National Institute for Health and Care Excellence

Final

Fertility problems: assessment and treatment

[W] Surgical interventions for obstructive azoospermia

NICE guideline NG257

Evidence review underpinning recommendation 1.25.1 in the NICE guideline

March 2026

Final
Developed by NICE

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Contents

Surgical interventions for fertility problems associated with obstructive azoospermia

Review question

What is the clinical and cost effectiveness of surgical interventions for fertility problems associated with obstructive azoospermia?

Introduction

Obstructive azoospermia is the absence of sperm in the ejaculate due to an obstruction in the epididymis, the vas deferens or the ejaculatory duct. The blockage can be congenital or can be acquired through injury or surgery (including vasectomy), infection, inflammation or prostatic cysts. Different surgical procedures to either remove or correct the anatomical blockage or retrieve sperm directly can be used as treatment options.

The aim of this review is to determine the most effective surgical intervention to improve fertility in people with obstructive azoospermia.

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 with fertility problems associated with obstructive azoospermia (including epididymal obstruction, ejaculatory duct obstruction, vasal obstruction) Exclusion: • People with congenital bilateral absence of vas deferens (CBAVD)
Intervention	Surgical interventions for the treatment of fertility problems associated with obstructive azoospermia, for example: • Epididymovasostomy or vasoepididymostomy (EV/VE) • (Trans) vasovasostomy (VV) • Transurethral resection of the ejaculatory ducts (TURED) • Surgery for ejaculatory duct obstruction
Comparison	• Head-to-head comparisons of different surgical interventions • Non-surgical interventions • No intervention • Surgical sperm retrieval (SSR)

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)
	• Improved semen parameters
	  ○ motile sperm count/concentration
	  ○ total sperm count
	• Adverse events
	  ○ testicular pain
	  ○ atrophy (shrinking of the testicle)
	  ○ haematoma
	  ○ infection

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 (supplement 1).

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

Effectiveness

Included studies

Eight retrospective cohort studies were included for this review (Belker 1991, Boorjian 2004, Heidenreich 2000, Hibi 2020, Kolettis 2002, Pai 1973, Rodrigues Netto Junior 1992, Uvin 2018).

The included studies are summarised in Table 2.

Six studies compared vasovasostomy (VV) to vasoepididymostomy or epididymovasostomy (VE/EV) (Belker 1991, Boorjian 2004, Hibi 2020, Kolettis 2002, Pai 1973, Rodrigues Netto Junior 1992), and 2 studies compared VV to surgical sperm retrieval (SSR) with either microsurgical epididymal sperm aspiration (MESA)/testicular extraction of sperm (TESE) (Heidenreich 2000) or TESE/fine need aspiration (FNA) (Uvin 2018).

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
Belker 1991 Retrospective cohort study USA	N=1,208 Patients who underwent vasectomy reversal Mean age (SD): 36.9 (NR) years Mean female partner age (SD): 29.6 (NR) years Mean duration of obstruction (SD): 7 (NR) years	VV Microsurgical 2-layer or modified microsurgical 1-layer (bilateral or unilateral)	VE Microsurgical end-to-end or end-to-side method (bilateral or unilateral)	• Pregnancy • Semen parameters	Postoperative semen analyses at 2 to 4-month intervals until conception occurred or the patient was lost to follow-up Patients with VV 1 side and VE other side and unspecified surgery type were not included in the review
Boorjian 2004 Retrospective cohort study USA	N=195 Men undergoing first time vasectomy reversals with bilateral reconstruction Mean age (SD): 43.2 (NR) years Mean female partner age (SD): 33.2 (NR) years Mean duration of obstruction: NR	VV Multilayer microsurgical approach (bilateral or unilateral)	VE Multilayer microsurgical approach (bilateral or unilateral)	• Pregnancy	Postoperative semen analyses began at 6 weeks and continued until pregnancy achieved or the patient was lost to follow-up Patients with VV/VE were not included in the review

Study	Population	Intervention	Comparison	Outcomes	Comments
	(most patients between 5-10 years)				
Heidenreich 2000 Retrospective cohort study Germany	N=225 Men who underwent VV for vasectomy reversal, and patients with obstructive azoospermia who were not amenable to microsurgical reconstruction and primary testicular failure or obstruction of the rete testis Mean age (SD): 37 (NR) years Mean female partner age (SD): 30 (NR) years Mean duration of obstruction (SD): 7.6 (NR) years	VV Microsurgical double-layer (bilateral)	SSR with MESA/TESE Sperm was retrieved by MESA or TESE before an ICSI treatment	• Pregnancy	Mean follow-up 20 months in VV group Mean age and female partner age were not reported in the VV group. The duration of obstruction was not reported in the MESA /TESE group
Hibi 2020 Retrospective cohort study Japan	N=90 Subjects with obstructive azoospermia referred to a male infertility clinic Mean age (SD) in vasovasostomy and vasoepididymostomy groups: 41 (NR) and 33 (NR) years Mean female partner age (SD) in vasovasostomy and vasoepididymostomy groups: 32 (NR) and 31 (NR) years Mean duration of obstruction (SD) in vasovasostomy	VV Two microlayer anastomotic technique under an operative microscope (bilateral or unilateral)	VE Double needle longitudinal intussusception technique (LIVE; bilateral or unilateral)	• Live birth • Pregnancy • Semen parameters	Post-operative follow-up consisted of serial semen analysis from 3 weeks to 3 years The duration of obstruction was not reported in the VE group

Study	Population	Intervention	Comparison	Outcomes	Comments
	and vasoepididymostomy groups: 12 (NR) and NR years				
Kolettis 2002 Retrospective cohort study USA	N=58 Patients undergoing microsurgical vasectomy reversal with an obstructive interval ≥10 years Mean age (SD): 44.5 (NR) years Mean female partner age (SD): 32.9 (NR) years Mean duration of obstruction (SD): 14.5 (NR) years	VV Modified one-layer anastomosis (bilateral or unilateral)	VE End-to-side two-layer technique (bilateral or unilateral)	• Pregnancy	Duration of follow-up was not reported but patients with <12 months of follow-up or no ongoing interest in establishing conception were excluded from the pregnancy rate analysis, unless they had established a pregnancy or had azoospermia at 6 or 12 months after VV or VE
Pai 1973 Retrospective cohort study India	N=36 Patients with post-vasectomy sterility (azoospermia) who sought vas reconstruction Mean age: NR (most patients between 31-40 years) Mean female partner age: NR Mean duration of obstruction: NR (most patients between 3-5 years)	VV Surgical methods unclear: Each half of the scrotal sac was examined for nodules. The proximity of the nodules indicated the retracted cut ends of the vas. Through a 4 to 6cm. incision, the scrotum was explored, and the cord was isolated and delivered	EV End-to-end anastomosis	• Pregnancy • Semen parameters	After 3 months semen was analysed monthly for 3 months, and thereafter at intervals of 3 months until pregnancy or normal sperm count was achieved
Rodrigues Netto Junior 1992 Retrospective cohort study	N=44 Infertile men with obstructive azoospermia Mean age (SD): 46 (NR) years	VV Two-layer microsurgical	VE Microsurgical end-to-end anastomosis	• Pregnancy	Mean follow-up 21 months in VV group The duration of obstruction was not

Study	Population	Intervention	Comparison	Outcomes	Comments
Brazil	Mean female partner age: NR Mean duration of obstruction (SD): 8 (NR)years				reported in the VE group
Uvin 2018 Retrospective cohort study Belgium	N=109 Patients with a renewed child wish after male sterilization Mean age (SD) in vasovasostomy and TESE/FNA groups: 43.2 (6.4) and 45.6 (7.7) years Mean female partner age (SD) in vasovasostomy and TESE/FNA groups: 33.4 (5.5) and 34.8 (5) years Mean duration of obstruction (SD): 9.5 (6.1) years	VV One-layer, two-layer or microdot multilayer techniques with surgical microscope (bilateral)	SSR with TESE/FNA Sperm was retrieved by FNA or TESE before an ICSI/IVF treatment	• Live birth • Pregnancy • Miscarriage	All patients had a follow-up period of a minimum 57 months (range: 57–120 months)

cm: centimetres; EV: epididymovasostomy; FNA: fine need aspiration; ICSI: intracytoplasmic sperm injection; IVF: in vitro fertilisation; LIVE: longitudinal intussusception technique; MESA: microsurgical epididymal sperm aspiration; NR: not reported; SD: standard deviation; SSR: surgical sperm retrieval; TESE: testicular extraction of sperm; USA: United States of America; VE: vasoepididymostomy; VV: vasovasostomy

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

Summary of the evidence

Very low quality evidence from 1 study showed a higher rate of live birth associated with VE/EV compared to VV, when pregnancy was obtained by intracytoplasmic sperm injection (ICSI) or when the results of participants who obtained pregnancy either spontaneously or by ICSI were combined. However, these findings could be impacted by the effectiveness of ICSI. Very low quality evidence from the same study showed no clinically important difference in live birth rate between VV and VE/EV when pregnancy was obtained naturally.

Very low quality evidence from 5 studies showed a higher rate of clinical pregnancy associated with VV compared to VE/EV. Although it should be noted that measurement of this outcome was not properly defined in 4 of these studies. Further subgroup analysis (conducted due to significant heterogeneity) showed no clinically important difference between VV and VE/EV for participants aged <45 years but showed an important benefit for VV compared to VE/EV in participants aged ≥45 years (very low quality evidence). However, in this subgroup analysis there was only 1 study that included participants aged ≥45 years and this study had very serious risk of bias.

Very low quality evidence from 2 studies showed a higher number of participants with sperm in their semen for those who received VV compared to VE/EV. However, another study

showed no clinically important difference between VV and VE/EV in the number of participants with normal sperm count, number of participants with low sperm count, or the number of participants with no sperm (very low quality evidence).

The evidence comparing VV with SSR was limited and inconsistent. Very low quality evidence from 1 study showed a higher rate of clinical pregnancy (measured by mailed questionnaire) associated with VV relative to SSR via MESA or TESE. However, very low quality evidence from another study showed a higher rate of clinical pregnancy (measured by the observation of fetal cardiac activity on ultrasonography at 7 weeks of gestation) associated with SSR via fine needle aspiration (FNA) or TESE compared to VV. Very low quality evidence from this study also showed a lower rate of miscarriage associated with VV relative to SSR via FNA or TESE. There was no clinically important difference between VV and SSR via FNA or TESE for the outcome live birth.

No eligible evidence was identified for the interventions transurethral resection of the ejaculatory ducts (TURED) or surgery for ejaculatory duct obstruction.

See appendix F for full GRADE tables.

Economic evidence

A total of 494 studies were identified in the health economic literature search for this review question. After duplicates were removed, 314 studies were screened on title and abstract. Of these 314 studies, 303 were excluded at this stage and 11 studies were ordered for screening on full text. When screening the full text, 8 studies were excluded, and 3 studies were screened in the third sift and formally check-listed. All three of these studies were also excluded at this stage as they did not meet the inclusion criteria.

Included studies

A systematic review of the economic literature was conducted but no economic studies were identified which were applicable to this review question.

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 J.

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

Table 3: Unit costs

Resource	Unit costs	Source
Epididymovasostomy or Vasoepididymostomy (EV/VE)	£2,436	National schedule of NHS costs 2023/24; Currency code: LB54A, Day case
(Trans) vasovasostomy (VV)	£2,436	National schedule of NHS costs 2023/24; Currency code: LB54A, Day case
Transurethral resection of the ejaculatory ducts (TURED)	£3,391	National schedule of NHS costs 2023/24; Currency code: LB25F, Day case

Resource	Unit costs	Source
		Elective inpatient £4,844
Surgery for ejaculatory duct obstruction	£2,436	National schedule of NHS costs 2023/24; Currency code: LB54A, Day case
Surgical extraction of sperm	£3,386	National schedule of NHS costs 2023/24; Currency code MC20Z, Day case procedure

The committee's discussion and interpretation of the evidence

The outcomes that matter most

The committee agreed that live birth is the most important outcome for people with fertility problems and reflects both pregnancy rates and antenatal loss. However, the committee were aware that clinical pregnancy rates are more commonly reported in studies and are often reported instead of live birth rates. The committee therefore agreed it was appropriate to make both live birth and clinical pregnancy critical outcomes to reflect the evidence available and to ensure evidence on direct measures of improved fertility were prioritised over other more indirect measures of effectiveness.

The committee agreed a number of other outcomes were important. Miscarriage was agreed to be an important outcome because it can be devastating for people trying to have a baby and can indicate when an intervention is effective for achieving pregnancy but does not lead to a live birth. The committee agreed that improved semen parameters were important as they provide an indication of male fertility. Motile sperm count/concentration was considered as the most reliable and informative measure, but total sperm count was also included as it was anticipated that this may be more frequently reported particularly in older studies. The rate of adverse events was also agreed to be an important outcome by the committee because it is important when discussing and deciding on treatment options that risks are considered and weighed up against potential benefits. Testicular pain, atrophy, haematoma, and infection were considered the most relevant adverse events associated with surgical interventions for obstructive azoospermia.

The quality of the evidence

The quality of the evidence was assessed with GRADE and rated as very low quality for all outcomes.

The evidence was downgraded for risk of bias due to serious concerns around confounding (studies did not control for or appropriately measure potentially important confounders including age and duration of infertility), selection of participants, lack of information about classification of interventions or any deviations from intended interventions, missing data, insufficient information about the measurement of outcomes and how the reported results were selected from among multiple analyses. 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 considered the evidence showing that vasovasostomy (VV), vasoepididymostomy (VE) and epididymovasostomy (EV) all increase the chance of live birth and clinical pregnancy for people with obstructive azoospermia who would not be able to conceive without intervention. The committee discussed the surgical options that are available to treat obstructive azoospermia and the difference between the procedures. They agreed that in clinical practice, a VV would be the preferred option relative to VE/EV for

individuals seeking surgery for obstructive azoospermia, as the procedure is more straightforward. The committee agreed that a VE/EV is typically only performed when VV is not possible because of the nature of the presentation of obstruction in an individual. The committee highlighted that the surgeon will often need to decide on the procedure during the operation, and so individuals are informed before surgery that the plan is to carry out a VV but there is a possibility of undergoing a VE/EV (VE/EV) if a VV is not possible. It is therefore not usually possible to give individuals the option to have one procedure or the other. The committee agreed that information about the benefits and harms of VV and VE/EV should be provided as part of the informed consent process for surgery.

The committee reviewed the evidence from the comparison of VV with VE/EV and noted that it showed no difference in live birth rates for spontaneous pregnancy. However, there was an increase in live birth rates with VE/EV for all pregnancies and in pregnancies using ICSI. However, the committee agreed that these results could be affected by the ICSI procedure and so did not show clear benefit for VE/EV compared to VV. There was some evidence of benefit for VV in terms of clinical pregnancy rates and some parameters measuring improved semen but for other sperm parameters there was no difference. Given the low quality and inconclusiveness of the evidence comparing VV and VE/EV the committee concluded that it was not possible to recommend one procedure over the other and that the choice of procedure could therefore remain a clinical decision at the time of surgery.

The committee discussed the evidence for surgical correction (VV) compared to surgical sperm retrieval (SSR) and noted that it was limited, and equivocal. There were only 2 studies that reported data for this comparison, and they could not be meta-analysed. One study compared VV with SSR using MESA or TESE and all participants received in vitro fertilisation (IVF) with ICSI, while the other study compared VV with SSR using fine need aspiration (FNA) or TESE and participants could receive IVF with or without ICSI. The committee agreed that the different SSR techniques could affect the outcome in the SSR arm.

For the comparison of VV with SSR using MESA or TESE the evidence showed a higher rate of clinical pregnancy (measured by mailed questionnaire) with VV. However, the committee noted the low pregnancy rates associated with the SSR arm and highlighted that at the time of this study ICSI was a relatively new technique, having only been introduced in 1992. Given the marked improvements in the success rate of ICSI over time, the committee questioned the applicability of this evidence to current practice.

The committee considered the more recent evidence from the other study that compared VV to SSR using FNA or TESE. This study showed a higher rate of clinical pregnancy (measured by the observation of fetal cardiac activity on ultrasonography at 7 weeks of gestation) with SSR (FNA or TESE), but also a higher rate of miscarriage with SSR compared to VV. The committee agreed that these findings were consistent with their clinical knowledge and experience where a higher miscarriage rate might be expected for assisted reproduction. There was no difference in live birth rate between VV and SSR in this comparison.

Given that the evidence did not show clear differential benefits in favour of surgical correction relative to surgical sperm retrieval or vice versa, the committee agreed that other factors should be taken into account when deciding between these treatments, including female fertility factors (age, ovarian reserve, tubal patency, ovulatory status), the obstructive interval if known, the risks and benefits of the surgical intervention and patient preference. The committee highlighted that based on their clinical knowledge and experience, obstructive intervals of less than 15 years are considered favourable to successful surgical reconstruction, although the length of obstruction may be less of an issue in situations where the partner with female reproductive organs is relatively young, with good ovarian reserve. On the other hand, where the partner with female reproductive organs is older with low ovarian reserve and there is a longer obstructive interval, assisted reproduction may be more

appropriate as it would be more likely to result in a pregnancy. The committee also discussed that for some patients surgical correction may be the preferred treatment option, particularly where there might be religious or other objections to IVF, and that these preferences should be taken into account.

