Global decline of male fertility: Fact or fiction?

A broad summary of the published evidence on sperm-count and fertility trends.

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ABSTRACT: For decades, researchers have been asking if sperm counts are decreasing worldwide, and if so, whether this presages 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. A large variety of factors, including tobacco, alcohol, and drug use; psychological stress; obesity; insufficient sleep; and environmental factors such as air pollutants and heavy metals, have been identified as potential risk factors affecting semen quality. Initial investigations recommended for a patient presenting with fertility concerns include a detailed history, physical examination, investigations based on the clinical context, and semen analysis for most patients. Although the evidence is conflicting, our review suggests that the potential decline in male sperm counts does not necessarily translate to a decline in male fertility.

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Concerns regarding declining sperm counts have existed for over 50 years, and even predate the use of a standard means to assess semen characteristics.[1] The scientific characterization of semen samples has also changed significantly since the World Health Organization's (WHO's) first publication of its *Laboratory Manual for the Examination and Processing of Human Semen* in 1999,[2] with the 6th edition released in July 2021.[3]

Dozens of articles have been published about a global reduction in male spermatogenesis, with *varying* results reported. However, the articles that report *declining* sperm counts are the ones more often picked up by news outlets, which leads to a widespread belief of globally declining sperm counts as fact. For example, the BBC released a podcast on this topic in 2021, stating, "the fall in men's sperm counts is more alarming than first thought."[4] This type of coverage has led to far-reaching claims of an imminent fertility disaster facing the world. However, in the field of reproduction, the contention that sperm counts are declining is not universally accepted and has been a hotly debated topic over the last several decades.[1,5-9] Although the evidence for declining sperm counts is conflicting, our review suggests that a decline in sperm counts does not necessarily translate to a decline in male fertility.

Evaluation of male fertility

Approximately 15% of male-female couples around the world will experience infertility.[10] The male is found to be the sole cause in 20% of those cases and a partial contributor in 30% to 40%.[10] Male sperm production (i.e., spermatogenesis) occurs in the seminiferous tubules of the testes. The 70-day process includes proliferation of spermatogonia, meiosis, and then acquisition of a head and tail structure to become mature spermatozoa. Endocrine drivers of male sexual function include follicle-stimulation hormone, which stimulates Sertoli cells in seminiferous tubules, and luteinizing hormone, which drives testosterone production in Leydig cells. Endogenous testosterone production is the single most important endocrine driver of spermatogenesis. Men can produce tens to hundreds of millions of sperm each day.[11]

History taking for men presenting with fertility concerns should include questions about general health, testicular symptoms, duration of infertility, sexual mechanics, difficulty with erection and/or ejaculation, coital frequency and timing, prior conceptions, medications, environmental exposures, and drug and alcohol use.[12] It is also important to ask specifically about consumption of muscle-building supplements or exogenous testosterone, as these substances can decrease or completely eliminate sperm production via negative feedback on pituitary follicle-stimulation hormone secretion.[13] It is important to obtain a medical history of prior injury (e.g., torsion), illness (e.g., mumps), surgery affecting the scrotum or testes, and childhood and pubertal development (e.g., delayed testicular descent).[12] A family history of infertility could suggest potential chromosomal or

