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SARS-CoV-2 Vaccine Effects on Semen Parameters: A Systematic Review and Meta-Analysis

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Objective: Vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) epitomizes the best preventative SARS-CoV-2 infection strategy to counteract the severe consequences of infection. However, concerns have been raised that the vaccines could have an adverse effect on sperm function and overall reproductive health. This combined systematic review and meta-analysis aimed to investigate the effects of different available SARS-CoV-2 vaccines on semen parameters.

Methods: A systematic PubMed, Scopus, Google Scholar, ScienceDirect, LILACS (Literatura Latinoamericana y del Caribe en Ciencias de la Salud), and Scilit database literature search until mid-June 2022 was conducted. Prospective and retrospective studies were eligible. No limitation was placed on language. Standardized mean differences (SMDs) with 95% confidence intervals (CIs) were thereafter obtained.

Results: Upon search completion, 122 studies were identified and retrieved and 110 were excluded, while the remaining 12 independent studies evaluating the effects of coronavirus disease 2019 (COVID-19) vaccines on semen parameters were included in this review. The total number of men included was 1551, aged 22.4–48 years. Following meta-analysis, the SMD summary measure with 95% CI for each semen parameter included a concentration of 0.22 (0–0.22); Total sperm count of 0.11 (0.18–0.24); Total motility of 0.02 (0.05–0.09); Volume of 0.02 (–0.1–0.14); Vitality of 0.55 (–0.19–0.29), progressive motility of –0.43 (–0.54 to –0.32); Total motile sperm count of –0.38 (–0.44 to –0.31); And normal morphology of 0.42 (–0.54 to –0.3). In brief, the total sperm count was slightly increased post-vaccination, while progressive motility, total motile sperm count, and normal morphology were marginally reduced post-vaccination, according to the meta-analysis.

Conclusions: No effects were observed regarding sperm viability and semen volume since the results of all the studies crossed the line of no effect. All seminal parameters analyzed showed a negligible or small change in relation to the vaccination effect. Furthermore, the parameters remained within the normal World Health Organization reference ranges, making the clinical significance unclear. Therefore, based on these results, it appears that vaccination does not have negative effects on semen quality. The individual study findings suggested that COVID-19 vaccines are not associated with decreased semen parameters.

Keywords: semen parameters; SARS-CoV-2; COVID-19; sperm; fertility

Introduction

In December 2019, the city of Wuhan, China reported the first severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection case, which has since become a global pandemic. SARS-CoV-2 infection, also called coronavirus disease 2019 (COVID-19), was recently reported to have infected more than 601 million people and caused about 6.4 million deaths globally. The common SARS-CoV-2 infection symptoms include upper and lower respiratory tract infections associated with fever, cough, anosmia, ageusia, fatigue, sputum production, shortness of breath, sore throat, and headache. Although many cases remain mild or asymptomatic, numerous patients display more severe symptoms, such as systemic inflammation, tissue damage, acute respiratory distress syndrome, thromboembolic complications, cardiac injury, and cytokine storm, which can cause death [1,2].

COVID-19 infection rates are similar in men and women (50%); However, COVID-19-related deaths among males are 1.6 times higher than in females [3]. This finding led some authors to suggest that men are more susceptible to contracting SARS-CoV-2 than women [4]. This view raised concerns about the possible adverse SARS-CoV-2 infection

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effects on male reproductive health [5–7]. Subsequent findings showed that SARS-CoV-2 infection caused altered gametogenesis and semen quality, which could be explained by fever, hormonal alteration, disrupted spermatogenesis, scrotal discomfort, orchitis, and inflammation as a result of COVID-19 disease [5,6,8,9]. Indeed, SARS-CoV-2 infection poses a great danger to the general well-being, including male reproductive health [10].

Based on current evidence, although the virus can cause adverse effects on the male reproductive tract, available evidence suggests that its presence in semen is very low (1.68%) [11]. This is still under debate.

Considering the critical SARS-CoV-2 infection effects on general health, including male and female reproductive and sexual health, it became pertinent to develop vaccines against this virus which would help prevent the severe infection effects.

Following authorization to administer approved vaccines (i.e., (1) mRNA vaccines: BNT162b2 (Pfizer-BioNTech), mRNA-1273 (Moderna); (2) Viral vector vaccines: AstraZeneca/Oxford, Janssen [12,13] and Sputnik V [14]; And (3) inactivated vaccines: Sinovac and Sinopharm [15]), another concern arose regarding the potential negative effects of these vaccines on fertility [16]. These suspicions led individuals and couples seeking fertility treatment to refuse to get vaccinated [4]. Thus, an investigation of the different SARS-CoV-2 vaccine effects on male reproductive parameters and functions became necessary. Studies began to evaluate this association and the outcomes are presented in the current study. Hence, this study's objective was to perform a systematic review and a meta-analysis to assess the SARS-CoV-2 vaccine's effects on semen parameters.

Materials and Methods

The Preferred Items for Systematic Reviews and Meta-analysis (PRISMA) reporting guidelines were used to perform the meta-analyses [17].

Literature Search Strategy

Literature was retrieved through a formal electronic database search (PubMed, Scopus, Google Scholar, ScienceDirect, LILACS, and Scilit) following the specifications for each database because they use different search query syntaxes [18].

The search strategy was performed using the following keywords in PubMed and Scopus: SARS-CoV-2 OR covid AND sperm OR spermatozoa OR sperm parameters AND COVID-19 vaccines. The search strategy in Google Scholar was as follows: "SARS-CoV-2" OR "covid" AND "sperm" OR "spermatozoa" AND "COVID-19 vaccines" AND "semen analysis" OR "semen parameters". The search strategy in ScienceDirect and LILACS (Literatura Latinoamericana y del Caribe en Ciencias de la Salud) was "sperm parameters" "COVID-19 vaccine". The search strategy in Scilit was the following: Sperm AND COVID-19 AND semen AND vaccine. The references of the included original studies were also manually screened to gather additional studies.

Study Selection

This study's search strategy was designed to include all published studies on semen parameters and the COVID-19 vaccine. Data until mid-June 2022 were extracted with no restriction to language. The PRISMA protocol for systematic review has four stages, which include identification, screening, eligibility, and inclusion. This protocol is followed in this study, as shown in Fig. 1. The study was registered in the International Prospective Register of Systematic Reviews (PROSPERO, CRD42022366849). Quality assessment was performed by two reviewers (WDCM and JSML) who independently assessed the articles that were considered relevant to this analysis using the Newcastle-Ottawa Scale (http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp) and data were extracted appropriately. They further assessed the bias risk for each study in the included following three main domains: Study group selection, group comparability, and outcome of interest ascertainment. Study bias was scaled as inferior quality (0–3 stars), medium quality (4–6 stars), and superior quality (7–9 stars). Disparities and disagreements were resolved by consensus (Table 1, Ref. [22,23,25–34]).

