HSPI The Open Access Publisher

CJOG CLINICAL JOURNAL OF OBSTETRICS AND GYNECOLOGY
ISSN 2640-2890

Short Review

# Decline in human sperm parameters: How to stop?

**Aboubakr Mohamed Elnashar***

Benha University Hospital, Egypt

## Abstract

A large systematic review and meta-regression analysis found that sperm counts all over the world appeared to be declining rather than stabilizing. The decline in male sperm counts does not necessarily translate to a decline in male fertility. The cause of declining sperm counts remains unknown; however, several potential causative factors have been identified: 1. Chronic diseases: diabetes mellitus, hypertension; hyperlipidemia, hyperuricemia and skin Diseases & metabolic syndrome. 2. Environmental factors: bisphenol a; phthalates; heavy metals and heat. 3. Lifestyle: obesity, diet, tobacco, alcohol, marijuana, stress, reduced sleep & sedentary life. Addressing these causes is required to stop or decrease male fertility decline. Action to improve semen quality such as prevention & treatment of chronic disease, decreasing unhealthy lifestyle behaviors such as smoking, poor diet, or lack of physical activity & eliminating toxic environmental chemicals.

**More Information**

***Address for Correspondence:**
Aboubakr Mohamed Elnashar, Professor, Aboubakr Elnashar, Benha University Hospital, 24 Gomhoria street, Elmansura, PC: 7650001, Egypt, Email: elnashar53@hotmail.com

**Submitted:** January 17, 2023
**Approved:** January 30, 2023
**Published:** January 31, 2023

**How to cite this article:** Elnashar AM. Decline in human sperm parameters: How to stop? Clin J Obstet Gynecol. 2023; 6: 016-020.

**DOI:** 10.29328/journal.cjog.1001122



**Keywords:** Male fertility; Semen analysis; Lifestyle

**Synopsis:** Action to improve semen quality such as prevention & treatment of chronic disease, decreasing unhealthy lifestyle behaviors & eliminating toxic environmental chemicals.



## Introduction

Evidence for declining sperm counts is conflicting. Despite the controversy and criticisms, the increasing data demonstrating a decline in sperm parameters cannot be ignored. A decline in sperm counts does not necessarily translate to a decline in male fertility. The dangers of neglecting a true decline in semen count are far more serious than reporting a decline that does not exist [1]. Ignoring the potential decline and its causes can lead to irreversible damage to human and planetary health. Environmental agents capable of altering semen quality could have long-term, even transgenerational, impacts. Action to improve semen quality such as decreasing unhealthy lifestyle behaviors such as smoking, poor diet, or lack of physical activity and eliminating toxic environmental chemicals will only serve to improve general health and sustainability. The cost of delayed action is high, whereas that of investment in research and precautionary measures is minimal in comparison to the potential damage.

### Who's semen parameters

WHO semen parameters are based on men who conceived a child within 1 year of trying [2]. It has changed significantly since WHO's first publication in 1999. The 6th edition released in July 2021 [3]. The lower reference limit for total sperm count was 39 million/ejaculate & sperm concentration was 16 million/Ml.

### Decline of sperm parameters: fact or fiction?

Evidence for declining sperm counts is conflicting, Nelson and Bunge 1974 [4] found that their patients have an average sperm concentration of 48 million/ml, which was significantly lower than the previously established average of 107 million/ml by MacLeod & Gold in 1951 [5]. Significantly lower semen volume and higher abnormal sperm morphology as compared with previous studies.

Carlsen, et al. 1992 [6] conducted the first SR. Seminal volume & mean sperm concentration had decreased over the previous 50 years (1938–1990). Significant criticisms and limitations for Carleson Systematic review: 1. Selection bias for the men selected for semen analysis [7]. 2. Failure to include studies not showing sperm count decline. 3. Failure to account for geographic variation. 4. Variability in sperm collection & measurement protocols. 5. Lack of control for abstinence durations, inability to control for seasonal variation, inability to control for lifestyle factors. 6. Inappropriate statistical considerations [8]

Levine, et al. 2017 performed a Large systematic review and meta-regression analysis to identify trends in sperm counts, between 1981 and 2013 [9]. 185 studies with data on sperm counts from 42935 men were included. They addressed the limitations of Carlsen, et al. study. They concluded that sperm concentration declined by 52.4% (~1.4% per year)

and total sperm counts declined by 59.3% (~1.6% per year). Sperm counts appeared to be continuing to decline rather than stabilizing.

