



Sperm DNA Fragmentation and Lifestyle Factors in Men Attending Infertility Clinics: A Review of the Evidence

Nour Okafor^{1*}, Kofi Sithole², Bekzat Carvalho³

¹Department of Medical Sciences, Achankovil Academy of Medical Sciences, Barbados

²Department of Medical Sciences, Volta Academy of Medical Sciences, Uzbekistan

³Department of Medical Sciences, Lapland Research Institute of Medical Sciences, Serbia

Article Info

Volume 1, Issue 1, 2026

doi: [10.62715/ijua.2026.v1.i1.pp1-7](https://doi.org/10.62715/ijua.2026.v1.i1.pp1-7)

Received: 25 October 2025

Accepted: 19 December 2025

Published: 26 February 2026

Abstract

Conventional semen analysis describes how many spermatozoa a man produces, how they move and what they look like, but it says nothing about the integrity of the genome they carry. Tests of sperm DNA fragmentation were developed to fill that gap, and they are now requested widely in infertility clinics, often together with advice to change habits that are thought to damage sperm chromatin. This narrative review examines what the published literature supports. It describes the principal assays and why their results are not interchangeable, summarises the biological account that links lifestyle exposures to DNA strand breaks through oxidative stress, and then considers the evidence for tobacco, alcohol, body weight and diet, scrotal heat, paternal age, environmental pollutants and abstinence interval. The associations are biologically plausible and fairly consistent for smoking, obesity and age, weaker for alcohol and heat, and almost all rest on cross-sectional comparisons in clinic populations where varicocele, infection and selection confound the picture. Evidence that changing behaviour lowers fragmentation, or that a lower value improves the chance of a live birth, remains thin. The review closes with the questions that well-designed longitudinal and interventional studies would need to answer.

Keywords: Sperm DNA fragmentation, Male infertility, Oxidative stress, Lifestyle factors, Semen analysis, Sperm chromatin

© 2026 Nour Okafor et al. This is an open access article under the CC BY license (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

1. Introduction

A man referred to an infertility clinic is assessed first by semen analysis, performed according to the laboratory manual of the World Health Organization, now in its sixth edition (WHO, 2021). The test counts spermatozoa and grades their motility and morphology. It was never designed to examine the DNA inside the sperm head, and men with entirely normal results may still father no pregnancy. Interest in sperm chromatin grew from that observation and from the early demonstration by Evenson et al. (1980) that the susceptibility of sperm DNA to denaturation differed between fertile and subfertile males.

Sperm DNA fragmentation, usually abbreviated SDF, refers to single-strand and double-strand breaks

* Corresponding author: Nour Okafor, Department of Medical Sciences, Achankovil Academy of Medical Sciences, Barbados. E-mail: nour.okafor@achankovil.edu

© 2026 Nour Okafor et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

in the nuclear DNA of the spermatozoon. Meta-analyses have associated higher fragmentation with miscarriage ([Robinson et al., 2012](#)) and with poorer results after in vitro fertilisation and intracytoplasmic sperm injection ([Simon et al., 2017](#)). Clinicians who order the test are therefore soon asked a practical question by the couple in front of them: whether the result can be improved. The usual answer is advice about smoking, drinking, weight, heat and supplements.

That advice is reasonable on general health grounds. Whether it is supported by evidence specific to sperm DNA is a separate matter, and it is the subject of this review. The focus is on men attending infertility clinics, because that is where the test is used and where most of the data come from, and because findings in such men cannot be assumed to hold in the general population or the reverse.

2. Scope and Approach

This is a narrative review of the published literature. It draws on landmark laboratory papers, on meta-analyses and large observational studies where they exist, and on the practice guidelines of professional societies. No formal search protocol was applied and no pooled estimates are offered. The aim is to set out what is reasonably established, what is suggested but unproven, and where the literature is too heterogeneous to support a firm statement. Occupational and iatrogenic causes of DNA damage, such as chemotherapy and radiotherapy, lie outside the scope, as does the technical question of sperm selection for assisted reproduction.

