National Institute for Health and Care Excellence

Draft for consultation

Fertility problems: assessment and treatment

[C] Screening hysteroscopy

NICE guideline NGXXX

Evidence reviews underpinning recommendation 1.10.4 in the NICE guideline

September 2025

Draft for consultation

This evidence review was developed by NICE

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ISBN:

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Screening hysteroscopy

Review question

What is the effectiveness of screening hysteroscopy (with or without treatment of any detected uterine cavity abnormalities) on reproductive outcomes for people with female factor fertility problems?

Introduction

Hysteroscopy can be used to diagnose and to treat intrauterine pathologies. These may be relevant to those people who have infertility related issues and require fertility treatment such as in vitro fertilisation (IVF). The current evidence on the routine use of hysteroscopy as a screening tool in people with female factor fertility problems is not clear. Therefore, the aim of this review is to determine if screening hysteroscopy has a beneficial effect on reproductive outcomes.

Summary of the protocol

See Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	Inclusion: • People undergoing screening hysteroscopy (where routine imaging did not show uterine cavity abnormalities), as an evaluation for unexplained infertility or prior to fertility treatment for a health-related fertility problem In this guideline, people with health-related fertility problems are those who have a known health-related impediment to fertility, or those who do not achieve a pregnancy: • after 12 months of regular unprotected sexual intercourse or • after 6 cycles of artificial insemination Exclusion: • People in whom routine imaging showed suspected uterine cavity abnormalities and hysteroscopy was for the purpose of treating these abnormalities (for example, hysteroscopic removal of endometrial polyps, submucous fibroids, uterine septum, or intrauterine adhesions)
Intervention	A screening hysteroscopy (with or without treatment of any detected uterine cavity abnormalities)
Comparison	No hysteroscopy

Outcome	Critical • Live birth (as defined by study, risk of bias assessments will reflect where this is not defined as a live birth to include a gestational age of ≥ 20 weeks) • Clinical pregnancy (as defined by study, risk of bias assessments will reflect where this is not defined as an ultrasound scan that has shown at least one fetal heart rate) Important • Miscarriage (loss of a baby before 24 weeks gestational age) • Any perioperative adverse event (including perforation, infection, and vasovagal attacks) • Pregnancy loss (including miscarriage, ectopic pregnancy, stillbirth, and termination of pregnancy)

For further details see the review protocol in appendix A.

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document (supplementary document 1).

Declarations of interest were recorded according to NICE's conflicts of interest policy.

Effectiveness evidence

Included studies

Twelve randomised controlled trials (RCTs) were included for this review (Aghahosseini 2012, Alleyassin 2017, Ben Abid 2021, Demirol 2004, El-Nashar 2011, Elsetohy 2015, El-Toukhy 2016, Moramezi 2012, Pounikar 2023, Rama Raju 2006, Shawki 2012 and Smit 2016). Two of the studies were published as abstracts only (Aghahosseini 2012 and El-Nashar 2011) and were included in this review as the data could be extracted and risk of bias assessed from the Kamath 2019 Cochrane Review.

All studies compared hysteroscopy to no hysteroscopy in people undergoing screening hysteroscopy prior to in vitro fertilisation (IVF) or intrauterine insemination (IUI).

The included studies are summarised in Table 2.

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies not included in this review are listed, and reasons for their exclusion are provided in appendix J.

Summary of included studies

Summaries of the studies that were included in this review are presented in Table 2.

Table 2: Summary of included studies

Study	Population	Intervention	Comparison	Outcomes	Comments
Aghahosseini 2012	N=353 Women aged <38	Hysteroscopy	No hysteroscopy	• Live birth • Clinical	Participants had ≥ 2

Study	Population	Intervention	Comparison	Outcomes	Comments
RCT (abstract only) Iran	years with normal hysterosalpingogram and no history of hysteroscopy in the last 2 months Mean age (SD) NR Interval between hysteroscopy and ICSI: NR	Hysteroscopy prior to ICSI	ICSI without hysteroscopy	pregnancy	implantation failures
Alleyassin 2017 RCT Iran	N=220 Women with normal uterine cavity appearances on vaginal ultrasonography and hysterosalpingography Mean age (SD) per group; hysteroscopy: 29.55 (3.85) years; no hysteroscopy: 29.14 (4.34) years Interval between hysteroscopy and ICSI: NR	Hysteroscopy Hysteroscopy prior to ICSI	No hysteroscopy ICSI without hysteroscopy	• Clinical pregnancy • Miscarriage	All participants were undergoing their first ICSI cycle 23% who underwent hysteroscopy had abnormal hysteroscopic findings that were treated in the same setting
Ben Abid 2021 RCT Tunisia	N=171 Infertile women <40 years old with normal uterine cavity shown by transvaginal ultrasound and HSG Mean age (SD) per group; hysteroscopy: 32.33 (4.38) years; no hysteroscopy: 33.32 (5.08) years Interval between hysteroscopy and IVF: IVF started in the cycle after hysteroscopy if hysteroscopy normal (not clear if abnormalities detected)	Hysteroscopy Hysteroscopy prior to IVF	No hysteroscopy IVF without hysteroscopy	• Clinical pregnancy • Live birth • Miscarriage	Participants scheduled for their first IVF 26/84 (31%) of those analysed in the hysteroscopy group had abnormalities, and 9 abnormalities were treated using operative hysteroscopy in a subsequent session
Demirol 2004 RCT Turkey	N=421 Participants aged 24-40 years with normal HSG Mean age (SD) per group; hysteroscopy:	Hysteroscopy Hysteroscopy prior to IVF	No hysteroscopy IVF without hysteroscopy	• Clinical pregnancy • Miscarriage	Participants had undergone ≥2 failed IVF cycles 27% of those

Study	Population	Intervention	Comparison	Outcomes	Comments
	35.6 (6.4) years; no hysteroscopy: 34.3 (11.6) years Interval between hysteroscopy and IVF: IVF was carried out on the menstrual cycle following hysteroscopy				who received hysteroscopy had intrauterine abnormalities diagnosed and treated during the office hysteroscopy
El-Nashar 2011 RCT (abstract only) Egypt	N=124 Women with primary infertility Mean age (SD) NR Interval between hysteroscopy and ICSI: NR	Hysteroscopy Hysteroscopy prior to ICSI	No hysteroscopy ICSI without hysteroscopy	• Clinical pregnancy	Participants were scheduled for ICSI Previous implantation failure NR
El-Toukhy 2016 RCT UK, Belgium, Italy, and the Czech Republic	N=702 Women <38 years who had a normal transvaginal ultrasound of the uterine cavity Mean age (SD) per group; hysteroscopy: 32.7 (3.1) years; no hysteroscopy: 32.7 (3.1) years Interval between hysteroscopy and IVF: 1 month	Hysteroscopy Hysteroscopy prior to IVF	No hysteroscopy IVF without hysteroscopy	• Live birth • Clinical pregnancy • Miscarriage	Participants had undergone 2-4 previous IVF treatment cycles 34/323 (11%) who received hysteroscopy had uterine abnormalities detected, and 15 were treated surgically
Elsetohy 2015 RCT Egypt	N=203 Women with primary or secondary infertility and normal transvaginal ultrasound (apart from intramural myomas without uterine cavity deformity) Mean age (SD) per group; hysteroscopy: 31.1 (5.8) years; no hysteroscopy: 29.9 (4.8) years Interval between hysteroscopy and ICSI: within 3 months	Hysteroscopy Hysteroscopy prior to ICSI	No hysteroscopy ICSI without hysteroscopy	• Live birth • Clinical pregnancy	Participants scheduled for their first IVF/ICSI treatment cycle 43% showed abnormal hysteroscopic findings that were treated in the same or a subsequent session
Moramezi 2012	N=110 Couples diagnosed with infertility who	Hysteroscopy Hysteroscopy	No hysteroscopy IUI without	• Clinical pregnancy • Miscarriage	Previous implantation failure NR

Study	Population	Intervention	Comparison	Outcomes	Comments
RCT Iran	were candidates for IUI and did not have a sexually transmitted disease, pelvic inflammatory disease, or pregnancy Mean age (SD) per group; hysteroscopy: 28.8 (3) years; no hysteroscopy: 29.8 (3) years Interval between hysteroscopy and IUI: If hysteroscopy normal IUI performed in the next cycle, if abnormalities detected IUI performed after 2-3 cycles	prior to IUI	hysteroscopy	• Any perioperative adverse event	47% of those receiving hysteroscopy had abnormalities identified and treated (not clear if treatment was performed in the same or a subsequent session)
Pounikar 2023 RCT India	N=180 Women <45 years old with primary or secondary infertility and normal uterine findings on transvaginal USG or HSG Mean age (SD) per group; hysteroscopy: 32.9 (1.97) years; no hysteroscopy: 33.57 (3.21) years Interval between hysteroscopy and IVF: IVF performed in the next cycle following hysteroscopy	Hysteroscopy Hysteroscopy prior to IVF	No hysteroscopy IVF without hysteroscopy	• Clinical pregnancy	Participants had undergone ≥1 embryo implantation failures in previous IVF cycles 40% of those receiving hysteroscopy had intrauterine abnormalities detected and treated (in the same session)
Rama Raju 2006 RCT India	N=520 Participants with primary infertility and normal uterine cavity on hysterosalpingography Mean age (SD) per group; hysteroscopy: between 27.4 (0.60) and 29.04 (0.92) years; no hysteroscopy: 26.72 (0.46) years Interval between	Hysteroscopy Hysteroscopy prior to IVF	No hysteroscopy IVF without hysteroscopy	• Live birth • Clinical pregnancy • Miscarriage	Participants had undergone ≥2 failed IVF cycles 37% of those receiving hysteroscopy had uterine cavity abnormalities identified and treated (during the same session)

Study	Population	Intervention	Comparison	Outcomes	Comments
	hysteroscopy and IVF: NR				
Shawki 2012 RCT Egypt	N=240 women with normal HSG and/or TVUS who had HSG in the past 2–3 months Mean age (SD) per group; hysteroscopy: 33 (11.14) years; no hysteroscopy: 31 (12.32) years Interval between hysteroscopy and ICSI: Not reported	Hysteroscopy Hysteroscopy prior to ICSI	No hysteroscopy ICSI without hysteroscopy	• Clinical pregnancy	46% had at least 1 previous ICSI/IVF failure 33% of participants analysed in the hysteroscopy group had abnormalities detected and treated (not clear if in same or subsequent session)
Smit 2016 RCT Netherlands	N=750 Infertile women with normal transvaginal ultrasound of the uterine cavity Mean age (SD) per group; hysteroscopy: 33 (4.4) years; no hysteroscopy: 33 (4.5) years Interval between hysteroscopy and IVF/ICSI: 1-3 months	Hysteroscopy Hysteroscopy prior to IVF/ICSI	No hysteroscopy IVF/ICSI without hysteroscopy	• Live birth • Clinical pregnancy • Miscarriage • Pregnancy loss	Participants scheduled for their first IVF treatment 10% of participants analysed in the hysteroscopy group had abnormalities detected and treated (in the same session)

HSG: hysterosalpingography; ICSI: intracytoplasmic sperm injection; IUI: intrauterine insemination; IVF: in vitro fertilisation; NR: not reported; RCT: randomised controlled trial; SD: standard deviation; TVUS: transvaginal ultrasound; UK: United Kingdom; USG: ultrasound sonography test

See the full evidence tables in appendix D and the forest plots in appendix E.

Summary of the evidence

Very low quality evidence from 6 randomised controlled trials (RCTs) showed a higher live birth rate in people receiving hysteroscopy relative to no hysteroscopy prior to in vitro fertilisation (IVF) or intrauterine insemination (IUI). However, there was serious heterogeneity in effect estimates across studies for this outcome. Planned subgroup analysis by age was not possible (all studies included mean age of under 35 years or mean age was not reported), and planned subgroup analysis by previous implantation failure did not account for the heterogeneity. Post-hoc subgroup analysis by risk of bias provided a potential explanation for the inconsistency as the test for subgroup differences was statistically significant. Studies with a lower risk of bias (some concerns) rating showed no clinically important difference in live birth rate between hysteroscopy and no hysteroscopy, and the studies with a high risk of bias rating showed a higher live birth rate for those receiving hysteroscopy relative to no hysteroscopy prior to IVF or IUI.

Very low quality evidence from 12 RCTs showed a higher rate of clinical pregnancy for people receiving hysteroscopy relative to no hysteroscopy prior to IVF or IUI. As there were more than 10 studies included in this meta-analysis the funnel plot (relationship between the magnitude of the effect estimate and study size) was examined and asymmetry was indicated raising the possibility of bias associated with small studies and publication bias. As per protocol, a fixed effect meta-analysis was conducted (in addition to the primary random effects analysis). However, no substantial difference in effect estimates between the two meta-analyses was observed. There was serious heterogeneity in effect estimates across studies for clinical pregnancy. As for live birth, planned subgroup analysis by age was not possible (all studies included mean age of under 35 years or mean age was not reported), and planned subgroup analysis by previous implantation failure did not account for the heterogeneity. Consistently to that observed for live birth, post-hoc subgroup analysis by risk of bias provided a potential explanation for the inconsistency as the test for subgroup differences was statistically significant. Studies with a lower risk of bias rating (some concerns) showed no clinically important difference in clinical pregnancy rate between hysteroscopy and no hysteroscopy, and the studies with a high risk of bias rating showed a higher clinical pregnancy rate for those receiving hysteroscopy relative to no hysteroscopy prior to IVF or IUI.

Low quality evidence from 7 RCTs showed no clinically important difference between hysteroscopy and no hysteroscopy prior to IVF or IUI on the rate of miscarriage. Although, low quality evidence from 1 RCT showed a higher rate of pregnancy loss (composite outcome, total pregnancy loss including biochemical and miscarriage) for people receiving hysteroscopy relative to no hysteroscopy prior to IVF or IUI.

Very low quality evidence from 1 RCT showed no clinically important difference between hysteroscopy and no hysteroscopy in the number of participants who experienced any perioperative adverse events.

See appendix F for full GRADE tables.

Economic evidence

A total of 388 studies were identified in the health economic literature search for this review question. After duplicates were removed, a total of 253 studies were screened on title and abstract. Of these 253 studies, one was subsequently included.

Included studies

One economic study was identified which was relevant to this question (Kasius 2013).

See the literature search strategy in appendix B and economic study selection flow chart in appendix G.

Excluded studies

Economic studies not included in this review are listed, and reasons for their exclusion are provided in appendix K.

Summary of included economic evidence

See Table 3 for the economic evidence profile of the included study.

Table 3: Economic evidence profile of a systematic review of economic evaluations of screening hysteroscopy (with or without treatment of any detected uterine cavity abnormalities) on reproductive outcomes for people with female factor fertility problems?

Study	Limitations	Applicability	Other comments	Incremental			Uncertainty
				Costs	Effect	Cost effectiveness	
Kasius 2013	Potentially serious limitations[1,2,3,4]	Partially applicable[5,6]	Study employed a decision-analytic model covering a period of up to 3 IVF cycles	-	i) Routine screening €9,341 per live birth ii) Conditional screening €10,570 per live birth iii) No screening €10,851 per live birth	Routine screening dominates	78% probability that routine screening dominates conditional screening and no screening.

[1] Time horizon not explicitly stated.
[2] No discounting applied and unclear whether this should be considered non-applicable because of the time horizon.
[3] Probabilistic sensitivity analysis is based on uniform distributions suggesting a lack of trial data on which to estimate treatment effectiveness. Authors also note that data is sparse and that trials confirming the effectiveness of hysteroscopy are required.
[4] Costs not reported separately for each strategy.
[5] Setting was the Netherlands and a cost year of 2008 (using 2004 prices adjusted for inflation).
[6] QALYs not used to quantify health benefits.

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation.

Unit costs

Resource	Unit costs	Source
Diagnostic hysteroscopy	£286.41	National Schedule of NHS Costs 2021-22, Outpatient procedure, Currency code MA31Z, Service code 502

The committee's discussion and interpretation of the evidence

The outcomes that matter most

Live birth and clinical pregnancy were prioritised as critical outcomes by the committee. They were selected as the best indicators of fertility and were specified in the core outcome set for fertility research (Duffy 2020).

Miscarriage, any perioperative adverse event, and pregnancy loss were identified as important outcomes by the committee. Miscarriage and pregnancy loss were prioritised as important outcomes as they provide meaningful information about the success of a pregnancy and can have a significant impact on the woman's psychological and physical health. Whilst it was important to include the composite outcome pregnancy loss (including miscarriage, ectopic pregnancy, stillbirth, and termination of pregnancy), the committee felt it was necessary to single out miscarriage due to its importance for clinical decision making. The committee prioritised any perioperative adverse event as an important outcome as it is necessary when discussing and deciding on whether to undertake hysteroscopy that risks are considered and weighed up against potential benefits.

The quality of the evidence

The quality of the evidence was assessed with GRADE and rated as low or very low quality for all outcomes except for the sub-group analyses by risk of bias where the evidence for the 'some concerns' subgroup was rated as moderate quality.

The evidence was downgraded for risk of bias because of lack of information on the randomisation techniques or concealment of the allocation sequence, lack of blinding, unavailability of intention-to-treat analyses for some studies, and unclear risk of selective reporting due to the absence of pre-registered protocols. The evidence was also downgraded for inconsistency (due to serious heterogeneity indicated by I^2 values between 50 and 80%), and for imprecision because of the 95% confidence intervals crossing clinical decision making thresholds.

Benefits and harms

The committee reviewed the evidence and discussed the lack of good quality evidence for the effectiveness of screening hysteroscopy on reproductive outcomes in people with female factor fertility problems. They considered the issue of serious heterogeneity in effect estimates across the studies for live birth and clinical pregnancy rate outcomes which could be explained by the risk of bias. This means that studies with a lower risk of bias rating showed no clinically important difference between hysteroscopy and no hysteroscopy prior to IVF or IUI for these outcomes, whereas studies with a high risk of bias rating showed a higher live birth and clinical pregnancy rate for those receiving hysteroscopy relative to no hysteroscopy. The committee also noted a lack of clinically important difference between hysteroscopy and no hysteroscopy for the majority of the remaining outcomes. Therefore, balancing the uncertainty in the evidence of any benefit against the invasiveness of the procedure, the committee agreed to recommend not offering hysteroscopy as a pre-treatment to improve the outcome of IVF. They wanted to stress that hysteroscopy before IVF may be indicated, for example, when uterine or endometrial abnormality is suspected, but not as means to improve IVF outcomes.

Cost effectiveness and resource use

One economic evaluation was identified for this review question but was only assessed as being partially applicable with potentially serious limitations. The unit cost of diagnostic hysteroscopy was also presented to the committee.

The included study by Kasius 2013 compared Routine Screening (hysteroscopy screening followed by up to 3 cycles of IVF) and Conditional Screening (up to 2 cycles of IVF with no hysteroscopy screening followed by hysteroscopy screening before a 3rd IVF cycle) to No Screening (Up to 3 IVF cycles without hysteroscopy screening). The study by Kasius 2013 found that there was a 78% probability that Routine Screening dominates Conditional Screening and No Screening. However, the committee noted the number of limitations with the study noting that the probabilistic sensitivity analysis was based on uniform distributions – suggesting a lack of trial data on which to estimate treatment effectiveness. In addition, it was discussed that the authors themselves had noted that the data used to inform the study was sparse and that further trials confirming the effectiveness of hysteroscopy are required.

Based on the potentially serious limitations of the health economic study included and the clinical evidence presented to the committee the committee decided to make a do not offer recommendation for hysteroscopy unless a uterine or endometrial abnormality is clinically suspected. This recommendation reflects current practice and so is not anticipated to result in a significant resource impact.

Recommendations supported by this evidence review

This evidence review supports recommendation 1.10.4.

