National Institute for Health and Care Excellence

Draft for consultation

Fertility problems: assessment and treatment

[Y] Surgical sperm retrieval techniques

NICE guideline NGXXX

Evidence reviews underpinning recommendations 1.4.8 and 1.4.9 in the NICE guideline

September 2025

Draft for consultation

Disclaimer

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ISBN:

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Surgical sperm retrieval

Review question

What is the clinical and cost effectiveness of surgical sperm retrieval (SSR) techniques for fertility problems associated with non-obstructive azoospermia or obstructive azoospermia?

Introduction

Azoospermia (an absence of sperm in the ejaculate) is identified in approximately 10% of infertile men and may be obstructive, where an obstruction is preventing the sperm entering the ejaculate, or non-obstructive where there is reduced sperm production. To overcome the fertility problems associated with azoospermia a surgical procedure called surgical sperm retrieval can be carried out to remove sperm directly from the testes or epididymis which can then be used for intracytoplasmic sperm injection (ICSI) treatment.

Various techniques can be used to carry out surgical sperm retrieval and the aim of this review was to identify which technique leads to better levels of sperm retrieval for ICSI, and better reproductive outcomes, while minimising adverse events.

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 non-obstructive azoospermia • People with fertility problems associated with obstructive azoospermia (including epididymal obstruction, ejaculatory duct obstruction, vasal obstruction) Exclusion: • People undergoing surgical sperm retrieval as part of fertility preservation
Intervention	Surgical sperm retrieval techniques for fertility problems associated with non-obstructive or obstructive azoospermia, for example: • single-site testicular sperm extraction (TESE)/ conventional TESE • multi-site testicular sperm extraction (TESE)/ conventional TESE • microdissection testicular sperm extraction (micro-TESE) • testicular sperm aspiration (TESA) • testicular fine-needle aspiration (TEFNA) • open epididymal spermatozoa aspiration (OESA) • microsurgical epididymal sperm aspiration (MESA) • percutaneous epididymal sperm aspiration (PESA)
Comparison	• Head-to-head comparisons of different surgical sperm retrieval techniques

Outcome	Critical • Sperm retrieval rate (as defined by study, risk of bias assessments will reflect where this is not defined as sperm suitable for ICSI) Important • 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 viable intrauterine pregnancy confirmed by ultrasound accounting for singleton pregnancy, twin pregnancy, and higher multiple pregnancy) • Miscarriage (loss of a baby before 24 weeks gestational age) • Adverse events o testicular pain o atrophy (shrinking of the testicle) and hypogonadism with a need for HRT o haematoma o infection

HRT: hormone replacement therapy; ICSI: intracytoplasmic sperm injection; MESA: microsurgical epididymal sperm aspiration; OESA: open epididymal spermatozoa aspiration; PESA: percutaneous epididymal sperm aspiration; TEFNA: testicular fine-needle aspiration; TESA: testicular sperm aspiration; TESE: testicular sperm extraction

For further details see the review protocol in appendix A.

Methods and process

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

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

Effectiveness evidence

Included studies

Two randomised controlled trials (RCT) were included for this review (Jensen 2022, Utlu 2023). The first RCT compared microdissection testicular sperm extraction (micro-TESE) to a combined group receiving testicular sperm aspiration (TESA) alone or TESA plus salvage micro-TESE (if spermatozoa were not found after TESA), in people with non-obstructive azoospermia. Another RCT compared bilateral micro-TESE to unilateral micro-TESE in people with non-obstructive azoospermia.

The included studies are summarised in Table 2.

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

Excluded studies

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

Summary of included studies

Summary of the studies that were included in this review is presented in Table 2.

Table 2: Summary of included studies

Study	Population	Intervention	Comparison	Outcomes	Comments
Jensen 2022 RCT Denmark and Sweden	N=100 Men with azoospermia according to WHO criteria Median age (iqi): 34 (30.5; 38.0) years Female age (SD): NR Presence of obstruction: non-obstructive azoospermia	Micro-TESE	TESA or TESA plus salvage micro-TESE	• Sperm retrieval rate • Adverse events including testicular pain, atrophy, haematoma and infection	Surgery stopped when spermatozoa were found or when both testes had been examined without finding spermatozoa If spermatozoa were not found after multiple needle-pass TESA, the patient underwent salvage micro-TESE while still in the operating room
Utlu 2023 RCT Turkey	N=84 Men with non-obstructive azoospermia Mean age (SD): bilateral micro-TESE 37.4 (NR); unilateral micro-TESE 32.2 (NR) Female age (SD): NR Presence of obstruction: non-obstructive azoospermia	Bilateral micro-TESE	Unilateral micro-TESE	• Sperm retrieval rate • Adverse event: infection	Duration of follow-up and source of funding were not reported

iqi: interquartile interval; Micro-TESE: microdissection testicular sperm extraction; NR: not reported; RCT: randomised controlled trial; SD: standard deviation; TESA: testicular sperm aspiration; WHO: world health organisation

See the full evidence tables in appendix D. No meta-analysis was conducted (and so there are no forest plots in appendix E).

Summary of the evidence

Low quality evidence from 1 study showed a clinically important difference between microdissection testicular sperm extraction (micro-TESE) compared to testicular sperm

aspiration (TESA) alone where sperm retrieval rate was higher in the former group. However, it should be noted that this comparison was made at midpoint rather than endpoint due to the design of the study with participants randomised to a combination arm (TESA or TESA plus salvage micro-TESE). When the data from this RCT was analysed at endpoint no clinically important difference was shown in sperm retrieval rate between micro-TESE compared to the combined group that received TESA alone or TESA plus salvage micro-TESE (if TESA was unsuccessful in locating spermatozoa, low quality evidence). Very low quality evidence also showed no clinically important difference between micro-TESE and TESA/TESA plus salvage micro-TESE for adverse events including testicular pain, atrophy, haematoma, and infection.

Very low quality evidence from 1 study showed no clinically important difference between bilateral and unilateral micro-TESE for sperm retrieval rate and adverse event such as infection.

No eligible evidence was identified for the outcomes live birth, clinical pregnancy, or miscarriage.

See appendix F for full GRADE tables.

Economic evidence

A total of 236 studies were identified in the health economic literature search for this review question. After duplicates were removed, 152 studies were screened on title and abstract, with 141 studies being excluded at this stage. Eleven studies were subsequently screened on full text, but all were excluded at this stage.

Included studies

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

Also see the literature search strategy in appendix B and the 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 there was insufficient clinical evidence available for different techniques to allow modelling to take place.

Unit costs

Table 3: Unit costs – National schedule of NHS costs

Resource	Unit costs	Source
Surgical extraction of sperm	£3,386	National schedule of NHS costs 2023/24; Currency code MC20Z, Day case procedure This currency code covers the following OPCS codes: • Microsurgical epididymal sperm aspiration • Percutaneous epididymal sperm aspiration

Resource	Unit costs	Source
		• Testicular sperm extraction
Minor, Scrotum, Testis or Vas Deferens Procedures, 19 years and over	£2,436	National schedule of NHS costs 2023/24; Currency code LB54A, Day case procedure This currency code covers open epididymal spermatozoa aspiration (OESA)

Using the National schedule of NHS costs, it was not possible to ascertain the differences in costs for many of the interventions listed in the protocol due to these interventions being listed under the same currency code. To illustrate the potential differences in costs for sperm extraction and sperm aspiration, costs from Manchester University NHS private fertility service (Saint Mary's) were obtained from their 2022 price list. Prices were available for testicular sperm extraction and percutaneous epididymal sperm aspiration (PESA). For the cost of TESE it was not noted, how and if this differentiated for micro-TESE and single-site or multiple-site TESE. Unit costs are presented in Table 4.

Table 4: Unit costs – private sector

Resource	Unit costs	Source
Testicular sperm extraction (TESE)	£3,075	TESE surgical sperm retrieval (SSR) https://mft.nhs.uk/app/uploads/2022/05/Price-List-May-2022.pdf
Percutaneous epididymal sperm aspiration (PESA)	£1,697	PESA surgical sperm retrieval (SSR) https://mft.nhs.uk/app/uploads/2022/05/Price-List-May-2022.pdf

The committee's discussion and interpretation of the evidence

The outcomes that matter most

Sperm retrieval rate was prioritised as a critical outcome by the committee as it was considered the most reliable and informative measure of the success of surgical sperm retrieval.

Live birth, clinical pregnancy, miscarriage, and adverse events were identified as important outcomes by the committee. Live birth and clinical pregnancy were selected as good indicators for the success of fertility treatment and were specified in the core outcome set for fertility research (Duffy 2020). Miscarriage rate was prioritised as an important outcome as it can be a devastating event for people trying to have a baby and it provides meaningful information about whether the different techniques for surgical sperm retrieval are effective for achieving pregnancy but do not lead to a live birth. Adverse events were agreed to be an important outcome by the committee because, when discussing and deciding on treatment options, it is important that the risks are considered and weighed up against potential benefits. Testicular pain, atrophy (shrinking of the testicle) and hypogonadism with a need for hormone replacement therapy, haematoma, and infection were considered the most relevant adverse events associated with surgical sperm retrieval for non-obstructive and obstructive azoospermia.