3. Measuring Sperm DNA Fragmentation

Four assays dominate clinical use. The sperm chromatin structure assay (SCSA) uses flow cytometry and acridine orange to measure the proportion of cells whose DNA denatures after a mild acid challenge, reported as the DNA fragmentation index ([Evenson et al., 1999](#)). The TUNEL assay labels the free 3'-hydroxyl ends of broken strands with a terminal transferase and counts the labelled cells by microscopy or flow cytometry. The sperm chromatin dispersion test infers fragmentation from the absence of a halo of dispersed DNA loops after denaturation and protein removal ([Fernández et al., 2003](#)). The comet assay, in alkaline or neutral form, measures DNA migration from single cells during electrophoresis.

These tests do not measure the same thing. TUNEL and the comet assay detect breaks directly, while SCSA and the dispersion test detect susceptibility to denaturation, which is related to breaks but also to chromatin compaction. Thresholds differ by assay and by laboratory. A fragmentation index of about 30 percent in the SCSA has been widely used to mark a group with reduced chances of natural and intrauterine conception ([Evenson et al., 1999](#); [Bungum et al., 2007](#)), but that figure does not transfer to other methods. Reviews of the tests have stressed this lack of standardisation for many years ([Sakkas and Alvarez, 2010](#)).

The consequence for the present question is direct. A study that reports higher fragmentation in smokers using one assay and a study that finds no difference using another are not necessarily in conflict, and results cannot simply be averaged. Professional guidance reflects the uncertainty. The American Society for Reproductive Medicine concluded that the evidence did not support routine use of the test ([ASRM, 2013](#)), and the joint guideline of the American Urological Association and the same society does not recommend it in the initial evaluation of the infertile couple ([Schlegel et al., 2021](#)). Other expert groups have set out specific scenarios, including unexplained infertility, recurrent pregnancy loss, varicocele and lifestyle risk, in which they consider testing informative ([Agarwal et al., 2016](#); [Esteves et al., 2021](#)).

4. How Lifestyle Could Damage Sperm DNA

The mature spermatozoon is unusually exposed. Its cytoplasm, and with it most of its antioxidant enzymes, is shed during spermiogenesis; its membranes are rich in polyunsaturated fatty acids; and it has very limited capacity to repair DNA. Protection depends on the tight packaging of the genome around protamines and on the antioxidants of seminal plasma. [Aitken and De Iuliis \(2010\)](#) proposed a two-step

account in which faulty chromatin remodelling during spermiogenesis leaves some cells poorly protaminated, and these vulnerable cells are then attacked by reactive oxygen species. Other recognised routes include abortive apoptosis in the testis and damage acquired during transit through the epididymis (Sakkas and Alvarez, 2010).