References – included studies

Effectiveness

Aghahosseini 2012

Aghahosseini, M., Ebrahimi, N., Mahdavi, A. et al. (2012) Hysteroscopy prior to assisted reproductive technique in women with recurrent implantation failure improves pregnancy likelihood. Fertility and Sterility 98(3suppl1): 4

Alleyassin 2017

Alleyassin A, Abiri A, Agha-Hosseini M et al. (2017) The Value of Routine Hysteroscopy before the First Intracytoplasmic Sperm Injection Treatment Cycle. Gynecologic and obstetric investigation 82(2): 125-130

Ben Abid 2021

Ben Abid, Haifa, Fekih, Myriam, Fathallah, Khadija et al. (2021) Office hysteroscopy before first in vitro fertilization. A randomized controlled trial. Journal of gynecology obstetrics and human reproduction 50(7): 102109

Demirol 2004

Demirol, Aygul and Gurgan, Timur (2004) Effect of treatment of intrauterine pathologies with office hysteroscopy in patients with recurrent IVF failure. Reproductive biomedicine online 8(5): 590-4

El-Nashar 2011

El-Nashar, IH and Nasr, A (2011) The role of hysteroscopy before intracytoplasmic sperm injection (ICSI): a randomized controlled trial. Fertility and sterility 96(3): 266

El-Toukhy 2016

El-Toukhy, Tarek, Campo, Rudi, Khalaf, Yacoub et al. (2016) Hysteroscopy in recurrent in-vitro fertilisation failure (TROPHY): a multicentre, randomised controlled trial. Lancet (London, England) 387(10038): 2614-2621

Elsetohy 2015

Elsetohy, Khaled Ahmed Abdel Aziz, Askalany, Ahmed H, Hassan, Mohamed et al. (2015) Routine office hysteroscopy prior to ICSI vs. ICSI alone in patients with normal transvaginal ultrasound: a randomized controlled trial. Archives of gynecology and obstetrics 291(1): 193-9

Moramezi 2012

Moramezi, Farideh, Barati, Mojgan, Mohammadjafari, Razieh et al. (2012) Effect of hysteroscopy before intra uterine insemination on fertility in infertile couples. Pakistan journal of biological sciences: PJBS 15(19): 942-6

Pounikar 2023

Pounikar, Minakshi, Shrivastava, Deepti, Sharma, Sapna et al. (2023) Role of Hysteroscopy in Patients with Previous In Vitro Fertilization Failure: An Institutional Experience in Rural Population. Journal of obstetrics and gynaecology of India 73(1): 77-82

Rama Raju 2006

Rama Raju GA, Shashi Kumari G, Krishna KM et al. (2006) Assessment of uterine cavity by hysteroscopy in assisted reproduction programme and its influence on pregnancy outcome. Archives of gynecology and obstetrics 274(3): 160-164

Shawki 2012

Shawki, H.E.; Elmorsy, M.; Eissa, M.K. (2012) Routine office hysteroscopy prior to ICSI and its impact on assisted reproduction program outcome: A randomized controlled trial. Middle East Fertility Society Journal 17: 14-21

Smit 2016

Smit, Janine G, Kasius, Jenneke C, Eijkemans, Marinus J C et al. (2016) Hysteroscopy before in-vitro fertilisation (inSIGHT): a multicentre, randomised controlled trial. Lancet (London, England) 387(10038): 2622-2629

Economic

Kasius 2013

Kasius JC, Eijkemans RJ, Mol BW, Fauser BC, Fatemi HM, Broekmans FJ. (2013) Cost-effectiveness of hysteroscopy screening for infertile women. Reproductive Biomedicine Online 26(6):619-26.

Other

Duffy 2020

Duffy JM, AlAhwany H, Bhattacharya S, Collura B, Curtis C, Evers JL, Farquharson RG, Franik S, Giudice LC, Khalaf Y, Knijnenburg JM. (2020) Developing a core outcome set for future infertility research: an international consensus development study. Human Reproduction 35(12): 2725-34

Kamath 2019

Kamath, Mohan S, Bosteels, Jan, D'Hooghe, Thomas M et al. (2019) Screening hysteroscopy in subfertile women and women undergoing assisted reproduction. The Cochrane database of systematic reviews 4: cd012856

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Appendices

Appendix A Review protocols

Review protocol for review question: What is the effectiveness of screening hysteroscopy (with or without treatment of any detected uterine cavity abnormalities) on reproductive outcomes for people with female factor fertility problems?

Table 4: Review protocol

ID	Field	Content
0.	PROSPERO registration number	CRD42023454994
1.	Review title	Effectiveness of screening hysteroscopy (with or without treatment of any detected uterine cavity abnormalities) on reproductive outcomes for people with female factor fertility problems
2.	Review question	What is the effectiveness of screening hysteroscopy (with or without treatment of any detected uterine cavity abnormalities) on reproductive outcomes for people with female factor fertility problems?
3.	Objective	To determine the effectiveness of screening hysteroscopy (with or without treatment of any detected uterine cavity abnormalities) on reproductive outcomes for people with female factor fertility problems
4.	Searches	The following databases will be searched (with no date restrictions): • Clinical searches • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE ALL • Epistemonikos Searches will be restricted by: • English language

		• Human studies The full search strategies for MEDLINE database will be published in the final review.
5.	Condition or domain being studied	Female factor fertility problems
6.	Population	Inclusion: • People undergoing screening hysteroscopy (where routine imaging did not show uterine cavity abnormalities), as an evaluation for unexplained infertility or prior to fertility treatment for a health-related fertility problem. In this guideline, people with health-related fertility problems are those who have a known health-related impediment to fertility, or those who do not achieve a pregnancy: • after 12 months of regular unprotected sexual intercourse or • after 6 cycles of artificial insemination. Exclusion: • People in whom routine imaging showed suspected uterine cavity abnormalities and hysteroscopy was for the purpose of treating these abnormalities (for example, hysteroscopic removal of endometrial polyps, submucous fibroids, uterine septum or intrauterine adhesions)
7.	Intervention/Exposure/Test	A screening hysteroscopy (with or without treatment of any detected uterine cavity abnormalities)
8.	Comparator/Reference standard/Confounding factors	No hysteroscopy
9.	Types of study to be included	• Systematic reviews of RCTs • RCTs • If no RCTs: Quasi-randomised controlled trials (experimental studies using a non-randomly assigned control group design with match comparison or another method of controlling for confounding variables)
10.	Other exclusion criteria	Other exclusion criteria: • Language limitations: non-English-language papers will be excluded (unless data can be obtained, and risk of bias assessed, from an existing systematic review)

		• Conference abstracts, dissertations and unpublished data will not be included unless the data can be extracted (and risk of bias assessed) from elsewhere (for instance, from an existing systematic review)
11.	Context	This guidance will fully update the following NICE guideline: Fertility problems: assessment and treatment (last updated 2017; CG156)
12.	Primary outcomes (critical outcomes)	• Live birth (as defined by study, risk of bias assessments will reflect where this is not defined as a live birth to include a gestational age of ≥ 20 weeks) • Clinical pregnancy (as defined by study, risk of bias assessments will reflect where this is not defined as an ultrasound scan that has shown at least one fetal heart rate)
13.	Secondary outcomes (important outcomes)	• Miscarriage (loss of a baby before 24 weeks gestational age) • Any perioperative adverse event (including perforation, infection, and vasovagal attacks) • Pregnancy loss (including miscarriage, ectopic pregnancy, stillbirth, and termination of pregnancy)
14.	Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI and de-duplicated. Titles and abstracts of the retrieved citations will be screened to identify studies that potentially meet the inclusion criteria outlined in the review protocol. Dual sifting will be performed on at least 10% of records; 90% agreement is required. Disagreements will be resolved via discussion between reviewers, and consultation with senior staff if necessary. Full versions of the selected studies will be obtained for assessment. Studies that fail to meet the inclusion criteria once the full version has been checked will be excluded at this stage. Each study excluded after checking the full version will be listed, along with the reason for its exclusion. A standardised form will be used to extract data from studies. The following data will be extracted: study details, participant characteristics, inclusion and exclusion criteria, details of the interventions, follow-up, relevant outcome data and source of funding. One reviewer will extract relevant data into a standardised form, and this will be quality assessed by a senior reviewer.
15.	Risk of bias (quality) assessment	Quality assessment of individual studies will be performed using the following checklists: • ROBIS tool for systematic reviews • Cochrane RoB tool v.2 for RCTs (and quasi-RCTs, if no RCT evidence identified) The quality assessment will be performed by one reviewer, and this will be quality assessed by a senior reviewer.
16.	Strategy for data synthesis	Depending on the availability of the evidence, the findings will be summarised narratively or quantitatively. Where there is available data, meta-analyses will be conducted using Cochrane Review Manager software, and data will be presented as risk ratios or odds ratios (all included outcomes are dichotomous outcomes). It is considered likely that a random-effects

		model will be used for meta-analyses (based on assumptions about methodological diversity of studies). Funnel plot asymmetry (relationship between the magnitude of the effect estimate and study size) will be considered (for meta-analyses that include at least 10 studies), and where asymmetry is indicated a fixed-effects model will be conducted (and both random-effects and fixed-effects analyses will be presented) or sensitivity analyses excluding small studies will be considered. Heterogeneity in the effect estimates of the individual studies will be assessed using the I2 statistic. Alongside visual inspection of the point estimates and confidence intervals, I2 values of greater than 50% and 80% will be considered as significant and very significant heterogeneity, respectively. Heterogeneity will be explored as appropriate using sensitivity analyses and pre-specified subgroup analyses. The confidence in the findings across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group: http://www.gradeworkinggroup.org/ Importance and imprecision of findings will be assessed against minimally important differences (MIDs). The following MIDs will be used: Live birth: statistical significance All other outcomes: 0.8 and 1.25 for all relative dichotomous outcomes

17.	Analysis of sub-groups	Evidence will be stratified by:
		• People undergoing screening hysteroscopy who are trying to conceive spontaneously
		• People undergoing screening hysteroscopy prior to in vitro fertilisation (IVF) or intrauterine insemination (IUI)
		
		Evidence will be sub-grouped by the following only in the event that there is significant heterogeneity in outcomes:
		• Age (based on mean age of participants in each study)
		  ○ <35 years
		  ○ ≥35 years
		• Previous implantation failure:
		  ○ Screening hysteroscopy prior to 1st embryo transfer
		  ○ Screening hysteroscopy after previous failed embryo transfer
		Where evidence is stratified or sub grouped the committee will consider on a case-by-case basis if separate

		recommendations should be made for distinct groups. Separate recommendations may be made where there is evidence of a differential effect of interventions in distinct groups. If there is a lack of evidence in one group, the committee will consider, based on their experience, whether it is reasonable to extrapolate and assume the interventions will have similar effects in that group compared with others.			
18.	Type and method of review	☒	Intervention		
		☐	Diagnostic		
		☐	Prognostic		
		☐	Qualitative		
		☐	Epidemiologic		
		☐	Service Delivery		
		☐	Other (please specify)		
19.	Language	English			
20.	Country	England			
21.	Anticipated or actual start date	June 2023			
22.	Anticipated completion date	November 2024			
23.	Stage of review at time of this submission	Review stage		Started	Completed
		Preliminary searches		☐	☑
		Piloting of the study selection process		☐	☑
		Formal screening of search results against eligibility criteria		☐	☑
		Data extraction		☐	☑
		Risk of bias (quality) assessment		☑	☐
		Data analysis		☑	☐
24.	Named contact	5a. Named contact			

		Guideline Development Team A 5b Named contact e-mail FertilityProblems@nice.org.uk 5e Organisational affiliation of the review Guideline Development Team A, Centre for Guidelines, National Institute for Health and Care Excellence (NICE)
25.	Review team members	• Senior Technical Analyst • Technical Analyst
26.	Funding sources/sponsor	This systematic review is being completed by NICE
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10263
29.	Other registration details	None
30.	Reference/URL for published protocol	https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=454994
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication

		• publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
32.	Keywords	Female factor fertility problems, infertility, hysteroscopy, screening, in vitro fertilisation, intrauterine insemination	
33.	Details of existing review of same topic by same authors	None	
34.	Current review status	☒	Ongoing
		☐	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated
		☐	Discontinued
35..	Additional information	None	
36.	Details of final publication	www.nice.org.uk	

NICE: National Institute for Health and Care Excellence; RCT: randomised controlled trial; RoB: risk of bias

Appendix B Literature search strategies

Literature search strategies for review question: What is the effectiveness of screening hysteroscopy (with or without treatment of any detected uterine cavity abnormalities) on reproductive outcomes for people with female factor fertility problems?

Database: Ovid MEDLINE(R) ALL

Date of last search: 27/09/2023

#	Searches
1	infertility, female/ or Infertility/ or fertility/
2	(infertil* or subfertil* or fertil* or hypofertil* or subfecund* or fecund* or infecund* or steril*).tw,kf.
3	((delay* or difficult* or inabilit* or unable or problem* or try or trying or attempt* or fail* or issue* or trouble* or loss or achiev* or improv*) adj4 (conceiv* or pregnan*)).tw,kf.
4	(preconception or conception).tw,kf.
5	((fallopian or factor*) adj2 (tubal or tube or tubes)).tw,kf.
6	Pregnancy/
7	pregnancy complications/ or abortion, spontaneous/ or abortion, habitual/ or embryo loss/ or fetal death/ or fetal resorption/
8	(abort* or miscarr*).tw,kf.
9	((embryo* or fetal or fetus* or blastocyst*) adj2 (loss or death or disintegrat* or resorption or reabsorp* or demise* or mummif*)).tw,kf.
10	exp reproductive techniques, assisted/
11	((ovar* or ovulat*) adj2 (induc* or stimulat*)).tw,kf.
12	((artificial or assisted or facilitat* or in vitro or invitro or intrauterine) adj2 (inseminat* or conception)).tw,kf.
13	(sperm adj2 inject*).tw,kf.
14	(ivf or fet or icsi or iui or GIFT).tw,kf.
15	((gamete* or embryo*) adj2 transfer*).tw,kf.
16	(implant* adj2 fail*).tw,kf.
17	Anovulation/
18	menstruation disturbances/ or amenorrhea/ or dysmenorrhea/ or menorrhagia/ or oligomenorrhea/
19	(anovulat* or oligoovulat* or oligo ovulat* or amenorrh* or dysmenorrh* or menorrh* or oligomenorrh* or hypomenorrh* or polymenorrh*).tw,kf.
20	((menses or menstrua* or period*) adj2 (absen* or irregular* or sporadic* or heav* or prolong* or excess* or pain* or abnormal* or infrequen* or disorder* or dysfunction* or disturb* or unpredictab*)).tw,kf.
21	((uterine or postcoital or post coital) adj2 bleed* adj2 (irregular* or sporadic* or heav* or prolong* or excess* or pain* or abnormal* or infrequen* or disorder* or dysfunction* or unpredictab*)).tw,kf.
22	or/1-21
23	(endoscopy/ or hysteroscopy/) and (biopsy/ or exp image-guided biopsy/ or diagnostic imaging/ or Mass Screening/)
24	((hysteroscop* or minihysteroscop*) adj5 (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*)).tw,kf.
25	((endoscop* or telescop* or microscop*) adj3 (womb or uter* or cervi*) adj5 (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*)).tw,kf.
26	(Uteroscop* adj5 (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*)).tw,kf.
27	or/23-26
28	22 and 27
29	letter/
30	editorial/
31	news/
32	exp historical article/
33	Anecdotes as topic/
34	comment/
35	case reports/
36	(letter or comment*).ti.

#	Searches
37	or/29-36
38	randomized controlled trial/ or random*.ti,ab.
39	37 not 38
40	animals/ not humans/
41	exp Animals, Laboratory/
42	exp Animal Experimentation/
43	exp Models, Animal/
44	exp Rodentia/
45	(rat or rats or rodent* or mouse or mice).ti.
46	or/39-45
47	28 not 46
48	limit 47 to english language
49	randomized controlled trial.pt.
50	controlled clinical trial.pt.
51	pragmatic clinical trial.pt.
52	randomi#ed.ab.
53	placebo.ab.
54	drug therapy.fs.
55	randomly.ab.
56	trial.ab.
57	groups.ab.
58	Clinical Trials as topic.sh.
59	trial.ti.
60	or/49-59
61	meta-analysis/
62	meta-analysis as topic/
63	(meta analy* or metanaly* or metaanaly*).ti,ab.
64	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
65	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
66	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
67	(search* adj4 literature).ab.
68	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
69	cochrane.jw.
70	or/61-69
71	48 and (60 or 70)

1 Database: Embase

2 Date of last search: 27/09/23

#	Searches
1	Fertility/ or Infertility/ or exp female infertility/
2	(infertil* or subfertil* or fertil* or hypofertil* or subfecund* or fecund* or infecund* or steril*).tw,kf.
3	((delay* or difficult* or inabilit* or unable or problem* or try or trying or attempt* or fail* or issue* or trouble* or loss or achiev* or improv*) adj4 (conceiv* or pregnan*)).tw,kf.
4	(preconception or conception).tw,kf.
5	((fallopian or factor*) adj2 (tubal or tube or tubes)).tw,kf.
6	Pregnancy/
7	pregnancy disorder/ or pregnancy complication/
8	recurrent abortion/ or spontaneous abortion/
9	embryo death/ or fetus death/ or fetus resorption/
10	(abort* or miscarr*).tw,kf.
11	((embryo* or fetal or fetus* or blastocyst*) adj2 (loss or death or disintegrat* or resorption or reabsorp* or demise* or mummif*)).tw,kf.
12	exp infertility therapy/

#	Searches
13	((ovar* or ovulat*) adj2 (induc* or stimulat*)).tw,kf.
14	((artifical or assisted or facilitat* or in vitro or invitro or intrauterine) adj2 (inseminat* or conception)).tw,kf.
15	(sperm adj2 inject*).tw,kf.
16	(ivf or fet or icsi or iui or GIFT).tw,kf.
17	((gamete* or embryo*) adj2 transfer*).tw,kf.
18	(implant* adj2 fail*).tw,kf.
19	anovulation/
20	exp menstruation disorder/
21	(anovulat* or oligoovulat* or oligo ovulat* or amenorrh* or dysmenorrh* or menorrh* or oligomenorrh* or hypomenorrh* or polymenorrh*).tw,kf.
22	((menses or menstrua* or period*) adj2 (absen* or irregular* or sporadic* or heav* or prolong* or excess* or pain* or abnormal* or infrequen* or disorder* or dysfunction* or disturb* or unpredictab*)).tw,kf.
23	((uterine or postcoital or post coital) adj2 bleed* adj2 (irregular* or sporadic* or heav* or prolong* or excess* or pain* or abnormal* or infrequen* or disorder* or dysfunction* or unpredictab*)).tw,kf.
24	or/1-23
25	(endoscopy/ or hysteroscopy/) and (screening/ or biopsy/ or exp image guided biopsy/ or diagnostic imaging/)
26	((hysteroscop* or minihysteroscop*) adj5 (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*)).tw,kf.
27	((endoscop* or telescop* or microscop*) adj3 (womb or uter* or cervi*) adj5 (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*)).tw,kf.
28	(Uteroscop* adj5 (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*)).tw,kf.
29	or/25-28
30	24 and 29
31	letter.pt. or letter/
32	note.pt.
33	editorial.pt.
34	case report/ or case study/
35	(letter or comment*).ti.
36	or/31-35
37	randomized controlled trial/ or random*.ti,ab.
38	36 not 37
39	animal/ not human/
40	nonhuman/
41	exp Animal Experiment/
42	exp Experimental Animal/
43	animal model/
44	exp Rodent/
45	(rat or rats or rodent* or mouse or mice).ti.
46	or/38-45
47	30 not 46
48	(conference abstract* or conference review or conference paper or conference proceeding).db,pt,su.
49	47 not 48
50	limit 49 to english language
51	random*.ti,ab.
52	factorial*.ti,ab.
53	(crossover* or cross over*).ti,ab.
54	((doubl* or singl*) adj blind*).ti,ab.
55	(assign* or allocat* or volunteer* or placebo*).ti,ab.
56	crossover procedure/
57	single blind procedure/
58	randomized controlled trial/
59	double blind procedure/
60	or/51-59
61	systematic review/

#	Searches
62	meta-analysis/
63	(meta analy* or metanaly* or metaanaly*).ti,ab.
64	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
65	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
66	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
67	(search* adj4 literature).ab.
68	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
69	((pool* or combined) adj2 (data or trials or studies or results)).ab.
70	cochrane.jw.
71	or/61-70
72	50 and (60 or 71)

Database: Cochrane Database of Systematic Reviews, Issue 9 of 12, September 2023 and Cochrane Central Register of Controlled Trials, Issue 8 of 12, August 2023

Date of last search: 27/09/23

#	Searches
#1	MeSH descriptor: [Infertility, Female] this term only
#2	MeSH descriptor: [Infertility] this term only
#3	MeSH descriptor: [Fertility] this term only
#4	(infertil* or subfertil* or fertil* or hypofertil* or subfecund* or fecund* or infecund* or steril*):ti,ab,kw
#5	((delay* or difficult* or inabilit* or unable or problem* or try or trying or attempt* or fail* or issue* or trouble* or loss or achiev* or improv*) NEAR/4 (conceiv* or pregnan*)):ti,ab,kw
#6	(preconception or conception):ti,ab,kw
#7	((fallopian or factor*) NEAR/2 (tubal or tube or tubes)):ti,ab,kw
#8	MeSH descriptor: [Pregnancy] this term only
#9	MeSH descriptor: [Pregnancy Complications] this term only
#10	MeSH descriptor: [Abortion, Spontaneous] this term only
#11	MeSH descriptor: [Abortion, Habitual] this term only
#12	MeSH descriptor: [Embryo Loss] this term only
#13	MeSH descriptor: [Fetal Death] this term only
#14	MeSH descriptor: [Fetal Resorption] this term only
#15	(abort* or miscarr*):ti,ab,kw
#16	((embryo* or fetal or fetus* or blastocyst*) NEAR/2 (loss or death or disintegrat* or resorption or reabsorp* or demise* or mummif*)):ti,ab,kw
#17	MeSH descriptor: [Reproductive Techniques, Assisted] explode all trees
#18	((ovar* or ovulat*) NEAR/2 (induc* or stimulat*)):ti,ab,kw
#19	((artificial or assisted or facilitat* or "in vitro" or invitro or intrauterine) NEAR/2 (inseminat* or conception)):ti,ab,kw
#20	(sperm NEAR/2 inject*):ti,ab,kw
#21	(ivf or fet or icsi or iui or GIFT):ti,ab,kw
#22	((gamete* or embryo*) NEAR/2 transfer*):ti,ab,kw
#23	(implant* NEAR/2 fail*):ti,ab,kw
#24	MeSH descriptor: [Anovulation] this term only
#25	MeSH descriptor: [Menstruation Disturbances] this term only
#26	MeSH descriptor: [Amenorrhea] this term only
#27	MeSH descriptor: [Dysmenorrhea] this term only
#28	MeSH descriptor: [Menorrhagia] this term only
#29	MeSH descriptor: [Oligomenorrhea] this term only
#30	(anovulat* or oligoovulat* or oligo NEXT ovulat* or amenorrh* or dysmenorrh* or menorrh* or oligomenorrh* or hypomenorrh* or polymenorrh*):ti,ab,kw
#31	((menses or menstrua* or period*) NEAR/2 (absen* or irregular* or sporadic* or heav* or prolong* or excess* or pain* or abnormal* or infrequen* or disorder* or dysfunction* or disturb* or unpredictab*)):ti,ab,kw
#32	((uterine or postcoital or "post coital") NEAR/2 bleed* NEAR/2 (irregular* or sporadic* or heav* or prolong* or excess* or pain* or abnormal* or infrequen* or disorder* or dysfunction* or unpredictab*)):ti,ab,kw