Statistical Analysis and Data Extraction Procedure

Mean and standard deviation were used when reporting the selected studies. When median with interquartile range or range were reported, the data to mean ± standard deviation were converted from the sample size. The median, interquartile range, minimum, and maximum values were calculated according to the formula published by Wan *et al*. [19].

Moreover, the summary measure was reported as standardized mean difference (SMD, the mean difference expressed in standard deviation units) with 95% confidence interval (CI). A SMDs refers to the raw difference in the sample treatment mean and the sample control mean divided by the pooled standard deviation of both the treatment and control groups [20] (https://meta-mar.shinyapps.io/meta-analysis-calculator/). Finally, the effect sizes' magnitude according to Cohen's categories was used, whereby an effect of $<$0.2 is considered negligible, between 0.2 and 0.49 is small, 0.5–0.8 is medium, and $>$0.8 is large [21].

All data were stored in a Microsoft Office Excel spread sheet and GraphPad Prism (version 9; GraphPad Software Inc., San Diego, CA, USA) was used to perform subsequent statistical analysis and plotting.

Results

Descriptive Data

Following literature search, a total of 122 publications were identified (Fig. 1). Of these, 109 were excluded due

Table 1. Newcastle-Ottawa Scale score for the included studies.

Study	Selection of the study				Comparability of the study	T in the study			Total scores
	Was the exposed cohort represen-tative?	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome of interest was not present at the start of the study	Comparability of the groups based on the design or analysis	Assessment of the outcome	Was the follow-up long enough for the outcome to occur?	Adequacy of the follow-up	
Sorokina TM *et al.* [33]	1	1	1	1	1	1	1	1	8
Drapkina YS *et al.* [32]	1	1	1	1	2	1	1	1	9
Esaulenko DI *et al.* [34]	1	1	1	1	2	1	1	1	9
Elagin VV *et al.* [31]	1	1	1	1	2	1	1	1	9
Rozhivanov RV *et al.* [30]	1	1	1	1	2	1	1	1	9
Lifshitz D *et al.* [27]	0	0	1	1	0	0	0	0	2
Zhu H *et al.* [22]	1	1	1	1	2	1	1	1	9
Safrai M *et al.* [23]	1	1	1	1	2	1	1	1	9
Barda S *et al.* [26]	1	1	1	1	1	1	1	1	8
Gonzalez *et al.* [28]	1	1	1	1	2	1	1	1	9
Reschini M *et al.* [25]	1	1	1	1	2	1	1	1	9
Xia W *et al.* [29]	1	1	1	1	1	1	1	0	7

to duplication (n = 46), non-related topics such as studies on women's health and pregnancy (n = 2), non-related article type such as reviews, letters, editorials, and others (n = 32), and papers not related to sperm and/or COVID-19 vaccines (n = 29). The remaining 13 studies that satisfied the inclusion criteria were included [22–34]. However, two studies were excluded because one was a case report [24] and the other had a high risk of bias [27]; The latter study only compared the semen parameters in vaccinated fertile men in relation to the World Health Organization (WHO) lower reference limits. Hence, 11 studies were included. Four articles were in Russian [30,31,33,34] and seven in English [22–26,28,29]. The total number of men included was 1551, aged 22.4–48 years. Additionally, due to the diversity in patients' clinical phenotypes, especially in the studies from Russia, the study cohorts were divided into the subgroups present. For instance, the population cohort from the study of Sorokina *et al.* [33] was subcategorized into (a) before and <75 days after vaccination, (b) before and >75 days after vaccination, (c) examination was performed before and <75 days after vaccination, (d) examination was performed before and >75 days after vaccination, (e) unvaccinated men in the year 2021, (f) <75 days after vaccination in the year 2021, (g) >75 days after vaccination in the year 2021, (h) after the first dose. Furthermore, the control group was used for comparison internally in each subgroup indicating the different conditions, which allowed for the proper analysis of the effect of the vaccine on seminal parameters. The study summary included is outlined in Table 2 (Ref. [22,23,25–34]).

SARS-CoV-2 Vaccine and Sperm Concentration

As shown in Fig. 2, only the study of Elagin *et al.* [31] showed that sperm concentration increased after the first Sputnik V dose. There were no significant changes in sperm concentration between pre- and post-vaccination in other studies, irrespective of the vaccine type received (Fig. 2). Hence, the overall summary showed that vaccination does not influence sperm concentration (SMD with 95% CI 0.22 [0–0.22]).

Table 2. Summary of the studies included in the meta-analysis.

