

The effect of obesity interventions on male fertility: a systematic review and meta-analysis

Andrew Peel ^{1,2,3,4,*}, Hannah Lyons ^{2,4}, Cathryn A. Tully ^{2,3,5}, Andrew D. Vincent ^{1,3,6}, David Jesudason ⁷, Gary Wittert ^{1,2,6,8,†}, Nicole O. McPherson ^{2,4,9,†}

¹Freemason Centre of Male Health and Wellbeing, South Australian Health and Medical Research Institute (SAHMRI), Faculty of Health and Medical Sciences, The University of Adelaide, Adelaide, Australia

²Robinson Research Institute, The University of Adelaide, Adelaide, Australia

³School of Medicine, University of Adelaide, Adelaide, Australia

⁴Discipline of Reproduction and Development, School of Biomedicine, The University of Adelaide, Adelaide, Australia

⁵Repromed, Adelaide, Australia

⁶Lifelong Health, South Australian Health and Medicine Research Institute (SAHMRI), Faculty of Health and Medical Sciences, The University of Adelaide, Adelaide, Australia

⁷Department of Endocrinology, The Queen Elizabeth Hospital, Adelaide, Australia

⁸Department of Endocrinology, The Royal Adelaide Hospital, Adelaide, Australia

⁹Genea, Sydney, Australia

*Correspondence address. Level 4, Adelaide Health and Medical Science Building, The University of Adelaide, 4 North Terrace, Adelaide 5000, Australia. E-mail: andrew.peel@adelaide.edu.au  <https://orcid.org/0000-0002-7498-8571>

†These authors contributed equally as joint senior authors.

TABLE OF CONTENTS

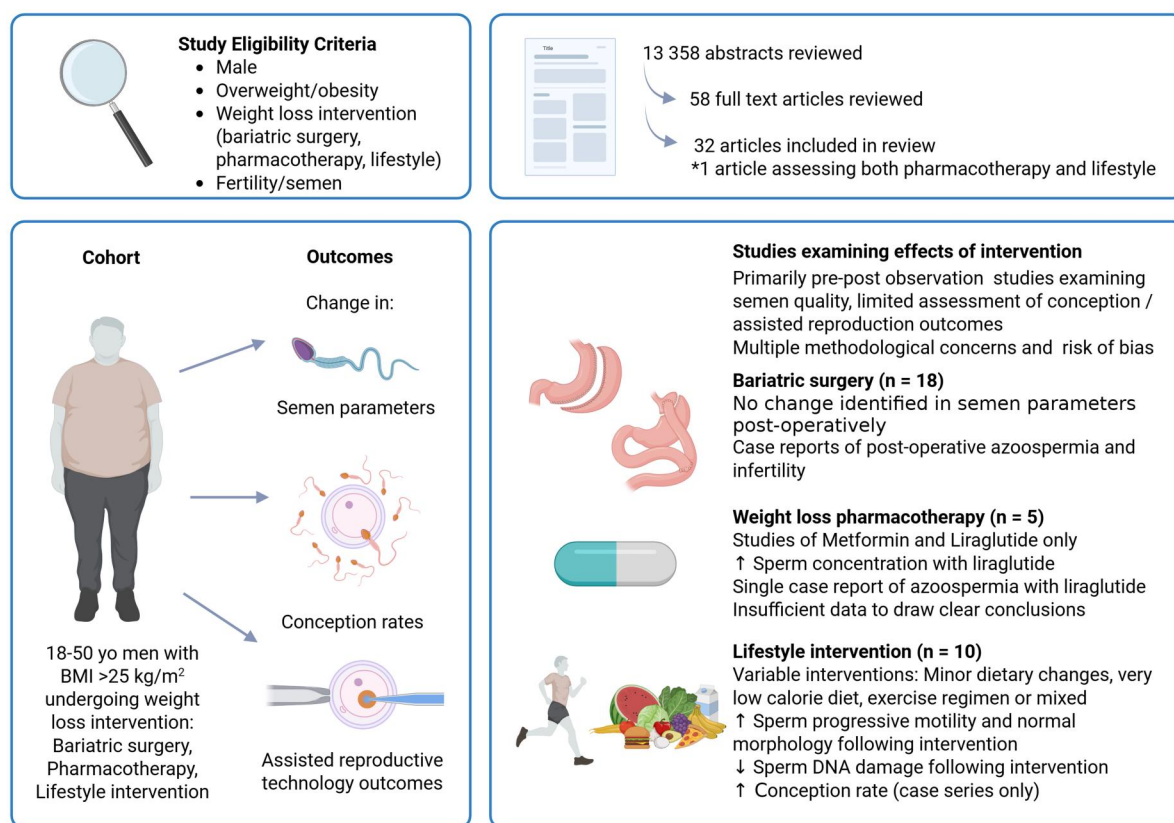
- **Introduction**
 - Review questions
- **Methods**
 - Search strategy
 - Inclusion and exclusion criteria
 - Outcomes
 - Study selection
 - Data analysis
- **Results**
 - Literature retrieval results
 - Bariatric surgery
 - Weight loss pharmacotherapy
 - Lifestyle intervention (diet/exercise)
- **Discussion**
 - Limitations
 - Preconception health messaging
- **Conclusion**

Received: April 28, 2025. Revised: September 2, 2025.

© The Author(s) 2025. Published by Oxford University Press on behalf of European Society of Human Reproduction and Embryology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact reprints@oup.com for reprints and translation rights for reprints. All other permissions can be obtained through our RightsLink service via the Permissions link on the article page on our site—for further information please contact journals.permissions@oup.com.

GRAPHICAL ABSTRACT



Systematic review of effects of weight loss interventions on measures of fertility. Created in BioRender. <https://BioRender.com/mkij81v>.

ABSTRACT

BACKGROUND: Obesity is a prevalent modifiable cause of male factor infertility. Preconception guidelines recommend men maintain a healthy weight; however, they provide limited guidance regarding methods or volume of weight loss for men with obesity. First-line interventions for weight loss involve lifestyle optimization (healthy diet and exercise), followed by pharmacotherapy or bariatric surgery in severe cases. Each modality has differing weight loss potential and complications for which the reproductive implications are currently unclear.

OBJECTIVE AND RATIONALE: To synthesize the available evidence regarding the reproductive effects of obesity interventions in men with obesity. Where possible, to evaluate whether the observed effects depend on the magnitude of weight loss.

SEARCH METHODS: Searches for articles published in English was performed using PubMed, Web of Science, Embase, Cochrane Central Register of Controlled Trials and Scopus from inception until December 2024, using prespecified keywords pertaining to four categories: male, overweight/obesity, weight loss (bariatric surgery, nutrition, diet, lifestyle, exercise, pharmacotherapy) and fertility (conception, assisted reproduction, sperm, semen). Studies of reproductive-aged men (18–50 years) who underwent an obesity intervention with established weight loss benefits and undertook repeated assessment of reproduction capacity (semen analysis, conception rates, assisted reproduction outcomes) before and after the intervention were included. Meta-analysis was performed when two or more studies of the same modality assessed an outcome measure in a manner suitable for meta-analysis. A meta-regression considering weight loss achieved was performed when five or more suitable studies were available. Narrative review of studies not suitable for meta-analysis occurred.

OUTCOMES: 32 studies were included in the analysis, with one study assessing both lifestyle interventions and pharmacotherapy. Assessment of conception rates and assisted reproduction was limited across all modalities. In almost all cases, the effect of obesity interventions on semen quality was examined as a surrogate for reproductive capacity and the certainty of evidence was low. Bariatric surgery was assessed in 18 studies, including 12 quasi-experimental studies, one randomized controlled trial, one case series and four case reports. Fixed- and random-effects meta-analysis of randomized controlled trials identified no differences in sperm parameters between control and intervention arms across any intervention, although small sample size limits interpretability. Random-effects meta-analyses of pre-post outcomes identified no clinically significant semen parameters or DNA damage changes following bariatric surgery. Pharmacotherapy (metformin and liraglutide) was assessed in five studies, including four quasi-experimental studies and one case report. There were insufficient data to draw clear conclusions regarding the impact of these agents on fertility outcomes. Lifestyle interventions were assessed in 10 studies, including five quasi-experimental studies and five randomized controlled trials. Fixed-effect meta-analysis identified improvements in sperm normal morphology (Mean difference = 0.59%, 95% Confidence interval = [0.23, 0.94]), and progressive motility (10.56% [8.97, 12.15]) following a lifestyle intervention.

WIDER IMPLICATIONS: Data regarding weight loss interventions and male fertility is limited primarily to observational studies examining semen quality. Improvements in semen quality following lifestyle interventions suggest a potential benefit of optimizing nutrition and physical activity, whereas a limited change with bariatric surgery indicates obesity-associated sperm dysfunction does

not resolve in a dose-dependent manner with weight loss and/or negative effects of rapid weight loss exist. Substantial knowledge gaps were identified, including limited randomized trials, inadequate examination of conception outcomes and limited assessment of GLP-1 agonist effects.

REGISTRATION NUMBER: CRD 42022349665.

Keywords: obesity / body mass index / fertility / sperm / semen / weight loss / nutrition

Introduction

Infertility is typically defined as the inability to achieve pregnancy after 12 months of unprotected sexual intercourse (Zegers-Hochschild et al., 2017). Current estimates suggest infertility affects approximately one in six people and in ~50% of cases, there is a causal or contributing male factor (Agarwal et al., 2015; World Health Organisation, 2023). Many causes of male factor infertility are not modifiable (e.g. genetic or chromosomal abnormalities, anatomical defects), others such as environmental exposures, health related behaviours (smoking, alcohol and other substance abuse) and chronic disorders (e.g. obesity, diabetes and obstructive sleep apnea) are emerging as critical, but modifiable risk factors (Agarwal et al., 2021; Bhattacharya et al., 2024).

Obesity (BMI ≥ 30 kg/m²) currently affects an estimated 40% of Americans aged 20–39 years and 23–30% of Australians aged 25–45 years (Australian Government, 2024; Hales et al., 2020). Infertility rates are ~50% higher in men with obesity compared with men of normal weight (Campbell and McPherson, 2019), and overall, conception is delayed (Boxem et al., 2024). Obesity is associated with reductions in basic sperm parameters (sperm count, motility, viability, and morphology), increases in DNA fragmentation, aberrant sperm acrosomal reaction, and markers of oxidative stress (Taha et al., 2016; Borges et al., 2017; Salas-Huetos et al., 2021; Li et al., 2024; Santi et al., 2024b). The mechanisms underlying these detrimental effects are multifactorial, involving oxidative stress, inflammation, and metabolic dysregulation (Kahn and Brannigan, 2017; Leisegang et al., 2021).

While meta-analyses identify minor variations in the specific semen parameters affected by obesity, a consistent negative trend is present (Salas-Huetos et al., 2021; Li et al., 2024; Santi et al., 2024b). Given the heterogeneous nature of obesity, it is not surprising that the effects on sperm quality are varied as these studies classify obesity by BMI only. BMI does not accurately reflect adiposity in all cohorts, provides limited information about adipose tissue distribution and does not characterize obesity related comorbidities (Nuttall, 2015; Rubino et al., 2025). While BMI is commonly utilized to assess obesity, use of this parameter when assessing fertility limits accurate assessment of multiple fertility-relevant factors, including adipose tissue distribution and changes, obesity related comorbidities and nutritional status.

Currently, international preconception guidelines provide dietary and weight reduction recommendations for women with overweight or obesity based on clear evidence of improvements in fertility and perinatal outcomes (Hanson et al., 2015; Federation of Obstetric and Gynaecological Societies of India (FOGSI) 2016; Shawe et al., 2019; Australian Government, 2021; Hunter et al., 2021; Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) 2021), with an evidence base present to guide management of maternal obesity-associated comorbidities and interventions that impair nutrition (e.g. bariatric surgery, very low-energy diet [VLED]) (Kominiarek, 2010; ACOG Practice Bulletin No. 201: Pregestational Diabetes Mellitus, 2018; National Institute for Health and Care Excellence: Guidelines, 2020; Cheah et al., 2022; Price and Sumithran, 2022;

Dominguez et al., 2023; 15. Management of Diabetes in Pregnancy: Standards of Care in Diabetes-2024, 2024). Contrastingly, preconception guidelines for men advocate a healthy weight, without more specific advice to achieve this (Rabiei et al., 2022; Healthy Male, 2024), or the relative merits of different dietary patterns/nutrient supplementation or physical activity independent of weight loss (Humaidan et al., 2022; Montano et al., 2022). Recent reviews of male weight loss lifestyle interventions have identified a lack of randomized controlled trials (Best et al., 2017; Hunter et al., 2021; Vitek and Hoeger, 2022), and a comprehensive review of all forms of interventional studies has not been identified.

For men with severe obesity, substantial weight loss can be achieved with bariatric surgery and recently available highly effective incretin-based pharmacotherapy. Different bariatric surgical procedures (e.g. Roux-en-Y gastric bypass (RYBG), sleeve gastrectomy) result in differing degrees of weight loss and effects on micronutrient balance (Gu et al., 2020; Sharples and Mahawar, 2020; Gomes-Rocha et al., 2022; De Luca et al., 2023). Recent meta-analyses do not clearly establish the effect of bariatric surgery on male fertility (Lee et al., 2019; Al Qurashi et al., 2022; Gao et al., 2022). While no identifiable change in basic sperm parameters occurs following bariatric surgery, these meta-analyses do not directly assess conception outcomes or specialized sperm parameters such as oxidative stress or DNA damage, which more closely reflect assisted reproduction outcomes (Marinero and Schlegel, 2023; Takalani et al., 2023). Glucagon-like peptide-1 (GLP-1) agonists are pharmaceutical agents that induce weight loss via appetite suppression. The newer agents are increasingly potent and can induce weight loss analogous to bariatric surgery (Jastreboff et al., 2022; Campbell et al., 2023). While significant cardiovascular benefits are established, there is limited data regarding the fertility implications of pharmacological weight loss (Andersen et al., 2022; La Vignera et al., 2023).

Despite the growing body of literature identifying detrimental effects of male obesity on fertility, there are limited high-quality studies evaluating the effect of specific obesity interventions on male reproduction. Studies that exist are small-scale, observational, and have significant heterogeneity in type and duration of intervention. This systematic review and meta-analysis aims to synthesize the evidence regarding obesity interventions' effects on male fertility, and where possible elucidate whether any change in fertility is related to degree of weight change or separate intervention-specific effects. By systematically reviewing studies across differing modalities, this review can contrast the effect of differing mechanisms, highlight critical knowledge gaps and provide a foundation for further investigation for optimizing male reproductive health.

Review questions

Q1. Is there a change in markers of fertility in men with overweight/obesity treated with (i) bariatric surgery; (ii) pharmacological treatment; or (iii) lifestyle interventions, including dietary change and exercise; for weight loss?

Q2. Is there a dose-response relationship between change in weight and markers of fertility after (i) bariatric surgery; (ii)

pharmacological treatments; or (iii) lifestyle interventions, including dietary change and exercise for weight loss?

Methods

This systematic review has been performed following a pre-approved protocol published in Joanna Briggs Institute (JBI) Evidence Synthesis (Peel et al., 2024). The following section briefly summarizes and outlines variations from initial protocol.

Search strategy

The systematic review was performed using the databases PubMed, Embase (Ovid), Cochrane Central Register of Controlled Trials, Web of Science and Scopus. Search terms (performed on 6 December 2023 and updated to 30 November 2024) utilized four categories: (i) male, man, men, paternal; (ii) obesity, overweight, overnutrition; (iii) weight loss, nutrition therapy, lifestyle, exercise, diet, weight reduction, nutrition, bariatric surgery, metabolic surgery, pharmacotherapy, glucagon-like peptide; and (iv) fertility, infertility, pregnancy, conception, foetal, assisted reproduction, stillbirth, miscarriage, semen, semen volume, spermatozoa, sperm count, motility, morphology, sperm maturation, aspermia, oligospermia, DNA damage, DNA fragmentation, reactive oxygen species (ROS), and lipid peroxidation (search criteria shown in [Supplementary Table S1](#)). Reference lists of all full-text articles were reviewed to capture missing literature. This review incorporated retrospective and prospective studies, including experimental studies, cohort studies, case reports, case studies, and case-control studies.

Inclusion and exclusion criteria

The inclusion criteria were studies of reproductive age men (age <50 years) with either overweight or obesity as determined by BMI (≥ 25 kg/m²) who underwent a health intervention typically associated with weight loss [divided into three primary methods: lifestyle change (dietary/exercise intervention), bariatric surgery, or pharmacotherapy] and had serial monitoring of either direct or indirect measures of fertility (see outcomes below). The age limit of 50 years was chosen to limit age-associated comorbidities that impact on fertility and based on census data indicating most male reproduction occurs prior to this age (Jimbo et al., 2022; Australian Government, 2023; Martinez and Daniels, 2023). Animal studies, letters, conference abstracts or previous meta-analyses were excluded, as were studies not published or translated to English. Where studies had a portion of patients greater than age 50 years, they were included if the mean age plus one SD was less than 50 years. Due to paucity of studies, studies that did not correct for female factors were not excluded for analysis.

Outcomes

Outcome measures that were assessed included both direct measures of fertility and semen quality (as a surrogate marker for fertility) (Peel et al., 2024). Direct measures of fertility assessed include time to conception, fecundity rate, and assisted reproduction outcomes (fertilization rate, embryo development, implantation rate, pregnancy rate). Semen quality outcomes measured include semen volume, sperm concentration, progressive motility and morphology, sperm DNA damage, lipid peroxidation and ROS as measured utilizing WHO laboratory manual for examination and processing of human semen (5th or 6th editions depending on time of publication) (World Health Organisation, 2010; Björndahl and Kirkman Brown, 2022). When serial monitoring was performed post-intervention, the latest data were utilized to increase probability that intervention-

related changes were captured. Study details including author, journal, year of publication, participant number, age, study design, intervention, were also collected.

Study selection

All identified citations were assessed by two independent reviewers against the dichotomous inclusion criteria. Relevant articles were subsequently reviewed in full text by two reviewers. Methodological risk of bias was assessed using the standard JBI critical appraisal checklist for experimental, quasi-experimental, cohort, case control, and case report studies (Moola et al., 2020; Munn et al., 2020; Tufanaru, 2020). Additionally, the Risk of Bias 2 (RoB2) tool was utilized to assess randomized controlled trials. Data extracted included: author, year of publication, journal of publication, participants, study methods, intervention, initial BMI, post-intervention BMI, follow-up duration, fertility parameters, and data analysis methods. Discrepancy was resolved through discussion between reviewers and authors were contacted if additional information was required.

Data analysis

The effect of individual health interventions (Study Q1) was assessed through meta-analyses of change in sperm outcomes (mean and standard error of the mean) before and after intervention, whereas influence on degree of weight loss on sperm outcomes (Study Q2) was assessed in random effects meta-regressions, with the inclusion of change in BMI as an effect moderator. We prespecified that a meta-analysis would be performed when at least two studies for an outcome measure were available, and a meta-regression when at least five studies were available. For all outcomes, treatment effect on mean differences (MD) was assessed. Studies were deemed available for inclusion if the following data were reported: type of intervention, pre- and post-intervention BMI mean, and SD and pre- and post-intervention outcome measurement mean and SD. Initial random effects meta-analyses were constructed. Heterogeneity was considered mild when the inconsistency statistic $I^2 < 30\%$ and the treatment effect was re-estimated using fixed effects models (Higgins and Thompson, 2002). Publication bias was assessed using the Egger's tests and funnel plots. If no evidence of publication bias was apparent, then significance was set at $\alpha = 0.05$ (two-sided).

Due to multiple randomized controlled trials being identified during study selection, a modification to the protocol was made whereby a systematic review and meta-analysis of the MD between intervention and control arms of randomized controlled trials was also examined and reported. Meta-analysis was performed when at least two randomized controlled trials examined an outcome measure in a manner suitable for meta-analysis were identified. Heterogeneity was deemed mild when inconsistency statistic $I^2 < 30\%$ and fixed effects models were utilized; otherwise, random effects models were used (Higgins and Thompson, 2002). Again, publication bias was examined via Egger's tests and funnel plots.