#	Searches
#33	{OR #1-#32}
#34	MeSH descriptor: [Endoscopy] this term only
#35	MeSH descriptor: [Hysteroscopy] this term only
#36	{OR #34-#35}
#37	MeSH descriptor: [Biopsy] this term only
#38	MeSH descriptor: [Image-Guided Biopsy] explode all trees
#39	MeSH descriptor: [Diagnostic Imaging] this term only
#40	MeSH descriptor: [Mass Screening] this term only
#41	{OR #37-#40}
#42	#36 AND #41
#43	((hysteroscop* or minihysteroscop*) NEAR/5 (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*)):ti,ab,kw
#44	((endoscop* or telescop* or microscop*) NEAR/3 (womb or uter* or cervi*) NEAR/5 (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*)):ti,ab,kw
#45	(Uteroscop* NEAR/5 (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*)):ti,ab,kw
#46	{or #42-#45}
#47	#33 AND #46

1 **Database: Epistemonikos**

2 **Date of last search: 08/09/2023**

#	Searches
1	(advanced_title_en:((infertil* OR subfertil* OR fertil* OR hypofertil* OR subfecund* OR fecund* OR infecund* OR steril*) OR ((delay* OR difficult* OR inabilit* OR unable OR problem* OR try OR trying OR attempt* OR fail* OR issue* OR trouble* OR loss OR achiev* OR improv*) AND (conceiv* OR pregnan*))) OR advanced_abstract_en:((infertil* OR subfertil* OR fertil* OR hypofertil* OR subfecund* OR fecund* OR infecund* OR steril*) OR ((delay* OR difficult* OR inabilit* OR unable OR problem* OR try OR trying OR attempt* OR fail* OR issue* OR trouble* OR loss OR achiev* OR improv*) AND (conceiv* OR pregnan*)))) AND (advanced_title_en:(((hysteroscop* OR minihysteroscop*) AND (screen* OR analy* OR assess* OR evaluat* OR detect* OR incidence* OR identif* OR predict* OR investigat* OR exam* OR biops* OR explor* OR diagnos* OR test* OR polyp* OR fibroid* OR myom*))) OR advanced_abstract_en:(((hysteroscop* OR minihysteroscop*) AND (screen* OR analy* OR assess* OR evaluat* OR detect* OR incidence* OR identif* OR predict* OR investigat* OR exam* OR biops* OR explor* OR diagnos* OR test* OR polyp* OR fibroid* OR myom*)))) [Filters: classification=systematic-review, cochrane=missing, protocol=no]
2	(advanced_title_en:((abort* OR miscarr* OR ivf OR fet OR icsi OR iui OR GIFT)) OR advanced_abstract_en:((abort* OR miscarr* OR ivf OR fet OR icsi OR iui OR GIFT))) OR (advanced_title_en:(((artificial OR assisted OR facilitat* OR in vitro OR invitro OR intrauterine) AND (inseminat* OR conception)))) OR advanced_abstract_en:(((artificial OR assisted OR facilitat* OR in vitro OR invitro OR intrauterine) AND (inseminat* OR conception)))) AND (advanced_title_en:(((hysteroscop* OR minihysteroscop*) AND (screen* OR analy* OR assess* OR evaluat* OR detect* OR incidence* OR identif* OR predict* OR investigat* OR exam* OR biops* OR explor* OR diagnos* OR test* OR polyp* OR fibroid* OR myom*))) OR advanced_abstract_en:(((hysteroscop* OR minihysteroscop*) AND (screen* OR analy* OR assess* OR evaluat* OR detect* OR incidence* OR identif* OR predict* OR investigat* OR exam* OR biops* OR explor* OR diagnos* OR test* OR polyp* OR fibroid* OR myom*)))) [Filters: classification=systematic-review, cochrane=missing, protocol=no]
3	(advanced_title_en:((anovulat* OR oligoovulat* OR amenorrh* OR dysmenorrh* OR menorrh* OR oligomenorrh* OR hypomenorrh* OR polymenorrh*)) OR advanced_abstract_en:((anovulat* OR oligoovulat* OR amenorrh* OR dysmenorrh* OR menorrh* OR oligomenorrh* OR hypomenorrh* OR polymenorrh*))) OR (advanced_title_en:(((menses OR menstrua* OR period*) AND (absen* OR irregular* OR sporadic* OR heav* OR prolong* OR excess* OR pain* OR abnormal* OR infrequen* OR disorder* OR dysfunction* OR disturb* OR unpredictab*))) OR advanced_abstract_en:(((menses OR menstrua* OR period*) AND (absen* OR irregular* OR sporadic* OR heav* OR prolong* OR excess* OR pain* OR abnormal* OR infrequen* OR disorder* OR dysfunction* OR disturb* OR unpredictab*)))) OR (advanced_title_en:(((uterine AND bleed*))) OR advanced_abstract_en:(((uterine AND bleed*)))) AND (advanced_title_en:(((hysteroscop* OR minihysteroscop*) AND (screen* OR analy* OR assess* OR evaluat* OR detect* OR incidence* OR identif* OR predict* OR investigat* OR exam* OR biops* OR explor* OR diagnos* OR test* OR polyp* OR fibroid* OR myom*))) OR advanced_abstract_en:(((hysteroscop* OR minihysteroscop*) AND (screen* OR analy* OR assess* OR evaluat* OR detect* OR incidence* OR identif* OR predict* OR investigat* OR exam* OR biops* OR explor* OR diagnos* OR test* OR polyp* OR fibroid* OR myom*)))) [Filters: classification=systematic-review, cochrane=missing, protocol=no]

3

1 Health Economic Literature Search Strategies

2 Database: Ovid MEDLINE(R) ALL <1946 to September 08, 2023>

3 Date of last search: 11/09/2023

#	Searches
1	infertility, female/ or Infertility/ or fertility/
2	(infertil* or subfertil* or fertil* or hypofertil* or subfecund* or fecund* or infecund* or steril*).tw,kf.
3	((delay* or difficult* or inabilit* or unable or problem* or try or trying or attempt* or fail* or issue* or trouble* or loss or achiev* or improv*) adj4 (conceiv* or pregnan*)).tw,kf.
4	(preconception or conception).tw,kf.
5	((fallopian or factor*) adj2 (tubal or tube or tubes)).tw,kf.
6	Pregnancy/
7	pregnancy complications/ or abortion, spontaneous/ or abortion, habitual/ or embryo loss/ or fetal death/ or fetal resorption/
8	(abort* or miscarr*).tw,kf.
9	((embryo* or fetal or fetus* or blastocyst*) adj2 (loss or death or disintegrat* or resorption or reabsorp* or demise* or mummif*)).tw,kf.
10	exp reproductive techniques, assisted/
11	((ovar* or ovulat*) adj2 (induc* or stimulat*)).tw,kf.
12	((artificial or assisted or facilitat* or in vitro or invitro or intrauterine) adj2 (inseminat* or conception)).tw,kf.
13	(sperm adj2 inject*).tw,kf.
14	(ivf or fet or icsi or iui or GIFT).tw,kf.
15	((gamete* or embryo*) adj2 transfer*).tw,kf.
16	(implant* adj2 fail*).tw,kf.
17	Anovulation/
18	menstruation disturbances/ or amenorrhea/ or dysmenorrhea/ or menorrhagia/ or oligomenorrhea/
19	(anovulat* or oligoovulat* or oligo ovulat* or amenorrh* or dysmenorrh* or menorrh* or oligomenorrh* or hypomenorrh* or polymenorrh*).tw,kf.
20	((menses or menstrua* or period*) adj2 (absen* or irregular* or sporadic* or heav* or prolong* or excess* or pain* or abnormal* or infrequen* or disorder* or dysfunction* or disturb* or unpredictab*)).tw,kf.
21	((uterine or postcoital or post coital) adj2 bleed* adj2 (irregular* or sporadic* or heav* or prolong* or excess* or pain* or abnormal* or infrequen* or disorder* or dysfunction* or unpredictab*)).tw,kf.
22	or/1-21
23	(endoscopy/ or hysteroscopy/) and (biopsy/ or exp image-guided biopsy/ or diagnostic imaging/ or Mass Screening/)
24	((hysteroscop* or minihysteroscop*) adj5 (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*)).tw,kf.
25	((endoscop* or telescop* or microscop*) adj3 (womb or uter* or cervi*) adj5 (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*)).tw,kf.
26	(Uteroscop* adj5 (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*)).tw,kf.
27	or/23-26
28	22 and 27
29	letter/
30	editorial/
31	news/
32	exp historical article/
33	Anecdotes as topic/
34	comment/
35	case reports/
36	(letter or comment*).ti.
37	or/29-36
38	randomized controlled trial/ or random*.ti,ab.
39	37 not 38
40	animals/ not humans/
41	exp Animals, Laboratory/
42	exp Animal Experimentation/

#	Searches
43	exp Models, Animal/
44	exp Rodentia/
45	(rat or rats or rodent* or mouse or mice).ti.
46	or/39-45
47	28 not 46
48	limit 47 to english language
49	Economics/
50	Value of life/
51	exp "Costs and Cost Analysis"/
52	exp Economics, Hospital/
53	exp Economics, Medical/
54	exp Resource Allocation/
55	Economics, Nursing/
56	Economics, Pharmaceutical/
57	exp "Fees and Charges"/
58	exp Budgets/
59	budget*.ti,ab.
60	cost*.ti,ab.
61	(economic* or pharmaco?economic*).ti,ab.
62	(price* or pricing*).ti,ab.
63	(financ* or fee or fees or expenditure* or saving*).ti,ab.
64	(value adj2 (money or monetary)).ti,ab.
65	resourc* allocat*.ti,ab.
66	(fund or funds or funding* or funded).ti,ab.
67	(ration or rations or rationing* or rationed).ti,ab.
68	ec.fs.
69	or/49-68
70	quality-adjusted life years/
71	sickness impact profile/
72	(quality adj2 (wellbeing or well being)).ti,ab.
73	sickness impact profile.ti,ab.
74	disability adjusted life.ti,ab.
75	(qal* or qtime* or qwb* or daly*).ti,ab.
76	(euroqol* or eq5d* or eq 5*).ti,ab.
77	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
78	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
79	(hui or hui1 or hui2 or hui3).ti,ab.
80	(health* year* equivalent* or hye or hyes).ti,ab.
81	discrete choice*.ti,ab.
82	rosser.ti,ab.
83	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
84	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
85	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
86	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
87	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
88	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
89	or/70-88
90	48 and (69 or 89)

1 **Database: Embase <1974 to 2023 September 08>**

2 **Date of last search: 11/09/2023**

#	Searches
1	Fertility/ or Infertility/ or exp female infertility/

#	Searches
2	(infertil* or subfertil* or fertil* or hypofertil* or subfecund* or fecund* or infecund* or steril*).tw,kf.
3	((delay* or difficult* or inabilit* or unable or problem* or try or trying or attempt* or fail* or issue* or trouble* or loss or achiev* or improv*) adj4 (conceiv* or pregnan*)).tw,kf.
4	(preconception or conception).tw,kf.
5	((fallopian or factor*) adj2 (tubal or tube or tubes)).tw,kf.
6	Pregnancy/
7	pregnancy disorder/ or pregnancy complication/
8	recurrent abortion/ or spontaneous abortion/
9	embryo death/ or fetus death/ or fetus resorption/
10	(abort* or miscarr*).tw,kf.
11	((embryo* or fetal or fetus* or blastocyst*) adj2 (loss or death or disintegrat* or resorption or reabsorp* or demise* or mummif*)).tw,kf.
12	exp infertility therapy/
13	((ovar* or ovulat*) adj2 (induc* or stimulat*)).tw,kf.
14	((artifical or assisted or facilitat* or in vitro or invitro or intrauterine) adj2 (inseminat* or conception)).tw,kf.
15	(sperm adj2 inject*).tw,kf.
16	(ivf or fet or icsi or iui or GIFT).tw,kf.
17	((gamete* or embryo*) adj2 transfer*).tw,kf.
18	(implant* adj2 fail*).tw,kf.
19	anovulation/
20	exp menstruation disorder/
21	(anovulat* or oligoovulat* or oligo ovulat* or amenorrh* or dysmenorrh* or menorrh* or oligomenorrh* or hypomenorrh* or polymenorrh*).tw,kf.
22	((menses or menstrua* or period*) adj2 (absen* or irregular* or sporadic* or heav* or prolong* or excess* or pain* or abnormal* or infrequen* or disorder* or dysfunction* or disturb* or unpredictab*)).tw,kf.
23	((uterine or postcoital or post coital) adj2 bleed* adj2 (irregular* or sporadic* or heav* or prolong* or excess* or pain* or abnormal* or infrequen* or disorder* or dysfunction* or unpredictab*)).tw,kf.
24	or/1-23
25	(endoscopy/ or hysteroscopy/) and (screening/ or biopsy/ or exp image guided biopsy/ or diagnostic imaging/)
26	((hysteroscop* or minihysteroscop*) adj5 (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*)).tw,kf.
27	((endoscop* or telescop* or microscop*) adj3 (womb or uter* or cervi*) adj5 (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*)).tw,kf.
28	(Uteroscop* adj5 (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*)).tw,kf.
29	or/25-28
30	24 and 29
31	letter.pt. or letter/
32	note.pt.
33	editorial.pt.
34	case report/ or case study/
35	(letter or comment*).ti.
36	or/31-35
37	randomized controlled trial/ or random*.ti,ab.
38	36 not 37
39	animal/ not human/
40	nonhuman/
41	exp Animal Experiment/
42	exp Experimental Animal/
43	animal model/
44	exp Rodent/
45	(rat or rats or rodent* or mouse or mice).ti.
46	or/38-45
47	30 not 46
48	(conference abstract* or conference review or conference paper or conference proceeding).db,pt,su.

#	Searches
49	47 not 48
50	limit 49 to english language
51	health economics/
52	exp economic evaluation/
53	exp health care cost/
54	exp fee/
55	budget/
56	funding/
57	resource allocation/
58	budget*.ti,ab.
59	cost*.ti,ab.
60	(economic* or pharmaco?economic*).ti,ab.
61	(price* or pricing*).ti,ab.
62	(financ* or fee or fees or expenditure* or saving*).ti,ab.
63	(value adj2 (money or monetary)).ti,ab.
64	resourc* allocat*.ti,ab.
65	(fund or funds or funding* or funded).ti,ab.
66	(ration or rations or rationing* or rationed).ti,ab.
67	or/51-66
68	quality adjusted life year/
69	"quality of life index"/
70	short form 12/ or short form 20/ or short form 36/ or short form 8/
71	sickness impact profile/
72	(quality adj2 (wellbeing or well being)).ti,ab.
73	sickness impact profile.ti,ab.
74	disability adjusted life.ti,ab.
75	(qal* or qtime* or qwb* or daly*).ti,ab.
76	(euroqol* or eq5d* or eq 5*).ti,ab.
77	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
78	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
79	(hui or hui1 or hui2 or hui3).ti,ab.
80	(health* year* equivalent* or hye or hyes).ti,ab.
81	discrete choice*.ti,ab.
82	rosser.ti,ab.
83	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
84	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
85	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
86	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
87	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
88	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
89	or/68-88
90	50 and (67 or 89)

1 **Database: INAHTA**

2 **Date of last search: 11/09/2023**

#	Searches
1	"infertility, female"[mh]
2	Infertility[mh]
3	fertility[mh]
4	(infertil* or subfertil* or fertil* or hypofertil* or subfecund* or fecund* or infecund* or steril*)
5	((delay* or difficult* or inabilit* or unable or problem* or try or trying or attempt* or fail* or issue* or trouble* or loss or achiev* or improv*) AND (conceiv* or pregnan*))
6	(preconception or conception)

#	Searches
7	((fallopian or factor*) AND (tubal or tube or tubes))
8	Pregnancy[mh]
9	"pregnancy complications"[mh]
10	"abortion, spontaneous"[mh]
11	"abortion, habitual"[mh]
12	"embryo loss"[mh]
13	"fetal death"[mh]
14	"fetal resorption"[mh]
15	(abort* or miscarr*)
16	((embryo* or fetal or fetus* or blastocyst*) AND (loss or death or disintegrat* or resorption or reabsorp* or demise* or mummif*))
17	"reproductive techniques, assisted"[mhe]
18	((ovar* or ovulat*) AND (induc* or stimulat*))
19	((artificial or assisted or facilitat* or "in vitro" or invitro or intrauterine) AND (inseminat* or conception))
20	(sperm AND inject*)
21	(ivf or fet or icsi or iui or GIFT)
22	((gamete* or embryo*) AND transfer*)
23	(implant* AND fail*)
24	Anovulation[mh]
25	"menstruation disturbances"[mh]
26	amenorrhea[mh]
27	dysmenorrhea[mh]
28	menorrhagia[mh]
29	oligomenorrhea[mh]
30	(anovulat* or oligoovulat* or (oligo AND ovulat*) or amenorrh* or dysmenorrh* or menorrh* or oligomenorrh* or hypomenorrh* or polymenorrh*)
31	((menses or menstrua* or period*) AND (absen* or irregular* or sporadic* or heav* or prolong* or excess* or pain* or abnormal* or infrequen* or disorder* or dysfunction* or disturb* or unpredictab*))
32	((uterine or postcoital or "post coital") AND bleed* AND (irregular* or sporadic* or heav* or prolong* or excess* or pain* or abnormal* or infrequen* or disorder* or dysfunction* or unpredictab*))
33	#32 OR #31 OR #30 OR #29 OR #28 OR #27 OR #26 OR #25 OR #24 OR #23 OR #22 OR #21 OR #20 OR #19 OR #18 OR #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1
34	endoscopy[mh]
35	hysteroscopy[mh]
36	#35 OR #34
37	biopsy[mh]
38	"image-guided biopsy"[mhe]
39	"diagnostic imaging"[mh]
40	"Mass Screening"[mh]
41	#40 OR #39 OR #38 OR #37
42	#41 AND #36
43	((hysteroscop* or minihysteroscop*) AND (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*))
44	((endoscop* or telescop* or microscop*) AND (womb or uter* or cervi*) AND (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*))
45	(Uteroscop* AND (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*))
46	#45 OR #44 OR #43 OR #42
47	#46 AND #33