The committee discussed the evidence and noted that it was largely from those receiving vasectomy reversal which might be easier to overcome than a non-acquired obstruction (because of localisation of the obstruction and more comprehensive clinical history including obstructive interval). The committee highlighted that the evidence reflects practice in which surgical correction was most commonly performed for vasectomy reversals but agreed that, in the absence of direct evidence, it was reasonable to extrapolate from this population.

Despite the low quantity and poor quality of the evidence for this review the committee agreed that the choice of surgical technique (VV or VE/EV) was likely to remain a clinical decision made at the time of surgery and so did not recommend further research. The committee noted that the guideline update included another question on SSR techniques (review question 1.3.1, see evidence review F) and that this provides additional advice on the optimal use of SSR. Therefore they did not make a research recommendation for the comparison of surgical correction and SSR.

Cost effectiveness and resource use

No health economic evidence was identified for this review question therefore the committee made a qualitative assessment regarding cost effectiveness.

The committee discussed the clinical evidence presented for VV and VE/EV, noting that VV would be the preferred option compared to VE/EV as the procedure is more straightforward and less resource intensive in terms of staff time. Although both procedures are grouped under the same currency code in the national schedule of NHS costs, the committee concluded that VE/EV would be the more expensive intervention of the two.

The committee acknowledged that in current clinical practice a VE/EV is typically only performed when a VV is not possible due to the presentation of an obstruction – and that the decision to perform VE/EV would be undertaken during the surgical procedure for a VV. The committee therefore concluded that it was not possible to recommend one procedure over the other.

The committee also discussed the clinical evidence presented for VV and SSR and concluded that it was not possible to recommend one treatment over the other. However, the committee recognised that SSR is more expensive than VV.

No clinical evidence was identified for transurethral resection of the ejaculatory ducts (TURED) and surgery for ejaculatory duct obstruction, but the committee noted that the costs for these procedures are similar those for SSR. The committee also discussed that in general, when treating obstructive azoospermia, the most appropriate course of treatment is dependent on several factors such as female fertility and the obstructive interval. The committee therefore made a recommendation to offer either surgical correction or SSR to treat obstructive azoospermia – noting that this recommendation is reflective of current clinical practice and therefore not expected to result in a significant resource impact.

Recommendations supported by this evidence review

This evidence review supports recommendation 1.25.1.

References – included studies

Effectiveness

Belker 1991

Belker, A M, Thomas, A J Jr, Fuchs, E F et al. (1991) Results of 1,469 microsurgical vasectomy reversals by the Vasovasostomy Study Group. The Journal of urology 145(3): 505-11

Boorjian 2004

Boorjian, Stephen; Lipkin, Michael; Goldstein, Marc (2004) The impact of obstructive interval and sperm granuloma on outcome of vasectomy reversal. The Journal of urology 171(1): 304-6

Heidenreich 2000

Heidenreich, A; Altmann, P; Engelmann, U H (2000) Microsurgical vasovasostomy versus microsurgical epididymal sperm aspiration/testicular extraction of sperm combined with intracytoplasmic sperm injection. A cost-benefit analysis. European urology 37(5): 609-14

Hibi 2020

Hibi, Hatsuki, Sugie, Miho, Ohori, Tadashi et al. (2020) Microsurgical seminal reconstruction; our experiences in a single institute. Nagoya journal of medical science 82(3): 477-485

Kolettis 2002

Kolettis, Peter N, Sabanegh, Edmund S, D'amico, Anna M et al. (2002) Outcomes for vasectomy reversal performed after obstructive intervals of at least 10 years. Urology 60(5): 885-8

Pai 1973

Pai, M G, Sampath Kumar, B T, Kaundinya, C et al. (1973) Vasovasostomy. A clinical study with 10 years' follow-up. Fertility and sterility 24(10): 798-801

Rodrigues Netto Junior 1992

Rodrigues Netto Junior, N, Claro, J A, Neves, P A et al. (1992) Surgical treatment of obstructive azoospermia. Archivos espanoles de urologia 45(10): 1053-5

Uvin 2018

Uvin, Valerie, De Brucker, S, De Brucker, M et al. (2018) Pregnancy after vasectomy: surgical reversal or assisted reproduction? Human reproduction (Oxford, England) 33(7): 1218-1227

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.

Appendices

Appendix A Review protocols

Review protocol for review question: What is the clinical and cost effectiveness of surgical interventions for fertility problems associated with obstructive azoospermia?

Table 4: Review protocol

ID	Field	Content
0.	PROSPERO registration number	CRD42023408979
1.	Review title	Clinical and cost effectiveness of surgical interventions for fertility problems associated with obstructive azoospermia
2.	Review question	What is the clinical and cost effectiveness of surgical interventions for fertility problems associated with obstructive azoospermia?
3.	Objective	To determine the clinical and cost effectiveness of surgical interventions for fertility problems associated with obstructive azoospermia.
4.	Searches	The following databases will be searched (with no date restriction): 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 guideline committee will decide whether and when to re-run the searches to retrieve further studies for inclusion.

ID	Field	Content
		The full search strategies for MEDLINE database will be published in the final review.
5.	Condition or domain being studied	Surgical interventions for fertility problems associated with obstructive azoospermia
6.	Population	Inclusion: People with fertility problems associated with obstructive azoospermia (including epididymal obstruction, ejaculatory duct obstruction, vasal obstruction) Exclusion: People with congenital bilateral absence of vas deferens (CBAVD).
7.	Intervention	Surgical interventions for the treatment of fertility problems associated with obstructive azoospermia, for example: • Epididymovasostomy or Vasoepididymostomy • (Trans) vasovasostomy • Transurethral resection of the ejaculatory ducts (TURED) • Surgery for ejaculatory duct obstruction
8.	Comparator	• Head-to-head comparisons of different surgical interventions • Non-surgical interventions • No intervention • Surgical sperm retrieval
9.	Types of study to be included	Include published full-text papers: • Systematic reviews of RCTs • 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) • Prospective or retrospective cohort studies* *Prospective and retrospective studies will be downgraded for risk of bias if they do not adequately adjust for the following covariates, but will not be excluded for this reason: • Age

ID	Field	Content
		• Different male factor fertility problems • Duration of infertility • Female factor diagnoses
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) • Improved semen parameters ○ motile sperm count/concentration ○ total sperm count • Adverse events ○ testicular pain ○ atrophy (shrinking of the testicle) ○ haematoma ○ infection
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 the two reviewers, and consultation with senior staff if necessary.

ID	Field	Content
		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 (reference, country where study was carried out, type and dates), 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 • Cochrane RoB tool v.2 for cluster-randomised trials • Cochrane RoB tool v.2 for crossover trials • Cochrane ROBINS-I tool for non-randomised (clinical) controlled trials and cohort studies 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 possible, meta-analyses will be conducted using Cochrane Review Manager software. A fixed effect meta-analysis will be conducted and data will be presented as risk ratios or odds ratios for dichotomous outcomes, and mean differences or standardised mean differences for continuous outcomes. 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. If heterogeneity cannot be explained through subgroup analysis then a random effects model will be used for meta-analysis, or the data will not be pooled. 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

ID	Field	Content	
		• Continuous outcomes: +/- 0.5x pooled control group SD for mean difference and SMD -0.5/0.5 for standardised mean difference. • Dichotomous outcomes (other than live birth): 0.8 and 1.25 for all relative dichotomous outcomes	
17.	Analysis of sub-groups	Evidence will be sub-grouped by the following: • Female partners age (based on the mean age reported in the study): ○ ≤35 years ○ >35 years Evidence will be sub-grouped by the following only if there is significant heterogeneity in outcomes: • Age (based on the mean age in the study): ○ <45 years ○ ≥45 years Where evidence is 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	March 2023	

ID	Field	Content		
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 5c. 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		

ID	Field	Content	
		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.	URL for published protocol	crd.york.ac.uk/PROSPERO/display_record.php?RecordID=408979	
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	Male factor fertility problems, infertility, surgical treatment, obstruction	
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	

CBAVD: congenital bilateral absence of vas deferens; CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; MID: minimally important difference; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation; TURED: transurethral resection of the ejaculatory ducts.

Appendix B Literature search strategies

Literature search strategies for review question: What is the clinical and cost effectiveness of surgical interventions for fertility problems associated with obstructive azoospermia?

Database: Ovid MEDLINE(R) ALL <1946 to January 06, 2025>

Date of last search: 07/01/2025

#	Searches
1	((sperm* or ejaculat* or epididym* or vasal* or seminal tract* or genital tract* or reproduct* tract*) adj3 (obstruct* or block*)).tw.
2	(CBAVD or (absen* adj3 (vasa deferentia or ((vas or duct*) adj deferens)))).tw.
3	Azoospermia/ or azoosperm*.tw.
4	or/1-3
5	(surg* or microsurg* or operat* or "minimal* invasive" or endoscop* or reconstruct* or resect* or disobstruct*).tw.
6	General Surgery/ or Urologic Surgical Procedures, Male/ or Minimally Invasive Surgical Procedures/ or Endoscopy/ or Microsurgery/ or su.fs.
7	or/5-6
8	4 and 7
9	((male steril* or vasectom*) adj3 revers*).tw.
10	(epididymovasostom* or vasoepididymostom* or transvasovasostom* or vasovasostom* or vasostom*).tw.
11	vasovasostomy/
12	ejaculatory ducts/su
13	(TURED or ((Transurethral or trans urethral) and ejaculatory duct*)).tw.
14	epididymis/su
15	vas deferens/su
16	or/8-15
17	letter/
18	editorial/
19	news/
20	exp historical article/
21	Anecdotes as Topic/
22	comment/
23	case reports/
24	(letter or comment*).ti.
25	or/17-24
26	randomized controlled trial/ or random*.ti,ab.
27	25 not 26
28	animals/ not humans/
29	exp Animals, Laboratory/
30	exp Animal Experimentation/
31	exp Models, Animal/
32	exp Rodentia/
33	(rat or rats or mouse or mice or rodent*).ti.
34	or/27-33
35	16 not 34
36	limit 35 to english language
37	randomized controlled trial.pt.
38	controlled clinical trial.pt.
39	pragmatic clinical trial.pt.
40	randomi#ed.ab.
41	placebo.ab.
42	randomly.ab.

#	Searches
43	Clinical Trials as topic.sh.
44	trial.ti.
45	or/37-44
46	Meta-Analysis/
47	Meta-Analysis as Topic/
48	(meta analy* or metanaly* or metaanaly*).ti,ab.
49	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
50	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
51	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
52	(search* adj4 literature).ab.
53	(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.
54	cochrane.jw.
55	or/46-54
56	36 and (45 or 55)
57	Observational Studies as Topic/
58	Observational Study/
59	Epidemiologic Studies/
60	exp Case-Control Studies/
61	exp Cohort Studies/
62	Cross-Sectional Studies/
63	Controlled Before-After Studies/
64	Historically Controlled Study/
65	Interrupted Time Series Analysis/
66	Comparative Study.pt.
67	case control$.tw.
68	case series.tw.
69	(cohort adj (study or studies)).tw.
70	cohort analy$.tw.
71	(follow up adj (study or studies)).tw.
72	(observational adj (study or studies)).tw.
73	longitudinal.tw.
74	prospective.tw.
75	retrospective.tw.
76	cross sectional.tw.
77	or/57-76
78	36 and 77
79	78 not 56

Database: Embase <1974 to 2025 January 06>

Date of last search: 07/01/2025

#	Searches
1	((sperm* or ejaculat* or epididym* or vasal* or seminal tract* or genital tract* or reproduct* tract*) adj3 (obstruct* or block*)).tw.
2	(CBAVD or (absen* adj3 (vasa deferentia or ((vas or duct*) adj deferens)))).tw.
3	Azoospermia/ or azoosperm*.tw.
4	or/1-3
5	(surg* or microsurg* or operat* or "minimal* invasive" or endoscop* or reconstruct* or resect* or disobstruct*).tw.
6	surgery/ or "minimally invasive procedure"/ or urologic surgery/ or endoscopic surgery/ or microsurgery/ or su.fs.
7	or/5-6
8	4 and 7
9	male sterilization reversal/
10	((male steril* or vasectom*) adj3 revers*).tw.

#	Searches
11	(epididymovasostom* or vasoepididymostom* or transvasovasostom* or vasovasostom* or vasostom*).tw.
12	vasovasostomy/
13	vasal obstruction/su
14	transurethral resection/ and ejaculatory duct/
15	ejaculatory duct/su or ejaculatory duct obstruction/su
16	(TURED or ((Transurethral or trans urethral) and ejaculatory duct*)).tw.
17	epididymis/su
18	vas deferens/su
19	or/8-18
20	letter.pt. or letter/
21	note.pt.
22	editorial.pt.
23	case report/ or case study/
24	(letter or comment*).ti.
25	or/20-24
26	randomized controlled trial/ or random*.ti,ab.
27	25 not 26
28	animal/ not human/
29	nonhuman/
30	exp Animal Experiment/
31	exp Experimental Animal/
32	animal model/
33	exp Rodent/
34	(rat or rats or mouse or mice or rodent*).ti.
35	or/27-34
36	19 not 35
37	limit 36 to english language
38	(conference abstract* or conference review or conference paper or conference proceeding).db,pt,su.
39	37 not 38
40	random*.ti,ab.
41	factorial*.ti,ab.
42	(crossover* or cross over*).ti,ab.
43	((doubl* or singl*) adj blind*).ti,ab.
44	(assign* or allocat* or volunteer* or placebo*).ti,ab.
45	crossover procedure/
46	single blind procedure/
47	randomized controlled trial/
48	double blind procedure/
49	or/40-48
50	systematic review/
51	meta-analysis/
52	(meta analy* or metanaly* or metaanaly*).ti,ab.
53	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
54	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
55	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
56	(search* adj4 literature).ab.
57	(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.
58	((pool* or combined) adj2 (data or trials or studies or results)).ab.
59	cochrane.jw.
60	or/50-59
61	39 and (49 or 60)
62	Clinical study/
63	Case control study/

#	Searches
64	Family study/
65	Longitudinal study/
66	Retrospective study/
67	comparative study/
68	Prospective study/
69	Randomized controlled trials/
70	68 not 69
71	Cohort analysis/
72	cohort analy$.tw.
73	(Cohort adj (study or studies)).tw.
74	(Case control$ adj (study or studies)).tw.
75	(follow up adj (study or studies)).tw.
76	(observational adj (study or studies)).tw.
77	(epidemiologic$ adj (study or studies)).tw.
78	(cross sectional adj (study or studies)).tw.
79	case series.tw.
80	prospective.tw.
81	retrospective.tw.
82	or/62-67,70-81
83	39 and 82
84	83 not 61

Database: Cochrane Database of Systematic Reviews Issue 1 of 12, January 2025

Date of last search: 07/01/2025

#	Searches
#1	((sperm* or ejaculat* or epididym* or vasal* or seminal NEXT tract* or genital NEXT tract* or reproduct* NEXT tract*) near/3 (obstruct* or block*)):ti,ab
#2	(CBAVD or (absen* near/3 (vasa next deferentia or ((vas or duct*) next deferens)))):ti,ab
#3	MeSH descriptor: [Azoospermia] this term only
#4	azoosperm*:ti,ab
#5	{or #1-#4}
#6	(surg* or microsurg* or operat* or minimal* next invasive or endoscop* or reconstruct* or resect* or disobstruct*):ti,ab
#7	MeSH descriptor: [General Surgery] this term only
#8	MeSH descriptor: [Urologic Surgical Procedures, Male] this term only
#9	MeSH descriptor: [Minimally Invasive Surgical Procedures] this term only
#10	MeSH descriptor: [Microsurgery] this term only
#11	MeSH descriptor: [Endoscopy] this term only
#12	MeSH descriptor: [] explode all trees and with qualifier(s): [surgery - SU]
#13	{or #6-#12}
#14	#5 and #13
#15	((male NEXT steril* or vasectom*) near/3 revers*):ti,ab
#16	(epididymovasostom* or vasoepididymostom* or transvasovasostom* or vasovasostom* or vasostom*):ti,ab
#17	MeSH descriptor: [Vasovasostomy] this term only
#18	MeSH descriptor: [Ejaculatory Ducts] this term only and with qualifier(s): [surgery - SU]
#19	(TURED or ((Transurethral or trans next urethral) and ejaculatory next duct*))
#20	MeSH descriptor: [Epididymis] this term only and with qualifier(s): [surgery - SU]
#21	MeSH descriptor: [Vas Deferens] this term only and with qualifier(s): [surgery - SU]
#22	{or #14-#21}
#23	conference:pt or (clinicaltrials or trialsearch):so
#24	#22 not #23 in Cochrane Reviews

Database: Cochrane Central Register of Controlled Trials Issue 12 of 12, December 2024

