# Table of contents

## Supplementary Material 1. Literature search.

September 27. 2020. 528 hits.

((((((((((((IVF) OR in vitro fertilization) OR fertilization in vitro)) OR (((infertile women) OR infertility) OR female infertility))) AND (("vaginitis"[MeSH Terms] OR "vaginitis"[All Fields]) OR ("vaginal diseases"[MeSH Terms] OR ("vaginal"[All Fields] AND "diseases"[All Fields]) OR "vaginal diseases"[All Fields] OR "vaginosis"[All Fields]) OR "vaginal microbiome"[All Fields] OR "vaginal microbiota"[All Fields] OR "vaginal infection"[All Fields] OR "vaginal infections"[All Fields] OR ("vaginosis, bacterial"[MeSH Terms] OR ("vaginosis"[All Fields] AND "bacterial"[All Fields]) OR "bacterial vaginosis"[All Fields] OR ("bacterial"[All Fields] AND "vaginosis"[All Fields])) OR ("vaginosis, bacterial"[MeSH Terms] OR ("vaginosis"[All Fields] AND "bacterial"[All Fields]) OR "bacterial vaginosis"[All Fields] OR ("bacterial"[All Fields] AND "vaginitis"[All Fields]) OR "bacterial vaginitis"[All Fields])))) NOT (((((((IVF) OR in vitro fertilization) OR fertilization in vitro)) OR (((infertile women) OR infertility) OR female infertility))) AND (("vaginitis"[MeSH Terms] OR "vaginitis"[All Fields]) OR ("vaginal diseases"[MeSH Terms] OR ("vaginal"[All Fields] AND "diseases"[All Fields]) OR "vaginal diseases"[All Fields] OR "vaginosis"[All Fields]) OR "vaginal microbiome"[All Fields] OR "vaginal microbiota"[All Fields] OR "vaginal infection"[All Fields] OR "vaginal infections"[All Fields] OR ("vaginosis, bacterial"[MeSH Terms] OR ("vaginosis"[All Fields] AND "bacterial"[All Fields]) OR "bacterial vaginosis"[All Fields] OR ("bacterial"[All Fields] AND "vaginosis"[All Fields])) OR ("vaginosis, bacterial"[MeSH Terms] OR ("vaginosis"[All Fields] AND "bacterial"[All Fields]) OR "bacterial vaginosis"[All Fields] OR ("bacterial"[All Fields] AND "vaginitis"[All Fields]) OR "bacterial vaginitis"[All Fields])))) AND Review[ptyp])))) NOT ((((((((((IVF) OR in vitro fertilization) OR fertilization in vitro)) OR (((infertile women) OR infertility) OR female infertility))) AND (("vaginitis"[MeSH Terms] OR "vaginitis"[All Fields]) OR ("vaginal diseases"[MeSH Terms] OR ("vaginal"[All Fields] AND "diseases"[All Fields]) OR "vaginal diseases"[All Fields] OR "vaginosis"[All Fields]) OR "vaginal microbiome"[All Fields] OR "vaginal microbiota"[All Fields] OR "vaginal infection"[All Fields] OR "vaginal infections"[All Fields] OR ("vaginosis, bacterial"[MeSH Terms] OR ("vaginosis"[All Fields] AND "bacterial"[All Fields]) OR "bacterial vaginosis"[All Fields] OR ("bacterial"[All Fields] AND "vaginosis"[All Fields])) OR ("vaginosis, bacterial"[MeSH Terms] OR ("vaginosis"[All Fields] AND "bacterial"[All Fields]) OR "bacterial vaginosis"[All Fields] OR ("bacterial"[All Fields] AND "vaginitis"[All Fields]) OR "bacterial vaginitis"[All Fields])))) NOT ((((((((IVF) OR in vitro fertilization) OR fertilization in vitro)) OR (((infertile women) OR infertility) OR female infertility))) AND (("vaginitis"[MeSH Terms] OR "vaginitis"[All Fields]) OR ("vaginal diseases"[MeSH Terms] OR ("vaginal"[All Fields] AND "diseases"[All Fields]) OR "vaginal diseases"[All Fields] OR "vaginosis"[All Fields]) OR "vaginal microbiome"[All Fields] OR "vaginal microbiota"[All Fields] OR "vaginal infection"[All Fields] OR "vaginal infections"[All Fields] OR ("vaginosis, bacterial"[MeSH Terms] OR ("vaginosis"[All Fields] AND "bacterial"[All Fields]) OR "bacterial vaginosis"[All Fields] OR ("bacterial"[All Fields] AND "vaginosis"[All Fields])) OR ("vaginosis, bacterial"[MeSH Terms] OR ("vaginosis"[All Fields] AND "bacterial"[All Fields]) OR "bacterial vaginosis"[All Fields] OR ("bacterial"[All Fields] AND "vaginitis"[All Fields]) OR "bacterial vaginitis"[All Fields])))) AND Review[ptyp])) AND Animals[Mesh:noexp])))) AND English[lang]

## Supplementary Material 2. New Castle – Ottawa Quality Assessment Scale - Cohort studies

**Study 1**
Bernabeu, A. *et al.* Effect of the vaginal microbiome on the pregnancy rate in women receiving assisted reproductive treatment. *Journal of assisted reproduction and genetics* **36**, 2111-2119, doi:10.1007/s10815-019-01564-0 (2019).

**A. Selection**
1) Representativeness of the exposed cohort: Good. Cohort came from Spain.

Although the cause of infertility has not been described.

2) Selection of the non-exposed cohort: Good, drawn from the same population as the exposed cohort.

3) Ascertainment of exposure: Good. Vaginal sample collection well defined. Use of NGS (16s rRNA) to analyze data.

4) Demonstration that outcome of interest was not present at start of study: yes

**B. Comparability**
1) Comparability of cohorts on the basis of the design or analysis: good, the endometrial preparation protocol of the study helped to normalize the cohort of the study.

**C. Outcome**
1) Assessment of outcome: Good.

2) Was follow-up long enough for outcomes to occur: Yes.

3) Adequacy of follow up of cohorts: Yes, on both biochemical and clinical pregnancies, however data regarding LBR on two subject (18%) who were verified clinical pregnant.

Total score = 4 + 1 + 2 = 7/9

**Study 2**
Kyono, K., Hashimoto, T., Nagai, Y. & Sakuraba, Y. Analysis of endometrial microbiota by 16S ribosomal RNA gene sequencing among infertile patients: a single-center pilot study. *Reproductive medicine and biology* 17, 297-306, doi:10.1002/rmb2.12105 (2018).

**A. Selection**
1) Representativeness of the exposed cohort: Study population from Japan.

2) Selection of the non-exposed cohort: Good, drawn from the same population as the exposed cohort.

3) Ascertainment of exposure: Good. Vaginal samples collected in different menstrual cycles. Use of NGS (16s rRNA) to analyze data.

4) Demonstration that outcome of interest was not present at start of study: yes

**B. Comparability**

1) Comparability of cohorts on the basis of the design or analysis: Poor, the article does not compare groups in relation to vaginal flora. Comparison is age dependent; >38 and <38. Limited sample size.

**C. Outcome**
1) Assessment of outcome: Poor description of the outcome data.

2) Was follow-up long enough for outcomes to occur: Only limited data on outcome, biochemical pregnancy, LBR and spontaneous abortion not thoroughly reported.

3) Adequacy of follow up of cohorts: A short follow up period. During the study period 15 out of 79 IVF patients achieved pregnancy. A longer follow-up period would have given data on different outcomes.

Total score = 3 + 0 + 0 = 3/9

**Study 3**
Vergaro, P. *et al.* Vaginal microbiota profile at the time of embryo transfer does not affect live birth rate in IVF cycles with donated oocytes. *Reproductive biomedicine online* **38**, 883-891, doi:10.1016/j.rbmo.2018.12.019 (2019).

**A. Selection**
1) Representativeness of the exposed cohort: Good. Cohort came from Spain.

2) Selection of the non-exposed cohort: Good, drawn from the same population as the exposed cohort.

3) Ascertainment of exposure: Good. Vaginal sample collection well defined. Used qPCR to analyze data.

4) Demonstration that outcome of interest was not present at start of study: yes

**B. Comparability**
1) Comparability of cohorts on the basis of the design or analysis: good

**C. Outcome**
1) Assessment of outcome: Good.

2) Was follow-up long enough for outcomes to occur: Yes. All outcomes reported.

3) Adequacy of follow up of cohorts: yes.

Total score = 4 + 1 + 3 = 8/9

**Study 4**
Koedooder, R. *et al.* The vaginal microbiome as a predictor for outcome of in vitro fertilization with or without intracytoplasmic sperm injection: a prospective study. *Human reproduction (Oxford, England)* **34**, 1042-1054, doi:10.1093/humrep/dez065 (2019).

