

# Delphi Consensus Global NOA Survey Recommendations: Round 1

Public: <https://forms.gle/SJZd8WSutEkLxK4w9>

Edit: [https://docs.google.com/forms/d/14Jla6xc5f7CGUe7Gx8Rvz\\_4eIGuyNaOPxnYC5BwP-pA/edit](https://docs.google.com/forms/d/14Jla6xc5f7CGUe7Gx8Rvz_4eIGuyNaOPxnYC5BwP-pA/edit)

Dear Colleagues:

We are nearing completion of two manuscripts on the Global NOA Survey. We would like to invite you to participate in the Delphi process to finalize our GAF expert recommendations. The "**initial expert recommendations**" were written by the authors for each of their respective subsection. These were written based on: 1) the results of our online survey; 2) the professional society recommendations presented in each draft; and 3) the evidence provided in the literature and presented by our authors in the discussion they wrote.

The survey consists of 23 recommendations (1 - 7 pertain to the first paper and 8 - 23 to the second paper). We will share a link to access the draft of two papers on NOA survey to those who take part in this Delphi review (to receive this access, please send an email to Ashok Agarwal: agarwaa32099@outlook.com). We are now starting the next stage of our project, which is to review, modify, and approve these recommendations based on Delphi method, and coordinated by one of our Senior Biostatistician, so they can be included in the draft.

We have invited you to take part in this process based on your extensive clinical experience in dealing with patients with NOA. You can quit this survey, if you lack the required clinical experience and feel that you have received this invitation by mistake.

## Instructions on Scoring:

A. If you agree with the recommendation and do not want this recommendation to be changed, give it a score of 7-10 with 7 indicating you agree and no changes necessary and 10 indicating you strongly agree and no changes necessary. If you score a recommendation 7-10, no further action is required for this recommendation and you may move forward to the next recommendation.

B. If you disagree with the recommendation (either entirely or part of it), give it a score of 1-6; with 1 indicating you strongly and completely disagree and you wish the entire recommendation to be changed, while 6 indicating you partly disagree and wish for some parts to be changed. If you do score a recommendation 1-6, you **MUST** write which parts you disagree with and provide an alternative recommendation. Write these alternatives in the space below the score for that recommendation.

C. After the first round survey for these recommendations is received, scores will be

calculated.

Recommendations that score 7-10 by more than 70% of the participants will pass and be accepted as complete.

D. Recommendations that score 6 or more than 30% of the participants will fail. The proposed alternatives for these recommendations will be analyzed and these recommendations will be submitted to review by a group of core experts. Final versions of the new recommendations will be created. These will then undergo the second round of Delphi (another survey which is similar to this), by the same invited experts. After the second round, the recommendations that still do not pass will be subject to the third round of Delphi, which will be done via a Zoom meeting. A final consensus will be reached during the meeting.

**Estimated time: 20-30 minutes.**

**The survey link will remain open for 7 days from Aug 1 to 8.**

Delphi: The Delphi technique is a method of collecting opinion on a particular research question. It is based on the premise that pooled intelligence enhances individual judgement and captures the collective opinion of a group of experts without being physically assembled. The conventional Delphi uses a series of questionnaires to generate expert opinion in an anonymous fashion and takes place over a series of rounds.

\* Indicates required question

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### Manuscript #1 Expert recommendations

1. **First (Given) Name :** \*

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2. **Middle Name :**

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3. **Last (Family) name :** \*

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4. **Email**

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5. **1. What is a Profession? \***

Mark only one oval.

- Urologist
- Andrologist
- Other

## 6.

Mark only one oval.

- 0 – 5 years
- >5 and <10
- >10 and <15
- >15 and <20
- >20

Please click on the link below to access the draft version of two NOA manuscripts.