Date of last search: 07/01/2025

#	Searches
#1	((sperm* or ejaculat* or epididym* or vasal* or seminal NEXT tract* or genital NEXT tract* or reproduct* NEXT tract*) near/3 (obstruct* or block*)):ti,ab
#2	(CBAVD or (absen* near/3 (vasa next deferentia or ((vas or duct*) next deferens)))):ti,ab
#3	MeSH descriptor: [Azoospermia] this term only
#4	azoosperm*:ti,ab
#5	{or #1-#4}
#6	(surg* or microsurg* or operat* or minimal* next invasive or endoscop* or reconstruct* or resect* or disobstruct*):ti,ab
#7	MeSH descriptor: [General Surgery] this term only
#8	MeSH descriptor: [Urologic Surgical Procedures, Male] this term only
#9	MeSH descriptor: [Minimally Invasive Surgical Procedures] this term only
#10	MeSH descriptor: [Microsurgery] this term only
#11	MeSH descriptor: [Endoscopy] this term only
#12	MeSH descriptor: [] explode all trees and with qualifier(s): [surgery - SU]
#13	{or #6-#12}
#14	#5 and #13
#15	((male NEXT steril* or vasectom*) near/3 revers*):ti,ab
#16	(epididymovasostom* or vasoepididymostom* or transvasovasostom* or vasovasostom* or vasostom*):ti,ab
#17	MeSH descriptor: [Vasovasostomy] this term only
#18	MeSH descriptor: [Ejaculatory Ducts] this term only and with qualifier(s): [surgery - SU]
#19	(TURED or ((Transurethral or trans next urethral) and ejaculatory next duct*))
#20	MeSH descriptor: [Epididymis] this term only and with qualifier(s): [surgery - SU]
#21	MeSH descriptor: [Vas Deferens] this term only and with qualifier(s): [surgery - SU]
#22	{or #14-#21}
#23	conference:pt or (clinicaltrials or trialsearch):so
#24	#22 not #23 in Trials

Database: Epistemonikos

Date of last search: 07/01/2025

#	Searches
1	(title:(((sperm* OR ejaculat* OR epididym* OR vasal* OR "seminal tract" OR "genital tract" OR "reproduct* tract") AND (obstruct* OR block*))) OR abstract:(((sperm* OR ejaculat* OR epididym* OR vasal* OR "seminal tract" OR "genital tract" OR "reproduct* tract") AND (obstruct* OR block*)))) OR (title:((CBAVD OR "vas deferens" OR "vasa deferentia" OR "duct deferens" OR azoosperm*)) OR abstract:((CBAVD OR "vas deferens" OR "vasa deferentia" OR "duct deferens" OR azoosperm*))) AND (title:(((surg* OR microsurg* OR operat* OR "minimally invasive" OR endoscop* OR reconstruct* OR resect* OR disobstruct*))) OR abstract:(((surg* OR microsurg* OR operat* OR "minimally invasive" OR endoscop* OR reconstruct* OR resect* OR disobstruct*))))
2	(title:(((vasectom* AND revers*) OR epididymovasostom* OR vasoepididymostom* OR transvasovasostom* OR vasovasostom* OR vasostom*)) OR abstract:(((vasectom* AND revers*) OR epididymovasostom* OR vasoepididymostom* OR transvasovasostom* OR vasovasostom* OR vasostom*))) OR (title:((TURED OR ((transurethral OR "trans urethral") AND ("ejaculatory duct" OR "ejaculatory ducts")))) OR abstract:((TURED OR ((transurethral OR "trans urethral") AND ("ejaculatory duct" OR "ejaculatory ducts")))))
3	#1 or #2 [Limited to systematic reviews]

Health Economic Literature search strategies

Database: Ovid MEDLINE(R) ALL <1946 to January 06, 2025>

Date of last search: 09/01/2025

#	Searches
1	((sperm* or ejaculat* or epididym* or vasal* or seminal tract* or genital tract* or reproduct* tract*) adj3 (obstruct* or block*)).tw.
2	(CBAVD or (absen* adj3 (vasa deferentia or ((vas or duct*) adj deferens)))).tw.

#	Searches
3	Azoospermia/ or azoosperm*.tw.
4	or/1-3
5	(surg* or microsurg* or operat* or "minimal* invasive" or endoscop* or reconstruct* or resect* or disobstruct*).tw.
6	General Surgery/ or Urologic Surgical Procedures, Male/ or Minimally Invasive Surgical Procedures/ or Endoscopy/ or Microsurgery/ or su.fs.
7	or/5-6
8	4 and 7
9	((male steril* or vasectom*) adj3 revers*).tw.
10	(epididymovasostom* or vasoepididymostom* or transvasovasostom* or vasovasostom* or vasostom*).tw.
11	vasovasostomy/
12	ejaculatory ducts/su
13	(TURED or ((Transurethral or trans urethral) and ejaculatory duct*)).tw.
14	epididymis/su
15	vas deferens/su
16	or/8-15
17	letter/
18	editorial/
19	news/
20	exp historical article/
21	Anecdotes as Topic/
22	comment/
23	case reports/
24	(letter or comment*).ti.
25	or/17-24
26	randomized controlled trial/ or random*.ti,ab.
27	25 not 26
28	animals/ not humans/
29	exp Animals, Laboratory/
30	exp Animal Experimentation/
31	exp Models, Animal/
32	exp Rodentia/
33	(rat or rats or mouse or mice or rodent*).ti.
34	or/27-33
35	16 not 34
36	limit 35 to english language
37	Economics/
38	Value of life/
39	exp "Costs and Cost Analysis"/
40	exp Economics, Hospital/
41	exp Economics, Medical/
42	exp Resource Allocation/
43	Economics, Nursing/
44	Economics, Pharmaceutical/
45	exp "Fees and Charges"/
46	exp Budgets/
47	budget*.ti,ab.
48	cost*.ti,ab.
49	(economic* or pharmaco?economic*).ti,ab.
50	(price* or pricing*).ti,ab.
51	(financ* or fee or fees or expenditure* or saving*).ti,ab.
52	(value adj2 (money or monetary)).ti,ab.
53	resourc* allocat*.ti,ab.
54	(fund or funds or funding* or funded).ti,ab.
55	(ration or rations or rationing* or rationed).ti,ab.

#	Searches
56	ec.fs.
57	or/37-56
58	quality-adjusted life years/
59	sickness impact profile/
60	(quality adj2 (wellbeing or well being)).ti,ab.
61	sickness impact profile.ti,ab.
62	disability adjusted life.ti,ab.
63	(qal* or qtime* or qwb* or daly*).ti,ab.
64	(euroqol* or eq5d* or eq 5*).ti,ab.
65	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
66	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
67	(hui or hui1 or hui2 or hui3).ti,ab.
68	(health* year* equivalent* or hye or hyes).ti,ab.
69	discrete choice*.ti,ab.
70	rosser.ti,ab.
71	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
72	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
73	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
74	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
75	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
76	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
77	or/58-76
78	36 and (57 or 77)

Database: Embase <1974 to 2025 January 07>

Date of last search: 09/01/2025

#	Searches
1	((sperm* or ejaculat* or epididym* or vasal* or seminal tract* or genital tract* or reproduct* tract*) adj3 (obstruct* or block*)).tw.
2	(CBAVD or (absen* adj3 (vasa deferentia or ((vas or duct*) adj deferens)))).tw.
3	Azoospermia/ or azoosperm*.tw.
4	or/1-3
5	(surg* or microsurg* or operat* or "minimal* invasive" or endoscop* or reconstruct* or resect* or disobstruct*).tw.
6	surgery/ or "minimally invasive procedure"/ or urologic surgery/ or endoscopic surgery/ or microsurgery/ or su.fs.
7	or/5-6
8	4 and 7
9	male sterilization reversal/
10	((male steril* or vasectom*) adj3 revers*).tw.
11	(epididymovasostom* or vasoepididymostom* or transvasovasostom* or vasovasostom* or vasostom*).tw.
12	vasovasostomy/
13	vasal obstruction/su
14	transurethral resection/ and ejaculatory duct/
15	ejaculatory duct/su or ejaculatory duct obstruction/su
16	(TURED or ((Transurethral or trans urethral) and ejaculatory duct*)).tw.
17	epididymis/su
18	vas deferens/su
19	or/8-18
20	letter.pt. or letter/
21	note.pt.
22	editorial.pt.
23	case report/ or case study/
24	(letter or comment*).ti.
25	or/20-24

#	Searches
26	randomized controlled trial/ or random*.ti,ab.
27	25 not 26
28	animal/ not human/
29	nonhuman/
30	exp Animal Experiment/
31	exp Experimental Animal/
32	animal model/
33	exp Rodent/
34	(rat or rats or mouse or mice or rodent*).ti.
35	or/27-34
36	19 not 35
37	limit 36 to english language
38	(conference abstract* or conference review or conference paper or conference proceeding).db,pt,su.
39	37 not 38
40	health economics/
41	exp economic evaluation/
42	exp health care cost/
43	exp fee/
44	budget/
45	funding/
46	resource allocation/
47	budget*.ti,ab.
48	cost*.ti,ab.
49	(economic* or pharmaco?economic*).ti,ab.
50	(price* or pricing*).ti,ab.
51	(financ* or fee or fees or expenditure* or saving*).ti,ab.
52	(value adj2 (money or monetary)).ti,ab.
53	resourc* allocat*.ti,ab.
54	(fund or funds or funding* or funded).ti,ab.
55	(ration or rations or rationing* or rationed).ti,ab.
56	or/40-55
57	quality adjusted life year/
58	"quality of life index"/
59	short form 12/ or short form 20/ or short form 36/ or short form 8/
60	sickness impact profile/
61	(quality adj2 (wellbeing or well being)).ti,ab.
62	sickness impact profile.ti,ab.
63	disability adjusted life.ti,ab.
64	(qal* or qtime* or qwb* or daly*).ti,ab.
65	(euroqol* or eq5d* or eq 5*).ti,ab.
66	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
67	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
68	(hui or hui1 or hui2 or hui3).ti,ab.
69	(health* year* equivalent* or hye or hyes).ti,ab.
70	discrete choice*.ti,ab.
71	rosser.ti,ab.
72	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
73	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
74	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
75	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
76	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
77	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
78	or/57-77
79	39 and (56 or 78)

Database: INAHTA

Date of last search: 09/01/2025

#	Searches
12	#11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1
11	"Vas Deferens"[mh]
10	(epididymis)
9	((TURED or ((Transurethral or trans urethral) and ejaculatory duct*)))
8	"Ejaculatory Ducts"[mh]
7	"Vasovasostomy"[mh]
6	((epididymovasostom* or vasoepididymostom* or transvasovasostom* or vasovasostom* or vasostom*))
5	(((male steril* or vasectom*) and revers*))
4	(((surg* or microsurg* or operat* or "minimal* invasive" or endoscop* or reconstruct* or resect* or disobstruct*))) AND (((sperm* or ejaculat* or epididym* or vasal* or seminal tract* or genital tract* or reproduct* tract*) and (obstruct* or block*)))
3	"Azoospermia"[mh]
2	(azoosperm*)
1	((CBAVD or "vasa deferentia")) OR (((vas or duct*) and deferens))

Database: HTA via CRD

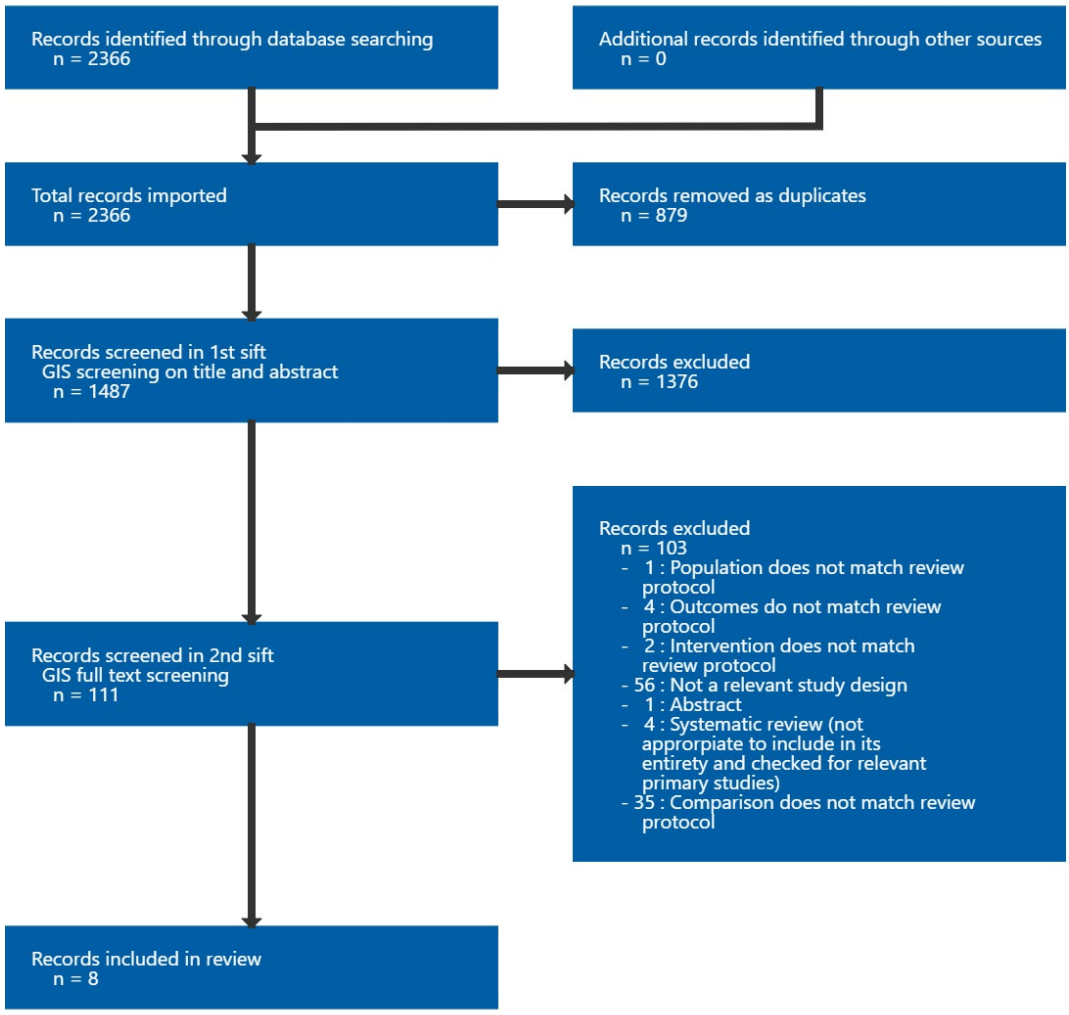
Date of last search: 09/01/2025

#	Searches
1	(((((sperm* or ejaculat* or epididym* or vasal* or seminal tract* or genital tract* or reproduct* tract*) adj3 (obstruct* or block*))))) and (Project record:ZDT OR Full publication record:ZDT) IN HTA
2	((((CBAVD or (absen* adj3 (vasa deferentia or ((vas or duct*) adj deferens)))))) and (Project record:ZDT OR Full publication record:ZDT) IN HTA
3	((azoosperm*)) and (Project record:ZDT OR Full publication record:ZDT) IN HTA
4	MeSH DESCRIPTOR Azoospermia EXPLODE ALL TREES
5	(((((male steril* or vasectom*) adj3 revers*))) and (Project record:ZDT OR Full publication record:ZDT) IN HTA
6	(((epididymovasostom* or vasoepididymostom* or transvasovasostom* or vasovasostom* or vasostom*))) and (Project record:ZDT OR Full publication record:ZDT) IN HTA
7	MeSH DESCRIPTOR vasovasostomy IN HTA
8	MeSH DESCRIPTOR vas deferens IN HTA
9	MeSH DESCRIPTOR epididymis IN HTA
10	(((TURED or ((Transurethral or trans urethral) and ejaculatory duct*)))) and (Project record:ZDT OR Full publication record:ZDT) IN HTA
11	MeSH DESCRIPTOR ejaculatory ducts IN HTA
12	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11

Appendix C Effectiveness

Study selection for review question: What is the clinical and cost effectiveness of surgical interventions for fertility problems associated with obstructive azoospermia?

Figure 1: Study selection flow chart



Appendix D Evidence tables

Evidence tables for review question: What is the clinical and cost effectiveness of surgical interventions for fertility problems associated with obstructive azoospermia?

Belker, 1991

Bibliographic Reference	Belker, A M; Thomas, A J Jr; Fuchs, E F; Konnak, J W; Sharlip, I D; Results of 1,469 microsurgical vasectomy reversals by the Vasovasostomy Study Group.; The Journal of urology; 1991; vol. 145 (no. 3); 505-11

Study details

Country where study was carried out	USA
Study type	Retrospective cohort study
Study dates	August 1976 to May 1985
Inclusion criteria	Men who underwent microsurgical vasectomy reversal procedures
Exclusion criteria	Not reported
Patient characteristics	Demographics of n=1,247 patients undergoing a first microsurgical vasectomy reversal procedure (including those with vasovasostomy 1 side, vasoepididymostomy other side and with procedure unspecified) **Mean age, years (range)** 36.9 (20.3-67.4) **Mean female age, years (range)** 29.6 (17-46) **Mean prior number of children (range)** 1.8 (0-9.0)

	Mean obstructive interval, years (range) 7.0 (<1.0-33.0) **Reasons for reversal in 1,213 patients** Divorce and remarriage: n=897 Religion: n=7 Scrotal pain: n=19 Child death: n=20 Divorced, not remarried: n=20 Other: n=239
Intervention(s)/control	**Vasovasostomy** A 2-layer microsurgical vasovasostomy was performed using interrupted 9/10-zero nylon to approximate the mucosal edges and interrupted 9-zero nylon to approximate the muscular and adventitial edges. A modified 1-layer microsurgical vasovasostomy was performed using 4 - 8 interrupted full thickness 9-zero nylon sutures and additional interrupted 9-zero nylon sutures through the muscularis and adventitia between the full thickness sutures. **Vasoepididymostomy** Microsurgical vasoepididymostomy was performed using either an end-to-end or end-to-side method by approximating the mucosa of the vas to the edges of the opened epididymal tubule with interrupted 10-zero nylon and then approximating the muscularis and adventitia of the vas to the edges of the incised epidydimal tunic with interrupted 9-zero nylon.
Duration of follow-up	Postoperative semen analyses at 2 to 4-month intervals until conception occurred or the patient was lost to follow-up
Sources of funding	Not reported
Sample size	N=1,208 patients undergoing a first microsurgical vasectomy reversal procedure (36 patients with vasovasostomy 1 side

	and vasoepididymostomy other side and 3 patients with unspecified surgery type were not included in the review).
Other information	The paper reports results for n=1,247 first-time and n=222 repeat microsurgical vasectomy reversal procedures, however results for repeat vasectomy reversal patients are not included in this review. Patients (n=192) were excluded from pregnancy rate calculations for the following reasons: reversal was performed for reasons other than restoration of fertility, postoperative information showed that the couple was divorced, using contraception or the wife's fertility was impaired, or combined factors.