Bonde, 2017 [10] criticized the 2017 systematic review for not assessing other indicators of sperm quality, such as motility or morphology & failing to take into account variation in sperm counting between laboratories and geographical variation.

Tiegs, et al. [2019] sought to address these limitations and conducted a retrospective analysis of 119 972 men looking at total motile sperm count trends from 2002 to 2017 [11]. A decline of approximately 10% points over the past 16 years

## Limitation of sperm count as a marker of fertility

A decline in sperm counts does not necessarily translate to a decline in male fertility [12]. Patients with low sperm counts can still conceive and patients with high sperm counts can have difficulties conceiving [13]. Additionally, there is not enough evidence to support the claims that subfertility has been increasing over recent decades [14]. Little evidence exists to show that sperm count is independently representative of male health status in isolation from other sperm parameters [15]. Although sperm concentration and total sperm count decreased from 1973 to 2011, the values still fall above the normal lower reference limit for fertility by a significant margin.

**Sperm Count Decline Hypothesis [9]:** Sperm count is a marker of male health. Low sperm counts may indicate a global decline in the general health of males because low sperm counts have been associated with increased morbidity and mortality in males [9].

**Sperm Count Biovariability Hypothesis [15]:** Sperm count naturally varies widely and fluctuations are not always pathological and are in fact typical for the human species [15]. A higher sperm count (above a certain threshold) does not equate to better health or fertility.

## Reasons for sperm parameters decline

**Chronic diseases:** Several recently published studies have examined associations between chronic diseases and declining sperm parameters.

1. **DM:** Prevalence has nearly quadrupled from 1980 to 2014, affecting over 400 million people worldwide [16]. Men with either type 1 or type 2 DM had a significantly lower sperm concentration and lower progressive motility compared with controls [17]. Men with type 1 DN had significantly lower seminal fluid volume: low ejaculate volumes due to lack of epididymal contraction. Type 2 DM patients may have decreased sperm parameters due to inflammatory processes.

2. **Hypertension:** Although the prevalence of hypertension decreased by 2.6% in high-income countries from 2000 to 2010, the prevalence actually increased by 7.7% in low and middle-income countries [18]. Hypertension had lower semen volume, sperm motility, total sperm count and total motile sperm count when compared with non-hypertensive men [19]. 17.8% of infertile men were diagnosed with hypertension while only 7.1% of fertile men shared the same diagnosis [20]. Men with newly diagnosed hypertension had higher levels of total motile sperm counts after 6 months of treatment for hypertension compared with their baseline and to poorly treated or untreated men.

3. **Hyperlipidemia:** hyperuricemia and skin diseases are significantly more prevalent in infertile men as compared with fertile men [21]. Treatment of various chronic diseases led to significant improvement in total motile sperm counts.

4. **Metabolic syndrome:** Combination of at least three of the following: central obesity, hypertension, hyperglycemia, high triglycerides, and low HLD cholesterol. Studies have shown a relationship between metabolic syndrome and sperm parameters [21]. Infertile men had higher BMIs, waist circumferences, fasting blood glucose levels and lower HDL cholesterol levels compared with fertile men. Significantly, this study did not note a difference in the prevalence of hypertension in the two groups. Metabolic syndrome is a significant independent risk factor for idiopathic infertility in men. It was associated with a reduced percentage of normal sperm morphology [22]. Individuals with an increased number of metabolic syndrome components had a progressively stronger association with reduced sperm progressive motility and percentage of normal sperm morphology. Hypertension, increased waist circumference, and increased serum glucose were associated with a decreased percentage of normal sperm morphology.

## Environmental factors

**Environmental exposures affecting sperm quality include:** Bisphenol A (BPA), Phthalates, Heavy metals and Heat [23].

1. BPA found in polycarbonate plastics, epoxy resin liners of aluminum cans, and thermal receipts a widely used chemical that has been demonstrated to have endocrine-disrupting effects [24]. Exposure was associated with decreased sperm concentrations and impaired sperm movement characteristics. Ji, et al. [25], abnormal sperm tail morphology compared with men with normal morphology; increased percentage of immature sperm and sperm sex chromosome disomy [26] and reduced testosterone levels [27].

