Environmental Science and Pollution Research (2023) 30:27884–27894
https://doi.org/10.1007/s11356-022-24182-3

RESEARCH ARTICLE

Association between per- and polyfluoroalkyl substances and semen quality

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Received: 7 September 2022 / Accepted: 9 November 2022 / Published online: 17 November 2022

Abstract

Some studies have suggested that perfluoroalkyl and polyfluoroalkyl substance (PFAS) exposure may be associated with semen quality in the general population, but with inconsistent results. To identify a more precise relationship between them, a meta-analysis was performed. We searched Embase, the PubMed, The Cochrane Library, Ovid databases, and Web of Science databases (before March 2022) for appropriate studies on the correlations of PFAS exposure with semen parameters. We extracted β value and 95% confidence intervals (CIs) to conduct meta-analysis. Subgroup analyses was performed by sample size, geographic location, and sample type. A total of seven articles involving 2190 participants were included in this study. The concentrations of perfluorooctanoic acid (PFOA) (β value = −1.38; 95% CI: −2.44, −0.32) and perfluorononanoic acid (PFNA) (β value = −1.31, 95% CI: −2.35, −0.26) were negatively associated with sperm progressive motility. Subgroup analysis revealed that PFNA exposure was related to sperm morphology in studies with the sample size exceeding 200 people (β value = −0.14; 95% CI: −0.26, −0.01). Our study supports that exposure to some PFASs (e.g., PFNA, PFOA) may be associated with semen quality, such as lower sperm progressive motility. Therefore, it is of great significance for the prevention of male infertility by control the use of PFASs.

Keywords Meta-analysis · PFAS exposure · Semen quality · Per- and polyfluorinated substances · Male infertility · Semen parameters

Introduction

Per- and polyfluoroalkyl substances (PFASs) are widely used in various fields of industrial processes and consumer products, such as waterproof fabrics, nonstick cookware, lubricant foam extinguishing agents, and carpets (Blake and Fenton 2020, Schaider et al. 2017; Trier et al. 2011). The family of PFASs has been estimated to include more than 4000 fluorinated substances (Kim et al. 2021). Of all the PFAS family members, the most commonly studied include perfluorooctanoic acid (PFOA), perfluorohexane sulfonate (PFHxS), perfluorooctane sulfonate (PFOS), perfluorodecanoic acid (PFDA), perfluorononanoic acid (PFNA), and perfluoroundecanoic acid (PFUnDA) (Birru et al. 2021). Among these, PFOS and PFOA were incorporated into the Stockholm Convention list as persistent organic pollutants (POPs). Although multiple countries are working to phase out or restrict these compounds, PFASs are still detected in wild animals, humans, and diverse environmental matrices (e.g., water and soil) (Jian et al. 2018; Schulz et al. 2020), and human serum levels of some less restrictive PFASs, such as PFNA and PFHxS, have remained unchanged and even increased in Japan and Sweden (Glynn et al. 2012; Okada et al. 2013; Stubleski et al. 2016). Thus, PFASs remain an important category of environmental pollutants that can cause serious health problems. Epidemiological studies have found that PFASs (specifically PFOS and PFOA) exposure is related to a variety of disease, including altered cholesterol levels, thyroid dysfunction, metabolic diseases,

Responsible Editor: Lotfi Aleya

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immunotoxicity, and reproductive toxicity (affecting pregnancy outcomes and fertility) (Braun 2017; Kim et al. 2018; Rappazzo et al. 2017; Stanifer et al. 2018).

Currently, infertility is a major global public health problem affecting approximately 15% of couples of reproductive ages worldwide (Boivin et al. 2007; Salas-Huetos et al. 2017). There are 25% of these cases that are caused by decreased semen quality, such as decreased sperm motility, decreased sperm number, abnormal sperm morphology, and low concentration of sperm (Salas-Huetos et al. 2017). The causes of decreased semen quality are unclear, and environmental factors are a major contributor (Skakkebaek et al. 2016). Recently, several studies involving infertile or general men suggested that exposure to PFASs (e.g., PFNA, PFOA, PFHxS, and PFOS) was correlated with sperm concentration, sperm count, and total sperm motility (Ma et al. 2021; Pan et al. 2019; Song et al. 2018; Vested et al. 2013) and sperm DNA fragmentation (Governini et al. 2015), whereas other studies have not found any significant correlation between PFAS exposure and semen quality (Joensen et al. 2013; Petersen et al. 2018). However, some studies suggest that exposure to some PFASs may have protective effects on some semen parameters (Huang et al. 2019; Toft et al. 2012).

To date, there is some evidence that exposure to PFAS may be associated with semen quality, but no systematic study has examined this relationship. Therefore, we conducted a meta-analysis to examine the impact of PFAS exposure on the quality of semen in a systematic and comprehensive manner.

Materials and methods

Literature search

We performed online literature searches in the PubMed, Ovid, Cochrane Library, Embase, and Web of Science databases through 1 March 2022. Medical subject heading terms related to "PFAS" and "semen quality" were used. Details about the MeSH terms are reported in Supplementary Table S1. All the references of relevant articles were further screened to identify additional literature.

Selection criteria

A study was considered eligible if (1) the study was a cohort, cross-sectional study, or case–control study exploring the relationship between PFAS and sperm quality; (2) PFASs (e.g., PFAS and PFAA) were the exposure of interest; (3) the study was written and published in English; and (4) sperm parameters (e.g., sperm count, semen volume, sperm morphology, and total sperm motility).