**A. Selection**

1) Representativeness of the exposed cohort: Good. Cohort from Greece. Long interval between vaginal swab and ET.

2) Selection of the non-exposed cohort: Good, drawn from the same population as the exposed cohort.

3) Ascertainment of exposure: Good. Vaginal sample collection well defined. Used IS-pro technique used.

4) Demonstration that outcome of interest was not present at start of study: yes

**B. Comparability**
1) Comparability of cohorts on the basis of the design or analysis: Good.

**C. Outcome**

1) Assessment of outcome: Fine, ultrasound proven heartbeat.

2) Was follow-up long enough for outcomes to occur: Did not report miscarriage, LBR and biochemical pregnancy.

3) Adequacy of follow up of cohorts: no.

Total score = 4 + 1 + 1 = 6/9

**Study 5**
Moragianni, D. *et al.* Genital tract infection and associated factors affect the reproductive outcome in fertile females and females undergoing in vitro fertilization. *Biomedical reports* **10**, 231-237, doi:10.3892/br.2019.1194 (2019).

**A. Selection**

1) Representativeness of the exposed cohort: Good. Cohort from Greece.

2) Selection of the non-exposed cohort: Good. Fertile woman with at least one child.

3) Ascertainment of exposure: Poor. Vaginal sample collection was not described. Used Nugent scoring system.

4) Demonstration that outcome of interest was not present at start of study: yes

**B. Comparability**
1) Comparability of cohorts on the basis of the design or analysis: Good.

**C. Outcome**

1) Assessment of outcome: Fine, ultrasound proven heartbeat and HCG concentration at week 8.

2) Was follow-up long enough for outcomes to occur: Yes.

3) Adequacy of follow up of cohorts: The follow-up period is not listed in the article, but authors were contacted and provided relevant information.

Total score = 3 + 1 + 3 = 7/9

Supplementary Material 3. Study Characteristic (VD prevalence)

| Studies | No. Participants (microbiom) | No. Participants (Microscopy) | Total no. participants | VD (Microbiom) | VD (Microscopy) | BV (total) |
|---|---|---|---|---|---|---|
| Haahr et al. | 130 | 130 | 130 | 36 | 27 | 36 |
| Mangot-Bertrand et al. | 307 | 307 | 307 | 29 | 17 | 29 |
| Selim et al. | - | 71 | 71 | - | 26 | 26 |
| Eckert et al. | - | 91 | 91 | - | 10 | 10 |
| Liversedge et al. | - | 301 | 301 | - | 77 | 77 |
| Gaudoin et al. | - | 246 | 246 | - | 40 | 40 |
| Boomsma et al. | - | 197 | 197 | - | 17 | 17 |
| Eldivan et al. | - | 45 | 45 | - | 17 | 17 |
| Moini et al. | - | 399 | 399 | - | 29 | 29 |
| Moore et al. | - | 91 | 91 | - | 12 | 12 |
| Ralph et al. | - | 771 | 771 | - | 190 | 190 |
| Spandorfer et al. | - | 331 | 331 | - | 14 | 14 |
| Moragianni et al. | - | 111 | 111 | - | 41 | 41 |
| Vergaro et al. | 150 | - | 150 | 35 | - | 35 |
| Koedooder et al | 192 | - | 192 | 34 | - | 34 |
| Kyono et al. | 79 | - | 79 | 35 | - | 35 |
| Bernabeu et al. | 31 | - | 31 | 2 | - | 2 |
| **Total** | **889** | **3091** | **3543** | **171** | **517** | **644** |

Supplementary Material 4. Live birth rate (Total)

| | | Chance of getting pregnant | | No. Participants | |
|---|---|---|---|---|---|
| **Studies** | **Analysis method** | **AVM** | **NVM** | **AVM** | **NVM** |
| Haahr et al. | qPCR | 2 (11) | 25 (45) | 18 | 57 |
| Mangot-Bertrand et al. | qPCR - Nugent score | 7 (28) | 67 (24) | 28 | 262 |
| Liversedge et al. | Nugent score | 20 (27) | 50 (24) | 75 | 212 |
| Moini et al. | Nugent score | 11 (44) | 102 (33) | 25 | 311 |
| Moore et al. | Nugent score | 2(10) | 25(31) | 10 | 81 |
| Spandorfer et al. | Nugent score | 8(58) | 123(39) | 14 | 317 |
| Vergaro et al. | qPCR | 11(31) | 45 (39) | 35 | 114 |
| Bernabeu et al. | 16S (microbiom) | 1(50) | 8(30) | 2 | 27 |
| Moragianni et al. | Nugent score | 10 | 22 | 41 | 70 |
| | **Total** | **72** | **467** | **248** | **1451** |

Supplementary Material 4. Live birth rate (Molecular)

| | | Chance of getting pregnant | | No. Participants | |
|---|---|---|---|---|---|
| **Studies** | **Analysis method** | **AVM** | **NVM** | **AVM** | **NVM** |
| Haahr et al. | qPCR | 2 | 25 | 18 | 57 |
| Mangot-Bertrand et al. | qPCR - Nugent score | 7 | 67 | 28 | 262 |
| Vergaro et al. | qPCR | 11 | 45 | 35 | 114 |
| Bernabeu et al. | 16S (microbiom) | 1 | 8 | 2 | 27 |
| | **Total** | **21** | **145** | **83** | **460** |

Supplementary Material 4. Live birth rate (Microscopy)

| | | Chance of getting pregnant | | No. Participants | |
|---|---|---|---|---|---|
| **Studies** | **Analysis method** | **AVM** | **NVM** | **AVM** | **NVM** |
| Haahr et al. | Nugent Score | 1 | 26 | 11 | 64 |
| Liversedge et al. | Nugent score | 20 | 50 | 75 | 212 |
| Moini et al. | Nugent score | 11 | 102 | 25 | 311 |
| Moore et al. | Nugent score | 2 | 25 | 10 | 81 |
| Spandorfer et al. | Nugent score | 8 | 123 | 14 | 317 |
| Moragianni et al. | Nugent score | 10 | 22 | 41 | 70 |
| | **Total** | **52** | **348** | **176** | **1055** |

Table legend: AVM=Abnormal vaginal microbiota, NVM=Normal vaginal microbiota

Supplementary Material 5. Early pregnancy loss (Total)

| | | Biochemical - Clinical pregnancy | | No. Participants | |
|---|---|---|---|---|---|
| **Studies** | **Analysis method** | **AVM** | **NVM** | **AVM** | **NVM** |
| Haahr et al. | qPCR | 4(67) | 5 (16) | 6 | 32 |
| Mangot-Bertrand et al. | qPCR - Nugent score | 1 (13) | 25 (25) | 8 | 101 |
| Selim et al. | Nugent score | 2 (35) | 2 (47) | 9 | 21 |
| Eckert et al. | Nugent score | 1 (33) | 13 (34) | 3 | 38 |
| Liversedge et al. | Nugent score | 4 (17) | 9 (14) | 24 | 64 |
| Gaudoin et al. | Nugent score | 3 (30) | 19 (26) | 10 | 72 |
| Boomsma et al. | Nugent score | 2 (25) | 18 (31) | 8 | 59 |
| Eldivan et al. | Nugent score | 0(0) | 0(0) | 4 | 12 |
| Moini et al. | Nugent score | 4 (27) | 19 (15) | 15 | 123 |
| Ralph et al. | Nugent score | 22 (36) | 34 (19) | 61 | 176 |
| Spandorfer et al. | Nugent score | 2(14) | 28 (9) | 14 | 317 |
| Moragianni et al. | Nugent score | 0 | 0 | 41 | 70 |
| Vergaro et al. | qPCR | 6(35) | 11 (17) | 17 | 64 |
| Bernabeu et al. | 16S (microbiom) | 0(0) | 1(7) | 2 | 15 |
| **Total** | | **51** | **184** | **222** | **1164** |

Supplementary Material 5. Early pregnancy loss (Molecular)

| | | Biochemical - Clinical pregnancy | | No. Participants | |
|---|---|---|---|---|---|
| **Studies** | **Analysis method** | **AVM** | **NVM** | **AVM** | **NVM** |
| Haahr et al. | qPCR | 4 | 5 | 6 | 32 |
| Mangot-Bertrand et al. | qPCR - Nugent score | 1 | 25 | 8 | 101 |
| Vergaro et al. | qPCR | 6 | 11 | 17 | 64 |
| Bernabeu et al. | 16S (microbiom) | 0 | 1 | 2 | 15 |
| **Total** | | **11** | **42** | **33** | **212** |

