# Reasons for worldwide decline in male fertility

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**Purpose of review**
To review the evidence regarding a decrease in worldwide sperm parameters and discuss potential causative factors.

**Recent findings**
The topic of worldwide decline in sperm parameters is contentious; however, recent high-quality studies have demonstrated that there is indeed a decline in sperm parameters. Several retrospective and basic science studies have shown possible links for this decline in sperm parameters such as obesity, diet, and environmental toxins.

**Summary**
There exist substantial data to suggest a decline in sperm counts over time. Although causative factors have yet to be fully elucidated, potential causes include, increased rates of obesity, poor diet, and exposure to environmental toxins. How this decline in sperm counts reflects fertility has yet to be determined. As such, further studies are necessary to evaluate whether this decline in sperm count correlates with decreased fecundity and how to identify and mitigate potential causative factors.

**Keywords**
chronic disease, environmental toxins, male fertility, sperm counts

## INTRODUCTION

The topic of worldwide decline in male fertility has sparked controversy as it was first proposed in 1974 by Nelson and Bunge [1]. This study found that their participants had an average sperm concentration of 48 million/ml, which was significantly lower than the previously established average of 107 million/ml by MacLeod and Gold in 1951 [2]. In addition to sperm concentration, Nelson *et al.* found that their participants also had significantly lower semen volume and higher abnormal sperm morphology as compared with previous studies. The study concluded that 'something has altered the fertile male population to depress the semen analysis remarkably. This is obviously speculative but the overall decrease in the sperm concentration and the semen volumes would tend to incriminate an environmental factor to which the entire population has been exposed' [1].

In 1992, Carlsen *et al.* [3] conducted the first systematic review investigating a decline in male fertility and concluded that seminal volume and mean sperm concentration had decreased over the previous 50 years (1938–1990). Since then, multiple other studies have been published that show a similar decline in sperm parameters [4–10]. However, the 1992 systematic review has been criticized for not accounting for geographic differences and the advancements made in laboratory technologies, including studies with various study designs and sperm counting methodologies, and the possibility of a selection bias existing for the men selected for semen analysis [11,12▪].

More recently, Levine *et al.* [13] published an updated systematic review which updates the 1992 review by covering 185 studies published from 1973 to 2011 with data on sperm counts from 42 935 men. This systematic review addressed limitations of the 1992 study by Carlsen *et al.* and also concluded that sperm counts declined significantly among men from North America, Europe, and Australia. However, Bonde [14] criticized the 2017 systematic review for failing to take into account variation in sperm counting between laboratories and geographical variation. Tiegs *et al.* [12▪] sought to address these limitations and conducted a retrospective analysis of 119 972 men looking at total

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## KEY POINTS

- The topic of declining male fertility remains contentious; however, there is a large body of evidence suggesting that semen parameters are declining.
- No clear etiologic factors have been identified; however, multiple factors have been shown to have correlative associations.
- Though studies in humans have been limited to observational and cross-sectional studies, there are randomized studies conducted in animal models which have shown possible causative associations.
- Potential causative factors include obesity, diet, chronic disease, tobacco, marijuana, and environmental toxins.

motile sperm count trends from 2002 to 2017. Their study 'revealed a decline of approximately 10 percentage points over the past 16 years' [12▪].

Despite the controversy and criticisms, the increasing data demonstrating a decline in sperm parameters cannot be ignored and the objective of this review is to discuss potential etiologic factors (Fig. 1).

## OBESITY

Obesity is defined as a BMI of greater than or equal to 30 kg/m$^2$. According to WHO statistics, the worldwide prevalence of obesity nearly tripled between 1975 and 2016. 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 (https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight). 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.