Reference	Vaccine	Sample size (study group)	Volunteers' age in years	Study characteristics	Description of the study groups
Sorokina TM *et al.* [33]	Sputnik V	32 (a) 21 (b) 5 (c, d) 759 (e) 73 (f) 58 (g)	35.2 ± 1 35 ± 1.6 38 ± 2 33.7 ± 0.3 34.6 ± 0.8 34.5 ± 0.9	Reproductive function in men who underwent vaccination or men who did not undergo vaccination.	a: Before and <75 days after vaccination. b: Before and >75 days after vaccination. c: Examination was performed before and <75 days after vaccination. d: Examination was performed before and >75 days after vaccination. e: Unvaccinated men in the year 2021. f: <75 days after vaccination in the year 2021. g: >75 days after vaccination in the year 2021.
Drapkina YS *et al.* [32]		45	36 (30–40)	The prospective study included 45 men who were vaccinated against COVID-19.	
Esaulenko DI *et al.* [34]		30	46 (42–48)	The pilot observational prospective study included 30 males with type 2 diabetes mellitus.	
Elagin VV *et al.* [31]		44	22.4 ± 4.65	Reproductive healthy men.	h: After the first dose. i: After the second dose.
Rozhivanov RV *et al.* [30]		30 (j) 30 (k)	31 (28–36) 23.5 (29–34)	The pilot observational prospective study included 30 men with normozoospermia and 30 with pathozoospermia.	j: Men with normozoospermia. k: Men with pathozoospermia.
Lifshitz D *et al.* [27]	Pfizer-BioNTech	75	38.6 ± 4.6	A prospective cohort study in fertile men.	
Zhu H *et al.* [22]		43	28.6 ± 5.9	A retrospective cohort study in the Human Sperm Bank. (1) Donation (T0) within 1 month before receiving the first dose of the COVID-19 vaccine; (2) Donation (T1) within 21 days of receiving the first dose of the COVID-19 vaccine; And (3) donation (T2) within 60 days of receiving the second dose of the COVID-19 vaccine.	l: About 10 days after the first dose. m: 30 days after the second dose.
Safrai M *et al.* [23]		72	35.7 (33.0–43.0)	Sperm samples of patients who had received two doses of the BNT162b2 vaccine were collected (post-vaccine) and compared with the same patients' retrospective data before vaccination (pre-vaccine) in patients attending the IVF unit.	
Barda S *et al.* [26]		898 (n) 666 (o)	27	This was a prospective cohort study in 33 donors from a sperm bank, before and after vaccination.	n: Sperm samples, 425 before fist dose vaccine and 473 after the second dose. o: Samples, 326 before vaccine, 80 after the first dose, and (p) 260 after the second dose.
Gonzalez *et al.* [28]		45	28 (25–31)	Prospective study, samples from healthy volunteers were obtain before and 75 days after the second dose. 21 men vaccinated with Pfizer and 24 with Moderna.	
Reschini M *et al.* [25]		106	39 (36–42)	Retrospective study in infertile men that have undergone two cycles of intrauterine insemination or *in vitro* fertilization (conventional IVF or ICSI) before and after vaccination.	Pfizer 73 (69%), Moderna 20 (19%), Oxford/AstraZeneca 10 (9%), Janssen 1 (1%), and mixed vaccines (2%).
Xia W *et al.* [29]	Sinovac and Sinopharm	105 (q) 155 (r)	33.9 ± 4.7 33.3 ± 4.4	Cohort study, IVF at the Reproductive Center, vaccine groups, and control group.	q: Completed two doses of inactivated vaccine. r: Not vaccinated men.

SARS-CoV-2 Vaccine and Total Sperm Count

Findings by Sorokina *et al.* [33] showed that the total sperm count (TSC) of men who were vaccinated with Sput-

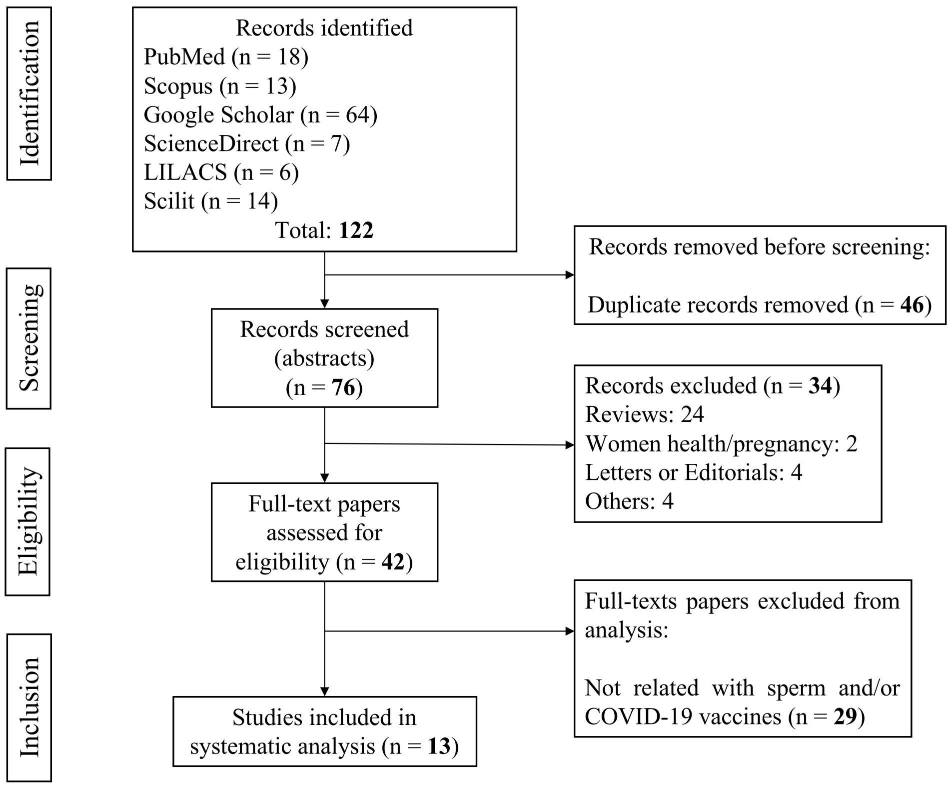

Fig. 1. Flow diagram of the study selection process.