Supplementary Material 5. Early pregnancy loss (Microscopy)

| | | Biochemical - Clinical pregnancy | | No. Participants | |
|---|---|---|---|---|---|
| **Studies** | **Analysis method** | **AVM** | **NVM** | **AVM** | **NVM** |
| Haahr et al. | Nugent score | 1 | 6 | 2 | 36 |
| Selim et al. | Nugent score | 2 | 2 | 9 | 21 |
| Eckert et al. | Nugent score | 1 | 13 | 3 | 38 |
| Liversedge et al. | Nugent score | 4 | 9 | 24 | 64 |
| Gaudoin et al. | Nugent score | 3 | 19 | 10 | 72 |
| Boomsma et al. | Nugent score | 2 | 18 | 8 | 59 |
| Eldivan et al. | Nugent score | 0 | 0 | 4 | 12 |
| Moini et al. | Nugent score | 4 | 19 | 15 | 123 |
| Ralph et al. | Nugent score | 22 | 34 | 61 | 176 |
| Spandorfer et al. | Nugent score | 2 | 28 | 14 | 317 |
| Moragianni et al. | Nugent score | 0 | 0 | 41 | 70 |
| **Total** | | **41** | **148** | **191** | **988** |

Table legend: AVM=Abnormal vaginal microbiota, NVM=Normal vaginal microbiota

## Supplementary Material 6. Clinical pregnancy (Total)

| | | Chance of getting pregnant | | No. Participants | |
|---|---|---|---|---|---|
| **Studies** | **Analysis method** | **AVM** | **NVM** | **AVM** | **NVM** |
| Haahr et al. | qPCR | 2 (9) | 27 (44) | 22 | 62 |
| Mangot-Bertrand et al. | qPCR - Nugent score | 8 (29) | 92 (35) | 28 | 262 |
| Selim et al. | Nugent score | 7 (27) | 19 (42) | 26 | 45 |
| Eckert et al. | Nugent score | 2 (20) | 25 (31) | 10 | 81 |
| Liversedge et al. | Nugent score | 24 (32) | 64 (30) | 75 | 212 |
| Gaudoin et al. | Nugent score | 7 (18) | 53 (26) | 40 | 206 |
| Boomsma et al. | Nugent score | 6 (35) | 41 (23) | 17 | 180 |
| Eldivan et al. | Nugent score | 4(24) | 12 (43) | 17 | 28 |
| Moini et al. | Nugent score | 12 (48) | 108 (35) | 25 | 311 |
| Moore et al. | Nugent score | 2(10) | 25(31) | 10 | 81 |
| Ralph et al. | Nugent score | 41(22) | 122 (25) | 190 | 493 |
| Spandorfer et al. | Nugent score | 8(58) | 147(46) | 14 | 317 |
| Moragianni et al. | Nugent score | 10 (24) | 22 (31) | 41 | 70 |
| Vergaro et al. | qPCR | 11(31) | 53 (46) | 35 | 115 |
| Koedooder et al | IS-pro (microbiom) | 2(6) | 65(41) | 34 | 158 |
| Kyono et al. | 16S (microbiom) | 5(14) | 9(32) | 35 | 44 |
| Bernabeu et al. | 16S (microbiom) | 1 (50) | 15 (52) | 2 | 29 |
| **Total** | | **152** | **899** | **621** | **2694** |

## Supplementary Material 6. Clinical pregnancy (Molecular)

| | | Chance of getting pregnant | | No. Participants | |
|---|---|---|---|---|---|
| **Studies** | **Analysis method** | **AVM** | **NVM** | **AVM** | **NVM** |
| Haahr et al. | qPCR | 2 | 27 | 22 | 62 |
| Mangot-Bertrand et al. | qPCR - Nugent score | 8 | 92 | 28 | 262 |
| Vergaro et al. | qPCR | 11 | 53 | 35 | 115 |
| Koedooder et al | IS-pro (microbiom) | 2 | 65 | 34 | 158 |
| Kyono et al. | 16S (microbiom) | 5 | 9 | 35 | 44 |
| Bernabeu et al. | 16S (microbiom) | 1 | 15 | 2 | 29 |
| **Total** | | **29** | **261** | **156** | **670** |

## Supplementary Material 6. Clinical pregnancy (Microscopy)

| | | Chance of getting pregnant | | No. Participants | |
|---|---|---|---|---|---|
| **Studies** | **Analysis method** | **AVM** | **NVM** | **AVM** | **NVM** |
| Haahr et al. | Nugent score | 1 | 28 | 12 | 72 |
| Selim et al. | Nugent score | 7 | 19 | 26 | 45 |
| Eckert et al. | Nugent score | 2 | 25 | 10 | 81 |
| Liversedge et al. | Nugent score | 24 | 64 | 75 | 212 |
| Gaudoin et al. | Nugent score | 7 | 53 | 40 | 206 |
| Boomsma et al. | Nugent score | 6 | 41 | 17 | 180 |
| Eldivan et al. | Nugent score | 4 | 12 | 17 | 28 |
| Moini et al. | Nugent score | 12 | 108 | 25 | 311 |
| Moore et al. | Nugent score | 2 | 25 | 10 | 81 |
| Ralph et al. | Nugent score | 41 | 122 | 190 | 493 |
| Spandorfer et al. | Nugent score | 8 | 147 | 14 | 317 |
| Moragianni et al. | Nugent score | 10 | 22 | 41 | 70 |
| **Total** | | **124** | **666** | **477** | **2096** |

Table legend: AVM=Abnormal vaginal microbiota, NVM=Normal vaginal microbiota

Supplementary Material 7. Biochemical pregnancy (Total)

| | | Chance of getting pregnant | | No. Participants | |
|---|---|---|---|---|---|
| **Studies** | **Analysis method** | **AVM** | **NVM** | **AVM** | **NVM** |
| Haahr et al. | qPCR | 6(27) | 32(52) | 22 | 62 |
| Mangot-Bertrand et al. | qPCR - Nugent score | 8 (29) | 101 (39) | 28 | 262 |
| Selim et al. | Nugent score | 9 (35) | 21 (47) | 26 | 45 |
| Eckert et al. | Nugent score | 3 (30) | 38 (47) | 10 | 81 |
| Gaudoin et al. | Nugent score | 10 (25) | 72 (35) | 40 | 206 |
| Boomsma et al. | Nugent score | 8 (47) | 59 (33) | 17 | 180 |
| Eldivan et al. | Nugent score | 4(24) | 12 (43) | 17 | 28 |
| Moini et al. | Nugent score | 15 (60) | 123 (40) | 25 | 311 |
| Moore et al. | Nugent score | 2(10) | 25(31) | 10 | 81 |
| Ralph et al. | Nugent score | 61(32) | 176 (30) | 190 | 581 |
| Spandorfer et al. | Nugent score | 10(71) | 175(55) | 14 | 317 |
| Moragianni et al. | Nugent score | 10 (24) | 22 (31) | 41 | 70 |
| Vergaro et al. | qPCR | 17(49) | 64 (56) | 35 | 115 |
| Bernabeu et al. | 16S (microbiom) | 1(50) | 16(55) | 2 | 29 |
| **Total** | | **164** | **936** | **477** | **2368** |

Supplementary Material 7. Biochemical pregnancy (Molecular)

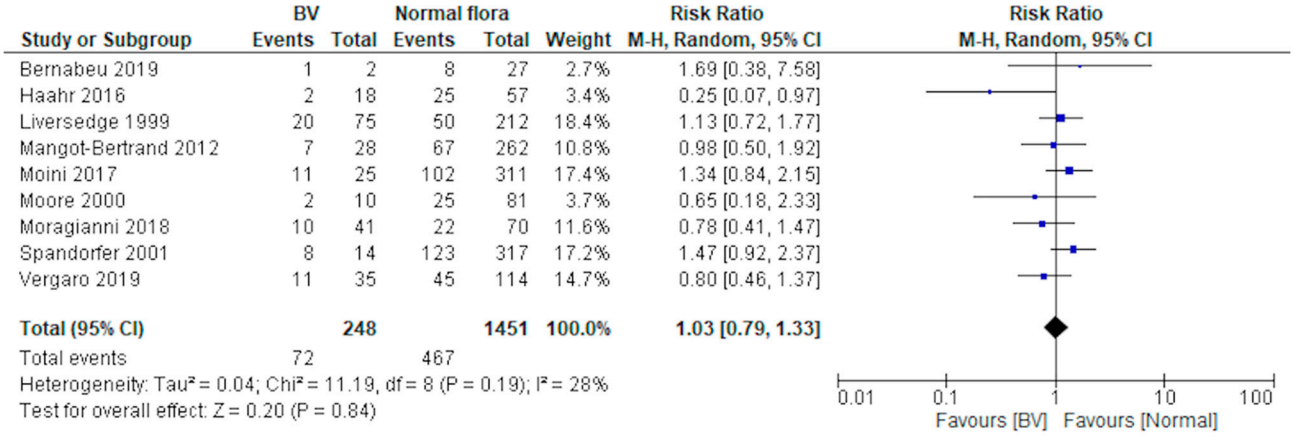
| | | Chance of getting pregnant | | No. Participants | |
|---|---|---|---|---|---|
| **Studies** | **Analysis method** | **AVM** | **NVM** | **AVM** | **NVM** |
| Haahr et al. | qPCR | 6 | 32 | 22 | 62 |
| Mangot-Bertrand et al. | qPCR - Nugent score | 8 | 101 | 28 | 262 |
| Vergaro et al. | qPCR | 17 | 64 | 35 | 115 |
| Bernabeu et al. | 16S (microbiom) | 1 | 16 | 2 | 29 |
| **Total** | | **32** | **213** | **87** | **468** |