We excluded studies for the following reasons: (1) the article type was a meta-analysis, review, comment, or case report; (2) the study was an animal study; (3) data on sperm parameters were incomplete or unavailable; (4) non-English writing articles.

Data extraction

Each eligible study was reviewed by at least two authors for the following information: (1) study design; (2) first author's name; (3) sample size; (4) publication year; (5) location; (6) number of participants; (7) date of outcomes (include sperm count, sperm concentration, progression of sperm motility, total motility of sperm, semen volume, and sperm morphology); (8) category of PFAS; and (9) statistical findings (β value and 95% confidence interval [CI]).

Data analysis

Stata version 16.0 was used to analyze the extracted data among the included studies and statistical significance was determined using $P < 0.05$. The β value and corresponding 95% CIs were calculated to assess the relationship between PFASs exposure and semen quality. We applied a random-effects model when the inconsistency statistic (I^2) is more than 50%, otherwise performed the fixed-effects models, as described by Higgins and Thompson. We performed subgroup analysis to confirm the sources of heterogeneity.

Results

Study selection

We retrieved 449 studies from the five databases of electronic bibliography: PubMed (80 articles), Web of Science (176 articles), Embase (106 articles), Ovid (87 articles), and Cochrane Library (0 article). After duplicated studies were removed automatically, 210 studies remained. Among them, 182 articles were excluded on the basis of their titles and abstracts because they were reviews, comments, animal studies, or were not relevant to the research subject. Twenty-one of the remaining 28 studies were excluded due to irrelevant exposure and/or outcomes (19 articles) or incomplete statistics (2 articles). Eventually, meta-analyses were conducted on seven studies (Fig. 1).

Study characteristics

A total of seven cross-sectional studies involving 2190 subjects were incorporated in this meta-analysis, and the characteristics of the seven articles are summarized in Table 1. All studies were conducted in Denmark, the USA,

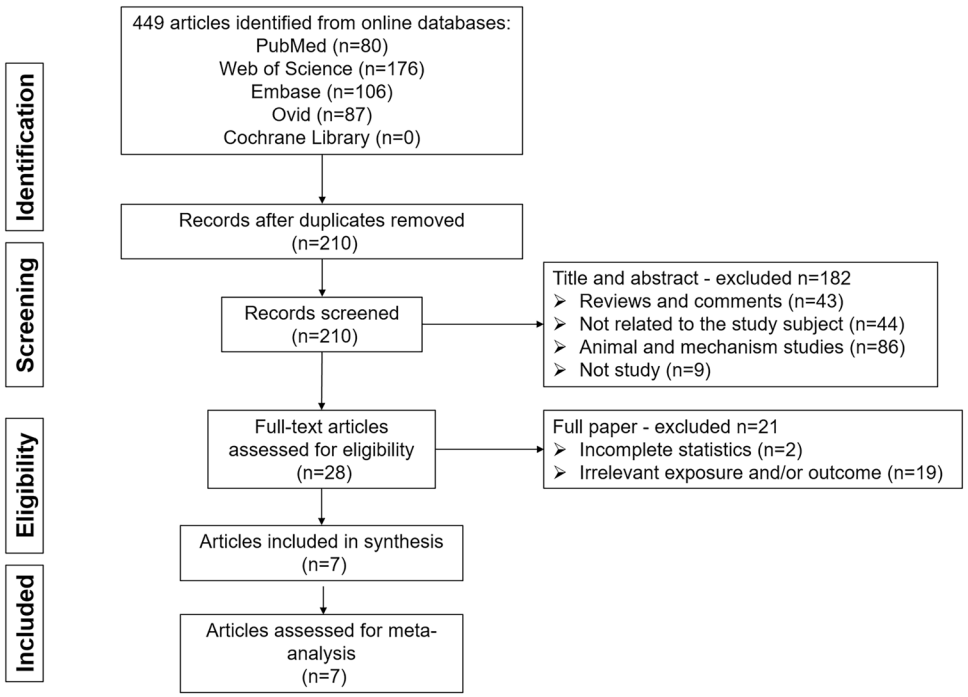

Fig. 1 The process of literature retrieval from the following electronic bibliographic databases: PubMed, Web of Science, Embase, Ovid, and Cochrane Library

Greenland, Poland, Ukraine, Faroese, and China (Huang et al. 2019; Joensen et al. 2009, 2013; Pan et al. 2019; Petersen et al. 2018; Raymer et al. 2012; Toft et al. 2012). Of the incorporated studies, all seven articles assessed the correlation between PFOA or PFOS exposure and the quality of semen (Huang et al. 2019; Joensen et al. 2009, 2013; Pan et al. 2019; Petersen et al. 2018; Raymer et al. 2012; Toft et al. 2012), four studies assessed the relationship between PFNA exposure and semen parameters (Huang et al. 2019; Joensen et al. 2013; Pan et al. 2019; Toft et al. 2012), and three studies evaluated the correlation between PFDA or PFHxS exposure and semen quality (Huang et al. 2019; Joensen et al. 2013; Pan et al. 2019; Toft et al. 2012). The following semen parameters were incorporated into the meta-analysis: sperm count (6 articles), sperm concentration (7 articles), progression of sperm motility (3 articles), total motility of sperm (5 articles), semen volume (7 articles), and sperm morphology (6 articles).