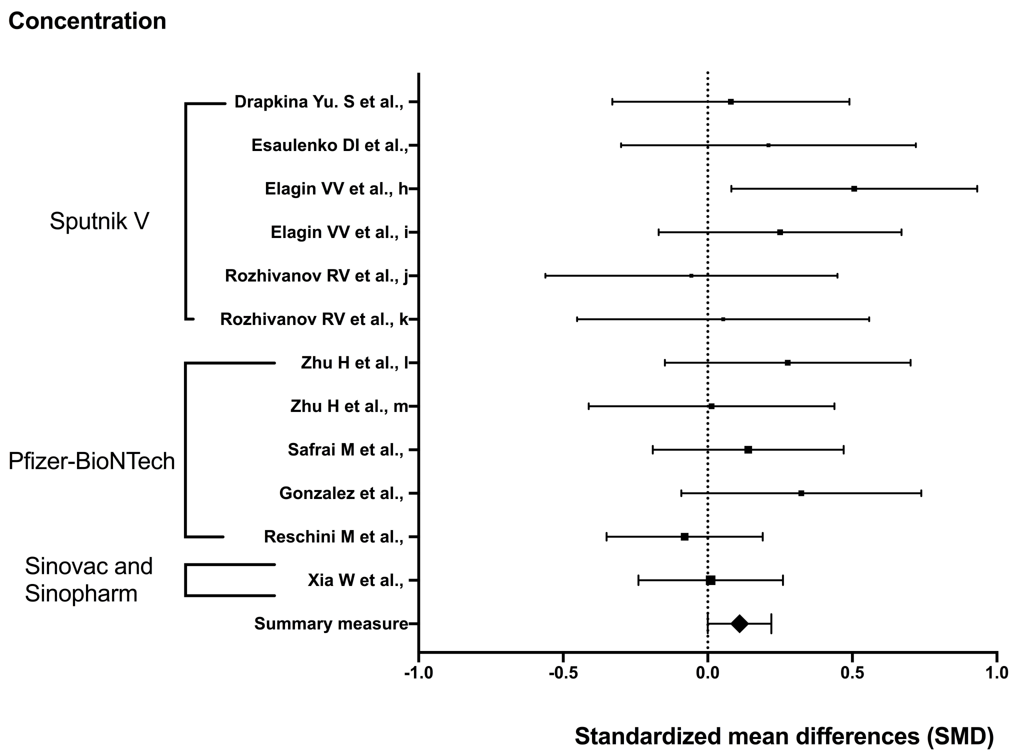

Fig. 2. Forest plot comparing sperm concentration before and after vaccination in each study using specific COVID-19 vaccines. (h) After the first dose. (i) After the second dose. (j) Men with normozoospermia. (k) Men with pathozoospermia. (l) About 10 days after the first dose. (m) 30 days after the second dose.

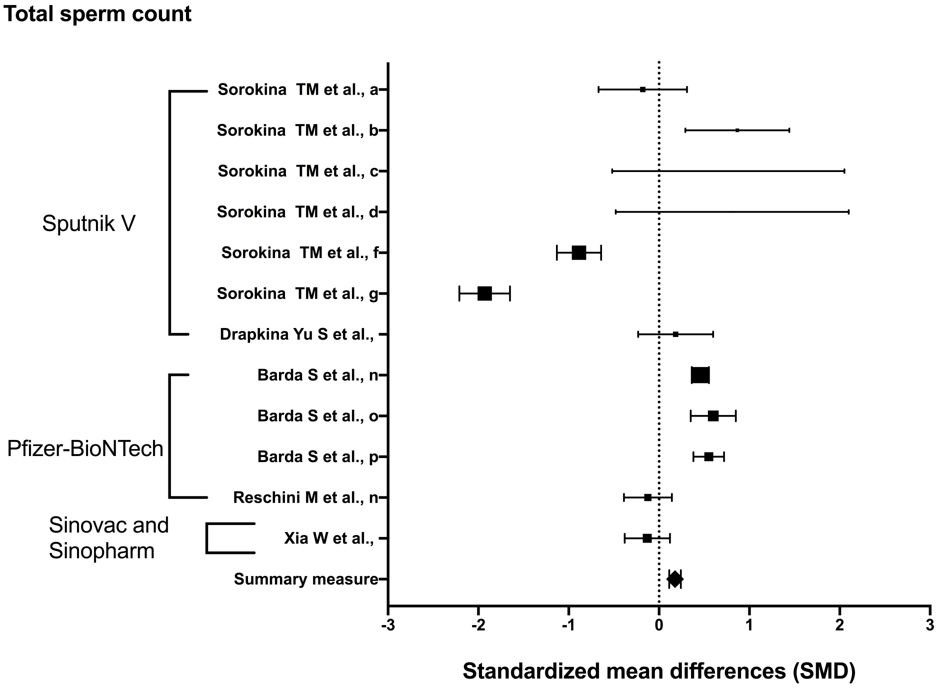

Fig. 3. Forest plot comparing total sperm count before and after vaccination, in each study for a specific COVID-19 vaccine. (a) Before and <75 days after vaccination. (b) Before and >75 days after vaccination. (c) Examination was performed before and <75 days after vaccination. (d) Examination was performed before and >75 days after vaccination. (f) <75 days after vaccination in the year 2021. (g) >75 days after vaccination in the year 2021. (n) Sperm samples, 425 before the vaccine and 473 after the second vaccine. (o) Samples, 326 before the vaccine, 80 after the first dose, and (p) 260 after the second dose.

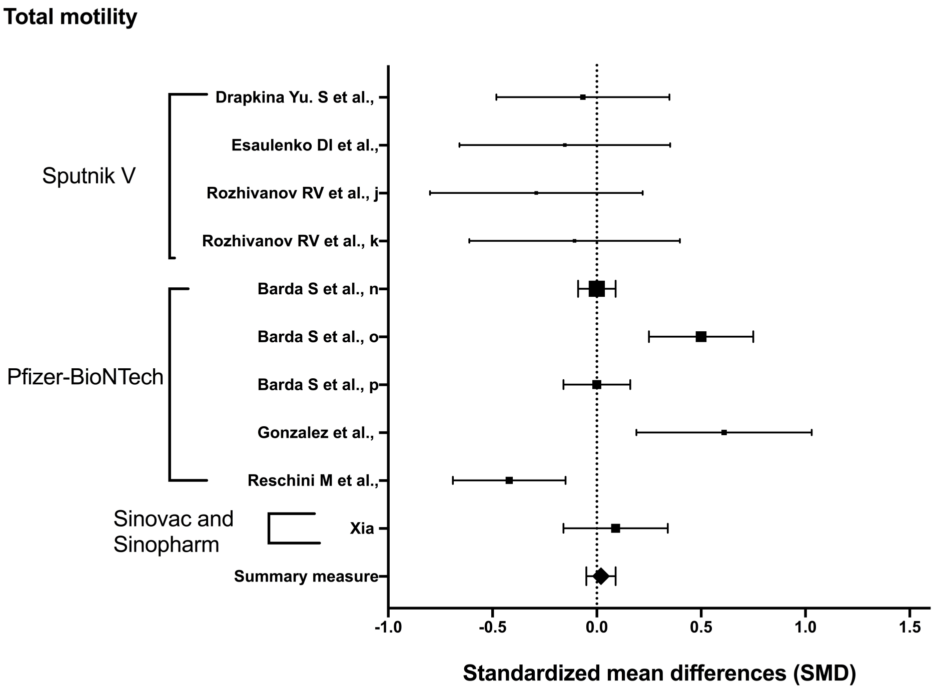

Fig. 4. Forest plot comparing total motility pre- and post-vaccination in each study using a specific COVID-19 vaccine. (j) Men with normozoospermia. (k) Men with pathozoospermia. (n) Sperm samples, 425 before the vaccine and 473 after the second vaccine. (o) Samples, 326 before the vaccine, 80 after the first dose, and (p) 260 after the second dose.