1 **Database: HTA via CRD**

2 **Date of last search: 27/09/23**

#	Searches
1	MESH DESCRIPTOR Infertility, Female

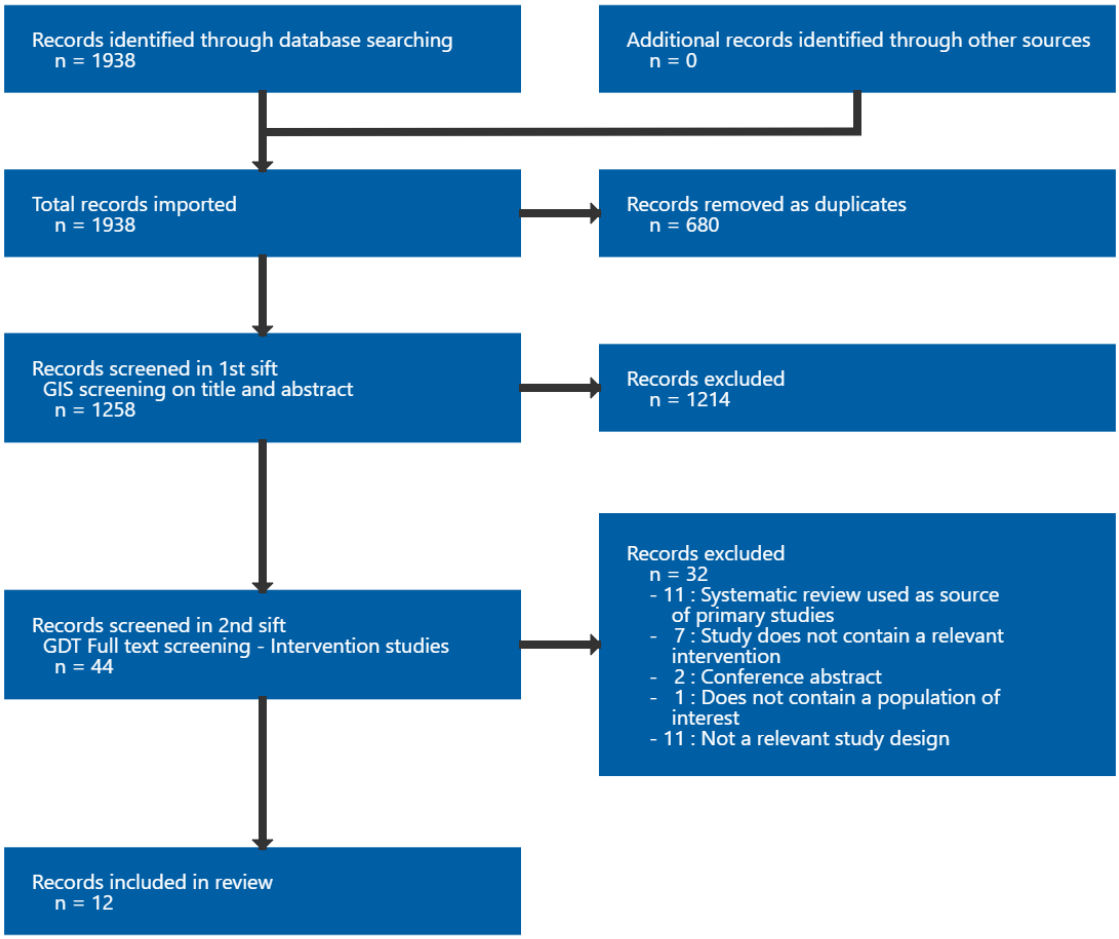
#	Searches
2	MESH DESCRIPTOR Infertility
3	MESH DESCRIPTOR Fertility
4	(infertil* or subfertil* or fertil* or hypofertil* or subfecund* or fecund* or infecund* or steril*)
5	((delay* or difficult* or inabilit* or unable or problem* or try or trying or attempt* or fail* or issue* or trouble* or loss or achiev* or improv*) NEAR4 (conceiv* or pregnan*))
6	(preconception or conception)
7	((fallopian or factor*) NEAR2 (tubal or tube or tubes))
8	MESH DESCRIPTOR Pregnancy
9	MESH DESCRIPTOR Pregnancy Complications
10	MESH DESCRIPTOR Abortion, Spontaneous
11	MESH DESCRIPTOR Abortion, Habitual
12	MESH DESCRIPTOR Embryo Loss
13	MESH DESCRIPTOR Fetal Death
14	MESH DESCRIPTOR Fetal Resorption
15	(abort* or miscarr*)
16	((embryo* or fetal or fetus* or blastocyst*) NEAR2 (loss or death or disintegrat* or resorption or reabsorp* or demise* or mummif*))
17	MESH DESCRIPTOR Reproductive Techniques, Assisted EXPLODE ALL TREES
18	((ovar* or ovulat*) NEAR2 (induc* or stimulat*))
19	((artificial or assisted or facilitat* or "in vitro" or invitro or intrauterine) NEAR2 (inseminat* or conception))
20	(sperm NEAR2 inject*)
21	(ivf or fet or icsi or iui or GIFT)
22	((gamete* or embryo*) NEAR2 transfer*)
23	(implant* NEAR2 fail*)
24	MESH DESCRIPTOR Anovulation
25	MESH DESCRIPTOR Menstruation Disturbances
26	MESH DESCRIPTOR Amenorrhea
27	MESH DESCRIPTOR Dysmenorrhea
28	MESH DESCRIPTOR Menorrhagia
29	MESH DESCRIPTOR Oligomenorrhea
30	(anovulat* or oligoovulat* or oligo NEXT ovulat* or amenorrh* or dysmenorrh* or menorrh* or oligomenorrh* or hypomenorrh* or polymenorrh*)
31	((menses or menstrua* or period*) NEAR2 (absen* or irregular* or sporadic* or heav* or prolong* or excess* or pain* or abnormal* or infrequen* or disorder* or dysfunction* or disturb* or unpredictab*))
32	((uterine or postcoital or "post coital") NEAR2 bleed* NEAR2 (irregular* or sporadic* or heav* or prolong* or excess* or pain* or abnormal* or infrequen* or disorder* or dysfunction* or unpredictab*))
33	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32
34	MESH DESCRIPTOR Endoscopy
35	MESH DESCRIPTOR Hysteroscopy
36	#34 or #35
37	MESH DESCRIPTOR Biopsy
38	MESH DESCRIPTOR Image-Guided Biopsy EXPLODE ALL TREES
39	MESH DESCRIPTOR Diagnostic Imaging
40	MESH DESCRIPTOR Mass Screening
41	#37 or #38 or #39 or #40
42	#36 AND #41
43	((hysteroscop* or minihysteroscop*) NEAR5 (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*))
44	((endoscop* or telescop* or microscop*) NEAR3 (womb or uter* or cervi*) NEAR5 (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*))
45	(Uteroscop* NEAR5 (screen* or analy* or assess* or evaluat* or detect* or incidence* or identif* or predict* or investigat* or exam* or biops* or explor* or diagnos* or test* or polyp* or fibroid* or myom*))
46	#42 or #43 or #44 or #45
47	#33 AND #46

#	Searches
48	(#33 AND #46) IN HTA

Appendix C Effectiveness evidence study selection

Study selection for review question: What is the effectiveness of screening hysteroscopy (with or without treatment of any detected uterine cavity abnormalities) on reproductive outcomes for people with female factor fertility problems?

Figure 1: Study selection flow chart



Appendix D Evidence tables

Evidence tables for review question: What is the effectiveness of screening hysteroscopy (with or without treatment of any detected uterine cavity abnormalities) on reproductive outcomes for people with female factor fertility problems?

Aghahosseini, 2012

Bibliographic Reference Aghahosseini, M.; Ebrahimi, N.; Mahdavi, A.; Aleyasin, A.; Safdarian, L.; Sina, S.; Hysteroscopy prior to assisted reproductive technique in women with recurrent implantation failure improves pregnancy likelihood; Fertility and Sterility; 2012; vol. 98 (no. 3suppl1); 4

Study details

Country where study was carried out	Iran
Study type	Randomised controlled trial (RCT) The study has been published as an abstract only
Study dates	Not reported
Inclusion criteria	• women undergoing intracytoplasmic sperm-embryo transfer (ICSI-ET) • had 2 or more implantation failures • aged less than 38 years old • BMI less than 35 kg/m2 • normal hysterosalpingogram and no history of hysteroscopy in the last 2 months
Exclusion criteria	Not reported
Patient	**Age, years: Mean (SD)**

characteristics	NR (inclusion criteria <38 years) **Duration of infertility, years: Mean (SD)** NR **Previous implantation failure** NR (inclusion criteria ≥2 implantation failures)
Intervention(s)/control	**Hysteroscopy (hysteroscopy prior to intracytoplasmic sperm injection: ICSI)** Not reported **No hysteroscopy (no hysteroscopy prior to ICSI)** Not reported **Ovarian stimulation and ICSI** Both groups received the same long term desensitization protocol and similar standard ovarian stimulation with gonadotropins
Duration of follow-up	Not reported - participants were followed until detection of fetal heart rate (clinical pregnancy) and delivery
Sources of funding	Supported by Tehran University of Medical Sciences
Sample size	N (total): 353 N (hysteroscopy): 142

	N (no hysteroscopy): 211 It is not clear from the abstract whether all participants were included in the analysis
Other information	This study was published as an abstract only. Extracted data is based on information available in the abstract only. The risk of bias assessment for this study has been taken from the following Cochrane review: Kamath, et al. Screening hysteroscopy in subfertile women and women undergoing assisted reproduction. The Cochrane database of systematic reviews; 2019; vol. 4; cd012856

Outcomes

Outcome	**Hysteroscopy, N = 142**	**No hysteroscopy, N = 211**
Live birth (defined as delivery rate)	n = 50; % = 35.5	n = 45; % = 21.1
Clinical pregnancy (defined in the study as detection of fetal heart rate)	n = 72; % = 50.7	n = 64; % = 30.3

Critical appraisal with Cochrane RoB 2.0

This study is published as an abstract only and the critical appraisal is based on the risk of bias assessment published in the following Cochrane review: Kamath, et al. Screening hysteroscopy in subfertile women and women undergoing assisted reproduction. The Cochrane database of systematic reviews; 2019; vol. 4; cd012856

Section	**Question**	**Answer**
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(The authors described the study as randomised and stated that both groups were comparable regarding participant characteristics. However, the information provided was insufficient for making a judgement and there is no information about concealment of the allocation sequence. An uneven distribution of randomised participants (142 in the hysteroscopy group and 211 in the non-hysteroscopy group),*

Section	Question	Answer
		with no clear available explanation)
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	High *(Participants and personnel were not blinded, although it is unlikely that an absence of blinding would influence outcomes. However, it is unclear whether an appropriate analysis was used)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	High *(There was no information provided regarding missing outcome data)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(There was no information provided on the method of measuring the outcome, however it was unlikely that the measurement or ascertainment of the outcome differed between intervention groups, nor that the assessment of the primary outcomes (live birth and pregnancy) could have been influenced by knowledge of the intervention received)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Some concerns *(There does not appear to be a published protocol, however both pregnancy and live birth were reported in the analysis)*
Overall bias and Directness	Risk of bias judgement	High *(The study is judged to be at high risk of bias or to have some concerns in the majority of the domains)*
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

Alleyassin, 2017

Bibliographic Reference	Alleyassin A; Abiri A; Agha-Hosseini M; Sarvi F; The Value of Routine Hysteroscopy before the First Intracytoplasmic Sperm Injection Treatment Cycle.; Gynecologic and obstetric investigation; 2017; vol. 82 (no. 2)

Study details

Country where study was carried out	Iran
Study type	Randomised controlled trial (RCT)
Study dates	May 2014 to March 2015
Inclusion criteria	• normal uterine cavity appearances on vaginal ultrasonography and hysterosalpingography
Exclusion criteria	• recurrent miscarriage • those who had previously received hysteroscopy treatment
Patient characteristics	**Age, years: Mean (SD)** Hysteroscopy: 29.55 (3.85) No hysteroscopy: 29.14 (4.34) **Duration of infertility, years: Mean (SD)** Hysteroscopy: 4.74 (3.44) No hysteroscopy: 4.59 (3.25) **Previous implantation failure**

	All participants were undergoing their first ICSI cycle
Intervention(s)/control	**Hysteroscopy (office hysteroscopy before intracytoplasmic sperm injection (ICSI):** Office hysteroscopy was performed between the 18th and 22nd day of the menstrual cycle using a rigid hysteroscope with continuous flow (30-degree view, 4 mm diameter diagnostic sheath). Diagnosis of intrauterine abnormalities was based on European Society of Human Reproduction and Embryology and European Society for Gynaecological Endoscopy classification and were treated during hysteroscopy. **No hysteroscopy (no office hysteroscopy before ICSI)** Women underwent ICSI without hysteroscopy evaluation **Ovarian stimulation and ICSI** The hysteroscopy was performed in the mid-luteal phase; afterwards downregulation was started using transdermal injection of Bucereline. After adequate downregulation (confirmed by oestradiol and LH measuring), recombinant follicle stimulating hormone was achieved for ovarian stimulation. Antral follicle count and the level of antimullerian hormone were used to adjust the dosage. hCG (human chorionic gonadotropin,10,000 IU) was injected when >=2 follicles were detected in the ultrasound scan. Oocyte retrieval was done 36 h after hCG injection by transvaginal guided ultrasonography and embryo transfer on day 3.
Duration of follow-up	Not reported (ultrasonography was completed 4 weeks after embryo transfer to confirm pregnancy)
Sources of funding	Not reported
Sample size	N (total): randomised=220, analysed=220 N (hysteroscopy): randomised=110, analysed=110 N (no hysteroscopy): randomised=110, analysed=110
Other information	25/110 (23%) who underwent hysteroscopy had abnormal hysteroscopic findings that were treated in the same setting

	Interval between hysteroscopy and IVF/ICSI treatment not reported

Outcomes

Outcome	Hysteroscopy, N = 110	No hysteroscopy, N = 110
Clinical pregnancy (defined as fetal heart pulsation visualized on ultrasound examination 4 weeks after embryo transfer)	n = 53; % = 48.2	n = 42; % = 38.6
Miscarriage (no definition provided)	n = 13; % = 12	n = 19; % = 17.3

Critical appraisal with Cochrane RoB v2.0

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(Participants were randomised into 2 equal groups using a computer-generated table of random numbers. However, it is not reported if the allocation sequence was concealed)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Some concerns *(Hysteroscopy participants and personnel were not blinded [although lab embryologists and the physician performing the embryo transfer were blinded], however it is unlikely that an absence of blinding would affect outcomes. ITT analysis was used)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(Outcome data were available for all randomised participants)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(The method of measuring the outcome was appropriate*

Section	Question	Answer
		and it is likely that the measurement or ascertainment of the outcome did not differ between the intervention groups and that the assessment of the outcome would not have been influenced by knowledge of the intervention received)
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	High *(There does not appear to be a published protocol, and only clinical pregnancy and not live birth was reported in the analysis)*
Overall bias and Directness	Risk of bias judgement	High *(The study is judged to be at high risk of bias or to have some concerns in the majority of the domains)*
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

Ben Abid, 2021

Bibliographic Reference	Ben Abid, Haifa; Fekih, Myriam; Fathallah, Khadija; Chachia, Salma; Bibi, Mohamed; Khairi, Hedi; Office hysteroscopy before first in vitro fertilization. A randomized controlled trial.; Journal of gynecology obstetrics and human reproduction; 2021; vol. 50 (no. 7); 102109

Study details

Country where study was carried out	Tunisia

Study type	Randomised controlled trial (RCT)
Study dates	January 2016 to September 2017
Inclusion criteria	• infertile women scheduled for their first IVF • younger than 40 years with regular cycles (28–32 days per cycle) • normal uterine cavity defined as normal systematic TVUS transvaginal ultrasound and HSG • FSH level less than 10 UI/l and an antral follicular count ≥12 • BMI between 19 to 30 Kg/m2
Exclusion criteria	• severe endometriosis • Polycystic Ovarian Syndrome (PCOS) according to Rotterdam criteria 2003 • hydrosalpinx (diagnosed by HSG or TVUS) and oocyte receivers
Patient characteristics	**Age, years: Mean (SD)** Hysteroscopy: 32.33 (4.38) No hysteroscopy: 33.32 (5.08) **Duration of infertility, years: Mean (SD)** Hysteroscopy: 4.28 (2.99) No hysteroscopy: 4.75 (3.43)
Intervention(s)/control	**Hysteroscopy (prior to In vitro fertilisation: IVF)** Participants were scheduled for diagnostic hysteroscopy in the mid-follicular phase. IVF was started the cycle after hysteroscopy if hysteroscopy was normal.

	The procedure was performed by an experienced operator (senior), without anaesthesia by vaginoscopy using a 2.9 mm diameter hysteroscope. **No hysteroscopy (immediate IVF)** Not reported **IVF** The IVF stimulation was either agonist or antagonist using recombinant or urinary gonadotrophins and Embryos were transferred after 2 or 3 days. A pregnancy test was performed 14 days after that.
Duration of follow-up	12 months
Sources of funding	The research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.
Sample size	N (total): randomised=171, embryo transfers/women followed within 12 months=151 N (hysteroscopy): randomised=84, embryo transfers/women followed within 12 months=68 (n=16 excluded) N (no hysteroscopy): randomised=87, embryo transfers/women followed within 12 months=83 (n=4 excluded)
Other information	Intrauterine abnormalities were detected in 26/84 (31%) of those analysed in the hysteroscopy group, and 9 abnormalities were treated using operative hysteroscopy in a subsequent session. Only polyps >1cm were treated. Interval between hysteroscopy and IVF: IVF started in the cycle after hysteroscopy if hysteroscopy normal (not clear if abnormalities detected)

Outcomes

Outcome	Hysteroscopy, N = 68	No hysteroscopy, N = 83

Outcome	Hysteroscopy, N = 68	No hysteroscopy, N = 83
Clinical pregnancy (defined as pregnancy rates per cycle per embryo transfer [defined as heart beating seen in pelvic ultrasound])	n = 22; % = 32.4	n = 18; % = 21.7
Live birth (defined as live birth rate per cycle per embryo transfer [defined as delivery of a live fetus after 24 weeks of gestation])	n = 17; % = 23.9	n = 16; % = 19.3
Miscarriage (defined as miscarriage rate per cycle per embryo transfer)	n = 5; % = 5.95	n = 2; % = 2.29

1 **Critical appraisal with Cochrane RoB v2.0**

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(Participants were assigned to the interventions groups using a computer-generated table of random numbers. However, it is not reported if the allocation sequence was concealed)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	High *(Participants and personnel were not blinded, however it is unlikely that an absence of blinding would affect outcomes. ITT analysis was not used and possible that the proportion excluded from the analysis sufficient to have an impact on the result)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	High *(ITT analysis was not used, there was some discrepancy in missing outcome data (19% missing in hysteroscopy group relative to 5% in no hysteroscopy group, and there was no evidence that the result was not biased by missing outcome data)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(The method of measuring the outcomes was appropriate and it is likely that the measurement or ascertainment of the*

Section	Question	Answer
		outcome did not differ between intervention groups and that the assessment of the outcome would not have been influenced by knowledge of the intervention received)
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Some concerns *(There does not appear to be a published protocol, however prespecified outcomes [clinical pregnancy and live birth] are reported in the analysis)*
Overall bias and Directness	Risk of bias judgement	High *(The study is judged to be at high risk of bias or to have some concerns in the majority of the domains)*
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

Demirol, 2004

Bibliographic Reference	Demirol, Aygul; Gurgan, Timur; Effect of treatment of intrauterine pathologies with office hysteroscopy in patients with recurrent IVF failure.; Reproductive biomedicine online; 2004; vol. 8 (no. 5); 590-4

Study details

Country where study was carried out	Turkey
Study type	Randomised controlled trial (RCT)
Study dates	May 2000 and February 2003

Inclusion criteria	• 2 or more failed IVF cycles, in which two or more good quality embryos were transferred • normal HSG (normal intrauterine cavity and bilaterally patent tubes) • aged 24 to 40 years • primary infertility
Exclusion criteria	Not reported
Patient characteristics	**Age, years: Mean (SD)** Hysteroscopy: 35.6 (6.4) No hysteroscopy: 34.3 (11.6) **Duration of infertility, years: Mean (SD)** Hysteroscopy: 5.9 (3.7) No hysteroscopy: 6.2 (4.4) **Number of failed transfer cycles: Mean (SD)** Hysteroscopy (with normal hysteroscopic findings): 2.6 (0.4) Hysteroscopy (with abnormal hysteroscopic findings): 3.1 (0.1) No hysteroscopy: 2.8 (0.2)
Intervention(s)/control	**Hysteroscopy (office hysteroscopy prior to In vitro fertilisation: IVF)** The procedure was performed in the early proliferative phase using saline distention medium and a 5 mm continuous flow office hysteroscope. The scope was based on a rod lens system (diameter of 2.9 mm and 30° view). The continuous flow sheath consisted of an oval profile and maximum 5 mm diameter with an incorporated 5Fr working channel. The

	procedures were carried out without anaesthesia. Diagnosed intrauterine lesions were operated during the office procedure. Hysteroscopies were performed 2-6 months after the last failed IVF cycles by the same physician. **No hysteroscopy (no hysteroscopy prior to IVF)** Not reported **IVF** IVF treatments were performed on the menstrual cycles after office hysteroscopies. Ovarian stimulation protocol started with daily subcutaneous injections of leuprolide acetate (1 mg) on day 21 of that cycle and continued until day 3 of the next menstrual cycle. After achieving ovarian suppression (oestradiol < 40 pg/ml) 225 IU/day of gonadotrophin (recombinant FSH) was started on day 3-4 and adjusted if needed. Ovulatory dose of 10,000 IU HCG (human chorionic gonadotrophin) was given when >=2 follicles of =>18 mm diameter were observed. Oocyte retrieval was performed using TVS, embryos were transferred on day 3 and a max of 4 embryos were transferred. Progesterone vaginal suppositories were used for luteal support.
Duration of follow-up	Not reported
Sources of funding	Not reported
Sample size	N (total): randomised=421, analysed=418 (n=3 excluded) N (hysteroscopy): randomised=210, analysed=209 (n=1 excluded) N (no hysteroscopy): randomised=211, analysed=209 (n=2 excluded) The study reported results separately for participants in the hysteroscopy group with normal hysteroscopic findings (N randomised=154, N analysed=154) and abnormal hysteroscopic findings (N randomised=56, N analysed=55)
Other information	56/210 (27%) of those who received hysteroscopy had intrauterine abnormalities diagnosed and treated during the office hysteroscopy.