Supplementary Material 7. Biochemical pregnancy (Microscopy)

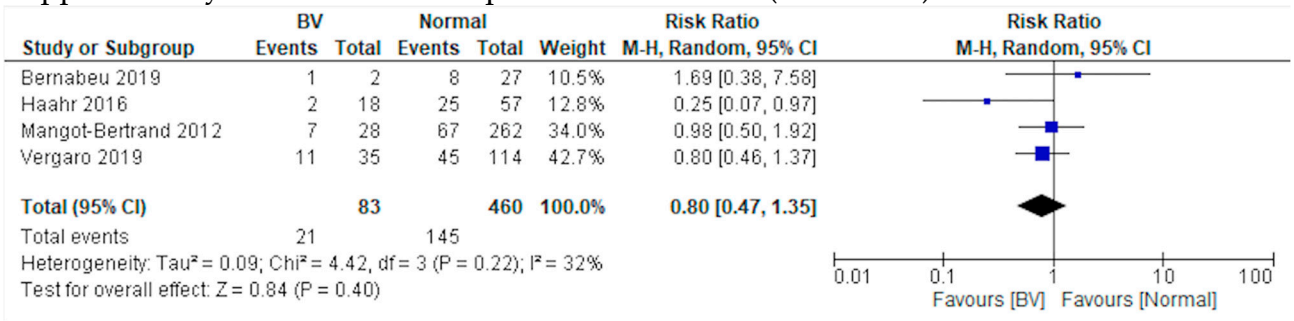
| | | Chance of getting pregnant | | No. Participants | |
|---|---|---|---|---|---|
| **Studies** | **Analysis method** | **AVM** | **NVM** | **AVM** | **NVM** |
| Haahr et al. | Nugent score | 2 | 36 | 12 | 72 |
| Selim et al. | Nugent score | 9 | 21 | 26 | 45 |
| Eckert et al. | Nugent score | 3 | 38 | 10 | 81 |
| Gaudoin et al. | Nugent score | 10 | 72 | 40 | 206 |
| Boomsma et al. | Nugent score | 8 | 59 | 17 | 180 |
| Eldivan et al. | Nugent score | 4 | 12 | 17 | 28 |
| Moini et al. | Nugent score | 15 | 123 | 25 | 311 |
| Moore et al. | Nugent score | 2 | 25 | 10 | 81 |
| Ralph et al. | Nugent score | 61 | 176 | 190 | 581 |
| Spandorfer et al. | Nugent score | 10 | 175 | 14 | 317 |
| Moragianni et al. | Nugent score | 10 | 22 | 41 | 70 |
| **Total** | | **134** | **759** | **402** | **1972** |

Table legend: AVM=Abnormal vaginal microbiota, NVM=Normal vaginal microbiota

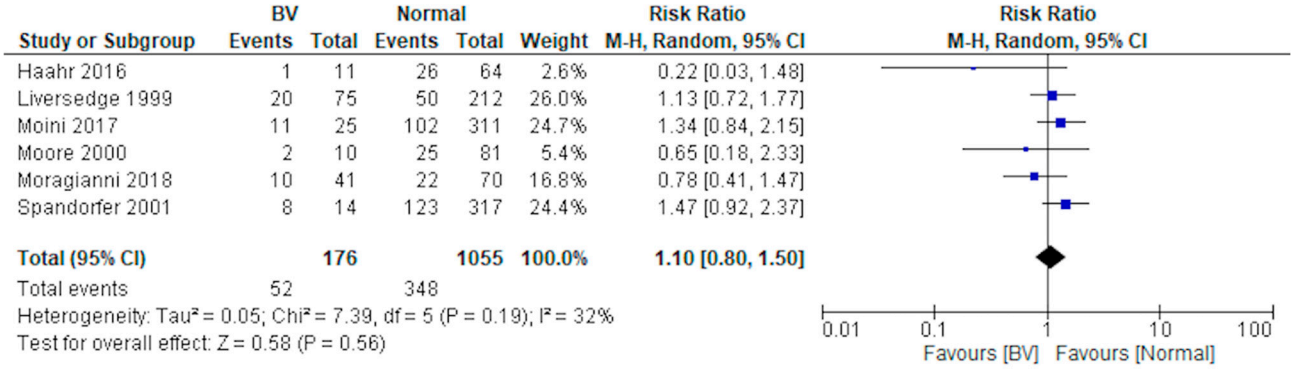
Supplementary Material 8. Forest plot. Live birth rate (Total)



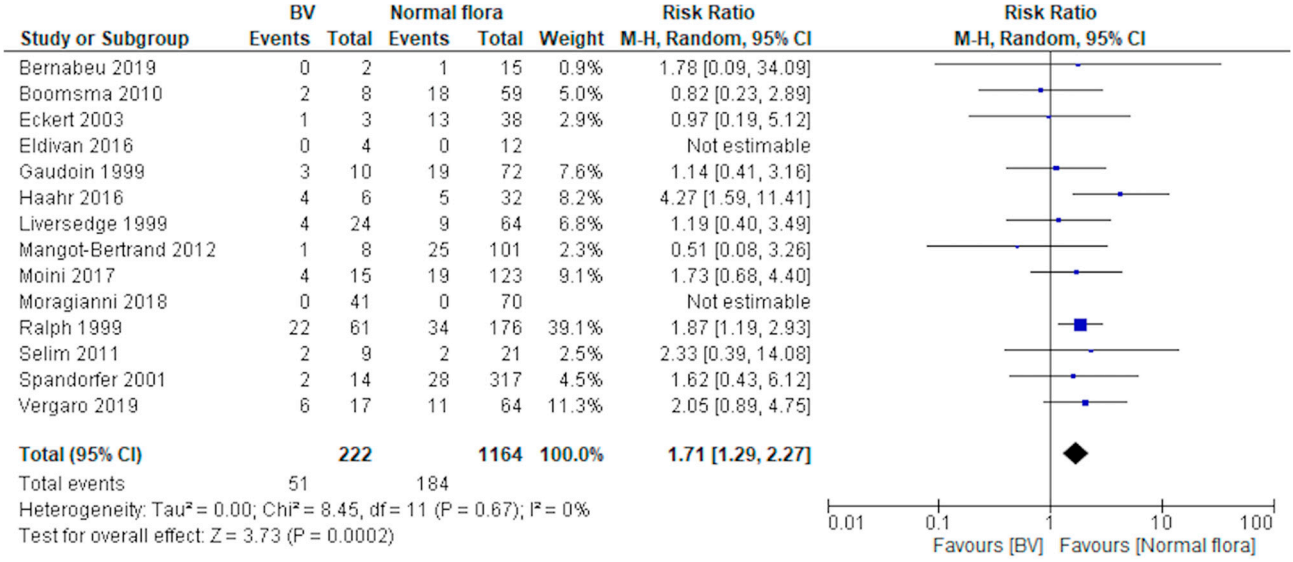

Supplementary Material 8. Forest plot. Live birth rate (Molecular)



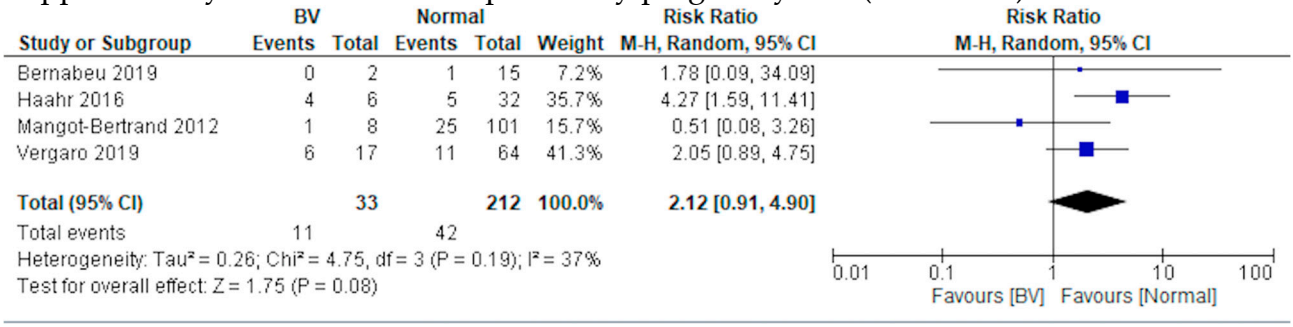

Supplementary Material 8. Forest plot. Live birth rate (Microscopy)