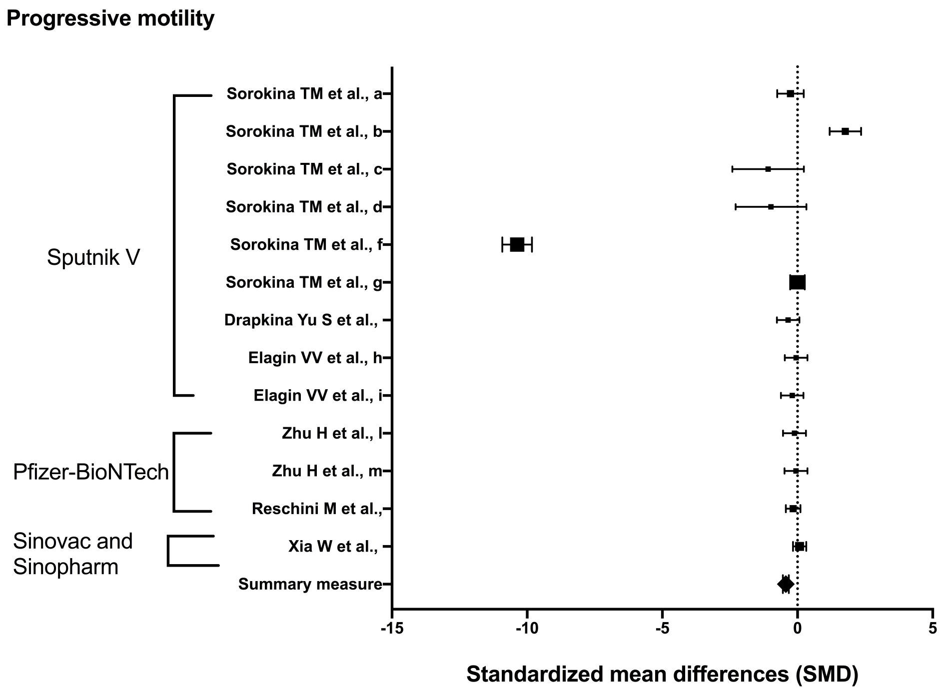

Fig. 5. Forest plot comparing progressive motility pre- and post-vaccination in each study using a specific COVID-19 vaccine. (a) Before and <75 days after vaccination. (b) Before and >75 days after vaccination. (c) Examination was performed before and <75 days after vaccination. (d) Examination was performed before and >75 days after vaccination. (f) <75 days after vaccination in the year 2021. (g) >75 days after vaccination in the year 2021. (h) After the first dose. (i) After the second dose. (l) About 10 days after the first dose; And (m) 30 days after the second dose.

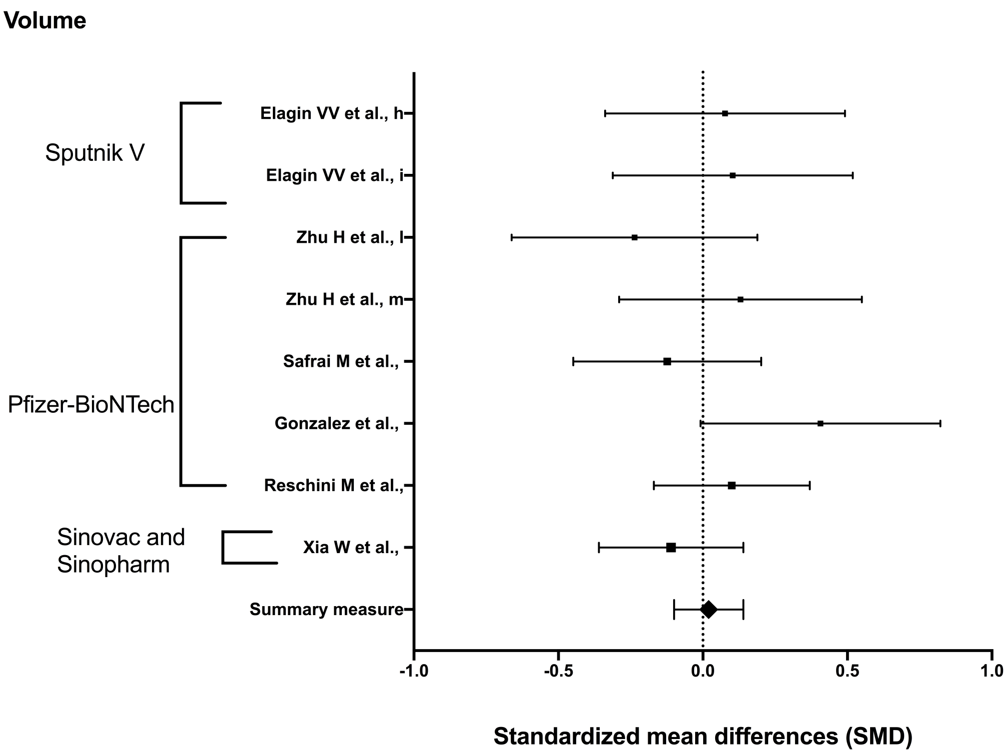

Fig. 6. Forest plot comparing volume pre- and post-vaccination in each study using a specific COVID-19 vaccine. (h) After the first dose. (i) After the second dose. (l) About 10 days after the first dose. (m) 30 days after the second dose.