	Paper reports data separately for those with normal and abnormal hysteroscopic findings but combined means calculated. The measure of variance that is reported for demographic data is not clear but it appears to be standard error and this has been converted to standard deviation for this review. Interval between hysteroscopy and IVF: IVF was carried out on the menstrual cycle following hysteroscopy

Outcomes

Outcome	Hysteroscopy, N = 209	No hysteroscopy, N = 209
Clinical pregnancy (defined as clinical pregnancy [confirmed by TVS at 6–7 weeks of gestation])	n = 67; % = 32	n = 45; % = 21.6
Miscarriage (defined as first trimester abortion)	n = 7; % = 3.3	n = 9; % = 4.2

Critical appraisal with Cochrane RoB v2.0

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(Participants were randomized using computer-generated random numbers. However, it is not reported if the allocation sequence was concealed)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Some concerns *(Participants and personnel were aware of the intervention. However, it is unlikely that an absence of blinding would affect outcomes. Modified ITT analysis [99% of N randomised] was used)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(Outcome data were available for 99% of randomised participants)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for	Low

Section	Question	Answer
	measurement of the outcome	*(The method of measuring the outcomes was appropriate and it is likely that the measurement or ascertainment of the outcome did not differ between intervention groups and that the assessment of the outcome would not have been influenced by knowledge of the intervention received)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	High *(There does not appear to be a published protocol, and only clinical pregnancy and not live birth was reported in the analysis)*
Overall bias and Directness	Risk of bias judgement	High *(The study is judged to be at high risk of bias or to have some concerns in the majority of the domains)*
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

El-Nashar, 2011

Bibliographic Reference	El-Nashar, IH; Nasr, A; The role of hysteroscopy before intracytoplasmic sperm injection (ICSI): a randomized controlled trial; Fertility and sterility; 2011; vol. 96 (no. 3); 266

Study details

Country where study was carried out	Egypt

Study type	Randomised controlled trial (RCT) This study has been published as an abstract only
Study dates	Not reported
Inclusion criteria	• women with primary infertility, who were scheduled for ICSI
Exclusion criteria	Not reported
Patient characteristics	Not reported
Intervention(s)/control	**Hysteroscopy (hysteroscopy prior to Intracytoplasmic sperm injection: ICSI)** A diagnostic hysteroscopy with directed biopsy was performed and any intrauterine abnormalities were corrected **No hysteroscopy (No hysteroscopy prior to ICSI)** Participants did not undergo diagnostic hysteroscopy **ICSI** Conventional methods for microinjection of oocytes and in vitro culture of oocytes and embryos were used
Duration of follow-up	Not reported
Sources of funding	Not reported
Sample size	N (total): 124 N (hysteroscopy): 62

	N (no hysteroscopy): 62 It is not clear from the abstract whether all participants were included in the analysis
Other information	This study was published as an abstract only. Extracted data is based on information available in the abstract only. The risk of bias assessment for this study has been taken from the following Cochrane review: Kamath, et al. Screening hysteroscopy in subfertile women and women undergoing assisted reproduction. The Cochrane database of systematic reviews; 2019; vol. 4; cd012856

Outcomes

Outcome	**Hysteroscopy, N = 62**	**No hysteroscopy, N = 62**
Clinical pregnancy (defined as fetal heartbeats visualized on transvaginal ultrasonography)	n = 25; % = 40.3	n = 15; % = 24.2

Critical appraisal with Cochrane RoB v2.0

This study is published as an abstract only and the critical appraisal is based on the risk of bias assessment published in the following Cochrane review: Kamath, et al. Screening hysteroscopy in subfertile women and women undergoing assisted reproduction. The Cochrane database of systematic reviews; 2019; vol. 4; cd012856

Section	**Question**	**Answer**
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(The authors described the study as randomised. However, there is no information about the randomisation method or concealment of the allocation sequence)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	High *(Participants and personnel were not blinded, although it is unlikely that an absence of blinding would influence outcomes. However, it is unclear whether an appropriate*

Section	Question	Answer
		analysis was used)
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	High *(There was no information provided about missing outcome data)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(There was no information on the method of measuring the outcome, however it is unlikely that the measurement or ascertainment of the outcome differed between intervention groups, nor that the assessment of the primary outcome [pregnancy] could have been influenced by knowledge of the intervention received)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	High *(There does not appear to be a published protocol, and only clinical pregnancy and not live birth was reported in the analysis)*
Overall bias and Directness	Risk of bias judgement	High *(The study is judged to be at high risk of bias or to have some concerns in the majority of the domains)*
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

Elsetohy, 2015

Bibliographic Reference	Elsetohy, Khaled Ahmed Abdel Aziz; Askalany, Ahmed H; Hassan, Mohamed; Dawood, Zamam; Routine office hysteroscopy prior to ICSI vs. ICSI alone in patients with normal transvaginal ultrasound: a randomized controlled trial.; Archives of gynecology and obstetrics; 2015; vol. 291 (no. 1); 193-9

1 **Study details**

Country where study was carried out	Egypt
Study type	Randomised controlled trial (RCT)
Study dates	January 2012 to June 2013
Inclusion criteria	• primary or secondary infertility • candidate for ICSI • normal transvaginal ultrasonographic examination performed during the follicular phase of the menstrual cycle, apart from intramural myomas without uterine cavity deformity
Exclusion criteria	• uterine factor of infertility • history of recurrent miscarriage • abnormal HSG, or abnormal transvaginal ultrasound • inter-menstrual blood loss • previous intrauterine surgery • contraindication for hysteroscopy
Patient characteristics	**Age, years: Mean (SD)** Hysteroscopy: 31.1 (5.8), range 16-44 No hysteroscopy: 29.9 (4.8), range 20-40 **Duration of infertility, years: Mean (SD)** Hysteroscopy: 5.9 (3.7), range 0.5-16

	No hysteroscopy: 5.7 (3.4), range 1-20 **Previous implantation failure** Participants were scheduled for a first IVF/ICSI treatment cycle
Intervention(s)/control	**Hysteroscopy (Intracytoplasmic sperm injection [ICSI] with hysteroscopy)** The procedure was scheduled in the early–mid follicular phase of a menstrual cycle (day 3–12) and was performed using a 4.3-mm outer-diameter continuous flow hysteroscope with a five French working channel and a 30 direction of view. **No hysteroscopy** Not reported **ICSI** Performed within 3 months of hysteroscopic examination. Induction of ovulation was performed using the long protocol and oocyte retrieval was carried out 36 h after HCG administration. 800 mg natural progesterone suppository in two separate dosages (Prontpgest/Cyclogest 400 mg 1 9 2/day) for 2 weeks after ovum pick-up were used for luteal support.
Duration of follow-up	Participants were followed until the end of pregnancy
Sources of funding	Not reported
Sample size	N (total): randomised=203, analysed=193 N (hysteroscopy): randomised=102, analysed=97 (n=5 excluded) N (no hysteroscopy): randomised=101, analysed=96 (n=5 excluded)

Other information	43% showed abnormal hysteroscopic findings that were treated in the same or a subsequent session. Interval between hysteroscopy and ICSI: within 3 months

Outcomes

Outcome	Hysteroscopy, N = 97	No hysteroscopy, N = 96
Live birth (defined as baby take home rate) The study doesn't describe baby-take-home rate, however it appears this may be the number of live births per number of IVF/ICSI treatments (cycles)	n = 58; % = 59.8	n = 33; % = 34.3
Pregnancy (defined as pregnancy by ultrasound) 3 weeks after embryo transfer	n = 68; % = 70.1	n = 44; % = 45.8

Critical appraisal with Cochrane RoB v2.0

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(Participants were randomised using a computer-generated table of random numbers. However, it is not reported if the allocation sequence was concealed)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Some concerns *(Participants and personnel were aware of the intervention. However, it is unlikely that an absence of blinding would affect outcomes. Modified ITT analysis [95% of N randomised] was used)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(Outcome data were available for 95% of randomised participants)*

Section	Question	Answer
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(The method of measuring the outcomes was appropriate and it is likely that the measurement or ascertainment of the outcome did not differ between intervention groups and that the assessment of the outcome would not have been influenced by knowledge of the intervention received)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Some concerns *(There does not appear to be a published protocol, however prespecified outcomes [clinical pregnancy and live birth] are reported in the analysis)*
Overall bias and Directness	Risk of bias judgement	High *(The study is judged to have some concerns across multiple domains that substantially lowers confidence in the result)*
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

El-Toukhy, 2016

Bibliographic Reference El-Toukhy, Tarek; Campo, Rudi; Khalaf, Yacoub; Tabanelli, Carla; Gianaroli, Luca; Gordts, Sylvie S; Gordts, Stephan; Mestdagh, Greet; Mardesic, Tonko; Voboril, Jan; Marchino, Gian L; Benedetto, Chiara; Al-Shawaf, Talha; Sabatini, Luca; Seed, Paul T; Gergolet, Marco; Grimbizis, Grigoris; Harb, Hoda; Coomarasamy, Arri; Hysteroscopy in recurrent in-vitro fertilisation failure (TROPHY): a multicentre, randomised controlled trial.; Lancet (London, England); 2016; vol. 387 (no. 10038); 2614-2621

Study details

Counties where study was carried out	United Kingdom, Belgium, Italy and the Czech Republic
Study type	Randomised controlled trial (RCT)
Study dates	January 2010 to December 2013
Inclusion criteria	• women below the age of 38 years of age (women aged 37 years only eligible if they had at least 8 oocytes retrieved in previous IVF cycle) • normal transvaginal ultrasound of the uterine cavity • previous 2-4 IVF treatment cycles ending in an embryo transfer but no pregnancy
Exclusion criteria	• hysteroscopy within 2 months before randomisation • submucous or intramural uterine fibroids diagnosed by ultrasound to be distorting the uterine cavity • untreated tubal hydrosalpinges • BMI above 35 kg/m2
Patient characteristics	**Age, years: Mean (SD)** Hysteroscopy: 32.7 (3.1) No hysteroscopy: 32.7 (3.1) **Duration of infertility, years: Mean (SD)** Hysteroscopy: 4.2 (3.4) No hysteroscopy: 4.2 (2.8) **Number of previous failed IVF cycles: Mean (SD)**

	Hysteroscopy: 2.7 (0.9) No hysteroscopy: 2.7 (1.0)
Intervention(s)/control	**Hysteroscopy (outpatient hysteroscopy prior to in vitro fertilisation: IVF)** The procedure was performed within 14 days of menstruation and IVF was started in the following month according to a standard IVF protocol. A rigid 30° view 2.9 mm diameter hysteroscope was used. Hysteroscopy was started with the single-flow 2.9 mm instrument to inspect the cervical canal and uterine cavity, and if necessary, the accessory diagnostic (3.7 mm) or operative (4.4 mm) sheath was used to establish a double-flow mode and allow operative intervention. Pre-operative analgesia, antibiotics, sedation or cervical preparation was not used routinely. **No hysteroscopy (no hysteroscopy prior to IVF)** The IVF treatment cycle was started according to a standard IVF protocol without undergoing hysteroscopy. **IVF** IVF was started in the menstrual cycle immediately following hysteroscopy. Multi-follicular ovarian stimulation was started by using follicle stimulating hormone injections (starting dose of 150-450 IU daily). 5,000-10,000 IU of hCG were used for oocyte maturation when =>2 18 mm follicles were detected on ultrasound scan. After 34-38 hours following hCG administration, ultrasound-guided oocyte retrieval was performed. 1-3 embryos were transferred. Luteal phase was supported with progesterone supplementation and continued for up to 8 weeks gestation if pregnancy had occurred.
Duration of follow-up	Not reported
Sources of funding	The European Society of Human Reproduction and Embryology and the European Society for Gynaecological Endoscopy provided funding for trial co-ordination and meetings. Karl Storz Company provided the hysteroscopy equipment for all centres and Tristel Solutions Limited (Snailwell, Cambridgeshire, United Kingdom) provided the equipment disinfecting systems for five of the eight participating centres.
Sample size	N (total): randomised=702, received IVF=640 (n=62 excluded)

	N (hysteroscopy): randomised=350, received intervention=323 (n=26 excluded, n=1 received saline hysterosonography) N (no hysteroscopy): randomised=352, received intervention=348 (n=4 received hysteroscopy at their request, prior to IVF)
Other information	The trial was registered on the ISRCTN Registry (#ISRCTN35859078) 34/323 (11%) who received hysteroscopy had uterine abnormalities detected, and 15 were treated surgically. Interval between hysteroscopy and IVF: 1 month

Outcomes

Outcome	**Hysteroscopy, N = 350**	**No hysteroscopy, N = 352**
Live birth (defined as live birth after 24 weeks gestation) Rate per participant randomly assigned to intervention	n = 102; % = 29	n = 102; % = 29
Clinical pregnancy (defined as the observation of fetal cardiac activity on ultrasound scan four or more weeks after embryo transfer) Rate per participant randomly assigned to intervention	n = 121; % = 35	n = 116; % = 33
Miscarriage (defined as pregnancy loss before 24 weeks gestation)	n = 29; % = 22	n = 33; % = 24

Critical appraisal with Cochrane RoB v2.0

Section	**Question**	**Answer**
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low *(Randomisation performed using a minimisation procedure with computer-based algorithm. Allocation was concealed by using centralised allocation)*

Section	Question	Answer
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Some concerns *(Hysteroscopy participants and personnel and the physician performing the embryo transfer were not blinded [although embryologists were blinded], however it is unlikely that an absence of blinding would affect outcomes. ITT analysis was used)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(ITT analysis was used)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(The method of measuring the outcome was appropriate and it is likely that the measurement or ascertainment of the outcome did not differ between intervention groups)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low *(There is a published protocol and all prespecified outcomes are reported in the analysis)*
Overall bias and Directness	Risk of bias judgement	Some concerns *(The study is judged to have some concerns due to lack of blinding but the method of analysis is appropriate and unlikely that an absence of blinding would affect outcomes)*
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

Moramezi, 2012

Bibliographic Reference	Moramezi, Farideh; Barati, Mojgan; Mohammadjafari, Razieh; Barati, Sara; Hemadi, Masoud; Effect of hysteroscopy before intra uterine insemination on fertility in infertile couples.; Pakistan journal of biological sciences: PJBS; 2012; vol. 15 (no. 19);

942-6

Study details

Country where study was carried out	Iran
Study type	Randomised controlled trial (RCT)
Study dates	June 2011 to April 2012
Inclusion criteria	• couples diagnosed with infertility who were candidates for IUI • absence of sexually transmitted disease, pelvic inflammatory disease or pregnancy
Exclusion criteria	• active vaginal bleeding
Patient characteristics	**Age, years: Mean (SD)** All participants: 32.3 (4.5), range 22-44 Hysteroscopy: 28.8 (3) No hysteroscopy: 29.8 (3) **Duration of infertility, years: Mean (SD)** All participants: Median 4.7 (1.4), range 1.4-6.1 Hysteroscopy: 4.4 (0.57) No hysteroscopy: 3.7 (0.49)

	Previous implantation failure Not reported
Intervention(s)/control	**Hysteroscopy (Hysteroscopy prior to Intrauterine insemination: IUI)** No details reported on the hysteroscopy procedure. **No hysteroscopy (IUI without Hysteroscopy)** Not reported **IUI and ovarian stimulation** First Clomifen (50-100g/day) and after 5 days HMG (75 units/day) were given. Transvaginal sonography was performed between day 12-14and a single dose of HCG was given to induce ovulation (when the follicles were 18-20mm). The swim up method was used to wash semen specimens and single IUI using (volume of 0.3mL) was performed 36 hours after rhCG injection.
Duration of follow-up	Not reported
Sources of funding	Supported by a research grant from the Ahvaz Jundishapur University of Medical Sciences
Sample size	N (total): 110 N (hysteroscopy): 55 N (no hysteroscopy): 55
Other information	26/55 (47%) of those receiving hysteroscopy had abnormalities identified and treated (not clear if treatment was performed in the same or a subsequent session). Interval between hysteroscopy and IUI: If hysteroscopy normal IUI performed in the next cycle, if abnormalities detected

	IUI performed after 2-3 cycles

Outcomes

Outcome	Hysteroscopy, N = 55	No hysteroscopy, N = 55
Clinical pregnancy (defined as clinical pregnancy confirmed with vaginal ultrasound) Carried out 2-4 weeks after IUI	n = 22; % = 40	n = 11; % = 20
Miscarriage (defined as abortion)	n = 1; % = 1.8	n = 2; % = 3.6
Any perioperative adverse event (defined as undesirable reaction or surgical complication)	n = 0; % = 0	n = 0; % = 0

Critical appraisal with Cochrane RoB v2.0

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(Reported that participants were divided randomly into 2 equal groups, however, no details reported on randomisation technique or allocation sequence concealment, although there does not appear to be a baseline imbalance between groups)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	High *(Participants and personnel were not blinded, although it is unlikely that an absence of blinding would influence outcomes. However, it is unclear whether an appropriate analysis was used)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	High *(There was no information provided about missing outcome*

Section	Question	Answer
		data)
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(The method of measuring the outcome was appropriate and it is likely that the measurement or ascertainment of the outcome did not differ between the intervention groups)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	High *(There does not appear to be a published protocol, and live birth was not reported in the analysis)*
Overall bias and Directness	Risk of bias judgement	High *(The study is judged to be at high risk of bias or to have some concerns in the majority of the domains)*
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

Pounikar, 2023

Bibliographic Reference	Pounikar, Minakshi; Shrivastava, Deepti; Sharma, Sapna; Tadghare, Jitendra; Role of Hysteroscopy in Patients with Previous In Vitro Fertilization Failure: An Institutional Experience in Rural Population.; Journal of obstetrics and gynaecology of India; 2023; vol. 73 (no. 1); 77-82

Study details

Country where study was carried out	India
Study type	Randomised controlled trial (RCT)

Study dates	September 2020 to August 2021
Inclusion criteria	• primary or secondary infertility • women under 45 years of age • one or more embryo implantation failures in previous IVF cycles • normal uterine findings on transvaginal USG or HSG
Exclusion criteria	• already diagnosed intrauterine pathology
Patient characteristics	**Age, years: Mean (SD)** Hysteroscopy: 32.90 (1.97) No hysteroscopy: 33.57 (3.21) **Duration of infertility: Mean (SD)** Hysteroscopy: 7.60 (3.87) No hysteroscopy: 8.13 (3.98) **1 previous IVF failure: Number (%)** Hysteroscopy: 18 (20) No hysteroscopy: 30 (33.3) **≥1 previous IVF failure: Number (%)** Hysteroscopy: 72 (80)

	No hysteroscopy: 60 (66.6)
Intervention(s)/control	**Hysteroscopy (Hysteroscopy prior to In vitro fertilisation: IVF)** No details reported on hysteroscopy procedure **No hysteroscopy (IVF without hysteroscopy)** Not reported **IVF** No details reported on the IVF treatment
Duration of follow-up	Not reported
Sources of funding	The authors received no financial support for the research
Sample size	N (total): 180 N (hysteroscopy): 90 N (no hysteroscopy): 90
Other information	36/90 (40%) of those receiving hysteroscopy had intrauterine abnormalities detected and treated (in the same session). Interval between hysteroscopy and IVF: IVF performed in the next cycle following hysteroscopy

1

2 **Outcomes**

Outcome	**Hysteroscopy, N = 90**	**No hysteroscopy, N = 90**

Outcome	Hysteroscopy, N = 90	No hysteroscopy, N = 90
Clinical pregnancy (defined as early scan showing live pregnancy with cardiac activity) The early scan took place 2 weeks after the positive beta HCG test	n = 27; % = 30	n = 21; % = 23.3

Critical appraisal with Cochrane RoB v2.0

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	High *(Paper reports 'prospective randomized study', however, no details reported on method of randomisation or allocation concealment. Baseline imbalance between groups (fewer participants had had only 1 previous IVF failure in the hysteroscopy relative to no hysteroscopy group, p<0.01) suggests a problem with the randomisation process)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	High *(Participants and personnel were not blinded, although it is unlikely that an absence of blinding would influence outcomes. However, it is unclear whether an appropriate analysis was used)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	High *(There was no information provided about missing outcome data)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(The method of measuring the outcome was appropriate and it is likely that the measurement or ascertainment of the outcome did not differ between the intervention groups)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	High *(There does not appear to be a published protocol, and only clinical pregnancy and not live birth was reported in the analysis)*
Overall bias and Directness	Risk of bias judgement	High *(The study is judged to be at high risk of bias across all but*

Section	Question	Answer
		one domain)
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

Rama Raju, 2006

Bibliographic Reference	Rama Raju GA; Shashi Kumari G; Krishna KM; Prakash GJ; Madan K; Assessment of uterine cavity by hysteroscopy in assisted reproduction programme and its influence on pregnancy outcome.; Archives of gynecology and obstetrics; 2006; vol. 274 (no. 3)

Study details

Country where study was carried out	India
Study type	Randomised controlled trial (RCT)
Study dates	January 2002 to February 2005
Inclusion criteria	• participants who had undergone 2 or more failed IVF cycles, in which 2 or more good quality embryos were transferred per procedure • primary infertility • normal appearance of the uterine cavity on hysterosalpingography
Exclusion criteria	Not reported

Patient characteristics	**Age, years: Mean (SD)** All participants: Range 26-30 Hysteroscopy (with normal hysteroscopic findings): 27.40 (0.60) Hysteroscopy (with abnormal hysteroscopic findings): 29.04 (0.92) No hysteroscopy: 26.72 (0.46) **Duration of infertility, years: Mean (SD)** All participants: Range 6-8 Hysteroscopy (with normal hysteroscopic findings): 6.94 (0.72) Hysteroscopy (with abnormal hysteroscopic findings): 7.12 (0.52) No hysteroscopy: 7.01 (0.10) **Failed transfer cycles: Number (%)** Hysteroscopy (with normal hysteroscopic findings): 2.8 (0.3) Hysteroscopy (with abnormal hysteroscopic findings): 2.4 (0.4) No hysteroscopy: 2.60 (0.1)
Intervention(s)/control	**Hysteroscopy (office hysteroscopy prior to In vitro fertilisation: IVF)** The procedure was performed in early proliferative phase using 1.9 mm miniature Karl Storz hysteroscope (30 degree view with a 3 mm Bettochi continuous flow sheath). No anaesthesia was used. **No hysteroscopy (no hysteroscopy prior to IVF)**