Manuscript No.1 NOA Global Survey : [https://docs.google.com/document/d/e/2PACX-1vSxpmRhyXrtZphEMxMOuZo2GQ3\\_f90Ogl5RdeM\\_w4bZrrd21yRfDRukonR5q5nGQOpyTld3ZT0oHWVo/pub](https://docs.google.com/document/d/e/2PACX-1vSxpmRhyXrtZphEMxMOuZo2GQ3_f90Ogl5RdeM_w4bZrrd21yRfDRukonR5q5nGQOpyTld3ZT0oHWVo/pub)

Manuscript No.2 NOA Global Survey : <https://docs.google.com/document/d/e/2PACX-1vQnD7bVey2soQv11LZz8K78WPApGHc-pju8ZdVYS7QsdSxRIEXgWxQNgcxHbRuhWKwgb7v318ApuXKo/pub>

- 7. **Recommendation 1 Incidence of NOA:** Though there are geographical variations \* in incidence, NOA accounts for the majority of azoospermia, with primary testicular failure being the main cause of NOA.

Please score from 1 to 10 on Likert scale. Ten being the highest.

*Mark only one oval.*

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- 8. **Recommendation 1.** Please use this box to type any change in the above recommendation.

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- 9. **Recommendation 2 Number of semen samples:** Due to possible fluctuations \* one semen sample might not be enough to diagnose azoospermia. At least two separate semen samples should be examined, with centrifugation to create a pellet, to establish a diagnosis of azoospermia.

Please score from 1 to 10 on Likert scale. Ten being the highest.

*Mark only one oval.*

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10. **Recommendation 2.** Please use this box to type any change in the above recommendation.

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11. **Recommendation 3 The interval between two semen tests:** Generally, at least \* a month's interval is preferable, but the physician's clinical judgment may be used to determine the duration between the two tests, depending on individual circumstances and history of any recent spermatotoxic event. Please score from 1 to 10 on Likert scale. Ten being the highest.

*Mark only one oval.*

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12. **Recommendation 3.** Please use this box to type any change in the above recommendation.

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- 13. **Recommendation 4 Hormone evaluation:** The initial evaluation of a patient with \* suspected NOA should include total testosterone level, FSH, and LH, as these hormones are the primary regulator for spermatogenesis. When the total testosterone level does not match the clinical symptoms or if there is any condition that could dramatically alter the SHBG level then calculation of free testosterone (after SHBG assay) is recommended. Estradiol should be measured in obese men, and prolactin should be assayed if there is associated decrease in libido and erection

Please score from 1 to 10 on Likert scale. Ten being the highest.

*Mark only one oval.*

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- 14. **Recommendation 4.** Please use this box to type any change in the above recommendation.

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- 15. **Recommendation 5 Genetic testing:** Karyotype and Y microdeletion tests should be performed for NOA patients, while CFTR gene mutation tests should be done only in cases of vas aplasia or congenital obstruction. Currently, other genetic tests like full exome or genome screening are not recommended as routine tests. \*

Please score from 1 to 10 on Likert scale. Ten being the highest.

Mark only one oval.

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- 16. **Recommendation 5.** Please use this box to type any change in the above recommendation.

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- 17. **Recommendation 6 Differentiating between OA and NOA:** Diagnostic testicular biopsy prior to definitive testicular sperm extraction is not recommended for use in routine clinical practice. Only in some cases where the FSH, LH and the testicular volumes are normal, a testicular biopsy may be indicated to provide a definitive diagnosis. In most cases clinical and laboratory results are sufficient to distinguish between NOA or OA. \*

Please score from 1 to 10 on Likert scale. Ten being the highest.

Mark only one oval.

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18. **Recommendation 6.** Please use this box to type any change in the above recommendation.

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19. **Recommendation 7 Predictors of spermatogenesis:** There are no preoperative \* biochemical and clinical variables that definitively predict positive sperm retrieval at surgery in patients with NOA. However, normal FSH, normal testicular volume, past history of sperm in the ejaculate, and histopathology with hypospermatogenesis predict higher chances of sperm retrieval.

Please score from 1 to 10 on Likert scale. Ten being the highest.

*Mark only one oval.*

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20. **Recommendation 7.** Please use this box to type any change in the above recommendation.