Outcome	**Vasovasostomy**	**Vasoepididymostomy**
Pregnancy achieved Information about postoperative pregnancies, spontaneous abortions, deliveries, and the gender and health of the child was obtained from the couple, obstetrician or referring physician	n = 412/777; % = 53	n = 2/8; % = 25
Sperm in semen	n = 837/966; % = 87	n = 5/12; % = 42

Critical appraisal – Cochrane ROBINS-I

Section	**Question**	**Answer**
1. Bias due to confounding	Risk of bias judgement for confounding	Serious *(There is insufficient information in the study to determine the reliability or validity of measurement, and so it is expected there is serious residual confounding)*
2. Bias in selection of participants into the study	Risk of bias judgement for selection of participants into the study	Low *(The study includes consecutive vasectomy reversal performed by selected surgeons, and so it is likely that all participants who would have been eligible for the target trial were included in the study. It appears for each participant, start of follow up and start of intervention coincided)*
3. Bias in classification of interventions	Risk of bias judgement for classification of interventions	Low *(The study is retrospective, but the intervention status is well defined and the definition is likely based on information collected at the time of intervention)*
4. Bias due to deviations from intended interventions	Risk of bias judgement for deviations from intended interventions	Low *(Since the study was retrospective in nature any deviations from usual practice were unlikely to impact on the outcome)*
5. Bias due to missing data	Risk of bias judgement for missing data	Serious *(Proportions of missing participants differ substantially across interventions (data on*

Section	Question	Answer
		pregnancy achieved data was available for 65% of participants in the VV group and 57% of participants in the VE group). The analysis did not appear to remove the risk of bias arising from the missing data)
6. Bias in measurement of outcomes	Risk of bias judgement for measurement of outcomes	Serious *(The methods of outcome assessment were not comparable across intervention groups; postoperative semen analyses were completed at 2 to 4-month intervals until conception occurred or the patient was lost to follow-up, subsequently participants could achieve outcomes at different times. Information about postoperative pregnancies, spontaneous abortions, deliveries, and the gender and health of the child was obtained from the couple, obstetrician or referring physician)*
7. Bias in selection of the reported result	Risk of bias judgement for selection of the reported result	Moderate *(The outcome measurements and analyses are defined, there is no indication of selection of the reported analysis from among multiple analyses, and there is no indication of selection of the cohort or subgroups for analysis and reporting on the basis of the results)*
Overall bias	Risk of bias judgement	Serious
Overall bias	Risk of bias variation across outcomes	This study has some important problems, and the risk of bias was rated as serious across several domains (confounding, missing data, and measurement of outcomes)
Overall bias	Directness	Indirect *(The study does not report whether participants had azoospermia)*

Boorjian, 2004

Bibliographic Reference	Boorjian, Stephen; Lipkin, Michael; Goldstein, Marc; The impact of obstructive interval and sperm granuloma on outcome of vasectomy reversal.; The Journal of urology; 2004; vol. 171 (no. 1); 304-6

Study details

Country where study was carried out	USA
Study type	Retrospective cohort study
Study dates	1984 to 2001

Inclusion criteria	Men undergoing first time vasectomy reversals with bilateral reconstruction
Exclusion criteria	Men who presented for repeat reconstruction, and cases of female factor infertility.
Patient characteristics	Demographics of n=213 patients (including those undergoing vasovasostomy/vasoepididymostomy) **Patients with an obstructive interval less than 5 year**s, n=45 Mean male age: 39 years Mean female partner age: 34 years Men who underwent at least a unilateral VE: 18% **Patients with an obstructive interval between 5-10 year**s, n=85 Mean male age: 41 years Mean female partner age: 33 years Men who underwent at least a unilateral VE: 29% **Patients with an obstructive interval between 10-15 year**s, n=56 Mean male age: 44 years Mean female partner age: 32 years Men who underwent at least a unilateral VE: 25% **Patients with an obstructive interval greater than 15 year**s, n=27 Mean male age: 49 years Mean female partner age: 34 years

	Men who underwent at least a unilateral VE: 26% Overall mean male age=43.2 years Overall mean female partner age=33.2 years
Intervention(s)/control	**Vasovasostomy (VV) and Vasoepididymostomy (VE)** Surgery was performed using a multilayer microsurgical approach. The entire vasectomy site including sperm granuloma, if present, was always excised.
Duration of follow-up	Postoperative evaluation included serial semen analyses beginning at 6 weeks and continuing until a pregnancy was achieved or patients were lost to follow-up. The minimum follow-up in patients yet to conceived was 6 months.
Sources of funding	Not reported
Sample size	N=195 patients undergoing vasovasostomy or vasoepididymostomy (n=18 patients undergoing vasovasostomy/ vasoepididymostomy were not included in the review).
Other information	Only naturally conceived pregnancies were included in the study and none of the female partners used assisted reproduction techniques to achieve pregnancy. Only clinical pregnancies with documented heartbeats were included in the study.

Outcome	**Vasovasostomy, N = 159**	**Vasoepididymostomy, N = 36**
Clinical pregnancy With a documented heartbeat, conceived naturally	n = 132; % = 83	n = 29; % = 81

Critical appraisal – Cochrane ROBINS-I

Section	**Question**	**Answer**
1. Bias due to confounding	Risk of bias judgement for confounding	Serious *(The study did not control for or appropriately measure important confounders.)*
2. Bias in selection of participants into the study	Risk of bias judgement for selection of participants into the study	Low *(The study retrospectively reviewed randomly selected vasectomy reversals performed by a single surgeon. It is likely that all participants who would have been eligible for the target trial were included in the study, and it appears that the start of follow up and start of intervention*

Section	Question	Answer
		coincided for all participants.)
3. Bias in classification of interventions	Risk of bias judgement for classification of interventions	Low *(Intervention status appears well defined and it is likely that the intervention definition is based solely on information collected at the time of intervention)*
4. Bias due to deviations from intended interventions	Risk of bias judgement for deviations from intended interventions	Low *(The study is retrospective so any deviations from usual practice were unlikely to impact on the outcome.)*
5. Bias due to missing data	Risk of bias judgement for missing data	Low *(Data appeared to be complete)*
6. Bias in measurement of outcomes	Risk of bias judgement for measurement of outcomes	Low *(The methods of outcome assessment were comparable across intervention groups; the outcome clinical pregnancy was measured by a documented heartbeat and was unlikely to be influenced by knowledge of the intervention received by study participants, and any error in measuring the outcome is unrelated to intervention status.)*
7. Bias in selection of the reported result	Risk of bias judgement for selection of the reported result	Moderate *(The outcome measurements and analyses are defined, there is no indication of selection of the reported analysis from among multiple analyses, and there is no indication of selection of the cohort or subgroups for analysis and reporting on the basis of the results.)*
Overall bias	Risk of bias judgement	Serious
Overall bias	Risk of bias variation across outcomes	This study has some important problems, and the risk of bias was rated as serious for one domain (confounding) and moderate for one domain (selection of the reported result)
Overall bias	Directness	Directly applicable

Heidenreich, 2000

Bibliographic Reference Heidenreich, A; Altmann, P; Engelmann, U H; Microsurgical vasovasostomy versus microsurgical epididymal sperm aspiration/testicular extraction of sperm combined with intracytoplasmic sperm injection. A cost-benefit analysis.; European urology; 2000; vol. 37 (no. 5); 609-14

Study details

Country where study was carried out	Germany
Study type	Retrospective cohort study
Study dates	January 1994 to December 1997
Inclusion criteria	Men who underwent microsurgical double-layer vasovasostomy for vasectomy reversal, and patients with obstructive azoospermia who were not amenable to microsurgical reconstruction and primary testicular failure or obstruction of the rete testis
Exclusion criteria	Not reported
Patient characteristics	n=156 patients n=165 vasovasostomy procedures n=62 MESA/ICSI procedures n=41 TESE/ICSI procedures Mean interval of vasal obstruction was 7.6 (0.5–18) years (in vasovasostomy group) Mean age of male patients in the MESA/TESE group was 37 (23-67) years Mean age of female partner in the MESA/TESE group was 30 (20-43) years The indication for MESA/TESE combined with ICSI n=82.5% obstruction of the vas deferens, epididymis or rete testis which is not amenable to microsurgical reconstruction n=10.2% testicular atrophy due to orchitis or cryptorchidism n=1.5% epididymal fibrosis n=5.8% ejaculatory disorders

Intervention(s)/control	**Vasovasostomy** The testicle, epididymis and vas deferens were exposed through a bilateral scrotal incision. The distal and proximal scarred stumps of the vas deferens were localized and excised. Fluid was aspirated from the testicular end of the vas and immediately examined microscopically. For microsurgical anastomosis, the mucosal layer was adapted with 6–8 sutures of 10–0 nylon and the seromuscularis was adapted with 10–12 sutures of 9–0 nylon. **Microsurgical epididymal sperm aspiration (MESA)/ICSI and testicular extraction of sperm (TESE)/ICSI** The testicle and epididymis were exposed through a scrotal incision. A single, preferentially distal dilated loop of the epididymis was isolated and unroofed with microsurgical scissors. The fluid was aspirated, examined microscopically and placed in HAM's F10 medium in case of positive sperm visualization. Regarding TESE, the testicle was exposed via a scrotal incision, 4 – 6 biopsies were taken, placed in medium and sent to the reproductive biology unit.
Duration of follow-up	Median follow-up for vasovasostomy was 21 months (range 2-60 months)
Sources of funding	Not reported
Sample size	N=225
Other information	A questionnaire was sent to all patients and their practicing urologists to obtain information concerning date of vasectomy, prior pregnancies, postoperative complications, and pregnancy and birth rates following vasovasostomy. Postoperative complications following vasovasostomy occurred in 4.7% of the male patients such as scrotal hematoma, wound infection or postoperative pain lasting for as long as 18 days following microsurgery. Local complications following MESA or TESE occurred in 4.3% of the men and comprised scrotal hematoma, wound infection and testalgia.

Outcome	**Vasovasostomy, N = 112**	**MESA/TESE, N = 69**
Pregnancy rate Measured by mailed questionnaire responses	n = 58; % = 52	n = 17; % = 24.5

Critical appraisal – Cochrane ROBINS-I

Section	**Question**	**Answer**
1. Bias due to confounding	Risk of bias judgement for confounding	Serious *(The study did not control for or appropriately measure important confounders)*
2. Bias in selection of	Risk of bias judgement for	Serious

Section	Question	Answer
participants into the study	selection of participants into the study	*(The study retrospectively reviewed the medical records of men undergoing vasectomy reversals. It is unclear whether all participants who would have been eligible for the target trial were included in the study and follow up is only reported for the vasovasostomy group.)*
3. Bias in classification of interventions	Risk of bias judgement for classification of interventions	Serious *(Intervention status is not well defined as there is a lack of reporting on whether participants underwent multiple surgeries. The study includes n=156 patients and reports on n=165 vasovasostomy procedures.)*
4. Bias due to deviations from intended interventions	Risk of bias judgement for deviations from intended interventions	Serious *(There is no information on whether deviations took place from usual practice, and since the number of patients does not match the number of procedures in the vasovasostomy group, this may have occurred and would likely affect the outcome.)*
5. Bias due to missing data	Risk of bias judgement for missing data	Serious *(Proportions of missing participants differ substantially across interventions (data on pregnancy rate was available for 71.8% of participants in the vasovasostomy group and 100% of participants in the MESA/TESE group). The analysis is unlikely to have removed the risk of bias arising from the missing data.)*
6. Bias in measurement of outcomes	Risk of bias judgement for measurement of outcomes	Moderate *(The methods of outcome assessment were comparable across intervention groups, the outcome clinical pregnancy rate was unlikely to be influenced by knowledge of the intervention received by study participants however this was measured by questionnaire. Any error in measuring the outcome is only minimally related to intervention status.)*
7. Bias in selection of the reported result	Risk of bias judgement for selection of the reported result	Serious *(There is a high risk of selective reporting from among multiple analyses, as the study reports percentages only and not number of events for each group. The pregnancy rate is reported as 53% for the vasovasostomy group in the text, but as 52% in table 1.)*
Overall bias	Risk of bias judgement	Serious
Overall bias	Risk of bias variation across outcomes	This study has some important problems, and the risk of bias was rated as serious across multiple domains (confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, the selection of the reported result)
Overall bias	Directness	Directly applicable

Hibi, 2020

Bibliographic Reference	Hibi, Hatsuki; Sugie, Miho; Ohori, Tadashi; Sonohara, Megumi; Fukunaga, Noritaka; Asada, Yoshimasa; Microsurgical seminal reconstruction; our experiences in a single institute.; Nagoya journal of medical science; 2020; vol. 82 (no. 3); 477-485

Study details

Country where study was carried out	Japan
Study type	Retrospective cohort study
Study dates	July 2002 and December 2018
Inclusion criteria	Obstructive azoospermic subjects referred to a male infertility clinic
Exclusion criteria	Not described
Patient characteristics	Vasovasostomy (VV group), Vasoepididymostomy (VE-group) **Cause of vasal obstruction in VV-group (N=45)** Inguinal herniorrhaphy (n=3) Previous vasectomy (n=42 subjects) **Cause of epidydimal obstruction in VE-group (N=45)** Orchidopexy (n=4) Young’s syndrome (n=3) Epididymitis (n=2) Unknown cause (n=36)

	Mean age, years (range) [significant difference between groups, p=0.0159] VV: 41 (27-61) VE: 33 (25-44) **Spouse mean age, years (range)** VV: 32 (20-45) VE: 31 (26-39) **Duration of obstruction, years (range)** VV: 12 (0.5-30) VE: unknown **Testicular volume (R/L) (mL)** VV: 20 (12-30)/18 (10-26) VE: 22 (8-30)/19 (8-28) **Testosterone, ng/mL (range)** VV: 4.48 (1.84-9.94) VE: 5.33 (3.04-9.25) **BMI (range)**

	VV: 23.9 (17.8-29.7) VE: 23.1 (18.8-32.1)
Intervention(s)/control	The surgical procedure was undertaken using an operative microscope under general anaesthesia. **Vasovasostomy (VV group)** VV was performed by the two-microlayer anastomotic technique under an operative microscope. Scrotal skin was incised longitudinally just above to the vas deferens (in cases of previous vasectomy), and skin incision was made on the previous operative scar (in cases of inguinal vasal obstruction). If adequate vasal length was obtained without any tension for the anastomosis, vasotomy was made. 2-3 mL of indigo carmine solution was gently injected to the distal vas. Distal patency was confirmed with drainage of blue-coloured-urine through a Foley's catheter inserted to the bladder during surgery. Although no sperm was obtained from bilateral vas deferens anastomoses performed, TESE was carried out and sperm cryopreserved in cases where patient had consented. Mucosal anastomosis was done using 6 sutures using 10-0 double armed nylon inside to outside fashion to ensure the mucosal adhesion. Additional 8 sutures by 9-0 nylon were used for adventitial anastomosis to complete VV. **Vasoepididymostomy (VE-group)** VE was performed using a double needle longitudinal intussusception technique. Vasotomy and confirmation of distal vasal patency were made by same manoeuvre as VV. The epididymal tunic was cut and trimmed to expose the dilated epididymal tubule with a micro-scissors. Two 10-0 double armed nylon sutures were parallelly placed to the epididymal tubule longitudinally. The tubulotomy was made and epididymal fluid was examined and collected. If spermatozoa were present, anastomosis and harvest of epididymal sperm for cryopreservation was carried out. The needles were pulled through and placed through the 4 microdots on the vasal ends in an inside-out fashion. To ligate these sutures, the epididymal tubule intussuscepted into the vas lumen. Then, the outer layer of 9-0 nylon sutures completed the anastomosis. If no sperm was found in the epididymis, the procedure was repeated more proximally. If no sperm were observed in the whole epididymis, anastomosis was not carried out.
Duration of follow-up	Post-operative follow-up consisted of serial semen analysis from 3 weeks to up to 3 years
Sources of funding	None
Sample size	N=90
Other information	In cases of unknown aetiology of epididymal obstruction, 3 subjects had a live birth following natural intercourse. Sperm harvest and cryopreservation during surgery was performed when requested by the patient.

