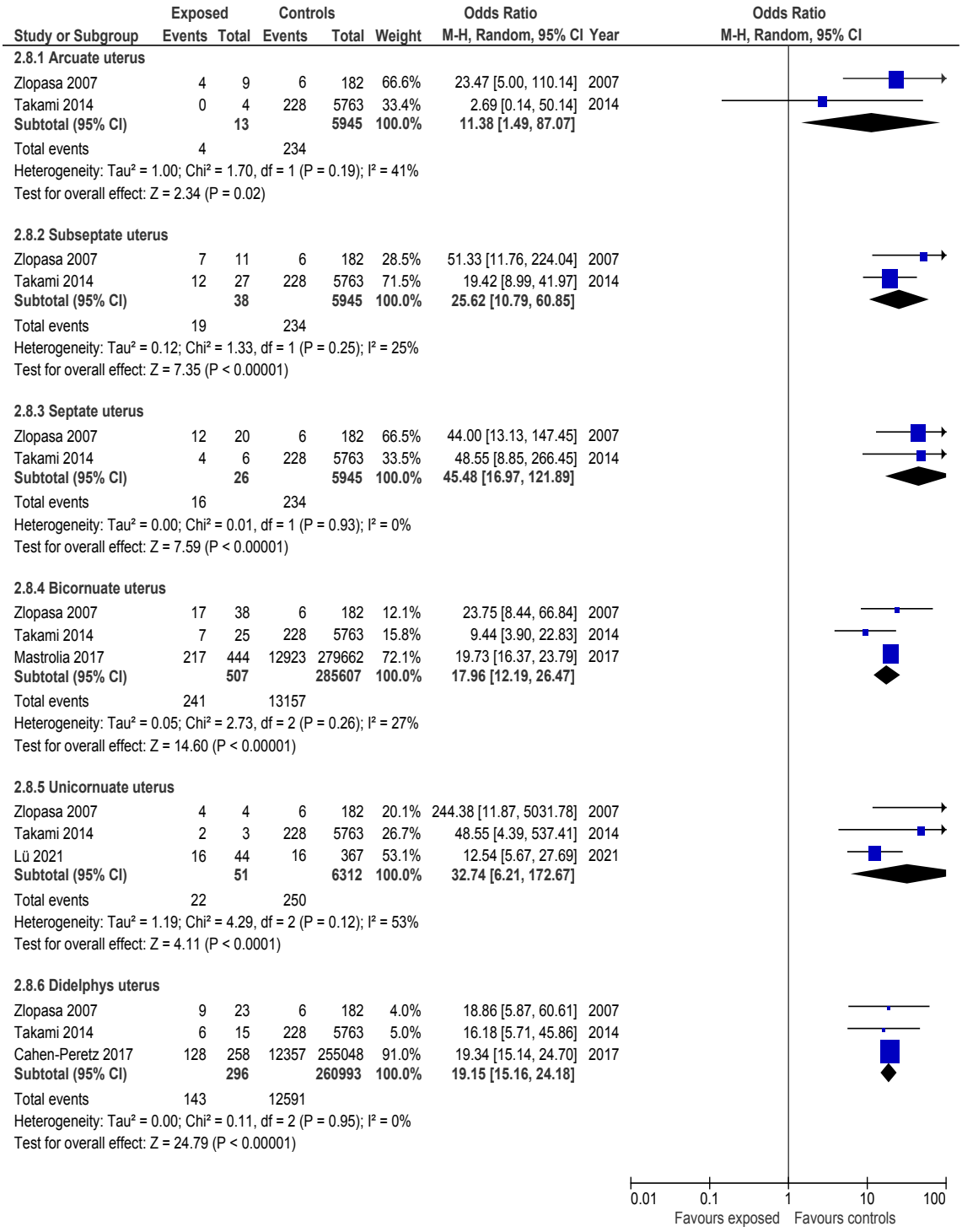


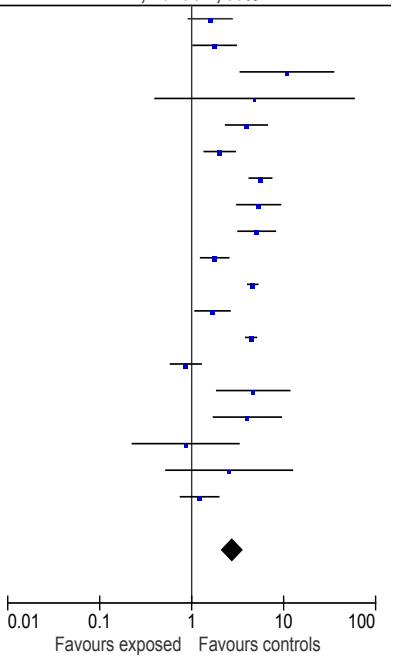
Figure S8: Forest plots of individual and pooled effects on fetal malpresentation at delivery by type of CUA.

Preterm delivery (all CUA)

A) Preterm birth

Study or Subgroup	Exposed Events	Exposed Total	Controls Events	Controls Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Chen 2018a	37	122	32	149	5.7%	1.59 [0.92, 2.76]	
Ben-Rafael 1991	29	245	29	413	5.8%	1.78 [1.03, 3.05]	1991
Crane 1992	14	52	4	122	3.2%	10.87 [3.37, 35.01]	1992
Leible 1998	2	14	1	30	1.1%	4.83 [0.40, 58.47]	1998
Zlopasa 2007	50	246	23	379	5.9%	3.95 [2.34, 6.67]	2007
Erez 2007	33	165	595	5406	6.4%	2.02 [1.37, 2.99]	2007
Hua 2011	80	203	6942	66753	6.8%	5.60 [4.22, 7.43]	2011
Takami 2014	17	80	276	5763	5.7%	5.36 [3.10, 9.29]	2014
Hiersch 2016	61	243	30	486	6.1%	5.09 [3.19, 8.15]	2016
Li 2017	57	238	123	818	6.6%	1.78 [1.25, 2.54]	2017
Cahen-Peretz 2017	332	1251	18516	255048	7.2%	4.61 [4.07, 5.24]	2017
Prior 2018	33	152	102	722	6.2%	1.69 [1.09, 2.61]	2018
Mastrolia 2018	287	1099	20682	279662	7.2%	4.43 [3.87, 5.07]	2018
Ouyang 2020	58	206	98	314	6.4%	0.86 [0.59, 1.27]	2020
Cai 2021	12	65	9	195	4.1%	4.68 [1.87, 11.70]	2021
Lü 2021	9	44	22	367	4.4%	4.03 [1.72, 9.43]	2021
Kong 2021	3	35	11	112	2.8%	0.86 [0.23, 3.28]	2021
Marianna 2022	2	22	10	266	2.2%	2.56 [0.52, 12.49]	2022
Qiu 2022	22	154	160	1331	6.0%	1.22 [0.75, 1.97]	2022
Total (95% CI)		**4636**		**618336**	**100.0%**	**2.79 [2.10, 3.70]**	
Total events	1138		47665				

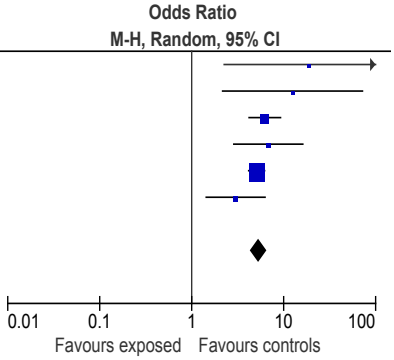
Heterogeneity: Tau² = 0.28; Chi² = 173.74, df = 18 (P < 0.00001); I² = 90%
Test for overall effect: Z = 7.12 (P < 0.00001)



B) Preterm birth < 34 weeks

Study or Subgroup	Exposed Events	Exposed Total	Controls Events	Controls Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Crane 1992	7	52	1	122	1.1%	18.82 [2.25, 157.29]	1992
Cooney 1998	5	17	2	62	1.6%	12.50 [2.17, 72.15]	1998
Hua 2011	29	203	1735	66753	24.5%	6.25 [4.20, 9.28]	2011
Hiersch 2016	22	243	7	486	6.2%	6.81 [2.87, 16.18]	2016
Cahen-Peretz 2017	106	1351	4199	255048	58.2%	5.09 [4.16, 6.22]	2017
Prior 2018	12	152	20	722	8.4%	3.01 [1.44, 6.30]	2018
Total (95% CI)		**2018**		**323193**	**100.0%**	**5.36 [4.29, 6.70]**	
Total events	181		5964				

Heterogeneity: Tau² = 0.01; Chi² = 5.71, df = 5 (P = 0.34); I² = 12%
Test for overall effect: Z = 14.81 (P < 0.00001)