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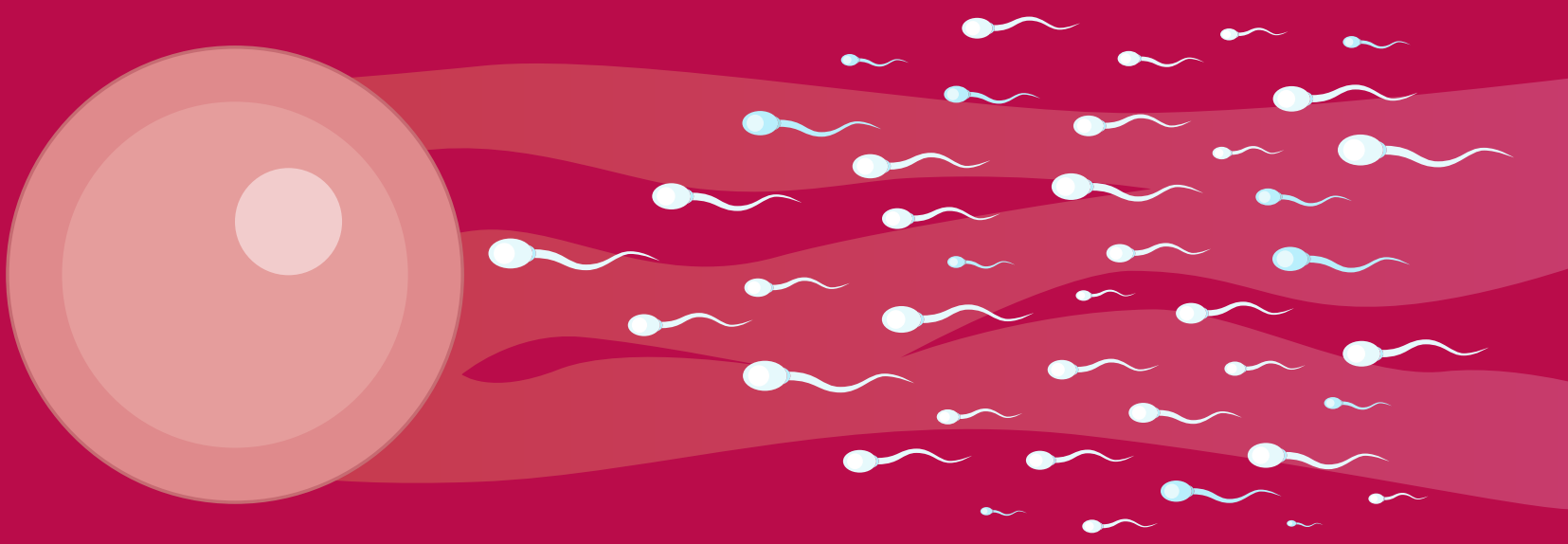

genetic causes of infertility such as Kallmann syndrome, myotonic dystrophy, androgen receptor defects, gonadotropin and gonadotropin receptor defects, cystic fibrosis, or chromosomal rearrangements.[12]

Physical examination should include evaluation of body mass index, secondary sexual characteristics such as presence of facial and chest hair, and the presence of gynecomastia.[12] The genitourinary exam includes a scrotal exam, assessment of testicular size (normal length is 4.5–5.1 cm, 15–19 g, or 20 mL), consistency, and presence of nodules, epididymal abnormalities such as dilatations and cysts, abnormalities of the vas deferens, and inspection/palpation for varicoceles.[12,14]

Investigations are selected based on the clinical context.[12] A semen analysis is a reasonable initial test to assess total sperm count (≥ 39 million per ejaculate), semen volume (≥ 1.4 mL), sperm concentration (≥ 16 million/mL), total motility (> 42%), and normal morphology (≥ 4%).[3,12] For men with oligozoospermia (concentration < 16 million/mL), a hormonal workup is indicated, including assessment of serum luteinizing hormone, follicle-stimulation hormone, prolactin, estradiol, and total testosterone.[12,15] In cases of severe oligozoospermia (concentration < 6 million/mL) genetic testing in the form of karyotype and Y chromosome microdeletion testing is indicated.[16]

As most pathology in the scrotum is palpable, scrotal ultrasound is reserved for cases where the physical exam is difficult, inadequate, or ambiguous, or when a testicular mass is suspected.[17] Other specialized testing such as retrograde semen analysis, transrectal ultrasound, and cystic fibrosis transmembrane regulator gene testing is typically arranged by those with subspecialty training given the specific instances in which they are indicated.[16]

Are sperm counts really declining?