Outcome	Vasovasostomy, N = 45	Vasoepididymostomy, N = 45
Natural pregnancy and delivery	n = 7; % = 15.6	N=7; % = 15.6
Pregnancy and delivery obtained by ICSI	n = 4; % = 8.9	n = 14; % = 31.1
Overall pregnancy and delivery (natural and ICSI combined)	n = 11; % = 24.4	n = 21; % = 46.7

Critical appraisal – Cochrane ROBINS-I

Section	Question	Answer
1. Bias due to confounding	Risk of bias judgement for confounding	Serious *(The study did not control for or appropriately measure important confounders and there is a significant difference in the mean age of the groups at baseline.)*
2. Bias in selection of participants into the study	Risk of bias judgement for selection of participants into the study	Moderate *(Participants were n=90 subjects selected from n=442 subjects diagnosed with obstructive azoospermia and referred to the male infertility clinic. It is unclear how those particular participants were selected. It appears that start of follow up and start of intervention do coincide for all participants.)*
3. Bias in classification of interventions	Risk of bias judgement for classification of interventions	Low *(Intervention status is well defined and it is likely that the intervention definition is based solely on information collected at the time of intervention.)*
4. Bias due to deviations from intended interventions	Risk of bias judgement for deviations from intended interventions	Low *(It appears as though there were no deviations from the intended interventions.)*
5. Bias due to missing data	Risk of bias judgement for missing data	Low *(Data appears to be complete)*
6. Bias in measurement of outcomes	Risk of bias judgement for measurement of outcomes	Moderate *(The methods of outcome assessment appear to be comparable across intervention groups however it is unclear how pregnancy and delivery were measured. Outcomes were unlikely to be influenced by knowledge of the intervention received by study participants, and any error in measuring the outcome be minimally related to intervention status)*
7. Bias in selection of	Risk of bias judgement for	Moderate

Section	Question	Answer
the reported result	selection of the reported result	*(The outcome measurements and analyses are defined, there is no indication of selection of the reported analysis from among multiple analyses, and there is no indication of selection of the cohort or subgroups for analysis and reporting on the basis of the results.)*
Overall bias	Risk of bias judgement	Serious
Overall bias	Risk of bias variation across outcomes	This study has some important problems, and the risk of bias was rated as serious for one domain (confounding) and moderate across several domains (selection of participants in the study, measurement of outcomes and selection of the reported results)
Overall bias	Directness	Directly applicable

Kolettis, 2002

Bibliographic Reference Kolettis, Peter N; Sabanegh, Edmund S; D'amico, Anna M; Box, Lyndon; Sebesta, Michael; Burns, John R; Outcomes for vasectomy reversal performed after obstructive intervals of at least 10 years.; Urology; 2002; vol. 60 (no. 5); 885-8

Study details

Country/ies where study was carried out	USA
Study type	Retrospective cohort study
Study dates	Not reported
Inclusion criteria	Patients undergoing microsurgical vasectomy reversal with an obstructive interval of at least 10 years
Exclusion criteria	Not reported
Patient characteristics	Demographics of n=70 patients (including patients who underwent Vasovasostomy/Vasoepididymostomy) **Mean patient age (years):** 44.5 (34–56) **Mean partner age (years)** 32.9 (21–43)

	Procedures (n=74, n=15 repeat) Bilateral VV: n=47 VV/VE: n=16 Unilateral VV: n=7 Bilateral VE: n=3 Unilateral VE: n=1 **Mean obstructive interval (years):** 14.5 (10–24)
Intervention(s)/control	**Vasovasostomy (VV)** Surgery was performed with a modified one-layer anastomosis with 9-0 nylon or a 2-layer technique with 10-0 and 9-0 nylon. **Vasoepididymostomy (VE)** Surgery was performed using an end-to-side two-layer technique with 10-0 and 9-0 nylon. 2 of the surgeons at the time of the study used an intussusception technique. The indications for VE varied between surgeons, but, in general, VE was performed after failed VV (azoospermic at 6 months and epididymal obstruction noted at reoperation) or in the setting of a prolonged obstructive interval when poor quality (thick, pasty) vasal fluid devoid of sperm was noted.
Duration of follow-up	Not reported
Sources of funding	Not reported
Sample size	N=58 (16 procedures with vasovasostomy/vasoepididymostomy were not included in the review).
Other information	Patients with less than 12 months of follow-up or no ongoing interest in establishing conception were excluded from the pregnancy rate analysis unless they had established a pregnancy or had azoospermia at 6 or 12 months after VV or VE. Therefore, patients with azoospermia at 6 months after VV or 12 months after VE (i.e., technical failures with sufficient follow-up) were included in the pregnancy rate calculations.

Outcome	Vasovasostomy, N = 46	Vasoepididymostomy, N = 4

Outcome	Vasovasostomy, N = 46	Vasoepididymostomy, N = 4
Pregnancy rate	n = 18; % = 39	n = 1; % = 25

Critical appraisal – Cochrane ROBINS-I

Section	Question	Answer
1. Bias due to confounding	Risk of bias judgement for confounding	Serious *(The study did not control for or appropriately measure important confounders and important confounders are not reported for each group. Patients with less than 12 months of follow-up or no ongoing interest in establishing conception were excluded from the pregnancy rate analysis unless they had established a pregnancy or were azoospermic at 6 months after VE or 12 months after VE.)*
2. Bias in selection of participants into the study	Risk of bias judgement for selection of participants into the study	Serious *(There is little information on the selection of participants in the study (participants were selected on the basis of vasectomy reversal performed by three surgeons with an obstructive interval of at least 10 years) however selection into the study would probably not be related to intervention and outcome. Follow-up time is not reported so it is unclear whether start of follow up and start of intervention do coincide for all participants.)*
3. Bias in classification of interventions	Risk of bias judgement for classification of interventions	Low *(Intervention status is fairly well defined and it is likely that the intervention definition is based solely on information collected at the time of intervention.)*
4. Bias due to deviations from intended interventions	Risk of bias judgement for deviations from intended interventions	Serious *(There were four repeat procedures performed due to a failed procedure by one of the surgeons, however it is not clear to which group these participants were assigned. All other repeat procedures were performed after an initial failed procedure at another institution and it is also unclear to which group these participants were assigned. It is likely these were deviations from usual practice that were possibly unbalanced between the intervention groups, and likely to have affected the outcome)*
5. Bias due to missing data	Risk of bias judgement for missing data	Serious *(It is unclear whether data was available for all, or nearly all participants and proportions of missing participants are not reported across groups. The analysis is unlikely to have removed the risk of bias arising from the missing data)*

Section	Question	Answer
6. Bias in measurement of outcomes	Risk of bias judgement for measurement of outcomes	Serious *(The methods of outcome assessment were not reported so it is unclear whether these were comparable across intervention groups. There is no information on how pregnancy rate was calculated although this is unlikely to be influenced by knowledge of the intervention.)*
7. Bias in selection of the reported result	Risk of bias judgement for selection of the reported result	Moderate *(The outcome measurements and analyses are defined, there is no indication of selection of the reported analysis from among multiple analyses, and there is no indication of selection of the cohort or subgroups for analysis and reporting on the basis of the results)*
Overall bias	Risk of bias judgement	Serious
Overall bias	Risk of bias variation across outcomes	This study has some important problems, and the risk of bias was rated as serious across multiple domains (confounding, selection of participants, deviations from intended interventions, missing data and measurement of outcomes)
Overall bias	Directness	Directly applicable

Pai, 1973

Bibliographic Reference	Pai, M G; Sampath Kumar, B T; Kaundinya, C; Bhat, H S; Vasovasostomy. A clinical study with 10 years' follow-up.; Fertility and sterility; 1973; vol. 24 (no. 10); 798-801

Study details

Country/ies where study was carried out	India
Study type	Retrospective cohort study
Study dates	1961-1971
Inclusion criteria	Patients with post-vasectomy sterility (azoospermia) who sought vas reconstruction
Exclusion criteria	Not reported
Patient characteristics	**Reason for vasectomies**

	Family planning: n=30 Poor health of wives: n=3 Fear of transmission of disease (leprosy): n=1 Accidental vasectomy: n=2 **Age, years** Majority of patients between 31-40 years, upper limit 43 years 23-30: n=5 31-35: n=12 36-40: n=16 41 and above: n=3 **Interval between Vasectomy and Vas Reconstruction, years** 0.-0.5: n=1 0.5-1: n=4 1-2: n=2 3-5: n=18 5-10: n=8 10 and above: n=3
Intervention(s)/control	Each half of the scrotal sac was examined for nodules. The proximity of the nodules indicated the retracted cut ends of

	the vas. Through a 4- to 6-cm. incision, the scrotum was explored, and the cord was isolated and delivered. Closely placed nodules in the scar tissue and in the whitish cord like structure were identified as the vas in the fibrous tissue. Extensive dissections were done for mobilization of the vas (n=8), the proximal cut end was completely fibrosed (n=6) and were fibrosed up to 2cm (n=2). After isolation of the vas, the cut ends were examined for colour, lumen, and strictures. At various levels, the vas was sectioned to identify the normal lumen. Usually, only 0.5-cm. sectioning of the ballooned proximal ends was required to locate the dilated lumen of the vas (n=30), whereas the distal cut end of the vas had to be sectioned for at least 1-3 cm. Patency of the vas was assessed by passing a 28-gauge monofilament nylon fiber into the lumen. Mter patency of the vas on both sides had been confirmed, an end-to-end anastomosis was carried out with 2-4 equidistant sutures of 5-0 arterial black silk on an atraumatic needle. Splints were used in n=28. The introduction of the splint was carried out as follows: a 20-gauge hypodermic needle was passed through the proximal end of the vas for a distance of 1-2 cm. and then brought out to the surface; a 28-gauge nylon monofilament fibre was then threaded through the needle and brought out through the proximal cut end. Later, the fibre was passed into the distal end of the vas to lie within the lumen for a distance of 5-8 cm. The free end of the splint was brought out to the skin and anchored. After ensuring good haemostasis, the scrotum was closed in layers. Postoperatively, all patients were treated with penicillin or streptopenicillin. The splint was retained for less than 5 days in 3 patients, until the fifth day in 3, until the sixth day in 12, and until the seventh day in 1.
Duration of follow-up	After 3 months, the semen was analysed monthly for 3 months, and thereafter at intervals of 3 months until pregnancy occurred or until a normal sperm count (40 million/mL with 40-50% motility) was observed.
Sources of funding	Not reported
Sample size	N=36

Outcome	Vasovasostomy, N = 30	Epididymovasostomy, N = 6
Pregnancy attained All of the pregnancies resulted in normal deliveries with healthy children	n = 5; % = 17	n = 0; % = 0
Normal sperm count Number of patients with normal sperm count (40 million/mi., with 40-50% motility)	n = 14; % = 47	n = 0; % = 0
Low sperm count Number of patients with low sperm count	n = 7; % = 23	n = 1; % = 17
No sperm count Number of patients with no sperm count	n = 9; % = 30	n = 5; % = 83

Critical appraisal – Cochrane ROBINS-I

Section	Question	Answer
1. Bias due to confounding	Risk of bias judgement for confounding	Serious *(The study did not control for or appropriately measure important confounders.)*
2. Bias in selection of participants into the study	Risk of bias judgement for selection of participants into the study	Serious *(It is unclear how participants were selected for the study, nor whether the start of follow up and start of intervention coincided for all participants, although this is likely.)*
3. Bias in classification of interventions	Risk of bias judgement for classification of interventions	Serious *(Intervention status is not well defined)*
4. Bias due to deviations from intended interventions	Risk of bias judgement for deviations from intended interventions	Moderate *(There is no information on whether deviations took place from usual practice, however the study is retrospective in nature and so it is likely that participants received the intervention as intended to be included in the study. If there were deviations from usual practice, their impact on the outcome is expected to be slight.)*
5. Bias due to missing data	Risk of bias judgement for missing data	Low *(Data appears to be complete)*
6. Bias in measurement of outcomes	Risk of bias judgement for measurement of outcomes	Serious *(There is limited information on the methods of outcome assessment, however it appears as these were comparable across intervention groups. It is unclear how the outcome pregnancy rate was attained, nor information on how low sperm count and no sperm count were defined. Any error in measuring the outcome is only minimally related to intervention status. Knowledge of the intervention received was unlikely to influence measurement of the outcomes.)*
7. Bias in selection of the reported result	Risk of bias judgement for selection of the reported result	Moderate *(The outcome measurements and analyses are defined, there is no indication of selection of the reported analysis from among multiple analyses, and there is no indication of selection of the cohort or subgroups for analysis and reporting on the basis of the results.)*
Overall bias	Risk of bias judgement	Serious
Overall bias	Risk of bias variation across outcomes	This study has some important problems, and the risk of bias was rated as serious across multiple domains (confounding, selection of participants, classification of intervention, and measurement of outcomes)

Section	Question	Answer
Overall bias	Directness	Directly applicable

Rodrigues Netto Junior, 1992

Bibliographic Reference	Rodrigues Netto Junior, N; Claro, J A; Neves, P A; Nobrega Junior, V D; Surgical treatment of obstructive azoospermia.; Archivos espanoles de urologia; 1992; vol. 45 (no. 10); 1053-5

Study details

Country where study was carried out	Brazil
Study type	Retrospective cohort study
Study dates	Not reported
Inclusion criteria	Infertile men with obstructive azoospermia
Exclusion criteria	Not reported
Patient characteristics	Demographics of N=48 patients undergoing surgery (including patients undergoing artificial spermatocele) Mean age: 46 years (Range 29 to 66) n=3 had observed vas deferens agenesia at physical examination and underwent artificial spermatocele n=31 had previous vasectomy and underwent microsurgical reversal with vasovasostomy n=14 with epididymal obstruction had normal findings and were treated with microsurgical vasoepididymostomy Mean period of time between vasectomy and reversal: 8 years (Range 2 to 17)
Intervention(s)/control	**Vasovasostomy** A 2-layer microsurgical vasovasostomy was performed using interrupted 9-zero prolene to approximate the mucosal edges and interrupted 9-zero prolene to approximate the muscular and adventitial edges. Usually 6 - 8 sutures were

	placed. In the last 8 cases a biological glue was used in the suture after placing four cardinal sutures in the mucosa to approximate the segments. **Vasoepididymostomy** Microsurgical vasoepididymostomy was performed using end to end anastomosis by approximating the mucosa of the vas to the edges of the opened epididymal tubule with interrupted 10-zero prolene and approximating the muscularis and adventitia of the vas to the edges of the incised epididymal tunic with interrupted 9-zero prolene.
Duration of follow-up	Mean follow-up of 21-months in Vasovasostomy group
Sources of funding	Not reported
Sample size	N=44 (3 patients underwent artificial spermatocele and were not included in the review)
Other information	There were n=3 patients who had vas deferens agnesia and underwent artificial spermatocele; they were not included in the review.

Outcome	**Vasovasostomy, N = 31**	**Vasoepididymostomy, N = 14**
Pregnancy rate Unclear how pregnancy was determined	n = 25; % = 80	n = 4; % = 30

Critical appraisal – Cochrane ROBINS-I

Section	**Question**	**Answer**
1. Bias due to confounding	Risk of bias judgement for confounding	Serious *(The study did not control for or appropriately measure important confounders)*
2. Bias in selection of participants into the study	Risk of bias judgement for selection of participants into the study	Moderate *(It is unclear how participants were selected for inclusion into the study and follow-up is only reported for the vasovasostomy group so it is unclear whether the start of follow up and start of intervention coincide for all participants.)*
3. Bias in classification of interventions	Risk of bias judgement for classification of interventions	Moderate *(Intervention status is fairly well defined the study retrospective reviews the records of patients so it is likely that the intervention definition is based solely on information collected at the time of intervention.)*

Section	Question	Answer
4. Bias due to deviations from intended interventions	Risk of bias judgement for deviations from intended interventions	Moderate *(The study does not report any deviations from intended interventions but the study was retrospective in nature any deviations from usual practice were unlikely to impact on the outcome)*
5. Bias due to missing data	Risk of bias judgement for missing data	Low *(Data appeared to be complete)*
6. Bias in measurement of outcomes	Risk of bias judgement for measurement of outcomes	Moderate *(It was unclear how outcomes were measured, including pregnancy rate. It is likely that the measured of outcomes was comparable across intervention groups, and are unlikely to be influenced by knowledge of the intervention received by study participants Any error in measuring the outcome is only minimally related to intervention status.)*
7. Bias in selection of the reported result	Risk of bias judgement for selection of the reported result	Serious *(Results are minimally reported and there are no graphs or tables located within the publications, subsequently there is a high risk of selective reporting from among multiple analyses)*
Overall bias	Risk of bias judgement	Serious
Overall bias	Risk of bias variation across outcomes	This study has some important problems, and the risk of bias was rated as serious across two domains (confounding and selection of the reported result) and moderate across several domains (selection of participants, classification of intervention, deviations from intended intervention, and measurement of outcomes)
Overall bias	Directness	Directly applicable

Uvin, 2018

Bibliographic Reference Uvin, Valerie; De Brucker, S; De Brucker, M; Vloeberghs, V; Drakopoulos, P; Santos-Ribeiro, S; Tournaye, H; Pregnancy after vasectomy: surgical reversal or assisted reproduction?.; Human reproduction (Oxford, England); 2018; vol. 33 (no. 7); 1218-1227