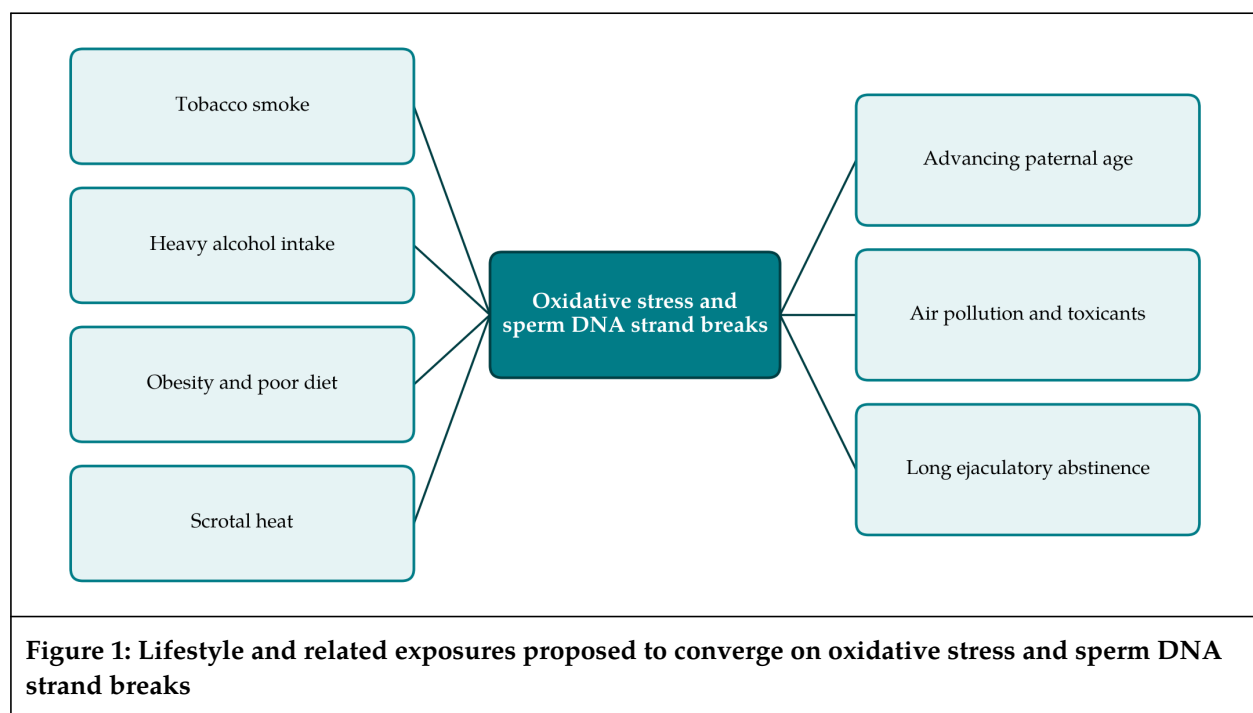
Oxidative stress is the mechanism through which most lifestyle exposures are thought to act. Reactive oxygen species arise from leukocytes in semen, from immature spermatozoa that retain excess cytoplasm and from systemic sources, and their production is increased by smoking, obesity, heat and pollutants (Tremellen, 2008; Wright et al., 2014). Figure 1 summarises this common pathway. The model is coherent and supported by laboratory work, but coherence of mechanism is not evidence of effect in patients, and the sections that follow consider each exposure against the clinical data.

5. Evidence for Individual Factors

Table 1 summarises the exposures most often discussed with patients, the mechanism proposed for each and the general state of the evidence. The paragraphs below give the reasoning behind each entry.

5.1. Tobacco

Smoking is the exposure with the largest literature. A meta-analysis restricted to studies using current World Health Organization methods found that smokers had lower sperm counts and motility and poorer morphology than non-smokers, with larger differences in infertile men and in moderate and heavy smokers (Sharma et al., 2016). Studies of DNA fragmentation in smokers are smaller and use a mixture of assays, but most report higher values, and cigarette smoke constituents and their metabolites have been identified in seminal plasma (Wright et al., 2014). What is lacking is good evidence on reversal: few studies have followed men after cessation with repeated measurement of sperm DNA.



5.2. Alcohol

For alcohol the picture is less clear. The meta-analysis by Ricci et al. (2017) found that intake was associated with lower semen volume and poorer morphology, and that the effect was confined largely to daily drinkers, with little sign of harm from occasional consumption. Data on DNA fragmentation specifically are few and inconsistent. Alcohol use is also closely tied to smoking, diet and body weight, so its independent contribution is difficult to isolate in observational data.

Table 1: Lifestyle and related factors linked to sperm DNA fragmentation, with the state of the published evidence

Factor	Proposed mechanism	State of the evidence	Representative sources
Tobacco smoking	Oxidants and genotoxic compounds reach seminal plasma	Fairly consistent association; mostly cross-sectional	Sharma et al., 2016 ; Wright et al., 2014
Alcohol	Oxidative metabolism; endocrine disturbance	Semen parameters affected by daily intake; DNA data sparse	Ricci et al., 2017
Obesity and diet	Systemic inflammation, raised scrotal temperature, altered hormones	Association reported; weight-loss studies small	Kort et al., 2006 ; Håkonsen et al., 2011
Scrotal heat	Impaired spermatogenesis and increased oxidant production	Plausible; exposure poorly measured	Jung and Schuppe, 2007
Paternal age	Accumulated oxidative damage, reduced apoptotic clearance	Consistent rise with age, including in healthy men	Wyrobek et al., 2006
Air pollution	Reactive metabolites of combustion products	Supported by a small number of cohort studies	Rubes et al., 2005
Antioxidant supplements	Scavenging of reactive oxygen species	Low-certainty evidence; a large trial found no benefit	Smits et al., 2019 ; Steiner et al., 2020