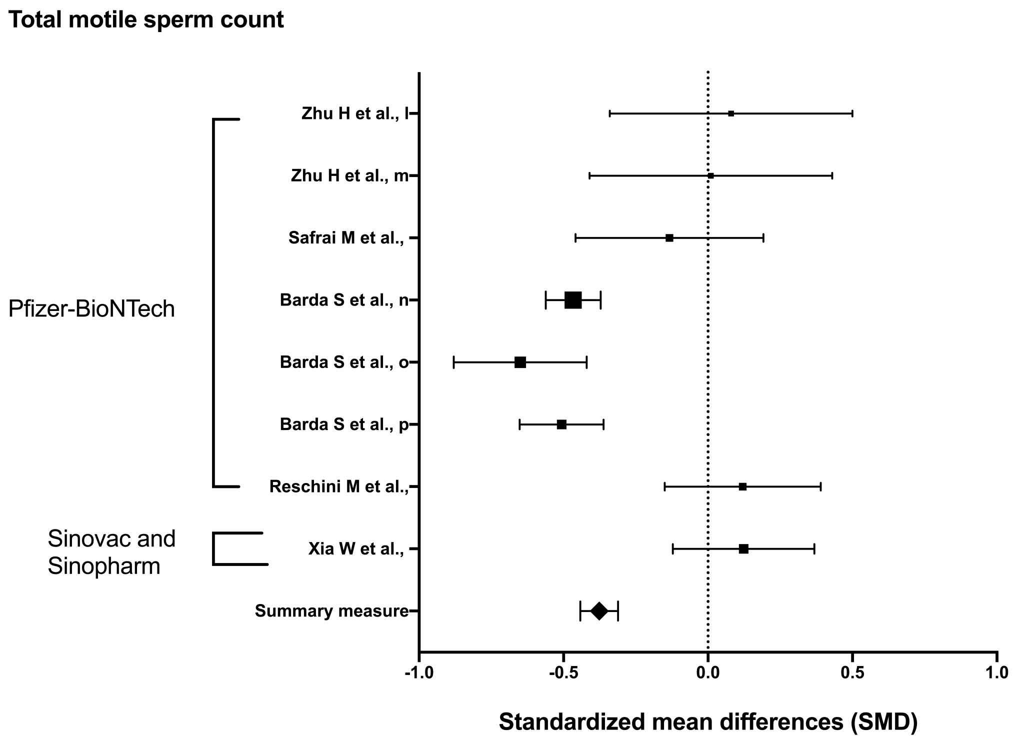

Fig. 7. Forest plot comparing total motile sperm count pre- and post-vaccination in each study using a specific COVID-19 vaccine. (l) About 10 days after the first dose. (m) 30 days after the second dose. (n) Sperm samples, 425 before the vaccine and 473 after the second vaccine. (o) Samples, 326 before the vaccine, 80 after the first dose, and (p) 260 after the second dose.

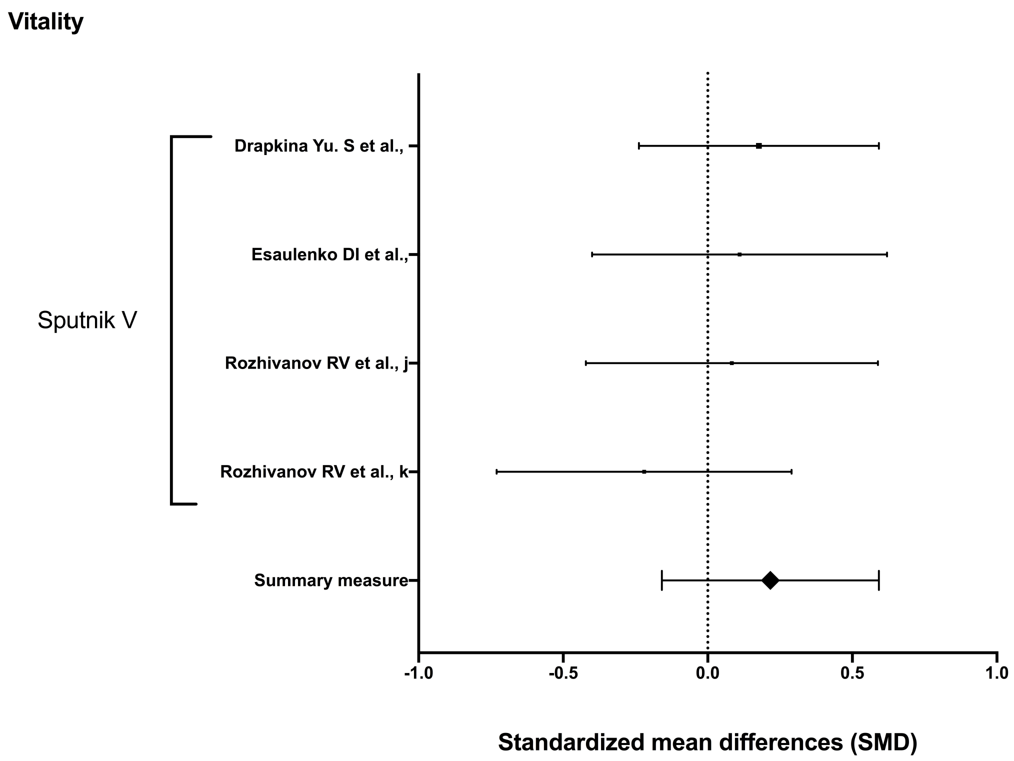

Fig. 8. Forest plot comparing vitality before and after vaccination in each study using a specific COVID-19 vaccine. (j) Men with normozoospermia. (k) Men with pathozoospermia.

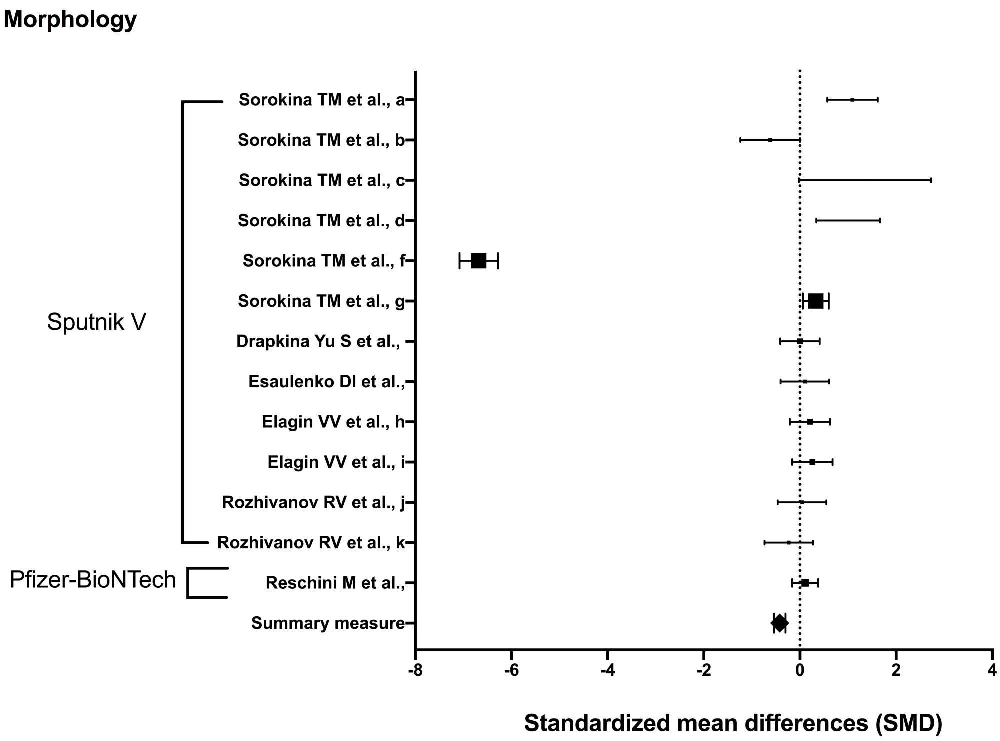

Fig. 9. Forest plot comparing morphology pre- and post-vaccination in each study using a specific COVID-19 vaccine. (a) Before and <75 days after vaccination. (b) Before and >75 days after vaccination. (c) Examination was performed before and <75 days after vaccination. (d) Examination was performed before and >75 days after vaccination. (f) <75 days after vaccination in the year 2021. (g) >75 days after vaccination in the year 2021. (h) After the first dose. (i) After the second dose. (j) Men with normozoospermia. (k) Men with pathozoospermia.