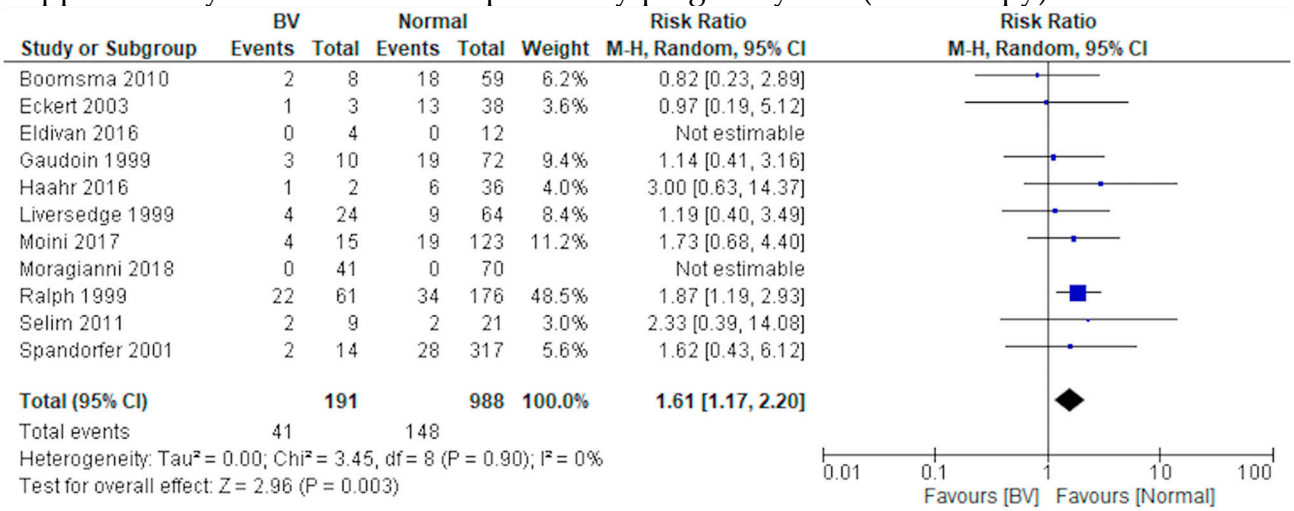
Supplementary Material 9. Forest plot. Early pregnancy loss (Total)




Supplementary Material 9. Forest plot. Early pregnancy loss (Molecular)



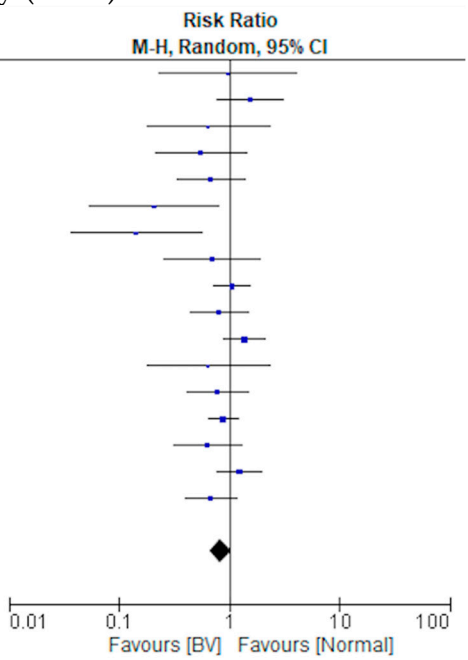

Supplementary Material 9. Forest plot. Early pregnancy loss (Microscopy)



Supplementary Material 10. Forest plot. Clinical pregnancy (Total)

| Study or Subgroup | BV Events | BV Total | Normal Events | Normal Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Bernabeu 2019 | 1 | 2 | 15 | 29 | 2.0% | 0.97 [0.23, 4.04] |
| Boomsma 2010 | 6 | 17 | 41 | 180 | 6.0% | 1.55 [0.77, 3.11] |
| Eckert 2003 | 2 | 10 | 25 | 81 | 2.4% | 0.65 [0.18, 2.33] |
| Eldivan 2016 | 4 | 17 | 12 | 28 | 3.8% | 0.55 [0.21, 1.43] |
| Gaudoin 1999 | 7 | 40 | 53 | 206 | 5.8% | 0.68 [0.33, 1.39] |
| Haahr 2016 | 2 | 22 | 27 | 62 | 2.2% | 0.21 [0.05, 0.81] |
| Koedooder 2019 | 2 | 34 | 65 | 158 | 2.1% | 0.14 [0.04, 0.56] |
| Kyono 2018 | 5 | 35 | 9 | 44 | 3.6% | 0.70 [0.26, 1.90] |
| Liversedge 1999 | 24 | 75 | 64 | 212 | 10.7% | 1.06 [0.72, 1.56] |
| Mangot-Bertrand 2012 | 8 | 28 | 92 | 262 | 7.1% | 0.81 [0.44, 1.50] |
| Moini 2017 | 12 | 25 | 108 | 311 | 9.8% | 1.38 [0.89, 2.14] |
| Moore 2000 | 2 | 10 | 25 | 81 | 2.4% | 0.65 [0.18, 2.33] |
| Moragianni 2018 | 10 | 41 | 22 | 70 | 6.7% | 0.78 [0.41, 1.47] |
| Ralph 1999 | 41 | 190 | 122 | 493 | 12.3% | 0.87 [0.64, 1.19] |
| Selim 2011 | 7 | 26 | 19 | 45 | 5.7% | 0.64 [0.31, 1.31] |
| Spandorfer 2001 | 8 | 14 | 147 | 317 | 9.2% | 1.23 [0.77, 1.97] |
| Vergaro 2019 | 11 | 35 | 53 | 115 | 8.2% | 0.68 [0.40, 1.16] |
| **Total (95% CI)** | | **621** | | **2694** | **100.0%** | **0.84 [0.68, 1.04]** |
| Total events | 152 | | 899 | | | |

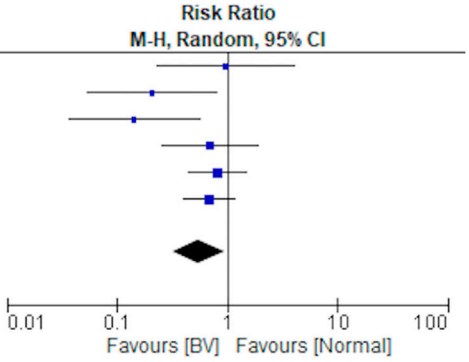
Heterogeneity: Tau² = 0.07; Chi² = 27.24, df = 16 (P = 0.04); I² = 41%
Test for overall effect: Z = 1.63 (P = 0.10)




Supplementary Material 10. Forest plot. Clinical pregnancy (Molecular)

| Study or Subgroup | BV Events | BV Total | Normal Events | Normal Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Bernabeu 2019 | 1 | 2 | 15 | 29 | 10.1% | 0.97 [0.23, 4.04] |
| Haahr 2016 | 2 | 22 | 27 | 62 | 10.9% | 0.21 [0.05, 0.81] |
| Koedooder 2019 | 2 | 34 | 65 | 158 | 10.8% | 0.14 [0.04, 0.56] |
| Kyono 2018 | 5 | 35 | 9 | 44 | 16.0% | 0.70 [0.26, 1.90] |
| Mangot-Bertrand 2012 | 8 | 28 | 92 | 262 | 25.0% | 0.81 [0.44, 1.50] |
| Vergaro 2019 | 11 | 35 | 53 | 115 | 27.2% | 0.68 [0.40, 1.16] |
| **Total (95% CI)** | | **156** | | **670** | **100.0%** | **0.55 [0.32, 0.93]** |
| Total events | 29 | | 261 | | | |

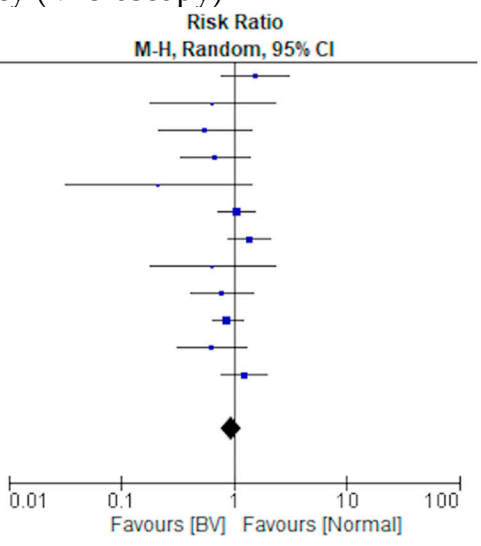
Heterogeneity: Tau² = 0.20; Chi² = 9.84, df = 5 (P = 0.08); I² = 49%
Test for overall effect: Z = 2.21 (P = 0.03)