C) Preterm birth < 32 weeks

Study or Subgroup	Exposed Events	Exposed Total	Controls Events	Controls Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Chen 2018a	6	122	4	129	15.6%	1.62 [0.44, 5.87]	
Crane 1992	5	52	1	122	6.9%	12.87 [1.46, 113.11]	1992
Hiersch 2016	10	243	3	486	15.4%	6.91 [1.88, 25.35]	2016
Li 2017	12	187	27	709	29.7%	1.73 [0.86, 3.49]	2017
Prior 2018	11	152	13	722	26.0%	4.25 [1.87, 9.69]	2018
Cai 2021	1	51	3	159	6.4%	1.04 [0.11, 10.22]	2021
Total (95% CI)		**807**		**2327**	**100.0%**	**2.98 [1.60, 5.54]**	
Total events	45		51				

Heterogeneity: Tau² = 0.21; Chi² = 7.98, df = 5 (P = 0.16); I² = 37%
Test for overall effect: Z = 3.45 (P = 0.0006)

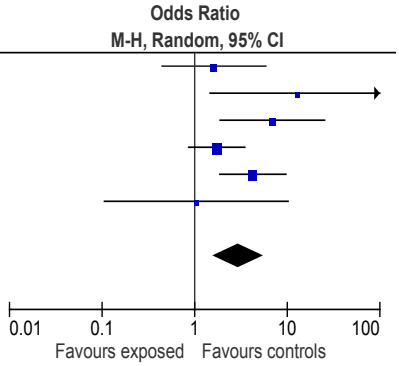


Figure S9: Forest plots of individual and pooled effects on preterm delivery (A) preterm delivery < 34 wweks (B) and preterm delivery < 32 weeks of all CUA (combined).

Preterm delivery by type of CUA
Preterm delivery

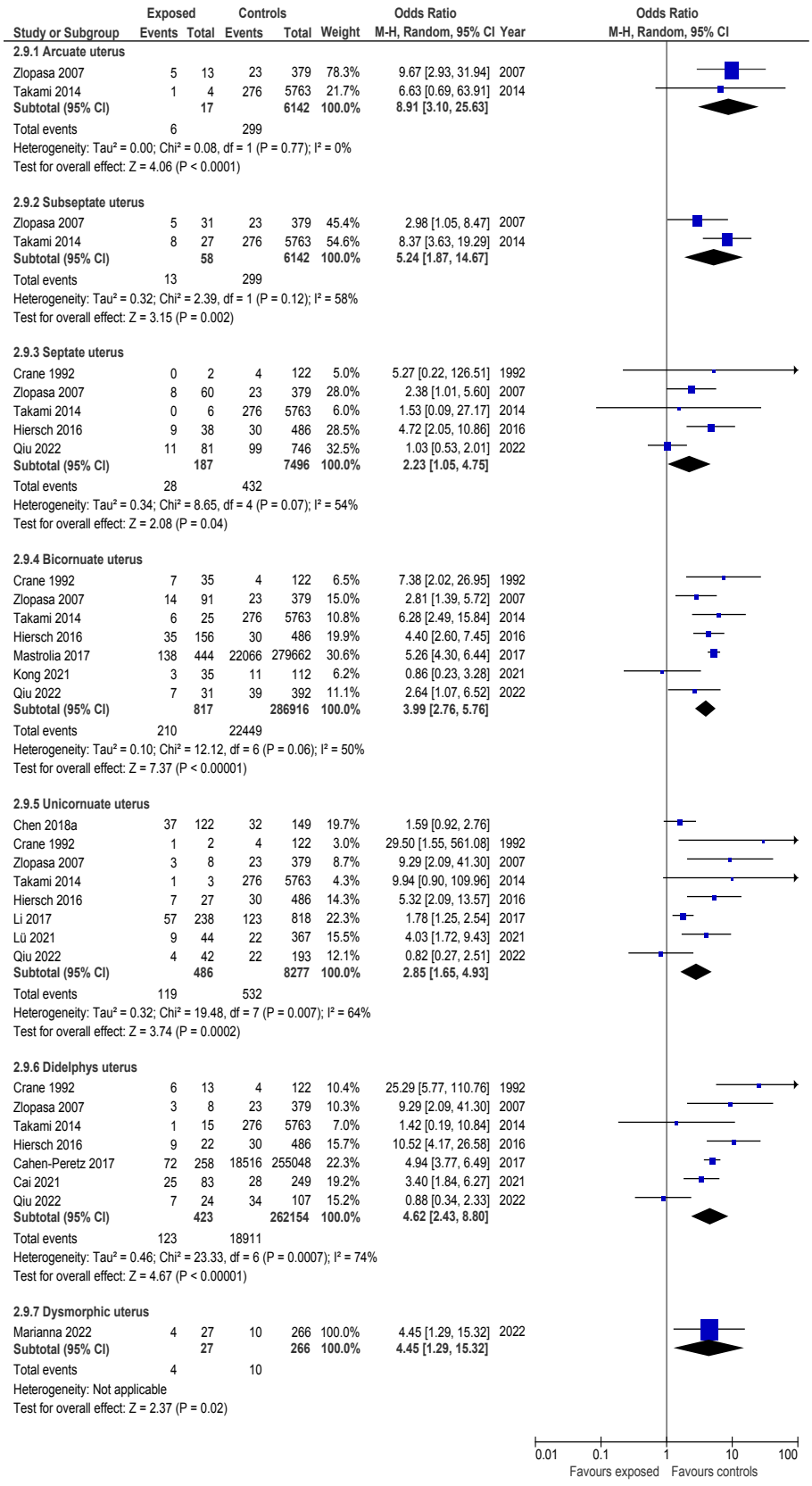


Figure S10: Forest plots of individual and pooled effects on preterm delivery by type of CUA.

Preterm delivery < 34 weeks

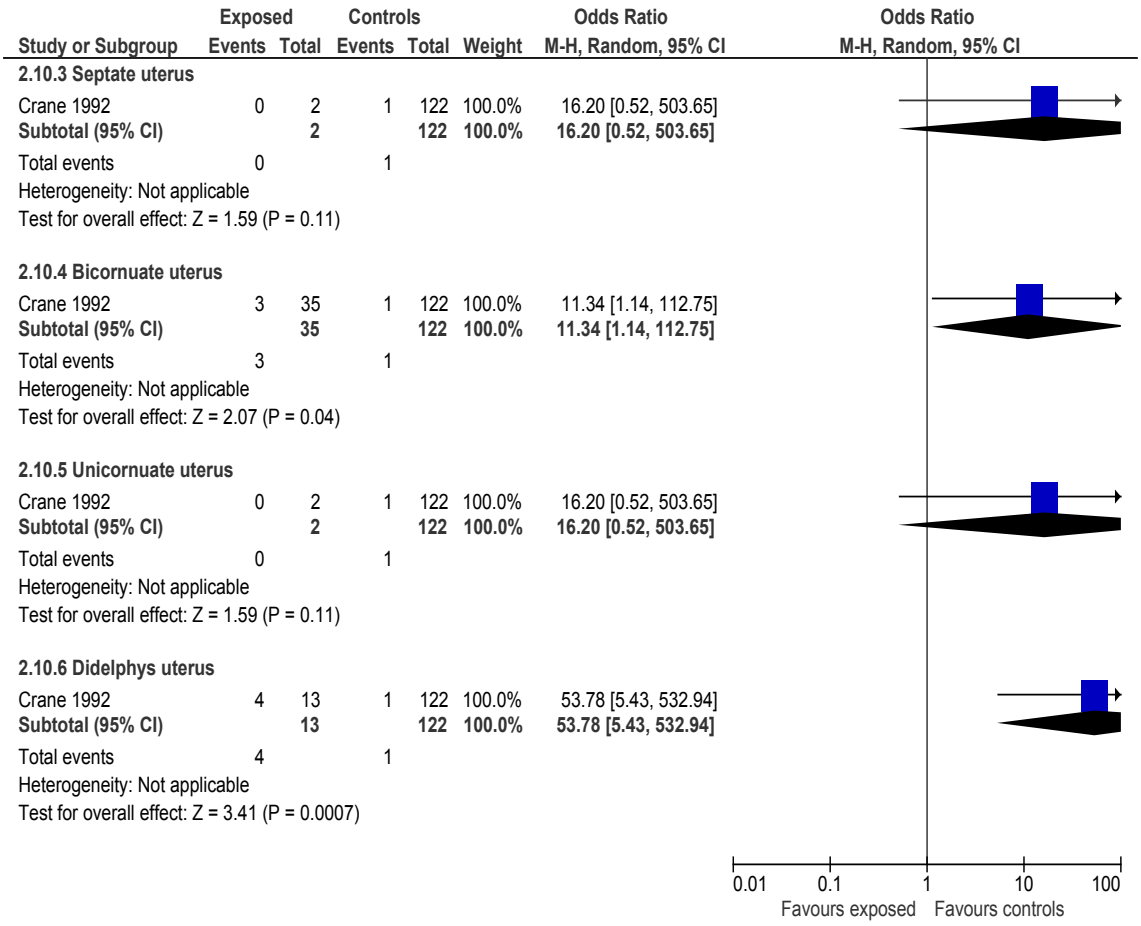


Figure S11: Forest plots of individual and pooled effects on preterm delivery < 34 weeks by type of CUA.