Quality of evidence for estimates of meta-analyses was assessed according to Grade of Recommendations, Assessment, Development and Evaluation (GRADE) classification (Guyatt et al., 2008). A narrative review was provided for studies not suitable for meta-analysis (e.g. case reports).

Where mean and SD were not available, equations established by Wan et al. (2014), which utilize alternative summary statistics (minimum value, first, second and third quartile, and maximum value) to determine an approximated mean and SD, were used to calculate said values. For studies that report 'median (minimum,

maximum)', equations 2, 7 ($n \leq 50$), and 9 ($n > 50$) were used. A deviation from protocol was performed for studies reporting 'median (interquartile range [IQR])' without the Q (Quartile) 1 and Q3 values, resulting in equations 14, 15 ($n \leq 50$), and 16 ($n > 50$) being unusable. Instead, the following inferences were made: median=mean and SD=IQR/1.35 (Wan et al., 2014). The formulas utilized are present in [Supplementary Table S2](#). When a variance estimate for the change score was not reported, we assumed a pre-post correlation of 0.5, conservatively based on two studies which reported pre-SD, post-SD and the SD of the difference (Samavat et al., 2018; Carette et al., 2019). In these studies, estimates of the pre-post correlations across sperm outcomes ranged from 0.46 to 0.96, with most being <0.7 . Sensitivity analyses excluding studies with inferred data were performed to ensure this assumption did not unduly affect results. All statistical analyses were performed using R package *metafor* version 4.6-0 (Free Software Foundation, Inc., Boston, USA).

There was significant heterogeneity of bariatric surgery study outcomes, and a subsequent *post hoc* exploratory meta-regression was performed to determine whether type of surgical intervention (RYGB, Sleeve gastrectomy or mixed) related to changes in sperm parameters. Two lifestyle intervention studies published by Mir/Jaffar et al. (Jaffar and Ashraf, 2017; Mir et al., 2018) utilized the same cohort, as did a further two bariatric intervention studies published by Calderón et al. (2019, 2020). Outcome data of these studies with identical cohorts were combined and analysed only once in meta-analyses (listed as studies Mir et al., 2018 and Calderón et al., 2019, respectively).

Results

Literature retrieval results

The PRIMSA flow chart presents the search results (Fig. 1). A total of 23 673 articles were identified (10 315 duplicates). Following reviewing titles and abstracts, a total of 58 full-text reviews were performed. A total of 32 studies met inclusion criteria, with one study assessing interventions across multiple modalities (Andersen et al., 2022). Reason for articles excluded at full-text review are available in [Supplementary Table S3](#). Study characteristics are presented based on the type of intervention (bariatric surgery, pharmacotherapy, and lifestyle intervention as [Tables 1–3](#), respectively). JBI Critical appraisal assessments classified by type of intervention ([Supplementary Tables S4–S6](#)), RoB2 Assessments ([Supplementary Table S7](#)) and GRADE quality of evidence profile ([Supplementary Table S8](#)) are presented in [supplementary data](#). In the following sections, specific outcomes are reported as mean (SD) unless otherwise specified.

Bariatric surgery

Bariatric surgery was assessed in a total of one randomized controlled trial (Reis et al., 2012), 13 quasi-experimental studies [classified as pre-post studies with controls (Samavat et al., 2018; Wood et al., 2020), and without controls (Legro et al., 2015; El Bardisi et al., 2016; Calderón et al., 2019, 2020; Carette et al., 2019; Fariello et al., 2021; Miñambres et al., 2022; Abouelgreed et al., 2023; Javani et al., 2023; Gao et al., 2024)], one case series (Velotti et al., 2021) and four case reports (di Frega et al., 2005; Lazaros et al., 2012; Sermondade et al., 2012; Razzaq et al., 2021) involving a total of 352 men. Outcome parameters were generally reported as mean (SD); however, calculation of these values from alternative summary statistics was required in two studies (El Bardisi et al., 2016; Wood et al., 2020). Notably, only three bariatric surgery studies reported prospective registration (Carette et al., 2019; Wood et al., 2020; Gao et al., 2024) with established trial registries

(e.g. International Clinical Trial Registry, Australian New Zealand Clinical Trials Registry).

Randomized controlled trials

A single randomized controlled trial examining the effect of bariatric surgery was identified (Reis et al., 2012), with a RoB2 score overall identifying 'some concerns' (specifically in domains two and five, [Supplementary Table S7](#)) and qualitative assessment of 9/13 limited by lack of blinding. The trial randomized 20 men (10 in each group) to either a strict dietary intervention followed by gastric bypass surgery or a brief dietary intervention (generalized dietary advice without stringent follow-up). The trial did not examine the sole effects of bariatric surgery as a semen analysis was not conducted between the dietary and surgical interventions. Additionally, substantial changes in BMI occurred following the initial dietary intervention resulting in differing patient demographics prior to surgical intervention [e.g. Pre-surgical intervention arm BMI: 43.1 kg/m² (4.7), control arm BMI: 51.9 kg/m² (5.7)]. Despite substantial weight loss in the intervention arm (post-surgical BMI 31.0 kg/m² (5.3). No differences in semen volume, concentration, normal morphology, or vitality were present between groups prior to dietary intervention or following bariatric surgery.

Observational studies and pre-post meta-analysis

The type of bariatric surgery performed across these studies included RYGB, sleeve gastrectomy, mixed (combination of RYGB with either sleeve or ventral gastrectomy) and unspecified. Mean age, pre- and post-surgical BMI and duration of follow-up are provided in [Table 1](#). Mean BMI pre-surgery ranged from 37.42 to 70.45 kg/m², reduction in BMI ranged from 7.56 to 24.70 kg/m² and mean critical appraisal assessment of 6/9. Common qualitative flaws identified across these studies included a lack of suitable control, lack of repeated outcome measurements, and lack of complete follow-up ([Supplementary Table S4](#)). Due to the predominance of observational studies, multiple study limitations and heterogeneity of data, a GRADE Quality assessment of 'Very Low' was assigned for all bariatric surgery meta-analysis outcomes ([Supplementary Table S8](#)).

Semen volume

Pre- and post-operative semen volume was assessed in 13 studies suitable for meta-analysis (Fig. 2A, $n = 336$) (Reis et al., 2012; Legro et al., 2015; El Bardisi et al., 2016; Samavat et al., 2018; Calderón et al., 2019; Carette et al., 2019; Wood et al., 2020; Fariello et al., 2021; Velotti et al., 2021; Miñambres et al., 2022; Abouelgreed et al., 2023; Javani et al., 2023; Gao et al., 2024). The random effects model identified no association between bariatric surgery and semen volume (MD = 0.13 ml, 95% CI = [−0.26, 0.52], $P = 0.50$) and no significant publication bias (Egger's test $P = 0.75$). A high degree of heterogeneity was identified ($I^2 = 88.6\%$). Following exclusion of studies with calculated mean and SD (consisting of a mix of RYGB and SG) (El Bardisi et al., 2016; Wood et al., 2020), we found a small increase in semen volume (MD = 0.34 ml, 95% CI = [0.05, 0.64], $P = 0.02$) and similar heterogeneity ($I^2 = 75.4\%$).

Due to the high heterogeneity, a *post hoc* meta-regression adjusting for type of surgery was undertaken. Heterogeneity reduced following adjusting for type of surgery undertaken ($I^2 = 80.1\%$), and studies undertaking solely RYGB had greater increments in semen volume compared to other forms of intervention (Mixed, Solely Sleeve gastrectomy, [Supplementary Table S9](#)). The relationship between change in BMI, surgical intervention and semen volume is displayed in [Supplementary Fig. S1A–D](#).

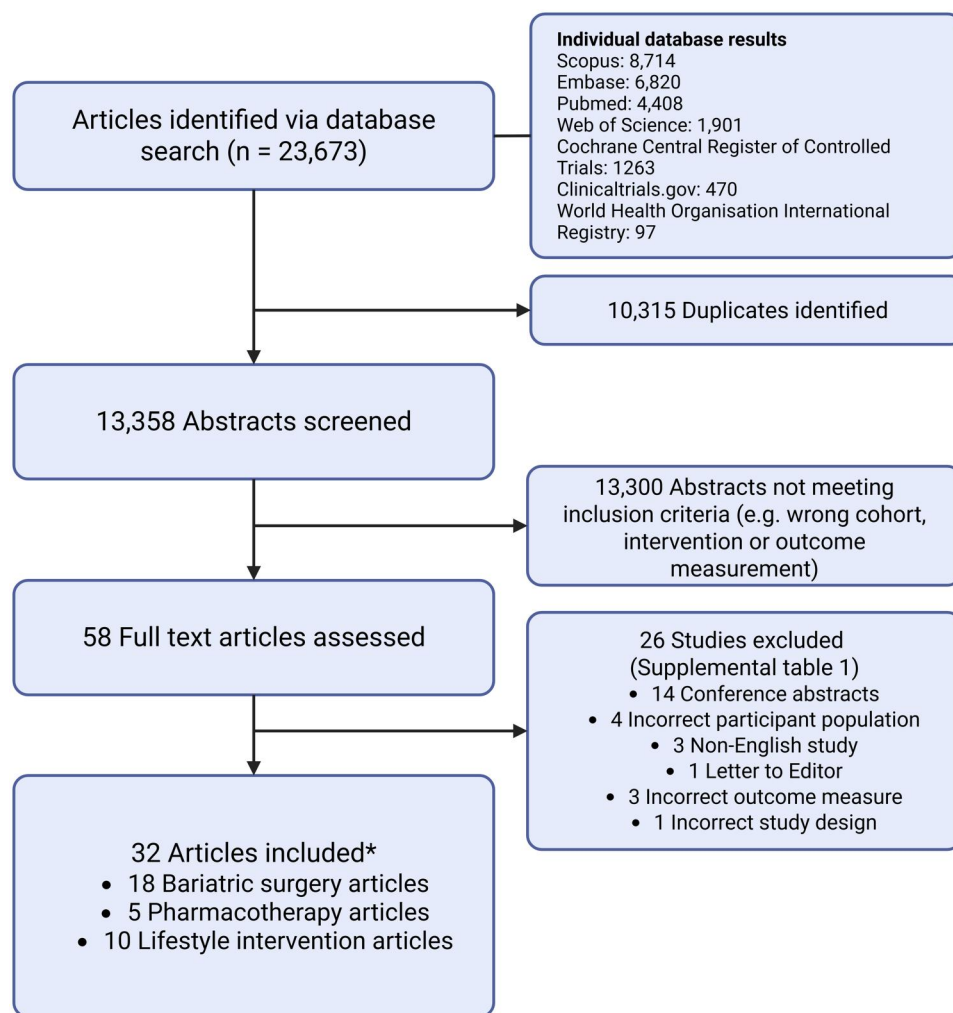


Figure 1. PRISMA flowchart of systematic review. *Single study (Andersen et al., 2022) was composed of both pharmacotherapy and lifestyle intervention cohorts and therefore included in both sections. Created in BioRender. McPherson, N. (2025) <https://BioRender.com/mkij81v>

Change in BMI after bariatric surgery was not identified as a significant moderating factor (MD=−0.01 ml, 95% CI=[−0.10, 0.08], $P=0.85$, $I^2=89.6\%$).

Sperm concentration

Sperm concentration was assessed pre- and post-operatively in 13 studies suitable for meta-analysis (Fig. 2B, $n=319$) (Reis et al., 2012; Sermondade et al., 2012; Legro et al., 2015; El Bardisi et al., 2016; Samavat et al., 2018; Calderón et al., 2019; Carette et al., 2019; Wood et al., 2020; Fariello et al., 2021; Velotti et al., 2021; Miñambres et al., 2022; Abouelgreed et al., 2023; Gao et al., 2024). The random effects model identified no association between bariatric surgery and sperm concentration (MD=−4.84 ml/ml, 95% CI=[−18.23, 8.54], $P=0.48$). No publication bias was identified by Egger's test ($P=0.13$) and a high heterogeneity was observed ($I^2=99.2\%$). Following exclusion of studies with calculated mean and SD (El Bardisi et al., 2016; Wood et al., 2020), we identified no change in sperm concentration following bariatric surgery (MD=−3.84 ml/ml, 95% CI=[−19.82, 12.13], $P=0.64$) with a similar degree of heterogeneity ($I^2=99.43\%$).

Due to the high heterogeneity, post hoc meta-regression adjusting for type of surgery was performed. Adjustment for surgical intervention identified that studies reporting mixed interventions had reductions in sperm concentration compared to RYGB

studies (Supplementary Table S10). There was no moderating effect of change in BMI on sperm concentration by random effects meta-regression (MD=0.68 ml/ml, 95% CI=[−3.54, 12.17], $P=0.64$, $I^2=97\%$). A graphical representation of the relationship between the change in BMI, surgical intervention and change in sperm concentration is displayed in Supplementary Fig. S2A–D.

Three case reports reporting on sperm concentration were not suitable for incorporation into the meta-analysis (di Frega et al., 2005; Lazaros et al., 2012; Razzaq et al., 2021). In a series of six Italian men with previously proven fertility who underwent Roux-en-Y gastric bypass (BMI >40 kg/m², weight loss of 60–80 kg each), serial semen analyses performed over the next year post-operatively ($n=3-4$ for each man) identified azoospermia (di Frega et al., 2005). In a second report, two men (BMI 40.1 and 38.2 kg/m², respectively) underwent assisted reproduction before and after bariatric surgery (gastric sleeve and not specified). Semen analysis performed 1–1.5 years following surgery showed reductions in sperm concentration compared to pre-operative assessments (59×10⁶/ml to 21×10⁶/ml and 32×10⁶/ml to azoospermia, respectively) (Lazaros et al., 2012). In the third report, two men (BMI 81.2 and 52 kg/m²) who also had previously fathered children underwent sleeve gastrectomy. Despite successful paternity pre-operatively, both men suffered from post-operative infertility and semen analyses confirmed

Table 1. Studies reporting bariatric surgery outcomes meeting inclusion criteria.

Study	Country	Design	Intervention sample size	Surgical intervention	Age years—mean (SD)	Mean follow-up duration	Pre-BMI kg/m ² —mean (SD)	Post-BMI kg/m ² —mean (SD)	Outcomes assessed
Di Frega <i>et al.</i> (2005)	Italy	Case report	6	RYGB	38.3 (2.4)	—	—	—	Concentration
Lazaros <i>et al.</i> (2012)	Greece	Case report	2	Unspecified	43.75*	—	39.85*	27.8*	Concentration, Morphology, Progressive motility, Embryo, quality, Fecundity rate
Sermondade <i>et al.</i> (2012)	France	Case report	3	RYGB (2), Sleeve gastrectomy (1)	33.7*	6 months	52.6 (13.6)*	30.4 (3)	Concentration, Morphology, Progressive motility, Fecundity rate
Reis <i>et al.</i> (2012)	Brazil	Randomized controlled trial	10	Gastric bypass	36.7 (11.5)	24 months	55.7 (7.8)	31 (5.3)	Volume, Concentration, Morphology, Progressive motility
Legro <i>et al.</i> (2015)	USA	Quasi-experimental (pre-post study without control arm)	6 (3 semen analyses)	RYGB	36.04 (3.95)*	12 months	48 (7)	32 (7)	Volume, Concentration, Morphology, Progressive motility
El Bardisi <i>et al.</i> (2016)	Qatar	Quasi-experimental (pre-post study without control arm)	46	Sleeve gastrectomy	36.74 (3.38)*	12 months	70.45 (12.02)*	50.81 (10.08)*	Volume, Concentration, Morphology, Progressive motility
Samavat <i>et al.</i> (2018)	Italy	Quasi-experimental (pre-post study with control arm)	23	RYGB	38 (9)	6 months	45.8 (7.4)	35.7 (5.3)	Volume, Concentration, Morphology, Progressive motility, DNA damage
Calderón <i>et al.</i> (2019, 2020)	Dominican Republic	Quasi-experimental (pre-post study without control arm)	20	Sleeve gastrectomy (4) Gastric bypass (16)	40 (8)	24 months	50 (10)	32 (7)	Volume, Concentration, Morphology, Progressive motility
Carette <i>et al.</i> (2019)	France	Quasi-experimental (pre-post study without control arm)	46	Gastric bypass (20) Sleeve gastrectomy (26)	38.9 (7.9)	12 months	44.1 (5.5)	31.4 (5.3)	Volume, Concentration, Morphology, Progressive motility, DNA damage
Wood <i>et al.</i> (2020)	Brazil	Quasi-experimental (pre-post study with control arm)	18	RYGB (15) Sleeve gastrectomy (3)	39 (11.85)*	6 months	43.9 (8.59)*	32.3 (4.07)*	Volume, Concentration, Morphology, Progressive motility, DNA damage
Fariello <i>et al.</i> (2021)	Brazil	Quasi-experimental (pre-post study without control arm)	15	RYGB	20–50	12 months	45.7 (8.3)	28 (2.8)	Volume, Concentration, Morphology, Progressive motility, DNA damage, Lipid peroxidation

(continued)

Table 1. (continued)

Study	Country	Design	Intervention sample size	Surgical intervention	Age years—mean (SD)	Mean follow-up duration	Pre-BMI kg/m ² —mean (SD)	Post-BMI kg/m ² —mean (SD)	Outcomes assessed
Razzaq et al. (2021)	Ireland	Case report	2	Sleeve gastrectomy	39*	—	—	—	Concentration, Fecundity rate
Velotti et al. (2021)	Italy	Case series	35	Sleeve gastrectomy	36.4 (5.17)	6 months	39.56 (1.51)	32 (1.22)	Volume, Concentration, Morphology, Progressive motility, Assisted reproduction outcomes
Minambres et al. (2022)	Spain	Quasi-experimental (pre-post study without control arm)	12	Gastric bypass (7) Sleeve gastrectomy (5)	45 (4.87)	18 months	42.37 (4.44)	29.6 (3.77)	Volume, Concentration, Morphology, Progressive motility, DNA damage
Abouelgreed et al. (2023)	Egypt	Quasi-experimental (pre-post study without control arm)	54	Sleeve gastrectomy	46 (4.83)	18 months	41.3 (4.1)	28.5 (3.32)	Volume, Concentration, Morphology, Progressive motility
Javani et al. (2023)	Iran	Quasi-experimental (pre-post study without control arm)	20	Gastric bypass (3) Sleeve gastrectomy (17)	34.74 (3.54)	12 months	42.45 (3.11)	32.02 (2.76)	Volume, Morphology
Gao et al. (2024)	China	Quasi-experimental (pre-post study without control arm)	34	Sleeve gastrectomy	20–35	12 months	37.42 (3.64)	28.21 (3.43)	Volume, Concentration Abnormal Morphology

RYGB, Roux-en-Y Gastric Bypass.

* Value inferred as outlined in methods as original data not presented as mean (SD).

Table 2. Studies reporting Pharmacotherapy outcomes meeting inclusion criteria.

Study	Country	Design	Intervention sample size	Intervention	Mean age	Follow-up duration	Pre-BMI kg/m ² —mean (SD)	Post-BMI kg/m ² —mean (SD)	Outcomes assessed
Morgante <i>et al.</i> (2011)	Italy	Quasi-experimental (pre-post study without control arm)	45	Metformin	—	6 months	28 (3.5)	27.3 (3.1)	Volume, Concentration, Morphology, Progressive motility
Fontoura <i>et al.</i> (2014)	Brazil	Case report	1	Liraglutide	35	—	—	—	Volume, Concentration, Morphology, Progressive motility, Pregnancy outcomes
Raghif (2015)	Iraq	Quasi-experimental (pre-post study without control arm)	18	Metformin	29 (5.49)*	3 months	35.93 (5.7)	34.85 (5.2)	Volume, Concentration, Morphology
Andersen <i>et al.</i> (2022) Sub-cohort 2	Denmark	Substudy of Randomized Controlled trial	7	Liraglutide	—	12 months	32.4 (2.8)	33.4 (5.26)	Volume, Concentration
Andersen <i>et al.</i> (2022) Sub-cohort 3	Denmark	Substudy of Randomized Controlled trial	13	Liraglutide+Exercise	—	12 months	31.6 (3)	31.6 (4.3)	Volume, Concentration
La Vignera <i>et al.</i> (2023)	Italy	Quasi-experimental (Non-randomized trial without control group)	35	Liraglutide	26 (6)	4 months	36 (3)	30 (3)	Concentration, Morphology, Progressive motility

* Value inferred as outlined in methods as original data not presented as mean (SD).