The quality of the evidence

The quality of the evidence was assessed with GRADE and rated as low to very low quality.

The evidence was downgraded for risk of bias because of deviations from the intended interventions (for example, when spermatozoa were not found, participants were offered the other intervention), lack of information on the randomisation techniques or concealment of the allocation sequence, lack of blinding and unclear risk of selective reporting due to the absence of pre-registered protocols. The evidence was also downgraded for imprecision because of the 95% confidence intervals crossing clinical decision making thresholds.

Benefits and harms

The committee discussed the evidence for microdissection testicular sperm extraction (micro-TESE) compared to testicular sperm aspiration (TESA) in people with non-obstructive azoospermia and noted that it was difficult to interpret the results for some of the outcomes as salvage micro-TESE was used in the TESA group when spermatozoa were not found (TESA plus salvage micro-TESE). However, the study did report the sperm retrieval rate in the micro-TESE group and the TESA group before any salvage treatments and this showed a higher sperm retrieval rate for people undergoing micro-TESE (42.9%) compared to TESA only (21.6%). The committee agreed that this finding was consistent with their own experience where micro-TESE is more likely to recover sperm than TESA and that in clinical practice it would be the preferred method of surgical sperm retrieval (where possible) for people with non-obstructive azoospermia. The committee noted that not all practitioners are currently trained and competent to conduct micro-TESE for surgical sperm retrieval and this may lead to variations in access to micro-TESE. However, the committee acknowledged that current variability in access is decreasing, and that recommending this procedure in the NICE guideline would be likely to improve access.

Since the study only reported adverse events from surgical sperm retrieval for people undergoing micro-TESE compared to TESA plus salvage micro-TESE (not for the TESA only group), the committee were limited in the conclusions they could make from the evidence for this outcome. The study showed no important difference between micro-TESE and TESA plus salvage micro-TESE for the adverse events testicular pain, atrophy, haematoma, and infection. The committee used their own experience and knowledge of non-randomised studies and agreed that less tissue is removed during a surgical sperm retrieval with micro-TESE, and the complication rate is reduced, when compared to conventional TESE. They acknowledged that although there is no randomised controlled trial evidence, evidence from non-randomised studies support micro-TESE for surgical sperm retrieval in people with non-obstructive azoospermia and this is in line with existing European Association of Urology (EAU) guidelines which recommend micro-TESE as the method of choice for surgical sperm retrieval.

The committee also reviewed the evidence from the comparison of bilateral micro-TESE with unilateral micro-TESE and noted that it showed no difference in sperm retrieval rate and infection.

The committee noted that the evidence was considered low or very low quality and that there was no evidence for the important outcomes live birth, clinical pregnancy, and miscarriage for people with non-obstructive azoospermia. The committee agreed the evidence was not sufficient to make a strong recommendation about a specific technique for surgical sperm retrieval for non-obstructive azoospermia, but that the use of micro-TESE could be considered.

The committee noted the lack of evidence in people with obstructive azoospermia and so did not make a recommendation on a specific surgical technique for this group. However, they noted that surgical retrieval of sperm was usually more successful from this population and so all surgical sperm retrieval techniques could be used, although it would be sensible and appropriate to use the least intrusive technique first. As the committee agreed that a variety of surgical sperm retrieval techniques could be used in people with obstructive azoospermia, they did not prioritise a research recommendation for this topic. They noted that they had

already considered the surgical management of obstructive azoospermia (see evidence review W) and advised that surgical correction or surgical sperm retrieval could both be used.

Cost effectiveness and resource use

No economic evidence was identified for this review question. Unit costs were therefore presented to aid the committee's consideration of cost-effectiveness. The following interventions were grouped under the same currency code in the national schedule of NHS costs: microsurgical epididymal sperm aspiration, percutaneous epididymal sperm aspiration and testicular sperm extraction. The committee discussed the categorisation of these costs and concluded that there were likely notable variations between these interventions – therefore concluding that it was difficult to make inferences on the comparative costs of these interventions using NHS reference costs alone.

Costs from an NHS fertility centre providing private services were therefore also presented to the committee. Costs were available for both TESE and PESA, with costs amounting to £3,075 and £1,697 respectively. However, for the cost of TESE, it was not noted how, and if, this differentiated for micro-TESE, single-site TESE or multiple-site TESE. These private sector costs do however highlight the committee's concerns surrounding the grouping of these interventions under the same currency code as regardless of the classification, notable differences in price are observed. In general, the committee agreed that micro-TESE was a more expensive procedure to carry out than TESA. The committee noted that TESA is usually done under local anaesthesia and is a relatively quick procedure, whereas Micro-TESE is nearly always done under general anaesthesia. As Micro-TESE is conducted under general anaesthesia, the procedure requires a full operating theatre - including a larger team of theatre staff. Micro-TESE also requires an operating microscope, in addition to specific equipment required for the case (for example, sutures and diathermy). Although Micro-TESE is more expensive than TESA, the committee noted that micro-TESE is also twice as effective at retrieving sperm suitable for ICSI compared to TESA. The committee did however acknowledge that this effectiveness measure was for before any salvage treatments were undertaken – but noted that this finding was also consistent with their own experience. Namely, that micro-TESE is more likely to recover sperm than TESA and that in clinical practice micro-TESE would be the preferred method of surgical sperm retrieval (where possible) for people with non-obstructive azoospermia.

The committee also discussed that in instances where TESA has failed to obtain sperm, micro-TESE is often undertaken as a second-line treatment option. The committee therefore concluded that micro-TESE is likely to be a cost-effective use of NHS resources and made recommendations reflective of this – and best clinical practice. The committee also concluded that the recommendations made will not result in a significant resource impact to the NHS.

Recommendations supported by this evidence review

This evidence review supports recommendations 1.4.8 and 1.4.9.

References – included studies

Effectiveness

Jensen 2022

Jensen, Christian Fuglesang S, Ohl, Dana A, Fode, Mikkel et al. (2022) Microdissection Testicular Sperm Extraction Versus Multiple Needle-pass Percutaneous Testicular Sperm

Aspiration in Men with Nonobstructive Azoospermia: A Randomized Clinical Trial. European urology 82(4): 377-384

Utlu 2023

Utlu, Adem, Ozkaya, Fatih, Aksakalli, Tugay et al. (2023) Comparison of unilateral and bilateral microdissection testicular sperm extraction (MD-TESE) in patients with non-obstructive azoospermia: a prospective study. International urology and nephrology 55(9): 2177-2182

Economic

None

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.

Schlegel 1999

Schlegel PN. (1999) Testicular sperm extraction: microdissection improves sperm yield with minimal tissue excision. Human Reproduction 14: 131–135

Appendices

Appendix A Review protocols

Review protocol for review question: What is the clinical and cost effectiveness of surgical sperm retrieval (SSR) techniques for fertility problems associated with non-obstructive azoospermia or obstructive azoospermia?

Table 5: Review protocol

ID	Field	Content
0.	PROSPERO registration number	CRD42023437737
1.	Review title	Clinical and cost effectiveness of surgical sperm retrieval (SSR) techniques for fertility problems associated with: non-obstructive azoospermia; obstructive azoospermia
2.	Review question	What is the clinical and cost effectiveness of surgical sperm retrieval (SSR) techniques for fertility problems associated with: • Non-obstructive azoospermia, • Obstructive azoospermia
3.	Objective	To determine the clinical and cost effectiveness of surgical sperm retrieval (SSR) techniques for fertility problems associated with: non-obstructive azoospermia; obstructive azoospermia
4.	Searches	The following databases will be searched: • 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

ID	Field	Content
		• Human studies The full search strategies for MEDLINE database will be published in the final review.
5.	Condition or domain being studied	Surgical sperm retrieval (SSR) techniques for fertility problems associated with: non-obstructive azoospermia; obstructive azoospermia
6.	Population	Inclusion: • People with fertility problems associated with non-obstructive azoospermia • People with fertility problems associated with obstructive azoospermia (including epididymal obstruction, ejaculatory duct obstruction, vasal obstruction) Exclusion: • People undergoing SSR as part of their fertility preservation
7.	Intervention	Surgical sperm retrieval (SSR) techniques for fertility problems associated with non-obstructive or obstructive azoospermia, for example: • single-site testicular sperm extraction (TESE)/ conventional TESE • multi-site testicular sperm extraction (TESE)/ conventional TESE • microdissection testicular sperm extraction (micro-TESE) • testicular sperm aspiration (TESA) • testicular fine-needle aspiration (TEFNA) • open epididymal spermatozoa aspiration (OESA) • microsurgical epididymal sperm aspiration (MESA) • percutaneous epididymal sperm aspiration (PESA)
8.	Comparator	• Head-to-head comparisons of different surgical sperm retrieval techniques
9.	Types of study to be included	Include published full-text papers: • Systematic reviews of RCTs • Parallel RCTs (individual or cluster) If no RCT evidence: ○ Quasi-randomised controlled trials (experimental studies using a non-randomly assigned control group design with matched comparison or another method of controlling for confounding variables)