Preterm delivery < 32 weeks

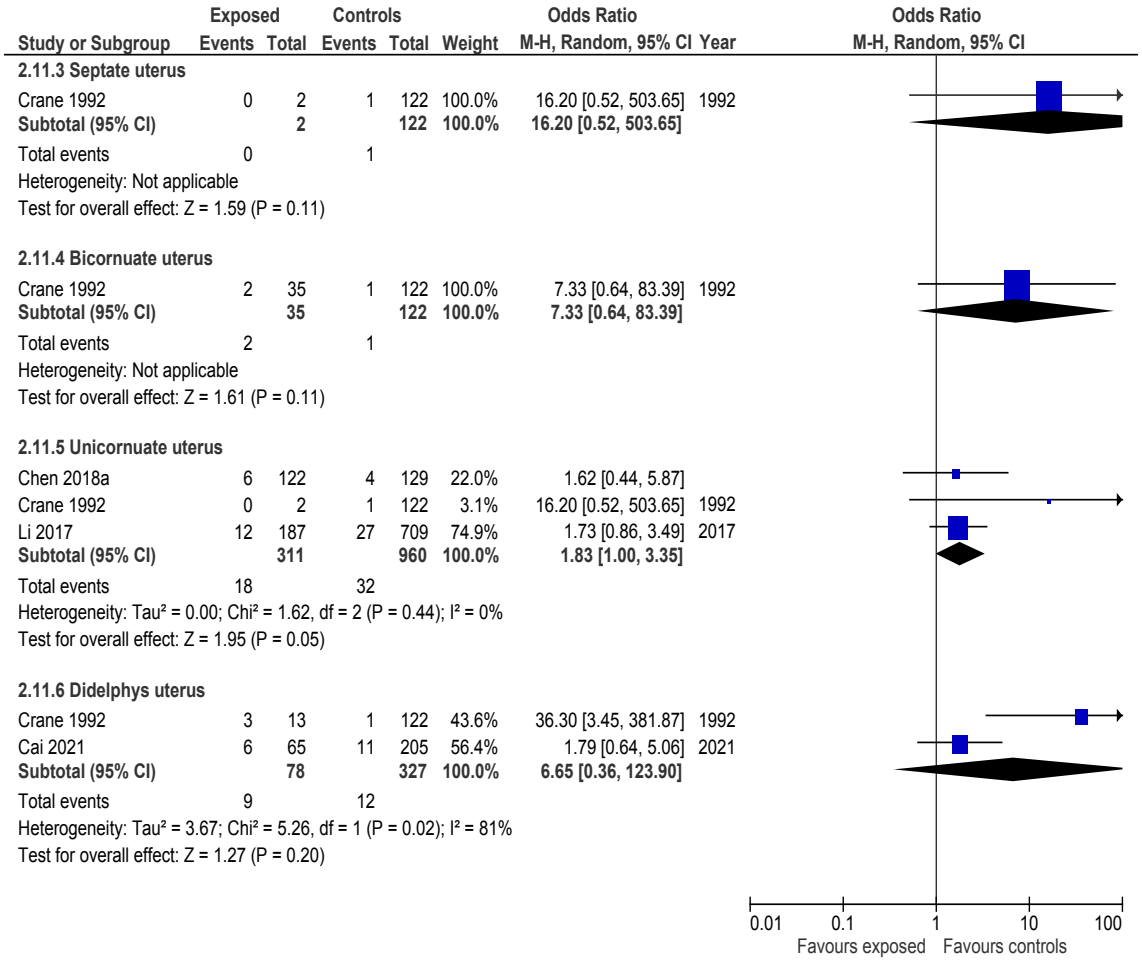


Figure S12: Forest plots of individual and pooled effects on preterm delivery < 32 weeks by type of CUA.

Cesarean delivery (all CUA)

Study or Subgroup	Exposed Events	Exposed Total	Controls Events	Controls Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Crane 1992	32	52	31	122	6.1%	4.70 [2.35, 9.38]	1992
Cooney 1998	8	17	19	62	5.6%	2.01 [0.67, 6.01]	1998
Erez 2007	103	165	2666	5406	6.4%	1.71 [1.24, 2.35]	2007
Zlopasa 2007	78	105	26	182	6.2%	17.33 [9.48, 31.69]	2007
Hua 2011	70	203	10814	66753	6.5%	2.72 [2.04, 3.64]	2011
Takami 2014	50	80	1025	5763	6.4%	7.70 [4.87, 12.18]	2014
Hiersch 2016	200	243	108	486	6.4%	16.28 [10.99, 24.11]	2016
Li 2017	155	187	557	709	6.4%	1.32 [0.87, 2.01]	2017
Cahen-Peretz 2017	975	1251	34739	255048	6.5%	22.40 [19.59, 25.62]	2017
Mastrolia 2017	346	444	38740	279662		Not estimable	2017
Mastrolia 2018	881	1099	38740	279622	6.5%	25.13 [21.66, 29.16]	2018
Prior 2018	66	152	291	722	6.4%	1.14 [0.80, 1.62]	2018
Ouyang 2020	168	206	268	314	6.3%	0.76 [0.47, 1.22]	2020
Kong 2021	26	35	52	112	5.9%	3.33 [1.43, 7.75]	2021
Lü 2021	38	44	134	367	5.9%	11.01 [4.54, 26.73]	2021
Cai 2021	52	65	146	205	6.1%	1.62 [0.82, 3.19]	2021
Qiu 2022	97	112	846	1100	6.3%	1.94 [1.11, 3.40]	2022
Total (95% CI)		**4016**		**616973**	**100.0%**	**4.15 [2.12, 8.15]**	
Total events	2999		90462				

Heterogeneity: Tau² = 1.81; Chi² = 931.70, df = 15 (P < 0.00001); I² = 98%

Test for overall effect: Z = 4.14 (P < 0.0001)

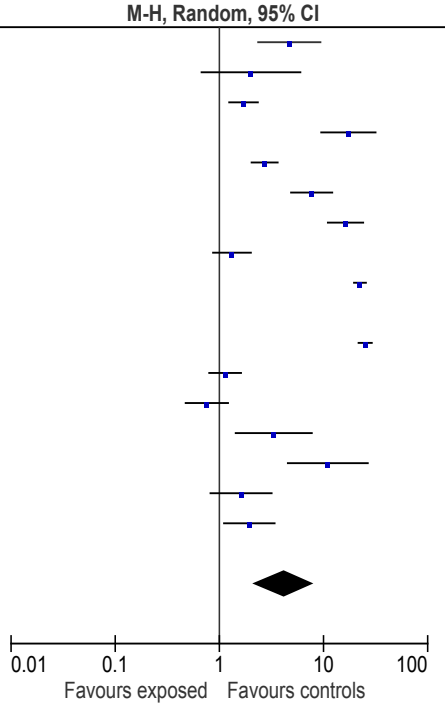


Figure S13: Forest plot of individual and pooled effects on cesarean delivery of all CUA (combined).