Table 3. Studies reporting lifestyle intervention outcomes meeting inclusion criteria.

Study	Country	Design	Intervention sample size	Intervention	Mean age	Follow-up duration	Pre-BMI kg/m ² —mean (SD)	Post-BMI kg/m ² —mean (SD)	Outcomes assessed
Håkonsen et al. (2011)	Denmark	Quasi-experimental (pre-post study without control arm)	43	Healthy diet/ Exercise	35.84 (8.91)*	3.5 months	45.53 (6.39)*	–	Volume, Concentration, Morphology, DNA damage
Faure et al. (2014)	France	Case series	6	Dietary change	31.83 (6.31)	5.4 months	30.58 (7.29)	29.37 (6.07)	Morphology, Progressive Motility, DNA damage, Pregnancy outcomes
Rafiee et al. (2016)	Iran	Randomized controlled trial	Inconsistent documentation	Exercise	35.2 (–)	6 months	–	–	Volume, Concentration, Morphology
Rosety et al. (2017)	Spain	Randomized controlled trial	45	Aerobic training program	36.3 (3.2)	4 months	31.2 (1.1)	–	Volume, Concentration, Morphology, Progressive Motility
Jaffar and Ashraf (2017)/Mir et al. (2018)	India	Quasi-experimental (pre-post study without control arm)	105	Healthy Diet/ Exercise	32.5 (7.5)	3 months	33.18 (5.06)	30.43 (5.98)	Volume, Concentration, Morphology, Progressive Motility, DNA damage
Mombeyni et al. (2021)	Iran	Randomized controlled trial	12	Exercise	34.36 (4.67)	3 months	32.84 (1.95)	33.03 (1.18)	Volume, Concentration, Morphology, Progressive Motility
Andersen et al. (2022) • Initial 8 weeks weight loss	Denmark	Substudy of Randomized Controlled trial—Initial weight loss component (pre-post study)	47	Very low-calorie diet 800 kcal/day (VLCD)	41 (9.66)*	2 months	37 (2.8)	32 (2.9)	Volume, Concentration
Andersen et al. (2022) • Exercise sub-cohort	Denmark	Substudy of Randomized Controlled trial	9	Exercise (following VLCD)	–	12 months	31.8 (3.7)	32.8 (4.5)	Volume, Concentration
Ismail et al. (2023)	Egypt	Randomized controlled trial	20	Exercise	33.6 (4.14)	3 months	32.55 (1.74)	30.99 (1.95)	Volume, Concentration, Morphology, Progressive Motility, DNA damage
Sharma et al. (2024) normo-zoospermic cohort	UK	Randomized controlled trial	12	VLCD	40.2 (9.6)	4 months	35.3 (4.1)	–	Concentration, Morphology, Progressive Motility, DNA damage
Sharma et al. (2024) oligo-zoospermic cohort	UK	Randomized controlled trial	20	VLCD	37.7 (6.6)	4 months	38.4 (4)	–	Concentration, Morphology, Progressive Motility, DNA damage, Reactive oxygen species

* Value inferred as outlined in methods as original data not presented as mean (SD).

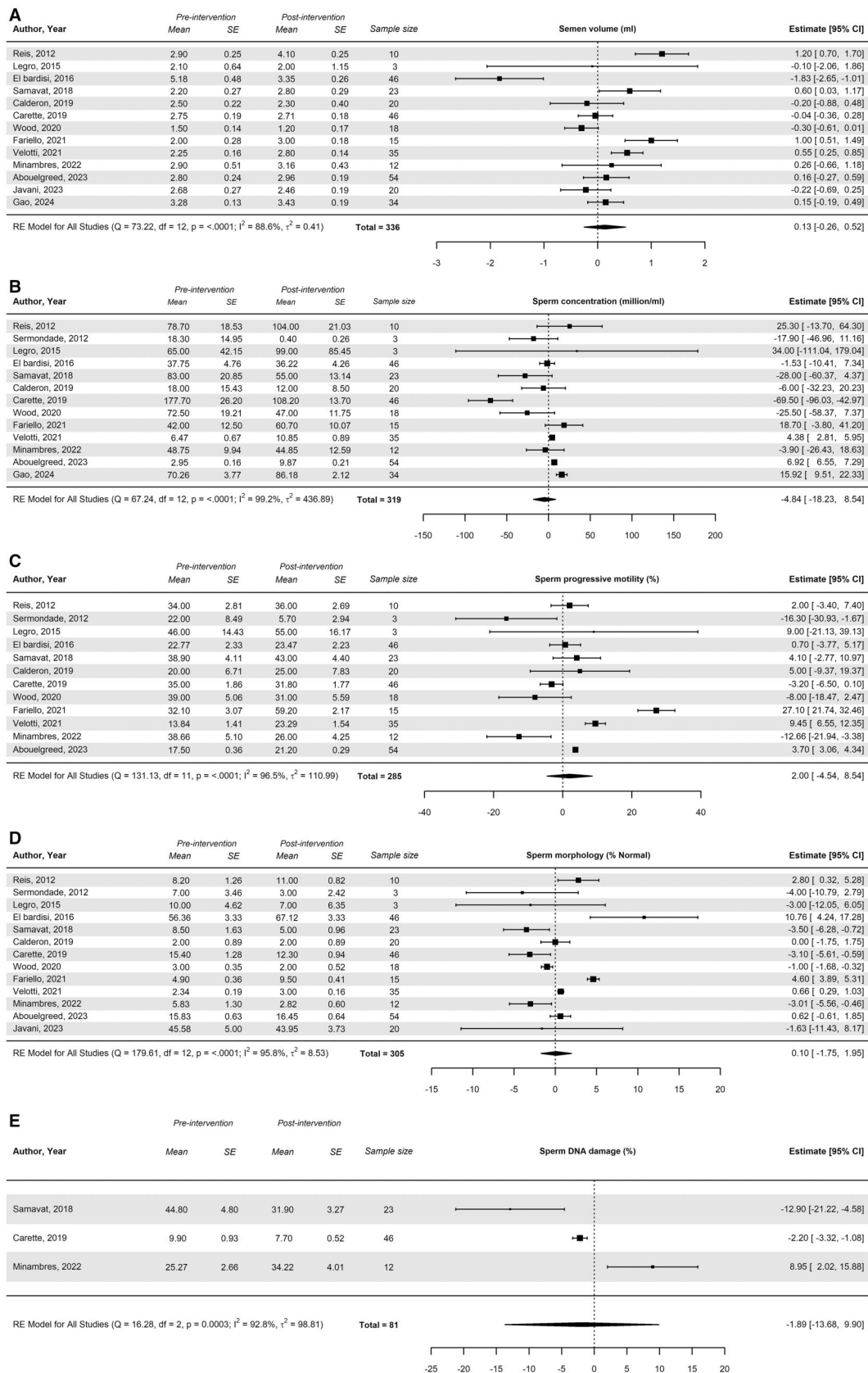


Figure 2. Meta-analysis forest plots of semen parameters in relation to bariatric surgery interventions. (A) Semen volume, (B) Sperm concentration, (C) Sperm progressive motility, (D) Sperm normal morphology, (E) Sperm DNA damage. SE, standard error of the mean, RE, random effects, FE, fixed effects, Q, Cochran's Q statistic, df, degrees of freedom, I², I² heterogeneity statistic, τ^2 , τ^2 variance statistic.

azoospermia (at 4 years and 1-year post-operation, respectively). (Razzaq et al., 2021).

Progressive motility

Sperm progressive motility was assessed in 12 studies suitable for meta-analysis (Fig. 2C, $n = 285$) (Reis et al., 2012; Sermondade et al., 2012; Legro et al., 2015; El Bardisi et al., 2016; Samavat et al., 2018; Calderón et al., 2019; Carette et al., 2019; Wood et al., 2020; Fariello et al., 2021; Velotti et al., 2021; Miñambres et al., 2022; Abouelgreed et al., 2023). The random effects model identified no association between bariatric surgery and sperm progressive motility (MD = 2.0%, 95% CI = [-4.54, 8.54], $P = 0.55$). No evidence of publication bias was identified via Egger's test ($P = 0.85$). A significant degree of heterogeneity was observed ($I^2 = 96.5\%$). Exclusion of studies with calculated mean and SD (El Bardisi et al., 2016; Wood et al., 2020) showed similar findings (MD = 3.06%, 95% CI = [-4.62, 10.75], $P = 0.43$) with similar heterogeneity ($I^2 = 97.1\%$).

Due to high heterogeneity, *post hoc* meta-regression adjusting for surgical intervention was performed, with studies examining solely RYGB being associated with increases in sperm concentration (Supplementary Table S11). There was no moderating effect of change in BMI on progressive motility by random effects meta-regression (MD = 0.09%, 95% CI = [-1.30, 1.48], $P = 0.90$, $I^2 = 96.8\%$). A graphical representation of the relationship between the change in BMI, surgical intervention and change in sperm concentration is displayed in Supplementary Fig. S3A–D.

One case report was unsuitable for inclusion in the meta-analysis. In the report, two men (BMI 41.1 and 38.2 kg/m²) underwent semen analysis before and after bariatric surgery (gastric sleeve and not specified, respectively). Compared to pre-operative assessment, sperm progressive motility assessed 1–1.5 years following surgery was reduced in both men (42% reduced to 17% and 41% with subsequent azoospermia, respectively) (Lazaros et al., 2012).

Normal morphology

Normal morphology was assessed in 13 studies suitable for meta-analysis (Fig. 2D, $n = 305$) (Reis et al., 2012; Sermondade et al., 2012; Legro et al., 2015; El Bardisi et al., 2016; Samavat et al., 2018; Calderón et al., 2019; Carette et al., 2019; Wood et al., 2020; Fariello et al., 2021; Velotti et al., 2021; Miñambres et al., 2022; Abouelgreed et al., 2023; Javani et al., 2023). The random effects model identified no association between bariatric surgery and sperm normal morphology (MD = 0.10%, 95% CI = [-1.75, 1.95], $P = 0.92$). No evidence of publication bias was identified (Egger's test $P = 0.64$). A significant degree of heterogeneity was observed ($I^2 = 95.8\%$). Similar findings (MD = -0.28%, 95% CI = [-2.14, 1.57], $P = 0.77$) and heterogeneity ($I^2 = 93.9\%$) were identified following exclusion of studies with calculated mean and SD (El Bardisi et al., 2016; Wood et al., 2020).

Due to significant heterogeneity, *post hoc* meta-regressions adjusting for surgical intervention were performed, with a minor reduction in heterogeneity ($I^2 = 89.4\%$) (Supplementary Table S12). There was no moderating effect of change in BMI on sperm normal morphology (MD = -0.29%, 95% CI = [-0.65, 0.06], $P = 0.10$, $I^2 = 92.5\%$). Supplementary Figure S4A–D shows the relationship between the change in BMI, surgical intervention and change in sperm normal morphology.

One case report and one interventional study reporting on normal morphology were not suitable for inclusion in the meta-analysis. In the report, two men (BMI 40.1 and 38.2 kg/m²) underwent bariatric surgery (gastric sleeve and not specified, respectively). A reduction in normal morphology was identified on semen analysis performed 1–1.5 years following bariatric surgery

(31% reduced to 18% and 25% with subsequent azoospermia, respectively) (Lazaros et al., 2012). In a series by Gao et al. (2024), 34 Chinese men (BMI 37.4 kg/m² [3.64]) underwent laparoscopic sleeve gastrectomy with serial semen analyses performed over the following 12 months. Normal morphology was not reported, however, the proportion of neck/middle segment deformities increased in the first 3 months following surgery, with subsequent reduction to below pre-surgical rates by 12 months post-operatively (Gao et al., 2024).

Sperm DNA damage

Sperm DNA damage was reported in five studies (Samavat et al., 2018; Carette et al., 2019; Wood et al., 2020; Fariello et al., 2021; Miñambres et al., 2022). The method of sperm DNA damage analysis varied between studies; and included terminal uridine nick end labelling (TUNEL) assay (Samavat et al., 2018; Carette et al., 2019), comet classification (Wood et al., 2020; Fariello et al., 2021) and sperm chromatin dispersion test (Miñambres et al., 2022). A meta-analysis was possible of the TUNEL and sperm chromatin dispersion test outcomes (Fig. 2E, $n = 81$). Included studies involved a mix of RYGB and SG interventions. The random effects model identified no association between bariatric surgery and change in sperm DNA damage (MD = -1.89%, 95% CI = [-13.68, 9.90], $P = 0.75$). No evidence of publication bias was identified (Egger's test $P = 0.943$). A significant degree of heterogeneity was observed ($I^2 = 92.8\%$). Due to the small sample size, analysis by type of surgical intervention was not performed.

Two studies were unable to be incorporated into the meta-analysis as DNA damage was assessed via Comet classification (Visual assessment of fragmentation) (Wood et al., 2020; Fariello et al., 2021). In a study of 18 men [BMI median 43.9 kg/m² (IQR 11.60)], the proportion of sperm with Comet class 1 (high DNA integrity) increased 6 months following bariatric surgery (mix of RYGB and SG) as compared to pre-operative assessment [Pre: 12.5% (19), Post: 30.5% (33)] (Wood et al., 2020). In a second study of 15 men [BMI mean 45.7 kg/m² (SD 8.3)], a similar increase in Comet class 1 sperm occurred 12 months following RYGB [Pre 24% (3.7), Post 47.3% (5.5)]. (Fariello et al., 2021).

Lipid peroxidation

Lipid peroxidation was reported in a cohort of 15 men [BMI 45.7 kg/m² (SD 8.3)] undergoing RYGB. There was a reduction in malondialdehyde concentration 12 months following bariatric surgery [pre: concentration 27.9 ng/ml (4.3), post: 14 ng/ml (3)] (Fariello et al., 2021).

Conception rate and assisted reproduction outcomes

Conception outcomes were reported in three case reports (Lazaros et al., 2012; Sermondade et al., 2012; Razzaq et al., 2021). A total of seven men, four of which had previously fathered children, developed infertility following bariatric surgery (either RYGB or SG) with post-operative follow-up ranging from 1 to 4 years. A total of three men across two of these series underwent ICSI, however, conception was not achieved (Lazaros et al., 2012; Sermondade et al., 2012).

Assisted reproduction outcomes were reported in one additional study of 35 men [BMI 39.56 kg/m² (1.51)] with idiopathic infertility who underwent assisted reproduction prior to and 6 months after laparoscopic sleeve gastrectomy (Velotti et al., 2021). An increase in top-quality embryos, implantation rate and pregnancy rate occurred post-operatively. However, this finding is confounded by concurrent increases in top-quality oocytes and number of fertilized oocytes in the post-operative collection,

which is unlikely to be solely due to paternal bariatric surgery (Velotti et al., 2021).

Weight loss pharmacotherapy

Pharmacotherapy targeted for weight loss or as an insulin sensitizer was assessed in a total of one sub-study of a randomized control trial (Andersen et al., 2022), three pre-post studies without controls (Morgante et al., 2011; Raghif, 2015; La Vignera et al., 2023) and one case report (Fontoura et al., 2014) with a total of 119 patients (Table 2). Two agents, metformin and liraglutide, were assessed and discussed individually.

Metformin

Metformin was assessed in two quasi-experimental studies ($n = 63$) (Morgante et al., 2011; Raghif, 2015). In the first study of 45 men with overweight/obesity [BMI 28 kg/m^2 (3.5)], 6 months of maximally tolerated metformin was associated with improvements in sperm concentration [$16.2 \times 10^6/\text{ml}$ (3.4) vs $20.0 \times 10^6/\text{ml}$ (4.2)], progressive motility [39% (8) vs 51% (7)] and normal morphology [25% (3) vs 30% (2)] without change in semen volume (results not reported) or BMI [post: 27.3 kg/m^2 (3.1)] (Morgante et al., 2011). In the second study of 18 men with obesity [35.93 kg/m^2 (5.7)], 3 months of maximally tolerated metformin was associated with a reduction in sperm concentration [$19.0 \times 10^6/\text{ml}$ (14.5) vs $16.1 \times 10^6/\text{ml}$ (13.8)] without change in semen volume [3.04 ml (1.12) vs 3.08 ml (0.93)] or normal morphology [62.1% (11.0) vs 64.6% (5.0)] (Raghif, 2015). The mean BMI was reduced by $\sim 1 \text{ kg}$ following metformin use (post-weight 34.85 kg/m^2 (5.2). Specialized sperm parameters, conception rates or assisted reproduction outcomes were not reported in either study.

A meta-analysis was performed where data were suitable from both studies, acknowledging that a meta-analysis of two small studies has limited representative capacity. Random effect meta-analysis (Fig. 3A, $n = 63$) identified no changes in sperm concentration following metformin use (MD = 1.28 ml/ml, 95% CI = [-5.07, 7.62], $P = 0.69$), with a high degree of heterogeneity ($I^2 = 74.2\%$). Random effects meta-analysis (Fig. 3B, $n = 63$) identified an increase in sperm normal morphology following metformin use (MD = 4.40, 95% CI = [1.94, 6.86], $P = 0.001$) with moderate heterogeneity ($I^2 = 33.6\%$). Due to study limitations, observational studies and limited sample size, GRADE Quality of assessment rating was 'Very Low' for meta-analysis outcomes (Supplementary Table S8).

Liraglutide

Liraglutide was assessed in one quasi-experimental pre-post study without control arm (La Vignera et al., 2023), one sub-study of a randomized controlled trial (Andersen et al., 2022) and one case report ($n = 56$) (Fontoura et al., 2014). Follow-up duration ranged from 4 to 12 months, and JBI Critical Appraisal scores were 7/9 (La Vignera et al., 2023), 10/13 (Andersen et al., 2022) and 8/8 (Fontoura et al., 2014) (Table 2, Supplementary Table S5). Mean pre-intervention BMI ranged from 31.6 to 36 kg/m^2 . Mean BMI change ranged from +1 to -6 kg/m^2 , noting that the two arms of the study by Andersen et al. (2022) utilized liraglutide following 8 weeks VLED which may mask weight loss potency of liraglutide alone. The primary limitation was a lack of repeated measurement of outcome variables in both cases.

The first study is a subgroup analysis of the S-Lite randomized control trial, where participants underwent an 8-week VLED with subsequent random allocation to one of four groups (exercise [$n = 9$], liraglutide [$n = 9$], liraglutide and exercise [$n = 13$] or control [$n = 8$]) for extended weight maintenance over 52 weeks with semen analysis before VLED, before randomization and after

weight maintenance (Andersen et al., 2022). RoB2 critical appraisal assessment identified 'some concerns' related to Domain two and five (Supplementary Table S7).

Mean pre-commencement BMI ranged from 35.76 to 38.2 kg/m^2 , and significant weight loss occurred following VLED resulting in mean pre-randomization BMI ranging from 30.8 to 32.4 kg/m^2 . Statistical analysis examined changes dependent on degree of weight loss maintained rather than specific intervention provided; identifying that sperm concentration increased in those who maintained a $>11.7 \text{ kg}$ weight loss over the entire trial (1.71-fold increase, 95% CI [1.22–3.18], $P < 0.05$). No changes in semen volume, sperm concentration or motility were identified. Intervention arm-based outcomes were available in supplementary data, and in both the liraglutide ($n = 7$) and liraglutide and exercise ($n = 13$) cohorts, no change in BMI occurred over the 52-week weight maintenance period. Liraglutide use was not associated with changes in semen volume or sperm concentration. Sperm progressive motility was not assessed; however, sperm total motility also did not change in either cohort.