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21. **Recommendation 8 Use of hormonal therapy prior to SSR in NOA patients:** \*

The quality of evidence supporting hormonal therapy before SSR in NOA patients is low with regards to the hormonal therapy before SSR. However, it may improve the SSR rates in some NOA patients. Given the limited and poor-quality evidence it is not routinely recommended but may be considered after adequate counseling Please score from 1 to 10 on Likert scale. Ten being the highest.

Mark only one oval.

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22. **Recommendation 8.** Please use this box to type any change in the above recommendation.

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23. **Recommendation 9 Use of exogenous testosterone in men with NOA** \*

**interested in fertility:** Exogenous testosterone should not be used for men with NOA who are still interested in testicular sperm retrieval and future fertility. Instead, SERMs, aromatase inhibitors, or hCG can be used to raise testosterone without compromising spermatogenesis.

Please score from 1 to 10 on Likert scale. Ten being the highest.

Mark only one oval.

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24. **Recommendation 9.** Please use this box to type any change in the above recommendation.

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25. **Recommendation 10 Surgical therapy with mTESE:** mTESE is the most efficient procedure for sperm retrieval in men with NOA who wish to have biological children. The experience of the surgeon and the time spent by the embryologist can impact the success of mTESE. \*

Please score from 1 to 10 on Likert scale. Ten being the highest.

*Mark only one oval.*

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26. **Recommendation 10.** Please use this box to type any change in the above recommendation.

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- 27. **Recommendation 11 SSR in Klinefelter patients:** The SSR rates reported in the literature in patients with Klinefelter syndrome undergoing mTESE ranges between 20-60%. m-TESE in patients with Klinefelter syndrome can be performed after explaining realistic success rates to patients. High volume mTESE centers may have better success in SSR in Klinefelter patients.

Please score from 1 to 10 on Likert scale. Ten being the highest.

Mark only one oval.

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- 28. **Recommendation 11.** Please use this box to type any change in the above recommendation.

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- 29. **Recommendation 12 Considerations related to sperm retrieval:** It is preferable for the laboratory team to be in reasonable proximity to the operating theater to facilitate the transfer of mTESE specimens and enhance the search for sperm. The samples should be subject to meticulous scrutiny and examination by the embryologist for at least 60 minutes in an attempt to identify sperm. Both fresh and cryopreserved sperm can be used dependent upon the expertise of the center and the embryologist.

Please score from 1 to 10 on Likert scale. Ten being the highest.

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30. **Recommendation 12.** Please use this box to type any change in the above recommendation.

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31. **Recommendation 13 Testicular biopsy at the time of surgical sperm retrieval:** Sending a testicular biopsy for histopathology during surgical sperm retrieval is recommended since it would establish the diagnosis and prognosis, help in counseling the patient if no sperm are found, and detect GCNIS if present. Please score from 1 to 10 on Likert scale. Ten being the highest.

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*Mark only one oval.*

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32. **Recommendation 13.** Please use this box to type any change in the above recommendation.

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33. **Recommendation 14 Surgical therapy in men with genetic abnormalities:** \*

The genetic status of a male has a significant impact on the success rate of SSR. There is a reasonable chance of finding sperm in men with Klinefelter Syndrome and Y chromosome AZFc microdeletion. A complete deletion of AZFa and AZFb correlate with severe spermatogenesis impairment and sperm retrieval is not advised in these situations. Sperm retrieval may be rarely successful in incomplete, aberrant, or non-classical AZFa, AZFb, and AZFbc microdeletions. It is essential to offer proper counseling regarding the likelihood of sperm retrieval, including the option for alternatives such as donor sperm and adoption.

Please score from 1 to 10 on Likert scale. Ten being the highest.

*Mark only one oval.*

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34. **Recommendation 14.** Please use this box to type any change in the above recommendation.

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35. **Recommendation 15 Varicocele repair in NOA:** Evidence supporting VR in men \* with NOA is limited. The decision to perform VR in cases of NOA is a shared decision between the physician and the couple after a detailed discussion of the risks and benefits. The decision may be guided by parameters such as testicular volume, FSH level, female partner’s age, testicular histology if available, and overall fertility status. VR for subclinical varicoceles is not recommended.