2. Phthalates. Exposure occurs via ingestion, inhalation, or absorption through the skin [28] Used as plasticizers to increase the elasticity of material can be found in materials such as cosmetics, paints, and lubricants [29]. Chronic phthalate exposure was associated with many

adverse sperm parameters including decreased sperm concentration, motility, morphology, and increased sperm DNA damage.

3. Heavy metal exposure and heat have also been associated with reduced sperm quality [23]. Triclosan, an antibacterial agent found in many household products, was shown by Nassan, et al. [30] to be correlated with a lower percentage of morphologically normal sperm. Cadmium was shown to affect sperm progressive motility [31].

4. Air pollutants have been associated with impaired sperm parameters, particularly impaired sperm morphology, though the difficulty of standardizing studies on this subject has led to mixed results [32].

## Lifestyle

**1. Obesity:** According to WHO statistics, the worldwide prevalence of obesity nearly tripled between 1975 and 2016 [33]. In the same time period, the prevalence of overweight and obesity among children and adolescents aged 5 – 19 has jumped from 4 to 18% and there has been an eight-fold increase in the prevalence of obesity in males aged 5 – 19. Given recent studies, there is increasing evidence that obesity may affect sperm parameters through a variety of methods such as an increased inflammatory state and oxidative stress. Several studies have established an inverse correlation between BMI and fertility or fertility-related parameters. Infertile men had higher BMIs and lower levels of FSH, LH, testosterone, and SHBG compared with fertile men [34]. A positive correlation between BMI and sperm DNA fragmentation and oxidative damage in men, while identifying increased intestinal permeability and metabolic endotoxemia as possible cause [35].

**2. Diet:** Diet and obesity are undoubtedly related. Diet may independently contribute to the ongoing decrease in sperm parameters. Several studies indicate that a high-fat diet is associated with impaired sperm parameters. The average calories consumed per person from 'added fats and oils' has risen from 337 in 1970 to 562 in 2010: an increase in the per capita availability of added fats and oils from 52.5 pounds per person in 1970 to 82.2 pounds in 2010 [36]. Low levels of vitamin D were thought to be associated with decreased sperm motility and the number of motile spermatozoa [37] however, in a randomized controlled trial assessing semen quality with vitamin D supplementation, no significant effect was observed in men who had a vitamin D deficiency [38].

**3. Tobacco:** Smoking appears to decrease sperm counts, increase DNA fragmentation and reduce motility and normal morphology [39]. The majority of tobacco products contain over 4000 different chemicals and constituents. Many of these, including nicotine and heavy metals such as cadmium and lead, have been individually linked to impaired sperm parameters, as has tobacco smoke in general. Tobacco smoking is associated with decreased sperm density, motility, viability, normal morphology, reduction in semen volume, and reproductive hormone dysfunction. Parental tobacco exposure in utero has been reported to affect male fertility in the offspring. {Increasing rates of male fertility despite decreasing rates of tobacco use in recent years}. Nonetheless, more than one-third of male adults worldwide continue to use tobacco, making it perhaps one of the most widespread contributors to declining male fertility [40].

**4. Alcohol:** Drinking 5 alcoholic beverages per week was enough to show effects on sperm concentration, total sperm count and proportion of sperm with normal morphology [41]. The effects were most pronounced in individuals who drank more than 25 drinks per week

**5. Marijuana:** With the recent legalization of marijuana in many countries and several states in the USA, there have been new studies investigating the effects of marijuana use on sperm parameters. Men with a history of recent or significant marijuana use were likely to have abnormal sperm motility and morphology [42]. Marijuana use may be linked with sperm morphological changes and a decrease in sperm counts, concentration, motility and viability [43].

**1. Stress:** Median sperm concentration significantly declined over a period of 5 years [44]. The decline in sperm concentration was more prominent in students versus nonstudents {sedentary lifestyle, stress and lack of sleep}. Association of high work stress with lower sperm concentration and total sperm count [45].

**2. Poor sleep:** Sleep duration has been implicated as a cause of reduced testosterone levels and fecundability [46]. Poor sleep quality and duration, possibly contributing to abnormal sperm morphology, higher rates of oligozoospermia and low sperm concentrations [47]. Sedentary lifestyle with more than 4 hours of sitting per day was significantly associated with higher immotile sperm [48].