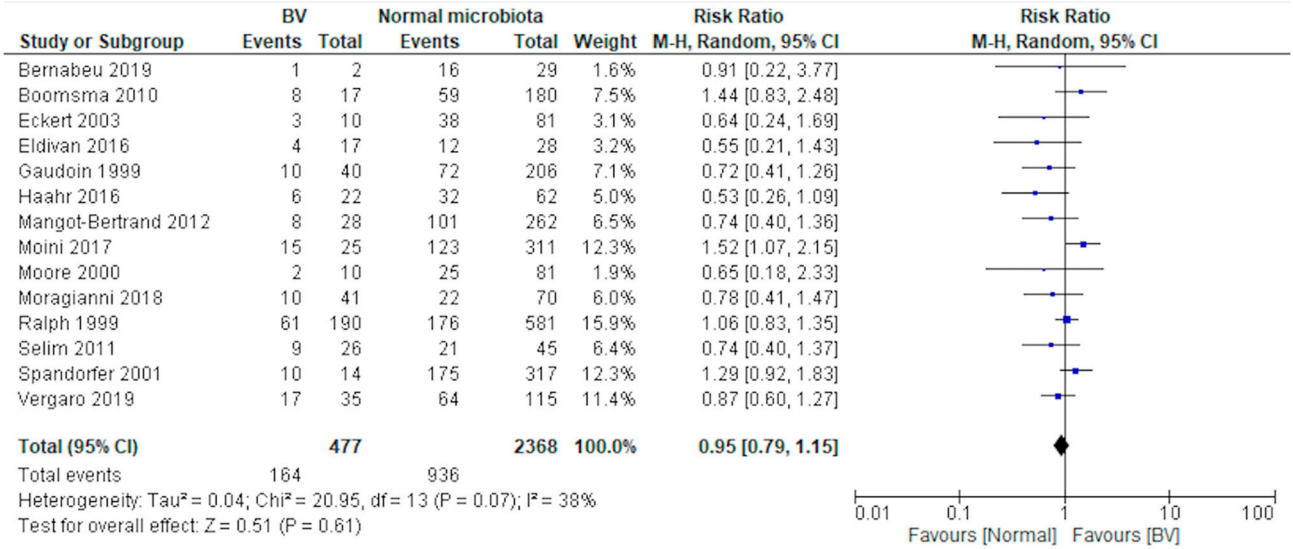

Supplementary Material 10. Forest plot. Clinical pregnancy (Microscopy)

| Study or Subgroup | BV Events | BV Total | Normal Events | Normal Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Boomsma 2010 | 6 | 17 | 41 | 180 | 6.8% | 1.55 [0.77, 3.11] |
| Eckert 2003 | 2 | 10 | 25 | 81 | 2.3% | 0.65 [0.18, 2.33] |
| Eldivan 2016 | 4 | 17 | 12 | 28 | 3.9% | 0.55 [0.21, 1.43] |
| Gaudoin 1999 | 7 | 40 | 53 | 206 | 6.5% | 0.68 [0.33, 1.39] |
| Haahr 2016 | 1 | 12 | 28 | 72 | 1.1% | 0.21 [0.03, 1.43] |
| Liversedge 1999 | 24 | 75 | 64 | 212 | 16.1% | 1.06 [0.72, 1.56] |
| Moini 2017 | 12 | 25 | 108 | 311 | 13.9% | 1.38 [0.89, 2.14] |
| Moore 2000 | 2 | 10 | 25 | 81 | 2.3% | 0.65 [0.18, 2.33] |
| Moragianni 2018 | 10 | 41 | 22 | 70 | 7.8% | 0.78 [0.41, 1.47] |
| Ralph 1999 | 41 | 190 | 122 | 493 | 20.5% | 0.87 [0.64, 1.19] |
| Selim 2011 | 7 | 26 | 19 | 45 | 6.4% | 0.64 [0.31, 1.31] |
| Spandorfer 2001 | 8 | 14 | 147 | 317 | 12.5% | 1.23 [0.77, 1.97] |
| **Total (95% CI)** | | **477** | | **2096** | **100.0%** | **0.95 [0.78, 1.16]** |
| Total events | 124 | | 666 | | | |

Heterogeneity: Tau² = 0.02; Chi² = 14.02, df = 11 (P = 0.23); I² = 22%
Test for overall effect: Z = 0.51 (P = 0.61)

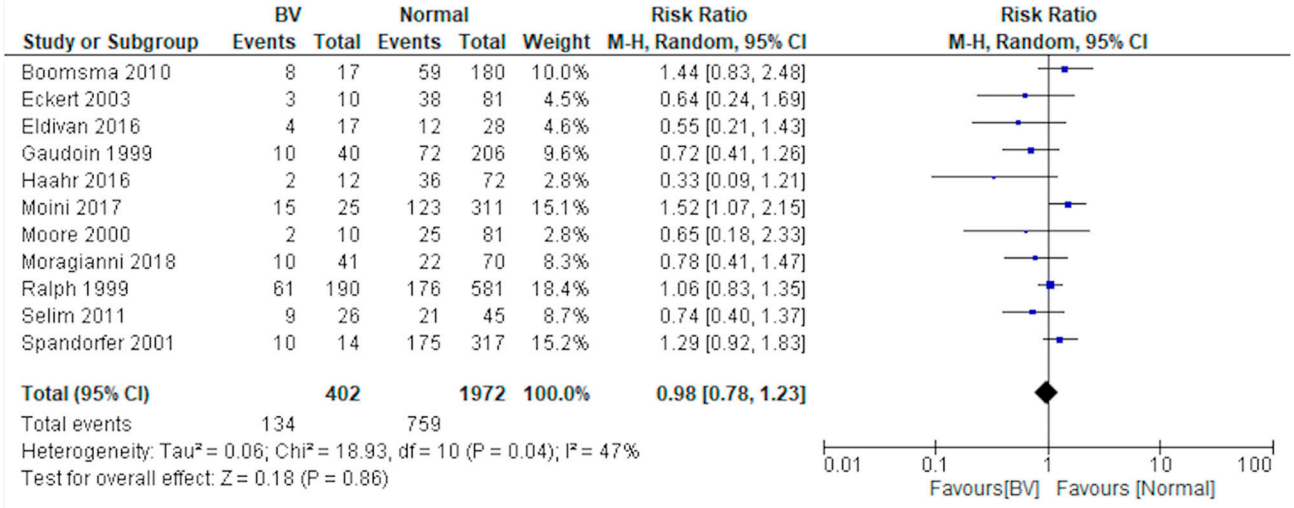


Supplementary Material 11. Forest plot. Biochemical pregnancy (Total)



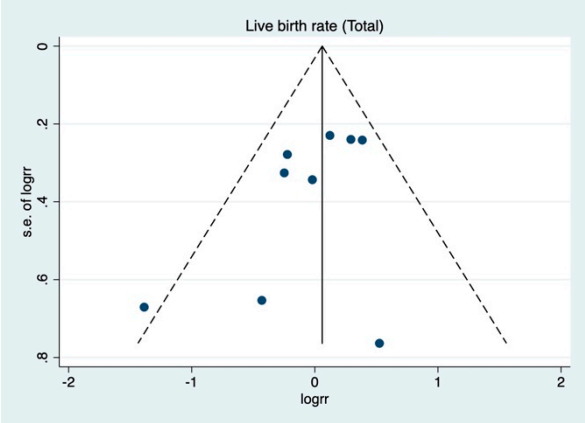

Supplementary Material 11. Forest plot. Biochemical pregnancy (Molecular)


Supplementary Material 11. Forest plot. Biochemical pregnancy (Microscopy)

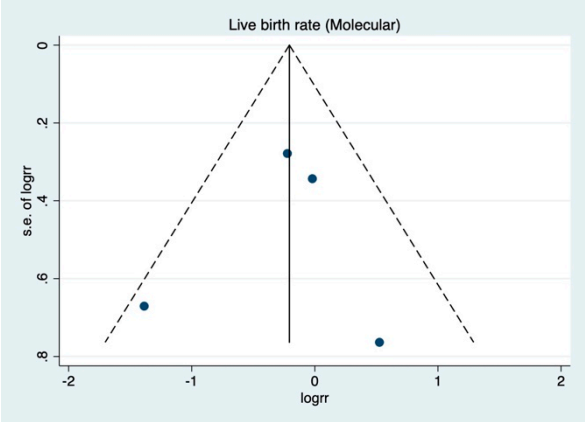


Supplementary Material 12. Funnel plot.