5.3. Body weight and diet

[Kort et al. \(2006\)](#) reported that overweight and obese men attending a fertility practice had a higher DNA fragmentation index and fewer normal motile sperm than men of normal weight, and several later studies have pointed in the same direction, although not all. Adipose tissue is a source of inflammatory mediators and of aromatase activity, and suprapubic and thigh fat may raise scrotal temperature, so more than one pathway is plausible. Evidence from weight reduction is limited. In a small cohort of severely obese men enrolled in a residential programme, weight loss was associated with better semen measures ([Håkonsen et al., 2011](#)), but the study had no control group and cannot separate the effect of weight from that of diet, exercise and abstinence from alcohol.

5.4. Heat, age and the environment

The testis functions a few degrees below core temperature, and experimental heating reliably suppresses spermatogenesis. The review by [Jung and Schuppe \(2007\)](#) found evidence that prolonged sitting, occupational heat and insulating clothing raise scrotal temperature, but the relation between everyday exposures and semen quality was inconsistent, in large part because exposure is rarely measured directly. Varicocele, which is common in clinic populations and is itself associated with raised fragmentation ([Zini and Dohle, 2011](#)), is an obvious confounder of any study of heat.

Age is not a lifestyle choice in the ordinary sense, but the timing of fatherhood is, and age modifies the interpretation of every other factor. In healthy non-clinical volunteers [Wyrobek et al. \(2006\)](#) found that DNA fragmentation rose steadily with age, with no evidence of a threshold. Environmental exposure has been examined in fewer studies. Young men in a Czech district with seasonal air pollution had higher fragmentation after periods of high exposure, without change in conventional semen measures ([Rubes et al., 2005](#)), a finding that illustrates how sperm DNA may respond to insults that routine analysis does not register.

The interval of abstinence before sample collection also affects the result. Longer storage in the epididymis prolongs exposure to oxidants, and shorter abstinence has been proposed as a simple means of lowering fragmentation before assisted reproduction ([Esteves et al., 2021](#)). The point matters for

research as well as practice, because uncontrolled differences in abstinence can create or conceal apparent effects of lifestyle.

6. Whether Changing Behaviour Lowers Fragmentation

An association between an exposure and DNA damage does not show that removing the exposure repairs it. The strongest test of the oxidative model in practice has been antioxidant supplementation. The Cochrane review of antioxidants for male subfertility found that supplements might increase live birth rates, but judged the evidence to be of low certainty because the trials were small and at risk of bias (Smits *et al.*, 2019). The subsequent multicentre randomised trial by Steiner *et al.* (2020) found that a combined antioxidant preparation did not improve semen parameters or DNA integrity in men with male factor infertility. For smoking cessation, alcohol reduction and exercise, comparable trials with sperm DNA as an outcome are not available.

Two further cautions follow. Spermatogenesis takes roughly ten weeks, so any intervention must be sustained before its effect can be assessed, and single measurements are subject to considerable biological variation within the same man. In addition, the outcome that matters to couples is a healthy child. A fall in fragmentation index is a surrogate, and its relation to live birth after lifestyle change has not been established. Advice to stop smoking, moderate alcohol and lose excess weight can be given with confidence on general health grounds; the claim that it will correct a DNA fragmentation result should be made with more reserve.

7. Gaps and Future Work

Several weaknesses recur across this literature. Most studies are cross-sectional and recruit from clinics, where men with risk factors and men with poor results are both over-represented. Exposure is self-reported. Assays and thresholds vary, and few studies adjust for age, abstinence, varicocele and genital tract infection together. Publication of positive associations is more likely than publication of null results. Each of these problems can be addressed: by prospective cohorts with repeated sampling, by agreed reporting of assay method and abstinence, by objective markers such as cotinine for tobacco exposure, and by trials of structured lifestyle programmes that follow couples to live birth.