## Conclusion

For decades, researchers have been asking if sperm counts are decreasing worldwide and if so, whether this heralds a global decline in male fertility. Most recently, a large systematic review and meta-regression analysis sought to identify trends in sperm counts between 1981 and 2013 and found that sperm counts appeared to be declining rather than stabilizing. One of the complicating features of relying on sperm count as a marker of fertility is that a low sperm count does not guarantee an inability to conceive. Sperm counts and fertility are not synonymous. The decline in male sperm counts does not necessarily translate to a decline in male fertility. The cause of declining sperm counts remains unknown; however, several potential causative factors have been identified.

## Chronic disease

DM, Hypertension; Hyperlipidemia, hyperuricemia and skin diseases & metabolic syndrome. Environmental: Bisphenol A; Phthalates; Heavy metals and Heat. III. Lifestyle: Obesity, Diet, Tobacco, Alcohol, Marijuana, Stress, Reduced sleep & sedentary life.

## Author contribution

Collection of data, writing the manuscript.

# References


1. Jorgensen N, Lamb DJ, Levine H, Pastuszak AW, Sigalos JT, Swan SH, Eisenberg ML. Are worldwide sperm counts declining? Fertil Steril. 2021 Dec;116(6):1457-1463. doi: 10.1016/j.fertnstert.2021.10.020. PMID: 34836581.
2. Shiraishi K, Matsuyama H. Effects of medical comorbidity on male infertility and comorbidity treatment on spermatogenesis. Fertil Steril. 2018 Nov;110(6):1006-1011.e2. doi: 10.1016/j.fertnstert.2018.07.002. PMID: 30396536.
3. World Health Organization. WHO laboratory manual for the examination and processing of human semen. 6th ed. Accessed 14 August 2021. www.who.int/publications-detail-redirect/9789240030787.
4. Nelson CM, Bunge RG. Semen analysis: evidence for changing parameters of male fertility potential. Fertil Steril. 1974 Jun;25(6):503-7. doi: 10.1016/s0015-0282(16)40454-1. PMID: 4835605.
5. MACLEOD J, GOLD RZ. The male factor in fertility and infertility. III. An analysis of motile activity in the spermatozoa of 1000 fertile men and 1000 men in infertile marriage. Fertil Steril. 1951 May-Jun;2(3):187-204. PMID: 14831643.
6. Carlsen E, Giwercman A, Keiding N, Skakkebaek NE. Evidence for decreasing quality of semen during past 50 years. BMJ. 1992 Sep 12;305(6854):609-13. doi: 10.1136/bmj.305.6854.609. PMID: 1393072; PMCID: PMC1883354.
7. Pastuszak AW, Lamb DJ. Counting your sperm before they fertilize: are sperm counts really declining? Asian J Androl. 2013 Mar;15(2):179-83. doi: 10.1038/aja.2012.105. Epub 2013 Jan 21. PMID: 23334199; PMCID: PMC3739138.
8. Fisch H. Declining worldwide sperm counts: disproving a myth. Urol Clin North Am. 2008 May;35(2):137-46, vii. doi: 10.1016/j.ucl.2008.01.001. PMID: 18423235.
9. Levine H, Jørgensen N, Martino-Andrade A, Mendiola J, Weksler-Derri D, Mindlis I, Pinotti R, Swan SH. Temporal trends in sperm count: a systematic review and meta-regression analysis. Hum Reprod Update. 2017 Nov 1;23(6):646-659. doi: 10.1093/humupd/dmx022. PMID: 28981654; PMCID: PMC6455044.
10. Bonde JP, Te Velde E. Male factor infertility: Declining sperm counts - the never-ending story. Nat Rev Urol. 2017 Nov;14(11):645-646. doi: 10.1038/nrurol.2017.153. Epub 2017 Sep 26. PMID: 28949326.
11. Tiegs AW, Landis J, Garrido N, Scott RT Jr, Hotaling JM. Total Motile Sperm Count Trend Over Time: Evaluation of Semen Analyses From 119,972 Men From Subfertile Couples. Urology. 2019 Oct;132:109-116. doi: 10.1016/j.urology.2019.06.038. Epub 2019 Jul 19. PMID: 31326545.
12. Guzick DS, Overstreet JW, Factor-Litvak P, Brazil CK, Nakajima ST, Coutifaris C, Carson SA, Cisneros P, Steinkampf MP, Hill JA, Xu D, Vogel DL; National Cooperative Reproductive Medicine Network. Sperm morphology, motility, and concentration in fertile and infertile men. N Engl J Med. 2001 Nov 8;345(19):1388-93. doi: 10.1056/NEJMoa003005. PMID: 11794171.