	Not reported **Ovarian stimulation and IVF** Down regulation was started using IM of Decapeptide 3.75 mg on day 21 of the cycle and was confirmed by measuring E2 (< 50 pg/ml) and LH levels (< 1 ng/ml). Controlled ovarian stimulation was achieved using recombinant FSH adjusting the dose if required. hCG (human chorionic gonadotropin) at a dose of 10,000 IU was given after 2 follicles of =>18 mm were detected in the ultrasound scan. Oocyte retrieval was planned 36 h later by TVS. Embryo transfer was performed on day 3 and luteal phase was supported with progesterone vaginal suppositories.
Duration of follow-up	Not reported (diagnosis of pregnancy was made 4 weeks after embryo transfer)
Sources of funding	Not reported
Sample size	N (total): randomised=520, analysed=515 (n=5 excluded) N (hysteroscopy): randomised=255, analysed=253 (n=2 excluded) N (no hysteroscopy): randomised=265, analysed=262 (n=3 excluded) The study reported results separately for participants in the hysteroscopy group with normal hysteroscopic findings (N randomised=160, N analysed=159) and abnormal hysteroscopic findings (N randomised=95, N analysed=94)
Other information	95/255 (37%) of those receiving hysteroscopy had uterine cavity abnormalities identified and treated (during the same session). Interval between hysteroscopy and IVF: Not reported

Outcomes

Outcome	**Hysteroscopy, N = 253**	**No hysteroscopy, N = 262**

Outcome	Hysteroscopy, N = 253	No hysteroscopy, N = 262
Live birth (defined as live birth)	n = 72; % = 28.4	n = 44; % = 16.6
Clinical pregnancy (defined as visualization of fetal heart pulsation four weeks after embryo transfer by transvaginal sonography)	n = 109; % = 42.7	n = 69; % = 26.2
Miscarriage (defined as miscarriage) Percentage of clinical pregnancies	n = 36; % = 33.3	n = 25; % = 36.2

1 **Critical appraisal with Cochrane RoB v2.0**

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(Participants were randomized into 2 groups using computer generated random numbers. However, no information is reported about concealment of the allocation sequence)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Some concerns *(Participants and personnel were aware of the intervention. However, it is unlikely that an absence of blinding would affect outcomes. Modified ITT analysis [99% of N randomised] was used)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(Outcome data were available for 99% of randomised participants)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Some concerns *(It is likely that the measurement or ascertainment of the outcome did not differ between the intervention groups, however definition of live birth was not provided)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for	Some concerns *(There does not appear to be a published protocol, however*

Section	Question	Answer
	selection of the reported result	*prespecified outcomes [clinical pregnancy and live birth] are reported in the analysis)*
Overall bias and Directness	Risk of bias judgement	High *(The study is judged to have some concerns across multiple domains that substantially lowers confidence in the result)*
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

Shawki, 2012

Bibliographic Reference	Shawki, H.E.; Elmorsy, M.; Eissa, M.K.; Routine office hysteroscopy prior to ICSI and its impact on assisted reproduction program outcome: A randomized controlled trial; Middle East Fertility Society Journal; 2012; 17, 14-21

Study details

Country where study was carried out	Egypt
Study type	Randomised controlled trial (RCT)
Study dates	October 2007 to October 2010
Inclusion criteria	• women with normal hysterosalpingogram (HSG) and/or transvaginal ultrasonography
Exclusion criteria	• uterine factor of infertility • previous intrauterine surgery or contraindication for hysteroscopy

	• had not had HSG in the 2-3 months prior to the study
Patient characteristics	**Age, years: Mean (SD)** Hysteroscopy: 33 (11.14), range 22-29 No hysteroscopy: 31 (12.32), range 23-37 **Duration of infertility, years: Mean (SD)** Hysteroscopy: 9.3 (1.15), range 4-14 No hysteroscopy: 7.5 (2.4), range 3-12 **Number of ICSI trial: Number (%)** **1st trial** Hysteroscopy: 22 (20.9) No hysteroscopy: 20 (18) **2nd trial** Hysteroscopy: 17 (16) No hysteroscopy: 15 (13) **More than 2** Hysteroscopy: 12 (11.4) No hysteroscopy: 8 (7.2)
Intervention(s)/control	**Hysteroscopy (Intracytoplasmic sperm injection [ICSI] after office hysteroscopy)**

	The procedure was performed using a 3.5-mm mini-hysteroscope with a 0 degree grade. No pharmacological preparations/local anaesthetics were given before the examination. **No hysteroscopy (ICSI without office hysteroscopy)** Not reported **Ovarian stimulation and ICSI** Down regulation was achieved using leucrine 0.1 mm daily for 10 days or until the start of menses and ovarian stimulation was achieved using recombinant FSH. The dose of gonadotropin was adjusted based on age, baseline day 3 FSH level and previous response to controlled ovarian hyperstimulation. HCG (10,000 IU) was given when =>3 follicles reached >18 mm in diameter and oocytes were retrieved 36 h after HCG injection using TVU. Standard ICSI techniques were used for fertilization of the oocytes. Luteal phase was supported with progesterone using prontogest vaginal suppositories (400 mg/day) starting on the day of oocyte retrieval and continued until the day of pregnancy test.
Duration of follow-up	Not reported
Sources of funding	The Department of Obstetrics and Gynecology and El-Menya Infertility Research and Treatment Center (MIRTC), Faculty of Medicine, El-Menya University, Egypt
Sample size	N (total): randomised=240, analysed=215 N (hysteroscopy): randomised=120, analysed=105 (n=15 excluded); The hysteroscopy group was further analysed according to participants with normal office hysteroscopy (n=70) and participants with abnormal office hysteroscopy findings (n=35) that were corrected before ICSI N (no hysteroscopy): randomised=120, analysed=110 (n=10 excluded)
Other information	35/105 (33%) of participants analysed in the hysteroscopy group had abnormalities detected and treated (not clear if in same or subsequent session).

	Interval between hysteroscopy and ICSI: Not reported

Outcomes

Outcome	Hysteroscopy, N = 105	No hysteroscopy, N = 110
Clinical pregnancy (defined as cases who had sonographic evidence of intrauterine pregnancy with positive fetal cardiac activity)	n = 40; % = 38	n = 30; % = 27.2

Critical appraisal with Cochrane RoB v2.0

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low *(Randomisation conducted using computer generated random numbers and the allocation sequence was concealed with sealed envelopes)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	High *(Participants and personnel were not blinded, however it is unlikely that an absence of blinding would affect outcomes. ITT analysis was not used and possible that the proportion excluded from the analysis sufficient to have an impact on the result)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	High *(ITT analysis was not performed)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(The method of measuring the outcome was appropriate and it is likely that the measurement or ascertainment of the outcome did not differ between intervention groups)*
Domain 5. Bias in selection of the reported	Risk-of-bias judgement for selection	High

Section	Question	Answer
result	of the reported result	*(There does not appear to be a published protocol, and only clinical pregnancy and not live birth was reported in the analysis)*
Overall bias and Directness	Risk of bias judgement	High *(The study is judged to have a high risk of bias across multiple domains)*
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

Smit, 2016

Bibliographic Reference	Smit, Janine G; Kasius, Jenneke C; Eijkemans, Marinus J C; Koks, Carolien A M; van Golde, Ronald; Nap, Annemiek W; Scheffer, Gabrielle J; Manger, Petra A P; Hoek, Annemieke; Schoot, Benedictus C; van Heusden, Arne M; Kuchenbecker, Walter K H; Perquin, Denise A M; Fleischer, Kathrin; Kaaijk, Eugenie M; Sluijmer, Alexander; Friederich, Jaap; Dykgraaf, Ramon H M; van Hooff, Marcel; Louwe, Leonie A; Kwee, Janet; de Koning, Corry H; Janssen, Ineke C A H; Mol, Femke; Mol, Ben W J; Broekmans, Frank J M; Torrance, Helen L; Hysteroscopy before in-vitro fertilisation (inSIGHT): a multicentre, randomised controlled trial.; Lancet (London, England); 2016; vol. 387 (no. 10038); 2622-2629

Study details

Country where study was carried out	Netherlands
Study type	Randomised controlled trial (RCT)
Study dates	May to August 2013

Inclusion criteria	• infertile women scheduled to start IVF or ICSI treatment • normal transvaginal ultrasound of the uterine cavity
Exclusion criteria	• history of 2 or more miscarriages or intermenstrual blood loss • undergone hysteroscopy previously
Patient characteristics	**Age, years: Mean (SD)** Hysteroscopy: 33 (4.4) No hysteroscopy: 33 (4.5) **Duration of infertility, years: Mean (SD)** Hysteroscopy: 2.6 (1.9) No hysteroscopy: 2.1 (2.7) **Previous implantation failure** Women were scheduled for their first IVF treatment
Intervention(s)/control	**Hysteroscopy (hysteroscopy followed by In vitro fertilisation: IVF)** The procedure was scheduled in the early to midfollicular phase of the cycle in an outpatient setting without anaesthesia. No further detail reported on the procedure. **No hysteroscopy (immediate IVF)** Not reported **IVF**

	Protocols such as rec-FSH or HMG combined with a GnRH agonist protocol or a GnRH antagonist protocol were used. Oocyte maturation was achieved by administering HCG when =>3 follicles of >16 mm were present. Oocyte retrieval was carried out 36 h after HCG administration. Luteal phase was supported with natural micronised progesterone (600 mg) in 3 separate dosages starting in the evening after oocyte retrieval and continued until 18 days after ovum pick-up.
Duration of follow-up	18 months
Sources of funding	The Dutch Organisation for Health Research and Development (ZonMW)
Sample size	N (total): randomised=750, completed 18 months of follow-up=708, included in analysis for outcomes in the table below=742 N (hysteroscopy): randomised=373, completed 18 months of follow-up=355, included in analysis=369 N (no hysteroscopy): randomised=377, completed 18 months of follow-up=353, included in analysis =373
Other information	According to the study protocol first IVF/ICSI treatment cycle. 37/369 (10%) of participants analysed in the hysteroscopy group had abnormalities detected and treated (in the same session). Interval between hysteroscopy and IVF/ICSI: 1-3 months

Outcomes

Outcome	**Hysteroscopy, N = 369**	**No hysteroscopy, N = 373**
Live birth (defined as ongoing pregnancy resulting in delivery of a live fetus after 24 weeks of gestation) Ongoing pregnancy within 18 months of randomisation and resulting in live birth	n = 209; % = 57	n = 200; % = 54
Clinical pregnancy (defined as ongoing pregnancy confirmed by transvaginal ultrasound)	n = 211; % = 57	n = 203; % = 54

Outcome	Hysteroscopy, N = 369	No hysteroscopy, N = 373
Miscarriage (defined as absence of a fetal heartbeat at week 7 or week 12 of gestation) Data per embryo transfer (n=266 in hysteroscopy group, n=231 in no hysteroscopy group)	n = 48; % = 18	n = 34; % = 15
Pregnancy loss (defined as total pregnancy loss including biochemical and miscarriage) Data per embryo transfer (n=266 in hysteroscopy group, n=231 in no hysteroscopy group)	n = 87; % = 33	n = 54; % = 23

1 **Critical appraisal – Cochrane RoB 2**

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low *(Participants were randomly assigned to 2 groups; web-based randomisation with a variable block size was used to allocate participants to groups and stratified assignment by centre)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Some concerns *(Participants and personnel were aware of the intervention. However, it is unlikely that an absence of blinding would affect outcomes. Modified ITT analysis [99% of N randomised] was used)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(Outcome data were available for 99% of randomised participants)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(The method of measuring the outcome was appropriate and it is likely that the measurement or ascertainment of the outcome did not differ between intervention groups)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low *(There is a published protocol and all prespecified outcomes are reported in the analysis)*
Overall bias and Directness	Risk of bias judgement	Some concerns

Section	Question	Answer
		(The study is judged to have some concerns due to lack of blinding but the method of analysis is appropriate and unlikely that an absence of blinding would affect outcomes)
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

RCT: randomised controlled trial; RoB: risk of bias

Appendix E Forest plots

Forest plots for review question: What is the effectiveness of screening hysteroscopy (with or without treatment of any detected uterine cavity abnormalities) on reproductive outcomes for people with female factor fertility problems?

This section includes forest plots only for outcomes that are meta-analysed. Outcomes from single studies are not presented here; the quality assessment for such outcomes is provided in the GRADE profiles in appendix F.

Figure 2: Hysteroscopy versus no hysteroscopy prior to IVF or IUI: Live birth (overall)

	Hysteroscopy		No hysteroscopy			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
Aghahosseini 2012	50	142	45	211	15.8%	1.65 [1.17, 2.32]
Ben Abid 2021	17	68	16	83	8.9%	1.30 [0.71, 2.37]
Elsetohy 2015	58	97	33	96	16.5%	1.74 [1.26, 2.40]
El-Toukhy 2016	102	350	102	352	19.7%	1.01 [0.80, 1.27]
Rama Raju 2006	72	253	44	262	16.1%	1.69 [1.21, 2.36]
Smit 2016	209	369	200	373	23.1%	1.06 [0.93, 1.20]
Total (95% CI)		**1279**		**1377**	**100.0%**	**1.34 [1.07, 1.67]**
Total events	508		440			

Heterogeneity: Tau² = 0.05; Chi² = 18.89, df = 5 (P = 0.002); I² = 74%

Test for overall effect: Z = 2.56 (P = 0.01)

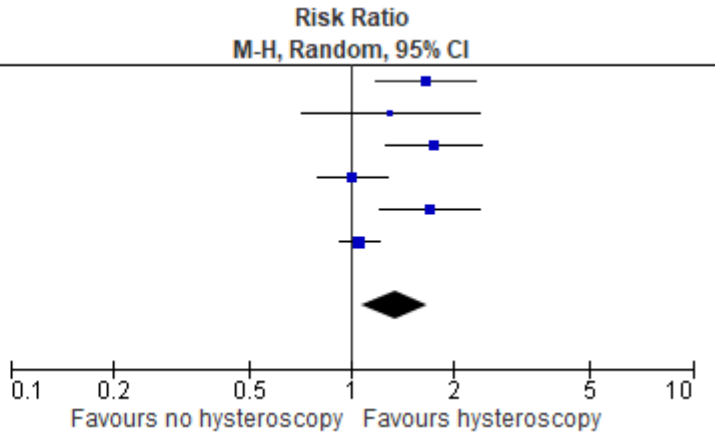


Figure 3: Hysteroscopy versus no hysteroscopy prior to IVF or IUI: Live birth (previous implantation failure subgroup)

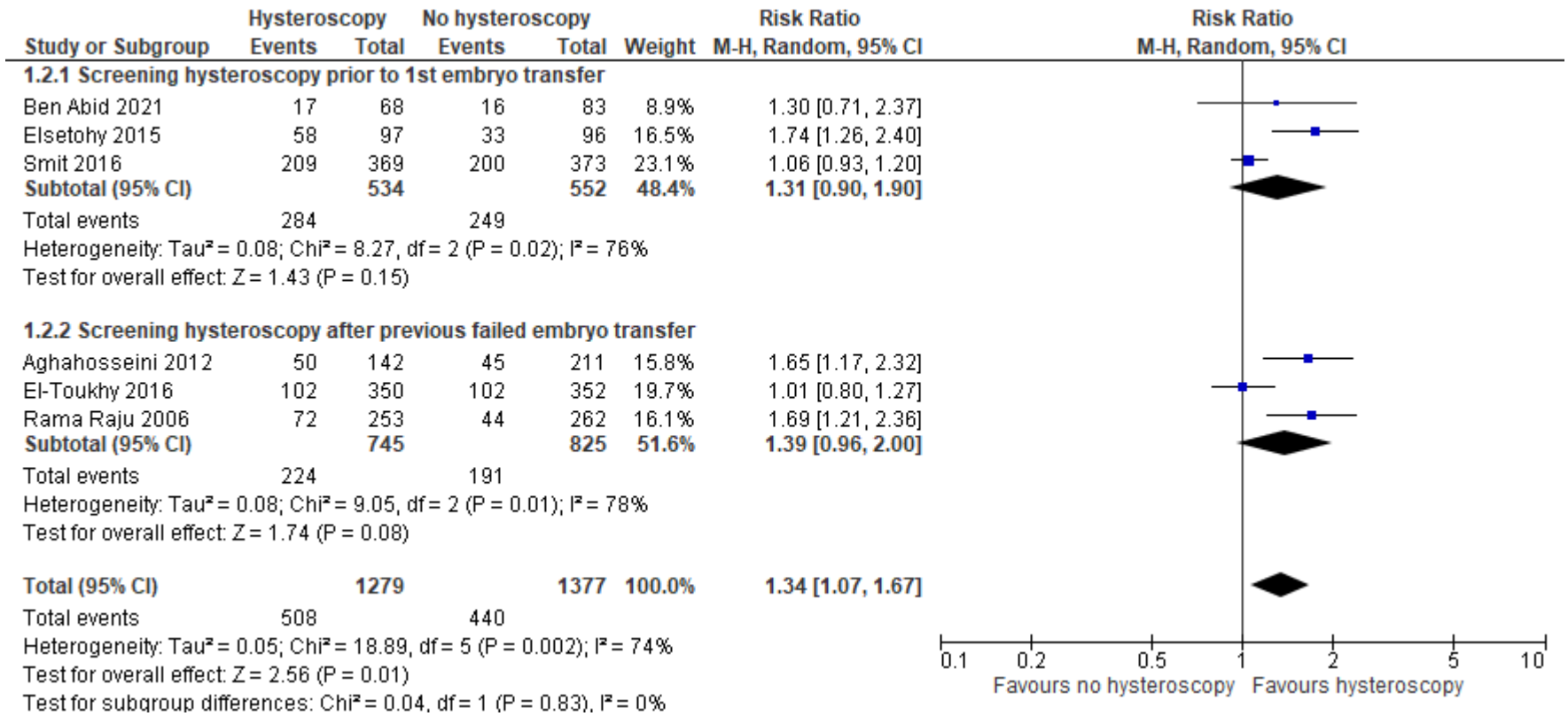


Figure 4: Hysteroscopy versus no hysteroscopy prior to IVF or IUI: Live birth (risk of bias subgroup)

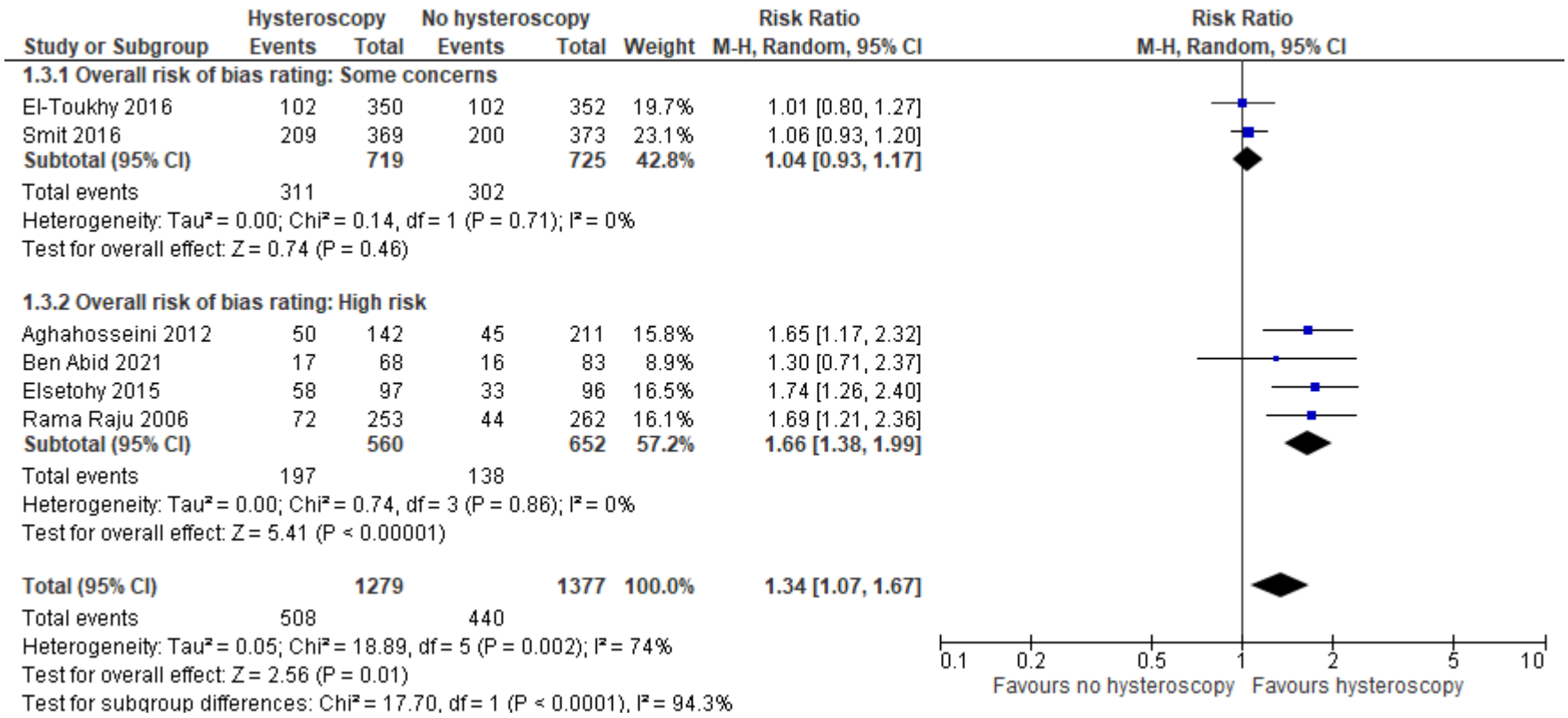


Figure 5: Hysteroscopy versus no hysteroscopy prior to IVF or IUI: Clinical pregnancy (overall; random effects meta-analysis)