There is also a question of who should be tested. If lifestyle counselling is appropriate for all men seeking fertility care, a test is useful only where its result changes management, for example by identifying men for whom varicocele repair, a shorter abstinence interval or a different mode of assisted reproduction should be discussed. That is the logic of the scenario-based recommendations (Agarwal *et al.*, 2016), and it deserves prospective evaluation.

8. Conclusion

Sperm DNA fragmentation is higher, on average, in men who smoke, who are obese and who are older, and a shared oxidative mechanism makes these associations credible. For alcohol, heat and environmental pollutants the evidence is suggestive and incomplete. The literature is weakened throughout by cross-sectional design, by confounding within clinic populations and by assays that do not agree with one another. Whether changing behaviour lowers fragmentation, and whether a lower value brings a better chance of a child, are questions that current studies do not settle. Clinicians can encourage healthier habits while being candid about what the test can and cannot promise.

Conflict of interest

To be declared by the author(s) before publication.

Funding

To be declared by the author(s) before publication.

References

- Agarwal, A., Majzoub, A., Esteves, S.C., Ko, E., Ramasamy, R. and Zini, A. (2016). [Clinical utility of sperm DNA fragmentation testing: practice recommendations based on clinical scenarios.](#) *Translational Andrology and Urology*, 5(6): 935-950. <https://doi.org/10.21037/tau.2016.10.03>
- Aitken, R.J. and De Iuliis, G.N. (2010). [On the possible origins of DNA damage in human spermatozoa.](#) *Molecular Human Reproduction*, 16(1): 3-13. <https://doi.org/10.1093/molehr/gap059>
- Bungum, M., Humaidan, P., Axmon, A., Spano, M., Bungum, L., Erenpreiss, J. and Giwercman, A. (2007). [Sperm DNA integrity assessment in prediction of assisted reproduction technology outcome.](#) *Human Reproduction*, 22(1): 174-179.
- Esteves, S.C., Zini, A., Coward, R.M., Evenson, D.P., Gosálvez, J., Lewis, S.E.M., Sharma, R. and Humaidan, P. (2021). [Sperm DNA fragmentation testing: summary evidence and clinical practice recommendations.](#) *Andrologia*, 53(2): e13874. <https://doi.org/10.1111/and.13874>
- Evenson, D.P., Darzynkiewicz, Z. and Melamed, M.R. (1980). [Relation of mammalian sperm chromatin heterogeneity to fertility.](#) *Science*, 210(4474): 1131-1133. <https://doi.org/10.1126/science.7444440>
- Evenson, D.P., Jost, L.K., Marshall, D., Zinaman, M.J., Clegg, E., Purvis, K., de Angelis, P. and Claussen, O.P. (1999). [Utility of the sperm chromatin structure assay as a diagnostic and prognostic tool in the human fertility clinic.](#) *Human Reproduction*, 14(4): 1039-1049. <https://doi.org/10.1093/humrep/14.4.1039>
- Fernández, J.L., Muriel, L., Rivero, M.T., Goyanes, V., Vazquez, R. and Alvarez, J.G. (2003). [The sperm chromatin dispersion test: a simple method for the determination of sperm DNA fragmentation.](#) *Journal of Andrology*, 24(1): 59-66.
- Håkonsen, L.B., Thulstrup, A.M., Aggerholm, A.S., et al. (2011). [Does weight loss improve semen quality and reproductive hormones? Results from a cohort of severely obese men.](#) *Reproductive Health*, 8: 24. <https://doi.org/10.1186/1742-4755-8-24>
- Jung, A. and Schuppe, H.-C. (2007). [Influence of genital heat stress on semen quality in humans.](#) *Andrologia*, 39(6): 203-215.
- Kort, H.I., Massey, J.B., Elsner, C.W., Mitchell-Leef, D., Shapiro, D.B., Witt, M.A. and Roudebush, W.E. (2006). [Impact of body mass index values on sperm quantity and quality.](#) *Journal of Andrology*, 27(3): 450-452.
- Practice Committee of the American Society for Reproductive Medicine (2013). [The clinical utility of sperm DNA integrity testing: a guideline.](#) *Fertility and Sterility*, 99(3): 673-677. <https://doi.org/10.1016/j.fertnstert.2012.12.049>
- Ricci, E., Al Beitawi, S., Cipriani, S., Candiani, M., Chiaffarino, F., Viganò, P., Noli, S. and Parazzini, F. (2017). [Semen quality and alcohol intake: a systematic review and meta-analysis.](#) *Reproductive BioMedicine Online*, 34(1): 38-47.
- Robinson, L., Gallos, I.D., Conner, S.J., Rajkhowa, M., Miller, D., Lewis, S., Kirkman-Brown, J. and Coomarasamy, A. (2012). [The effect of sperm DNA fragmentation on miscarriage rates: a systematic review and meta-analysis.](#) *Human Reproduction*, 27(10): 2908-2917. <https://doi.org/10.1093/humrep/des261>
- Rubes, J., Selevan, S.G., Evenson, D.P., Zudova, D., Vozdova, M., Zudova, Z., Robbins, W.A. and Perreault, S.D. (2005). [Episodic air pollution is associated with increased DNA fragmentation in human sperm without other changes in semen quality.](#) *Human Reproduction*, 20(10): 2776-2783.
- Sakkas, D. and Alvarez, J.G. (2010). [Sperm DNA fragmentation: mechanisms of origin, impact on reproductive outcome, and analysis.](#) *Fertility and Sterility*, 93(4): 1027-1036. <https://doi.org/10.1016/j.fertnstert.2009.10.046>
- Schlegel, P.N., Sigman, M., Collura, B., et al. (2021). [Diagnosis and treatment of infertility in men: AUA/ASRM guideline part I.](#) *Journal of Urology*, 205(1): 36-43. <https://doi.org/10.1097/JU.0000000000001521>