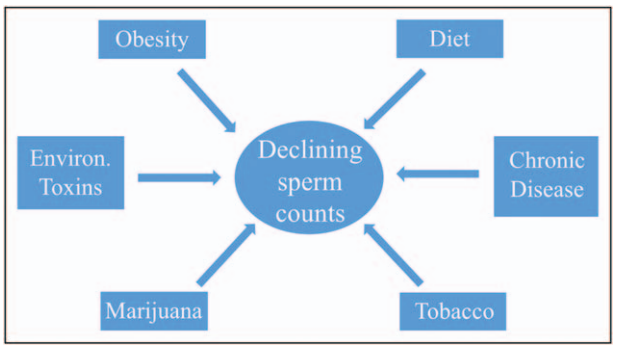


**FIGURE 1.** Factors associated with declining sperm counts.

Several studies have established an inverse correlation between BMI and fertility or fertility-related parameters. Amjad *et al.* [15] found that infertile men had higher BMIs and lower levels of follicle stimulating hormone (FSH), Luteinizing hormone (LH), testosterone and Sex hormone-binding globulin (SHBG) compared with fertile men. At the sperm level, Pearce *et al.* [16] identified a positive correlation between BMI and sperm DNA fragmentation and oxidative damage in men, while identifying increased intestinal permeability and metabolic endotoxemia as a possible cause. The link between obesity and sperm parameters is supported by animal models as well. Abdel-Fadeil *et al.* [17▪] found that obesity-induced rats had inferior semen quality parameters such as sperm concentration and percentage of motile, viable, and morphologically viable sperm compared with controls.

## DIET

Though diet and obesity are undoubtedly related, there is increasing evidence that diet may independently contribute to the ongoing decrease in sperm parameters. Specifically, there have been several studies indicating that a high-fat diet is associated with impaired sperm parameters. According to the US Department of Agriculture, the average calories consumed per person from 'added fats and oils' has risen from 337 in 1970 to 562 in 2010. This was associated with an increase of the per capita availability of added fats and oils from 52.5 pounds per person in 1970 to 82.2 pounds in 2010 [18]. Crean and Senior [19▪] conducted a systematic review of animal model studies on this subject and concluded that a high-fat diet has strong negative effects on sperm parameters including sperm number, sperm motility, progressive motility, sperm morphology, and sperm viability. Moreover, a high-fat diet was associated with smaller testes, lower seminal vesicle mass, and lower epididymal mass relative to body size. Most importantly, a high-fat diet was also associated with reduced fertilization success. Nematollahi *et al.*'s study on mice also characterizes the effects of diet and demonstrates their independence from obesity. Their study found that in obese mice, a low-fat diet was associated with higher sperm motility, whereas a high-fat diet in nonobese mice was associated with lower sperm motility [20▪]. More relevant to humans, Jurewicz *et al.*'s [21] study investigated dietary patterns, semen parameters, and sperm DNA fragmentation in 336 men. They classified dietary intake as either Prudent or Western pattern; Prudent pattern diet included a high intake of fish, chicken, fruit, vegetables, tomatoes, and whole grains, whereas the Western pattern diet included a high intake of red and processed

meats, butter, high-fat dairy, snacks, mayonnaise, and sweets. This study noted that the Prudent pattern diet was associated with increased sperm concentration, increased serum levels of testosterone, and decreased percentage of sperm DNA fragmentation as compared with a Western pattern diet.

Recent studies have also focused on the Mediterranean diet and shown that it may improve sperm parameters. One study involving 309 men presenting to an infertility clinic found that a higher adherence to a Mediterranean diet was associated with a lower risk of low sperm concentration and low total sperm count [22]. Similarly, Salas-Huetos *et al.* [23▪] also conducted a cross-sectional analysis on 106 men and concluded that men with higher adherence to a Mediterranean diet was associated with higher total sperm motility.

## CHRONIC DISEASE

There are now numerous articles that suggest a link between sperm parameters and overall male health [24▪,25]. Several recently published studies have examined associations between chronic diseases and declining sperm parameters.