nik V increased 75 days post-vaccination. The results of Barda *et al.* [26] were similar in that the sperm concentration of men who received the Pfizer vaccine increased post-vaccination compared with pre-vaccination (Fig. 3). However, TSC was reduced when the samples were examined either <75 or >75 days after vaccination with Sputnik V. Overall, the summary measure showed that the TSC was increased after vaccination (SMD with 95% CI 0.11 [0.18–0.24]).

SARS-CoV-2 Vaccine and Total Motility

Barda *et al.* [26] and Gonzalez *et al.* [28] showed that total motility increased, while Reschini *et al.* [25] showed a post-vaccination decrease with Pfizer (Fig. 4). Overall, the summary measure showed that there is no significant difference in total motility between pre- and post-vaccination (SMD with 95% CI 0.02 [0.05–0.09]).

SARS-CoV-2 Vaccine and Progressive Motility

Following Sputnik V vaccination, Sorokina *et al.* [33] showed that progressive motility increased post-vaccination (samples analyzed >75 days). Other studies showed no significant difference in progressive motility between pre- and postvaccination, irrespective of the vaccine type. However, the summary measure showed that vaccination negatively affected progressive motility (Fig. 5) (SMD with 95% CI –0.43 [–0.54 to –0.32]).

SARS-CoV-2 Vaccine and Semen Volume

There were no significant changes in semen volume between the pre- and postvaccination samples, irrespective of the vaccine type administered (Fig. 6) (SMD with 95% CI 0.02 [–0.1–0.14]).

SARS-CoV-2 Vaccine on Total Motile Sperm Count

Barda *et al.* [26] showed that total motile sperm count was higher before Pfizer vaccination, while no difference was observed in the other studies. However, the summary measure shows that total motile sperm count was reduced post-vaccination (Fig. 7) (SMD with 95% CI –0.38 [–0.44 to –0.31]).

SARS-CoV-2 Vaccine and Vitality

All studies showed that there is no difference in vitality between pre- and postvaccination (Fig. 8) (SMD with 95% CI 0.55 [–0.19–0.29]).

SARS-CoV-2 Vaccine and Morphology

Sorokina *et al.* [33] showed that morphologically normal spermatozoa improved between pre- and <75 days post-vaccination. When the unvaccinated samples versus the samples collected <75 days post-vaccination were compared, spermatozoa with normal morphology increased. Other study findings showed no differences between pre- and post-vaccination. Nevertheless, the summary measure indicates that the number of spermatozoa with normal morphology was higher pre-vaccination compared with post-vaccination (Fig. 9) (SMD with 95% CI 0.42 [–0.54 to –0.3]).

SARS-CoV-2 Vaccine and Sperm DNA Fragmentation

While most studies evaluated the vaccine's effect on fertility by determining the effect on conventional semen parameters, two [24,32] evaluated the effect pre- and post-vaccination (BNT162b2 and Sputnik V, respectively) on sperm DNA fragmentation. Both studies reported that sperm DNA quality improved postvaccination. Drapkina *et al*. [32] showed that the DNA fragmentation rate pre-vaccination was 13.9% (11.5%–17.5%), while 90 days post-vaccination was 11.9% (8.6%–16.8%). Similarly, Chatzimeletiou *et al*. [24] showed that the sperm DNA fragmentation percentage decreased from 7.6% prevaccination to 6.8% post-vaccination.

Discussion

The current study evaluated the SARS-CoV-2 vaccines' effect on semen parameters by performing a systematic review and meta-analysis of previously published data. The current study findings showed a small effect in magnitude in relation to the effect of SARS-CoV-2 vaccines (Sputnik V, Pfizer, or Sinovac and Sinopharm) on semen parameters.

Gonzalez *et al*. [28] evaluated the effect of two messager ribonucleic acid (mRNA) vaccines (BNT162b2 and mRNA-1273) on semen parameters by assessing the semen samples of 45 men (n = 21 for BNT162b2; n = 24 for mRNA-1273) before vaccination and 70 days after the second dose administration. They reported that all sperm parameters, including semen volume, sperm concentration, total motility, and total motile sperm count, increased post-vaccination. Similarly, Barda *et al*. [26] examined the Pfizer vaccine's effect (BNT162b) on sperm quality on the samples collected from sperm donors with each donor serving as its own control. Samples were collected prevaccination and 72 days after the second dose administration. The authors showed that TSC and total motile sperm count increased after the second dose. The total motility percentage did not change and vaccination did not affect the quality of freeze–thaw sperm, suggesting that the spermatozoa of vaccinated men can be cryopreserved. Another study assessed alterations between pre-vaccination and 3 months post-vaccination with 4BNT162b2, and showed no significant differences were observed in semen parameters, reactive oxygen species levels, electrolyte levels (Ca_2^+, Cl^-, K^+, Mg^{2+}, Na_2^+), and inflammatory cytokine expression (interleukin-6) [35]. Safrai *et al*. [23] also reported that the BNT162b2 mRNA vaccine did not impair semen parameters in both normozoospermic and infertile male patients 71 days post-vaccination. The 72 patients included in their study served as their own control for pre-vaccination versus post-vaccination comparison. Furthermore, Lifshitz *et al*. [27] investigated whether BNT162b2 would have detrimental effects on sperm quality; They analyzed the semen samples of 75 fertile men between 1–2 months of receiving the second dose. The post-vaccination samples were analyzed and compared to the WHO reference values. They concluded that the semen parameters of these men are in the normal range. On the other hand, Zhu *et al*. [22] retrospectively evaluated the COVID-19 BNT162b2 vaccine's effect on semen parameters of men (n = 43) who had never been infected with SARS-CoV-2. They also showed that there were no significant changes in semen parameters (semen volume, sperm concentration, total motility, progressive motility, and total progressive motile sperm count) following vaccination, either between pre-vaccination and 21 days of receiving the first dose or between pre-vaccination and 60 days of receiving the second dose. Reschini *et al*. [25] also found that reproductive parameters were not affected after vaccination. The study retrospectively compared the semen parameters and fertilization rate in 106 men between the first and second assisted reproductive technology (ART) attempts performed before and after receiving the COVID-19 vaccine. The median time between the first dose administration and the second ART attempt was 75 days (39–112 days). Upon assessment, no significant difference was observed in semen parameters between the pre- and postvaccination samples. The fertilization rate was also comparable before and after vaccination. It was concluded that the COVID-19 vaccine had no effect on male reproductive health.