ID	Field	Content
10.	Other exclusion criteria	Other exclusion criteria: • Language limitations: studies published not in English-language • Conference abstracts will not be included because these do not typically have sufficient information to allow full critical appraisal.
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)	• Sperm retrieval rate (as defined by study, risk of bias assessments will reflect where this is not defined as sperm suitable for ICSI)

13.	Secondary outcomes (important 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 viable intrauterine pregnancy confirmed by ultrasound accounting for singleton pregnancy, twin pregnancy, and higher multiple pregnancy)
		• Miscarriage (loss of a baby before 24 weeks gestational age)
		• Adverse events
		  ○ testicular pain
		  ○ atrophy (shrinking of the testicle) and hypogonadism with a need for HRT
		  ○ 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. 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

ID	Field	Content
		was carried out, type and dates), participant characteristics, inclusion and exclusion criteria, details of the interventions if relevant, setting and 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 The quality assessment will be performed by one reviewer and this will be quality assessed by a senior reviewer.
16.	Strategy for data synthesis	Depending on the availability of the evidence, the findings will be summarised narratively or quantitatively. Where there is available data, meta-analyses will be conducted using Cochrane Review Manager software, and data will be presented as risk ratios or odds ratios (all included outcomes are dichotomous outcomes). It is considered likely that a random-effects model will be used for meta-analyses (based on assumptions about methodological diversity of studies). Funnel plot asymmetry (relationship between the magnitude of the effect estimate and study size) will be considered, and where asymmetry is indicated a fixed-effects model will be conducted (and both random-effects and fixed-effects analyses will be presented) or sensitivity analyses excluding small studies will be considered. Heterogeneity in the effect estimates of the individual studies will be assessed using the I2 statistic. Alongside visual inspection of the point estimates and confidence intervals, I2 values of greater than 50% and 80% will be considered as significant and very significant heterogeneity, respectively. Heterogeneity will be explored as appropriate using sensitivity analyses and pre-specified subgroup analyses. The confidence in the findings across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group: http://www.gradeworkinggroup.org/Importance and imprecision of findings will be assessed against minimally important differences (MIDs). The following MIDs will be used: ○ Live birth: statistical significance ○ Dichotomous outcomes (other than live birth): 0.8 and 1.25 for all other relative dichotomous outcomes
17.	Analysis of sub-groups	Evidence will be stratified by: • Presence of obstruction:

ID	Field	Content	
		○ Non-obstructive azoospermia ○ Obstructive azoospermia Evidence will be sub-grouped by the following (for relevant outcomes): • Female 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 reported in the study): ○ <45 years ○ ≥45 years Where evidence is stratified or sub-grouped the committee will consider on a case-by-case basis if separate recommendations should be made for distinct groups. Separate recommendations may be made where there is evidence of a differential effect of interventions in distinct groups. If there is a lack of evidence in one group, the committee will consider, based on their experience, whether it is reasonable to extrapolate and assume the interventions will have similar effects in that group compared with others.	
18.	Type and method of review	☒	Intervention
		☐	Diagnostic
		☐	Prognostic
		☐	Qualitative
		☐	Epidemiologic
		☐	Service Delivery
		☐	Other (please specify)
19.	Language	English	
20.	Country	England	
21.	Anticipated or actual start date	June 2023	

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 member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any		

ID	Field	Content	
		changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.	
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10263	
29.	Other registration details	None	
30.	Reference/URL for published protocol	https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=437737	
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 sperm retrieval, azoospermia	
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	

GRADE: Grading of Recommendations Assessment, Development and Evaluation; HRT: hormone replacement therapy; ICSI: intracytoplasmic sperm injection; MESA: microsurgical epididymal sperm aspiration; micro-TESE: microdissection testicular sperm extraction; MID: minimally important difference; PESA: percutaneous epididymal

sperm aspiration; RCT: randomised controlled trial; SSR: surgical sperm retrieval; TEFNA: testicular fine-needle aspiration; TESA: testicular sperm aspiration; TESE; testicular sperm extraction.

Appendix B Literature search strategies

Literature search strategies for review question: What is the clinical and cost effectiveness of surgical sperm retrieval (SSR) techniques for fertility problems associated with non-obstructive azoospermia or obstructive azoospermia?

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

Date of last search: 07/01/2025

#	Searches
1	Azoospermia/ or azoosperm*.tw.
2	(sperm* adj2 absen*).tw.
3	1 or 2
4	Sperm Retrieval/
5	"Tissue and Organ Harvesting"/
6	((sperm* or testi* or testes* or needle* or epididym*) adj3 (retriev* or aspirat* or extract* or procur* or harvest*)).tw.
7	(PESA or MESA or TESA or TESE or MicroTESE or mTESE or TEFNA or FNA or FNAC or SSR or OESA).tw.
8	or/4-7
9	3 and 8
10	letter/
11	editorial/
12	news/
13	exp historical article/
14	Anecdotes as topic/
15	comment/
16	case reports/
17	(letter or comment*).ti.
18	or/10-17
19	randomized controlled trial/ or random*.ti,ab.
20	18 not 19
21	animals/ not humans/
22	exp Animals, Laboratory/
23	exp Animal Experimentation/
24	exp Models, Animal/
25	exp Rodentia/
26	(rat or rats or rodent* or mouse or mice).ti.
27	or/20-26
28	9 not 27
29	limit 28 to English language
30	randomized controlled trial.pt.
31	controlled clinical trial.pt.
32	pragmatic clinical trial.pt.
33	randomi#ed.ab.
34	placebo.ab.
35	randomly.ab.
36	Clinical Trials as topic.sh.
37	trial.ti.
38	or/30-37
39	meta-analysis/
40	meta-analysis as topic/
41	(meta analy* or metanaly* or metaanaly*).ti,ab.
42	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
43	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
44	(search strategy or search criteria or systematic search or study selection or data extraction).ab.

#	Searches
45	(search* adj4 literature).ab.
46	(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.
47	cochrane.jw.
48	or/39-47
49	38 or 48
50	Observational Studies as Topic/
51	Observational Study/
52	Epidemiologic Studies/
53	exp Case-Control Studies/
54	exp Cohort Studies/
55	Cross-Sectional Studies/
56	Controlled Before-After Studies/
57	Historically Controlled Study/
58	Interrupted Time Series Analysis/
59	Comparative Study.pt.
60	case control$.tw.
61	case series.tw.
62	(cohort adj (study or studies)).tw.
63	cohort analy$.tw.
64	(follow up adj (study or studies)).tw.
65	(observational adj (study or studies)).tw.
66	longitudinal.tw.
67	prospective.tw.
68	retrospective.tw.
69	cross sectional.tw.
70	or/50-69
71	29 and 49
72	29 and 70

1 **Database: Embase <1974 to 2025 January 06>**

2 **Date of last search: 07/01/2025**

#	Searches
1	Azoospermia/ or azoosperm*.tw.
2	(sperm* adj2 absen*).tw.
3	1 or 2
4	exp sperm retrieval/
5	graft harvesting/
6	((sperm* or testi* or testes* or needle* or epididym*) adj3 (retriev* or aspirat* or extract* or procur* or harvest*)).tw.
7	(PESA or MESA or TESA or TESE or MicroTESE or mTESE or TEFNA or FNA or FNAC or SSR or OESA).tw.
8	or/4-7
9	3 and 8
10	letter.pt. or letter/
11	note.pt.
12	editorial.pt.
13	case report/ or case study/
14	(letter or comment*).ti.
15	or/10-14
16	randomized controlled trial/ or random*.ti,ab.
17	15 not 16
18	animal/ not human/
19	nonhuman/
20	exp Animal Experiment/

#	Searches
21	exp Experimental Animal/
22	animal model/
23	exp Rodent/
24	(rat or rats or rodent* or mouse or mice).ti.
25	or/17-24
26	9 not 25
27	limit 26 to English language
28	(conference abstract* or conference review or conference paper or conference proceeding).db,pt,su.
29	27 not 28
30	random*.ti,ab.
31	factorial*.ti,ab.
32	(crossover* or cross over*).ti,ab.
33	((doubl* or singl*) adj blind*).ti,ab.
34	(assign* or allocat* or volunteer* or placebo*).ti,ab.
35	crossover procedure/
36	single blind procedure/
37	randomized controlled trial/
38	double blind procedure/
39	or/30-38
40	systematic review/
41	meta-analysis/
42	(meta analy* or metanaly* or metaanaly*).ti,ab.
43	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
44	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
45	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
46	(search* adj4 literature).ab.
47	(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.
48	((pool* or combined) adj2 (data or trials or studies or results)).ab.
49	cochrane.jw.
50	or/40-49
51	39 or 50
52	Clinical study/
53	Case control study/
54	Family study/
55	Longitudinal study/
56	Retrospective study/
57	comparative study/
58	Prospective study/
59	Randomized controlled trials/
60	58 not 59
61	Cohort analysis/
62	cohort analy$.tw.
63	(Cohort adj (study or studies)).tw.
64	(Case control$ adj (study or studies)).tw.
65	(follow up adj (study or studies)).tw.
66	(observational adj (study or studies)).tw.
67	(epidemiologic$ adj (study or studies)).tw.
68	(cross sectional adj (study or studies)).tw.
69	case series.tw.
70	prospective.tw.
71	retrospective.tw.
72	or/52-57,60-71
73	29 and 51