The second study assessed the effect multiple pharmacotherapies (urofillotropin [$n = 35$], maximally tolerated liraglutide [$n = 35$], transdermal testosterone [$n = 40$]) in men with obesity for 4 months (La Vignera et al., 2023). In the Liraglutide cohort [BMI 36 kg/m^2 (3)], liraglutide use was associated significant weight reduction to 30 kg/m^2 (2) with an increase in sperm concentration (mean $6 \times 10^6/\text{ml}$ vs $16 \times 10^6/\text{ml}$, $P < 0.05$), progressive motility [14% (2) vs 35% (4)] and normal morphology (mean 4% vs 10%, $P < 0.05$).

A meta-analysis was performed where data were suitable from both studies, again acknowledging that meta-analysis of two studies has limited representative capacity. In this section, Andersen (1) refers to the S-Lite subgroup who underwent the liraglutide intervention ($n = 7$), whereas Andersen (2) refers to the subgroup who underwent liraglutide and exercise intervention ($n = 13$). Regarding sperm concentration, the random effects meta-analysis (Fig. 3C, $n = 55$) identified moderate heterogeneity ($I^2 = 38.1\%$) and no change in sperm concentration in response to treatment with liraglutide (MD = 0.58 ml/ml, 95% CI = [-24.76, 25.91], $P = 0.96$). GRADE Quality of assessment rating was 'Very Low' (Supplementary Table S8).

The single case report describes a man with obesity (weight 100 kg) who was undergoing an infertility assessment (Fontoura et al., 2014). Serial semen analysis identified a gradual onset of azoospermia occurring ~ 5 months following commencement of liraglutide 0.6 mg daily. Liraglutide was ceased at this time, and three serial semen analyses performed over the following 5 months showed incremental partial recovery of sperm concentration. No significant changes in semen volume or sperm motility occurred over this period, although sperm normal morphology did not recover (8% initial vs 2.5% 5 months post-cessation). ICSI was performed 5 months following liraglutide cessation and a successful twin pregnancy occurred.

Lifestyle intervention (diet/exercise)

Lifestyle interventions were assessed in five randomized controlled trials (Rafiee et al., 2016; Rosety et al., 2017; Mombeyni et al., 2021; Ismail et al., 2023; Sharma et al., 2024), one sub-study of a randomized controlled trial (with two components, an initial pre-post study followed by the randomized intervention) (Andersen et al., 2022), three pre-post studies without control arms (Håkonsen et al., 2011; Jaffar and Ashraf, 2017; Mir et al., 2018) and one case series (Faure et al., 2014) with a total of 319 participants (Table 3). Only one study was found to have

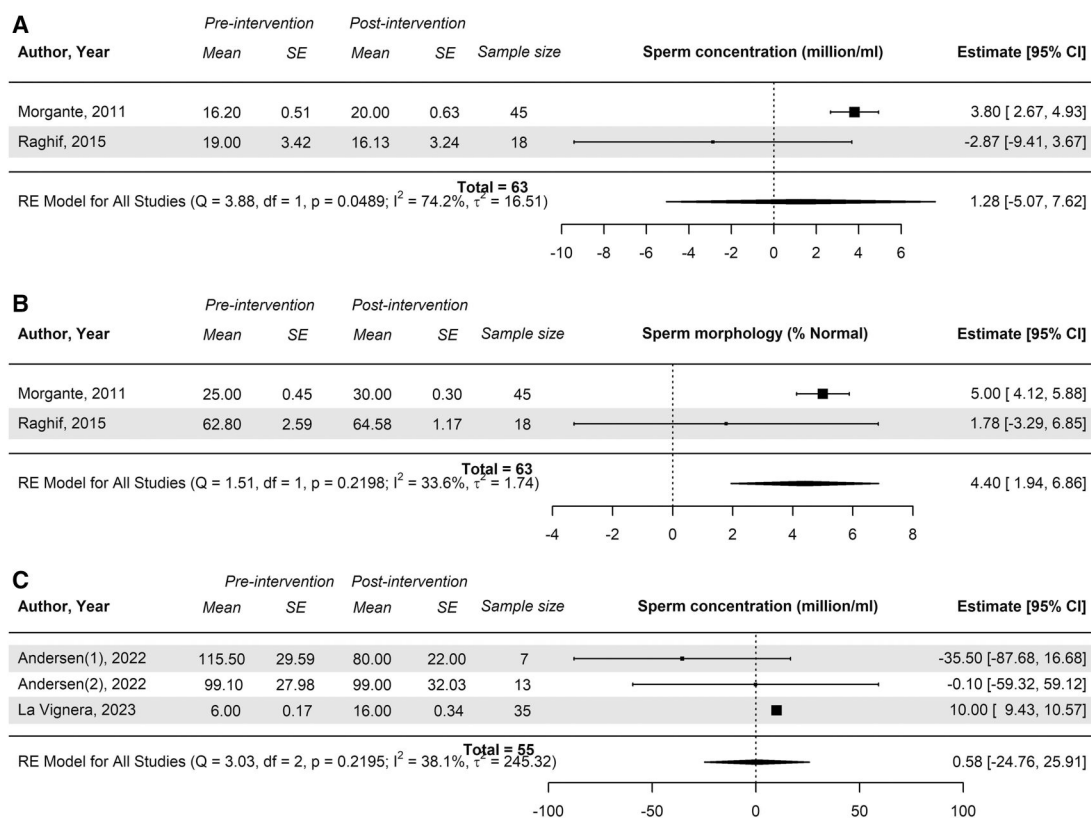


Figure 3. Meta-analysis forest plots of semen parameters in relation to weight loss pharmacotherapy use interventions. (A) Sperm concentration following metformin, (B) Sperm normal morphology following metformin, (C) Sperm concentration following liraglutide. SE, standard error of the mean, RE, random effects, FE, fixed effects, Q, Cochran's Q statistic, df, degrees of freedom, I², I² heterogeneity statistic, τ^2 , τ^2 variance statistic.

prospective registration with an established trial registry (Andersen et al., 2022).

Randomized controlled trials and intervention-control meta-analyses

A total of six parallel arm randomized controlled trials were performed examining lifestyle interventions, five of which examined varying exercise interventions (Rafiee et al., 2016; Rosety et al., 2017; Mombeyni et al., 2021; Andersen et al., 2022; Ismail et al., 2023), and one examined dietary optimization (Sharma et al., 2024). All studies had varying degrees of biases resulting in mean JBI Critical Appraisal assessment of 7.5/13 (Supplementary Table S6) and RoB2 scores ranging from 'some concerns' to 'high risk' (Supplementary Table S7). Duration of interventions ranged from 3 to 12 months. Due to limitations in study design and sample size, GRADE Quality of assessment rating of 'Low' for meta-analysis outcomes (Supplementary Table S8).

Meta-analysis forest plots are shown in Fig. 4A–D. Each included study had small sample sizes, with total participants in each arm (intervention/control) ranging from 32 to 53 participants. No heterogeneity was identified for meta-analyses of semen volume (I²=0%). Fixed effects model identified no association between lifestyle intervention and changes in semen volume (MD=0.03 ml, 95% CI=[0.12, 0.18] P=0.7), with no evidence of publication bias identified (Egger's test P=0.21). A high degree of heterogeneity was observed in meta-analyses of sperm concentration, progressive motility and normal morphology (I²=51.9%, 89.4% and 85.3%, respectively). Random effects meta-analysis identified no change in sperm concentration (MD 6.66 ml/ml, 95% CI=[−7.21, 20.53], P=0.35) or sperm progressive motility (MD=9.24%, 95% CI=[−1.94, 20.41], P=0.11) with no

evidence of publication bias (Egger's test P=0.54 and P=0.84, respectively). Random effects meta-analysis also identified no change in sperm normal morphology (MD=4.77%, 95% CI=[−4.67, 14.20], P=0.32).

Two trials presented data not suitable for meta-analysis (Rafiee et al., 2016; Rosety et al., 2017).

In first, sperm quality was assessed in men randomly allocated to either a 6-month intensive exercise program or vitamin C supplementation. Significant qualitative concerns are present including unclear control cohort, unclear sample size and incomplete participant demographics, resulting in a RoB2 assessment identified 'high risk' (Supplementary Table S7). Outcomes were categorized based on baseline BMI categorization. Following an exercise intervention, an increase in semen volume (2.64 ml (3.15) vs 3.52 ml (3.51)), sperm concentration (48.5×10⁶/ml (1.95) vs 55.8×10⁶/ml (2.13)) and normal morphology (40.2% vs 58.1%) was identified in men who were overweight at baseline. Similar improvements in semen volume (1.8 ml (2.95) vs 2.85 ml (3.1)), sperm concentration (35.3×10⁶/ml (2.11) vs 48.9×10⁶/ml (3.11)) and normal morphology (28.2–35%) occurred in men with obesity (Rafiee et al., 2016). Demographic data comparing the control cohort to exercise intervention cohort was not reported. Comparison of outcomes between the control and intervention arm was not available.

The second study involved 90 men with obesity (BMI 31.2 kg/m² (1.1)) randomized to either a 16-week aerobic training program or no intervention. RoB2 assessment identified 'some concerns' in domains one, two and five. No significant change in semen volume was identified following the intervention (median [5th, 95th percentile]—2.81 mls [0.89, 6.2] vs 2.92 mls [1.12, 6.5], P=0.18) (Rosety et al., 2017). Increases in sperm concentration

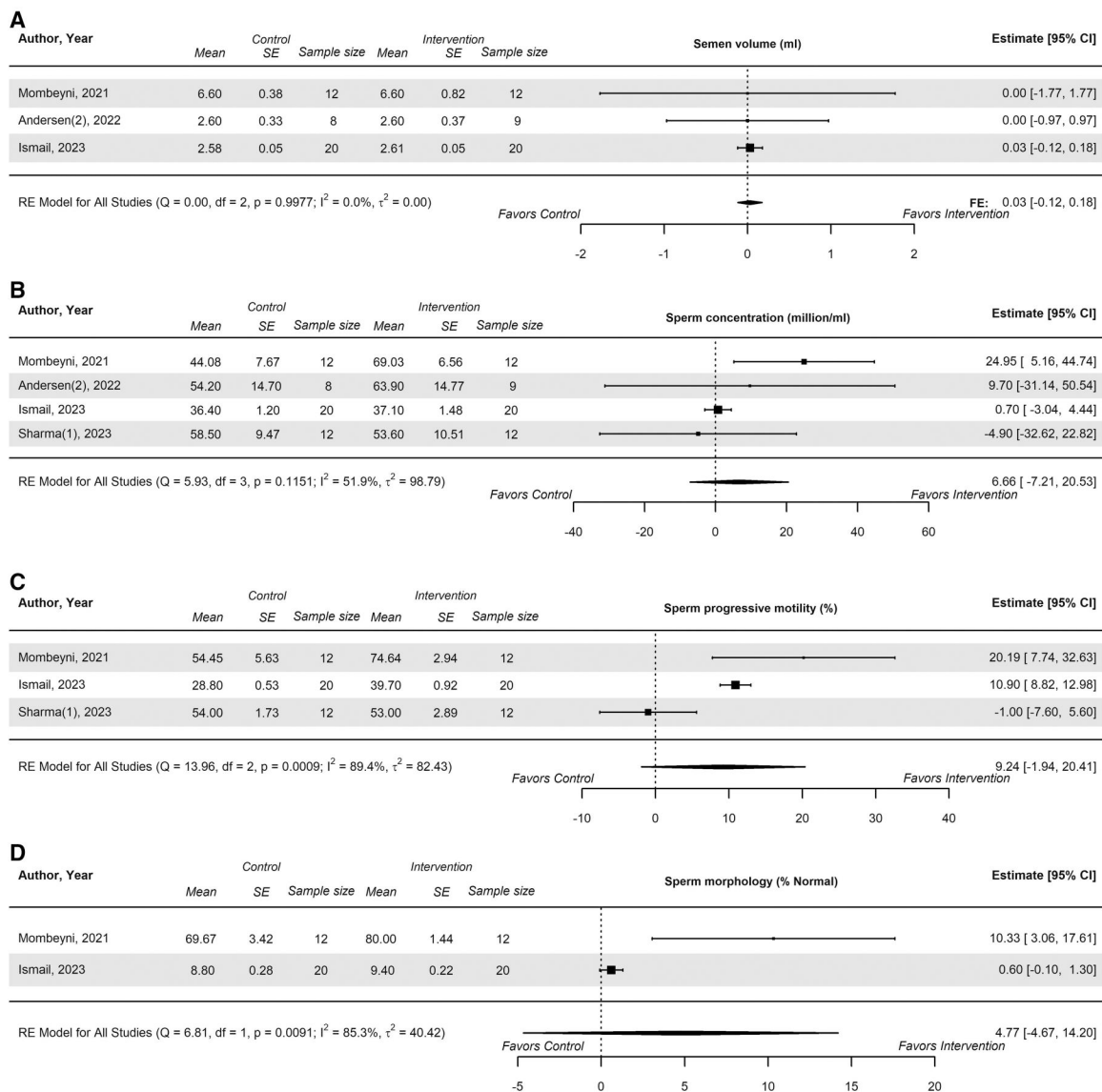


Figure 4. Meta-analysis forest plots of semen parameters comparing lifestyle intervention versus placebo in parallel arm randomized controlled trials. (A) Semen volume, (B) Sperm concentration, (C) Sperm progressive motility, (D) Sperm normal morphology. SE, standard error of the mean, RE, random effects, FE, fixed effects, Q, Cochran's Q statistic, df, degrees of freedom, I^2 , I^2 heterogeneity statistic, τ^2 , τ^2 variance statistic.

(45 mil/ml [4.70, 296.4] vs 48.8 mil/ml [5.3–312.8] $P=0.04$), progressive motility (42.6% [9.0, 56.8] vs 46.2% [10.2, 60.0], $P=0.02$) and normal morphology (21% [2.70, 61.8] vs 23.3% [3.9, 64.6], $P=0.03$) were identified following the exercise intervention (Rosety et al., 2017). Both the control and intervention cohorts were similar at baseline (age, BMI, high-density lipoprotein concentration, triglyceride concentration, glycaemia, energy intake). Analyses only examined pre-post differences within the same cohort, and no changes in sperm parameters in the control cohort were identified.

Observational studies and pre-post meta-analyses

Mean pre-intervention BMI of observational studies ranged from 30.58 to 45.33 kg/m², and when reported, mean weight change ranged from +1 to –5 kg/m². Mean JBI Critical Appraisal assessments were 5.67/9 for quasi-experimental studies and 7/10 for the case series (Supplementary Table S6). Consistent qualitative limitations of quasi-experimental studies included lack of suitable control and lack of multiple measures. Types of

interventions included healthy dietary changes, exercise, VLED, or a combination. Duration of interventions ranged from 2 to 12 months, although most were less than 6 months. Limitations in study design and likely insufficient sample size again resulted in a GRADE Quality of assessment rating was 'Low' for meta-analysis outcomes (Supplementary Table S8).

Outcomes from one observational study were presented in a manner not suitable for incorporation to any meta-analysis (Håkonsen et al., 2011). A narrative review of this study occurs following meta-analysis results. Two studies utilized the same cohort of patients and have been amalgamated for the purposes of meta-analysis (Jaffar and Ashraf, 2017; Mir et al., 2018). The study by Andersen et al. (2022) had two components that were assessed separately; an initial weight loss intervention via a VLED for 2 months, followed by randomization into four groups (exercise, liraglutide, both or control), for which the exercise cohort is assessed in this section. Andersen (1) will refer to the initial pre-post VLED intervention (Weeks 0–8), whereas Andersen (2) will refer to the subsequent 'exercise' randomized subgroup

(Weeks 8–60). Similarly, Sharma (1) refers to the cohort with normozoospermia within the Sharma et al. (2024) study, whereas Sharma (2) refers to the cohort with oligozoospermia.

Semen volume

Semen volume was assessed before and after a lifestyle intervention in seven studies (Håkonsen et al., 2011; Rafiee et al., 2016; Rosety et al., 2017; Mir et al., 2018; Mombeyni et al., 2021; Andersen et al., 2022; Ismail et al., 2023), of which four studies were suitable for meta-analysis (Fig. 5A, $n = 193$) (Mir et al., 2018; Mombeyni et al., 2021; Andersen et al., 2022; Ismail et al., 2023). No heterogeneity was observed ($I^2 = 0\%$). Fixed effects model identified no association between lifestyle intervention and change in semen volume (MD = 0.07 ml, 95% CI = [−0.03, 0.16], $P = 0.17$). Egger's test did not identify evidence of publication bias ($P = 0.33$).

Sperm concentration

Sperm concentration was assessed before and after a lifestyle intervention in eight studies (Håkonsen et al., 2011; Rafiee et al., 2016; Rosety et al., 2017; Mir et al., 2018; Mombeyni et al., 2021; Andersen et al., 2022; Ismail et al., 2023; Sharma et al., 2024), of which five were suitable for meta-analysis (Fig. 5B, $n = 205$) (Mir et al., 2018; Mombeyni et al., 2021; Andersen et al., 2022; Ismail et al., 2023; Sharma et al., 2024). There was no evidence of publication bias (Egger's Test $P = 0.44$) and low heterogeneity ($I^2 = 23.64\%$). The fixed effects model identified no association between lifestyle intervention and change in sperm concentration (MD = 1.29 mil/ml, 95% CI = [−1.03, 3.61], $P = 0.26$). There was no detectable association of effect of change in BMI with change in sperm concentration (MD = −2.06 mil/ml, 95% CI = [−5.73, 1.61], $P = 0.27$). Graphical representation of weight loss and semen volume is shown in Supplementary Fig. S5A.

In the subgroup with oligozoospermia of Sharma et al. (2024) ($n = 43$) the median (IQR) was reported before and after a 16-week VLED. No significant change in sperm concentration was identified after the dietary intervention [pre: 5.6 mil/ml (6.0), post: 3.4 mil/ml (13.1)] (Sharma et al., 2024).

Sperm progressive motility

Progressive motility was assessed in six studies (Faure et al., 2014; Rosety et al., 2017; Mir et al., 2018; Mombeyni et al., 2021; Ismail et al., 2023; Sharma et al., 2024), of which five were suitable for meta-analysis ($n = 155$, Fig. 5C) (Faure et al., 2014; Mir et al., 2018; Mombeyni et al., 2021; Ismail et al., 2023; Sharma et al., 2024). There was neither publication bias Egger's test ($P = 1.0$) or heterogeneity ($I^2 = 0\%$). The fixed effects model identified a positive association between lifestyle intervention and progressive motility (MD = 10.6%, 95% CI = [8.97, 12.15], $P < 0.001$). There was no effect of change in BMI on change in progressive sperm motility (Supplementary Fig. S5B).

In the subgroup of Sharma et al. (2024) with oligozoospermia ($n = 43$) the median (IQR) was reported before and after a 16-week VLED. An increase in sperm progressive motility was identified after the dietary intervention [pre: 28.7% (23), post: 44% (25)] (Sharma et al., 2024).

Normal sperm morphology

Normal morphology was assessed in seven studies (Håkonsen et al., 2011; Faure et al., 2014; Rafiee et al., 2016; Rosety et al., 2017; Mir et al., 2018; Mombeyni et al., 2021; Ismail et al., 2023), of which four studies were suitable for meta-analysis (Fig. 5D, $n = 143$) (Faure et al., 2014; Mir et al., 2018; Mombeyni et al., 2021; Ismail et al., 2023). There was no evidence of publication bias (Egger's

test $P = 0.21$), nor heterogeneity ($I^2 = 0\%$). The fixed effects model identified a positive association between lifestyle intervention and normal sperm morphology (MD = 0.59%, 95% CI = [0.23, 0.94], $P = 0.001$).

Sperm DNA damage

Sperm DNA damage was reported in four studies (Håkonsen et al., 2011; Mir et al., 2018; Ismail et al., 2023; Sharma et al., 2024) and one case series (Faure et al., 2014). Differing methods of assessing sperm DNA damage or fragmentation were performed, including TUNEL assay (Faure et al., 2014; Sharma et al., 2024), sperm chromatin dispersion test (Mir et al., 2018; Ismail et al., 2023) and sperm chromatin structure assay (Håkonsen et al., 2011). Four studies were suitable for meta-analysis ($n = 143$, Fig. 5E) (Faure et al., 2014; Mir et al., 2018; Ismail et al., 2023; Sharma et al., 2024). There was no publication bias (Egger's test $P = 0.409$) and a high degree of heterogeneity was identified ($I^2 = 98.3\%$). The random effects model identified no reduction in sperm DNA damage following a lifestyle intervention (MD = −6.95%, 95% CI = [−16.05, 2.15], $P = 0.13$).