13. Patel AS, Leong JY, Ramasamy R. Prediction of male infertility by the World Health Organization laboratory manual for assessment of semen analysis: A systematic review. Arab J Urol. 2017 Nov 20;16(1):96-102. doi: 10.1016/j.aju.2017.10.005. PMID: 29713540; PMCID: PMC5922004.
14. Inhorn MC, Patrizio P. Infertility around the globe: new thinking on gender, reproductive technologies and global movements in the 21st century. Hum Reprod Update. 2015 Jul-Aug;21(4):411-26. doi: 10.1093/humupd/dmv016. Epub 2015 Mar 22. PMID: 25801630.
15. Boulicault M, Perret M, Galka J, Borsa A, Gompers A, Reiches M, Richardson S. The future of sperm: a biovariability framework for understanding global sperm count trends. Hum Fertil (Camb). 2022 Dec;25(5):888-902. doi: 10.1080/14647273.2021.1917778. Epub 2021 May 10. PMID: 33969777.
16. World Health Organization. Global report on diabetes. Geneva, Switzerland: World Health Organization. 2016; 88.
17. Condorelli RA, La Vignera S, Mongioì LM, Alamo A, Calogero AE. Diabetes Mellitus and Infertility: Different Pathophysiological Effects in Type 1 and Type 2 on Sperm Function. Front Endocrinol (Lausanne). 2018 May 25;9:268. doi: 10.3389/fendo.2018.00268. PMID: 29887834; PMCID: PMC5980990.
18. Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM, Reynolds K, Chen J, He J. Global Disparities of Hypertension Prevalence and Control: A Systematic Analysis of Population-Based Studies From 90 Countries. Circulation. 2016 Aug 9;134(6):441-50. doi: 10.1161/CIRCULATIONAHA.115.018912. PMID: 27502908; PMCID: PMC4979614.
19. Guo D, Li S, Behr B, Eisenberg ML. Hypertension and Male Fertility. World J Mens Health. 2017 Aug;35(2):59-64. doi: 10.5534/wjmh.2017.35.2.59. PMID: 28868816; PMCID: PMC5583372.
20. Shiraishi K, Matsuyama H. Effects of medical comorbidity on male infertility and comorbidity treatment on spermatogenesis. Fertil Steril. 2018 Nov;110(6):1006-1011.e2. doi: 10.1016/j.fertnstert.2018.07.002. PMID: 30396536.
21. Dupont C, Faure C, Daoud F, Gautier B, Czernichow S, Lévy R; ALIFERT collaborative group. Metabolic syndrome and smoking are independent risk factors of male idiopathic infertility. Basic Clin Androl. 2019 Jul 1;29:9. doi: 10.1186/s12610-019-0090-x. PMID: 31304019; PMCID: PMC6600889.
22. Chen YY, Kao TW, Peng TC, Yang HF, Wu CJ, Chen WL. Metabolic syndrome and semen quality in adult population. J Diabetes. 2020 Apr;12(4):294-304. doi: 10.1111/1753-0407.12995. Epub 2019 Nov 24. PMID: 31605564.
23. Henry TD, Porucznik CA, Honda TJ, VanDerslice JA, Blackburn BE, Cox KJ, Carrell DT. Differential impacts of particulate air pollution exposure on early and late stages of spermatogenesis. Ecotoxicol Environ Saf. 2021 Sep 1;220:112419. doi: 10.1016/j.ecoenv.2021.112419. Epub 2021 Jun 11. PMID: 34126304; PMCID: PMC8383784.
24. Mima M, Greenwald D, Ohlander S. Environmental Toxins and Male Fertility. Curr Urol Rep. 2018 May 17;19(7):50. doi: 10.1007/s11934-018-0804-1. PMID: 29774504.
25. Ji H, Miao M, Liang H, Shi H, Ruan D, Li Y, Wang J, Yuan W. Exposure of environmental Bisphenol A in relation to routine sperm parameters and sperm movement characteristics among fertile men. Sci Rep. 2018 Dec 3;8(1):17548. doi: 10.1038/s41598-018-35787-5. PMID: 30510208; PMCID: PMC6277384.
26. Radwan M, Wielgomas B, Dziewirska E, Radwan P, Kałużny P, Klimowska A, Hanke W, Jurewicz J. Urinary Bisphenol A Levels and Male Fertility. Am J Mens Health. 2018 Nov;12(6):2144-2151. doi: 10.1177/1557988318799163. Epub 2018 Sep 27. PMID: 30261816; PMCID: PMC6199454.
27. Srivastava S, Gupta P. Alteration in apoptotic rate of testicular cells and sperms following administration of Bisphenol A (BPA) in Wistar albino rats. Environ Sci Pollut Res Int. 2018 Aug;25(22):21635-21643. doi: 10.1007/s11356-018-2229-2. Epub 2018 May 21. PMID: 29785601.