Quality assessment

Seven included cross-sectional articles were assessed for quality by the Agency for Healthcare Research and Quality (AHRQ) (Viswanathan et al. 2008), yielding an average score of 7.3, and all the studies met the criteria of the meta-analysis.

Association between PFOA exposure and semen quality

Seven articles were incorporated in the meta-analysis of the relationship between PFOA exposure and sperm concentration (Huang et al. 2019; Joensen et al. 2009, 2013; Pan et al. 2019; Petersen et al. 2018; Raymer et al. 2012; Toft et al. 2012). The pooled β value between PFOA and sperm concentration was no significant (β value = 0.06; 95% CI: 0.00, 0.11). In light of the low heterogeneity among the seven studies ($I^2 = 30.2\%$, $P = 0.167$), the fixed-effects model was performed to evaluate the relationship between PFOA exposure and sperm concentration (Fig. 2A).

Three studies on the correlation between PFOA exposure and sperm progressive motility were included (Huang et al. 2019; Joensen et al. 2013; Pan et al. 2019). The overall results suggested that exposure to PFOA at higher levels was significantly associated with a decline in sperm progressive motility (β value = −1.38; 95% CI: −2.44, −0.32), with no significant heterogeneity ($I^2 = 2.6\%$, $P = 0.38$). Thus, the fixed-effects model was applied to the meta-analysis and revealed a correlation between PFOA exposure and sperm progressive motility (Fig. 2B).

Five studies on the relationship between PFOA exposure and total motility of sperm were meta-analyzed (Huang et al. 2019; Joensen et al. 2009; Petersen et al. 2018; Raymer et al. 2012; Toft et al. 2012). Due to high heterogeneity

Table 1 Characteristics of all included studies in the meta-analysis

Study	Research design	Country	Sampling year	PFASs	Outcomes	Method of chemical analysis	Adjusted variables	AHRQ
Ulla Nordström Joensen et al., 2009	Cross-sectional study	Denmark	105	PFOS PFOA	Sperm concentration Sperm motility Total sperm count Morphology Semen volume	LC–MS-MS	Smoking and BMI	7
James H. Raymer et al., 2012	Cross-sectional study	United States	256	PFOS PFOA	Initial total motile (10^6/mL) Percent motile Sperm concentration (10^6/mL) Volume (mL)	HPLC–MS/MS	Age, period of abstinence, and tobacco use	6
G. Toft et al., 2012	Cross-sectional study	Greenland, Poland, Ukraine	588	PFOS PFOA PFHxS PFNA	Percent motile sperm Sperm concentration (10^6/mL) Total count (10^6) Volume (mL)	LC/MS/MS	Age, abstinence time, spillage, smoking, urogenital infections, and BMI. Combined analyses were adjusted for country as well	8
Ulla Nordstro¨m Joensen et al., 2013	Cross-sectional study	Denmark	247	PFHxS PFOS PFOA PFNA PFDA	Concentration Morphologically normal Progressively motile Total count Volume	HPLC–MS/MS	Abstinence time, BMI, and smoking (cigarettes per day), time to semen analysis	8
Maria Skaalum Petersen et al., 2018	Cross-sectional study	Faroese	263	PFOA PFOS	Motile sperm (%) Normal morphology (%) Semen volume (mL) Sperm concentration (mill/mL) Total sperm count (mill)	HPLC–MS/MS	Duration from ejaculation to assessment, period of abstinence, age, BMI, current smoking, and time of sampling	7
Qingyu Huang et al., 2019	Cross-sectional study	China	67	PFOA PFOS PFHxS PFDA PFNA	Progressive motility Semen volume Sperm concentration Sperm count Sperm morphology Total motility	UPLC/MS/MS	Age, BMI, abstinence time, smoking, and alcohol drinking status	7
Yitao Pan et al., 2019	Cross-sectional study	China	664	PFOA PFNA PFDA PFOS	Morphologically normal (%) Progressive motile (%) Semen volume (mL) Sperm conc. (million/mL) Sperm count (million)	UPLC	Age, BMI, smoking, alcohol intake, and abstinence time	8