Cesarean delivery by type of CUA

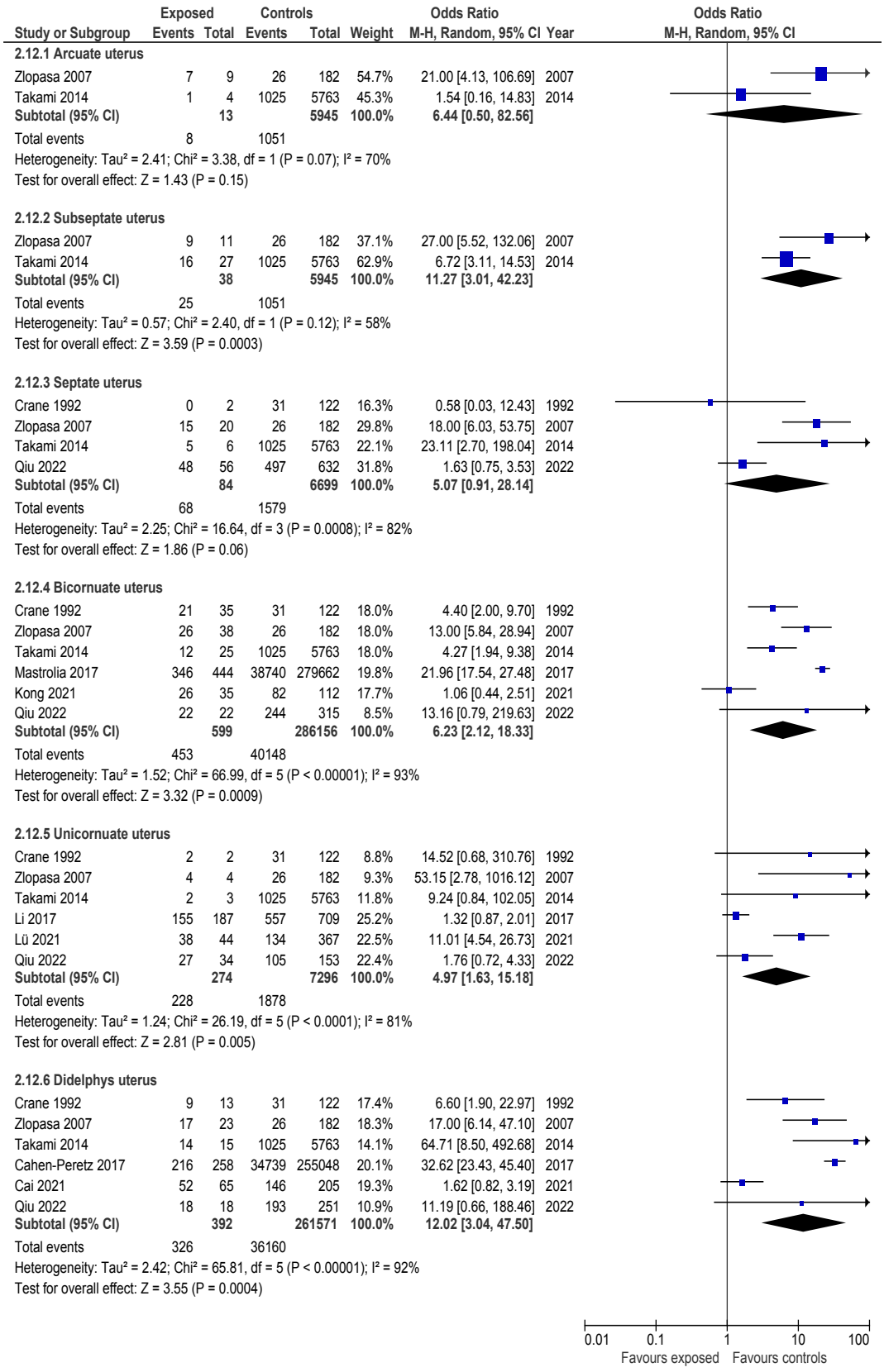


Figure S14: Forest plots of individual and pooled effects on cesarean delivery by type of CUA.

IUGR/SGA (all CUA)

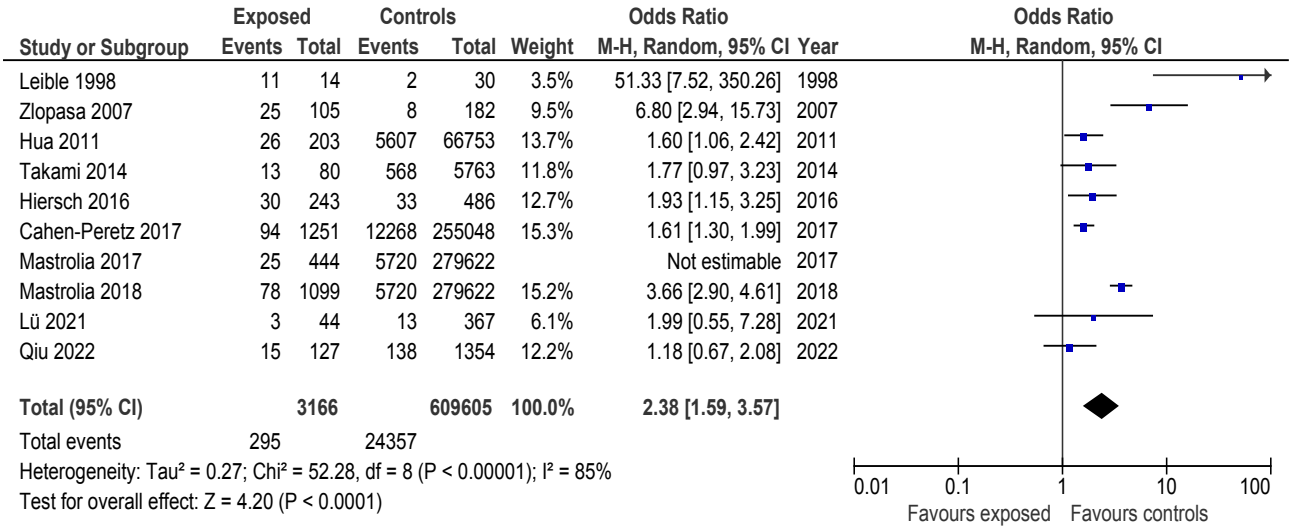


Figure S15: Forest plot of individual and pooled effects on IUGR/SGA of all CUA (combined).

IUGR/SGA by type of CUA

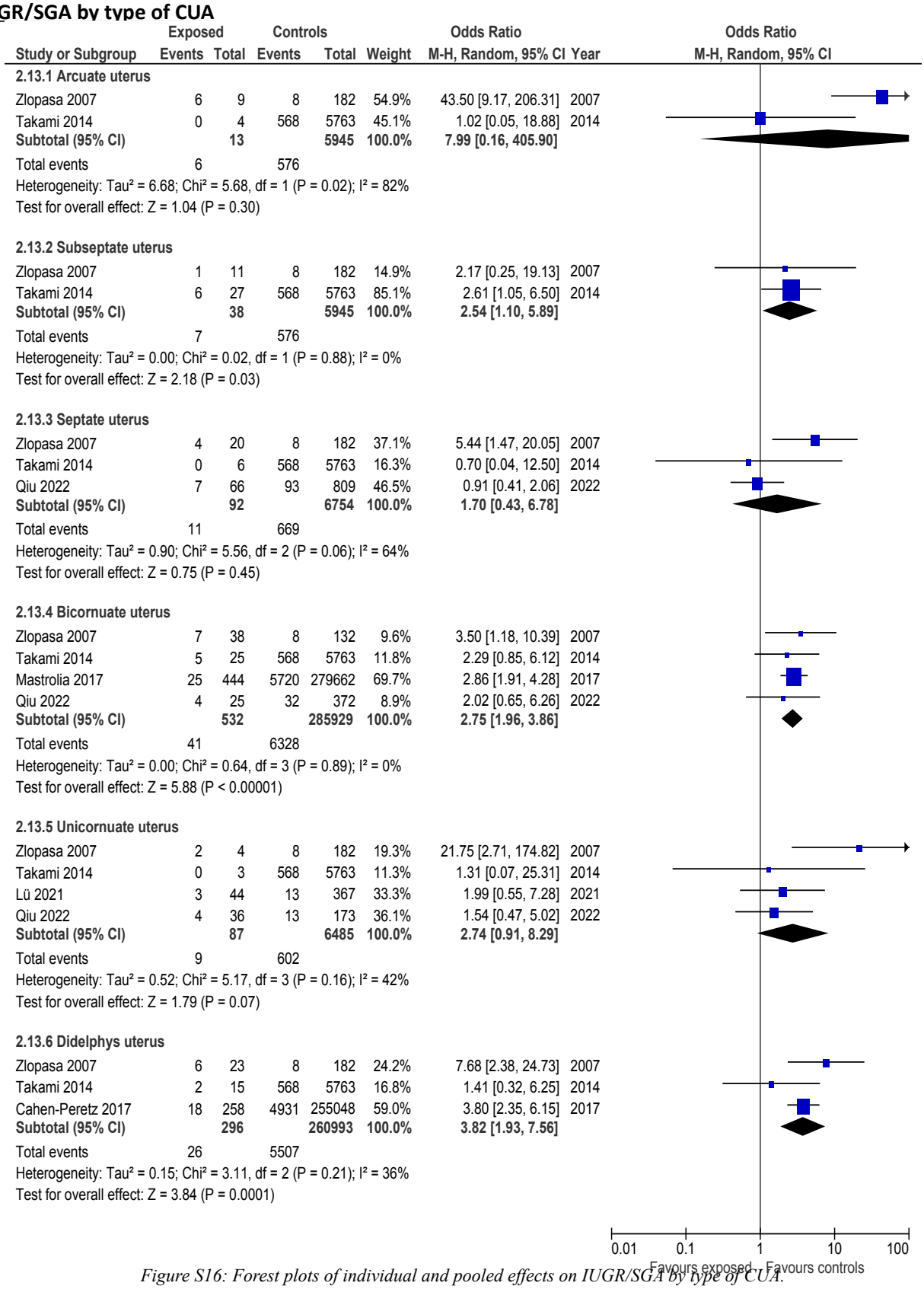


Figure S16: Forest plots of individual and pooled effects on IUGR/SGA by type of CUA.