Reactive oxygen species

In the Sharma et al. cohort with oligozoospermia, ROS was measured by a chemiluminescence assay utilizing luminol. The degree of ROS luminescence increased following a 12-week VLED and 4-week food reintroduction phase (median [IQR] relative light units—pre: 8.5 [171.5], post: 13.02 [36.14]) (Sharma et al., 2024).

Conception rate and assisted reproduction outcomes

A single case series assessed conception rates before and after a lifestyle intervention. 15 infertile men from the ALIFERT cohort met the inclusion criteria of: non-smoking, DNA fragmentation >25%, abdominal fat >4 measured by impedance, and in an established relationship. Eight of the men agreed to participate in a dietary program involving a complete nutritional assessment and advice based on the French national nutrition and health programme. All eight men who participated in the program achieved pregnancy within 8 months of the intervention. Comparatively, only one of the seven men who did not participate in the dietary program achieved pregnancy (although time-frame for follow-up is unclear) (Faure et al., 2014).

Narrative review of study not suitable for meta-analysis

A single observational study reported findings in a manner not suitable for incorporation into aforementioned meta-analyses (Håkonsen et al., 2011). In this study, men with obesity ($n = 43$ at enrolment, 26 at completion, BMI median 44 kg/m²), underwent a 14-week healthy diet and exercise program with serial monitoring of sperm parameters before and after the intervention. The change in sperm parameters was reported in relation to tertile of weight loss (Tertile A: 3.5–12.1%; Tertile B 12.1–17.1%; Tertile C: 17.2–25.4%). An increase in normal morphology was identified only in the men achieving the greatest weight loss (Tertile 3: mean increase 4%, 95% CI [1,7]). No changes in semen volume, sperm concentration, or sperm DNA damage irrespective of degree of weight lost were detected (Håkonsen et al., 2011).

Discussion

This review is the first comprehensive systematic review and meta-analysis of various methods of weight loss on fertility parameters in men with obesity. Our review assessed several measures of fertility and identified that current data involve multiple small sample size studies that are highly heterogeneous

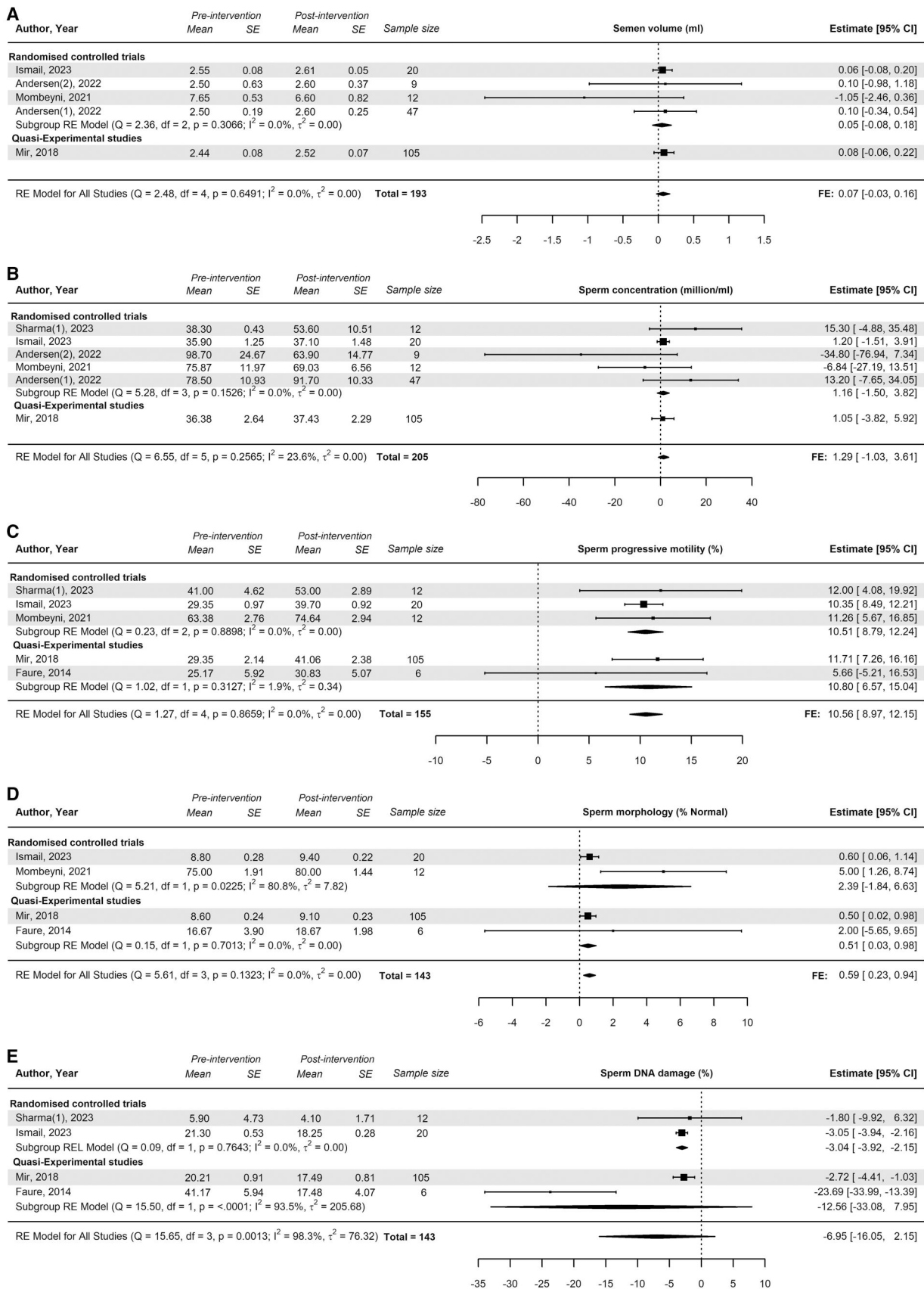


Figure 5. Meta-analysis forest plots of semen parameters in relation to lifestyle interventions. (A) Semen Volume, (B) Sperm concentration, (C) Sperm progressive motility, (D) Sperm normal morphology, (E) Sperm DNA damage. SE, standard error of the mean, RE, random effects, FE, fixed effects, Q, Cochran's Q statistic, df, degrees of freedom, I², I² heterogeneity statistic, τ^2 , τ^2 variance statistic.

in terms of participant demographics, intervention performed, and outcomes assessed. Both pre-commencement BMI and degree of weight loss were substantially different between each type of intervention in this analysis, with those undergoing bariatric surgery having on average higher BMI and greater weight loss compared to other modalities. Greater BMI is associated with an increased frequency of medical comorbidities (Liu et al., 2021; Kivimäki et al., 2022), which may affect the efficacy of individual interventions. As such, comparison of efficacy between interventions is not possible, and findings of the review are limited to the cohort BMI examined. In most cases, semen parameters are assessed as a surrogate marker for fertility, while data related to conception and assisted reproduction outcomes are limited.

Our meta-analyses of semen parameters are consistent with recent meta-analyses identifying the absence of significant sperm parameter changes following bariatric surgery (Lee et al., 2019; Al Qurashi et al., 2022; Gao et al., 2022), while incorporating additional prospective studies (Aboulghar et al., 2016; Miñambres et al., 2022). Post hoc meta-regression was performed due to high degrees of heterogeneity identified differing reproductive outcomes dependent on the type of surgery performed, although interpretation is limited by the need for a 'mixed' cohort as many different procedures outcomes were reported together in multiple studies (Carette et al., 2019; Calderón et al., 2020; Wood et al., 2020; Miñambres et al., 2022; Javani et al., 2023). This review is also the first to systematically assess the effect of bariatric surgery on sperm DNA damage, and while our meta-analysis did not identify a change in DNA damage, the small sample size and inability to incorporate studies utilizing the visualization method of assessment necessitate further assessment (Wood et al., 2020; Fariello et al., 2021). Sperm DNA damage is associated with higher rates of miscarriage, poorer embryo implantation and lower ART pregnancy rates (Agarwal et al., 2019; Ribas-Maynou et al., 2021; Lourenço et al., 2023), as such clearly establishing the impact of bariatric surgery is necessary while data regarding direct conception outcomes are limited. Data regarding conception outcomes are limited primarily to case reports and case series, with multiple reports of detrimental fertility outcomes following bariatric surgery.

Chronic obesity related disorders such as OSA or diabetes mellitus have independent adverse effects on sperm quality (Peel et al., 2023). Intermittent hypoxia in animal models (Torres et al., 2014; Wang et al., 2020) and OSA in humans (Kyrou et al., 2022; Alvarenga et al., 2023; Wang et al., 2023) cause reductions in sperm count and motility, increased sperm DNA damage and infertility. The severity of OSA, defined as the apnoea hypopnoea index, correlates with degree of impairment (Wang et al., 2023). Men with diabetes mellitus also have sperm dysfunction characterized by reductions in normal morphology and motility (Imani et al., 2021; Facondo et al., 2022; Lotti and Maggi, 2023), and animal models of both Type 1 (autoimmune insulin deficiency) and Type 2 diabetes mellitus (insulin resistance and metabolic dysfunction) reveal testicular microarchitectural disruption and increased seminal reactive oxygen species, DNA damage and apoptotic pathways (Shrilatha and Muralidhara, 2007; Mangoli et al., 2013; Zhu et al., 2019; Omolayo and Du Plessis, 2021; Wang et al., 2021), mitigated by reduction in hyperglycaemia by insulin administration (Zhu et al., 2019). Bariatric surgery is associated with profound improvements in metabolic comorbidities of obesity including functional hypogonadism, steatotic liver disease, dyslipidaemia, diabetes mellitus, hypertension, and obstructive sleep apnoea (Arterburn et al., 2020; Courcoulas et al., 2023). The lack of change in sperm quality despite resolution of these

comorbidities suggests factors unrelated to adiposity likely also contribute to impaired sperm and reproductive capacity in these men.

A likely factor contributing to sperm dysfunction is nutritional insufficiency, which is common in men requiring bariatric surgery both preoperatively (Krzizek et al., 2018; Mohapatra et al., 2020; González-Sánchez et al., 2023) and post-operatively (Weng et al., 2015; Mohapatra et al., 2020; Ha et al., 2021; Gasmi et al., 2022; Cao et al., 2023; González-Sánchez et al., 2023). While micronutrient supplementation is standard of care, adherence to supplementation is often limited (Ha et al., 2021). In men requiring bariatric surgery, nutritional deficiencies such as zinc, iron, and copper) have been associated with detrimental changes in sperm parameters (Calderón et al., 2020). Additionally, supplementation of various micronutrients (in non-bariatric surgery cohorts) (e.g. antioxidants, Ω -3 fatty acids, Vitamin C, Vitamin E) has also been associated with improvements in sperm parameters (Su et al., 2022; Zhou et al., 2022; Chen et al., 2023). The degree of nutritional insufficiency varies depending on the type of surgery performed (Vix et al., 2014; Salminen et al., 2022; Steenackers et al., 2023), which is consistent with our post hoc analysis finding that correction for type of surgery significantly reduced heterogeneity of sperm quality outcomes.

A second hypothesis to explain the lack of sperm improvement following bariatric surgery is due to increased exposure to endocrine-disrupting chemicals (EDCs) (Magalhaes et al., 2022). EDCs are environmental molecules that disrupt normal endocrine function (Heindel and Blumberg, 2019; Lahimer et al., 2023). Due to their lipophilic nature, they become concentrated in adipose tissue, and serum concentrations increase following significant weight loss (Hue et al., 2006; Kim et al., 2011). Exposure to some EDCs such as dichloro-diphenyl-dichloroethylene has been cross-sectionally associated with changes in basic sperm parameters and DNA fragmentation (Magalhaes et al., 2022). The consistent increase in serum LH and testosterone concentration following bariatric surgery (Lee et al., 2019; Moxthe et al., 2020), and the lack of relationship between change in sperm parameters to degree of weight lost argue against EDC exposure as a major factor causing infertility post-bariatric surgery.

The limited assessment of pregnancy outcomes identified in this review hampers stratification of reproductive risk; however, repeated reports of azoospermia suggest reproductive complications are not infrequent (Lazaros et al., 2012; Sermondade et al., 2012; Razzaq et al., 2021). Current guidelines suggest delaying pregnancy by 12–18 months following female bariatric surgery due to antenatal and perinatal risks (ACOG Committee Opinion No. 549: Obesity in Pregnancy, 2013; Busetto et al., 2017). Establishing the timing, mechanism, and degree of effect on sperm is necessary to establish similar male recommendations.

Data relating to the effect of weight loss medications on male reproductive outcomes are sparse and at least insofar as criteria for inclusion, identified studies only related to metformin and liraglutide. The effect of other weight loss pharmaceutical may not have been captured by the search criteria, and the effect of these agents cannot be commented on. Additionally, within the study (Andersen et al., 2022) pharmacotherapy use was preceded by an 8-week VLED with resultant substantial weight loss, which likely confounds attempts to elucidate the effects of liraglutide alone. Fixed effects models identified minor positive effect of both metformin (normal morphology) and liraglutide (sperm concentration), however, the number of studies and sample size limiting the generalizability of data.

The limited changes identified for men with obesity are consistent with studies of metformin and GLP-1 agonists across different cohorts. A single study of 15 men with hyperinsulinemia (weight not specified) provided with a multivitamin and metformin therapy showed a minor improvement normal morphology (Bosman *et al.*, 2015). Further, Dulaglutide use in 13 men with normal weight for 4 weeks was associated with no change in sperm parameters (Lengsfeld *et al.*, 2024). A study of 13 men with obesity aged 46–60 years treated with Semaglutide and an increased protein low-carbohydrate diet for 6 months was excluded from inclusion due to the reproductive age limitation. On average, these men had 16 kg weight reduction and normal sperm morphology increased from 2% to 4% (Gregorič *et al.*, 2025). Notably, the effect of isolated GLP-1 agonist-associated weight loss on male fertility in men with obesity is limited primarily to two studies (La Vignera *et al.*, 2023; Gregorič *et al.*, 2025), highlighting a knowledge gap requiring further investigation (Du Plessis *et al.*, 2024).

The seminal concentration of metformin induced by therapeutic metformin use is unclear, however, *in vitro* incubation of sperm with metformin shows benefits to capacitation and sperm function at low concentration, while impairing sperm function at higher (100× larger) concentrations (Calle-Guisado *et al.*, 2019; Yang *et al.*, 2020). Metformin use in obese animal models shows improvements in basic sperm parameters with concurrent reductions in testicular ROS, testicular inflammation, and sperm DNA damage (Yan *et al.*, 2015; Liu *et al.*, 2020; McPherson and Lane, 2020). Similarly, the use of a GLP-1 agonist in obese animal models is also associated with reduced testicular inflammation improvement and improvements in basic sperm parameters (Zhang *et al.*, 2015; Correia *et al.*, 2022; Attia *et al.*, 2024).

The underlying mechanism for these benefits is not established and is likely multifactorial in nature. Metformin and liraglutide both cause weight loss, with liraglutide being associated with a more prominent effect (Konwar *et al.*, 2022; Haber *et al.*, 2024). They both also improve metabolic complications of obesity such as diabetes, obstructive sleep apnoea and fatty liver disease (Armstrong *et al.*, 2016; Madsen *et al.*, 2019; Huang *et al.*, 2022; Jiang *et al.*, 2023). Additionally, the presence of GLP-1 receptors within both human and animal testis highlights possible direct effects on spermatogenesis (Caltabiano *et al.*, 2020; Rago *et al.*, 2020). Human and animal studies across multiple cohorts (e.g. without obesity, with obesity, with obesity and metabolic complications) are necessary to further delineate the precise fertility implications and elucidate the underlying mechanisms.

The single case report on pregnancy outcomes highlights that GLP-1 agonist use is not without risk (Fontoura *et al.*, 2014). While in this case, azoospermia and infertility resolved following liraglutide cessation, the underlying aetiology is not established. GLP-1 agonists have a significant adverse reaction profile characterized by nausea, vomiting and diarrhoea with a resultant high discontinuation rate (Lincoff *et al.*, 2023; Ryan *et al.*, 2024). As newer agents such as tirzepatide induce weight loss analogous to bariatric surgery (Tan *et al.*, 2023), the probability of exacerbating nutritional deficiencies also increases. Nutritional concerns already limited the use of these agents in some cohorts (Despain and Hoffman, 2024), and given the reproductive implication of nutritional deficiencies outlined above, further assessment of the nutritional implications of these agents is necessary.

Irrespective of the type of intervention, lifestyle changes broadly were effective at improving sperm quality in observational studies, with an improvement in sperm progressive motility, normal morphology and DNA damage identified in this

meta-analysis. While no benefit to sperm parameters was identified in randomized controlled trials, small sample size and qualitative limitations substantially hamper the interpretation of these findings. Larger randomized trials are necessary to adequately characterize the effect of these interventions.

Lifestyle interventions were associated with smaller volumes of weight loss compared to surgical or pharmacotherapy weight loss. Additionally, type of lifestyle intervention performed was also heterogeneous, and it is likely that differing methods have unique risks and benefits. Due to limited number in studies available, further subcategorization of lifestyle intervention was not performed. The duration of follow-up of lifestyle intervention studies was short (typically 2–4 months) indicating the rapidity with which beneficial changes can occur. Given the duration of spermatozoa formation is ~64 days (Heller and Clermont, 1963), it is likely that maximal benefit may only be determined with studies of a longer duration.

Dietary choices have significant implications for fertility. Diets with a high proportion of ultra processed foods (classically described as a 'Western diet') are obesogenic and proinflammatory (Cao *et al.*, 2017; García-Montero *et al.*, 2021), and cross-sectionally associated with poorer sperm quality and increased risk of male infertility in comparison with the 'Mediterranean diet', with limited processed food and increase fruits, vegetables, whole grains and monounsaturated fats (Karayiannis *et al.*, 2017; Salas-Huetos *et al.*, 2017, 2019; Efrat *et al.*, 2018; Cutillas-Tolín *et al.*, 2019; Ricci *et al.*, 2019; Cristodoro *et al.*, 2024). Further, consistent healthy dietary changes are also associated with improvements in sperm quality in both healthy and infertile cohorts (Caruso *et al.*, 2020; Humaidan *et al.*, 2022; Montano *et al.*, 2022), indicating inherent benefits unrelated to changes in adiposity. These benefits likely are derived from underlying dietary nutritional differences. Micronutrient deficiencies are more likely to occur with the Western Diet (Astrup and Bügel, 2019; Jiang *et al.*, 2020; Jun *et al.*, 2020), many of which are associated with impaired spermatogenesis in animal models (Tvrda *et al.*, 2015; Peng *et al.*, 2022; Pouriayevali *et al.*, 2022; Tsao *et al.*, 2022; Ren *et al.*, 2023). Differences in consumption of monounsaturated fatty acids, Ω -3 fatty acid and antioxidants can also impact on basic sperm parameters (Safarinejad *et al.*, 2010; Ferramosca *et al.*, 2017; Salas-Huetos *et al.*, 2018).

The effect of solely exercise interventions has recently been assessed by meta-analysis of randomized controlled trials, identifying similar improvements in sperm concentration, motility, count and morphology to our combined lifestyle analysis (Lo Giudice *et al.*, 2024), although meta-analyses were not limited by adiposity and were limited to two to three studies of varying durations ranging from 3 to 12 months. The beneficial effects of exercise include increased insulin sensitivity, and lowered blood glucose, improved testicular blood flow and reduced inflammation and oxidative stress (Adelowo *et al.*, 2024). The effects of differing forms of exercise (e.g. low vs high intensity, endurance vs resistance) remain to be determined (Abedpoor *et al.*, 2024).