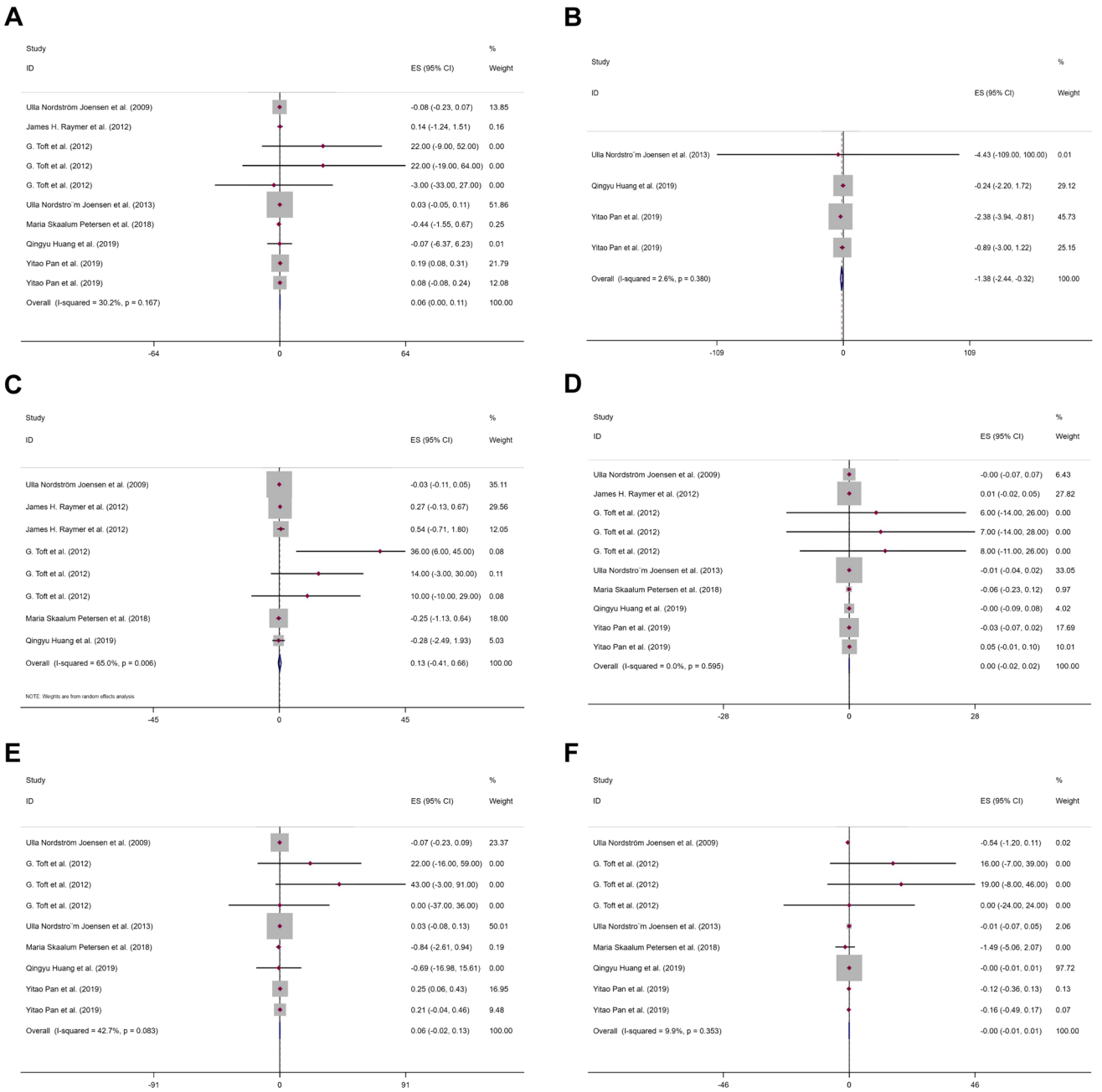

Fig. 2 Forest plot (fixed-effects model or random-effects model) for β value and their corresponding 95% CIs for the association between PFOA exposure and semen quality

($I^2 = 65.0\%$, $P = 0.006$), the random-effects model was used to analyze the correlations between PFOA exposure and total motility of sperm. There was no relationship between PFOA exposure and total motility of sperm (β value = 0.13; 95% CI: − 0.41, 0.66) (Fig. 2C).

Seven of the included studies reported semen volume, and all seven of them suggested that PFOA exposure had no significant correlation with semen volume (Huang et al. 2019; Joensen et al. 2009, 2013; Pan et al. 2019; Petersen et al. 2018; Raymer et al. 2012; Toft et al. 2012). Our results also revealed no correlation between PFOA exposure and semen volume (β value = 0.00; 95% CI: − 0.02, 0.02). The studies exhibited low heterogeneity ($I^2 = 0.00\%$, $P = 0.595$), and we used the fixed-effects model to analyze the overall data (Fig. 2D).

Six articles were applied to meta-analysis which investigated the relationship between PFOA exposure and sperm count (Huang et al. 2019; Joensen et al. 2009, 2013; Pan

et al. 2019; Petersen et al. 2018; Toft et al. 2012). The pooled estimate β value was 0.06 (95% CI: − 0.02, 0.13), and there was no significant relationship between PFOA exposure and sperm count across studies. Moreover, the studies exhibited low heterogeneity ($I^2 = 42.7\%$, $P = 0.083$), and a fixed-effects model was applied to evaluate the association between PFOA exposure and sperm count (Fig. 2E).

The relationship between PFOA exposure and sperm morphology was evaluated in six studies (Huang et al. 2019; Joensen et al. 2009, 2013; Pan et al. 2019; Petersen et al. 2018; Toft et al. 2012). Overall, the results showed that PFOA exposure does not significantly affect sperm morphology, with a pooled β value of − 0.00 (95% CI: − 0.01, 0.01). In addition, the included studies showed low heterogeneity ($I^2 = 9.9\%$, $P = 0.353$), and the fixed-effects model was applied (Fig. 2F).

Correlation between PFOS exposure and semen quality

Seven articles met the inclusion criteria for meta-analysis of the association between PFOS exposure and semen quality: seven for sperm concentration, three for sperm progressive motility, five for sperm total motility, seven for semen volume, and six for sperm count and sperm morphology (Huang et al. 2019; Joensen et al. 2009, 2013; Pan et al. 2019; Petersen et al. 2018; Raymer et al. 2012; Toft et al. 2012). There were no correlations between PFOS exposure and the above six semen parameters (Supplementary Fig. S1). Three studies in the meta-analysis of the association between PFOS exposure and sperm progressive motility had high heterogeneity ($I^2 = 55.9\%$, $P = 0.078$), and the random-effects model was used for the overall analysis (Supplementary Fig. S1B). The others had low or no heterogeneity, and we performed the meta-analysis via a fixed-effects model (Supplementary Fig S1).