28. Khasin LG, Della Rosa J, Petersen N, Moeller J, Kriegsfeld LJ, Lishko PV. The Impact of Di-2-Ethylhexyl Phthalate on Sperm Fertility. Front Cell Dev Biol. 2020 Jun 30;8:426. doi: 10.3389/fcell.2020.00426. PMID: 32695775; PMCID: PMC7338605.

29. Wang C, Yang L, Wang S, Zhang Z, Yu Y, Wang M, Cromie M, Gao W, Wang SL. The classic EDCs, phthalate esters and organochlorines, in relation to abnormal sperm quality: a systematic review with meta-analysis. Sci Rep. 2016 Jan 25;6:19982. doi: 10.1038/srep19982. PMID: 26804707; PMCID: PMC4726156.

30. Nassan FL, Mínguez-Alarcón L, Williams PL, Dadd R, Petrozza JC, Ford JB, Calafat AM, Hauser R; EARTH Study Team. Urinary triclosan concentrations and semen quality among men from a fertility clinic. Environ Res. 2019 Oct;177:108633. doi: 10.1016/j.envres.2019.108633. Epub 2019 Aug 6. PMID: 31421444; PMCID: PMC6717534.

31. Marchiani S, Tamburrino L, Farnetani G, Muratori M, Vignozzi L, Baldi E. Acute effects on human sperm exposed in vitro to cadmium chloride and diisobutyl phthalate. Reproduction. 2019 Sep 1;158(3):281-290. doi: 10.1530/REP-19-0207. PMID: 31437814.

32. Deng Z, Chen F, Zhang M, Lan L, Qiao Z, Cui Y, An J, Wang N, Fan Z, Zhao X, Li X. Association between air pollution and sperm quality: A systematic review and meta-analysis. Environ Pollut. 2016 Jan;208(Pt B):663-9. doi: 10.1016/j.envpol.2015.10.044. Epub 2015 Nov 6. PMID: 26552539.

33. WHO. Obesity and overweight. 2021. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

34. Amjad S, Baig M, Zahid N, Tariq S, Rehman R. Association between leptin, obesity, hormonal interplay and male infertility. Andrologia. 2019 Feb;51(1):e13147. doi: 10.1111/and.13147. Epub 2018 Sep 25. PMID: 30255520.

35. Pearce KL, Hill A, Tremellen KP. Obesity related metabolic endotoxemia is associated with oxidative stress and impaired sperm DNA integrity. Basic Clin Androl. 2019 May 13;29:6. doi: 10.1186/s12610-019-0087-5. PMID: 31114691; PMCID: PMC6513521.

36. Bentley J. US. Trends in Food Availability and a Dietary Assessment of Loss- Adjusted Food Availability, 1970-2014, EIB-166, US. Department of Agriculture, Economic Research Service. January 2017.

37. Blomberg Jensen M, Gerner Lawaetz J, Andersson AM, Petersen JH, Nordkap L, Bang AK, Ekbom P, Joensen UN, Prætorius L, Lundstrøm P, Boujida VH, Lanske B, Juul A, Jørgensen N. Vitamin D deficiency and low ionized calcium are linked with semen quality and sex steroid levels in infertile men. Hum Reprod. 2016 Aug;31(8):1875-85. doi: 10.1093/humrep/dew152. Epub 2016 Jun 19. PMID: 27496946.