There is insufficient data from this review to form a conclusion regarding the effect of lifestyle interventions on pregnancy outcomes. The aforementioned meta-analysis of exercise interventions did report an improvement in pregnancy rates following an exercise intervention (Lo Giudice *et al.*, 2024), however, this conclusion depended solely on three studies by Maleki *et al.* (Hajizadeh Maleki and Tartibian, 2017, 2018; Maleki and Tartibian, 2017). The reliability of these studies is uncertain, as two additional articles by the same group have been retracted

due to concerns of duplicate publication and statistical anomalies (Maleki and Tartibian, 2023, 2024).

Multiple studies are currently in progress examining the impact of paternal and maternal lifestyle interventions in infertile cohorts, which will provide much-needed guidance regarding this topic (Boedt et al., 2019; Dupont et al., 2020).

Limitations

While this review provides the most recent review of studies assessing the weight loss interventions and fertility in men with obesity, significant qualitative limitations result in GRADE quality classifications of 'very low' and 'low'. Notably, meta-analysis of randomized controlled trials could only be performed for lifestyle interventions, with qualitative limitations and small sample size greatly impacts reliability and generalizability of the findings. Significant qualitative limitations were identified including lack of or inappropriate control arms, and in the few randomized trials, unclear or lack of appropriate randomization. Where possible, these limitations were overcome by a narrative review of data not suitable for meta-analysis. Additionally, most studies (both randomized and observational) were not prospectively registered, suggesting a possibility of other unpublished, unregistered data.

While categorization by modality of weight loss is necessary due to differences in participant demographics and intervention-specific reproductive effects, this limited the sample size of each meta-analysis. Within each modality, further subcategorization is possible (e.g. type of surgery, type of lifestyle intervention) with likely differing effects, evidenced by exploratory meta-regressions which showed differing changes in sperm parameters based on the type of surgical intervention performed (RYGB vs Sleeve gastrectomy vs mixed intervention studies).

It is also possible that weight loss pharmaceutical agents beyond metformin and GLP-1 agonists have reproductive implications, however, were not captured by the search criteria and review of cited articles in all full-text articles.

As BMI is the most common measure of adiposity, it was used to define obesity in this review. It is not, however, reliable in all populations and alternative parameters such as waist circumference may be more accurate at reflecting visceral adiposity (Flegal et al., 2009; Escamilla et al., 2024). Similarly, relevant comorbidities such as diabetes or metabolic syndrome, which have independent effects on sperm quality (Zhou et al., 2020; Facondo et al., 2022), were not regularly reported and therefore could not be accounted for in this analysis. There was also significant variation in follow-up duration across studies, with surgical studies typically assessing outcomes ~6–12 months following intervention, whereas lifestyle interventions were shorter at 2–4 months following intervention commencement. Weight loss following bariatric surgery predominantly occurs in the first 3 months and plateaus at ~12 months (Xu et al., 2020; Sylivris et al., 2022) with corresponding dietary pattern changes over this timeframe (Giusti et al., 2016; Livingstone et al., 2022). While short-term negative energy balance (VLED interventions) shows beneficial sperm effects (Andersen et al., 2022; Sharma et al., 2024), it is unclear whether sperm quality changes depending on degree and duration of negative energy balance. Serial monitoring extending beyond weight stabilization is necessary to fully characterize the impact of surgical procedures. Contrastingly, longer duration of follow-up in lifestyle intervention studies is necessary due to the risk of false negative results related to the duration of spermatogenesis.

Our study did not identify a dose-dependent relationship between change in BMI and change in sperm parameters following

either bariatric surgery or a lifestyle intervention. This finding is inconsistent with a recent meta-analysis suggesting a dose-dependent benefit of weight loss for semen quality (Santi et al., 2024). There are, however, significant limitations of the previous meta-analysis, including a limited search strategy (identifying a total of 12 studies), repeated analysis of multiple study time-points and incorporation of studies from differing weight loss modalities. Further, the meta-regressions performed for 'weight loss' appear to have an erroneous interpretation as the graphical representation suggests that greater weight loss was detrimental.

Overall, the paucity of high-quality data is consistent with prior reports of reduced male reproductive research and health-care (Roudsari et al., 2023; Lyons et al., 2025). Paternal involvement in reproductive care is anticipated to improve pregnancy outcomes (Yargawa and Leonardi-Bee, 2015; Fletcher et al., 2024) and as such, identification and minimization of barriers is necessary to allow further research and improved care for couples worldwide (Roudsari et al., 2023).

Preconception health messaging

The relationship between adiposity and fertility is more nuanced than a dose-dependent effect of fat on sperm quality, with multiple contributing factors including dietary quality, nutritional status, and obesity related comorbidities. Current guidelines provide limited information regarding appropriate methods or degree of weight loss in men with obesity attempting to improve fertility, and current data are limited primarily to observational studies of small cohorts. Data suggest that lifestyle interventions may have benefit irrespective of small degrees of weight loss achieved, and that normalization of BMI is not necessary to improve sperm quality. Contrastingly, surgical interventions with potent weight loss effects have unclear/limited reproductive benefits and possible short-term detrimental effects, especially as the effect of nutritional (in)sufficiency is poorly characterized in this cohort. Similarly, marked knowledge deficits regarding the effect of GLP-1 agonists on conception require addressing due to the increasing use worldwide (Han et al., 2023; Du Plessis et al., 2024; Shareef et al., 2024; Watanabe et al., 2024).

Significant knowledge deficiencies were identified from this review, including:

- Lack of high-quality randomized controlled trials across all interventions,
- Need for more accurate measurements of adiposity beyond BMI in reproductive studies,
- Need to assess effects of individual interventions rather than combined (e.g. Roux-en-Y gastric bypass vs Gastric sleeve, specific dietary changes, specific exercise regimen),
- Need to account for the effect for confounders (nutritional sufficiency, obesity related comorbidities), and determine reversibility of these effects via differing modalities,
- Need to further characterize specialized sperm parameters such as DNA damage, lipid peroxidation or ROS across all modalities of weight loss,
- Need for further assessment of direct pregnancy outcomes including conception rate and assisted reproduction outcomes across all modalities of weight loss,
- Urgent need to establish the impact of weight loss pharmacotherapy, particularly more potent GLP-1 receptor agonists, on sperm parameters in both men with and without obesity, and
- Need for serial monitoring of sperm quality to further characterize the impact of rate of weight loss (specifically with surgery or pharmacotherapy where weight loss is more profound).

Conclusion

Despite data primarily examining sperm parameters as a surrogate for fertility outcomes, current evidence highlights likely differing reproductive implications of weight loss modalities in men with obesity. Lifestyle interventions such as dietary and exercise optimization are associated with measurable improvements in sperm quality (in observational studies) despite limited weight loss, whereas limited benefit and potential harm have been identified from medical weight loss interventions (e.g. bariatric surgery, pharmacotherapy) despite greater weight loss potential. There is a need for large, randomized studies incorporating assessment of known confounders to further elucidate potential mechanisms of fertility improvement and subsequently establish optimal preconception weight loss recommendations.

Supplementary data

Supplementary data are available at *Human Reproduction Update* online.

Data availability

Data available on request.

Authors' roles

Abstract review, full text review and data collection performed by all authors. Statistical analysis performed by A.P. and A.D.V. Manuscript written by A.P. and revised by all members.

Funding

No funding was sought for this research.

Conflict of interest

No conflict of interests exists.

References

15. Management of diabetes in pregnancy: standards of care in diabetes-2024. *Diabetes Care* 2024;**47**:S282–S294.
- Abedpoor N, Taghian F, Hajibabae F. Exploring the dynamics of exercise intensity on male fertility and reproductive health: advancements and implications for fertility research. *Front Reprod Health* 2024;**6**:1423916.
- Abouelgreed TA, Elatreisy A, El-Sherbeiny AF, Abdelaal MA, Saafan T, Shalkamy O, Farag H, Ghoneimy OM, El-Dydamony EM, Ibrahim EH et al. Long-term effect of sleeve gastrectomy surgery on hormonal profile, semen parameters and sexual functions of obese infertile men; a prospective observational study. *Basic Clin Androl* 2023;**33**:16.
- Aboughar M, Albertini DF, Allen JF, Bhattacharya S, Terralis JC, Evers JLH, Geraedts JPM, Glasier A, Hunt K, Hussein J et al. The influence of social factors on gender^{aEuro} health. *Hum Reprod* 2016;**31**:1631–1637.
- ACOG Committee Opinion No. 549: Obesity in Pregnancy. *Obstet Gynecol* 2013;**121**:213–217.
- ACOG Practice Bulletin No. 201: Pre gestational Diabetes Mellitus. *Obstet Gynecol* 2018;**132**:e228–e248.
- Adelowo OE, Akindele BM, Adegbola CA, Oyedokun PA, Akhigbe TM, Akhigbe RE. Unraveling the complexity of the impact of physical exercise on male reproductive functions: a review of both sides of a coin. *Front Physiol* 2024;**15**:1492771.
- Agarwal A, Baskaran S, Parekh N, Cho CL, Henkel R, Vij S, Arafa M, Panner Selvam MK, Shah R. Male infertility. *Lancet* 2021;**397**:319–333.
- Agarwal A, Mulgund A, Hamada A, Chyatte MR. A unique view on male infertility around the globe. *Reprod Biol Endocrinol* 2015;**13**:37.
- Agarwal A, Panner Selvam MK, Baskaran S, Cho CL. Sperm DNA damage and its impact on male reproductive health: a critical review for clinicians, reproductive professionals and researchers. *Expert Rev Mol Diagn* 2019;**19**:443–457.
- Al Qurashi AA, Qadri SH, Lund S, Ansari US, Arif A, Durdana AR, Maryam R, Saadi M, Zohaib M, Khan MK et al. The effects of bariatric surgery on male and female fertility: a systematic review and meta-analysis. *Ann Med Surg (Lond)* 2022;**80**:103881.
- Alvarenga TA, Fernandes GL, Bittencourt LR, Tufik S, Ml A. The effects of sleep deprivation and obstructive sleep apnea syndrome on male reproductive function: a multi-arm randomised trial. *J Sleep Res* 2023;**32**:e13664.
- Andersen E, Juhl CR, Kj  ller ET, Lundgren JR, Janus C, Dehestani Y, Saupstad M, Ingerslev LR, Duun OM, Jensen SBK et al. Sperm count is increased by diet-induced weight loss and maintained by exercise or GLP-1 analogue treatment: a randomized controlled trial. *Hum Reprod* 2022;**37**:1414–1422. and
- Armstrong MJ, Gaunt P, Aithal GP, Barton D, Hull D, Parker R, Hazlehurst JM, Guo K, Abouda G, Aldersley MA et al.; LEAN Trial Team. Liraglutide safety and efficacy in patients with non-alcoholic steatohepatitis (LEAN): a multicentre, double-blind, randomised, placebo-controlled phase 2 study. *Lancet* 2016;**387**:679–690.
- Arterburn DE, Telem DA, Kushner RF, Courcoulas AP. Benefits and risks of bariatric surgery in adults: a review. *Jama* 2020;**324**:879–887.
- Astrup A, B  gel S. Overfed but undernourished: recognizing nutritional inadequacies/deficiencies in patients with overweight or obesity. *Int J Obes (Lond)* 2019;**43**:219–232.
- Attia SM, Alshamrani AA, Ahmad SF, Albekairi NA, Nadeem A, Attia MSM, Ansari MA, Alqahtani F, Bakheet SA, Harisa GI. Dulaglutide rescues the elevated testicular dysfunction in a mouse model of high-fat diet-induced obesity. *Mutat Res Genet Toxicol Environ Mutagen* 2024;**898**:503805.
- Australian Government. *Your Healthy Pregnancy*. Department of Health and Aged Care, Canberra, Australian Capital Territory, Australia, 2021.
- Australian Government. *Births, Australia*. Australian Bureau of Statistics, Canberra, Australian Capital Territory, Australia, 2023.
- Australian Government. *Overweight and Obesity*. Australian Institute of Health and Welfare. Canberra, Australian Capital Territory, Australia, 2024.
- Best D, Avenell A, Bhattacharya S. How effective are weight-loss interventions for improving fertility in women and men who are overweight or obese? A systematic review and meta-analysis of the evidence. *Hum Reprod Update* 2017;**23**:681–705.
- Bhattacharya I, Sharma SS, Majumdar SS. Etiology of male infertility: an update. *Reprod Sci* 2024;**31**:942–965.
- Bj  rmdahl L, Kirkman Brown J; Other Editorial Board Members of the WHO Laboratory Manual for the Examination and Processing of Human Semen. The sixth edition of the WHO Laboratory Manual for the Examination and Processing of Human Semen: ensuring quality and standardization in basic examination of human ejaculates. *Fertil Steril* 2022;**117**:246–251.

- Boedt T, Dancet E, Lie Fong S, Peeraer K, De Neubourg D, Pelckmans S, van de Vijver A, Seghers J, Van der Gucht K, Van Calster B et al. Effectiveness of a mobile preconception lifestyle programme in couples undergoing in vitro fertilisation (IVF): the protocol for the PreLiFe randomised controlled trial (PreLiFe-RCT). *BMJ Open* 2019; **9**:e029665.
- Borges BC, Garcia-Galiano D, da Silveira Cruz-Machado S, Han X, Gavrilina GB, Saunders TL, Auchus RJ, Hammoud SS, Smith GD, Elias CF. Obesity-induced infertility in male mice is associated with disruption of *Crisp4* expression and sperm fertilization capacity. *Endocrinology* 2017; **158**:2930–2943.
- Bosman E, Esterhuizen AD, Rodrigues FA, Becker PJ, Hoffmann WA. Effect of metformin therapy and dietary supplements on semen parameters in hyperinsulinaemic males. *Andrologia* 2015; **47**:974–979.
- Boxem AJ, Blaauwendraad SM, Mulders AGMJ, Bekkers EL, Kruithof CJ, Steegers EAP, Gaillard R, Jaddoe VVW. Preconception and early-pregnancy body mass index in women and men, time to pregnancy, and risk of miscarriage. *JAMA Netw Open* 2024; **7**:e2436157.
- Busetto L, Dicker D, Azran C, Batterham RL, Farpour-Lambert N, Fried M, Hjelmæsæth J, Kinzl J, Leitner DR, Makaronidis JM et al. Practical recommendations of the obesity management task force of the European Association for the Study of Obesity for the post-bariatric surgery medical management. *Obes Facts* 2017; **10**:597–632.
- Calderón B, Gómez-Martín JM, Cuadrado-Ayuso M, Cobeta P, Vega-Piñero B, Mateo R, Galindo J, Botella-Carretero JI. Circulating zinc and copper levels are associated with sperm quality in obese men after metabolic surgery: a pilot study. *Nutrients* 2020; **12**:3354.
- Calderón B, Huerta L, Galindo J, González Casbas JM, Escobar-Morreale HF, Martín-Hidalgo A, Botella-Carretero JI. Lack of improvement of sperm characteristics in obese males after obesity surgery despite the beneficial changes observed in reproductive hormones. *Obes Surg* 2019; **29**:2045–2050.
- Calle-Guisado V, Gonzalez-Fernandez L, Martin-Hidalgo D, Garcia-Marin LJ, Bragado MJ. Metformin inhibits human spermatozoa motility and signalling pathways mediated by protein kinase A and tyrosine phosphorylation without affecting mitochondrial function. *Reprod Fertil Dev* 2019; **31**:787–795.
- Caltabiano R, Condorelli D, Panza S, Boitani C, Musso N, Ježek D, Memeo L, Colarossi L, Rago V, Mularoni V et al. Glucagon-like peptide-1 receptor is expressed in human and rodent testis. *Andrology* 2020; **8**:1935–1945.
- Campbell JE, Müller TD, Finan B, DiMarchi RD, Tschöp MH, D'Alessio DA. GIPR/GLP-1R dual agonist therapies for diabetes and weight loss—chemistry, physiology, and clinical applications. *Cell Metab* 2023; **35**:1519–1529.
- Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. *Obes Res Clin Pract* 2019; **13**:511–521.
- Cao L, Liang S, Yu X, Guan B, Yang Q, Ming WK, Chen Y. Change in mineral status after bariatric surgery: a meta-analysis. *Obes Surg* 2023; **33**:3907–3931.
- Cao Y, Wittert G, Taylor AW, Adams R, Appleton S, Shi Z. Nutrient patterns and chronic inflammation in a cohort of community dwelling middle-aged men. *Clin Nutr* 2017; **36**:1040–1047.
- Carette C, Levy R, Eustache F, Baron G, Coupaye M, Msika S, Barrat C, Cohen R, Catheline JM, Brugnon F et al. Changes in total sperm count after gastric bypass and sleeve gastrectomy: the BARIASPERM prospective study. *Surg Obes Relat Dis* 2019; **15**:1271–1279.
- Caruso P, Caputo M, Cirillo P, Scappaticcio L, Longo M, Maiorino MI, Bellastella G, Esposito K. Effects of Mediterranean diet on semen parameters in healthy young adults: a randomized controlled trial. *Minerva Endocrinol* 2020; **45**:280–287.
- Cheah S, Gao Y, Mo S, Rigas G, Fisher O, Chan DL, Chapman MG, Talbot ML. Fertility, pregnancy and post partum management after bariatric surgery: a narrative review. *Med J Aust* 2022; **216**:96–102.
- Chen Z, Hong Z, Wang S, Qiu J, Wang Q, Zeng Y, Weng H. Effectiveness of non-pharmaceutical intervention on sperm quality: a systematic review and network meta-analysis. *Aging (Albany NY)* 2023; **15**:4253–4268.
- Correia AS, Pereira SC, Morais T, Martins AD, Monteiro MP, Alves MG, Oliveira PF. Obesity-related genes expression in testes and sperm parameters respond to GLP-1 and caloric restriction. *Biomedicines* 2022; **10**:2609.
- Courcoulas AP, Daigle CR, Arterburn DE. Long term outcomes of metabolic/bariatric surgery in adults. *BMJ* 2023; **383**:e071027.
- Cristodoro M, Zambella E, Fietta I, Inversetti A, Di Simone N. Dietary patterns and fertility. *Biology (Basel)* 2024; **13**:131.
- Cutillas-Tolín A, Adoamnei E, Navarrete-Muñoz EM, Vioque J, Moñino-García M, Jørgensen N, Chavarro JE, Mendiola J, Torres-Cantero AM. Adherence to diet quality indices in relation to semen quality and reproductive hormones in young men. *Hum Reprod* 2019; **34**:1866–1875.
- De Luca M, Zese M, Silveri GA, Ragghianti B, Bandini G, Forestieri P, Zappa MA, Navarra G, Foschi D, Musella M et al. Bariatric surgery for patients with overweight/obesity. A comprehensive grading methodology and network metanalysis of randomized controlled trials on weight loss outcomes and adverse events. *Obes Surg* 2023; **33**:4147–4158.
- Despain D, Hoffman BL. Optimizing nutrition, diet, and lifestyle communication in GLP-1 medication therapy for weight management: a qualitative research study with registered dietitians. *Obes Pillars* 2024; **12**:100143.
- di Frega AS, Dale B, Di Matteo L, Wilding M. Secondary male factor infertility after Roux-en-Y gastric bypass for morbid obesity: case report. *Hum Reprod* 2005; **20**:997–998.
- Dominguez JE, Cantrell S, Habib AS, Izci-Balserak B, Lockhart E, Louis JM, Miskovic A, Nadler JW, Nagappa M, O'Brien LM et al. Society of anesthesia and sleep medicine and the society for obstetric anesthesia and perinatology consensus guideline on the screening, diagnosis, and treatment of obstructive sleep apnea in pregnancy. *Obstet Gynecol* 2023; **142**:403–423.
- Du Plessis SS, Omolayo TS, Cardona Maya WD. Potential impact of GLP-1 receptor agonists on male fertility: a fable of caution. *Front Physiol* 2024; **15**:1496416.
- Dupont C, Aegerter P, Foucaut AM, Reyre A, Lhuissier FJ, Bourgain M, Chabbert-Buffet N, Cédric-Durnerin I, Selleret L, Cosson E et al. Effectiveness of a therapeutic multiple-lifestyle intervention taking into account the periconceptional environment in the management of infertile couples: study design of a randomized controlled trial—the PEPIC study. *BMC Pregnancy Childbirth* 2020; **20**:322.
- Efrat M, Stein A, Pinkas H, Unger R, Birk R. Dietary patterns are positively associated with semen quality. *Fertil Steril* 2018; **109**:809–816.
- El Bardisi H, Majzoub A, Arafa M, AlMalki A, Al Said S, Khalafalla K, Jabbour G, Basha M, Al Ansari A, Sabanegh E Jr. Effect of bariatric surgery on semen parameters and sex hormone concentrations: a prospective study. *Reprod Biomed Online* 2016; **33**:606–611.
- Escamilla RF, Yamashiro K, Asuncion R, MacLean D, Thompson IS, McKeough M. Comparison of four quick and reliable methods of assessing body fat appropriate for clinical settings among young,