Fetal mortality (all CUA)

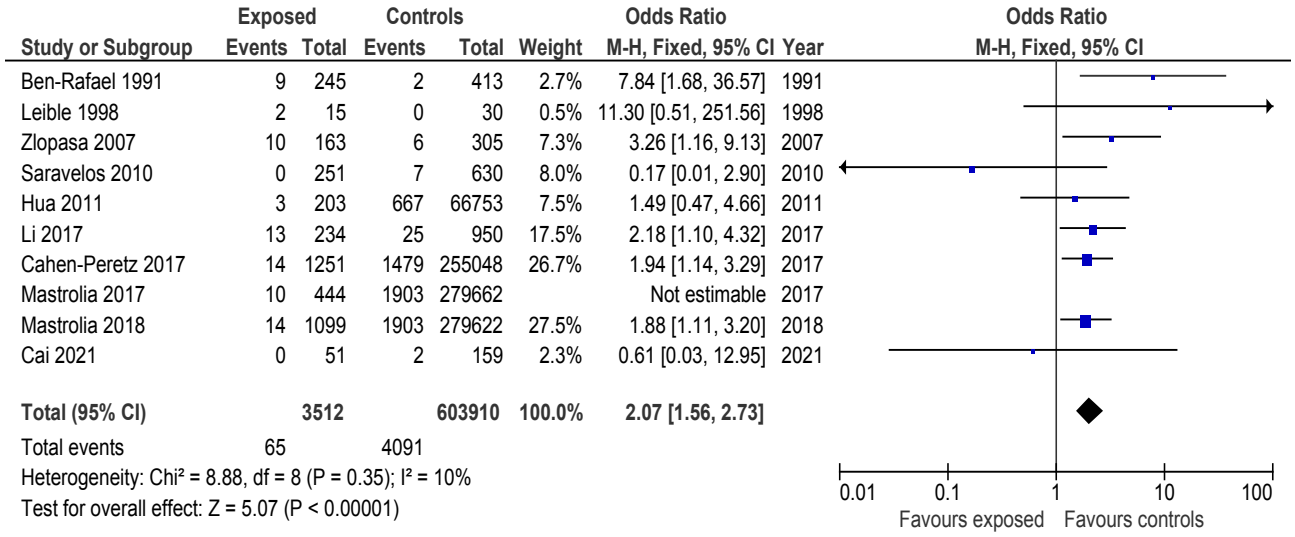


Figure S17: Forest plot of individual and pooled effects on fetal mortality of all CUA (combined).

Fetal mortality by type of CUA

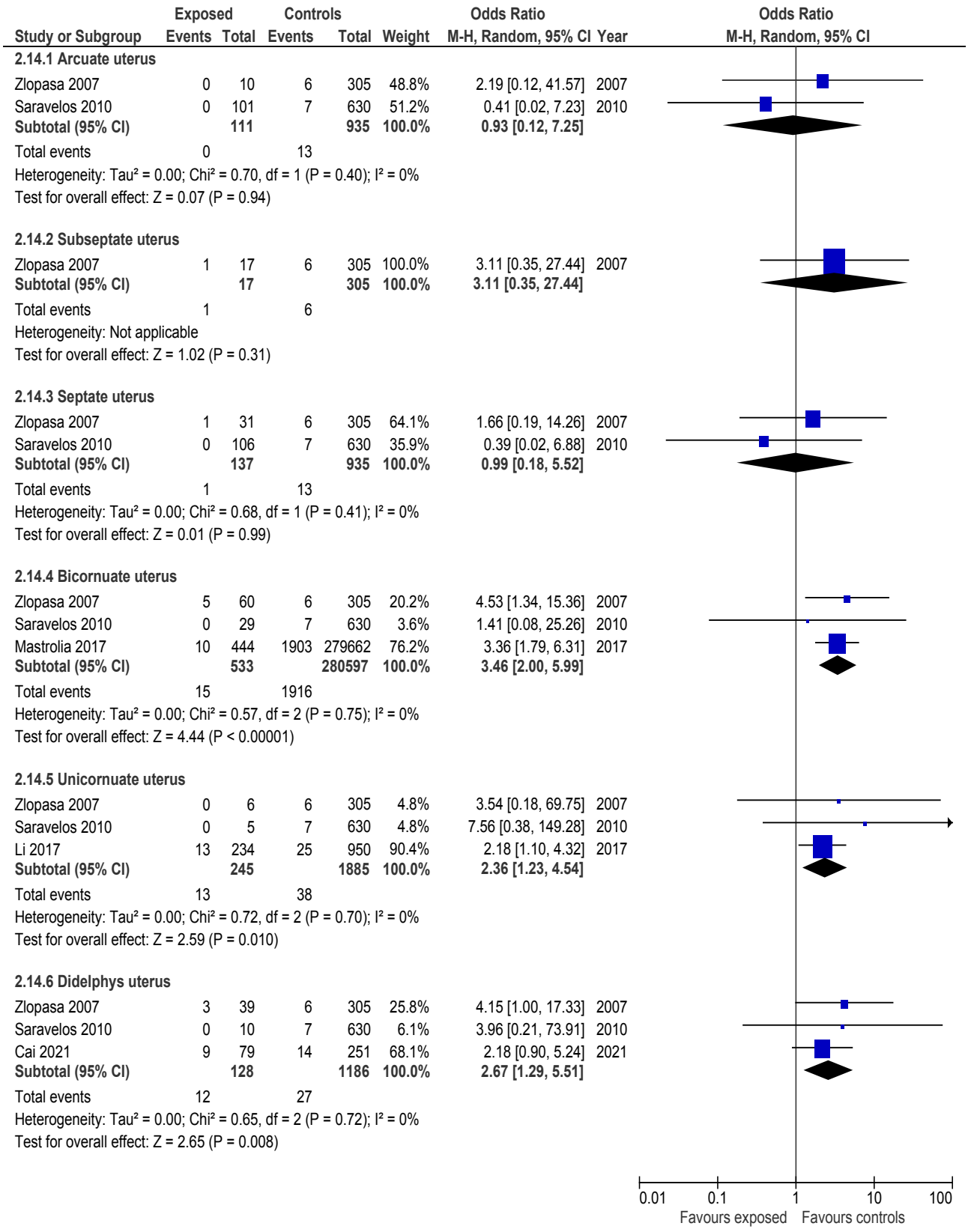


Figure S18: Forest plots of individual and pooled effects on fetal mortality by type of CUA.

Perinatal mortality (all CUA)

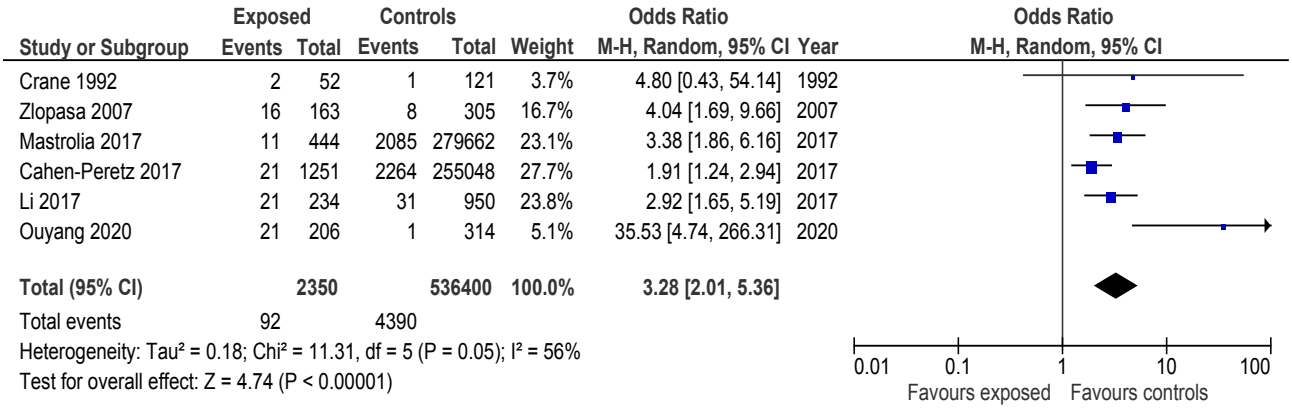


Figure S19: Forest plot of individual and pooled effects on perinatal mortality of all CUA (combined).