Study details

Country/ies where	Belgium

study was carried out	
Study type	Retrospective cohort study
Study dates	2006 to December 2011
Inclusion criteria	Patients with a renewed child wish after male sterilization
Exclusion criteria	Not reported
Patient characteristics	Demographics of n=109 patients (primary IVF/ICSI and primary reanastomosis) **Primary IVF/ICSI (TESE/FNA group, n=64)** Mean male age (SD): 45.6 (7.7), range 27-66 years Mean female age (SD): 34.8 (5.0), range 21-42 years Nulliparous: n=42 (65.6%) Multiparous: n=22 (34.4%) **Primary reanastomosis (Vasovasostomy group, n=45)** Mean male age (SD): 43.2 (6.4), range 31-58 years Mean female age (SD): 33.4 (5.5), range 20-45 years Nulliparous: n=28 (62.2%) Multiparous: n=17 (37.8%)
Intervention(s)/control	**Vasovasostomy (Primary reanastomosis)** High bilateral vertical scrotal incisions were made depending on where the defect was palpable and both ends of the vas deferens were dissected. Both ends were transected at a 90° angle with a scalpel, followed by visual inspection of the following layers of the vas: the inner mucosal layer, the muscularis and the vasal sheath. For the anastomosis, the mucosa of both ends were approximated after verifying the patency of both ends. Both ends were connected by using: 1-

	layer, 2-layer or microdot multilayer techniques. Whenever some traction was present on the vas, the 1-layer technique was performed. In the absence of any traction, a 2-layer technique was preferred, where 1 inner layer of sutures close the mucosa and another outer layer of sutures was performed to close the seromuscular layer. In these techniques, a variant of the microdot principle was performed in which the lumen of the vas deferens are marked with methylene-blue at 3, 6, 9 and 12 o'clock, to approximate the ends more precisely. Intraoperative harvesting of testicular sperm was combined with the reanastamosis by performing an unilateral TESE during the procedure. **FNA/TESE with IVF/ICSI (Primary IVF/ICSI)** The 'primary IVF/ICSI' pathway included all cases in which no reanastomosis was performed or in which the reanastomosis of the vas deferens failed. In these cases, sperm was retrieved by fine needle aspiration (FNA), testicular sperm extraction (TESE) or a percutaneous epididymal sperm aspiration (PESA) before an ICSI treatment. In the majority of cases, a single embryo was transferred five days after oocyte retrieval. For luteal phase support, 200 mg progesterone was given intravaginally 3 times daily, starting on the day after oocyte retrieval until 7 weeks of pregnancy. When 3follicles with a diameter of ≥17 mm were visualized on a pelvic ultrasound scan, 5000 or 10 000 IU hCG was administered to trigger final oocyte maturation, followed after 36 hours by the transvaginal aspiration of the cumulus oocyte complexes. In n=29 patients (45.3%) of the primary IVF/ICSI group, an agonist protocol was used the long GnRH-agonist protocol was used in 71.4% and the short agonist protocol was used in 28.6% of the agonist cases.
Duration of follow-up	All patients had a follow-up period of a minimum 57 months (range: 57–120 months). The first delivery was the endpoint of this study.
Sources of funding	No funding
Sample size	N=109 (54 patients who switched treatments were not included in the review).
Other information	The choice between surgical reversal or IVF/ICSI with sperm retrieval was made after counselling and explanation of both options and was based on patient's and physician's preference. Of the 99 patients who underwent microsurgical vasovasostomy, a subgroups of patients (n=54) known as 'switchers' underwent a reanastomosis but later switched to assisted reproductive technology and were not included in the review.

Outcome	**Vasovasostomy, N = 45**	**FNA/TESE, N = 64**
Live birth Reported as delivery	n = 18; % = 85.7	n = 28; % = 65.1
Clinical pregnancy	n = 21; % = 46.7	n = 43; % = 67.2

Outcome	Vasovasostomy, N = 45	FNA/TESE, N = 64
Defined as the observation of fetal cardiac activity on ultrasonography at seven weeks of gestation		
Miscarriage Time frame not defined	n = 3; % = 14.3	n = 15; % = 34.9

Critical appraisal – Cochrane ROBINS-I

Section	Question	Answer
1. Bias due to confounding	Risk of bias judgement for confounding	Serious *(The study did not control for or appropriately measure important confounders)*
2. Bias in selection of participants into the study	Risk of bias judgement for selection of participants into the study	Moderate *(The study retrospectively included participants from a single centre. It is unclear how participants were selected but it is likely that all participants who would have been eligible for the target trial were included in the study and it appears that the start of follow up and start of intervention coincided for all participants.)*
3. Bias in classification of interventions	Risk of bias judgement for classification of interventions	Low *(Intervention status is well defined it is likely the intervention definition is based solely on information collected at the time of intervention.)*
4. Bias due to deviations from intended interventions	Risk of bias judgement for deviations from intended interventions	Serious *(There were deviations from usual practice that were unbalanced between the intervention groups and likely to have affected the outcome. This included participants known as 'switchers' who underwent a reanastomosis but later switched to assisted reproductive technology.)*
5. Bias due to missing data	Risk of bias judgement for missing data	Low *(Data appeared to be complete)*
6. Bias in measurement of outcomes	Risk of bias judgement for measurement of outcomes	Low *(The methods of outcome assessment were comparable across intervention groups; the outcome clinical pregnancy was measured by observation of fetal cardiac activity on ultrasonography at seven weeks of gestation and was unlikely to be influenced by knowledge of the intervention received by study participants, and any error in measuring the outcome is unrelated to intervention status.)*
7. Bias in selection of the reported result	Risk of bias judgement for selection of the reported	Moderate *(The outcome measurements and analyses are defined, there is no indication of selection of*

Section	Question	Answer
	result	*the reported analysis from among multiple analyses, and there is no indication of selection of the cohort or subgroups for analysis and reporting on the basis of the results.)*
Overall bias	Risk of bias judgement	Serious
Overall bias	Risk of bias variation across outcomes	This study has some important problems, and the risk of bias was rated as serious across two domains (confounding and deviations from intended interventions) and across two domains (selection of participants and selection of the reported result).
Overall bias	Directness	Indirect *(The study does not report whether participants had azoospermia)*

Appendix E Forest plots

Forest plots for review question: What is the clinical and cost effectiveness of surgical interventions for fertility problems associated with obstructive azoospermia?

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: Vasovasostomy compared to vasoepididymostomy or epididymovastomy for clinical pregnancy

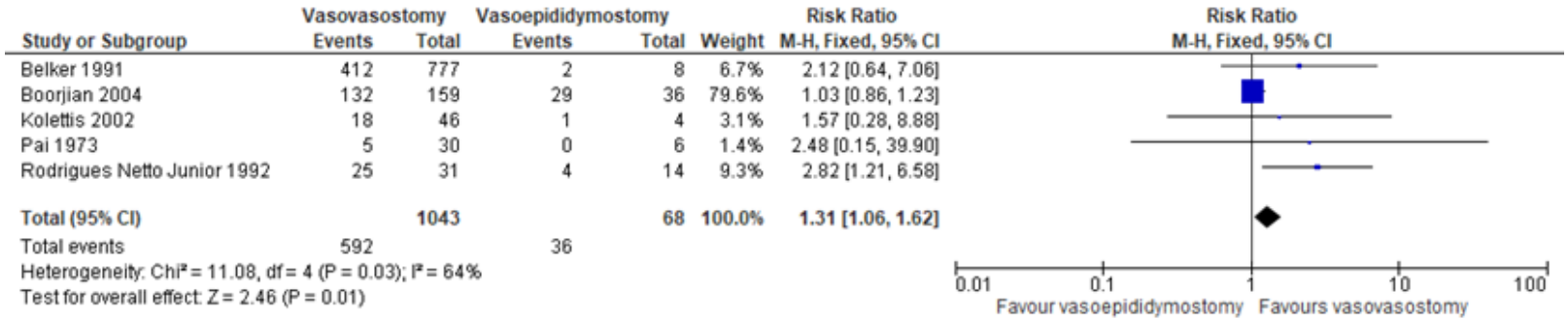
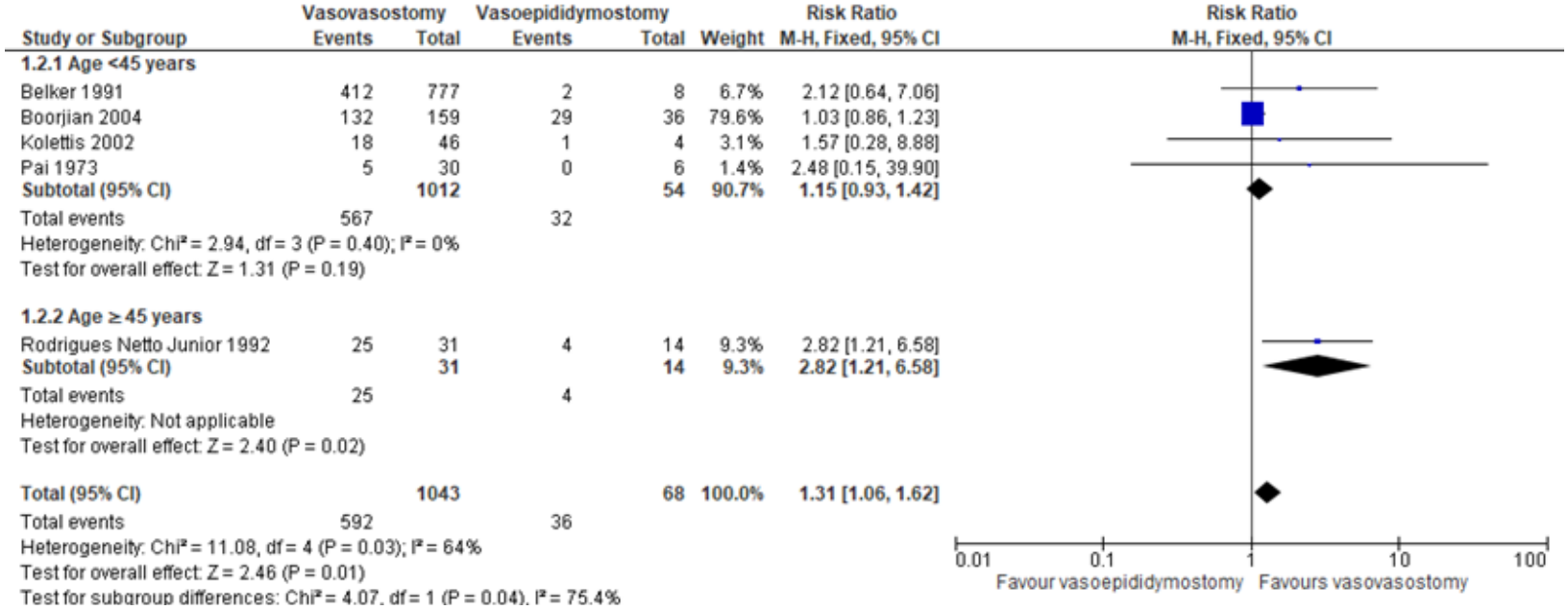


Figure 3: Vasovasostomy compared to vasoepididymostomy or epididymovastomy for clinical pregnancy subgrouped by age



Appendix F GRADE tables

GRADE tables for review question: What is the clinical and cost effectiveness of surgical interventions for fertility problems associated with obstructive azoospermia?

Table 5: Evidence profile for comparison 1: vasovasostomy versus vasoepididymostomy or epididymovasostomy

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vasovasostomy	Vasoepididymostomy or epididymovasostomy	Relative (95% CI)	Absolute		
Live birth (defined as pregnancy and delivery obtained naturally; better indicated by higher values)												
1 (Hibi 2020)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	7/45 (15.6%)	7/45 (15.6%)	RR 1.00 (0.38 to 2.62)	0 fewer per 1000 (from 96 fewer to 252 more)	VERY LOW	CRITICAL
Live birth (defined as pregnancy and delivery obtained by intracytoplasmic sperm injection (ICSI); better indicated by higher values)												
1 (Hibi 2020)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/45 (8.9%)	14/45 (31.1%)	RR 0.29 (0.10 to 0.80)	221 fewer per 1000 (from 62 fewer to 280 fewer)	VERY LOW	CRITICAL
Live birth (overall, defined as pregnancy and delivery obtained either naturally or ICSI; better indicated by higher values)												
1 (Hibi 2020)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	11/45 (24.4%)	21/45 (46.7%)	RR 0.52 (0.29 to 0.96)	224 fewer per 1000 (from 19 fewer to 331 fewer)	VERY LOW	CRITICAL
Clinical pregnancy (defined in Boorjian 2004 as clinical pregnancy with documented heartbeat achieved via natural conception, defined in Kollettis 2002 and Rodrigues Netto Junior 1992 as pregnancy rate and defined in Belker 1991 and Pai 1973 as pregnancy achieved or attained; better indicated by higher values)												
5[3]	observational studies	very serious[1]	serious[4]	serious[5]	serious[6]	none	592/1043 (56.8%)	36/68 (52.9%)	RR 1.31 (1.06 to 1.62)	164 more per 1000 (from 32 more to 328 more)	VERY LOW	CRITICAL
Clinical pregnancy subgrouped by age <45 years (defined in Boorjian 2004 as clinical pregnancy with documented heartbeat achieved via natural conception, defined in Kollettis 2002 as pregnancy rate and defined in Belker 1991 and Pai 1973 as pregnancy achieved or attained; better indicated by higher values)												
4[7]	observational studies	very serious[1]	no serious inconsistency	serious[5]	serious[6]	none	567/1012 (56%)	32/54 (59.3%)	RR 1.15 (0.93 to 1.42)	89 more per 1000 (from 41 fewer to 249 more)	VERY LOW	CRITICAL
Clinical pregnancy subgrouped by age ≥45 years (defined as pregnancy rate; better indicated by higher values)												
1 (Rodrigues	observational	very	no serious	no serious	serious[6]	none	25/31	4/14	RR 2.82	520 more per	VERY	CRITICAL

Netto Junior 1992)	studies	serious[1]	inconsistency	indirectness			(80.6%)	(28.6%)	(1.21 to 6.58)	1000 (from 60 more to 1000 more)	LOW	
Improved semen parameters: total sperm count (defined as sperm in semen; better indicated by higher values)												
1 (Belker 1991)	observational studies	very serious[1]	no serious inconsistency	serious[5]	serious[6]	none	837/966 (86.6%)	5/12 (41.7%)	RR 2.08 (1.06 to 4.06)	450 more per 1000 (from 25 more to 1000 more)	VERY LOW	IMPORTANT
Improved semen parameters: total sperm count (defined as normal count of 40 million/mL with 40-50% motility; better indicated by higher values)												
1 (Pai 1973)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[8]	none	14/30 (46.7%)	0/6 (0%)	POR 6.55 (0.44 to 97.17)	-	VERY LOW	IMPORTANT
Improved semen parameters: total sperm count (defined in the study as low count; better indicated by lower values)												
1 (Pai 1973)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[8]	none	7/30 (23.3%)	1/6 (16.7%)	RR 1.40 (0.21 to 9.39)	67 more per 1000 (from 132 fewer to 1000 more)	VERY LOW	IMPORTANT
Improved semen parameters: total sperm count (defined as no sperm; better indicated by lower values)												
1 (Pai 1973)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	9/30 (30%)	5/6 (83.3%)	RR 0.36 (0.19 to 0.69)	533 fewer per 1000 (from 258 fewer to 675 fewer)	VERY LOW	IMPORTANT

CI: confidence interval; ICSI: intracytoplasmic sperm injection; MID: minimally important difference; mL: millilitres; POR: Peto odds ratio; RR: risk ratio
[1] Very serious risk of bias in the evidence contributing to the outcomes as per ROBINS-I
[2] <150 events
[3] Belker 1991, Boorjian 2004, Kolettis 2002, Pai 1973, Rodrigues Netto Junior 1992
[4] Serious inconsistency (I^2=50-80%)
[5] Population is indirect due to the study not reporting whether participants had azoospermia
[6] 95% CI crosses 1 clinical decision making threshold
[7] Belker 1991, Boorjian 2004, Kolettis 2002, Pai 1973
[8] 95% CI crosses 2 clinical decision making thresholds

Table 6: Evidence for comparison 2: vasovasostomy versus surgical sperm retrieval via microsurgical epididymal sperm aspiration (MESA) or testicular extraction of sperm (TESE)

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Vasovasostomy**	**Surgical sperm retrieval (MESA or TESE)**	**Relative (95% CI)**	**Absolute**		
Clinical pregnancy (defined as pregnancy reported by mailed questionnaire response; better indicated by higher values)												
1 (Heidenreich 2000)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	58/112 (51.8%)	17/69 (24.6%)	RR 2.1 (1.34 to 3.3)	271 more per 1000 (from 84 more to 567 more)	VERY LOW	CRITICAL

MESA: microsurgical epididymal sperm aspiration; RR: risk ratio; TESE: testicular extraction of sperm

[1] Very serious risk of bias in the evidence contributing to the outcomes as per ROBINS-I

Table 7: Evidence for comparison 3: vasovasostomy versus surgical sperm retrieval via fine needle aspiration (FNA) or testicular extraction of sperm (TESE)