Association between PFDA exposure and semen quality

Three articles stated the relationship between PFDA exposure and semen quality: three for sperm concentration, sperm progressive motility, sperm morphology, sperm count, and semen volume (Huang et al. 2019; Joensen et al. 2013; Pan et al. 2019). There were no associations between PFDA exposure and the above five semen parameters in our meta-analysis (Supplementary Fig. S2). Considering the significant heterogeneity among the three studies ($I^2 = 69.6\%$, $P = 0.02$), the relationship between PFDA exposure and sperm progressive motility was studied using a random-effects model (Supplementary Fig. S2B). For others with low or no heterogeneity, the fixed-effects model was applied (Supplementary Fig. S2).

Relationship between PFHxS exposure and semen quality

Three studies were incorporated in the meta-analysis of the association between PFHxS exposure and semen quality including the concentration of sperm, semen volume, sperm count, and sperm morphology (Huang et al. 2019; Joensen et al. 2013; Toft et al. 2012). There was no significant association between PFHxS exposure and sperm concentration (β value = 7.23; 95% CI: − 11.94, 26.40). Due to high heterogeneity ($I^2 = 74.2\%$, $P = 0.021$), we applied the random-effects model to analyze the above data (Supplementary Fig. S3A). The pooled β value between PFHxS and semen volume suggested no correlation (β value = 0.04; 95% CI: − 0.02, 0.11; $I^2 = 0.0\%$, $P = 0.503$) (Supplementary Fig. S3B). PFHxS showed no correlation with sperm count (β value = 0.21; 95% CI: − 0.03, 0.45; $I^2 = 43.9\%$, $P = 0.168$) (Supplementary Fig. S3C). There was also no association between PFHxS exposure and sperm morphology (β value = 0.05; 95% CI: − 0.11, 0.21); due to high heterogeneity ($I^2 = 68.2\%$, $P = 0.043$), the random-effects model was applied (Supplementary Fig. S3D).

Relationship between PFNA exposure and semen quality

Four articles were incorporated in the meta-analysis of the relationship between PFNA exposure and semen quality: four for sperm concentration, three for sperm progressive motility, and four for semen volume, sperm morphology, and sperm count (Huang et al. 2019; Joensen et al. 2013; Pan et al. 2019; Toft et al. 2012). The present results revealed that PFNA exposure was negatively associated with sperm progressive motility, and the pooled β value was − 1.31 (95% CI: − 2.35, − 0.26), without significant heterogeneity ($I^2 = 37.4\%$, $P = 0.188$) (Fig. 3B). However, PFNA exposure showed no correlation with sperm concentration (β value = 0.05; 95% CI: − 0.03, 0.12), with no heterogeneity ($I^2 = 0.0\%$, $P = 0.442$), and the fixed-effects model was applied (Fig. 3A). Similarly, PFNA exposure had no effect on semen volume (β value = − 0.00; 95% CI: − 0.03, 0.02; $I^2 = 17.2\%$, $P = 0.305$) (Fig. 3C). Additionally, there was no association between PFNA exposure and sperm count (β value = 0.06; 95% CI: − 0.05, 0.18; $I^2 = 0.0\%$, $P = 0.673$) (Fig. 3D). PFNA exposure was not associated with sperm morphology (β value = − 0.03; 95% CI: − 0.08, 0.02), with no heterogeneity ($I^2 = 34.1\%$, $P = 0.208$); therefore, the fixed-effects model was applied to the meta-analysis (Fig. 3E).

Subgroup analysis

PFNA and PFOA exposure had negative associations with sperm progressive, while PFOS, PFDA, and PFHxS