The question of whether sperm counts are declining remains controversial. A prominent article from Carlsen and colleagues in 1992 brought about concern about declining sperm counts between the 1930s and 1990s.[8] Significant criticisms and limitations in the article were subsequently identified, including variability in sperm collection and measurement protocols, lack of control for abstinence durations, inability to control for seasonal variation, inability to control for lifestyle factors, failure to include studies not showing sperm count decline, failure to account for geographic variation, and inappropriate statistical considerations.[18] Most notably, geographic disparities have been shown pertaining to the United States. Significantly more semen samples from New York were included than from other regions. In Carlsen's article, 80% of the included studies were derived from New York prior to 1970, but only three studies were derived from the United States after 1970. After removing the New York semen analyses, the declining trend was reversed and not statistically significant.[18]

More recently, Levine and colleagues conducted a large systematic review and meta-regression analysis to identify more contemporary trends in sperm counts, between 1981 and 2013.[19] They found that an overall decline in sperm counts was observed from 1973 to 2011.[19] Sperm concentration declined 52.4% (~1.4% per year) and total sperm counts declined 59.3% (~1.6% per year) in studies completed in North America, Europe, Australia, and New Zealand.[19] Sperm counts appeared to be continuing to decline rather than stabilizing.[19] The systematic review did not assess for other indicators of sperm quality, such as motility or morphology.[19] The study concluded that declining sperm counts are a reason to be concerned about worldwide subfertility or infertility in the future. Some further concluded that low sperm counts may serve as a canary in a coal mine, indicating a global decline in the general health of males because low sperm counts have been associated with increased morbidity and mortality in males.[19-22]

A critique of Levine and colleagues' meta-analysis (conducted in 2021 by Boulicault and colleagues) highlights several limitations that may provide alternative explanations for the trends they identified.[23] Levine offers what Boulicault and colleagues call the Sperm Count Decline Hypothesis.[23] In the hypothesis, sperm count is a marker of male health.[23] Causes of the decline in sperm count are attributed to endocrine disruptors, environmental pollutants, and lifestyle.[23] Boulicault offers an alternative framework called the Sperm Count Biovariability Hypothesis,[23] in which sperm count naturally varies widely and fluctuations are not always pathological and are in fact typical for the human species.[23] A central tenet of this theory is that a higher sperm count (above a certain threshold) does not equate to better health or fertility.[23] The WHO's reference intervals for semen characteristics are based on men who conceived a child within 1 year of trying.[24] Based on those parameters, the lower reference limit for total sperm count was 39 million/ejaculate and sperm concentration was 16 million/mL.[24] Levine and colleagues report total sperm counts of 212 million and sperm concentration of 66.4 million/mL in 2011.[19] 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.[24]

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.[25] Patients with low sperm counts can still conceive and patients with high sperm counts can have difficulties conceiving.[26] Additionally, there is not enough evidence to support the claims that subfertility has been increasing over recent decades.[27] Little evidence exists to show that sperm count is independently representative of male health status in isolation of other sperm parameters.[23]

Do environmental and lifestyle factors affect fertility?

While it is difficult to determine if sperm counts are declining, and if so, if that will translate to an impact on fertility, it is worthwhile to understand the potential impact of environmental and lifestyle factors on sperm parameters and fertility. Tobacco, alcohol, and drug use; psychological stress; obesity; insufficient sleep; and environmental factors such as air pollutants and heavy metals have all been identified as potential risk factors that affect semen quality **[Table]**.[28-45]

TABLE. Environmental and lifestyle factors that may affect male fertility.