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vasovasostomy	Surgical sperm retrieval (FNA or TESE)	Relative (95% CI)	Absolute		
Live birth (defined as delivery; better indicated by higher values												
1 (Uvin 2018)	observational studies	very serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	18/45 (40%)	28/64 (43.8%)	RR 0.91 (0.58 to 1.44)	39 fewer per 1000 (from 184 fewer to 193 more)	VERY LOW	CRITICAL
Clinical pregnancy (defined as the observation of fetal cardiac activity on ultrasonography at seven weeks of gestation; better indicated by higher values)												
1 (Uvin 2018)	observational studies	very serious[1]	no serious inconsistency	serious[2]	serious[4]	none	21/45 (46.7%)	43/64 (67.2%)	RR 0.69 (0.49 to 0.99)	208 fewer per 1000 (from 7 fewer to 343 fewer)	VERY LOW	CRITICAL
Miscarriage (defined as miscarriage; better indicated by lower values)												
1 (Uvin 2018)	observational studies	very serious[1]	no serious inconsistency	serious[2]	serious[4]	none	3/45 (6.7%)	15/64 (23.4%)	RR 0.28 (0.09 to 0.93)	169 fewer per 1000 (from 16 fewer to 213 fewer)	VERY LOW	IMPORTANT

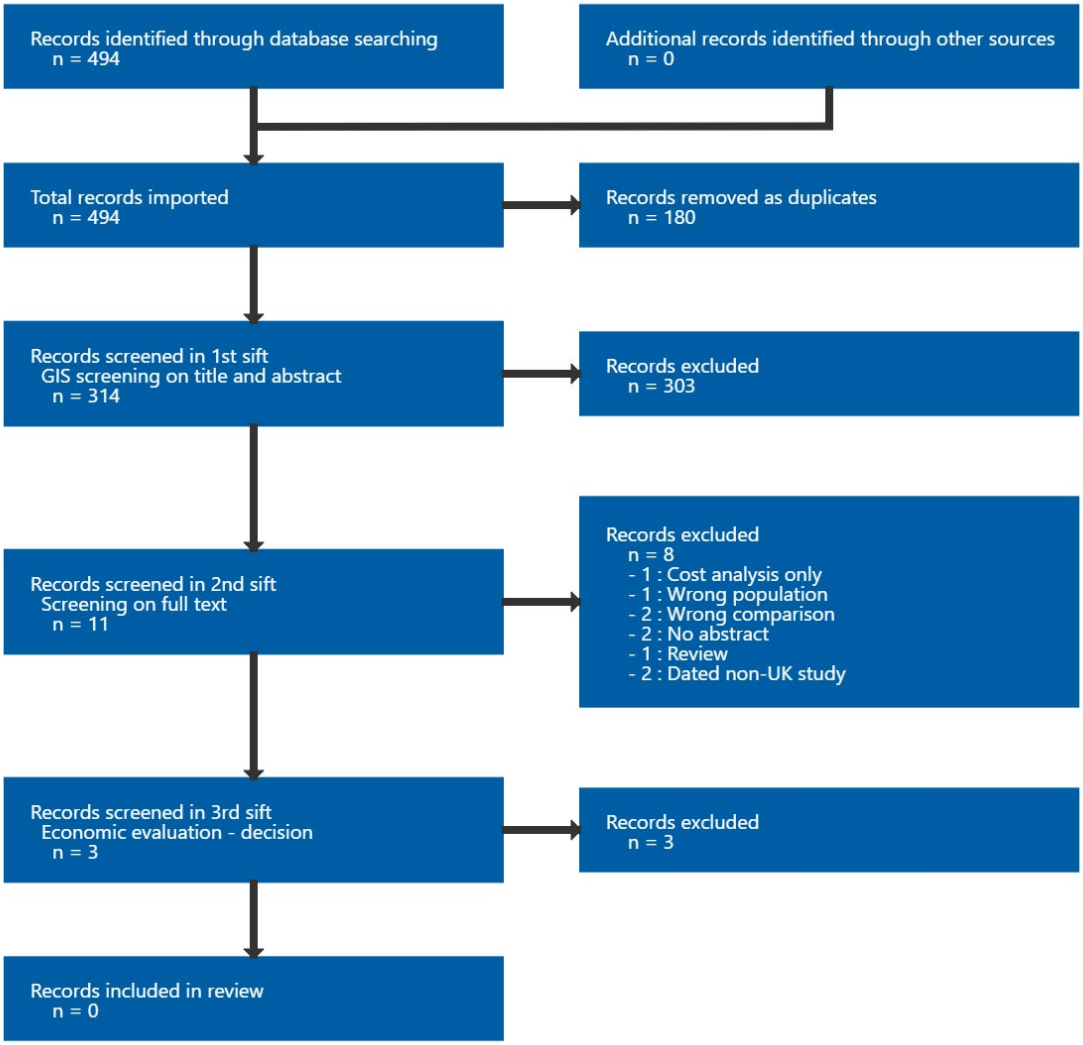
CI: confidence interval; FNA: fine needle aspiration; MID: minimally important difference; RR: risk ratio; TESE: testicular extraction of sperm
[1] Very serious risk of bias in the evidence contributing to the outcomes as per ROBINS-I
[2] Population is indirect due to the study not reporting whether participants had azoospermia
[3] <150 events
[4] 95% CI crosses 1 clinical decision making threshold

Appendix G Economic evidence study selection

Study selection for review question: What is the clinical and cost effectiveness of surgical interventions for fertility problems associated with obstructive azoospermia?

No relevant health economic studies were included for this review question.

Figure 4: Study selection flow chart



Appendix H Economic evidence tables

Economic evidence tables for review question: What is the clinical and cost effectiveness of surgical interventions for fertility problems associated with obstructive azoospermia?

No evidence was identified which was applicable to this review question.

Appendix I Economic model

Economic model for review question: What is the clinical and cost effectiveness of surgical interventions for fertility problems associated with obstructive azoospermia?

No economic analysis was conducted for this review question.

Appendix J Excluded studies

Excluded studies for review question: What is the clinical and cost effectiveness of surgical interventions for fertility problems associated with obstructive azoospermia?

Excluded effectiveness studies

Table 8: Excluded studies and reasons for their exclusion

Study	Code [Reason]
Abdel-Al, Ibrahim, Elatreisy, Adel, Hassan, Gamal M et al. (2022) Long-Term Success Durability of Transurethral Resection of Ejaculatory Duct in Treating Infertile Men with Ejaculatory Duct Obstruction. Journal of endourology 36(7): 982-988	- Not a relevant study design
Allameh, Farzad, Hosseini, Jalil, Qashqai, Hamidreza et al. (2019) Efficacy of Intraoperative Mitomycin-C in Vasovasostomy Procedure: A Randomized Clinical Trial. International journal of fertility & sterility 13(3): 240-244	- Comparison does not match review protocol
Amjadi, M., Jahantabi, E., Nouri, H. et al. (2023) One-layer macroscopic verus two-layer microscopic vasovasostomy: Our experience in two referral hospitals. Urologia Journal 90(2): 322	- Comparison does not match review protocol
Banerjee, A K; Bajwa, F M; Simpson, A (1994) Vasovasostomy: 10 years' experience in a district general hospital showing improved results with luminal dilatation. Journal of the Royal College of Surgeons of Edinburgh 39(3): 153-5	- Not a relevant study design
Belker, A M, Fuchs, E F, Konnak, J W et al. (1985) Transient fertility after vasovasostomy in 892 patients. The Journal of urology 134(1): 75-6	- Not a relevant study design
Boeckx, W and Van Helden, S (1996) Microsurgical vasoepididymostomy in the treatment of occlusive azoospermia. British journal of urology 77(4): 577-9	- Comparison does not match review protocol
Chan, Peter T (2013) The evolution and refinement of vasoepididymostomy techniques. Asian journal of andrology 15(1): 49-55	- Not a relevant study design
Chan, Peter T K; Brandell, Roy A; Goldstein, Marc (2005) Prospective analysis of outcomes after microsurgical intussusception vasoepididymostomy. BJU international 96(4): 598-601	- Not a relevant study design
Chan, Peter T K and Goldstein, Marc (2004) Superior	- Comparison does not match review

Study	Code [Reason]
outcomes of microsurgical vasectomy reversal in men with the same female partners. Fertility and sterility 81(5): 1371-4	protocol
Chen, Xiang-Feng, Chen, Bin, Liu, Wei et al. (2016) Microsurgical vasoepididymostomy for patients with infectious obstructive azoospermia: cause, outcome, and associated factors. Asian journal of andrology 18(5): 759-62	- Not a relevant study design
Chen, Xiang-Feng, Wang, Hong-Xiang, Liu, Yi-Dong et al. (2014) Clinical features and therapeutic strategies of obstructive azoospermia in patients treated by bilateral inguinal hernia repair in childhood. Asian journal of andrology 16(5): 745-8	- Not a relevant study design
Denton, SE; Bohnert, WW; Kurtz, CW (1983) Vasectomy reversal technique and results. Arizona medicine 40(1): 33-6	- Not a relevant study design
Dewire, D M and Lawson, R K (1994) Experience with macroscopic vasectomy reversal at the Medical College of Wisconsin. Wisconsin medical journal 93(3): 107-9	- Not a relevant study design
Douroumis, Konstantinos, Spartalis, Eleftherios, Stravodimos, Konstantinos et al. (2023) Robotic-assisted microsurgery in andrology: a systematic review. Asian journal of andrology	- Not a relevant study design
Duijn, M.; van der Zee, J.A.; Bachour, Y. (2023) Outcomes of Three Vasovasostomy Surgical Techniques in Vasectomized Men: A Systematic Review of the Current Literature. SN Comprehensive Clinical Medicine 5(1): 56	- Comparison does not match review protocol
Duijn, M.; van der Zee, J.A.; Bachour, Y. (2021) Outcomes of Macrosurgical Versus Microsurgical Vasovasostomy in Vasectomized Men: a Systematic Review and Meta-analysis. SN Comprehensive Clinical Medicine 3(10): 2193-2203	- Comparison does not match review protocol
Eguchi, J, Nomata, K, Hirose, T et al. (1999) Clinical experiences of microsurgical side-to-end epididymovasostomy for epididymal obstruction. International journal of urology : official journal of the Japanese Urological Association 6(5): 271-4	- Not a relevant study design
Eisenberg, Michael L, Walsh, Thomas J, Garcia, Maurice M et al. (2008) Ejaculatory duct manometry in normal men and in patients with ejaculatory duct obstruction. The Journal of urology 180(1): 255-260	- Not a relevant study design
El-Assmy, Ahmed, El-Tholoth, Hosam, Abouelkheir, Rasha T et al. (2012) Transurethral resection of ejaculatory duct in infertile men: outcome and predictors of success. International urology and nephrology 44(6): 1623-30	- Not a relevant study design

Study	Code [Reason]
Etafy, M., Gudeloglu, A., Brahmbhatt, J.V. et al. (2018) Review of the role of robotic surgery in male infertility. Arab Journal of Urology 16(1): 148-156	- Not a relevant study design
Farber, Nicholas J, Flannigan, Ryan, Li, Peng et al. (2019) The Kinetics of Sperm Return and Late Failure Following Vasovasostomy or Vasoepididymostomy: A Systematic Review. The Journal of urology 201(2): 241-250	- Outcomes do not match review protocol
Feber, K M and Ruiz, H E (1999) Vasovasostomy: Macroscopic approach and retrospective review. Techniques in urology 5(1): 8-11	- Not a relevant study design
Fischer, M A and Grantmyre, J E (2000) Comparison of modified one- and two-layer microsurgical vasovasostomy. BJU international 85(9): 1085-8	- Comparison does not match review protocol
Fogdestam, I.; Fall, M.; Nilsson, S. (1986) Microsurgical epididymovasostomy in the treatment of occlusive azoospermia. Fertility and Sterility 46(5): 925-929	- Not a relevant study design
Fox, M (1997) Failed vasectomy reversal: is a further attempt worthwhile using microsurgery?. European urology 31(4): 436-40	- Not a relevant study design
Fox, M (1994) Vasectomy reversal--microsurgery for best results. British journal of urology 73(4): 449-53	- Comparison does not match review protocol
Fuchs, Eugene F and Burt, Richard A (2002) Vasectomy reversal performed 15 years or more after vasectomy: correlation of pregnancy outcome with partner age and with pregnancy results of in vitro fertilization with intracytoplasmic sperm injection. Fertility and sterility 77(3): 516-9	- Comparison does not match review protocol
Fuselier, H A Jr and Lesser, D A (1980) Vasovasostomy: four year experience at Ochsner Medical Institutions. The Journal of the Louisiana State Medical Society : official organ of the Louisiana State Medical Society 132(12): 195-6	- Not a relevant study design
Garibyan, H and De Jong, E A (1990) Microsurgical vaso-epididymostomy in 2 layers. British journal of urology 65(6): 634-7	- Not a relevant study design
Gerrard, Edward R Jr, Sandlow, Jay I, Oster, Robert A et al. (2007) Effect of female partner age on pregnancy rates after vasectomy reversal. Fertility and sterility 87(6): 1340-4	- Not a relevant study design
Gopi, S S and Townell, N H (2007) Vasectomy reversal: is the microscope really essential?. Scottish medical journal 52(2):	- Not a relevant study design

Study	Code [Reason]
18-20	
Gozen, Ali Serdar, Tokas, Theodoros, Tawfick, Ahmed et al. (2020) Robot-assisted vasovasostomy and vasoepididymostomy: Current status and review of the literature. Turkish journal of urology 46(5): 329-334	- Comparison does not match review protocol
Grober, Ethan D, Jarvi, Keith, Lo, Kirk C et al. (2011) Mini-incision vasectomy reversal using no-scalpel vasectomy principles: efficacy and postoperative pain compared with traditional approaches to vasectomy reversal. Urology 77(3): 602-6	- Comparison does not match review protocol
Gurnani, Nishant, Goel, Ritesh, Kumar, Manoj et al. (2023) Unilateral Versus Bilateral Vasoepididymal Anastomosis for Idiopathic Obstructive Azoospermia: A Randomised Controlled Trial. European urology open science 52: 30-35	- Comparison does not match review protocol
Harza, Mihai, Voinea, Sebastian, Ismail, Gener et al. (2014) Predictive factors for natural pregnancy after microsurgical reconstruction in patients with primary epididymal obstructive azoospermia. International journal of endocrinology 2014: 873527	- Not a relevant study design
Hauser, R, Temple-Smith, P D, Southwick, G J et al. (1995) Pregnancies after microsurgical correction of partial epididymal and vasal obstruction. Human reproduction (Oxford, England) 10(5): 1152-5	- Comparison does not match review protocol
Hernandez, J and Sabanegh, E S (1999) Repeat vasectomy reversal after initial failure: overall results and predictors for success. The Journal of urology 161(4): 1153-6	- Intervention does not match review protocol
Herrel, Lindsey A, Goodman, Michael, Goldstein, Marc et al. (2015) Outcomes of microsurgical vasovasostomy for vasectomy reversal: a meta-analysis and systematic review. Urology 85(4): 819-25	- Not a relevant study design
Ho, K L; Wong, M H; Tam, P C (2009) Microsurgical vasoepididymostomy for obstructive azoospermia. Hong Kong medical journal = Xianggang yi xue za zhi 15(6): 452-7	- Not a relevant study design
Hsieh, Ming-Li, Huang, Hsin Chieh, Chen, Yu et al. (2005) Loupe-assisted vs microsurgical technique for modified one-layer vasovasostomy: is the microsurgery really better?. BJU international 96(6): 864-6	- Comparison does not match review protocol
Huang, Hsin-Chieh, Hsieh, Ming-Li, Huang, Shih-Tsung et al. (2002) Microsurgical vasectomy reversal: ten-years' experience in a single institute. Chang Gung medical journal 25(7): 453-7	- Not a relevant study design

Study	Code [Reason]
Jee, Sang Hyun and Hong, Young Kwon (2010) One-layer vasovasostomy: microsurgical versus loupe-assisted. Fertility and sterility 94(6): 2308-11	- Comparison does not match review protocol
Jenkins, I L and Blacklock, N J (1979) Experience with vasovasostomy: operative technique and results. British journal of urology 51(1): 43-5	- Not a relevant study design
Johnson, Christopher W, Bingham, Jonathan B, Goluboff, Erik T et al. (2005) Transurethral resection of the ejaculatory ducts for treating ejaculatory symptoms. BJU international 95(1): 117-9	- Not a relevant study design
Judge, C. and Stahl, P. (2017) A systematic review of the efficacy and safety of transurethral surgery for ejaculatory duct obstruction-related infertility. Andrology: 92	- Abstract
Kadioglu, A, Cayan, S, Tefekli, A et al. (2001) Does response to treatment of ejaculatory duct obstruction in infertile men vary with pathology?. Fertility and sterility 76(1): 138-42	- Not a relevant study design
Kapadia, Akash A, Anthony, Marcus, Martinez Acevedo, Ann et al. (2018) Reconsidering vasectomy reversal over assisted reproduction in older couples. Fertility and sterility 109(6): 1020-1024	- Comparison does not match review protocol
Karpman, E.; Williams IV, D.H.; Lipshultz, L.I. (2006) Is microsurgical intussusception vasoepididymostomy a suitable option for men with obstructive azoospermia?. Nature Clinical Practice Urology 3(1): 20-21	- Not a relevant study design
Kavoussi, Parviz K (2015) Validation of robot-assisted vasectomy reversal. Asian journal of andrology 17(2): 245-7	- Comparison does not match review protocol
Kim, E D, Winkel, E, Orejuela, F et al. (1998) Pathological epididymal obstruction unrelated to vasectomy: results with microsurgical reconstruction. The Journal of urology 160(6pt1): 2078-80	- Not a relevant study design
Kochakarn, W, Leenanupunth, C, Muangman, V et al. (2001) Ejaculatory duct obstruction in the infertile male: experience of 7 cases at Ramathibodi Hospital. Journal of the Medical Association of Thailand = Chotmaihet thangphaet 84(8): 1148-52	- Not a relevant study design
Kolettis, P N and Thomas, A J Jr (1997) Vasoepididymostomy for vasectomy reversal: a critical assessment in the era of intracytoplasmic sperm injection. The Journal of urology 158(2): 467-70	- Comparison does not match review protocol