- middle-age, and older healthy male and female adults. *J Phys Ther Sci* 2024;**36**:518–525.
- Facondo P, Di Lodovico E, Delbarba A, Anelli V, Pezzaioli LC, Filippini E, Cappelli C, Corona G, Ferlin A. The impact of diabetes mellitus type 1 on male fertility: systematic review and meta-analysis. *Andrology* 2022;**10**:426–440.
- Fariello RM, de Carvalho RC, Spaine DM, Andretta RR, Caetano EM, Sá GPD, Cedenho AP, Fraietta R. Analysis of the functional aspects of sperm and testicular oxidative stress in individuals undergoing metabolic surgery. *Obes Surg* 2021;**31**:2887–2895.
- Faure C, Dupont C, Baraibar MA, Ladouce R, Cedrin-Durnerin I, Wolf JP, Lévy R. In subfertile couple, abdominal fat loss in men is associated with improvement of sperm quality and pregnancy: a case-series. *PLoS One* 2014;**9**:e86300.
- Federation of Obstetric and Gynaecological Societies of India (FOGSI). *Good Clinical Practice Recommendations on Preconception Care*. Mumbai, India, 2016.
- Ferramosca A, Moscatelli N, Di Giacomo M, Zara V. Dietary fatty acids influence sperm quality and function. *Andrology* 2017;**5**:423–430.
- Flegal KM, Shepherd JA, Looker AC, Graubard BI, Borrud LG, Ogden CL, Harris TB, Everhart JE, Schenker N. Comparisons of percentage body fat, body mass index, waist circumference, and waist-stature ratio in adults. *Am J Clin Nutr* 2009;**89**:500–508.
- Fletcher R, Forbes F, Dadi AF, Kassa GM, Regan C, Galle A, Beyene A, Liackman R, Temmerman M. Effect of male partners' involvement and support on reproductive, maternal and child health and well-being in East Africa: a scoping review. *Health Sci Rep* 2024;**7**:e2269.
- Fontoura P, Cardoso MC, Erthal-Martins MC, Werneck C, Sartorio C, Ramos CF. The effects of liraglutide on male fertility: a case report. *Reprod Biomed Online* 2014;**29**:644–646.
- Gao X, Li PZ, Wang GH, Li WZ, Song Z, Zhu SH, Zhu LY. Effect of laparoscopic sleeve gastrectomy on male reproductive function in Chinese men with obesity: a prospective cohort study. *Int J Surg* 2024;**110**:3373–3381.
- Gao Z, Liang Y, Yang S, Zhang T, Gong Z, Li M, Yang J. Bariatric surgery does not improve semen quality: evidence from a meta-analysis. *Obes Surg* 2022;**32**:1341–1350.
- García-Montero C, Fraile-Martínez O, Gómez-Lahoz AM, Pekarek L, Castellanos AJ, Nogueiras-Fraguas F, Coca S, Guijarro LG, García-Honduvilla N, Asúnsolo A et al. Nutritional components in western diet versus mediterranean diet at the gut microbiota-immune system interplay. implications for health and disease. *Nutrients* 2021;**13**:699.
- Gasmi A, Bjørklund G, Mujawdiya PK, Semenova Y, Peana M, Dosa A, Piscopo S, Gasmi Benahmed A, Costea DO. Micronutrients deficiencies in patients after bariatric surgery. *Eur J Nutr* 2022;**61**:55–67.
- Giusti V, Theytaz F, Di Vetta V, Clarisse M, Suter M, Tappy L. Energy and macronutrient intake after gastric bypass for morbid obesity: a 3-y observational study focused on protein consumption. *Am J Clin Nutr* 2016;**103**:18–24.
- Gomes-Rocha SR, Costa-Pinho AM, Pais-Neto CC, de Araújo Pereira A, Nogueiro JPM, Carneiro SPR, Santos-Sousa H, Lima-da-Costa EJ, Bouça-Machado R, Preto JR; CRI-O Group. Roux-en-Y gastric bypass vs sleeve gastrectomy in super obesity: a systematic review and meta-analysis. *Obes Surg* 2022;**32**:170–185.
- González-Sánchez DL, Murillo-Prado BR, Zaragoza-Calderón CM, Armenta-Rojas E, Cornejo-Bravo JM, Andrade-Soto VH, Pineda-García G, Serrano-Medina A. Micronutrient deficiency pre- and post-bariatric metabolic surgery in Latin America: a systematic review. *Obes Surg* 2023;**33**:635–664.
- Gregorič N, Šikonja J, Janež A, Jensterle M. Semaglutide improved sperm morphology in obese men with type 2 diabetes mellitus and functional hypogonadism. *Diabetes Obes Metab* 2025;**27**:519–528.
- Gu L, Fu R, Chen P, Du N, Chen S, Mao D, Chen B, Mao F, Khadaroo PA, Jin Q. In terms of nutrition, the most suitable method for bariatric surgery: laparoscopic sleeve gastrectomy or Roux-en-Y gastric bypass? A systematic review and meta-analysis. *Obes Surg* 2020;**30**:2003–2014.
- Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ; GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;**336**:924–926.
- Ha J, Kwon Y, Kwon JW, Kim D, Park SH, Hwang J, Lee CM, Park S. Micronutrient status in bariatric surgery patients receiving post-operative supplementation per guidelines: insights from a systematic review and meta-analysis of longitudinal studies. *Obes Rev* 2021;**22**:e13249.
- Haber R, Zarzour F, Ghezzawi M, Saadeh N, Bacha DS, Al Jebbawi L, Chakhtoura M, Mantzoros CS. The impact of metformin on weight and metabolic parameters in patients with obesity: a systematic review and meta-analysis of randomized controlled trials. *Diabetes Obes Metab* 2024;**26**:1850–1867.
- Hajizadeh Maleki B, Tartibian B. Combined aerobic and resistance exercise training for improving reproductive function in infertile men: a randomized controlled trial. *Appl Physiol Nutr Metab* 2017;**42**:1293–1306.
- Hajizadeh Maleki B, Tartibian B. Resistance exercise modulates male factor infertility through anti-inflammatory and antioxidative mechanisms in infertile men: a RCT. *Life Sci* 2018;**203**:150–160.
- Håkonsen LB, Thulstrup AM, Aggerholm AS, Olsen J, Bonde JP, Andersen CY, Bungum M, Ernst EH, Hansen ML, Ernst EH et al. Does weight loss improve semen quality and reproductive hormones? Results from a cohort of severely obese men. *Reprod Health* 2011;**8**:24.
- Hales CM, Carroll MD, Fryar CD, Ogden CL. Prevalence of obesity and severe obesity among adults: United States, 2017–2018. *NCHS Data Brief* 2020;**(360)**:1–8.
- Han SH, Safeek R, Ockerman K, Trieu N, Mars P, Klenke A, Furnas H, Soric-Virk S. Public interest in the off-label use of glucagon-like peptide 1 agonists (ozempic) for cosmetic weight loss: a Google trends analysis. *Aesthet Surg J* 2023;**44**:60–67.
- Hanson MA, Bardsley A, De-Regil LM, Moore SE, Oken E, Poston L, Ma RC, McAuliffe FM, Maleta K, Purandare CN et al. The International Federation of Gynecology and Obstetrics (FIGO) recommendations on adolescent, preconception, and maternal nutrition: “Think Nutrition First”. *Int J Gynaecol Obstet* 2015;**131**:S213–S253.
- Healthy Male. *Preconception Health Checklist for Men*. Melbourne, Victoria, Australia: Healthy Male, 2024.
- Heindel JJ, Blumberg B. Environmental obesogens: mechanisms and controversies. *Annu Rev Pharmacol Toxicol* 2019;**59**:89–106.
- Heller CG, Clermont Y. Spermatogenesis in man: an estimate of its duration. *Science* 1963;**140**:184–186.
- Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002;**21**:1539–1558.
- Huang Y, Wang X, Yan C, Li C, Zhang L, Zhang L, Liang E, Liu T, Mao J. Effect of metformin on nonalcoholic fatty liver based on meta-analysis and network pharmacology. *Medicine (Baltimore)* 2022;**101**:e31437.
- Hue O, Marcotte J, Berrigan F, Simoneau M, Doré J, Marceau P, Marceau S, Tremblay A, Teasdale N. Increased plasma levels of

- toxic pollutants accompanying weight loss induced by hypocaloric diet or by bariatric surgery. *Obes Surg* 2006;**16**:1145–1154.
- Humaidan P, Haahr T, Povlsen BB, Kofod L, Laursen RJ, Alsbjerg B, Elbaek HO, Esteves SC. The combined effect of lifestyle intervention and antioxidant therapy on sperm DNA fragmentation and seminal oxidative stress in IVF patients: a pilot study. *Int Braz J Urol* 2022;**48**:131–156.
- Hunter E, Avenell A, Maheshwari A, Stadler G, Best D. The effectiveness of weight-loss lifestyle interventions for improving fertility in women and men with overweight or obesity and infertility: a systematic review update of evidence from randomized controlled trials. *Obes Rev* 2021;**22**:e13325.
- Imani M, Talebi AR, Fesahat F, Rahiminia T, Seifati SM, Dehghanpour F. Sperm parameters, DNA integrity, and protamine expression in patients with type II diabetes mellitus. *J Obstet Gynaecol* 2021;**41**:439–446.
- Ismail A, Abdelghany A, Atef H. Response of testosterone and semen parameters to a 14-week aerobic training in sedentary obese men with hyperglycaemia. *Physiother Quart* 2023;**31**:28–33.
- Jaffar M, Ashraf M. Does weight loss improve fertility with respect to semen parameters—results from a large cohort study. *Int J Infertil Fetal Med* 2017;**8**:12–17.
- Jastreboff AM, Aronne LJ, Ahmad NN, Wharton S, Connery L, Alves B, Kiyosue A, Zhang S, Liu B, Bunck MC et al.; SURMOUNT-1 Investigators. Tirzepatide once weekly for the treatment of obesity. *N Engl J Med* 2022;**387**:205–216.
- Javani S, Mosapour E, Hoseine S, Ashrafi A, Farhadi E. Analysis of semen parameters, and hormonal changes of FSH, LH, testosterone, and libido following bariatric surgery. *J Family Med Prim Care* 2023;**12**:2596–2601.
- Jiang S, Ma X, Li M, Yan S, Zhao H, Pan Y, Wang C, Yao Y, Jin L, Li B. Association between dietary mineral nutrient intake, body mass index, and waist circumference in U.S. adults using quantile regression analysis NHANES 2007–2014. *PeerJ* 2020;**8**:e9127.
- Jiang W, Li W, Cheng J, Li W, Cheng F. Efficacy and safety of liraglutide in patients with type 2 diabetes mellitus and severe obstructive sleep apnea. *Sleep Breath* 2023;**27**:1687–1694.
- Jimbo M, Kunisaki J, Ghaed M, Yu V, Flores HA, Hotaling JM. Fertility in the aging male: a systematic review. *Fertil Steril* 2022;**118**:1022–1034.
- Jun S, Cowan AE, Bhadra A, Dodd KW, Dwyer JT, Eicher-Miller HA, Gahche JJ, Guenther PM, Potischman N, Tooze JA et al. Older adults with obesity have higher risks of some micronutrient inadequacies and lower overall dietary quality compared to peers with a healthy weight, National Health and Nutrition Examination Surveys (NHANES), 2011–2014. *Public Health Nutr* 2020;**23**:2268–2279.
- Kahn BE, Brannigan RE. Obesity and male infertility. *Curr Opin Urol* 2017;**27**:441–445.
- Karayianis D, Kontogianni MD, Mendorou C, Douka L, Mastrominas M, Yiannakouris N. Association between adherence to the Mediterranean diet and semen quality parameters in male partners of couples attempting fertility. *Hum Reprod* 2017;**32**:215–222.
- Kim MJ, Marchand P, Henegar C, Antignac JP, Alili R, Poitou C, Bouillot JL, Basdevant A, Le Bizec B, Barouki R et al. Fate and complex pathogenic effects of dioxins and polychlorinated biphenyls in obese subjects before and after drastic weight loss. *Environ Health Perspect* 2011;**119**:377–383.
- Kivimäki M, Strandberg T, Pentti J, Nyberg ST, Frank P, Jokela M, Ervasti J, Suominen SB, Vahtera J, Sipilä PN et al. Body-mass index and risk of obesity-related complex multimorbidity: an observational multicohort study. *Lancet Diabetes Endocrinol* 2022;**10**:253–263.
- Kominiarek MA. Pregnancy after bariatric surgery. *Obstet Gynecol Clin North Am* 2010;**37**:305–320.
- Konwar M, Bose D, Jaiswal SK, Maurya MK, Ravi R. Efficacy and safety of liraglutide 3.0 mg in patients with overweight and obese with or without diabetes: a systematic review and meta-analysis. *Int J Clin Pract* 2022;**2022**:1201977.
- Krzizek EC, Brix JM, Herz CT, Kopp HP, Schernthaner GH, Schernthaner G, Ludvik B. Prevalence of micronutrient deficiency in patients with morbid obesity before bariatric surgery. *Obes Surg* 2018;**28**:643–648.
- Kyrkou K, Alevrakis E, Baou K, Alchanatis M, Pouloupoulou C, Kanopoulos C, Vagiakis E, Dikeos D. Impaired human sexual and erectile function affecting semen quality, in obstructive sleep apnea: a pilot study. *J Pers Med* 2022;**12**:980.
- La Vignera S, Condorelli RA, Calogero AE, Cannarella R, Aversa A. Sexual and Reproductive Outcomes in Obese Fertile Men with Functional Hypogonadism after Treatment with Liraglutide: Preliminary Results. *J Clin Med* 2023;**12**:672.
- Lahimer M, Abou Diwan M, Montjean D, Cabry R, Bach V, Ajina M, Ben Ali H, Benkhalifa M, Khorsi-Cauet H. Endocrine disrupting chemicals and male fertility: from physiological to molecular effects. *Front Public Health* 2023;**11**:1232646.
- Lazaros L, Hatzis E, Markoula S, Takenaka A, Sofikitis N, Zikopoulos K, Georgiou I. Dramatic reduction in sperm parameters following bariatric surgery: report of two cases. *Andrologia* 2012;**44**:428–432.
- Lee Y, Dang JT, Switzer N, Yu J, Tian CH, Birch DW, Karmali S. Impact of bariatric surgery on male sex hormones and sperm quality: a systematic review and meta-analysis. *Obes Surg* 2019;**29**:334–346.
- Legro RS, Kunselman AR, Meadows JW, Kesner JS, Krieg EF, Rogers AM, Cooney RN. Time-related increase in urinary testosterone levels and stable semen analysis parameters after bariatric surgery in men. *Reprod Biomed Online* 2015;**30**:150–156.
- Leisegang K, Sengupta P, Agarwal A, Henkel R. Obesity and male infertility: mechanisms and management. *Andrologia* 2021;**53**:e13617.
- Lengsfeld S, Probst L, Emara Y, Werlen L, Vogt DR, Bathelt C, Baur F, Cavielz B, Vukajlovic T, Fischer M et al. Effects of the glucagon-like peptide-1 receptor agonist dulaglutide on sexuality in healthy men: a randomised, double-blind, placebo-controlled crossover study. *EBioMedicine* 2024;**107**:105284.
- Li YX, Lin Y, Ou CK, Xu RJ, Liu TT, Zhong ZH, Liu LK, Zheng Y, Hou SH, Lv ZQ et al. Association between body mass index and semen quality: a systematic review and meta-analysis. *Int J Obes (Lond)* 2024;**48**:1383–1401.
- Lincoff AM, Brown-Frandsen K, Colhoun HM, Deanfield J, Emerson SS, Esbjerg S, Hardt-Lindberg S, Hovingh GK, Kahn SE, Kushner RF et al.; SELECT Trial Investigators. Semaglutide and cardiovascular outcomes in obesity without diabetes. *N Engl J Med* 2023;**389**:2221–2232.
- Liu CY, Chang TC, Lin SH, Wu ST, Cha TL, Tsao CW. Metformin ameliorates testicular function and spermatogenesis in male mice with high-fat and high-cholesterol diet-induced obesity. *Nutrients* 2020;**12**:1932.
- Liu N, Birstler J, Venkatesh M, Hanrahan L, Chen G, Funk L. Obesity and BMI cut points for associated comorbidities: electronic health record study. *J Med Internet Res* 2021;**23**:e24017.
- Livingstone MBE, Redpath T, Naseer F, Boyd A, Martin M, Finlayson G, Miras AD, Bodnar Z, Kerrigan D, Pournaras DJ et al. Food intake following gastric bypass surgery: patients eat less but do not eat differently. *J Nutr* 2022;**152**:2319–2332.
- Lo Giudice A, Asmundo MG, Cimino S, Morgia G, Cocci A, Falcone M, Sokolakis I, Capogrosso P, Morgado A, Russo GI; EAU-YAU Sexual and Reproductive Health Group. Effects of physical activity on