#	Searches
74	29 and 72

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

Date of last search: 07/01/2025

#	Searches
#1	MeSH descriptor: [Azoospermia] this term only
#2	azoosperm*:ti,ab,kw
#3	(sperm* NEAR/2 absen*):ti,ab,kw
#4	{OR #1-#3}
#5	MeSH descriptor: [Sperm Retrieval] this term only
#6	MeSH descriptor: [Tissue and Organ Harvesting] this term only
#7	((sperm* or testi* or testes* or needle* or epididym*) NEAR/3 (retriev* or aspirat* or extract* or procur* or harvest*)):ti,ab,kw
#8	(PESA or MESA or TESA or TESE or MicroTESE or mTESE or TEFNA or FNA or FNAC or SSR or OESA):ti,ab,kw
#9	{OR #5-#8}
#10	#4 AND #9
#11	conference:pt or (clinicaltrials or trialsearch):so
#12	#10 NOT #11 in Cochrane Reviews

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

Date of last search: 07/01/2025

#	Searches
#1	MeSH descriptor: [Azoospermia] this term only
#2	azoosperm*:ti,ab,kw
#3	(sperm* NEAR/2 absen*):ti,ab,kw
#4	{OR #1-#3}
#5	MeSH descriptor: [Sperm Retrieval] this term only
#6	MeSH descriptor: [Tissue and Organ Harvesting] this term only
#7	((sperm* or testi* or testes* or needle* or epididym*) NEAR/3 (retriev* or aspirat* or extract* or procur* or harvest*)):ti,ab,kw
#8	(PESA or MESA or TESA or TESE or MicroTESE or mTESE or TEFNA or FNA or FNAC or SSR or OESA):ti,ab,kw
#9	{OR #5-#8}
#10	#4 AND #9
#11	conference:pt or (clinicaltrials or trialsearch):so
#12	#10 NOT #11 in Trials

Database: Epistemonikos

Date of last search: 07/01/2025

#	Searches
1	(azoosperm* OR (sperm* OR testi* OR testes* OR needle* OR epididym*) AND (retriev* OR aspirat* OR extract* OR procur* OR harvest*))
2	(PESA OR MESA OR TESA OR TESE OR MicroTESE OR mTESE OR TEFNA OR FNA OR FNAC OR SSR OR OESA)
3	#1 AND #2
4	Limit to systematic reviews

Health Economic Literature Search Strategies:

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

2 **Date of last search: 08/01/2025**

#	Searches
1	Azoospermia/ or azoosperm*.tw.
2	(sperm* adj2 absen*).tw.
3	1 or 2
4	Sperm Retrieval/
5	"Tissue and Organ Harvesting"/
6	((sperm* or testi* or testes* or needle* or epididym*) adj3 (retriev* or aspirat* or extract* or procur* or harvest*)).tw.
7	(PESA or MESA or TESA or TESE or MicroTESE or mTESE or TEFNA or FNA or FNAC or SSR or OESA).tw.
8	or/4-7
9	3 and 8
10	letter/
11	editorial/
12	news/
13	exp historical article/
14	Anecdotes as topic/
15	comment/
16	case reports/
17	(letter or comment*).ti.
18	or/10-17
19	randomized controlled trial/ or random*.ti,ab.
20	18 not 19
21	animals/ not humans/
22	exp Animals, Laboratory/
23	exp Animal Experimentation/
24	exp Models, Animal/
25	exp Rodentia/
26	(rat or rats or rodent* or mouse or mice).ti.
27	or/20-26
28	9 not 27
29	limit 28 to English language
30	Economics/
31	Value of life/
32	exp "Costs and Cost Analysis"/
33	exp Economics, Hospital/
34	exp Economics, Medical/
35	exp Resource Allocation/
36	Economics, Nursing/
37	Economics, Pharmaceutical/
38	exp "Fees and Charges"/
39	exp Budgets/
40	budget*.ti,ab.
41	cost*.ti,ab.
42	(economic* or pharmaco?economic*).ti,ab.
43	(price* or pricing*).ti,ab.
44	(financ* or fee or fees or expenditure* or saving*).ti,ab.
45	(value adj2 (money or monetary)).ti,ab.
46	resourc* allocat*.ti,ab.
47	(fund or funds or funding* or funded).ti,ab.
48	(ration or rations or rationing* or rationed).ti,ab.
49	ec.fs.
50	or/30-49

#	Searches
51	quality-adjusted life years/
52	sickness impact profile/
53	(quality adj2 (wellbeing or well being)).ti,ab.
54	sickness impact profile.ti,ab.
55	disability adjusted life.ti,ab.
56	(qal* or qtime* or qwb* or daly*).ti,ab.
57	(euroqol* or eq5d* or eq 5*).ti,ab.
58	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
59	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
60	(hui or hui1 or hui2 or hui3).ti,ab.
61	(health* year* equivalent* or hye or hyes).ti,ab.
62	discrete choice*.ti,ab.
63	rosser.ti,ab.
64	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
65	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
66	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
67	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
68	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
69	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
70	or/51-69
71	50 or 70
72	29 and 71

1 Database: Embase <1974 to 2025 January 07>

2 Date of last search: 08/01/2025

#	Searches
1	Azoospermia/ or azoosperm*.tw.
2	(sperm* adj2 absen*).tw.
3	1 or 2
4	exp sperm retrieval/
5	graft harvesting/
6	((sperm* or testi* or testes* or needle* or epididym*) adj3 (retriev* or aspirat* or extract* or procur* or harvest*)).tw.
7	(PESA or MESA or TESA or TESE or MicroTESE or mTESE or TEFNA or FNA or FNAC or SSR or OESA).tw.
8	or/4-7
9	3 and 8
10	letter.pt. or letter/
11	note.pt.
12	editorial.pt.
13	case report/ or case study/
14	(letter or comment*).ti.
15	or/10-14
16	randomized controlled trial/ or random*.ti,ab.
17	15 not 16
18	animal/ not human/
19	nonhuman/
20	exp Animal Experiment/
21	exp Experimental Animal/
22	animal model/
23	exp Rodent/
24	(rat or rats or rodent* or mouse or mice).ti.
25	or/17-24
26	9 not 25

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

1 Database: HTA via CRD

2 Date of last search: 08/01/2025

#	Searches
1	MeSH DESCRIPTOR Azoospermia IN HTA
2	((azoosperm*)) and (Project record:ZDT OR Full publication record:ZDT) IN HTA
3	(((sperm* adj2 absen*))) and (Project record:ZDT OR Full publication record:ZDT) IN HTA
4	#1 OR #2 OR #3

#	Searches
5	MeSH DESCRIPTOR Sperm Retrieval IN HTA
6	MeSH DESCRIPTOR Tissue and Organ Harvesting IN HTA
7	((((sperm* or testi* or testes* or needle* or epididym*) adj3 (retriev* or aspirat* or extract* or procur* or harvest*)))) and (Project record:ZDT OR Full publication record:ZDT) IN HTA
8	(((PESA or MESA or TESA or TESE or MicroTESE or mTESE or TEFNA or FNA or FNAC or SSR or OESA))) and (Project record:ZDT OR Full publication record:ZDT) IN HTA
9	#5 OR #6 OR #7 OR #8
10	#4 AND #9