	Hysteroscopy		No hysteroscopy			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
Aghahosseini 2012	72	142	64	211	10.2%	1.67 [1.29, 2.17]
Alleyassin 2017	53	110	42	110	8.9%	1.26 [0.93, 1.71]
Ben Abid 2021	22	68	18	83	4.6%	1.49 [0.87, 2.54]
Demirol 2004	67	209	45	209	8.4%	1.49 [1.08, 2.06]
El-Nashar 2011	25	62	15	62	4.6%	1.67 [0.98, 2.84]
Elsetohy 2015	68	97	44	96	10.4%	1.53 [1.19, 1.97]
El-Toukhy 2016	121	350	116	352	11.9%	1.05 [0.85, 1.29]
Moramezi 2012	22	55	11	55	3.7%	2.00 [1.08, 3.72]
Pounikar 2023	27	90	21	90	5.2%	1.29 [0.79, 2.10]
Rama Raju 2006	109	253	69	262	10.6%	1.64 [1.28, 2.09]
Shawki 2011	40	105	30	110	7.0%	1.40 [0.95, 2.06]
Smit 2016	211	369	203	373	14.3%	1.05 [0.92, 1.19]
Total (95% CI)		**1910**		**2013**	**100.0%**	**1.38 [1.20, 1.58]**
Total events	837		678			

Heterogeneity: Tau² = 0.03; Chi² = 26.91, df = 11 (P = 0.005); I² = 59%

Test for overall effect: Z = 4.62 (P < 0.00001)

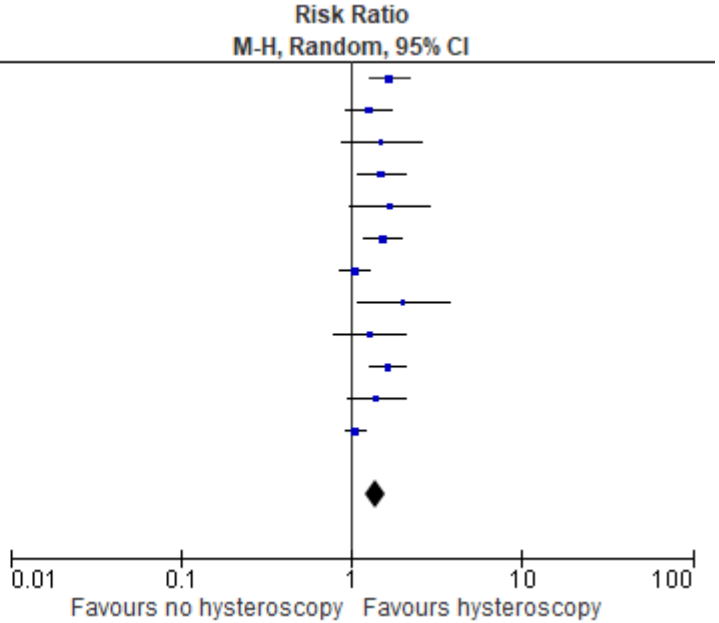


Figure 6: Hysteroscopy versus no hysteroscopy prior to IVF or IUI: Clinical pregnancy (overall; fixed effects meta-analysis)

Study or Subgroup	Hysteroscopy Events	Hysteroscopy Total	No hysteroscopy Events	No hysteroscopy Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Aghahosseini 2012	72	142	64	211	7.8%	1.67 [1.29, 2.17]
Alleyassin 2017	53	110	42	110	6.4%	1.26 [0.93, 1.71]
Ben Abid 2021	22	68	18	83	2.5%	1.49 [0.87, 2.54]
Demirol 2004	67	209	45	209	6.8%	1.49 [1.08, 2.06]
El-Nashar 2011	25	62	15	62	2.3%	1.67 [0.98, 2.84]
Elsetohy 2015	68	97	44	96	6.7%	1.53 [1.19, 1.97]
El-Toukhy 2016	121	350	116	352	17.5%	1.05 [0.85, 1.29]
Moramezi 2012	22	55	11	55	1.7%	2.00 [1.08, 3.72]
Pounikar 2023	27	90	21	90	3.2%	1.29 [0.79, 2.10]
Rama Raju 2006	109	253	69	262	10.3%	1.64 [1.28, 2.09]
Shawki 2011	40	105	30	110	4.4%	1.40 [0.95, 2.06]
Smit 2016	211	369	203	373	30.6%	1.05 [0.92, 1.19]
Total (95% CI)		**1910**		**2013**	**100.0%**	**1.30 [1.20, 1.40]**
Total events	837		678			

Heterogeneity: Chi² = 26.91, df = 11 (P = 0.005); I² = 59%

Test for overall effect: Z = 6.57 (P < 0.00001)

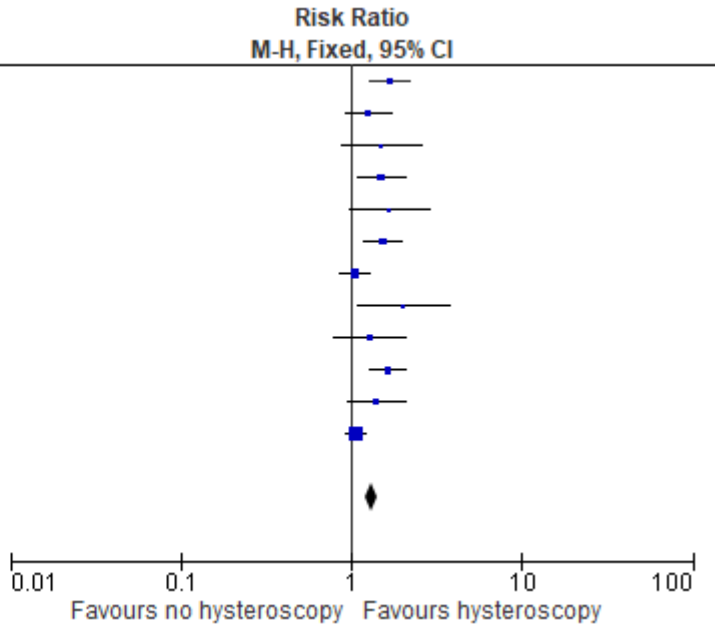


Figure 7: Hysteroscopy versus no hysteroscopy prior to IVF or IUI: Clinical pregnancy (previous implantation failure subgroup)

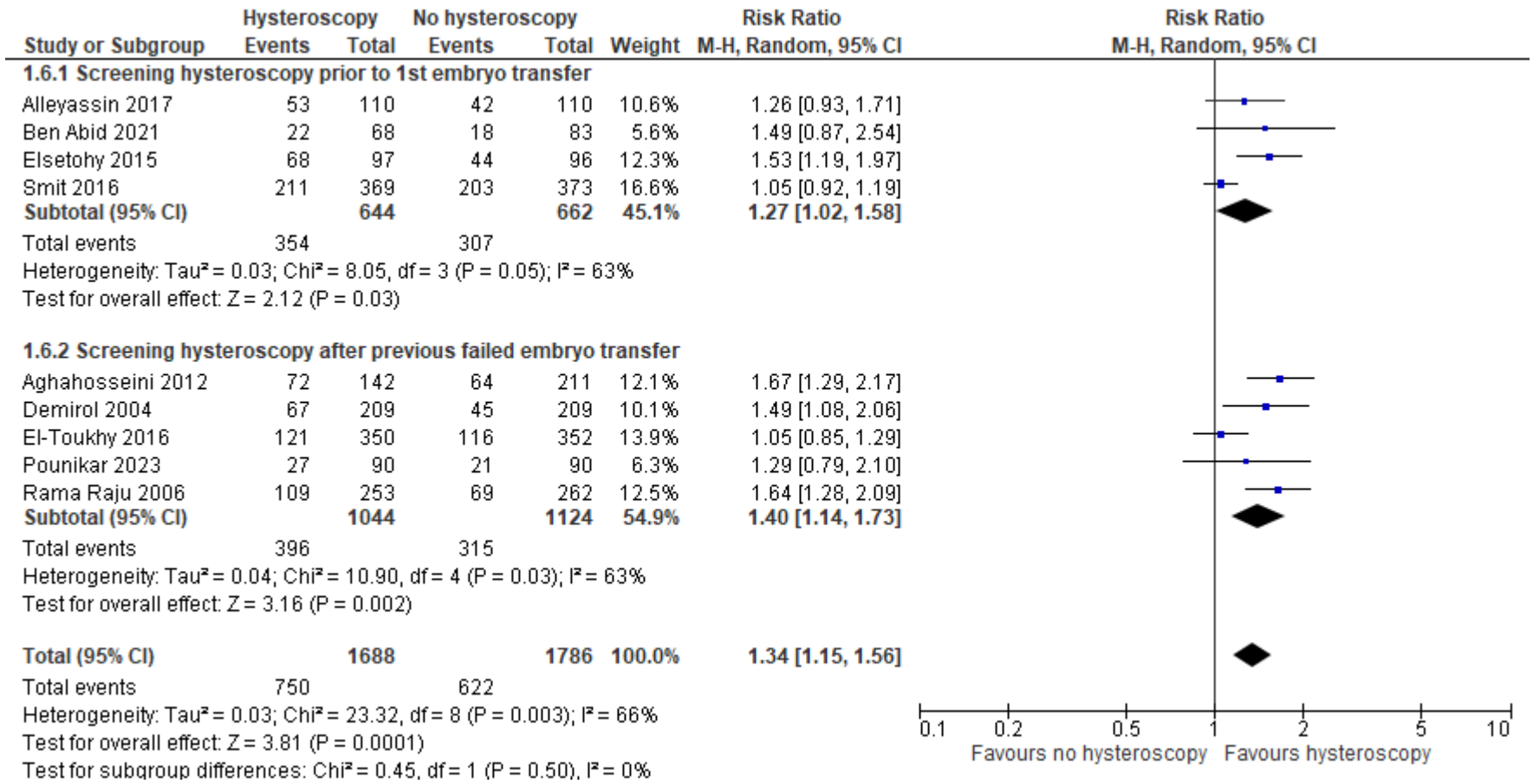


Figure 8: Hysteroscopy versus no hysteroscopy prior to IVF or IUI: Clinical pregnancy (risk of bias subgroup)

Study or Subgroup	Hysteroscopy Events	Hysteroscopy Total	No hysteroscopy Events	No hysteroscopy Total	Weight	Risk Ratio M-H, Random, 95% CI
1.7.1 Overall risk of bias rating: Some concerns						
El-Toukhy 2016	121	350	116	352	11.9%	1.05 [0.85, 1.29]
Smit 2016	211	369	203	373	14.3%	1.05 [0.92, 1.19]
Subtotal (95% CI)		**719**		**725**	**26.1%**	**1.05 [0.94, 1.17]**
Total events	332		319			
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.99); I² = 0%						
Test for overall effect: Z = 0.88 (P = 0.38)						
1.7.2 Overall risk of bias rating: High risk						
Aghahosseini 2012	72	142	64	211	10.2%	1.67 [1.29, 2.17]
Alleyassin 2017	53	110	42	110	8.9%	1.26 [0.93, 1.71]
Ben Abid 2021	22	68	18	83	4.6%	1.49 [0.87, 2.54]
Demirol 2004	67	209	45	209	8.4%	1.49 [1.08, 2.06]
El-Nashar 2011	25	62	15	62	4.6%	1.67 [0.98, 2.84]
Elsetohy 2015	68	97	44	96	10.4%	1.53 [1.19, 1.97]
Moramezi 2012	22	55	11	55	3.7%	2.00 [1.08, 3.72]
Pounikar 2023	27	90	21	90	5.2%	1.29 [0.79, 2.10]
Rama Raju 2006	109	253	69	262	10.6%	1.64 [1.28, 2.09]
Shawki 2011	40	105	30	110	7.0%	1.40 [0.95, 2.06]
Subtotal (95% CI)		**1191**		**1288**	**73.9%**	**1.52 [1.37, 1.70]**
Total events	505		359			
Heterogeneity: Tau² = 0.00; Chi² = 3.78, df = 9 (P = 0.93); I² = 0%						
Test for overall effect: Z = 7.71 (P < 0.00001)						
Total (95% CI)		**1910**		**2013**	**100.0%**	**1.38 [1.20, 1.58]**
Total events	837		678			
Heterogeneity: Tau² = 0.03; Chi² = 26.91, df = 11 (P = 0.005); I² = 59%						
Test for overall effect: Z = 4.62 (P < 0.00001)						
Test for subgroup differences: Chi² = 22.81, df = 1 (P < 0.00001), I² = 95.6%						

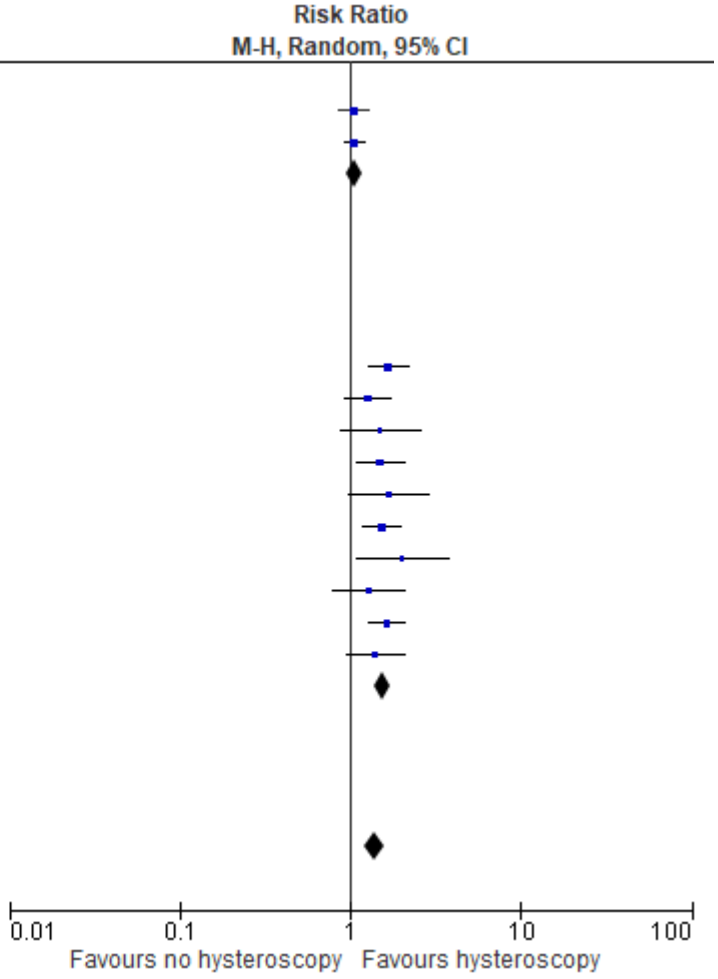
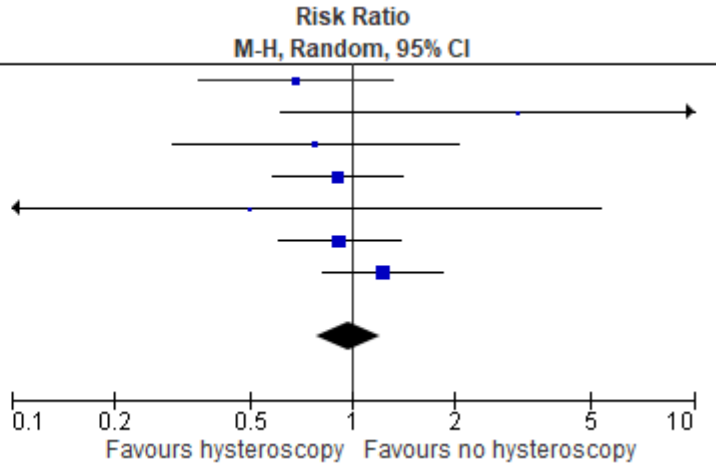


Figure 9: Hysteroscopy versus no hysteroscopy prior to IVF or IUI: Miscarriage

Study or Subgroup	Hysteroscopy Events	Hysteroscopy Total	No hysteroscopy Events	No hysteroscopy Total	Weight	Risk Ratio M-H, Random, 95% CI
Alleyassin 2017	13	110	19	110	11.0%	0.68 [0.36, 1.32]
Ben Abid 2021	5	68	2	83	1.8%	3.05 [0.61, 15.24]
Demirol 2004	7	209	9	209	5.0%	0.78 [0.30, 2.05]
El-Toukhy 2016	29	131	33	135	24.6%	0.91 [0.58, 1.40]
Moramezi 2012	1	55	2	55	0.8%	0.50 [0.05, 5.36]
Rama Raju 2006	36	109	25	69	27.7%	0.91 [0.60, 1.38]
Smit 2016	48	266	34	231	29.0%	1.23 [0.82, 1.83]
Total (95% CI)		**948**		**892**	**100.0%**	**0.97 [0.78, 1.20]**
Total events	139		124			

Heterogeneity: Tau² = 0.00; Chi² = 5.03, df = 6 (P = 0.54); I² = 0%

Test for overall effect: Z = 0.28 (P = 0.78)



Appendix F GRADE tables

GRADE tables for review question: What is the effectiveness of screening hysteroscopy (with or without treatment of any detected uterine cavity abnormalities) on reproductive outcomes for people with female factor fertility problems?

Table 5: Evidence profile for comparison between hysteroscopy versus no hysteroscopy prior to in vitro fertilisation (IVF) or intrauterine insemination (IUI)

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hysteroscopy	No hysteroscopy	Relative (95% CI)	Absolute		
Live birth (overall)												
6[1]	randomised trials	very serious[2]	serious[3]	no serious indirectness	no serious imprecision	none	508/1279 (39.7%)	440/1377 (32%)	RR 1.34 (1.07 to 1.67)	109 more per 1000 (from 22 more to 214 more)	VERY LOW	CRITICAL
Live birth: Previous implantation failure subgroup analysis (screening hysteroscopy prior to 1st embryo transfer)												
3[5]	randomised trials	very serious[2]	serious[3]	no serious indirectness	no serious imprecision	none	284/534 (53.2%)	249/552 (45.1%)	RR 1.31 (0.9 to 1.9)	140 more per 1000 (from 45 fewer to 406 more)	VERY LOW	CRITICAL
Live birth: Previous implantation failure subgroup analysis (screening hysteroscopy after previous failed embryo transfer)												
3[6]	randomised trials	very serious[2]	serious[3]	no serious indirectness	no serious imprecision	none	224/745 (30.1%)	191/825 (23.2%)	RR 1.39 (0.96 to 2)	90 more per 1000 (from 9 fewer to 232 more)	VERY LOW	CRITICAL
Live birth: Risk of bias subgroup analysis (some concerns)												
2[7]	randomised trials	serious[8]	no serious inconsistency	no serious indirectness	no serious imprecision	none	311/719 (43.3%)	302/725 (41.7%)	RR 1.04 (0.93 to 1.17)	17 more per 1000 (from 29 fewer to 71 more)	MODERATE	CRITICAL
Live birth: Risk of bias subgroup analysis (high risk)												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hysteroscopy	No hysteroscopy	Relative (95% CI)	Absolute		
4[9]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	197/560 (35.2%)	138/652 (21.2%)	RR 1.66 (1.38 to 1.99)	140 more per 1000 (from 80 more to 210 more)	LOW	CRITICAL
Clinical pregnancy (overall; random effects meta-analysis)												
12[10]	randomised trials	very serious[2]	serious[3]	no serious indirectness	serious[4]	reporting bias[11]	837/1910 (43.8%)	678/2013 (33.7%)	RR 1.38 (1.2 to 1.58)	128 more per 1000 (from 67 more to 195 more)	VERY LOW	CRITICAL
Clinical pregnancy (overall; fixed effects meta-analysis)												
12[10]	randomised trials	very serious[2]	serious[3]	no serious indirectness	serious[4]	reporting bias[11]	837/1910 (43.8%)	678/2013 (33.7%)	RR 1.3 (1.2 to 1.4)	101 more per 1000 (from 67 more to 135 more)	VERY LOW	CRITICAL
Clinical pregnancy: Previous implantation failure subgroup analysis (screening hysteroscopy prior to 1st embryo transfer)												
4[12]	randomised trials	very serious[2]	serious[3]	no serious indirectness	serious[4]	none	354/644 (55%)	307/662 (46.4%)	RR 1.27 (1.02 to 1.58)	125 more per 1000 (from 9 more to 269 more)	VERY LOW	CRITICAL
Clinical pregnancy: Previous implantation failure subgroup analysis (screening hysteroscopy after previous failed embryo transfer)												
5[13]	randomised trials	very serious[2]	serious[3]	no serious indirectness	serious[4]	none	396/1044 (37.9%)	315/1124 (28%)	RR 1.4 (1.14 to 1.73)	112 more per 1000 (from 39 more to 205 more)	VERY LOW	CRITICAL
Clinical pregnancy: Risk of bias subgroup analysis (some concerns)												
2[7]	randomised trials	serious[8]	no serious inconsistency	no serious indirectness	no serious imprecision	none	332/719 (46.2%)	319/725 (44%)	RR 1.05 (0.94 to 1.17)	22 more per 1000 (from 26 fewer to 75 more)	MODERATE	CRITICAL
Clinical pregnancy: Risk of bias subgroup analysis (high risk)												
10[14]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	505/1191 (42.4%)	359/1288 (27.9%)	RR 1.52 (1.37 to 1.7)	145 more per 1000 (from 103 more to 195 more)	LOW	CRITICAL