Xia *et al*. [29] investigated COVID-19 vaccines (Sinovac and Sinopharm)' effect on semen parameters, embryo quality, and *in vitro* fertilization (IVF) outcomes. The vaccinated group (n = 105) received two vaccine doses before the IVF cycle, whereas the unvaccinated group (n = 155) were not vaccinated before the start of the IVF cycle. Upon examination, similar findings were observed between the two groups in terms of semen volume, sperm concentration, sperm count, progressive motility, total motility, total motile sperm count, and IVF outcomes. The embryo quality was also similar in both groups.

Rozhivanov and Mokrysheva [30] investigated semen quality and testosterone levels in Spuntnik-V-vaccinated men. They recruited 30 normozoospermic and 30 pathozoospermic men and analyzed their semen samples pre- and post-vaccination. The changes were not significant, although the total sperm motility in normozoospermic men decreased by 5%. Thus, they concluded that Sputnik V does not affect sperm quality. Another study that investigated Sputnik V's effect on semen quality reported that no changes were seen in semen parameters when pre-vaccination samples were compared with 90 days post-vaccination samples. Additionally, no changes were observed in hormonal profiles (FSH, LH, TSH, and testosterone) postvaccination compared with pre-vaccination [32]. Similarly, Esaulenko *et al*. [34] showed that Sputnik V did not affect the sperm quality of vaccinated diabetic and nondiabetic men.

On the other hand, Sorokina *et al*. [33] showed that the progressive motility and percentage of morphologically normal spermatozoa was slightly reduced in semen samples analyzed <75 days after administration of the second Sputnik V dose, while no difference was observed in the cohort analyzed >75 days after the second dose. It was concluded that there are no significant changes in semen parameters postvaccination, especially in the cohort analyzed >75 days after receiving the vaccine. These findings suggest that Sputnik V does not have long-term consequences on sperm quality, though the short-term adverse effects need to be verified.

Overall, the findings on the different COVID-19 vaccines' effects on semen parameters and IVF outcomes indicate no effect [36]. However, due to the mild and moderate decreases in some semen parameters when comparing various groups of individuals pre- and post-vaccination, it is necessary to carry out more detailed research to validate any possible negative fertility effects.

The Society for Male Reproduction and Urology and the Society for the Study of Male Reproduction stated that the COVID-19 vaccine should not be withheld from men desiring fertility as it would also not be withheld from men not desiring fertility if they meet the vaccination criteria [37] based on the available evidence that COVID-19 vaccines does not affect IVF outcomes negatively [36]. The benefits outweigh the minimal risk associated with the decrease in semen parameters, and no alteration to zero has been observed in any parameter [38].

Following this analysis, two new articles were published. First, in a retrospective, longitudinal, multicenter study, Gat *et al*. [39] investigated the effects of the Pfizer vaccine on the semen parameters of semen donors (n = 37) from a sperm bank. A decrease in sperm concentration and total motile count was reported 3 months after vaccination, but these semen parameters recovered to normal levels >145 days post-vaccination.

Second, a prospective observational study by Abd *et al*. [40] found that the Pfizer vaccine has no deleterious effects on semen parameters (n = 60), apart from a slight reduction in total sperm motility and progressive motility. However, the observed differences were clinically insignificant because the values remained within the normal ranges, according to WHO semen parameters. Since the post-vaccination results were recorded at least 90 days after vaccination, it could be speculated that perhaps, as shown in the study by Gat *et al*. [39], the effects were transient and any potential deleterious effects might have lessened by the time of testing.

It is important to emphasize that there are not enough data to compare the vaccines, nor will there be enough data to be completely sure of a negative effect on seminal quality. Therefore, grouping the studies according to the vaccines helps to analyze the information, but could also be interpreted as a major bias. Another prejudice of this study is attempting to compare various studies with different sample sizes, consisting of patients, volunteers, and donors, including some with unvaccinated individuals serving as controls and having different post-vaccination sampling times.

Conclusions

This systematic review and meta-analysis has presented findings from recent studies that elucidated the SARS-CoV-2 vaccines' effect on male reproductive parameters. Upon meta-analysis assessment, the overall summary effect showed that vaccination does not influence semen parameters.

With the available evidence, a definitive conclusion on the SARS-CoV-2 vaccines' effects on sperm quality cannot be reached. Nevertheless, individual study findings suggest that the COVID-19 vaccines are not associated with decreased semen parameters. Perhaps as more studies get published, it may be possible to determine if specific vaccines are more or less detrimental to male reproductive parameters than others.

As such, the vaccine will not correct pre-existing semen alterations, but it is anticipated that the effects are transient and only impact the gametes present in the different phases of gametogenesis at the time of vaccination. Therefore, based on the premise that the vaccine has more benefits than risks on health and specifically male sexual health, vaccination should not be discouraged.

Author Contributions

TSO—participated in the design of the study, contributed to data collection, data analysis, interpretation of results and contributed to the manuscript; PAV—participated in the design of the study, contributed to data collection, data analysis, interpretation of results and contributed to the manuscript; JSML—participated in the design of the study, contributed to data collection, data analysis, interpretation of results and contributed to the manuscript; SSdP—participated in the design of the study, contributed to data collection, data analysis, interpretation of results and contributed to the manuscript; WDCM—participated in the design of the study, contributed to data collection, data analysis, interpretation of results and contributed to the manuscript. All authors have read and agreed to the published version of the manuscript.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

Given his role as Editorial Board Member, Walter D. Cardona Maya had no involvement in the peer-review of this article and has no access to information regarding its peer-review. The authors declare no conflict of interest.

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