Factors	Effects	References
Tobacco	Decreased sperm counts Increased DNA fragmentation Decreased sperm motility Decreased normal sperm morphology	29, 30
Alcohol use	Decreased sperm concentration Decreased sperm count Decreased normal sperm morphology	31
Illicit drug use (marijuana, cocaine, anabolic steroids)	Decreased sperm count Decreased sperm motility	32
Sedentary lifestyle	Decreased sperm concentration Decreased sperm motility Decreased normal sperm morphology	29, 33
Diet high in total fat	Decreased sperm concentration Decreased sperm count	34
Psychological stress	Decreased sperm concentration Decreased sperm motility	35
Obesity	Decreased sperm concentration Decreased sperm count	36
Poor sleep (quality and duration)	Decreased sperm concentration Decreased sperm count Increased abnormal sperm morphology	37
Air pollutants	Decreased semen concentration Decreased normal sperm morphology	38
Heavy metals	Decreased normal sperm morphology	39
Low levels of vitamin D	Decreased sperm motility	40,41
Bisphenol A	Decreased sperm concentration	42
Phthalates	Decreased sperm concentration Decreased sperm motility Increased abnormal sperm morphology Increased sperm DNA damage	43, 44
Heat	Decreased sperm concentration Decreased sperm count Decreased sperm motility	45

Drinking five alcoholic beverages per week was enough to show effects on sperm concentration, total sperm count, and proportion of sperm with normal morphology.[31] The effects were most pronounced in individuals who drank more than 25 drinks per week.[31] Smoking appears to decrease sperm counts, increase DNA fragmentation, and reduce motility and normal morphology.[20,30]

A sedentary lifestyle with more than 4 hours of sitting per day was significantly associated with higher immotile sperm.[29,33] Other lifestyle factors affecting fertility include poor sleep quality and duration, possibly contributing to abnormal sperm morphology, higher rates of oligozoospermia, and low sperm concentrations.[37]

Low levels of vitamin D were thought to be associated with decreased sperm motility and number of motile spermatozoa;[40] 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.[41]

Environmental exposures affecting sperm quality include bisphenol A (BPA), phthalates, heavy metals, and heat.[38,39,42-44,46] BPA is found in polycarbonate plastics, epoxy resin liners of aluminum cans, and thermal receipts, and was found to be associated with lower sperm concentrations.[38] Phthalates are ubiquitous and exposure occurs via ingestion, inhalation, or absorption through the skin.[46] Phthalates are used as plasticizers to increase the elasticity of material and can be found in materials such as cosmetics, paints, and lubricants.[43,44] Chronic phthalate exposure was associated with many adverse sperm parameters including decreased sperm concentration, motility, morphology, and increased sperm DNA damage.[44,45] Higher levels of occupational heavy metal exposure and heat have also been associated with reduced sperm quality.[38,39,45]

Conclusion

The debate over whether sperm counts are declining will likely be a contentious topic until better study designs are implemented. Importantly, this question is separate from whether a decline in male fertility exists, because sperm counts and fertility are not synonymous. Ultimately, the evidence is conflicting, limiting our ability to draw accurate conclusions. While it is possible that sperm counts are declining, methodologic limitations, biological variability, and technical inconsistency significantly weaken this conclusion. Furthermore, even if sperm counts are declining, this likely does not have as significant an impact on fertility as is portrayed in the media.

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.

While researchers report that lifestyle and environmental factors are negatively associated with sperm parameters, it is difficult to interpret the impact seen in today's society. Certainly, a healthy lifestyle and environment are important not only for fertility, but also for general health in society and the natural world.

Researchers should caution against drawing the conclusion that male infertility is on the rise based on literature showing declining sperm counts because these studies have significant methodological limitations. While the most recent meta-analysis attempts to address several confounding variables, the data remain highly heterogeneous with immeasurable confounding biases that cannot be addressed with currently available retrospective data. Furthermore, sperm counts by themselves are not a precise marker of male fertility. Research that implements prospective, meticulously designed studies is likely required to further investigate trends of sperm production and fertility. ■

Competing interests

Dr Dunne is a member of the *BCMJ* Editorial Board, but did not participate in the decision making regarding this article. No other competing interests have been declared.

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