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hysteroscopy	No hysteroscopy	Relative (95% CI)	Absolute		
Miscarriage												
7[15]	randomised trials	serious[8]	no serious inconsistency	no serious indirectness	serious[4]	none	139/948 (14.7%)	124/892 (13.9%)	RR 0.97 (0.78 to 1.2)	4 fewer per 1000 (from 31 fewer to 28 more)	LOW	IMPORTANT
Pregnancy loss												
1 (Smit 2016)	randomised trials	serious[8]	no serious inconsistency	no serious indirectness	serious[4]	none	87/266 (32.7%)	54/231 (23.4%)	RR 1.4 (1.05 to 1.87)	94 more per 1000 (from 12 more to 203 more)	LOW	IMPORTANT
Any perioperative adverse event												
1 (Moramezi 2012)	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[16]	none	0/55 (0%)	0/55 (0%)	RD 0.00 (-0.03 to 0.03)	0 fewer per 1000 (from 30 fewer to 30 more)[17]	VERY LOW	IMPORTANT

CI: confidence interval; RR; risk ratio

[1] *Aghahosseini 2012, Ben Abid 2021, El-Toukhy 2016, Elsetohy 2015, Rama Raju 2006, Smit 2016*

[2] *Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2*

[3] *Serious inconsistency (I2=50-80%)*

[4] *95% CI crosses 1 clinical decision making threshold*

[5] *Ben Abid 2021, Elsetohy 2015, Smit 2016*

[6] *Aghahosseini 2012, El-Toukhy 2016, Rama Raju 2006*

[7] *El-Toukhy 2016, Smit 2016*

[8] *Serious risk of bias in the evidence contributing to the outcomes as per RoB 2*

[9] *Aghahosseini 2012, Ben Abid 2021, Elsetohy 2015, Rama Raju 2006*

[10] *Aghahosseini 2012, Alleyassin 2017, Ben Abid 2021, Demirol 2004, El-Nashar 2011, El-Toukhy 2016, Elsetohy 2015, Moramezi 2012, Pounikar 2023, Rama Raju 2006, Shawki 2012, Smit 2016*

[11] *Funnel plot indicates asymmetry*

[12] *Alleyassin 2017, Ben Abid 2021, Elsetohy 2015, Smit 2016*

[13] *Aghahosseini 2012, Demirol 2004, El-Toukhy 2016, Pounikar 2023, Rama Raju 2006*

[14] *Aghahosseini 2012, Alleyassin 2017, Ben Abid 2021, Demirol 2004, El-Nashar 2011, Elsetohy 2015, Moramezi 2012, Pounikar 2023, Rama Raju 2006, Shawki 2012*

[15] *Alleyassin 2017, Ben Abid 2021, Demirol 2004, El-Toukhy 2016, Moramezi 2012, Rama Raju 2006, Smit 2016*

[16] *Zero events in both arms and small sample size*

[17] *Absolute effect calculated based on risk difference*

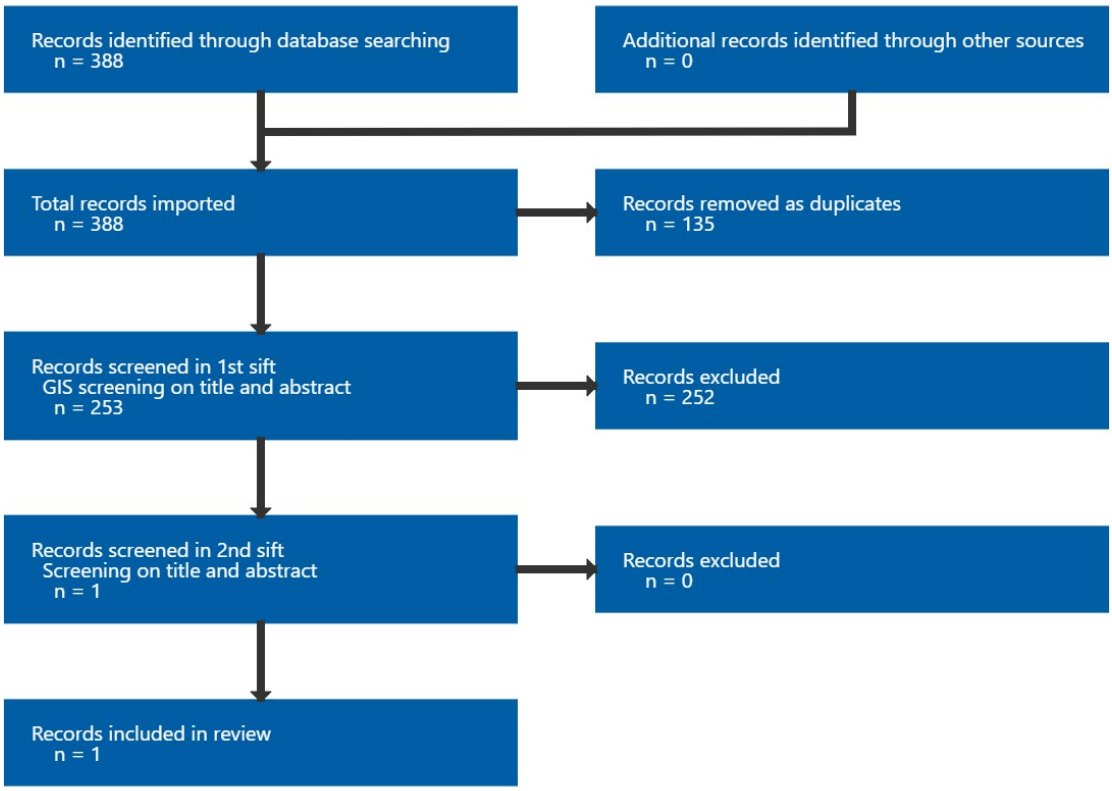
1

2
3

Appendix G Economic evidence study selection

Study selection for review question: What is the effectiveness of screening hysteroscopy (with or without treatment of any detected uterine cavity abnormalities) on reproductive outcomes for people with female factor fertility problems?

Figure 10: Study selection flow chart



Appendix H Economic evidence tables

Economic evidence tables for review question: What is the effectiveness of screening hysteroscopy (with or without treatment of any detected uterine cavity abnormalities) on reproductive outcomes for people with female factor fertility problems?

Table 6: Economic evidence tables

Study country and type	Intervention and comparator	Study population, design and data sources	Costs and outcomes (descriptions and values)	Results	Comments
Author and year: Kasius 2013 **Country:** Netherlands **Type of economic analysis:** CEA **Source of funding:** None declared	**Intervention:** i) Routine screening Hysteroscopy screening followed by up to 3 cycles of IVF. ii) Conditional screening Up to 2 cycles of IVF with no hysteroscopy screening followed by hysteroscopy screening before a 3rd IVF cycle. **Comparator:** iii) No screening Up to 3 IVF cycles without hysteroscopy screening	**Population characteristics:** Infertile women, eligible for indicated for IVF/intracytoplasmic sperm injection treatment and with no symptoms of intrauterine pathology and a normal transvaginal sonography **Modelling approach:** Decision analytic model **Source of baseline data:** Kremer 2012 **Source of effectiveness data**: Bosteels 2010 Bozdag 2008 El-Toukhy 2008 Demirol 2004 Rama Raju 2006 **Source of cost data:**	**Costs:** Health care perspective **Mean cost per participant:** Not reported **Primary measure of outcome**: Cost per live births **Mean outcome per participant:** i) Routine screening €9,341 per live birth ii) Conditional screening €10,570 per live birth iii) No screening €10,851 per live birth	**ICERs:** Routine screening dominates. **Probability of being cost effective:** 78% probability that routine screening dominates conditional screening and no screening. **Subgroup analysis**: Assumed benefit would only accrue to those with intrauterine pathology and that hysteroscopy would lead to normal IVF pregnancy rates. *Base case analysis relative to no screening:* *i) Routine screening ICER €3,938 per live birth*	**Currency:** Euros (€) **Cost year:** 2008 **Time horizon:** Not stated but implicitly time to complete 3 cycles of IVF. **Discounting:** None **Applicability:** Partially applicable **Limitations:** Potentially serious limitations **Other comments:** Probabilistic sensitivity analysis was undertaken using uniform distributions for effectiveness. Authors note that randomised trials are needed to

Study country and type	Intervention and comparator	Study population, design and data sources	Costs and outcomes (descriptions and values)	Results	Comments
		Estimate/assumption **Source of unit cost data:** Bouwmans 2008 es Hakkaart-Roijen 2010.		*ii) Conditional screening* *€10,004 per live birth* **Sensitivity analysis:** Variables varied so as not to favour hysteroscopy. *ICERs calculated relative to no screening:* *i) Routine screening* *ICER €6,728 per live birth* *ii) Conditional screening* *€15,000 per live birth*	confirm the effectiveness of hysteroscopy.

CEA = Cost-effectiveness analysis; ICER = Incremental cost-effectiveness ratio; IVF = In vitro fertilisation

Appendix I Economic model

Economic model for review question: What is the effectiveness of screening hysteroscopy (with or without treatment of any detected uterine cavity abnormalities) on reproductive outcomes for people with female factor fertility problems?

No economic analysis was conducted for this review question.

Appendix J - Excluded studies

Excluded studies for review question: What is the effectiveness of screening hysteroscopy (with or without treatment of any detected uterine cavity abnormalities) on reproductive outcomes for people with female factor fertility problems?

Excluded effectiveness studies

Table 7: Excluded studies and reasons for their exclusion

Study	Code [Reason]
Berntsen, S., Hare, K.J., Berntsen, S. et al. (2020) Endometrial scratch injury with office hysteroscopy before IVF/ICSI: A randomised controlled trial. Eur. J. Obstet. Gynecol. Reprod. Biol. 252: 112-117	- Study does not contain a relevant intervention *The intervention in the study is endometrial scratch injury with office hysteroscopy*
Bilir, E and Kahramanoğlu, İ (2023) The role of hysteroscopy in fertility preservation in endometrial cancer and atypical endometrial hyperplasia: a semi-systematic literature review. Archives of gynecology and obstetrics	- Not a relevant study design *Study is a systematic review of non randomised studies only*
Bozdag, Gurkan, Aksan, Guldeniz, Esinler, Ibrahim et al. (2008) What is the role of office hysteroscopy in women with failed IVF cycles?. Reproductive biomedicine online 17(3): 410-5	- Narrative review
Bosteels, Jan, Weyers, Steven, Puttemans, Patrick et al. (2010) The effectiveness of hysteroscopy in improving pregnancy rates in subfertile women without other gynaecological symptoms: a systematic review. Human reproduction update 16(1): 1-11	- Systematic review, included studies checked for relevance
Cao, H, You, D, Yuan, M et al. (2018) Hysteroscopy after repeated implantation failure of assisted reproductive technology: A meta-analysis. The journal of obstetrics and gynaecology research 44(3): 365-373	- Systematic review, included studies checked for relevance
Carrera, Maria, Alonso, Luis, Dominguez, Jose Antonio et al. (2022) Hysteroscopic metroplasty for the treatment of the dysmorphic uterus: A SWOT analysis. Frontiers in surgery 9: 1097248	- Narrative review
Carrera, Maria, Perez Millan, Federico, Alcazar, Juan Luis et al. (2022) Effect of Hysteroscopic Metroplasty on Reproductive Outcomes in Women with Septate Uterus: Systematic Review and Meta-Analysis. Journal of minimally invasive gynecology 29(4): 465-475	- Systematic review, included studies checked for relevance
Cholkeri-Singh, Aarathi and Sasaki, Kirsten J (2015) Hysteroscopy for infertile women: a review. Journal of minimally invasive gynecology 22(3): 353-62	- Narrative review
De Angelis, C, Antinori, M, Cerusico, V et al. (2010) Hysteroscopic surgery prior to IVF. Reproductive biomedicine online 20: 81	- Conference abstract
Di Spiezio Sardo, Attilio, Di Carlo, Costantino, Minozzi, Silvia et al. (2016) Efficacy of hysteroscopy	- Systematic review, included studies checked for relevance

Study	Code [Reason]
in improving reproductive outcomes of infertile couples: a systematic review and meta-analysis. Human reproduction update 22(4): 479-96	
El-Toukhy, T, Sunkara, SK, Coomarasamy, A et al. (2008) Outpatient hysteroscopy and subsequent IVF cycle outcome: a systematic review and meta-analysis. Reproductive biomedicine online 16(5): 712-9	- Systematic review, included studies checked for relevance
Genovese, Fortunato, Di Guardo, Federica, Monteleone, Morena Maria et al. (2021) Hysteroscopy as An Investigational Operative Procedure in Primary and Secondary Infertility: A Systematic Review. International journal of fertility & sterility 15(2): 80-87	- Systematic review, included studies checked for relevance used as source of primary studies *The study is a systematic review of both randomised and non randomised studies and so cannot be included as whole. The systematic review includes 11 randomised controlled trials which have been checked for relevance*
Ghasemi, M; Aleyasine, A; Aghahosseini, M (2018) The effect of uterine cavity irrigation with office, hysteroscopy during antagonist cycle 0varian stimulation on IVF outcome. Human reproduction (Oxford, England) 33: i353	- Conference abstract
Ghasemi, Marzieh, Aleyasin, Ashraf, Fatemi, Human M et al. (2022) Uterine Cavity Irrigation With Office Hysteroscopy During Ovarian Stimulation for IVF: A Randomized Controlled Trial. Frontiers in endocrinology 13: 778988	- Study does not contain a relevant intervention
Gui, Juan, Xu, Wangming, Yang, Jing et al. (2019) Impact of local endometrial injury on in vitro fertilization/intracytoplasmic sperm injection outcomes: A systematic review and meta-analysis. The journal of obstetrics and gynaecology research 45(1): 57-68	- Systematic review used as source of primary studies *The study is a systematic review of both randomised and non randomised studies and so cannot be included as whole. The study includes 8 randomised controlled trial (RCTs) which have been checked for relevance*
IRCT2016011022795N2 (2016) evaluation of hysteroscopic effect on endometrial receptivity of the patients in the IVF cycle. https://trialsearch.who.int/Trial2.aspx?TrialID=IRCT2016011022795N2	- Not a relevant study design Trial registry only
Kalaitzopoulos, Dimitrios Rafail, Themeli, Maria Zografou, Grigoriadis, Georgios et al. (2023) Fertility, pregnancy and perioperative outcomes after operative hysteroscopy for uterine septum: a network meta-analysis. Archives of gynecology and obstetrics	- Study does not contain a relevant intervention *The study is a systematic review which included studies that compared two or more different hysteroscopic septoplasty techniques*
Kamath, Mohan S, Bosteels, Jan, D'Hooghe, Thomas M et al. (2019) Screening hysteroscopy in subfertile women and women undergoing assisted reproduction. The Cochrane database of systematic reviews 4: cd012856	- Systematic review used as source of primary studies *The study is a Cochrane review which includes 3 conference abstracts and so cannot be included as whole. The study includes 11 randomised controlled trials which have been checked for relevance and included where they match the review protocol*
Kilic, Yusuf; Bastu, Ercan; Ergun, Bulent (2013) Validity and efficacy of office hysteroscopy before in	- Not a relevant study design

Study	Code [Reason]
vitro fertilization treatment. Archives of gynecology and obstetrics 287(3): 577-81	*Non randomised study*
Krishnan, Monica, Narice, Brenda F, Ola, Bolarinde et al. (2021) Does hysteroscopic resection of uterine septum improve reproductive outcomes: a systematic review and meta-analysis. Archives of gynecology and obstetrics 303(5): 1131-1142	- Study does not contain a relevant intervention *The study is a systematic review which includes studies with hysteroscopic septum resection as the intervention*
Lin, L.-J., Liu, J., Xu, L.-Z. et al. (2022) The impact of endometrial mechanical stimulation in women with normal hysteroscopic findings undergoing IVF/ICSI: a meta-analysis. Clinical and Experimental Obstetrics and Gynecology 49(1): 027	- Study does not contain a relevant intervention *The study is a systematic review of randomised and non-randomised studies which examine hysteroscopic endometrial mechanical stimulation as the intervention of interest*
Liu, H; Xia, E; Xu, Y (2018) Clinical efficacy of hysteroscopic surgery combined with extensive care by professional nursing teams in the treatment of patients with intrauterine adhesions. Biomedical research (india) 29(9): 1829-1832	- Does not contain a population of interest *The study includes people with intrauterine adhesions*
Makrakis, Evangelos and Pantos, Konstantinos (2010) The outcomes of hysteroscopy in women with implantation failures after in-vitro fertilization: findings and effect on subsequent pregnancy rates. Current opinion in obstetrics & gynecology 22(4): 339-43	- Not a relevant study design *Narrative literature review*
Marchand, Greg J, Masoud, Ahmed Taher, Ulibarri, Hollie et al. (2023) Effect of the decision to perform hysteroscopy on asymptomatic patients before undergoing assisted reproduction technologies-a systematic review and meta-analysis. AJOG global reports 3(2): 100178	- Systematic review used as source of primary studies *The study is a systematic review of randomised and non randomised studies, and includes abstracts in the analysis. Subsequently it cannot be included as whole. The study includes 11 randomised controlled trials which have been checked for relevance*
NCT01743391 (2012) Hysteroscopy Before in Vitro Fertilization - Does it Improve the Outcome?. https://clinicaltrials.gov/show/NCT01743391	- Not a relevant study design *Trial registry*
NCT03173404 (2017) Benefits of Hysteroscopy Prior to Performing a Cycle of in Vitro Fertilization/Intracytoplasmic Sperm Injection. https://clinicaltrials.gov/show/NCT03173404	- Not a relevant study design *Trial registry*
Pundir, Jyotsna, Pundir, Vishal, Omanwa, Kireki et al. (2014) Hysteroscopy prior to the first IVF cycle: a systematic review and meta-analysis. Reproductive biomedicine online 28(2): 151-61	- Systematic review used as source of primary studies *The study is a systematic review of randomised and non randomised studies and cannot be included as whole. The systematic review includes 1 randomised controlled trial which was checked for relevance*
Roig, Maria Carrera, Milan, Federico Perez, Alonso, Luis et al. (2023) A controversial old topic revisited: Should diagnostic hysteroscopy be routinely performed prior to the first IVF cycle? A systematic review and updated meta-analysis. Journal of minimally invasive gynecology	- Systematic review used as source of primary studies *The study is a systematic review of randomised and non randomised studies so cannot be included as whole. The systematic review includes 6 randomised controlled trials which have been checked for relevance*

Study	Code [Reason]
Smit, JG, Kasius, JC, Eijkemans, MJ et al. (2012) The inSIGHT study: costs and effects of routine hysteroscopy prior to a first IVF treatment cycle. A randomised controlled trial. BMC women's health 12: 22	- Not a relevant study design *Trial protocol*
Varlas, V, Rhazi, Y, Cloțea, E et al. (2021) Hysterolaparoscopy: A Gold Standard for Diagnosing and Treating Infertility and Benign Uterine Pathology. Journal of clinical medicine 10(16)	- Not a relevant study design *Narrative review of randomised and non randomised studies*
Yang, Soo Yeon; Chon, Seung-Joo; Lee, Seon Heui (2020) The effects of diagnostic hysteroscopy on the reproductive outcomes of infertile women without intrauterine pathologies: a systematic review and meta-analysis. Korean journal of women health nursing 26(4): 300-317	- Systematic review used as source of primary studies *The study was a systematic review of randomised and non randomised studies and so cannot be included as whole. The systematic review includes 6 randomised controlled trials which have been checked for relevance*
Zhang, Huixia, He, Xueqing, Tian, Wenyan et al. (2019) Hysteroscopic Resection of Endometrial Polyps and Assisted Reproductive Technology Pregnancy Outcomes Compared with No Treatment: A Systematic Review. Journal of minimally invasive gynecology 26(4): 618-627	- Study does not contain a relevant intervention *The study is a systematic review of randomised and non randomised studies with hysteroscopic resection of polyps as the intervention of interest. The systematic review includes 1 RCT which has been checked for relevance*

Excluded economic studies

No economic evidence was excluded for this review.

Appendix K Research recommendations – full details

Research recommendations for review question: What is the effectiveness of screening hysteroscopy (with or without treatment of any detected uterine cavity abnormalities) on reproductive outcomes for people with female factor fertility problems?

No research recommendations were made for this review question.