According to the WHO, the prevalence of diabetes has nearly quadrupled from 1980 to 2014, affecting over 400 million people worldwide [26]. In addition to obesity as previously noted, Abdel-Fadeil *et al.* [17▪] studied diabetes in rats and found that diabetic rats had reduced sperm concentration, percentage of motile sperm, and LH and testosterone levels compared with nondiabetic rats. Condorelli *et al.* [27] also studied the effect of diabetes on sperm function but in humans. Their study found that men with either type 1 or type 2 diabetes mellitus had a significantly lower sperm concentration and lower progressive motility compared with controls. As well, men with type 1 diabetes mellitus had significantly lower seminal fluid volume. The study concluded that type 1 diabetes mellitus patients may have low ejaculate volumes due to a lack of epididymal contraction, whereas type 2 diabetes mellitus patients may have decreased sperm parameters due to inflammatory processes.

In addition to diabetes, hypertension is another chronic disease that has been implicated in the recent decline in sperm parameters. 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 [28]. Guo *et al.* [29] found that men with hypertension had lower semen volume, sperm motility, total sperm count, and total motile sperm count when compared with nonhypertensive men. A recent study by Shiraishi and Matsuyama [24▪] assessed over 3700 men and found that the prevalence of comorbidities was significantly higher in infertile men compared with fertile men. Specifically, 17.8% of infertile men were diagnosed with hypertension while only 7.1% of fertile men shared the same diagnosis. Furthermore, 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. In addition to hypertension, Shiraishi *et al.* identified hyperlipidemia, hyperuricemia, and skin diseases as being significantly more prevalent in infertile men as compared with fertile men. This study found that treatment of the various chronic diseases led to significant improvement in total motile sperm counts.

Metabolic syndrome is generally defined as the combination of at least three of the following: central obesity, hypertension, hyperglycemia, high triglycerides, and low HLD cholesterol. Given the evidence discussed above regarding obesity, diabetes, and hypertension, it is unsurprising that studies have also shown a relationship between metabolic syndrome and sperm parameters. Dupont *et al.* [30▪] found that 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. Ultimately the study concluded that metabolic syndrome is a significant independent risk factor for idiopathic infertility in men. Similarly, Chen *et al.* [31▪] found that metabolic syndrome was associated with a reduced percentage of normal sperm morphology. In fact, 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. Specifically, hypertension, increased waist circumference, and increased serum glucose were associated with decreased percentage of normal sperm morphology.

## ENVIRONMENTAL TOXINS

Environmental toxins have been postulated as a major contributor to declining sperm parameters. Several review articles have been published on the subject, listing environmental toxins such as bisphenol A (BPA), phthalates, cadmium, and triclosan as potential offending agents [7,32–36,37▪].

As an important precursor to many plastics, BPA is a widely used chemical that has been demonstrated to have endocrine-disrupting effects [38]. There have been multiple studies in the recent past investigating the effects of BPA on sperm parameters.

Specifically, Ji *et al.* [37▪] conducted a cross-sectional study in which they found that environmental exposure to BPA was associated with decreased sperm concentrations and impaired sperm movement characteristics. Conversely, a different study has shown that although no association was found between sperm counts and exposure to BPA, a higher exposure to BPA was found in men with abnormal sperm tail morphology compared with men with normal morphology [39]. Radwan *et al.* [40] studied semen samples from 315 men and concluded that exposure to BPA was associated with increased percentage of immature sperm and sperm sex chromosome disomy, and decreased sperm motility. Of special interest, a recent study in rats found that increasing exposure to BPA led to increased rates of apoptosis in testes and reduced testosterone levels [41]. Specifically, Srivastava *et al.* found that rats fed higher levels of BPA had lower testicular weights, lower sperm counts, increased degenerative changes in the germinal layer of seminiferous tubules, and lower levels of testosterone. In addition, rats exposed to BPA had increased rates of apoptosis in the testes and epididymal sperm. This study sheds light on the possible mechanisms that may lead to decreased sperm counts secondary to BPA exposure.