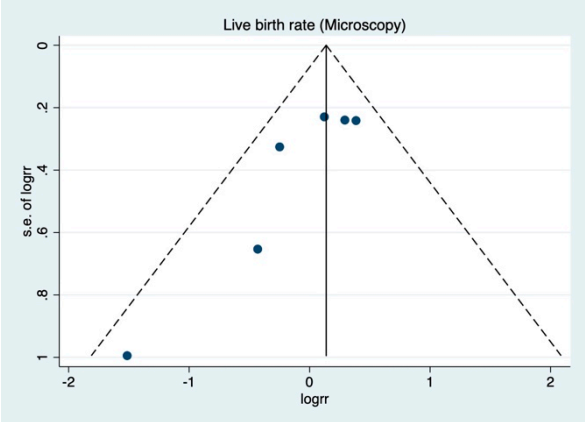
Live birth rate




*Funnel plot. Live birth rate (Total).*
Egger's test: Bias coef. -1.6 (95%CI -3.8-0.6), P=0.135.

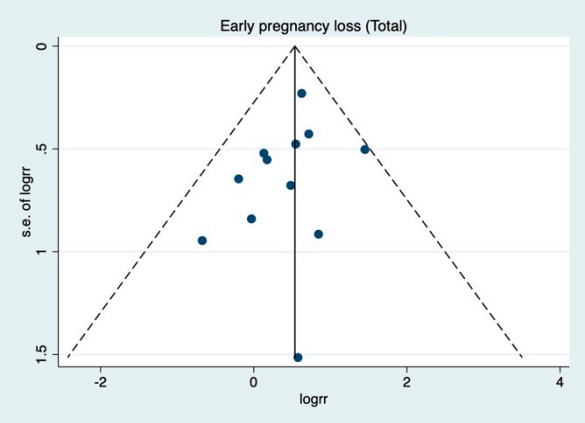



*Funnel plot. Live birth rate (Molecular).*
Egger's test: Bias coef. -0.5 (95%CI -8.7-7.6), P=0.799

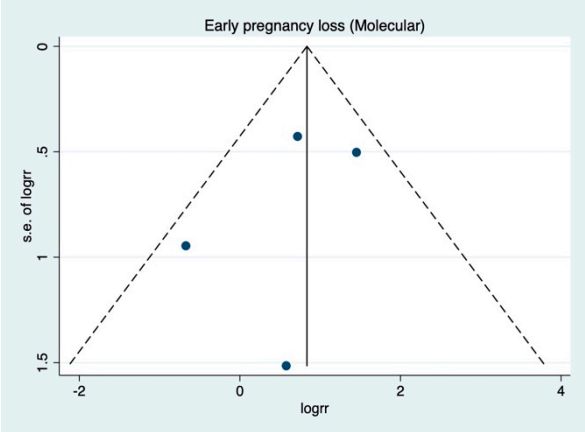



*Funnel plot. Live birth rate (Microscopy).*
Egger's test: Bias coef. -2.2 (95%CI -4.1- -0.3), P=0.031

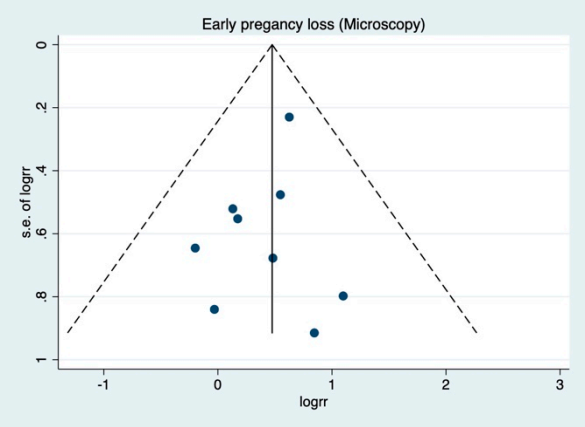
Early pregnancy loss.




*Funnel plot. Early pregnancy loss (Total).*
Egger's test: Bias coef. -0.66 (95%CI -1.9-0.6), P=0.254

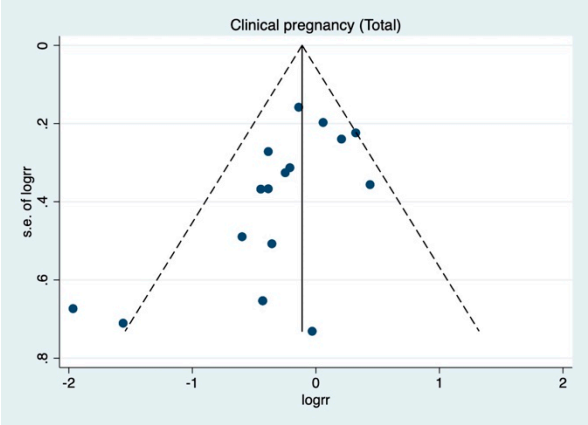



*Funnel plot. Early pregnancy loss (Molecular).*
Egger's test: Bias coef. -1.2 (95%CI -7.8-5.4), P=0.514

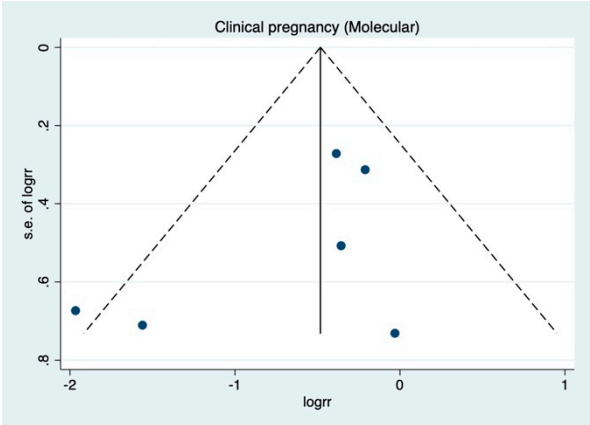



*Funnel plot. Early pregnancy loss (Microscopy).*
Egger's test: Bias coef. -0.5 (95%CI -1.6-0.7), P=0.366

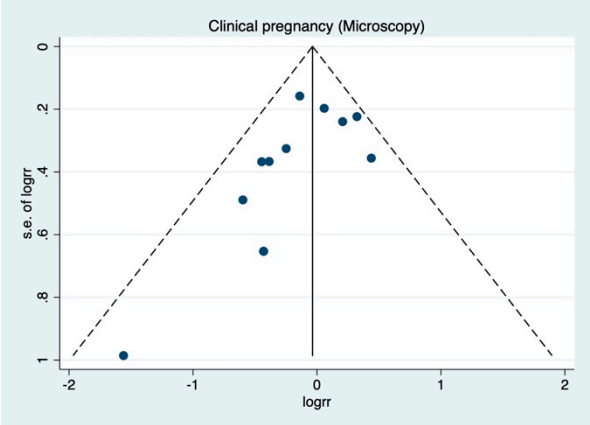
Clinical pregnancy.




*Funnel plot. Clinical pregnancy (Total).*
Egger's test: Bias coef. -1.6 (95%CI -2.9- -0.3), P=0.017

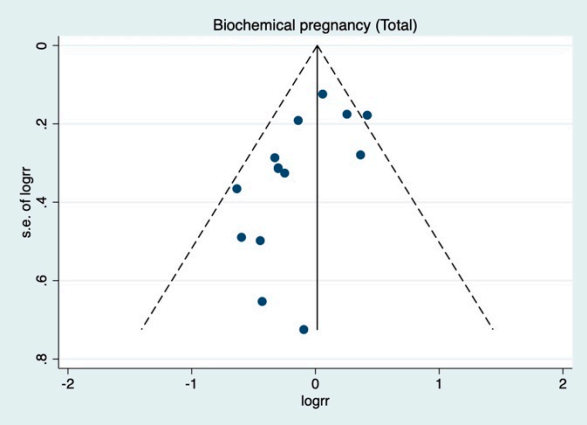



*Funnel plot. Clinical pregnancy (Molecular).*
*Egger's test: Bias coef. -1.8 (95%CI -5,2-1.6), P=0.217*

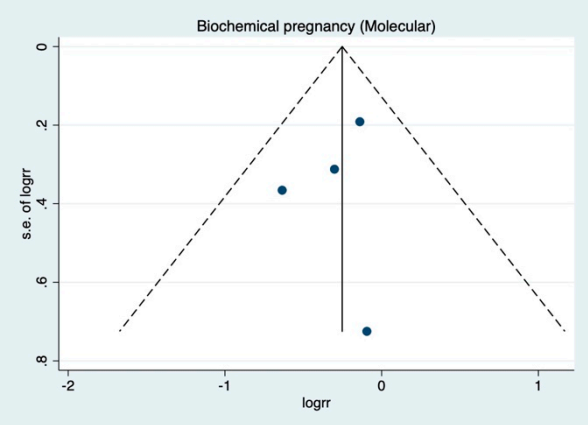



*Funnel plot. Clinical pregnancy (Microscopy).*
*Egger's test: Bias coef. -1.2 (95%CI -2.7-0.2), P=0.083*

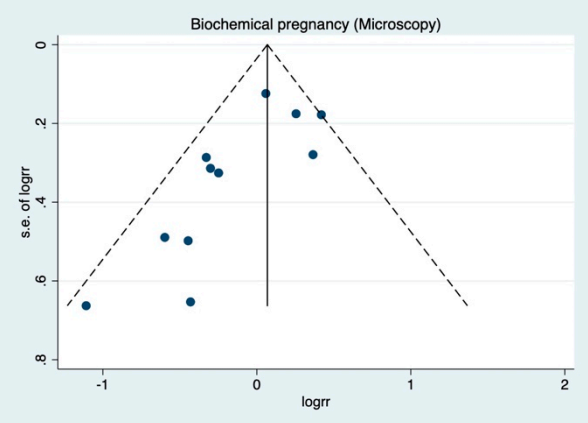
Biochemical pregnancy.