- fertility parameters: a meta-analysis of randomized controlled trials. *World J Mens Health* 2024;**42**:555–562.
- Lotti F, Maggi M. Effects of diabetes mellitus on sperm quality and fertility outcomes: clinical evidence. *Andrology* 2023;**11**:399–416.
- Lourenço ML, Moura GA, Rocha YM, Rodrigues JPV, Monteiro PB. Impact of sperm DNA fragmentation on the clinical outcome of assisted reproduction techniques: a systematic review of the last five years. *JBRA Assist Reprod* 2023;**27**:282–291.
- Lyons HE, Peel A, Gonzalez M, Deluao J, Olatunji O, Nikitaras V, McPherson NO. Unlocking the power of semen analysis in primary health care—a path to men's health and lifestyle transformation. *Nat Rev Urol* 2025. Doi: [10.1038/s41585-025-01047-1](https://doi.org/10.1038/s41585-025-01047-1).
- Madsen KS, Chi Y, Metzendorf M-I, Richter B, Hemmingsen B. Metformin for prevention or delay of type 2 diabetes mellitus and its associated complications in persons at increased risk for the development of type 2 diabetes mellitus. *Cochrane Database Syst Rev* 2019;**11**:CD013516, CD008558.
- Magalhaes DP, Mahalingaiah S, Perry MJ. Exploring the causes of semen quality changes post-bariatric surgery: a focus on endocrine-disrupting chemicals. *Hum Reprod* 2022;**37**:902–921.
- Maleki BH, Tartibian B. High-intensity exercise training for improving reproductive function in infertile patients: a randomized controlled trial. *J Obstet Gynaecol Can* 2017;**39**:545–558.
- Maleki BH, Tartibian B. “High-intensity interval training modulates male factor infertility through anti-inflammatory and antioxidative mechanisms in infertile men: a randomized controlled trial” [Cytokine 125 (2020) 154861]. *Cytokine* 2023;**168**:156250.
- Maleki BH, Tartibian B. Retraction notice to “Moderate aerobic exercise training for improving reproductive function in infertile patients: a randomized controlled trial” [Cytokine 92 (2017) 55–67]. *Cytokine* 2024;**173**:156453.
- Mangoli E, Talebi AR, Anvari M, Pouretezar M. Effects of experimentally-induced diabetes on sperm parameters and chromatin quality in mice. *Iran J Reprod Med* 2013;**11**:53–60.
- Marinaro JA, Schlegel PN. Sperm DNA damage and its relevance in fertility treatment: a review of recent literature and current practice guidelines. *Int J Mol Sci* 2023;**24**:1446.
- Martinez GM, Daniels K. Fertility of men and women aged 15–49 in the United States: national survey of family growth, 2015–2019. *Natl Health Stat Report* 2023;**(179)**:1–22.
- McPherson NO, Lane M. Metformin treatment of high-fat diet-fed obese male mice restores sperm function and fetal growth, without requiring weight loss. *Asian J Androl* 2020;**22**:560–568.
- Miñambres I, Sardà H, Urgell E, Genua I, Ramos A, Fernández-Ananin S, Balagué C, Sánchez-Quesada JL, Bassas L, Pérez A. Obesity surgery improves hypogonadism and sexual function in men without effects in sperm quality. *J Clin Med* 2022;**11**:5126.
- Mir J, Franken D, Andrabi SW, Ashraf M, Rao K. Impact of weight loss on sperm DNA integrity in obese men. *Andrologia* 2018;**50**:e12957.
- Mohapatra S, Gangadharan K, Pitchumoni CS. Malnutrition in obesity before and after bariatric surgery. *Dis Mon* 2020;**66**:100866.
- Mombeyni A, Shakerian S, Habibi A, Ghanbarzadeh M. The effect of 12 weeks of concurrent training on hypothalamic-pituitary-gonadal axis hormones and semen fertility indices of sedentary obese men. *Med Sport* 2021;**74**:269–283.
- Montano L, Ceretti E, Donato F, Bergamo P, Zani C, Viola GCV, Notari T, Pappalardo S, Zani D, Ubaldi S et al.; FASt Study Group. Effects of a lifestyle change intervention on semen quality in healthy young men living in highly polluted areas in Italy: the FASt Randomized Controlled Trial. *Eur Urol Focus* 2022;**8**:351–359.
- Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sftcu R, Currie M, Qureshi R, Mattis P, Lisy K, Mu P-F. Chapter 7: systematic reviews of etiology and risk. In: Aromataris E, Munn Z (eds). *JBIR Reviewer's Manual*, Adelaide, South Australia, Australia: Joanna Briggs Institute, 2020.
- Morgante G, Tosti C, Orvieto R, Musacchio MC, Piomboni P, De Leo V. Metformin improves semen characteristics of oligo-terato-asthenozoospermic men with metabolic syndrome. *Fertil Steril* 2011;**95**:2150–2152.
- Moxthe LC, Sauls R, Ruiz M, Stern M, Gonzalvo J, Gray HL. Effects of bariatric surgeries on male and female fertility: a systematic review. *J Reprod Infertil* 2020;**21**:71–86.
- Munn Z, Barker TH, Moola S, Tufanaru C, Stern C, McArthur A, Stephenson M, Aromataris E. Methodological quality of case series studies: an introduction to the JBI critical appraisal tool. *JBI Evid Synth* 2020;**18**:2127–2133.
- National Institute for Health and Care Excellence: Guidelines. Diabetes in pregnancy: management from preconception to the postnatal period. 2020. National Institute for Health and Care Excellence (NICE) Copyright © NICE 2020; London.
- Nuttall FQ. Body mass index: obesity, BMI, and health: a critical review. *Nutr Today* 2015;**50**:117–128.
- Omolaoye TS, Du Plessis SS. The effect of streptozotocin induced diabetes on sperm function: a closer look at AGEs, RAGEs, MAPKs and activation of the apoptotic pathway. *Toxicol Res* 2021;**37**:35–46.
- Peel A, Mathews N, Vincent AD, Jesudason D, Wittert G, McPherson NO. Impact of bariatric surgery, lifestyle change, and pharmacotherapy on fertility in men with obesity: a systematic review protocol. *JBI Evid Synth* 2024;**22**:1393–1400.
- Peel A, Saini A, Deluao JC, McPherson NO. Sperm DNA damage: the possible link between obesity and male infertility, an update of the current literature. *Andrology* 2023;**11**:1635–1652.
- Peng C, Cheng Q, Liu Y, Zhang Z, Wang Z, Ma H, Liu D, Wang L, Wang C. Marginal zinc deficiency in mice increased the number of abnormal sperm and altered the expression level of spermatogenesis-related genes. *Biol Trace Elem Res* 2022;**200**:3738–3749.
- Pouriaeyevali F, Tavalaei M, Taktaz-Hafshejani T, Dattilio M, Nasr-Esfahani MH. Overlapping sperm damages from vitamin B or D deficiency in mice: insights into the role of clinical supplementations. *Andrologia* 2022;**54**:e14592.
- Price SA, Sumithran P. Using a very low energy diet to achieve substantial preconception weight loss in women with obesity: a review of the safety and efficacy. *Nutrients* 2022;**14**:4423.
- Rabiei Z, Shariati M, Mogharabian N, Tahmasebi R, Ghiasi A, Motaghi Z. A review of guidelines, recommendations and framework of men's preconception care. *Reprod Dev Med* 2022;**6**:254–259.
- Rafiee B, Morowvat MH, Rahimi-Ghalati N. Comparing the effectiveness of dietary vitamin C and exercise interventions on fertility parameters in normal obese men. *Urol J* 2016;**13**:2635–2639.
- Raghif A. Effects of metformin on hormonal profile and seminal fluid analysis in obese infertile male. *Iraqi JMS* 2015;**13**:295–301.
- Rago V, De Rose D, Santoro M, Panza S, Malivindi R, Andò S, D'Agata R, Aquila S. Human sperm express the receptor for glucagon-like peptide-1 (GLP-1), which affects sperm function and metabolism. *Endocrinology* 2020;**161**:bqaa031.
- Razzaq A, Soomro FH, Siddiq G, Khizar S, Ali Khan M. Decrease in sperm count after bariatric surgery: case reports. *Cureus* 2021;**13**:e20388.
- Reis LO, Zani EL, Saad RD, Chaim EA, de Oliveira LC, Fregonesi A. Bariatric surgery does not interfere with sperm quality—a preliminary long-term study. *Reprod Sci* 2012;**19**:1057–1062.
- Ren H, Wang K, Liu Z, Zhong X, Liang M, Liao Y. Effect of low dietary folate on mouse spermatogenesis and spindle assembly checkpoint dysfunction may contribute to folate deficiency-induced

- chromosomal instability in cultured mouse spermatogonia. *DNA Cell Biol* 2023;**42**:515–525.
- Ribas-Maynou J, Yeste M, Becerra-Tomás N, Aston KI, James ER, Salas-Huetos A. Clinical implications of sperm DNA damage in IVF and ICSI: updated systematic review and meta-analysis. *Biol Rev Camb Philos Soc* 2021;**96**:1284–1300.
- Ricci E, Bravi F, Noli S, Ferrari S, De Cosmi V, La Vecchia I, Cavadini M, La Vecchia C, Parazzini F. Mediterranean diet and the risk of poor semen quality: cross-sectional analysis of men referring to an Italian Fertility Clinic. *Andrology* 2019;**7**:156–162.
- Rosety M, Díaz AJ, Rosety JM, Pery MT, Brenes-Martín F, Bernardi M, García N, Rosety-Rodríguez M, Ordoñez FJ, Rosety I. Exercise improved semen quality and reproductive hormone levels in sedentary obese adults. *Nutr Hosp* 2017;**34**:603–607.
- Roudsari RL, Sharifi F, Goudarzi F. Barriers to the participation of men in reproductive health care: a systematic review and meta-synthesis. *BMC Public Health* 2023;**23**:818.
- Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG). *Pre-Pregnancy Counselling (C-Obs-3a) Clinical Guideline Version 13.1*. Melbourne, Victoria, Australia, 2021.
- Rubino F, Cummings DE, Eckel RH, Cohen RV, Wilding JPH, Brown WA, Stanford FC, Batterham RL, Farooqi IS, Farpour-Lambert NJ et al. Definition and diagnostic criteria of clinical obesity. *Lancet Diabetes Endocrinol* 2025;**13**:221–262.
- Ryan DH, Lingvay I, Deanfield J, Kahn SE, Barros E, Burguera B, Colhoun HM, Cercato C, Dicker D, Horn DB et al. Long-term weight loss effects of semaglutide in obesity without diabetes in the SELECT trial. *Nat Med* 2024;**30**:2049–2057.
- Safarinejad MR, Hosseini SY, Dadkhah F, Asgari MA. Relationship of omega-3 and omega-6 fatty acids with semen characteristics, and anti-oxidant status of seminal plasma: a comparison between fertile and infertile men. *Clin Nutr* 2010;**29**:100–105.
- Salas-Huetos A, Babio N, Carrell DT, Bulló M, Salas-Salvadó J. Adherence to the Mediterranean diet is positively associated with sperm motility: a cross-sectional analysis. *Sci Rep* 2019;**9**:3389.
- Salas-Huetos A, Bulló M, Salas-Salvadó J. Dietary patterns, foods and nutrients in male fertility parameters and fecundability: a systematic review of observational studies. *Hum Reprod Update* 2017;**23**:371–389.
- Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, Becerra-Tomás N, Javid AZ, Abed R, Torres PJ et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. *Obes Rev* 2021;**22**:e13082.
- Salas-Huetos A, Rosique-Esteban N, Becerra-Tomás N, Vizmanos B, Bulló M, Salas-Salvadó J. The effect of nutrients and dietary supplements on sperm quality parameters: a systematic review and meta-analysis of randomized clinical trials. *Adv Nutr* 2018;**9**:833–848.
- Salminen P, Grönroos S, Helmiö M, Hurme S, Juuti A, Juusela R, Peromaa-Haavisto P, Leivonen M, Nuutila P, Ovaska J. Effect of laparoscopic sleeve gastrectomy vs Roux-en-Y gastric bypass on weight loss, comorbidities, and reflux at 10 years in adult patients with obesity: the SLEEVEPASS randomized clinical trial. *JAMA Surg* 2022;**157**:656–666.
- Samavat J, Cantini G, Lotti F, Di Franco A, Tamburrino L, Degl'Innocenti S, Maseroli E, Filimberti E, Facchiano E, Lucchese M et al. Massive weight loss obtained by bariatric surgery affects semen quality in morbid male obesity: a preliminary prospective double-armed study. *Obes Surg* 2018;**28**:69–76.
- Santi D, Greco C, Barbonetti A, Simoni M, Maggi M, Corona G. Weight loss as therapeutic option to restore fertility in obese men: a meta-analytic study. *World J Mens Health* 2024a;**43**:333–343.
- Santi D, Lotti F, Sparano C, Rastrelli G, Isidori AM, Pivonello R, Barbonetti A, Salonia A, Minhas S, Krausz C et al. Does an increase in adipose tissue 'weight' affect male fertility? A systematic review and meta-analysis based on semen analysis performed using the WHO 2010 criteria. *Andrology* 2024b;**12**:123–136.
- Sermondade N, Massin N, Boitrelle F, Pfeffer J, Eustache F, Sifer C, Czernichow S, Lévy R. Sperm parameters and male fertility after bariatric surgery: three case series. *Reprod Biomed Online* 2012;**24**:206–210.
- Shareef LG, Khalid SS, Raheem MF, Al-Hussainy AF, Al-Khayyat NS, Al Arajy AZ, Noori MM, Qasim MA, Jasim HH. Population-level interest in glucagon-like peptide-1 receptor agonists for weight loss using Google trends statistics in a 12-month retrospective analysis: an infodemiology and infoveillance study. *Cureus* 2024;**16**:e71569.
- Sharma A, Papanikolaou N, Abou Sherif S, Dimakopolou A, Thaventhiran T, Go C, Holtermann Entwistle O, Brown A, Luo R, Jha R et al. Improvements in sperm motility following low- or high-intensity dietary interventions in men with obesity. *J Clin Endocrinol Metab* 2024;**109**:449–460.
- Sharples AJ, Mahawar K. Systematic review and meta-analysis of randomised controlled trials comparing long-term outcomes of Roux-En-Y gastric bypass and sleeve gastrectomy. *Obes Surg* 2020;**30**:664–672.
- Shawe J, Ceulemans D, Akhter Z, Neff K, Hart K, Heslehurst N, Štötl I, Agrawal S, Steegers-Theunissen R, Taheri S et al. Pregnancy after bariatric surgery: consensus recommendations for preconception, antenatal and postnatal care. *Obes Rev* 2019;**20**:1507–1522.
- Shrilatha B, Muralidhara. Early oxidative stress in testis and epididymal sperm in streptozotocin-induced diabetic mice: its progression and genotoxic consequences. *Reprod Toxicol* 2007;**23**:578–587.
- Steenackers N, Van der Schueren B, Augustijns P, Vanuytsel T, Matthys C. Development and complications of nutritional deficiencies after bariatric surgery. *Nutr Res Rev* 2023;**36**:512–525.
- Su L, Qu H, Cao Y, Zhu J, Zhang SZ, Wu J, Jiao YZ. Effect of antioxidants on sperm quality parameters in subfertile men: a systematic review and network meta-analysis of randomized controlled trials. *Adv Nutr* 2022;**13**:586–594.
- Sylivris A, Mesinovic J, Scott D, Jansons P. Body composition changes at 12 months following different surgical weight loss interventions in adults with obesity: a systematic review and meta-analysis of randomized control trials. *Obes Rev* 2022;**23**:e13442.
- Taha EA, Sayed SK, Gaber HD, Abdel Hafez HK, Ghandour N, Zahran A, Mostafa T. Does being overweight affect seminal variables in fertile men? *Reprod Biomed Online* 2016;**33**:703–708.
- Takalani NB, Monageng EM, Mohlala K, Monsees TK, Henkel R, Opuwari CS. Role of oxidative stress in male infertility. *Reprod Fertil* 2023;**4**:e230024.
- Tan B, Pan XH, Chew HSJ, Goh RSJ, Lin C, Anand VV, Lee ECZ, Chan KE, Kong G, Ong CEY et al. Efficacy and safety of tirzepatide for treatment of overweight or obesity. A systematic review and meta-analysis. *Int J Obes (Lond)* 2023;**47**:677–685.
- Torres M, Laguna-Barraza R, Dalmases M, Calle A, Pericuesta E, Montserrat JM, Navajas D, Gutierrez-Adan A, Farré R. Male fertility is reduced by chronic intermittent hypoxia mimicking sleep apnea in mice. *Sleep* 2014;**37**:1757–1765.
- Tsao CW, Liao YR, Chang TC, Liew YF, Liu CY. Effects of iron supplementation on testicular function and spermatogenesis of iron-deficient rats. *Nutrients* 2022;**14**:2063.

- Tufanaru C, Munn Z, Aromataris E, Campbell J, Hopp L. Chapter 3: systematic reviews of effectiveness. In: Aromataris E, Munn Z (eds). *JBIR Reviewer's Manual, JBI Manual for Evidence Synthesis, Adelaide, South Australia, Australia: Joanna Briggs Institute, 2020.*
- Tvrda E, Peer R, Sikka SC, Agarwal A. Iron and copper in male reproduction: a double-edged sword. *J Assist Reprod Genet* 2015;**32**:3–16.
- Velotti N, Elisa De Palma FD, Sosa Fernandez LM, Manigrasso M, Galloro G, Vitiello A, Berardi G, Milone M, D, Palma GD, Musella M. Effect of bariatric surgery on in vitro fertilization in infertile men with obesity. *Surg Obes Relat Dis* 2021;**17**:1752–1759.
- Vitek WS, Hoeger KM. Worth the wait? Preconception weight reduction in women and men with obesity and infertility: a narrative review. *Fertil Steril* 2022;**118**:447–455.
- Vix M, Liu KH, Diana M, D'Urso A, Mutter D, Marescaux J. Impact of Roux-en-Y gastric bypass versus sleeve gastrectomy on vitamin D metabolism: short-term results from a prospective randomized clinical trial. *Surg Endosc* 2014;**28**:821–826.
- Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol* 2014;**14**:135.
- Wang J, Bao B, Feng J, Zhao Q, Dai H, Meng F, Deng S, Wang B, Li H. Effects of diabetes mellitus on sperm quality in the Db/Db mouse model and the role of the FoxO1 pathway. *Med Sci Monit* 2021;**27**:e928232.
- Wang J, Gong X, Meng F, Deng S, Dai H, Bao B, Feng J, Li H, Wang B. Biological network model of effect of chronic intermittent hypoxia on spermatogenesis in rats. *Med Sci Monit* 2020;**26**:e925579.
- Wang Z, Zhang Q, Ding J, Yan S, Jin W, Luo L, Zha S, Liu Q, Zhang Z, Chen H et al. Effect of obstructive sleep apnea on semen quality. *Sleep Breath* 2023;**27**:2341–2349.
- Watanabe JH, Kwon J, Nan B, Reikes A. Trends in glucagon-like peptide 1 receptor agonist use, 2014 to 2022. *J Am Pharm Assoc (2003)* 2024;**64**:133–138.
- Weng TC, Chang CH, Dong YH, Chang YC, Chuang LM. Anaemia and related nutrient deficiencies after Roux-en-Y gastric bypass surgery: a systematic review and meta-analysis. *BMJ Open* 2015;**5**:e006964.
- Wood GJA, Tiseo BC, Paluello DV, de Martin H, Santo MA, Nahas W, Srougi M, Cocuzza M. Bariatric surgery impact on reproductive hormones, semen analysis, and sperm DNA fragmentation in men with severe obesity: prospective study. *Obes Surg* 2020;**30**:4840–4851.
- World Health Organisation. *WHO Laboratory Manual for the Examination and Processing of Human Semen*, 5th edn. Geneva: World Health Organisation, 2010.
- Infertility Prevalence Estimates, 1990–2021. Geneva: World Health Organisation, 2023. <https://iris.who.int/server/api/core/bitstreams/a22ced65-46b1-4482-bf85-058719fec649/content>
- Xu T, Wang C, Zhang H, Han X, Liu W, Han J, Yu H, Chen J, Zhang P, Di J. Timing of maximal weight reduction following bariatric surgery: a study in Chinese patients. *Front Endocrinol (Lausanne)* 2020;**11**:615.
- Yan WJ, Mu Y, Yu N, Yi TL, Zhang Y, Pang XL, Cheng D, Yang J. Protective effects of metformin on reproductive function in obese male rats induced by high-fat diet. *J Assist Reprod Genet* 2015;**32**:1097–1104.
- Yang Y, Chen H, Weng S, Pan T, Chen W, Wang F, Luo T, Tang Y. In vitro exposure to metformin activates human spermatozoa at therapeutically relevant concentrations. *Andrology* 2020;**8**:663–670.
- Yargawa J, Leonardi-Bee J. Male involvement and maternal health outcomes: systematic review and meta-analysis. *J Epidemiol Community Health* 2015;**69**:604–612.
- Zegers-Hochschild F, Adamson GD, Dyer S, Racowsky C, de Mouzon J, Sokol R, Rienzi L, Sunde A, Schmidt L, Cooke ID et al. The International Glossary on Infertility and Fertility Care, 2017. *Hum Reprod* 2017;**32**:1786–1801.
- Zhang EH, Xu F, Liang H, Yan JH, Xu HX, Li Z, Wen XQ, Weng JP. GLP-1 receptor agonist exenatide attenuates the detrimental effects of obesity on inflammatory profile in testis and sperm quality in mice. *Am J Reprod Immunol* 2015;**74**:457–466.
- Zhou L, Han L, Liu M, Lu J, Pan S. Impact of metabolic syndrome on sex hormones and reproductive function: a meta-analysis of 2923 cases and 14062 controls. *Aging (Albany NY)* 2020;**13**:1962–1971.
- Zhou X, Shi H, Zhu S, Wang H, Sun S. Effects of vitamin E and vitamin C on male infertility: a meta-analysis. *Int Urol Nephrol* 2022;**54**:1793–1805.
- Zhu X, Guo F, Tang H, Huang C, Xie G, Huang T, Li Y, Liu C, Wang H, Chen B. Islet transplantation attenuating testicular injury in Type 1 diabetic rats is associated with suppression of oxidative stress and inflammation via Nrf-2/HO-1 and NF- κ B pathways. *J Diabetes Res* 2019;**2019**:8712492.