1 **Database: INAHTA International HTA Database**

2 **Date of last search: 08/01/2025**

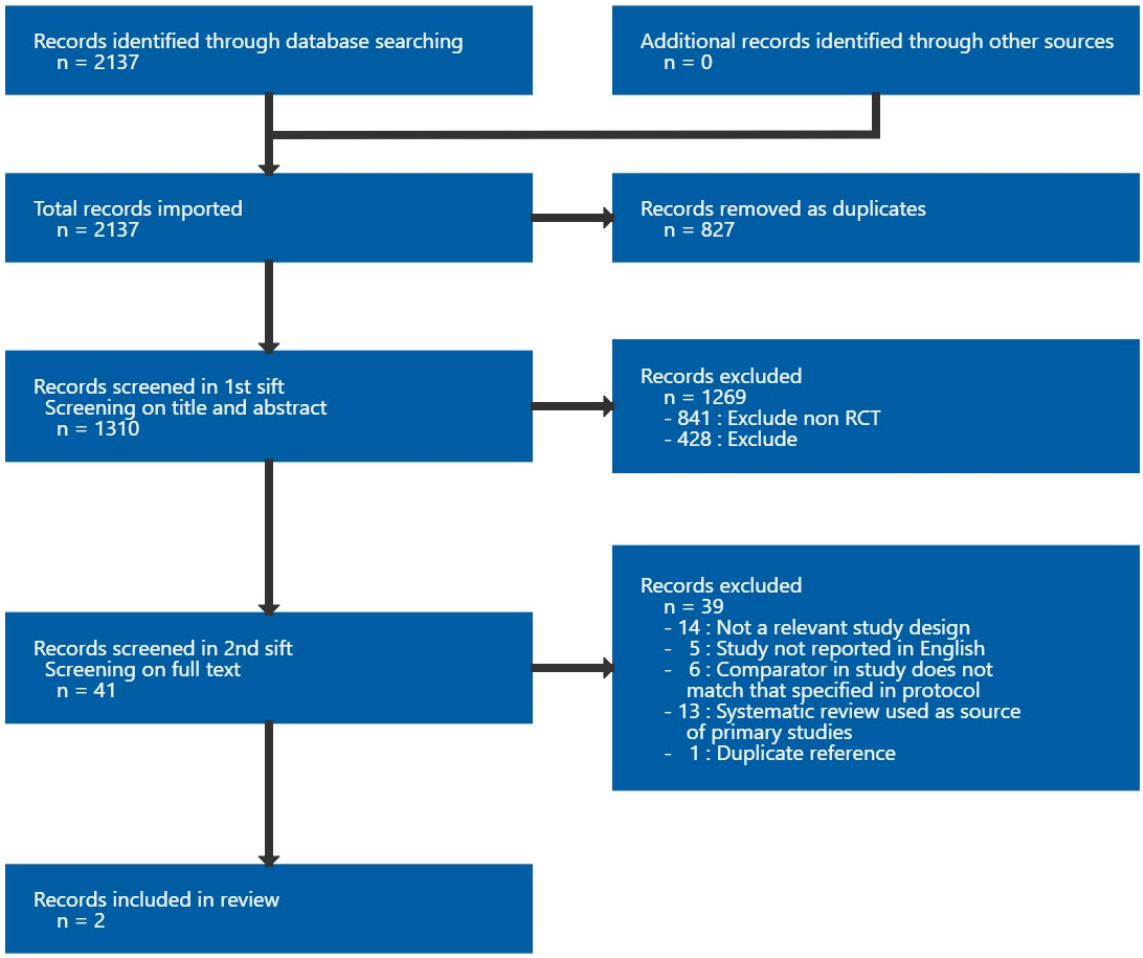
#	Searches
10	#9 AND #4
9	#8 OR #7 OR #6 OR #5
8	((PESA or MESA or TESA or TESE or MicroTESE or mTESE or TEFNA or FNA or FNAC or SSR or OESA))[Title] OR ((PESA or MESA or TESA or TESE or MicroTESE or mTESE or TEFNA or FNA or FNAC or SSR or OESA))[abs]
7	(((sperm* or testi* or testes* or needle* or epididym*) AND (retriev* or aspirat* or extract* or procur* or harvest*)))[Title] OR (((sperm* or testi* or testes* or needle* or epididym*) AND (retriev* or aspirat* or extract* or procur* or harvest*)))[abs]
6	"Tissue and Organ Harvesting"[mh]
5	"Sperm Retrieval"[mh]
4	#3 OR #2 OR #1
3	((sperm* AND absen*))[Title] OR ((sperm* AND absen*))[abs]
2	(azoosperm*)[Title] OR (azoosperm*)[abs]
1	"Azoospermia"[mh]

3

Appendix C Effectiveness evidence study selection

Study selection for review question: What is the clinical and cost effectiveness of surgical sperm retrieval (SSR) techniques for fertility problems associated with non-obstructive azoospermia or 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 sperm retrieval (SSR) techniques for fertility problems associated with non-obstructive azoospermia or obstructive azoospermia?

Jensen, 2022

Bibliographic Reference Jensen, Christian Fuglesang S; Ohl, Dana A; Fode, Mikkel; Jorgensen, Niels; Giwercman, Aleksander; Bruun, Niels Henrik; Elenkov, Angel; Klajnbard, Anna; Andersen, Claus Y; Aksglaede, Lise; Grondahl, Marie Louise; Bekker, Mette C; Sonksen, Jens; Microdissection Testicular Sperm Extraction Versus Multiple Needle-pass Percutaneous Testicular Sperm Aspiration in Men with Nonobstructive Azoospermia: A Randomized Clinical Trial.; European urology; 2022; vol. 82 (no. 4); 377-384

Study details

Countries where study was carried out	Denmark and Sweden
Study type	Randomised controlled trial (RCT)
Study dates	June 19, 2017 to August 24, 2020
Inclusion criteria	Men with azoospermia according to World Health Organization criteria; testis volume (Prader's orchidometer) ≤15 ml on both sides; no indication of obstructive causes of azoospermia in previous medical history or on physical examination
Exclusion criteria	People with previous open surgical sperm retrieval or testicular biopsy, anejaculation, retrograde ejaculation, Klinefelter's syndrome, XX male syndrome, azoospermia factor (AZFa and/or AZFb) microdeletion, cystic fibrosis transmembrane conductance regulator (CFTR) gene mutation, or bleeding disorders, or if they were unsuitable for full anaesthesia. People where testicular histology during a study biopsy showed normal spermatogenesis.
Patient characteristics	Microdissection testicular sperm extraction (micro-TESE) and Testicular sperm aspiration (TESA) **Age (years), median (interquartile range (iqi))** Micro-TESE=34.0 (30.5; 38.0) TESA=31.0 (29.0; 35.0)

	BMI (kg/m2), median (iqi) Micro-TESE=26.8 (24.6; 29.9) TESA=26.9 (23.6; 29.5) **Left testis volume (ml), median (iqi)** Micro-TESE=12 (8.0; 15.0) TESA=12 (8.0; 15.0) **Right testis volume (ml), median (iqi)** Micro-TESE=12 (8.0; 15.0) TESA=10 (8.0; 15.0)
Intervention(s)/control	**Microdissection testicular sperm extraction (micro-TESE)** The micro-TESE procedure was performed according to Schlegel (1999). The layers surrounding the testis were opened, and under the operating microscope, an equatorial incision of the tunica albuginea was made and the testis bivalved to expose the tissue. **Testicular sperm aspiration (TESA)** The multiple needle-pass TESA was conducted with an 18-gauge needle inserted percutaneously into the testis. While applying a vacuum with a syringe, multiple needle passes (50– 100), targeting the entire testis tissue, were performed through one puncture site before releasing the vacuum and briskly removing the needle. All patients were operated under full anaesthesia by the same 2 surgeons at the same institution, except for the last 11 patients (n=5 needle-pass TESA and n=6 micro-TESE) for whom a third surgeon replaced one of the previous surgeons. The surgery was stopped when spermatozoa were found or when both testes had been examined without finding spermatozoa. If spermatozoa were not found after the multiple needle-pass TESA, salvage micro-TESE was performed

	while the patient was still in the operating room. All extracted tissue from multiple needle-pass TESA and micro-TESE was kept separate for a subsequent analysis in the laboratory. Perioperative antibiotics using a single dose of 2 g ampicillin and 5 mg/kg gentamicin were used for the last 30 procedures due to an unexpectedly high infection rate.
Duration of follow-up	2 days, 3 months, and 6 months post-surgery. Note: Follow-up ended on April 30, 2021, 6 months after surgery on the last patient
Sources of funding	The trial was supported by unrestricted grants from the European Research Council (ReproUnion), Beckett Fonden, Grosserer Chr. Andersen og Hustru Ingeborg Andersen f. Schmidts legat, and Gangstedfonden.
Sample size	N=100 (total) Micro-TESE, N=49; TESA, N=51 Note: N=40 received both TESA and salvage micro-TESE; N=11 received TESA only; N=49 received micro-TESE only

Study arms

Micro-TESE (N = 49)

TESA (N = 51)

Outcomes

Outcome	Micro-TESE, N = 49	TESA + salvage micro-TESE, N = 51
Sperm retrieval rate assessed by successful sperm retrieval defined as laboratory isolation of spermatozoa deemed suitable for IVF/ICSI) No of events	n = 21; % = 43	n = 15; % = 29
Testicular tenderness measured by testicular tenderness No of events	n = 1; % = 2	n = 0; % = 0

Outcome	Micro-TESE, N = 49	TESA + salvage micro-TESE, N = 51
Smaller testicular size No of events	n = 0; % = 0	n = 1; % = 2
Haematoma No of events	n = 4; % = 8	n = 1; % = 2
Infection No of events	n = 2; % = 4	n = 0; % = 0

microTESA: microdissection testicular sperm aspiration; micro-TESE: microdissection testicular sperm extraction
Sperm retrieval rate - Polarity - Higher values are better
Sperm retrieval rate with TESA + salvage mTESE - Polarity - Higher values are better
Surgical complications (including severe pain, hematoma, testicular tenderness, fever, vasovagal syncope, superficial bleeding, wound dehiscence, scrotal swelling, suture loosened, smaller testicular size, infection, abscess, and defect in the tunica albuginea) - Polarity - Lower values are better
Testicular tenderness - Polarity - Lower values are better
Smaller testicular size - Polarity - Lower values are better
Haematoma - Polarity - Lower values are better
Infection - Polarity - Lower values are better

Critical appraisal with Cochrane RoB v2

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low *(Participants were randomised using computer-generated randomization list with five blocks, with block sizes of 20 (four blocks) or 30 (one block). The order of the blocks was not known to the investigators. Patients were randomized in the operating room after receiving full anaesthesia based on externally produced concealed envelopes)*
Domain 2a: Risk of bias due to deviations from the intended	Risk of bias for deviations from the intended interventions	High *(Participants were blinded to the intervention during the operation however*