- Sharma, R., Harlev, A., Agarwal, A. and Esteves, S.C. (2016). Cigarette smoking and semen quality: a new meta-analysis examining the effect of the 2010 World Health Organization laboratory methods for the examination of human semen. *European Urology*, 70(4): 635-645. <https://doi.org/10.1016/j.eururo.2016.04.010>
- Simon, L., Zini, A., Dyachenko, A., Ciampi, A. and Carrell, D.T. (2017). A systematic review and meta-analysis to determine the effect of sperm DNA damage on in vitro fertilization and intracytoplasmic sperm injection outcome. *Asian Journal of Andrology*, 19(1): 80-90.
- Smits, R.M., Mackenzie-Proctor, R., Yazdani, A., Stankiewicz, M.T., Jordan, V. and Showell, M.G. (2019). Antioxidants for male subfertility. *Cochrane Database of Systematic Reviews*, 3: CD007411. <https://doi.org/10.1002/14651858.CD007411.pub4>
- Steiner, A.Z., Hansen, K.R., Barnhart, K.T., et al. (2020). The effect of antioxidants on male factor infertility: the Males, Antioxidants, and Infertility (MOXI) randomized clinical trial. *Fertility and Sterility*, 113(3): 552-560.
- Tremellen, K. (2008). Oxidative stress and male infertility: a clinical perspective. *Human Reproduction Update*, 14(3): 243-258. <https://doi.org/10.1093/humupd/dmn004>
- World Health Organization (2021). *WHO Laboratory Manual for the Examination and Processing of Human Semen, 6th edition*. World Health Organization, Geneva.
- Wright, C., Milne, S. and Leeson, H. (2014). Sperm DNA damage caused by oxidative stress: modifiable clinical, lifestyle and nutritional factors in male infertility. *Reproductive BioMedicine Online*, 28(6): 684-703. <https://doi.org/10.1016/j.rbmo.2014.02.004>
- Wyrobek, A.J., Eskenazi, B., Young, S., Arnheim, N., Tiemann-Boege, I., Jabs, E.W., Glaser, R.L., Pearson, F.S. and Evenson, D. (2006). Advancing age has differential effects on DNA damage, chromatin integrity, gene mutations, and aneuploidies in sperm. *Proceedings of the National Academy of Sciences of the United States of America*, 103(25): 9601-9606. <https://doi.org/10.1073/pnas.0506468103>
- Zini, A. and Dohle, G. (2011). Are varicoceles associated with increased deoxyribonucleic acid fragmentation? *Fertility and Sterility*, 96(6): 1283-1287.