Perinatal mortality by type of CUA

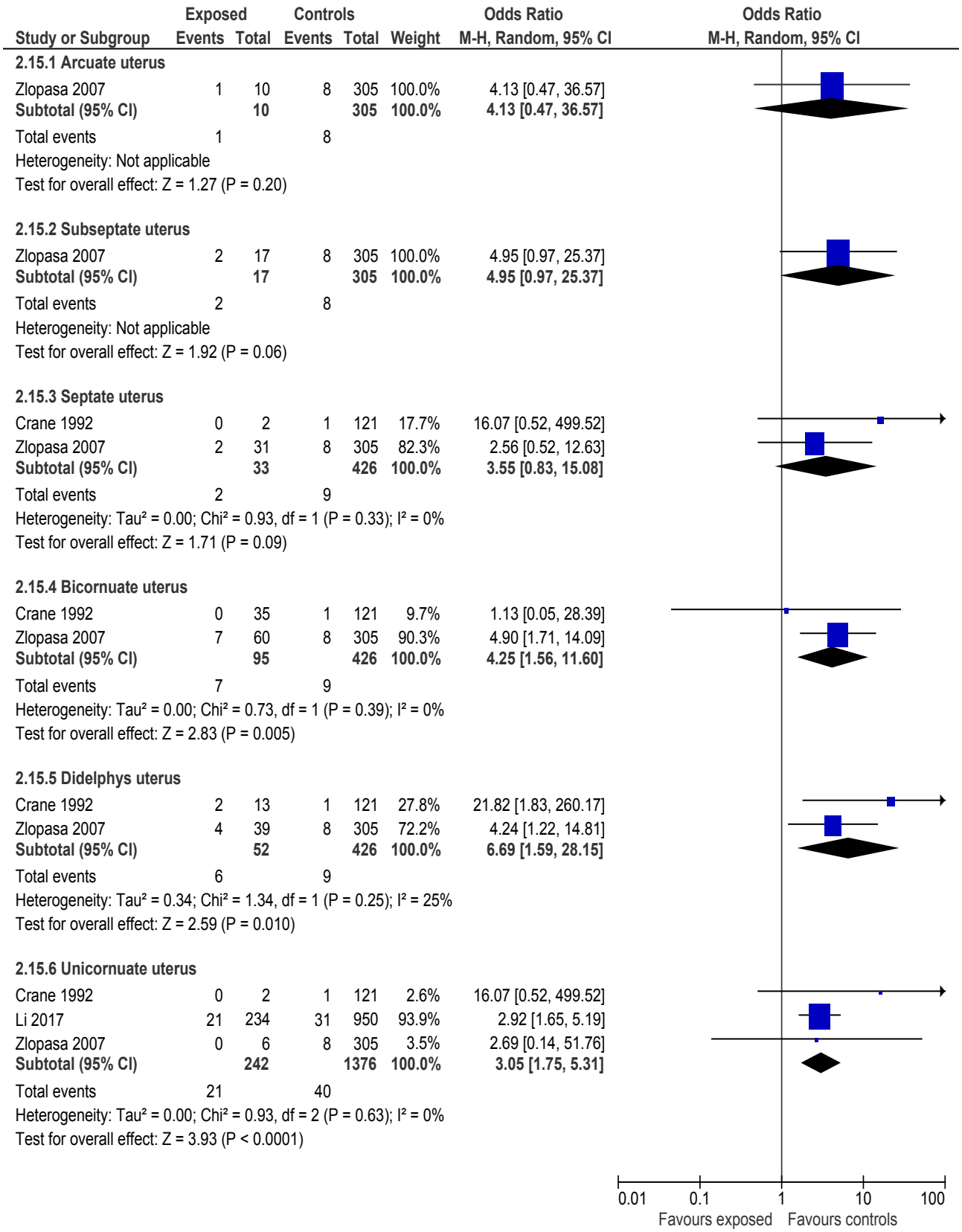


Figure S20: Forest plots of individual and pooled effects on perinatal mortality by type of CUA.

Appendix 1: NLM (PUBMED) structured search

(congenital uterine anomalies OR müllerian anomalies OR arcuate uterus OR septate uterus OR subseptate uterus OR bicornuate uterus OR unicornuate uterus OR didelphis uterus OR dysmorphic uterus OR T-shaped uterus) AND ('pregnancy OR miscarriage OR spontaneous abortion OR ectopic pregnancy OR delivery OR live birth', 'pregnancy outcome OR perinatal outcome OR premature birth OR prematurity OR preterm delivery OR preterm labor OR premature rupture of membranes OR preterm premature rupture of membranes OR intrauterine growth restriction OR (infant, small for gestational age) OR placental abruption OR cesarean delivery OR fetal malposition OR abnormal presentation OR fetal mortality OR stillbirth OR perinatal mortality OR pregnancy complications OR obstetric labor complications AND (1000/1/1:2021/10/3[pdat])) Filters: **from 1000/1/1 - 2022/04/30[pdat])**

((((“congenital”[MeSH Subheading] OR “congenital”[All Fields] OR “congenitally”[All Fields]) AND (“uterine anomalies”[Supplementary Concept] OR “uterine anomalies”[All Fields] OR “uterine anomalies”[All Fields])) OR (“mullerian”[All Fields] AND (“abnormalities”[MeSH Subheading] OR “abnormalities”[All Fields] OR “anomalies”[All Fields] OR “anomalie”[All Fields] OR “anomaly”[All Fields])) OR (“arcuate”[All Fields] AND (“uterus”[MeSH Terms] OR “uterus”[All Fields] OR “uteri”[All Fields])) OR ((“septate”[All Fields] OR “septated”[All Fields] OR “septates”[All Fields] OR “septation”[All Fields] OR “septations”[All Fields]) AND (“uterus”[MeSH Terms] OR “uterus”[All Fields] OR “uteri”[All Fields])) OR (“subseptate”[All Fields] AND (“uterus”[MeSH Terms] OR “uterus”[All Fields] OR “uteri”[All Fields])) OR (“bicornuate”[All Fields] AND (“uterus”[MeSH Terms] OR “uterus”[All Fields] OR “uteri”[All Fields])) OR (“unicornuate”[All Fields] AND (“uterus”[MeSH Terms] OR “uterus”[All Fields] OR “uteri”[All Fields])) OR ((“didelphis”[MeSH Terms] OR “didelphis”[All Fields]) AND (“uterus”[MeSH Terms] OR “uterus”[All Fields] OR “uteri”[All Fields])) OR ((“congenital abnormalities”[MeSH Terms] OR (“congenital”[All Fields] AND “abnormalities”[All Fields]) OR “congenital abnormalities”[All Fields] OR “dysmorphism”[All Fields] OR “dysmorphisms”[All Fields] OR “dysmorphic”[All Fields]) AND (“uterus”[MeSH Terms] OR “uterus”[All Fields] OR “uteri”[All Fields])) OR (“T-shaped”[All Fields] AND (“uterus”[MeSH Terms] OR “uterus”[All Fields] OR “uteri”[All Fields]))) AND ((“pregnancy”[MeSH Terms] OR “pregnancy”[All Fields] OR “pregnancies”[All Fields] OR “pregnancy s”[All Fields] OR (“abortion, spontaneous”[MeSH Terms] OR (“abortion”[All Fields] AND “spontaneous”[All Fields]) OR “spontaneous abortion”[All Fields] OR “miscarriage”[All Fields] OR “miscarriages”[All Fields]) OR (“abortion, spontaneous”[MeSH Terms] OR (“abortion”[All Fields] AND “spontaneous”[All Fields]) OR “spontaneous abortion”[All Fields] OR (“spontaneous”[All Fields] AND “abortion”[All Fields])) OR (“pregnancy, ectopic”[MeSH Terms] OR (“pregnancy”[All Fields] AND “ectopic”[All Fields]) OR “ectopic pregnancy”[All Fields] OR (“ectopic”[All Fields] AND “pregnancy”[All Fields])) OR (“deliveries”[All Fields] OR “delivery, obstetric”[MeSH Terms] OR (“delivery”[All Fields] AND “obstetric”[All Fields]) OR “obstetric delivery”[All Fields] OR “delivery”[All Fields]) OR ((“live birth”[MeSH Terms] OR (“live”[All Fields] AND “birth”[All Fields]) OR “live birth”[All Fields]) AND (“pregnancy outcome”[MeSH Terms] OR (“pregnancy”[All Fields] AND “outcome”[All Fields]) OR “pregnancy outcome”[All Fields])) OR ((“perinatal”[All Fields] OR “perinatally”[All Fields] OR “perinatals”[All Fields]) AND (“outcome”[All Fields] OR “outcomes”[All Fields])) OR (“premature birth”[MeSH Terms] OR (“premature”[All Fields] AND “birth”[All Fields]) OR “premature birth”[All Fields]) OR (“premature birth”[MeSH Terms] OR (“premature”[All Fields] AND “birth”[All Fields]) OR “premature birth”[All Fields] OR “premature”[All Fields] OR “prematurely”[All Fields] OR “prematures”[All Fields] OR “prematurities”[All Fields] OR “prematurity”[All Fields]) OR (“premature birth”[MeSH Terms] OR (“premature”[All Fields] AND “birth”[All Fields]) OR “premature birth”[All Fields] OR (“preterm”[All Fields] AND “delivery”[All Fields]) OR “preterm delivery”[All Fields]) OR (“obstetric labor, premature”[MeSH Terms] OR (“obstetric”[All Fields] AND “labor”[All Fields] AND “premature”[All Fields]) OR “premature obstetric labor”[All Fields] OR (“preterm”[All Fields] AND “labor”[All Fields]) OR “preterm labor”[All Fields]) OR (“fetal membranes, premature rupture”[MeSH Terms] OR (“fetal”[All Fields] AND “membranes”[All Fields] AND