Section	Question	Answer
interventions (effect of assignment to intervention)	(effect of assignment to intervention)	*surgeons and carers were aware of intervention groups during the trial. If spermatozoa from intraoperative microscopic examination were not found after the multiple needle-pass TESA, the patient continued directly with salvage micro-TESE while still in the operating room. This deviation was likely to affect the outcome and was unbalanced across groups. However, an analysis is provided for all individuals randomised to the original intervention (TESA) group (intention to treat))*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(Outcome data were available for all randomised participants)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(The method of measuring the outcome was appropriate and the measurement or ascertainment of the outcome did not differ between intervention groups. It is unclear whether the outcome assessors were aware of the intervention received by study participants however the assessment of the primary outcome (sperm retrieval rates) could not have been influenced by knowledge of the intervention received)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	High *(The result being assessed is likely to have been selected, on the basis of the results, from multiple eligible analyses of the data)*
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

RoB: risk of bias; micro-TESA: microdissection testicular sperm aspiration; micro-TESE: microdissection testicular sperm extraction

Utlu, 2023

Bibliographic Reference Utlu, Adem; Ozkaya, Fatih; Aksakalli, Tugay; Cinislioglu, Ahmet Emre; Demirdogen, Saban Oguz; Altay, Mehmet Sefa; Karabulut, Ibrahim; Ozbey, Isa; Guclu Utlu, Sibel; Comparison of unilateral and bilateral microdissection testicular sperm

extraction (MD-TESE) in patients with non-obstructive azoospermia: a prospective study.; International urology and nephrology; 2023; vol. 55 (no. 9); 2177-2182

Study details

Country/ies where study was carried out	Turkey
Study type	Randomised controlled trial (RCT)
Study dates	January 2019 to January 2020
Inclusion criteria	Azoospermic primary infertile male patients, married for at least one year and had no history of infertility in their female partners, and diagnosed with non-obstructive azoospermia (NOA)
Exclusion criteria	NR
Patient characteristics	**Age, mean (years)** bilateral micro-TESE=37.4 unilateral micro-TESE=32.2 **Left testis volume, mean (ml)** bilateral micro-TESE=11.6 unilateral micro-TESE=12.5 **Right testis volume, mean (ml)** bilateral micro-TESE=11.5 unilateral micro-TESE=12.9
Intervention(s)/control	**Bilateral microdissection testicular sperm extraction**

	Unilateral microdissection testicular sperm extraction (micro-TESE) An incision was made of approximately 5cm over the raphe, opening the tunica albuginea with transverse incision, and removing the testicular tissue. Then an incision was made in the non-vascularised area near the middle of the testis and approximately 10 large white, shiny tubules were selected and placed into a medium. The micro-TESE procedure was performed under general anaesthesia and by a single surgeon.
Duration of follow-up	NR
Sources of funding	NR
Sample size	N=84 (total) bilateral micro-TESE, N=41; unilateral micro-TESE, N=43

Study arms

Bilateral micro-TESE (N = 41)

Unilateral micro-TESE (N = 43)

Outcomes

Outcome	Bilateral micro-TESE, N = 41	Unilateral micro-TESE, N = 43
Sperm retrieval rate no definition provided No of events	n = 23; % = 56.1	n = 26; % = 60.5
Infection no definition provided No of events	n = 2; % = 4.9	n = 0; % = 0

micro-TESE: microdissection testicular sperm extraction
Sperm retrieval rate - Polarity - Higher values are better
Infection - Polarity - Lower values are better

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	High *(Reported that participants were randomised but the method of randomization was not reported. Not reported if the allocation sequence was concealed. Some significant baseline differences between the 2 groups, men in the bilateral micro-TESE group were older and had a higher oestradiol level than those in the unilateral micro-TESE group)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Some concerns *(The surgeon was aware of interventions groups during the trial. No intention to treat analysis was done as it looks like all randomised participants underwent the originally assigned intervention)*
Domain 2b: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)	Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention)	Some concerns *(The surgeon was aware of interventions groups during the trial. No intention to treat analysis was done as it looks like all randomised participants underwent the originally assigned intervention)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(Outcome data were available for all randomised participants)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Some concerns *(The method of measuring the outcome was appropriate and the measurement. It is unclear whether the outcome assessors were aware of the intervention received by study participants however the assessment of the primary outcome (sperm retrieval rates) could not have been influenced by knowledge of the intervention received. However, sperm was not defined as suitable for ICSI)*

Section	Question	Answer
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Some concerns *(There appears to be no published protocol, however it is unlikely that the result being assessed has been selected on the basis of the results)*
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

ICSI: intracytoplasmic sperm injection; RoB: risk of bias; micro-TESE: microdissection testicular sperm extraction

Appendix E Forest plots

Forest plots for review question: What is the clinical and cost effectiveness of surgical sperm retrieval (SSR) techniques for fertility problems associated with non-obstructive azoospermia or obstructive azoospermia?

No meta-analysis was conducted for this review question and so there are no forest plots.

Appendix F GRADE tables

GRADE tables for review question: What is the clinical and cost effectiveness of surgical sperm retrieval (SSR) techniques for fertility problems associated with non-obstructive azoospermia or obstructive azoospermia?

Table 6: Evidence profile for comparison between micro-TESE and TESA only

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Micro-TESE	TESA	Relative (95% CI)	Absolute		
Sperm retrieval rate (assessed by successful sperm retrieval defined as laboratory isolation of spermatozoa deemed suitable for IVF/ICSI; better indicated by higher values)												
1 (Jensen 2022)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	21/49 (42.9%)	11/51 (21.6%)	RR 1.99 (1.07 to 3.68)	214 more per 1000 (from 15 more to 578 more)	LOW	CRITICAL

CI: confidence interval; ICSI: intracytoplasmic sperm injection; IVF: in vitro fertilisation; Micro-TESE: microdissection testicular sperm extraction; RoB2: Cochrane risk of bias version 2; RR: risk ratio; TESA: testicular sperm aspiration.

1 Serious risk of bias in the evidence contributing to the outcomes as per RoB2

2 95% CI crosses 1 clinical decision making threshold

Table 7: Evidence profile for comparison between micro-TESE and TESA (including TESA plus salvage micro-TESE)

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Micro-TESE	TESA + salvage micro-TESE	Relative (95% CI)	Absolute		
Sperm retrieval rate (assessed by successful sperm retrieval defined as laboratory isolation of spermatozoa deemed suitable for IVF/ICSI; better indicated by higher values)												
1 (Jensen 2022)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	21/49 (42.9%)	15/51 (29.4%)	RR 1.46 (0.85 to 2.49)	135 more per 1000 (from 44 fewer to 438 more)	LOW	CRITICAL
Adverse events: testicular pain (measured by testicular tenderness; better indicated by lower values)												
1 (Jensen 2022)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	1/49 (2%)	0/51 (0%)	RR 3.12 (0.13 to 74.8)	-	VERY LOW	IMPORTANT
Adverse events: atrophy (measured by smaller testicular size; better indicated by lower values)												
1 (Jensen 2022)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/49 (0%)	1/51 (2%)	RR 0.35 (0.01 to 8.31)	13 fewer per 1000 (from 19 fewer to 143 more)	VERY LOW	IMPORTANT
Adverse events: haematoma (measured by haematoma; better indicated by lower values												

1 (Jensen 2022)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	4/49 (8.2%)	1/51 (2%)	RR 4.16 (0.48 to 35.95)	62 more per 1000 (from 10 fewer to 685 more)	VERY LOW	IMPORTANT
Adverse events: infection (measured by infection; better indicated by lower values)												
1 (Jensen 2022)	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	2/49 (4.1%)	0/51 (0%)	RR 5.2 (0.26 to 105.65)	0 fewer per 1,000 (from 0 fewer to 0 fewer)	VERY LOW	IMPORTANT

CI: confidence interval; ICSI: intracytoplasmic sperm injection; IVF: in vitro fertilisation; Micro-TESE: microdissection testicular sperm extraction; RoB2: Cochrane risk of bias version 2; RR: risk ratio; TESA: testicular sperm aspiration.

[1] Serious risk of bias in the evidence contributing to the outcomes as per RoB2

[2] 95% CI crosses 1 clinical decision making threshold

[3] 95% CI crosses 2 clinical decision making thresholds

Table 8: Evidence profile for comparison between bilateral micro-TESE and unilateral micro-TESE

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Bilateral micro-TESE**	**Unilateral micro-TESE**	**Relative (95% CI)**	**Absolute**		
Sperm retrieval rate (no definition provided; better indicated by higher values)												
1 (Utlu 2023)	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	23/41 (56.1%)	26/43 (60.5%)	RR 0.93 (0.65 to 1.33)	42 fewer per 1,000 (from 212 fewer to 200 more)	VERY LOW	CRITICAL
Adverse events: infection (no definition provided; better indicated by lower values)												
1 (Utlu 2023)	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	2/41 (4.9%)	0/43 (0%)	RR 5.24 (0.26 to 105.93)	0 fewer per 1,000 (from 0 fewer to 0 fewer)	VERY LOW	IMPORTANT

CI: confidence interval; micro-TESE: microdissection testicular sperm extraction; RoB2: Cochrane risk of bias version 2; RR: risk ratio; TESA: testicular sperm aspiration.