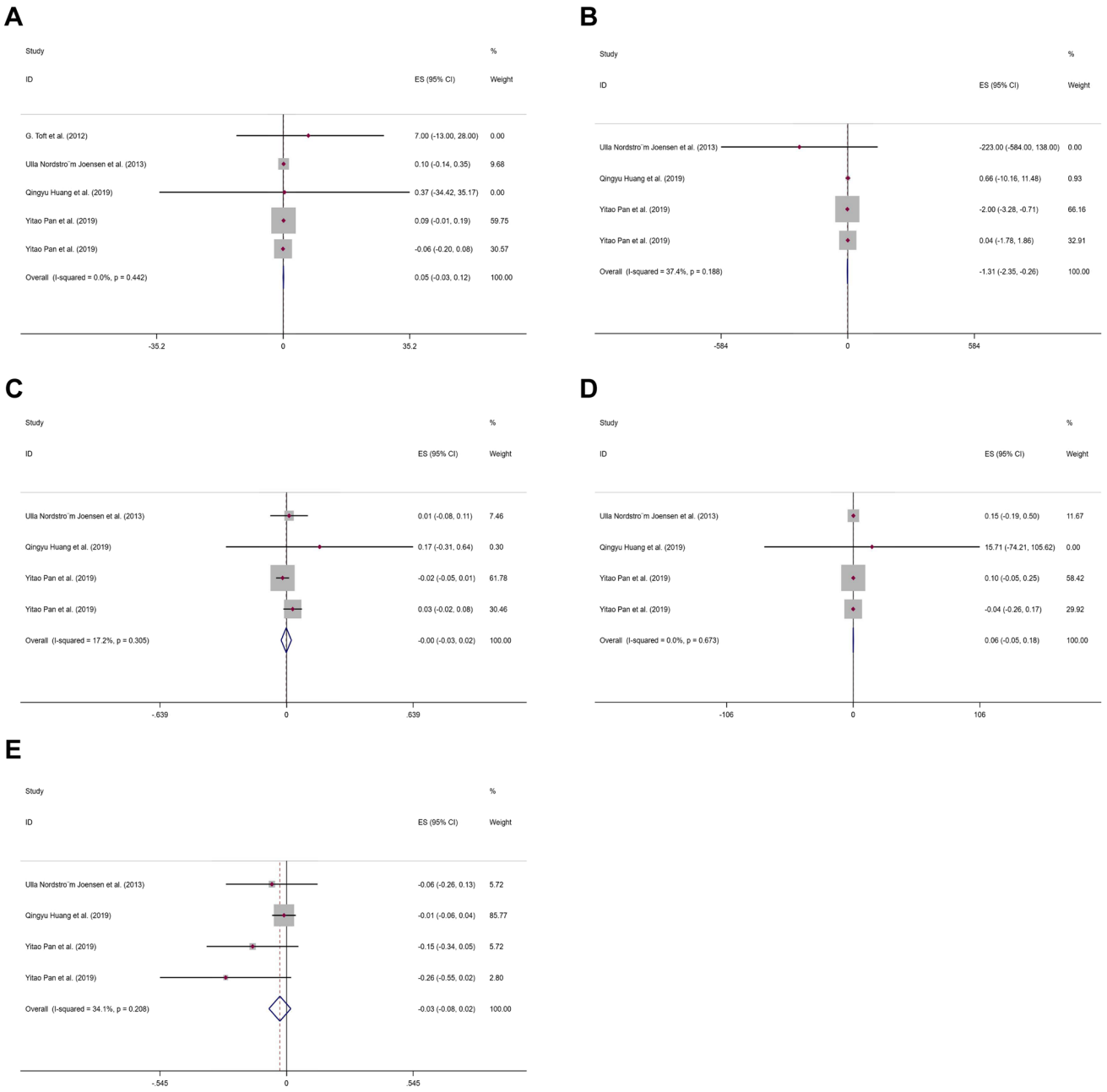

Fig. 3 Forest plot (fixed-effects model) for β value and their corresponding 95% CIs for the association between PFNA exposure and semen quality

exposure were nonsignificantly correlated with semen quality. Thus, to explore the correlation analysis results more deeply, subgroup analyses were performed to explore the relationship between PFAS exposure and semen quality according to study characteristics. The subgroup analyses were based on the following possible influencing factors: geographic location, sample size, and sample type.

There was no significant relationship between PFNA exposure and semen quality when stratified by geographic location, without significant heterogeneity (Supplementary Fig. S4). The relationship of PFOS exposure and semen quality was also not significantly different when stratified by geographic location (Supplementary Fig. S5). When the geographic location was used to stratify, the pooled estimates of the correlation between PFOA exposure and sperm concentration were 0.15 (95% CI: 0.06, 0.25; $I^2 = 0.0\%$, $P = 0.55$) for Asian countries and 0.00 (95% CI: −0.06, 0.07; $I^2 = 0.0\%$, $P = 0.492$) for Western countries (Supplementary Fig. S6A). Moreover, the pooled estimates of the relationship between sperm count and PFOA exposure were 0.23

(95% CI: 0.08, 0.38; $I^2 = 0.0\%$, $P = 0.966$) for Asian countries and −0.01 (95% CI: −0.10, 0.08; $I^2 = 22.0\%$, $P = 0.268$) for Western countries when stratified by geographic location (Supplementary Fig. S6B). When stratified by geographic location, PFOA exposure had no significant association with sperm morphology (Supplementary Fig. S6C).

There was no significant association between PFNA exposure and sperm count, semen volume, or sperm concentration when stratified by sample size (Fig. 4A–C). Interestingly, a significant negative correlation between PFNA exposure and sperm morphology was shown in studies when the sample size was greater than 200 people (β value = −0.14; 95% CI: −0.26, −0.01; $I^2 = 0.0\%$, $P = 0.522$) but not in studies with sample size of less than 200 people (β value = −0.01; 95% CI: −0.06, 0.04; $I^2 = 8.2\%$, $P = 0.297$) (Fig. 4D). PFOA exposure was not significantly correlated with sperm count, semen volume, sperm morphology, or total sperm motility when stratified by sample size for Asian and Western countries (Supplementary Figs. S7A, S7C-S7E). In studies with sample sizes greater than 200 people, PFOA exposure was demonstrated to be positively associated with sperm concentration (β value = 0.08; 95% CI: 0.02, 0.14; $I^2 = 34.1\%$, $P = 0.194$) but not in studies with sample sizes of less than 200 people (β value = −0.08; 95% CI: −0.23, 0.07; $I^2 = 0.0\%$, $P = 0.535$) (Supplementary Fig. S7B). There was no significant association between PFOS exposure and semen volume, sperm concentration, sperm morphology, or total sperm motility when stratified by sample size (Supplementary Figs. S8A, B, D, E). However, a positive relationship between PFOS exposure and sperm count was observed in studies with sample sizes of over 200 participants (β value = 0.06; 95% CI: 0.01, 0.11; $I^2 = 0.0\%$, $P = 0.584$) but not in studies with sample sizes of less than 200 people (β value = −0.02 95% CI: −0.05, 0.01; $I^2 = 0.0\%$, $P = 0.681$) (Supplementary Fig. S8C). When stratified by sample type, there was no association between PFOS exposure and sperm concentration in studies that analyzed serum sample, but a positive association between PFOS exposure and sperm concentration was revealed in studies that analyzed semen samples (β value = 0.01; 95% CI: 0.01, 0.19; $I^2 = 0.0\%$, $P = 0.638$) (Supplementary Fig. S9).