"premature"[All Fields] AND "rupture"[All Fields]) OR "premature rupture fetal membranes"[All Fields] OR ("premature"[All Fields] AND "rupture"[All Fields] AND "membranes"[All Fields]) OR "premature rupture of membranes"[All Fields]) OR (("premature birth"[MeSH Terms] OR ("premature"[All Fields] AND "birth"[All Fields]) OR "premature birth"[All Fields] OR "preterm"[All Fields] OR "preterms"[All Fields]) AND ("fetal membranes, premature rupture"[MeSH Terms] OR ("fetal"[All Fields] AND "membranes"[All Fields] AND "premature"[All Fields] AND "rupture"[All Fields]) OR "premature rupture fetal membranes"[All Fields] OR ("premature"[All Fields] AND "rupture"[All Fields] AND "membranes"[All Fields]) OR "premature rupture of membranes"[All Fields])) OR ("fetal growth retardation"[MeSH Terms] OR ("fetal"[All Fields] AND "growth"[All Fields] AND "retardation"[All Fields]) OR "fetal growth retardation"[All Fields] OR ("intrauterine"[All Fields] AND "growth"[All Fields] AND "restriction"[All Fields]) OR "intrauterine growth restriction"[All Fields]) OR ("infant, small for gestational age"[MeSH Terms] OR ("infant"[All Fields] AND "small"[All Fields] AND "gestational"[All Fields] AND "age"[All Fields]) OR "small for gestational age infant"[All Fields] OR ("infant"[All Fields] AND "small"[All Fields] AND "gestational"[All Fields] AND "age"[All Fields]) OR "infant small for gestational age"[All Fields]) OR ("abruptio placentae"[MeSH Terms] OR ("abruptio"[All Fields] AND "placentae"[All Fields]) OR "abruptio placentae"[All Fields] OR ("placental"[All Fields] AND "abruption"[All Fields]) OR "placental abruption"[All Fields]) OR ("cesarean section"[MeSH Terms] OR ("cesarean"[All Fields] AND "section"[All Fields]) OR "cesarean section"[All Fields] OR ("cesarean"[All Fields] AND "delivery"[All Fields]) OR "cesarean delivery"[All Fields]) OR (("fetale"[All Fields] OR "fetally"[All Fields] OR "fetals"[All Fields] OR "fetus"[MeSH Terms] OR "fetus"[All Fields] OR "fetal"[All Fields] OR "foetal"[All Fields]) AND ("malposition"[All Fields] OR "malpositioned"[All Fields] OR "malpositioning"[All Fields] OR "malpositionings"[All Fields] OR "malpositions"[All Fields])) OR (("abnormal"[All Fields] OR "abnormalities"[MeSH Subheading] OR "abnormalities"[All Fields] OR "congenital abnormalities"[MeSH Terms] OR ("congenital"[All Fields] AND "abnormalities"[All Fields]) OR "congenital abnormalities"[All Fields] OR "abnormality"[All Fields] OR "abnormally"[All Fields] OR "abnormals"[All Fields] OR "abnormities"[All Fields] OR "abnormity"[All Fields]) AND ("present"[All Fields] OR "presentation"[All Fields] OR "presentations"[All Fields] OR "presented"[All Fields] OR "presenter"[All Fields] OR "presenters"[All Fields] OR "presenting"[All Fields] OR "presents"[All Fields])) OR ("fetal mortality"[MeSH Terms] OR ("fetal"[All Fields] AND "mortality"[All Fields]) OR "fetal mortality"[All Fields]) OR ("stillbirth"[MeSH Terms] OR "stillbirth"[All Fields] OR "stillbirths"[All Fields]) OR ("perinatal mortality"[MeSH Terms] OR ("perinatal"[All Fields] AND "mortality"[All Fields]) OR "perinatal mortality"[All Fields] OR "perinatal death"[MeSH Terms] OR ("perinatal"[All Fields] AND "death"[All Fields]) OR "perinatal death"[All Fields] OR ("perinatal"[All Fields] AND "mortality"[All Fields])) OR ("pregnancy complications"[MeSH Terms] OR ("pregnancy"[All Fields] AND "complications"[All Fields]) OR "pregnancy complications"[All Fields]) OR ("obstetric labor complications"[MeSH Terms] OR ("obstetric"[All Fields] AND "labor"[All Fields] AND "complications"[All Fields]) OR "obstetric labor complications"[All Fields])) AND 1000/01/01:2021/10/03[Date - Publication])) AND (1000/1/1:2022/04/30[pdat])

Translations

congenital: "congenital"[Subheading] OR "congenital"[All Fields] OR "congenitally"[All Fields]

uterine anomalies: "Uterine Anomalies"[Supplementary Concept] OR "Uterine Anomalies"[All Fields] OR "uterine anomalies"[All Fields]

anomalies: "abnormalities"[Subheading] OR "abnormalities"[All Fields] OR "anomalies"[All Fields] OR "anomalie"[All Fields] OR "anomaly"[All Fields]

uterus: "uterus"[MeSH Terms] OR "uterus"[All Fields] OR "uteri"[All Fields]

septate: "septate"[All Fields] OR "septated"[All Fields] OR "septates"[All Fields] OR "septation"[All Fields] OR "septations"[All Fields]

uterus: "uterus"[MeSH Terms] OR "uterus"[All Fields] OR "uteri"[All Fields]

uterus: "uterus"[MeSH Terms] OR "uterus"[All Fields] OR "uteri"[All Fields]

uterus: "uterus"[MeSH Terms] OR "uterus"[All Fields] OR "uteri"[All Fields]

uterus: "uterus"[MeSH Terms] OR "uterus"[All Fields] OR "uteri"[All Fields]

didelphis: "didelphis"[MeSH Terms] OR "didelphis"[All Fields]

uterus: "uterus"[MeSH Terms] OR "uterus"[All Fields] OR "uteri"[All Fields]

dysmorphic: "congenital abnormalities"[MeSH Terms] OR ("congenital"[All Fields] AND "abnormalities"[All Fields]) OR "congenital abnormalities"[All Fields] OR "dysmorphism"[All Fields] OR "dysmorphisms"[All Fields] OR "dysmorphic"[All Fields]
uterus: "uterus"[MeSH Terms] OR "uterus"[All Fields] OR "uteri"[All Fields]
uterus: "uterus"[MeSH Terms] OR "uterus"[All Fields] OR "uteri"[All Fields]
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miscarriage: "abortion, spontaneous"[MeSH Terms] OR ("abortion"[All Fields] AND "spontaneous"[All Fields]) OR "spontaneous abortion"[All Fields] OR "miscarriage"[All Fields] OR "miscarriages"[All Fields]
spontaneous abortion: "abortion, spontaneous"[MeSH Terms] OR ("abortion"[All Fields] AND "spontaneous"[All Fields]) OR "spontaneous abortion"[All Fields] OR ("spontaneous"[All Fields] AND "abortion"[All Fields])
ectopic pregnancy: "pregnancy, ectopic"[MeSH Terms] OR ("pregnancy"[All Fields] AND "ectopic"[All Fields]) OR "ectopic pregnancy"[All Fields] OR ("ectopic"[All Fields] AND "pregnancy"[All Fields])
delivery: "deliveries"[All Fields] OR "delivery, obstetric"[MeSH Terms] OR ("delivery"[All Fields] AND "obstetric"[All Fields]) OR "obstetric delivery"[All Fields] OR "delivery"[All Fields]
live birth',: "live birth"[MeSH Terms] OR ("live"[All Fields] AND "birth"[All Fields]) OR "live birth"[All Fields]
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premature birth: "premature birth"[MeSH Terms] OR ("premature"[All Fields] AND "birth"[All Fields]) OR "premature birth"[All Fields]
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premature rupture of membranes: "fetal membranes, premature rupture"[MeSH Terms] OR ("fetal"[All Fields] AND "membranes"[All Fields] AND "premature"[All Fields] AND "rupture"[All Fields]) OR "premature rupture fetal membranes"[All Fields] OR ("premature"[All Fields] AND "rupture"[All Fields] AND "membranes"[All Fields]) OR "premature rupture of membranes"[All Fields]
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premature rupture of membranes: "fetal membranes, premature rupture"[MeSH Terms] OR ("fetal"[All Fields] AND "membranes"[All Fields] AND "premature"[All Fields] AND "rupture"[All Fields]) OR "premature rupture fetal membranes"[All Fields] OR ("premature"[All Fields] AND "rupture"[All Fields] AND "membranes"[All Fields]) OR "premature rupture of membranes"[All Fields]
intrauterine growth restriction: "fetal growth retardation"[MeSH Terms] OR ("fetal"[All Fields] AND "growth"[All Fields] AND "retardation"[All Fields]) OR "fetal growth retardation"[All Fields] OR ("intrauterine"[All Fields] AND "growth"[All Fields] AND "restriction"[All Fields]) OR "intrauterine growth restriction"[All Fields]
infant, small for gestational age: "infant, small for gestational age"[MeSH Terms] OR ("infant"[All Fields] AND "small"[All Fields] AND "gestational"[All Fields] AND "age"[All Fields]) OR "small for gestational age infant"[All Fields] OR ("infant"[All Fields] AND "small"[All Fields] AND "gestational"[All Fields] AND "age"[All Fields]) OR "infant small for gestational age"[All Fields]
placental abruption: "abruptio placentae"[MeSH Terms] OR ("abruptio"[All Fields] AND "placentae"[All Fields]) OR "abruptio placentae"[All Fields] OR ("placental"[All Fields] AND "abruption"[All Fields]) OR "placental abruption"[All Fields]
cesarean delivery: "cesarean section"[MeSH Terms] OR ("cesarean"[All Fields] AND