*Funnel plot. Biochemical pregnancy (Total).*
*Egger's test: Bias coef. -1.6 (95%CI -2.9- -0.2), P=0.026*




*Funnel plot. Biochemical pregnancy (Molecular).*
*Egger's test: Bias coef. -0.6 (95%CI -4.9-3.6), P=0.596*




*Funnel plot. Clinical pregnancy (Microscopy).*
*Egger's test: Bias coef. -1.8 (95%CI -3.2- -0.3), P=0.021*

Supplementary Material 13. Moose guidelines and PRISMA Guideline.

MOOSE guideline

| Reporting Criteria | Reported | Page number |
|---|---|---|
| **Reporting of Background** | | |
| Problem definition | Yes | 1+2 |
| Hypothesis statement | Yes | 1+2 |
| Description of Study Outcome(s) | Yes | 10 |
| Type of exposure or intervention used | Yes | 10 |
| Type of study design used | Yes | 11 |
| Study population | Yes | 11 |
| **Reporting of Search Strategy** | | |
| Qualifications of searchers (eg, librarians and investigators) | Yes | 11 |
| Search strategy, including time period included in the synthesis and keywords | Yes | 11 |
| Effort to include all available studies, including contact with authors | Yes | 11 |
| Databases and registries searched | Yes | 11 |
| Search software used, name and version, including special features used (eg, explosion) | Yes | 12 |
| Use of hand searching (eg, reference lists of obtained articles) | No | |
| List of citations located and those excluded, including justification | Yes | 2+11 |
| Method for addressing articles published in languages other than English | No | |
| Method of handling abstracts and unpublished studies | Yes | 11 |
| Description of any contact with authors | Yes | 11 |
| **Reporting of Methods** | | |
| Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested | Yes | 11 |
| Rationale for the selection and coding of data (eg, sound clinical principles or convenience) | Yes | 11 |
| Documentation of how data were classified and coded (eg, multiple raters, blinding, and interrater reliability) | Yes | 11 |
| Assessment of confounding (eg, comparability of cases and controls in studies where appropriate | Yes | 11 |
| Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results | Yes | 11 |
| Assessment of heterogeneity | Yes | 12 |
| Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated | Yes | 12 |
| Provision of appropriate tables and graphics | No | |
| **Reporting of Results** | | |
| Table giving descriptive information for each study included | Yes | 5 |
| Results of sensitivity testing (eg, subgroup analysis) | Yes | 7 + Supplementary Material |
| Indication of statistical uncertainty of findings | Yes | 4+7 |
| **Reporting of Discussion** | | |
| Quantitative assessment of bias (eg, publication bias) | Yes | 8 |
| Justification for exclusion (eg, exclusion of non–English-language citations) | No | |

| | | |
|---|---|---|
| Assessment of quality of included studies | Yes | 8 |
| **Reporting of Conclusions** | | |
| Consideration of alternative explanations for observed results | Yes | 12 |
| Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review) | Yes | 12 |
| Guidelines for future research | Yes | 12 |
| Disclosure of funding source | Yes | 13 |

## PRISMA Guideline

| Section/Topic | # | CHECKLIST ITEM | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 1 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 2 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 2 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 10 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 11 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 11 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 11 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 11 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 11 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 11 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 11+12 |

| | | | |
|---|---|---|---|
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 12 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | 12 |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 12 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | 12 |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 2 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 4 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 4+7+8 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 7 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 4+7+8 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | 7 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | 4+7+8 |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 8 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 8+9 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 9+10 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 13 |

Supplementary Material 14. GRADE. Quality of evidence.

| Outcome | No of studies | Design | Risk of Bias | Inconsistency | Indirectness | Imprecision | Risk of publication bias |
|---|---|---|---|---|---|---|---|
| **Live birth rate (Total)** | 9 | Observation studies | High | $I^2$=28%. The inconsistency was low. | Although all patients were treated with IVF, the indirectness was affected as the populations were different in many ways including origin of country and IVF cycle of sampling. | Imprecision moderate due to a confidence interval that included potential for important harm or benefit. | Risk of publication bias was low according to Egger's test (P=0.135). See Supplementary Material 12. |
| **Live birth rate (Molecular)** | 4 | Observation studies | High | $I^2$=32%. The inconsistency was low. | Although all patients were treated with IVF, the indirectness was affected as the populations were different in many ways including origin of country and IVF cycle of sampling. | Imprecision high due to a confidence interval that included potential for important harm or benefit. Also, small sample size. | As only four studies are included in the Funnel Plot, the power of tests is too low to evaluate the risk of publication bias. See Supplementary Material 12. |
| **Live birth rate (Microscopy)** | Quality of evidence: Very low. Assessment can be found in our previous study see the Material and Methods section in the Article. The addition of Moragianni et al. did no change the level of evidence. | | | | | | |
| **Early pregnancy loss (Total)** | 14 | Observation studies | High | $I^2$=0%. The inconsistency was low. | Although all patients were treated with IVF, the indirectness was affected as the populations were different in many ways including origin of country and IVF cycle of sampling. | Imprecision low. | Risk of publication bias was low according to Egger's test (P=0.254) See Supplementary Material 12. |
| **Early pregnancy loss (Molecular)** | 4 | Observation studies | High | $I^2$=37%. The inconsistency was low. | Although all patients were treated with IVF, the indirectness was affected as the populations were different in many ways including origin of country and IVF cycle of sampling. | Imprecision high due to a wide CI interval that included potential for important harm or benefit. Also, small sample size. | As only four studies are included in the Funnel Plot, the power of tests is too low to evaluate the risk of publication bias. See Supplementary Material 12. |
| **Early pregnancy loss (Microscopy)** | Quality of evidence: Very low. Assessment can be found in our previous study see the Material and Methods section in the Article. The addition of Moragianni et al. did no change the level of evidence. | | | | | | |
| **Clinical pregnancy (Total)** | 17 | Observation studies | High | $I^2$=41%. The inconsistency was moderate. | Although all patients were treated with IVF, the indirectness was affected as the populations were different in many ways including origin of country and IVF cycle of sampling. | Imprecision moderate due to a confidence interval that included potential for important harm or benefit. | Risk of publication bias high according to Egger's test (P=0.017). See Supplementary Material 12. |
| **Clinical Pregnancy (Molecular)** | 6 | Observation studies | High | $I^2$=49%. The inconsistency was moderate. | Although all patients were treated with IVF, the indirectness was affected as the populations were different in many ways including origin of country and IVF cycle of sampling. | Imprecision low | As only six studies are included in the Funnel Plot, the power of tests is too low to evaluate the risk of publication bias. See Supplementary Material 12. |
| **Clinical Pregnancy (Microscopy)** | Quality of evidence: Very low. Assessment can be found in our previous study see the Material and Methods section in the Article. The addition of Moragianni et al. did no change the level of evidence. | | | | | | |
| **Biochemical pregnancy (Total)** | 14 | Observation studies | High | $I^2$=38%. The inconsistency was low. | Although all patients were treated with IVF, the indirectness was affected as the populations were different in many ways including origin of country and IVF cycle of sampling. | Imprecision moderate due to a confidence interval that included potential for important harm or benefit. | Risk of publication bias high according to Egger's test (P=0.026). See Supplementary Material 12. |
| **Biochemical pregnancy (Molecular)** | 4 | Observation studies | High | $I^2$=0%. The inconsist | Although all patients were treated with IVF, the indirectness was affected as the populations were different | Imprecision high due to a wide CI interval that included potential | As only four studies are included in the Funnel Plot, the power of tests is too low to evaluate the risk of |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | ency was low. | in many ways including origin of country and IVF cycle of sampling. | for important harm or benefit. Also, small sample size. | publication bias. See Supplementary Material 12. |
| **Biochemical pregnancy (Microscopy)** | Quality of evidence: Very low. Assessment can be found in our previous study see the Material and Methods section in the Article. The addition of Moragianni et al. did no change the level of evidence. | | | | | | |