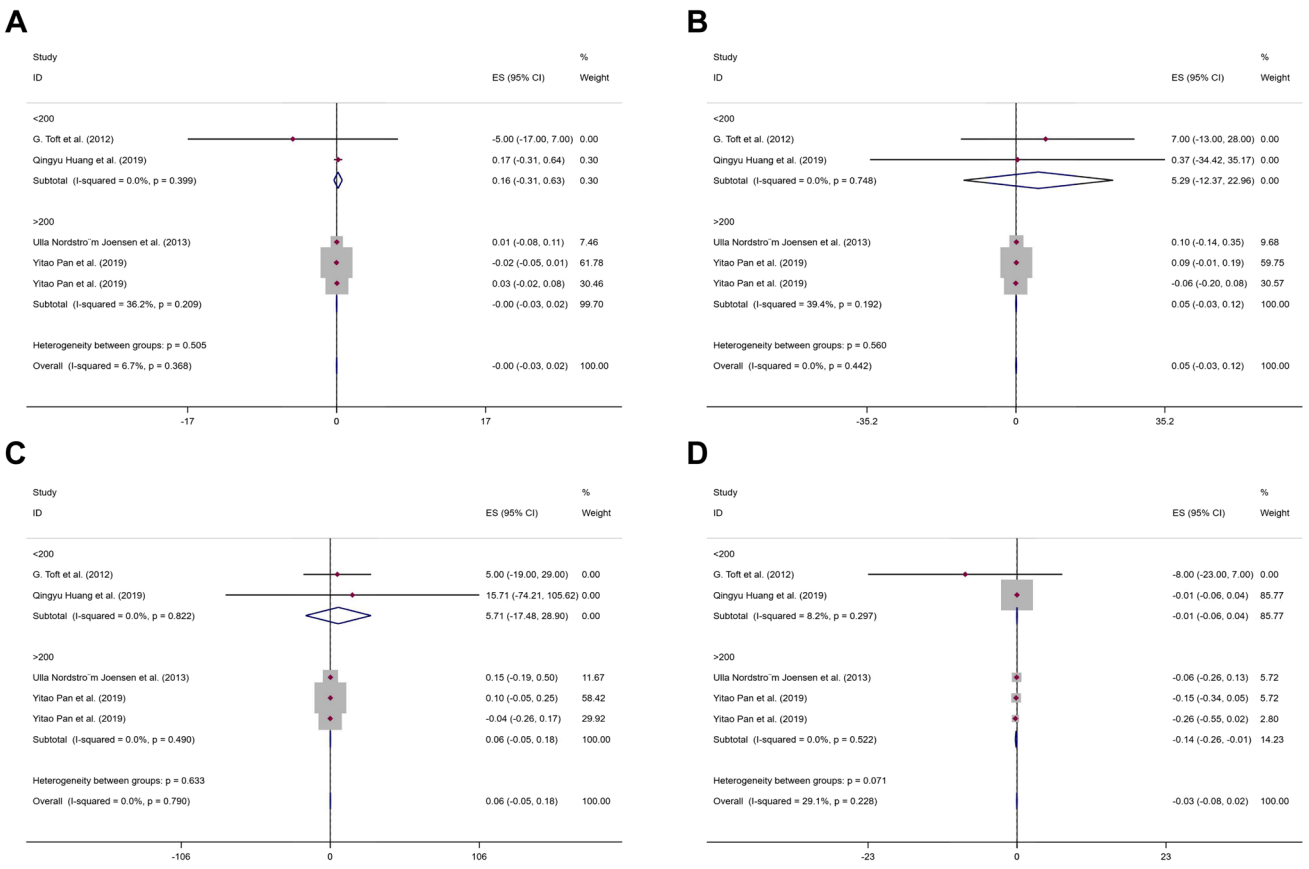

Fig. 4 Forest plot (fixed-effects model) for β value and their corresponding 95% CIs for the association between PFNA exposure and semen quality when stratified by sample size

Discussion

The current study is the first attempt to investigate the connection between PFAS exposure and semen quality parameters utilizing meta-analysis. In the present study, seven studies that involved 2190 participants were eligible for inclusion. Our results revealed that PFOA and PFNA had deleterious effects on sperm progressive motility, but not other sperm parameters. Exposure to PFOS and PFDA had no effect on sperm quality parameters, including sperm concentration, sperm progressive motility, semen volume, sperm count, and sperm morphology in our meta-analysis. Moreover, no significant correlation between PFHxS exposure and semen parameters including sperm concentration, semen volume, sperm morphology, and sperm count was found in our study.