"section"[All Fields]) OR "cesarean section"[All Fields] OR ("cesarean"[All Fields] AND "delivery"[All Fields]) OR "cesarean delivery"[All Fields]

fetal: "fetale"[All Fields] OR "fetally"[All Fields] OR "fetals"[All Fields] OR "fetus"[MeSH Terms] OR "fetus"[All Fields] OR "fetal"[All Fields] OR "foetal"[All Fields]

malposition: "malposition"[All Fields] OR "malpositioned"[All Fields] OR "malpositioning"[All Fields] OR "malpositionings"[All Fields] OR "malpositions"[All Fields]

abnormal: "abnormal"[All Fields] OR "abnormalities"[Subheading] OR "abnormalities"[All Fields] OR "congenital abnormalities"[MeSH Terms] OR ("congenital"[All Fields] AND "abnormalities"[All Fields]) OR "congenital abnormalities"[All Fields] OR "abnormality"[All Fields] OR "abnormally"[All Fields] OR "abnormals"[All Fields] OR "abnormities"[All Fields] OR "abnormity"[All Fields]

presentation: "present"[All Fields] OR "presentation"[All Fields] OR "presentations"[All Fields] OR "presented"[All Fields] OR "presenter"[All Fields] OR "presenter's"[All Fields] OR "presenters"[All Fields] OR "presenting"[All Fields] OR "presents"[All Fields]

fetal mortality: "fetal mortality"[MeSH Terms] OR ("fetal"[All Fields] AND "mortality"[All Fields]) OR "fetal mortality"[All Fields]

stillbirth: "stillbirth"[MeSH Terms] OR "stillbirth"[All Fields] OR "stillbirths"[All Fields]

perinatal mortality: "perinatal mortality"[MeSH Terms] OR ("perinatal"[All Fields] AND "mortality"[All Fields]) OR "perinatal mortality"[All Fields] OR "perinatal death"[MeSH Terms] OR ("perinatal"[All Fields] AND "death"[All Fields]) OR "perinatal death"[All Fields] OR ("perinatal"[All Fields] AND "mortality"[All Fields])

pregnancy complications: "pregnancy complications"[MeSH Terms] OR ("pregnancy"[All Fields] AND "complications"[All Fields]) OR "pregnancy complications"[All Fields]

obstetric labor complications: "obstetric labor complications"[MeSH Terms] OR ("obstetric"[All Fields] AND "labor"[All Fields] AND "complications"[All Fields]) OR "obstetric labor complications"[All Fields]

First author, year	Newcastle-Ottawa Scale domains								Total Score	Quality (AHRQ standards)†
	Selection*				Comparability*	Outcome*				
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis controlled for confounders	Assessment of outcome	Follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts		
Ben-Rafael, 1991	*	*	*		*	*	*	*	7	Good
Cooney, 1998	*	*		*	*	*	*	*	7	Good
Leible, 1998			*	*	*	*	*	*	6	Fair
Erez, 2007	*	*		*	*	*	*	*	7	Good
Zlopasa, 2007	*	*	*	*	*	*	*	*	8	Good
Ban-Frangez, 2009	*	*	*	*	*	*	*	*	8	Good
Sugiura-Ogasawara, 2010	*	*		*	**	*	*	*	8	Good
Saravelos, 2010	*	*	*	*	**	*	*	*	9	Good
Tomazevic, 2010	*	*	*	*	**	*	*	*	9	Good
Hua, 2011	*	*	*	*	**	*	*	*	9	Good
Jayaprakasan, 2011	*	*	*	*	*	*	*	*	8	Good
Crane, 2012	*	*		*	*	*	*	*	7	Good
Takami, 2014	*	*	*	*	*	*	*	*	8	Good
Hiersch, 2016	*	*		*	**	*	*	*	8	Good
Li, 2017	*	*		*	*	*	*	*	7	Good
Ozgur, 2017	*	*		*	*	*	*	*	7	Good
Mastrolia, 2017	*	*		*	*	*	*	*	7	Good
Cahen-Peretz, 2017	*	*		*	**	*	*	*	9	Good
Mastrolia, 2018	*	*		*	*	*	*	*	7	Good
Ples, 2018	*	*	*	*	**	*	*	*	9	Good
Prior, 2018	*	*	*	*	**	*	*	*	9	Good
Surrey, 2018	*	*	*	*	**	*	*	*	9	Good
Chen, 2018a	*	*		*	*	*	*	*	7	Good
Chen, 2018b	*	*		*	*	*	*	*	7	Good
Ouyang, 2020	*	*	*	*	**	*	*	*	9	Good

Cai, 2021	*	*	*	*	*	*	*	*	8	Good
Kong, 2021	*	*	*	*	**	*	*	*	9	Good
Lü, 2021	*	*	*	*	**	*	*	*	9	Good
Zambrotta, 2021	*	*	*	*	**	*	*	*	9	Good
Zhang, 2021	*	*		*	**	*	*	*	8	Good
Marianna, 2022	*	*	*	*	**	*	*	*	9	Good
Qiu, 2022	*	*	*	*	**	*	*	*	9	Good

*** Specific scoring criteria:**

– Representativeness of the exposed cohort: Hospital-based cohorts including all exposed patients (n≥30) registered during the observation period were granted with one star.

– Selection of the non-exposed cohort: Hospital-bases cohorts including all non-exposed patients (n≥30) from the same population registered during the observation period were granted with one star.

– Ascertainment of exposure: müllerian abnormality assessment by laparoscopy, ultrasonography or histeroscopy was granted with one star.

– Comparability of cohorts on the basis of the design or analysis controlled for confounders:

  Studies controlling basic potential confounders (age, parity and number of transferred embryos in IVF patients) were granted with one star.

  Studies controlling also one or more additional relevant potential confounders were granted with two stars.

– Assessment of outcome: confirmation of outcome provided by clinical records was granted with one star.

– Adequacy of follow-up of cohorts: Follow up rate > 90% was granted with one star.

†USA Agency for Healthcare Research and Quality standards:

– Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain

– Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain

– Poor quality: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/exposure domain

Appendix 3: PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Pages 3-4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 5
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 6
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supp. File 1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Pages 6-7
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 7
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 7
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	NA
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 7
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 7
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 8
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 8
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 8
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 8
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 8
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 8
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 8
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Table I & Page 8
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Table II (Supp. File 2)
Study characteristics	17	Cite each included study and present its characteristics.	Table I
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supp. File 2
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Pages 9-13, Table III & Supp. File 3
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Supp. File 3
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Pages 9-13, Table III & Supp. File 3
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Pages 9-13, Table III & Supp. File 3
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Pages 9-13 & Supp. File 3
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Page 13
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Supp. File 2

Section and Topic	Item #	Checklist item	Location where item is reported
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Pages 13-14
	23b	Discuss any limitations of the evidence included in the review.	Pages 16-17
	23c	Discuss any limitations of the review processes used.	Pages 16-17
	23d	Discuss implications of the results for practice, policy, and future research.	Page 17
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 6
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 6
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 18
Competing interests	26	Declare any competing interests of review authors.	Page 18
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	NA

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71
For more information, visit: http://www.prisma-statement.org/