Pthalates are another class of environmental toxins that are ubiquitous in consumer goods and have been implicated in declining sperm parameters. Sumner *et al.* [42] conducted studies on both canine and human semen and found that in vitro incubation of semen with a specific phthalate (diethyhexyl phthalate) was correlated with lower progressive motility and higher sperm DNA fragmentation. Similarly, Marchiani *et al.* [43] studied the effects on sperm after in-vitro incubation with a phthalate (diisobutyl phthalate) and found that incubation with this phthalate led to a significant decrease in sperm progressive motility and induced spontaneous sperm acrosome reaction. Another recent study investigated the effects of prenatal exposure of phthalates on sperm parameters [44▪]. Barakat *et al.* found that mice that were prenatally exposed to phthalates had smaller gonads, prostates, and seminal vesicles. In addition to these anatomic differences, mice exposed to phthalates prenatally also had lower serum testosterone and impaired spermatogenesis. Significantly, sperm concentration and sperm motility were also affected by phthalate exposure, though it was not a dose-dependent correlation [44▪]. This new evidence lends support to the argument that phthalates affect sperm parameters through a variety of mechanisms and may play a role in the decline in sperm parameters.

Other environmental toxins have also been investigated and found to have effects on sperm parameters. One such example is triclosan, an antibacterial agent found in many household products, which was shown by Nassan *et al.* [45] to be correlated with lower percentage of morphologically normal sperm. Another toxin that has been studied is cadmium, which was shown to effect sperm progressive motility [43]. Finally, various air pollutants have been associated with impaired sperm parameters, particularly impaired sperm morphology, though the difficulty of standardizing studies on this subject have led to mixed results [46,47].

## TOBACCO

The majority of tobacco products contain over 4000 different chemicals and constituents. Many of these, including as nicotine and heavy metals such as cadmium and lead, have been individually linked to impaired sperm parameters, as has tobacco smoke in general. The significant prevalence of smoking has allowed large-scale epidemiological studies to be performed on the subject. Overall, tobacco smoking is associated with decreased sperm density, motility, viability, normal morphology, and reduction in semen volume. Tobacco is also associated with reproductive hormone dysfunction. Furthermore, parental tobacco exposure *in utero* has been reported to affect male fertility in the offspring. This may contribute to 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 [48,49].

## MARIJUANA

With recent legalization of marijuana in many countries and several states in USA, there have been new studies investigating the effects of marijuana use on sperm parameters. Carroll *et al.* [50] found that men with a history of recent or significant marijuana use were likely to have abnormal sperm motility and morphology. In addition, Payne *et al.* [51] conducted a systematic review of 48 studies and concluded that though the field is underresearched, evidence thus far suggests that marijuana use may be linked with sperm morphological changes and decrease in sperm counts, concentration, motility, and viability.

## OTHER LIFESTYLE FACTORS

A study investigating sperm counts of over 9000 men by Yuan *et al.* [9] found that median sperm concentration significantly declined over a period of 5 years. Significantly, the data showed that the

decline in sperm concentration was more prominent in students versus nonstudents. The authors of the study proposed sedentary lifestyle, stress, and lack of sleep as possible reasons to explain the finding. Nematollahi *et al.* [20▪] found that mice exposed to exercise had higher sperm concentration and motility compared with sedentary mice. In addition, there is evidence associating high work stress with lower sperm concentration and total sperm count [52]. Finally, reduced sleep duration in particular has been implicated as a cause of reduced testosterone levels and fecundability [53,54]. Basic science research has shown that sleep restriction in mice led to changes in the blood-testis and blood-epididymis barriers, as well as reduced the number of pregnancies [55].

## CONCLUSION

The topic of declining male fertility remains contentious. Though not yet conclusive, the overall body of evidence certainly suggests that semen parameters are indeed decreasing. Whether or not this translates to reduced male fertility in terms of fecundity remains to be definitively proven. Several hypotheses have been proposed to explain the decline in sperm parameters, including many that are reviewed in this article. There is likely a multitude of reasons to account for the decline in sperm parameters and no one clear etiologic factor has been identified. Although randomized studies have been conducted in animal models, there are ethical limitations to conducting similar experiments in humans and thus we are limited to observational and cross-sectional studies. The cause of declining sperm counts remains unknown; however, several potential causative factors are obesity, diet, chronic disease, and environmental toxin exposure.

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### Conflicts of interest

*There are no conflicts of interest.*

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- ▪ of special interest
- ▪▪ of outstanding interest

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