According to a recent cross-sectional study conducted in China, PFOA and PFNA levels in the semen were associated with a lower sperm progressivity (Pan et al. 2019), consistent with our results. Nevertheless, some other study results confirmed that serum PFOA or PFDA levels were not consistently associated with sperm progressive motility (Huang et al. 2019; Joensen et al. 2013). This variability may be partly because PFASs were measured in different sample types, and semen levels of PFAS may be more representative of male reproductive system levels than serum levels. In future studies, we will explore this hypothesis in a larger population. In addition, several studies found that serum PFOS levels were not associated with semen parameters such as sperm motility, sperm volume, sperm morphology, and sperm count (Huang et al. 2019; Joensen et al. 2009, 2013; Pan et al. 2019; Petersen et al. 2018; Raymer et al. 2012; Toft et al. 2012), which is in agreement with our results. In a cross-sectional study from China, semen PFOS levels were positively correlated with sperm concentration (Pan et al. 2019), but the difference was nonsignificant. These studies also showed that there was no statistical correlation between PFOA exposure and semen parameters, including sperm volume, concentration, count, total motility, and morphology, consistent with our findings. Moreover, no significant associations between PFNA and PFDA exposure and sperm quality parameters, including the concentration of sperm, total number of sperms, semen volume, and sperm morphology, were found (Huang et al. 2019; Joensen et al. 2009, 2013; Pan et al. 2019; Petersen et al. 2018; Raymer et al. 2012; Toft et al. 2012), and our meta-analysis results were consistent with these findings. However, a cross-sectional study from China observed a positive association between PFHxS exposure and sperm concentration (Huang et al. 2019). One plausible explanation for this observation may be difference in pollutant exposure levels and sample sizes between the different study populations.

According to the analyses of subgroups, there was a positive association between PFOA exposure and sperm concentration and count in the Asian population, but not in Western studies. When stratified by sample size, a positive relationship between PFOS exposure and sperm count and PFOA exposure and sperm concentration were observed in studies with sample sizes of more than 200 people. However, PFNA exposure and sperm morphology were negatively correlated in studies when the sample sizes of over 200 participants. Given that the reported results appear inconsistent, further more population and animal studies are warranted.

Recently, several PFASs (i.e., PFOS, PFOA, PFNA, and PFHxS) and their roles in the pathogenesis of male infertility and impaired semen quality have been confirmed in animal studies. One study indicated that exposure to PFOS causes dose-dependent decreases in sperm count and Sertoli cell vacuolization when the dose exceeded 2.5 mg/kg/day (Qiu et al. 2013). Other studies found that PFOS exposure affected testicular parameters (i.e., sperm count, testosterone) by perturbating lipid mediators (Lai et al. 2017) or impeding testicular signaling (Wan et al. 2011). PFOA exposure reduced testosterone levels, damaged the seminiferous tubules, and reduced sperm quality, including sperm count, motility, and progressiveness, in mouse testes in a dose-dependent manner (Lu et al. 2016; Raymer et al. 2012; Wan et al. 2020; Zhang et al. 2014). Further study found that low-level PFOA exposure strengthen StAR expression via the repression of H3K9me1/3, which promotes the production of steroid hormones in rat testes, and other study found that PFOS and PFOA treatments destroyed mRNA expression by sequencing the transcriptome of rat testis Sertoli cell (Han et al. 2022; Wan et al. 2020). PFNA-treated mice also experienced adverse effects on sperm parameters (i.e., sperm count, sperm motility, and testosterone) and damage to the seminiferous tubules (Singh & Singh 2019). In addition, Yi et al. found impairment of specific secretory functions in Sertoli cells by PFNA treatment of testicular Sertoli cell in rats, and others found that chronic exposure to PFNA causes impaired biological synthesis of testosterone and elevated levels of oxidative stress in the mice testes (Feng et al. 2010, Singh & Singh 2019). However, there are currently no animal studies on PFHxS and PFDA exposure and male reproduction, and further laboratory animal studies are warranted in the future.

The present study has several limitations that warrant consideration. Our study used PFAS concentration as the categorical variable and only selected the highest quantile. Since PFAS concentration quantile criteria varied between studies, bias was possible. Moreover, not all the included articles adjusted for potential confounding factors (i.e., abstinence time, alcohol consumption status, and urogenital infections), which may affect the results of the present

meta-analysis. In addition, only seven studies were included according to the criteria, which may cause some bias. Therefore, more studies related to the association between PFAS exposure and semen quality are required in the future.

Conclusion

In this study, we discovered that exposure to PFNA and PFOA was negatively associated with sperm progressive motility. Further animal studies should be performed to uncover the causality and elucidate underlying mechanisms. It is necessary to reduce ambient PFAS exposure to prevent male infertility and improve human reproductive health.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11356-022-24182-3.

Acknowledgements We are grateful to Prof. Chuncheng Lu and Dr. Zhi Li for assistance with the method, and we would like to thank American Journal Experts for English language editing.

Author contribution Huanqiang Wang: investigation and writing—original draft preparation; Kai Wei: validation and data extraction; Zhixin Wu: investigation and data check; Fucun Liu and Xianzheng Peng: data curation; Danhua Wang: software; Yongyou Liu and Jida Xu: writing—review and editing; A'pei Jiang and Yan Zhang: funding acquisition, conceptualization, and supervision.

Funding This work was supported by the National Natural Science Foundation of China (82101679) and the Project Supported by Science Foundation of Kangda College of Nanjing Medical University (KD2022KYCXTD001, KD2021KYRC016, and KD2021KYRC009).

Data availability All data analyzed and/or generated during this study can be obtained from the corresponding author on a reasonable request.

Declarations

Ethics approval and consent to participate Not applicable.

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

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