[1] Very serious risk of bias in the evidence contributing to the outcomes as per RoB2

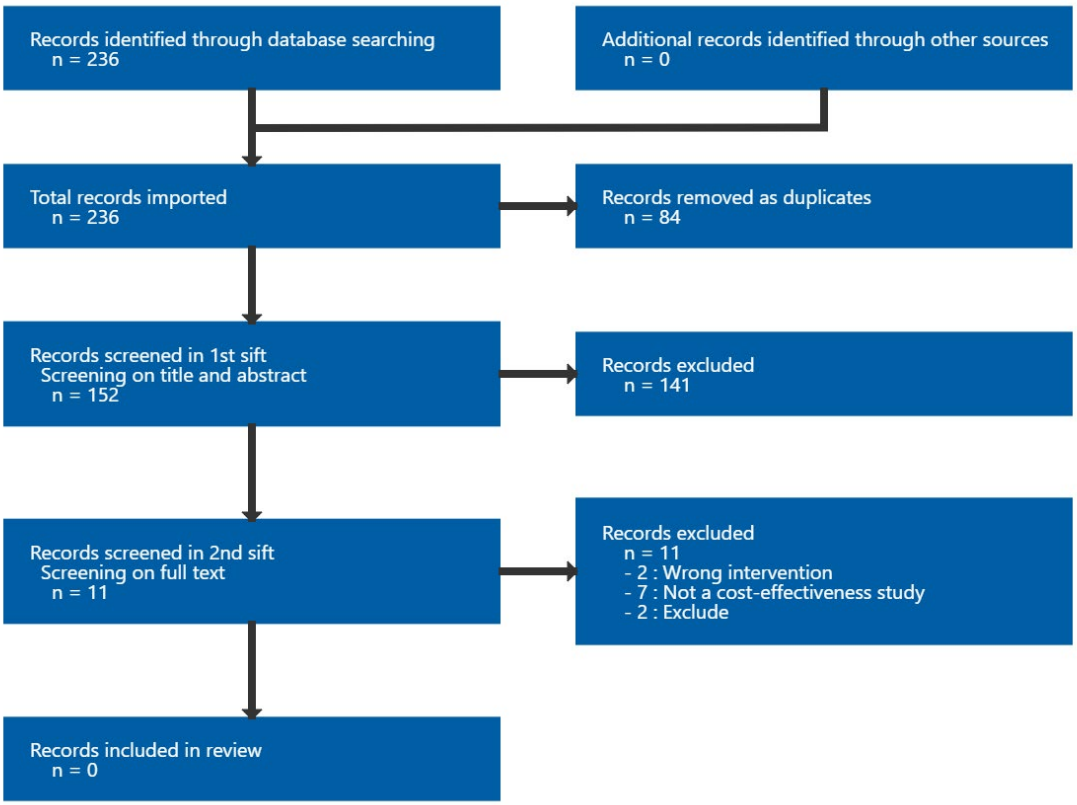
[2] 95% CI crosses 2 clinical decision making thresholds

Appendix G Economic evidence study selection

Study selection for review question: What is the clinical and cost effectiveness of surgical sperm retrieval (SSR) techniques for fertility problems associated with non-obstructive azoospermia or obstructive azoospermia?

No economic evidence was identified which was applicable to this review question. Reasons for study exclusion can be found in Appendix J.

Figure 2: Study selection flow chart



Appendix H Economic evidence tables

Economic evidence for review question: What is the clinical and cost effectiveness of surgical sperm retrieval (SSR) techniques for fertility problems associated with non-obstructive azoospermia or 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 sperm retrieval (SSR) techniques for fertility problems associated with non-obstructive azoospermia or 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 sperm retrieval (SSR) techniques for fertility problems associated with non-obstructive azoospermia or obstructive azoospermia?

Excluded effectiveness studies

Table 9: Excluded studies and reasons for their exclusion

Study	Code [Reason]
Achermann, Arnold P P; Pereira, Thairo A; Esteves, Sandro C (2021) Microdissection testicular sperm extraction (micro-TESE) in men with infertility due to nonobstructive azoospermia: summary of current literature. International urology and nephrology 53(11): 2193-2210	- Narrative summary
Akhvlediani, ND, Reva, IA, Chernushenko, AS et al. (2021) [Sperm retrieval techniques in patients with non-obstructive azoospermia]. Urologiia (Moscow, Russia: 1999): 106-113	- Study not reported in English
Aldemir, Muhammed Ebuzer, Aksakalli, Tugay, Demirdogen, Saban Oguz et al. (2024) A Comparative Study of Equatorial and Longitudinal Incision Techniques in Micro-Dissection Sperm Extraction for Non-Obstructive Azoospermic Patients. Urology	- Not a relevant study design
Aliakbari, Fereshteh, Taghizabet, Neda, Rezaei-Tazangi, Fatemeh et al. (2023) Evaluation of Predicting Factors Affecting Sperm Retrieval in Patients with Klinefelter Syndrome: A Prospective Study. International journal of fertility & sterility 17(4): 276-280	- Comparator in study does not match that specified in protocol
Alkhayal, Abdullah, Aljumaiah, Sahar, Alyami, Ali et al. (2024) Varicocelectomy outcomes among patients with azoospermia and severe oligasthenoteratozoospermia. Urology annals 16(1): 60-63	- Not a relevant study design
Avci, Ali Egemen; Kendirci, Muammer; Basar, Mehmet Murad (2024) Psychological and Pain Factors in Microsurgical Testicular Sperm Extraction (Micro-TESE) for Non-Obstructive Azoospermia: A Comparative Study of Successful and Unsuccessful Cases. Urology journal 21(6): 415-419	- Not a relevant study design
Belenky, A, Avrech, OM, Bachar, GN et al. (2001) Ultrasound-guided testicular sperm aspiration in azoospermic patients: a new sperm retrieval method for intracytoplasmic sperm injection. Journal of clinical ultrasound 29(6): 339-343	- Comparator in study does not match that specified in protocol
Bernie, Aaron M, Mata, Douglas A, Ramasamy, Ranjith et al. (2015) Comparison of microdissection testicular sperm extraction, conventional testicular sperm extraction, and testicular sperm aspiration for nonobstructive azoospermia: a systematic review and meta-analysis. Fertility and sterility 104(5): 1099-	- Systematic review used as source of primary studies

Study	Code [Reason]
3	
Colpi, Giovanni M, Colpi, Elisabetta M, Piediferro, Guido et al. (2009) Microsurgical TESE versus conventional TESE for ICSI in non-obstructive azoospermia: a randomized controlled study. Reproductive biomedicine online 18(3): 315-9	- Not a relevant study design
Corona, G, Pizzocaro, A, Lanfranco, F et al. (2017) Sperm recovery and ICSI outcomes in Klinefelter syndrome: a systematic review and meta-analysis. Human reproduction update 23(3): 1-11	- Systematic review used as source of primary studies
Corona, Giovanni, Minhas, Suks, Giwercman, Aleksander et al. (2019) Sperm recovery and ICSI outcomes in men with non-obstructive azoospermia: a systematic review and meta-analysis. Human reproduction update 25(6): 733-757	- Systematic review used as source of primary studies
Deruyver, Y; Vanderschueren, D; Van der Aa, F (2014) Outcome of microdissection TESE compared with conventional TESE in non-obstructive azoospermia: a systematic review. Andrology 2(1): 20-4	- Systematic review used as source of primary studies
Eliveld, Jitske, van Wely, Madelon, Meisner, Andreas et al. (2018) The risk of TESE-induced hypogonadism: a systematic review and meta-analysis. Human reproduction update 24(4): 442-454	- Systematic review used as source of primary studies
Esteves, S.C. and Pereira, T.A. (2020) SPERM RETRIEVAL RATES BY MICRO-TESE VERSUS CONVENTIONAL TESE IN MEN WITH HISTOPATHOLOGY CONFIRMED NON-OBSTRUCTIVE AZOOSPERMIA: A SYSTEMATIC REVIEW. Fertil. Steril. 114(3): e378-e379	- Conference abstract
Flannigan, Ryan K and Schlegel, Peter N (2019) Microdissection testicular sperm extraction: preoperative patient optimization, surgical technique, and tissue processing. Fertility and sterility 111(3): 420-426	- Systematic review used as source of primary studies
Hayden, R. and Tanrikut, C. (2015) Detection and Management of Obstructive Azoospermia. Urology Practice 2(1): 33-37	- Not a relevant study design
Hu, YY, Wang, LY, Song, BT et al. (2017) Impacts of different procedures of testicular sperm retrieval on testicular function and antisperm antibodies in azoospermia patients. Zhonghua nan ke xue [National journal of andrology] 23(7): 620-625	- Study not reported in English
Jiang, Yan, Cao, Qinying, Zhao, Xiujun et al. (2013) Percutaneous epididymal sperm aspiration and short time insemination in the treatment of men with obstructive azoospermia. Journal of assisted reproduction and genetics 30(9): 1175-9	- Comparator in study does not match that specified in protocol
Kapadia, A.A., Greear, G.M., Chen, T. et al. (2024) Testicular mapping-guided sperm retrieval vs. upfront microTESE in non-obstructive azoospermia: a comparison of sperm retrieval, pregnancy and live-birth rates. Translational Andrology and Urology 13(12): 2672	- Not a relevant study design
Klami, Rauni, Tomas, Candido, Mankonen, Harri et al. (2024) ICSI outcome after microdissection	- Not a relevant study design