38. Blomberg Jensen M, Lawaetz JG, Petersen JH, Juul A, Jørgensen N. Effects of Vitamin D Supplementation on Semen Quality, Reproductive Hormones, and Live Birth Rate: A Randomized Clinical Trial. J Clin Endocrinol Metab. 2018 Mar 1;103(3):870-881. doi: 10.1210/jc.2017-01656. PMID: 29126319.

39. Jensen TK, Heitmann BL, Blomberg Jensen M, Halldorsson TI, Andersson AM, Skakkebæk NE, Joensen UN, Lauritsen MP, Christiansen P, Dalgård C, Lassen TH, Jørgensen N. High dietary intake of saturated fat is associated with reduced semen quality among 701 young Danish men from the general population. Am J Clin Nutr. 2013 Feb;97(2):411-8. doi: 10.3945/ajcn.112.042432. Epub 2012 Dec 26. PMID: 23269819.

40. Sansone A, Di Dato C, de Angelis C, Menafra D, Pozza C, Pivonello R, Isidori A, Gianfrilli D. Smoke, alcohol and drug addiction and male fertility. Reprod Biol Endocrinol. 2018 Jan 15;16(1):3. doi: 10.1186/s12958-018-0320-7. PMID: 29334961; PMCID: PMC5769315.

41. Jensen TK, Gottschau M, Madsen JO, Andersson AM, Lassen TH, Skakkebæk NE, Swan SH, Priskorn L, Juul A, Jørgensen N. Habitual alcohol consumption associated with reduced semen quality and changes in reproductive hormones; a cross-sectional study among 1221 young Danish men. BMJ Open. 2014 Oct 2;4(9):e005462. doi: 10.1136/bmjopen-2014-005462. PMID: 25277121; PMCID: PMC4185337.

42. Carroll K, Pottinger AM, Wynter S, DaCosta V. Marijuana use and its influence on sperm morphology and motility: identified risk for fertility among Jamaican men. Andrology. 2020 Jan;8(1):136-142. doi: 10.1111/andr.12670. Epub 2019 Jul 2. PMID: 31267718.

43. Payne KS, Mazur DJ, Hotaling JM, Pastuszak AW. Cannabis and Male Fertility: A Systematic Review. J Urol. 2019 Oct;202(4):674-681. doi: 10.1097/JU.0000000000000248. Epub 2019 Sep 6. PMID: 30916627; PMCID: PMC7385722.

44. Yuan HF, Shangguan HF, Zheng Y, Meng TQ, Xiong CL, Guan HT. Decline in semen concentration of healthy Chinese adults: evidence from 9357 participants from 2010 to 2015. Asian J Androl. 2018 Jul-Aug;20(4):379-384. doi: 10.4103/aja.aja_80_17. PMID: 29493550; PMCID: PMC6038153.

45. Zou P, Sun L, Chen Q, Zhang G, Yang W, Zeng Y, Zhou N, Li Y, Liu J, Ao L, Cao J, Yang H. Social support modifies an association between work stress and semen quality: Results from 384 Chinese male workers. J Psychosom Res. 2019 Feb;117:65-70. doi: 10.1016/j.jpsychores.2018.10.013. Epub 2018 Oct 27. PMID: 30391000.

46. Patel P, Shiff B, Kohn TP, Ramasamy R. Impaired sleep is associated with low testosterone in US adult males: results from the National Health and Nutrition Examination Survey. World J Urol. 2019 Jul;37(7):1449-1453. doi: 10.1007/s00345-018-2485-2. Epub 2018 Sep 17. PMID: 30225799.

47. Demirkol MK, Yıldırım A, Gıca Ş, Doğan NT, Resim S. Evaluation of the effect of shift working and sleep quality on semen parameters in men attending infertility clinic. Andrologia. 2021 Sep;53(8):e14116. doi: 10.1111/and.14116. Epub 2021 May 12. PMID: 33978248.

48. Montano L, Ceretti E, Donato F, Bergamo P, Zani C, Viola GCV, Notari T, Pappalardo S, Zani D, Ubaldi S, Bollati V, Consales C, Leter G, Trifuoggi M, Amoresano A, Lorenzetti S; FASt study group. Effects of a Lifestyle Change Intervention on Semen Quality in Healthy Young Men Living in Highly Polluted Areas in Italy: The FASt Randomized Controlled Trial. Eur Urol Focus. 2022 Jan;8(1):351-359. doi: 10.1016/j.euf.2021.01.017. Epub 2021 Feb 10. PMID: 33579652.