Please score from 1 to 10 on Likert scale. Ten being the highest.

*Mark only one oval.*

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36. **Recommendation 15.** Please use this box to type any change in the above recommendation.

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37. **Recommendation 16 Techniques to optimize sperm retrieval:** The evidence \* supporting the utility of diagnostic testicular FNA mapping prior to SSR is limited and the procedure may cause testicular damage. Hence, it is not routinely recommended. There is currently no evidence supporting the use of imaging techniques to improve the success of sperm retrieval.

Please score from 1 to 10 on Likert scale. Ten being the highest.

*Mark only one oval.*

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38. **Recommendation 16.** Please use this box to type any change in the above recommendation.

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39. **Recommendation 17 Comparison of sperm retrieval techniques:** mTESE is \* considered the preferred method for sperm extraction due to its overall higher SSR rate compared to other procedures such as TESA and cTESE, but this is true only for some testicular histologies. Hence, it may be acceptable, in some cases, to perform a cTESE as the first step of a mTESE.

Please score from 1 to 10 on Likert scale. Ten being the highest.

*Mark only one oval.*

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40. **Recommendation 17.** Please use this box to type any change in the above recommendation.

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- 41. **Recommendation 18** Repeat mTESE: A repeat mTESE can still be successful regardless of the outcome of the initial sperm retrieval procedure, although the chance of successful SSR during a repeat operation is higher if the original surgery found sperm. The recommended duration between the two procedures is 6 months. Waiting for 6 months after the first procedure may allow for the testicles to recover their function from the previous surgery.. \*

Please score from 1 to 10 on Likert scale. Ten being the highest.

Mark only one oval.

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- 42. **Recommendation 18.** Please use this box to type any change in the above recommendation.

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- 43. **Recommendation 19 mTESE miscellaneous questions:** With a negative mTESE on one side, mTESE can be attempted on the opposite side in bilateral symmetrical testes with a 10% chance of finding sperm on the second side. Though there is no defined cutoff value for FSH, higher success rates have been reported with FSH < 40 IU/ml. \*

Please score from 1 to 10 on Likert scale. Ten being the highest.

Mark only one oval.

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44. **Recommendation 19.** Please use this box to type any change in the above recommendation.

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45. **Recommendation 20 PGT in men with 47XXY:** In embryos formed from 47 XXY \* men, pre-implantation genetic testing can be offered whenever feasible, however studies suggest that the majority of embryos from men with Klinefelter syndrome have no chromosomal abnormalities.

Please score from 1 to 10 on Likert scale. Ten being the highest.

*Mark only one oval.*

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46. **Recommendation 20.** Please use this box to type any change in the above recommendation.

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47. **Recommendation 21 Stem cells and PRP use:** Currently, there is not enough \* evidence to recommend the routine use of stem cells and PRP in the treatment of NOA. These are evolving and promising therapies but currently their use should be restricted to experimental settings.

Please score from 1 to 10 on Likert scale. Ten being the highest.

*Mark only one oval.*

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48. **Recommendation 21.** Please use this box to type any change in the above recommendation.

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49. **Recommendation 22 MRI prior to SSR:** More evidence is needed before its use \* can be routinely recommended for identifying areas of spermatogenesis or potentially favorable patients for SSR.

Please score from 1 to 10 on Likert scale. Ten being the highest.

*Mark only one oval.*

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50. **Recommendation 22.** Please use this box to type any change in the above recommendation.

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51. **Recommendation 23 Biggest advancement in NOA:** Gene therapy with CRISPR-Cas9 may be able to cure NOA in selected patients. This is possible in theory, but future studies are needed to demonstrate its applicability. \*  
Please score from 1 to 10 on Likert scale. Ten being the highest.

*Mark only one oval.*

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52. **Recommendation 23.** Please use this box to type any change in the above recommendation.

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