Study	Code [Reason]
Kolettis, Peter N, Burns, John R, Nangia, Ajay K et al. (2006) Outcomes for vasovasostomy performed when only sperm parts are present in the vasal fluid. Journal of andrology 27(4): 565-7	- Comparison does not match review protocol
Kolettis, Peter N, Sabanegh, Edmund S, Nalesnik, Jeffrey G et al. (2003) Pregnancy outcomes after vasectomy reversal for female partners 35 years old or older. The Journal of urology 169(6): 2250-2	- Not a relevant study design
Kuang, Wayne, Shin, Paul R, Matin, Surena et al. (2004) Initial evaluation of robotic technology for microsurgical vasovasostomy. The Journal of urology 171(1): 300-3	- Population does not match review protocol
Kumar, Rajeev; Gautam, Gagan; Gupta, Narmada P (2006) Early patency rates after the two-suture invagination technique of vaso-epididymal anastomosis for idiopathic obstruction. BJU international 97(3): 575-7	- Not a relevant study design
Kumar, Rajeev and Mukherjee, Satyadip (2010) "4 x 4 vasovasostomy": A simplified technique for vasectomy reversal. Indian journal of urology : IJU : journal of the Urological Society of India 26(3): 350-2	- Not a relevant study design
Kumar, Rajeev; Mukherjee, Satyadip; Gupta, Narmada P (2010) Intussusception vasoepididymostomy with longitudinal suture placement for idiopathic obstructive azoospermia. The Journal of urology 183(4): 1489-92	- Not a relevant study design
Liang, Zhong-Yan, Zhang, Feng-Bin, Li, Le-Jun et al. (2019) Clinical application of cross microsurgical vasovasostomy in scrotum for atypical obstructive azoospermia. Journal of Zhejiang University. Science. B 20(3): 282-286	- Comparison does not match review protocol
Lorenzini, Mariana S; Lorenzini, Fernando; Bezerra, Cicero A (2021) Vasectomy re-reversal: effectiveness and parameters associated with its success. International braz j urol : official journal of the Brazilian Society of Urology 47(3): 544-548	- Not a relevant study design
Lyu, Kun-Long, Zhuang, Jin-Tao, Li, Philip S et al. (2018) A novel experience of deferential vessel-sparing microsurgical vasoepididymostomy. Asian journal of andrology 20(6): 576-580	- Not a relevant study design
Meacham, R B; Hellerstein, D K; Lipshultz, L I (1993) Evaluation and treatment of ejaculatory duct obstruction in the infertile male. Fertility and sterility 59(2): 393-7	- Not a relevant study design
Mehrotra, M L, Gupta, R L, Nagar, A M et al. (1981) Fertility status of men following vaso-vasostomy. The Indian journal of	- Not a relevant study design

Study	Code [Reason]
medical research 73: 33-40	
Mekhaimar, Ayah, Goble, Mary, Brunckhorst, Oliver et al. (2020) A systematic review of transurethral resection of ejaculatory ducts for the management of ejaculatory duct obstruction. Turkish journal of urology 46(5): 335-347	- Systematic review (not appropriate to include in its entirety and checked for relevant primary studies)
Middleton, R G, Smith, J A, Moore, M H et al. (1987) A 15-year followup of a nonmicrosurgical technique for vasovasostomy. The Journal of urology 137(5): 886-7	- Not a relevant study design
Mui, P, Perkins, A, Burrows, P J et al. (2014) The need for epididymovasostomy at vasectomy reversal plateaus in older vasectomies: a study of 1229 cases. Andrology 2(1): 25-9	- Not a relevant study design
Namekawa, Takeshi, Imamoto, Takashi, Kato, Mayuko et al. (2018) Vasovasostomy and vasoepididymostomy: Review of the procedures, outcomes, and predictors of patency and pregnancy over the last decade. Reproductive medicine and biology 17(4): 343-355	- Outcomes do not match review protocol
Niederberger, C and Ross, L S (1993) Microsurgical epididymovasostomy: predictors of success. The Journal of urology 149(5pt2): 1364-7	- Not a relevant study design
Nyame, Yaw A, Babbar, Paurush, Almassi, Nima et al. (2016) Comparative Cost-Effectiveness Analysis of Modified 1-Layer versus Formal 2-Layer Vasovasostomy Technique. The Journal of urology 195(2): 434-8	- Comparison does not match review protocol
Ozer, C. and Goren, M.R. (2019) Transurethral resection of ejaculatory duct in primary infertile men with distal ejaculatory duct obstruction. Journal of Urological Surgery 6(2): 135-138	- Not a relevant study design
Pace, Gianna, Galatioto, Giuseppe Paradiso, Guala, Luana et al. (2008) Ejaculatory duct obstruction caused by a right giant seminal vesicle with an ipsilateral upper urinary tract agenesia: an embryologic malformation. Fertility and sterility 89(2): 390-4	- Not a relevant study design
Parekattil, Sijo J, Gudeloglu, Ahmet, Brahmbhatt, Jamin et al. (2012) Robotic assisted versus pure microsurgical vasectomy reversal: technique and prospective database control trial. Journal of reconstructive microsurgery 28(7): 435-44	- Comparison does not match review protocol
Patel, Sutchin R and Sigman, Mark (2008) Comparison of outcomes of vasovasostomy performed in the convoluted and straight vas deferens. The Journal of urology 179(1): 256-9	- Comparison does not match review protocol
Peng, Jing, Yuan, Yiming, Zhang, Zhichao et al. (2014) Microsurgical vasoepididymostomy is an effective treatment	- Not a relevant study design

Study	Code [Reason]
for azoospermic patients with epididymal obstruction and prior failure to achieve pregnancy by sperm retrieval with intracytoplasmic sperm injection. Human reproduction (Oxford, England) 29(1): 1-7	
Peng, Jing, Zhang, Zhichao, Yuan, Yiming et al. (2017) Pregnancy and live birth rates after microsurgical vasoepididymostomy for azoospermic patients with epididymal obstruction. Human reproduction (Oxford, England) 32(2): 284-289	- Not a relevant study design
Ramasamy, R, Mata, D A, Jain, L et al. (2015) Microscopic visualization of intravasal spermatozoa is positively associated with patency after bilateral microsurgical vasovasostomy. Andrology 3(3): 532-5	- Not a relevant study design
Rosemberg, S K (1988) Further clinical experience with CO2 laser in microsurgical vasovasostomy. Urology 32(3): 225-7	- Not a relevant study design
Rothman, I, Berger, R E, Cummings, P et al. (1997) Randomized clinical trial of an absorbable stent for vasectomy reversal. The Journal of urology 157(5): 1697-700	- Comparison does not match review protocol
Safarinejad, Mohammad Reza, Lashkari, Mohammad Hossein, Asgari, Seyyed Alaeddin et al. (2013) Comparison of macroscopic one-layer over number 1 nylon suture vasovasostomy with the standard two-layer microsurgical procedure. Human fertility (Cambridge, England) 16(3): 194-9	- Comparison does not match review protocol
Savage, Joshua, Manka, Madeleine, Rindels, Tiffany et al. (2020) Reinforcing vasal suture technique improves sperm concentration and pregnancy rates in men undergoing vasovasostomy for vasectomy reversal. Translational andrology and urology 9(1): 73-81	- Comparison does not match review protocol
Schiff, Jonathan, Chan, Peter, Li, Philip S et al. (2005) Outcome and late failures compared in 4 techniques of microsurgical vasoepididymostomy in 153 consecutive men. The Journal of urology 174(2): 651-801	- Not a relevant study design
Schlegel, P N and Goldstein, M (1993) Microsurgical vasoepididymostomy: refinements and results. The Journal of urology 150(4): 1165-8	- Comparison does not match review protocol
Seth, Ishith, Gibson, Damien, Bulloch, Gabriella et al. (2024) Vasovasostomy: A systematic review and meta-analysis comparing macroscopic, microsurgical, and robot-assisted microsurgical techniques. Andrology 12(4): 740-767	- Systematic review (not appropriate to include in its entirety and checked for relevant primary studies)
Shaeer, Osama K Z and Shaeer, Kamal Z (2005) Pelviscrotal vasovasostomy: refining and troubleshooting. The Journal of	- Comparison does not match review protocol

Study	Code [Reason]
urology 174(5): 1935-7	
Sharlip, I D (1981) Vasovasostomy: comparison of two microsurgical techniques. Urology 17(4): 347-52	- Comparison does not match review protocol
Shiraishi, Koji and Matsuyama, Hideyasu (2020) Outcomes of partial intussusception and endo-to-side vasoepididymostomy in men with epididymal obstructive azoospermia. International journal of urology : official journal of the Japanese Urological Association 27(12): 1124-1129	- Comparison does not match review protocol
Shridharani, Anand and Sandlow, Jay I (2010) Vasectomy reversal versus IVF with sperm retrieval: which is better?. Current opinion in urology 20(6): 503-9	- Not a relevant study design
Singh, I and Kaza, R C (1996) A case in favour of one sided microscopic vasovasostomy--the New Delhi experience. International urology and nephrology 28(1): 27-31	- Comparison does not match review protocol
Tang, Songxi, Chen, Qiang, Ding, Yilang et al. (2024) Comparison of clinical characteristics and surgical outcomes in non-vasectomized epididymal obstructive azoospermia patients with or without concurrent vas-deferens obstruction. Andrology	- Comparison does not match review protocol
Thomas, A J Jr (1987) Vasoepididymostomy. The Urologic clinics of North America 14(3): 527-38	- Not a relevant study design
Tung, M.-C., Ou, Y.-C., Lu, C.-H. et al. (2020) The expansion condition of amount and complexity of urologic robotic surgery in 2000 patients: A 13-year experience sharing. Formosan Journal of Surgery 53(6): 223-229	- Intervention does not match review protocol
Vazquez-Levin, M H; Dressler, K P; Nagler, H M (1994) Urine contamination of seminal fluid after transurethral resection of the ejaculatory ducts. The Journal of urology 152(6pt1): 2049-52	- Not a relevant study design
Wagenknecht, L V; Klosterhalfen, H; Schirren, C (1980) Microsurgery in andrologic urology. I. Refertilization. Journal of microsurgery 1(5): 370-6	- Outcomes do not match review protocol
Wan, Bangbei, Wu, Yamei, Wu, Zhong et al. (2023) Current progress on the curative effects of vasoepididymostomy for patients with obstructive azoospermia: An updated systematic review and meta-analysis of human studies. Andrology 11(1): 103-111	- Comparison does not match review protocol
Wang, Bin; Liu, Ziming; Jiang, Hongtao (2020) Comparison of low-power magnification one-layer vasovasostomy with stent	- Comparison does not match review protocol

Study	Code [Reason]
and microscopic two-layer vasovasostomy for vasectomy reversal. International journal of impotence research 32(6): 617-622	
Wang, Shou-Yang and Fang, Yang-Yi (2023) Outcomes of microsurgical vasoepididymostomy using intussusception technique: a systematic review and meta-analysis. Scientific reports 13(1): 3340	- Comparison does not match review protocol
Wang, Zilong, Wang, Xinkun, Song, Changze et al. (2023) The pregnancy outcomes in patients with epididymal obstructive azoospermia after microsurgical vasoepididymostomy: a systematic review and meta-analysis. Frontiers in medicine 10: 1186729	- Systematic review (not appropriate to include in its entirety and checked for relevant primary studies)
Xiao, Hong, Zhou, Shan, Chen, Qiang et al. (2024) Comparative evaluation of double- and single-armed two-suture longitudinal intussusception techniques in microsurgical vasoepididymostomy: An updated systematic review and meta-analysis. PloS one 19(2): e0298019	- Systematic review (not appropriate to include in its entirety and checked for relevant primary studies)
Yang, Glen, Walsh, Thomas J, Shefi, Shai et al. (2007) The kinetics of the return of motile sperm to the ejaculate after vasectomy reversal. The Journal of urology 177(6): 2272-6	- Outcomes do not match review protocol
Yoon, Young Eun, Lee, Hyung Ho, Park, Sung Yul et al. (2018) The role of vasoepididymostomy for treatment of obstructive azoospermia in the era of in vitro fertilization: a systematic review and meta-analysis. Asian journal of andrology	- Not a relevant study design
Zhang, Hao, Huang, Wen-Tao, Ruan, Xing-Xing et al. (2013) Microsurgical transverse 2-suture intussusception vasoepididymostomy: effectiveness and rationality. Chinese medical journal 126(24): 4670-3	- Not a relevant study design
Zhang, Zheng; Zhang, Yong; Zhang, Nan (2022) Clinical outcome of microsurgical vasoepididymostomy versus epididymal or testicular sperm retrieval combined with intracytoplasmic sperm injection in obstructive azoospermia males. Andrologia 54(8): e14458	- Not a relevant study design
Zhao, Liang, Deng, Chun-Hua, Sun, Xiang-Zhou et al. (2013) A modified single-armed technique for microsurgical vasoepididymostomy. Asian journal of andrology 15(1): 79-82	- Not a relevant study design

Excluded economic studies

Table 9: Excluded health economic studies and reasons for their exclusion

Study	Code [Reason]
Excluded when check listing (final sift)	
Hsieh, Michael H; Meng, Maxwell V; Turek, Paul J (2007) Markov modeling of vasectomy reversal and ART for infertility: how do obstructive interval and female partner age influence cost effectiveness?. Fertility and sterility; 2007; vol. 88 (no. 4); 840-6	- US study – costs not applicable to UK setting
Cheng, Philip J; Kim, Jaewhan; Craig, James R et al. (2021) "The Back-up Vasectomy Reversal." Simultaneous Sperm Retrieval and Vasectomy Reversal in the Couple With Advanced Maternal Age: A Cost-Effectiveness Analysis. Urology; 2021; vol. 153; 175-180	- US study – costs not applicable to UK setting
Meng, Maxwell V; Greene, Kirsten L; Turek, Paul J (2005) Surgery or assisted reproduction? A decision analysis of treatment costs in male infertility. The Journal of urology; 2005; vol. 174 (no. 5); 1926-1931	- - Limited information provided on methodology - Older study so costs may be less applicable
Excluded on full text review (2nd sift)	
Heidenreich, A; Altmann, P; Engelmann, U H et al. (2000) Microsurgical vasovasostomy versus microsurgical epididymal sperm aspiration/testicular extraction of sperm combined with intracytoplasmic sperm injection. A cost-benefit analysis.. European urology; 2000; vol. 37 (no. 5); 609-14	- Costs based on one institution from Germany with only a simple cost per outcome analysis conducted, based on a small number of patients. - Old study with patients recruited between 1994 and 1997. A high proportion of multiple gestations are reported for MESA/TESE and ICSI (15.8%), indicating the clinical procedures are not reflective of current practice – employing single embryo transfer (SET). SET has been established clinical practice for a long time and therefore costs are not reflective of current practice.
Nyame, Yaw A; Babbar, Paurush; Almassi, Nima; Polackwich, Alan S; Sabanegh, Edmund (2016) Comparative Cost-Effectiveness Analysis of Modified 1-Layer versus Formal 2-Layer Vasovasostomy Technique. The Journal of urology; 2016; vol. 195 (no. 2); 434-8	- Cost analysis only

Study	Code [Reason]
Lee, Richard; Li, Philip S; Goldstein, Marc et al (2009) A decision analysis of treatments for nonobstructive azoospermia associated with varicocele. Fertility and sterility; 2009; vol. 92 (no. 1); 188-96	- Wrong population
Lee, R; Li, P S; Goldstein, M; Tanrikut, C (2008) A decision analysis of treatments for obstructive azoospermia. Human reproduction (Oxford, England); 2008; vol. 23 (no. 9); 2043-9	- US study – costs not applicable to UK setting
Dubin, Justin M; Greer, Aubrey B et al (2018) Men With Severe Oligospermia Appear to Benefit From Varicocele Repair: A Cost-effectiveness Analysis of Assisted Reproductive Technology. Urology; 2018; vol. 111; 99-103	- Wrong comparator
Chiles, Kelly A; Schlegel, Peter N (2016) Cost-effectiveness of varicocele surgery in the era of assisted reproductive technology. Asian journal of andrology; 2016; vol. 18 (no. 2); 259-61	- Wrong comparator - Not a cost-effectiveness analysis
Savage, P M Jr (1971) An economic and efficient vasectomy program. HSMHA health reports; 1971; vol. 86 (no. 8); 682-3	- Old study - Abstract only
Honig, S.C. (2005) Finding the best and most cost-effective approach for treating obstructive azoospermia American Journal of Urology Review; 2005; vol. 3 (no. 5); 219-223	- Abstract only

Appendix K Research recommendations – full details

Research recommendations for review question: What is the clinical and cost effectiveness of surgical interventions for fertility problems associated with obstructive azoospermia?

No research recommendations were made for this review question.