Study	Code [Reason]
testicular sperm extraction, testicular sperm aspiration and ejaculated sperm. Reproductive biology 24(1): 100825	
Nicopoullos, James D M, Gilling-Smith, Carole, Almeida, Paula A et al. (2004) Use of surgical sperm retrieval in azoospermic men: a meta-analysis. Fertility and sterility 82(3): 691-701	- Systematic review used as source of primary studies
Ogouma, Ludmilla, Berthaut, Isabelle, Levy, Rachel et al. (2022) Testicular sperm extraction (TESE) outcomes in the context of malignant disease: a systematic review. Asian journal of andrology 24(6): 584-590	- Systematic review used as source of primary studies
Pan, D., Xianfeng, C., Yunshan, Z. et al. (2012) Meta-analysis of surgical sperm retrieval in non-obstructive azoospermia patients. Chinese Journal of Andrology 26(9): 41-45	- Study not reported in English
Persily, Jesse B; Vijay, Varun; Najari, Bobby B (2021) How do we counsel men with obstructive azoospermia due to CF mutations?-a review of treatment options and outcomes. Translational andrology and urology 10(3): 1467-1478	- Systematic review used as source of primary studies
Qin, ZiHan, Xiong, QiaoHua, Lu, MingHan et al. (2024) Sperm recovery and ICSI outcomes in non-obstructive azoospermia with cryptorchidism treated by orchiopexy: a systematic review and meta-analysis. Reproductive biomedicine online: 104392	- Systematic review used as source of primary studies
Shah, Rupin and Gupta, Chirag (2018) Advances in sperm retrieval techniques in azoospermic men: A systematic review. Arab journal of urology 16(1): 125-131	- Systematic review used as source of primary studies
Shih, Kuan-Wei, Shen, Ping-You, Wu, Chien-Chih et al. (2019) Testicular versus percutaneous epididymal sperm aspiration for patients with obstructive azoospermia: a systematic review and meta-analysis. Translational andrology and urology 8(6): 631-640	- Systematic review used as source of primary studies
Sikiru, Akeem Babatunde; Truong, Manh Nguyen; Zohdy, Wael (2024) Future prospects for the advancement of treatment of men with NOA: focus on gene editing, artificial sperm, stem cells, and use of imaging. Asian journal of andrology	- Narrative summary
Silber, S J, Nagy, Z P, Liu, J et al. (1994) Conventional in-vitro fertilization versus intracytoplasmic sperm injection for patients requiring microsurgical sperm aspiration. Human reproduction (Oxford, England) 9(9): 1705-9	- Comparator in study does not match that specified in protocol
Sun, X., Zhu, H., Yang, X. et al. (2023) Outcomes of Microdissection Testicular Sperm Extraction/ Intracytoplasmic Sperm Injection in Cases of Nonobstructive Azoospermia: A Retrospective Study. Andrologia 2023	- Not a relevant study design
Tai, T., Miyamoto, W., Fukuoka, Y. et al. (2024) Micromapping testicular sperm extraction: A new technique for microscopic testicular sperm extraction in nonobstructive azoospermia. Reproductive Medicine and Biology 23(1): e12566	- Comparator in study does not match that specified in protocol
Tournaye, H, Clasen, K, Aytoz, A et al. (1998) Fine	- Not a relevant study design

Study	Code [Reason]
needle aspiration versus open biopsy for testicular sperm recovery: a controlled study in azoospermic patients with normal spermatogenesis. Human reproduction (Oxford, England) 13(4): 901-4	
Turunc, Tahsin, Gul, Umit, Haydardedeoglu, Bulent et al. (2010) Conventional testicular sperm extraction combined with the microdissection technique in nonobstructive azoospermic patients: a prospective comparative study. Fertility and sterility 94(6): 2157-60	- Not a relevant study design
Van Peperstraten, A, Proctor, M L, Johnson, N P et al. (2006) Techniques for surgical retrieval of sperm prior to ICSI for azoospermia. The Cochrane database of systematic reviews: cd002807	- Duplicate reference
Van Peperstraten, A, Proctor, M L, Johnson, N P et al. (2008) Techniques for surgical retrieval of sperm prior to intra-cytoplasmic sperm injection (ICSI) for azoospermia. The Cochrane database of systematic reviews: cd002807	- Systematic review used as source of primary studies
Van Wijck, C.K.I.; Wijnands, K.P.J.; Dohle, C.R. (2009) What is the best technique to harvest spermatozoa from the testis in patients with non-obstructive azoospermia?. Nederlands Tijdschrift voor Urologie 17(3): 69-73	- Study not reported in English
Xu, Shuai, Huang, Yuhua, Yao, Chencheng et al. (2023) Stepwise mini-incision microdissection testicular sperm extraction in NOA patients with a history of cryptorchidism: a case-control study. Basic and clinical andrology 33(1): 21	- Not a relevant study design
Yamamoto, M, Hibi, H, Miyake, K et al. (1996) Microsurgical epididymal sperm aspiration versus epididymal micropuncture with perivascular nerve stimulation for intracytoplasmic sperm injection to treat unreconstructable obstructive azoospermia. Archives of andrology 36(3): 217-24	- Comparator in study does not match that specified in protocol
Yang, J, Liu, JH, Zou, XF et al. (2008) [Sperm retrieval and the predictive parameter of non-obstructive azoospermia: a meta-analysis of literatures 1990 to 2008]. Zhonghua yi xue za zhi 88(30): 2131-5	- Study not reported in English

Excluded economic studies

Table 10: Excluded studies and reasons for their exclusion

Study	Code [Reason]
Asanad, K., Matthew Coward, R., Mehta, A. et al. (2021) Factors Influencing the Decision for Fresh Versus Cryopreserved Microdissection Testicular Sperm Extraction for Non-Obstructive Azoospermia. Urology	- Not a cost-effectiveness study
Chiles, Kelly A and Schlegel, Peter N (2016) Cost-effectiveness of varicocele surgery in the era of assisted reproductive technology. Asian journal of andrology 18(2): 259-61	- USA study

Study	Code [Reason]
Guneri, Cagri; Alkibay, Turgut; Tunc, Lutfi (2016) Effects of clinical, laboratuary and pathological features on successful sperm retrieval in non-obstructive azoospermia. Turkish journal of urology 42(3): 168-77	- Not a cost-effectiveness study
Han, Tracy X; Berk, Brittany; Ghayada, Ramy A; Ernadez et al. (2024) Financial decision analysis based on "willingness to pay" for surgical sperm retrieval approaches among men with non-obstructive azoospermia in the United States. Andrology 12(2) 422-428	- Not a cost-effectiveness study
Harza, M.C.; Voinea, S.N.; Vladareanu, R. (2013) The role of microsurgery in the treatment of male infertility in Romania. Gineco.eu 9(3): 151-153	- Not a cost-effectiveness study
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	- Old study with patients recruited between 1994 and 1997 where more than one embryo was typically transferred. So costs not reflective of current practice. - Wrong comparator
Lee, R, Li, P S, Goldstein, M et al. (2008) A decision analysis of treatments for obstructive azoospermia. Human reproduction (Oxford, England) 23(9): 2043-9	- Wrong intervention
Lee, Richard, Li, Philip S, Goldstein, Marc et al. (2009) A decision analysis of treatments for nonobstructive azoospermia associated with varicocele. Fertility and sterility 92(1): 188-96	- Wrong comparator
Lisek, E W and Levine, L A (1997) Percutaneous technique for aspiration of sperm from the epididymis and testicle. Techniques in urology 3(2): 81-5	- Not a cost-effectiveness study
Patel, Sagar R, Park, Bridget, Reddy, Amit et al. (2023) Testicular Core Extraction: Important Technique for Determining Sperm Retrieval Method in Non-obstructive Azoospermia. Urology 173: 87-91	- Not a cost-effectiveness study
Sacca, A, Pastore, A L, Roscigno, M et al. (2016) Conventional testicular sperm extraction (TESE) and non-obstructive azoospermia: is there still a chance in the era of microdissection TESE? Results from a single non-academic community hospital. Andrology 4(3): 425-9	- Not a cost-effectiveness study

1

2

Appendix K Research recommendations – full details

Research recommendations for review question: What is the clinical and cost effectiveness of surgical sperm retrieval (SSR) techniques for fertility problems associated with non-obstructive azoospermia or obstructive azoospermia?

No research recommendations were made for this review question.