QUALITY IN SPORT
eISSN 2450-3118 · Open Access · Peer-reviewed
apcz.umk.pl/QS Nicolaus Copernicus University in Toruń

MLICZEK, Aleksandra, ROCZYŃSKI, Brajan, POLOK, Izabela, OBERSZTYN, Julia, and SZCZECIŃSKA, Adrianna. The Impact of GLP-1 Receptor Agonists on Semen Parameters and the Hypothalamic-Pituitary-Gondal Axis in Men with Obesity – A Literature Review. Quality in Sport. 2026;71:75106. https://doi.org/10.12775/QS.2026.71.75106

ARTICLE TIMELINE
Received: 07.08.2026. Revised: 26.08.2026. Accepted: 06.09.2026. Published: 13.09.2026.

The journal has been awarded 20 points in the parametric evaluation by the Polish Ministry of Higher Education and Science (Annex to the announcement of 05.01.2024, No. 32553). Unique Journal Identifier: 201398. Scientific disciplines assigned: Economics and Finance (Field of Social Sciences); Management and Quality Sciences (Field of Social Sciences).
Punkty Ministerialne z 2019 – aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The Impact of GLP-1 Receptor Agonists on Semen Parameters and the Hypothalamic–Pituitary–Gonadal Axis in Men with Obesity — A Literature Review

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Abstract

Background: Rising global obesity prevalence has coincided with a debated decline in semen quality. GLP-1 receptor agonists (GLP-1 RAs) are now widely used for weight reduction in men of reproductive age, raising questions about their effect on fertility, particularly relative to testosterone replacement therapy (TRT), which suppresses spermatogenesis.

Aim: To review evidence on GLP-1 RAs and the male reproductive system, focusing on semen parameters and the hypothalamic-pituitary-gonadal axis, and whether effects are drug-specific or mediated by weight loss.

Material and methods: Narrative review of PubMed, Scopus and Web of Science on GLP-1 RAs, semen quality, male fertility, testosterone, functional hypogonadism, obesity and weight loss, with reference-list screening and ClinicalTrials.gov. English-language studies only; no time restriction.

Results: GLP-1 receptors are expressed in human testis and spermatozoa. Obesity impairs semen quality via endocrine, inflammatory and thermal mechanisms. GLP-1 RAs raise testosterone while preserving gonadotropic function, unlike TRT; a randomized trial showed semaglutide improved sperm morphology while testosterone worsened sperm count. Weight loss, not the drug itself, appears the principal mediator, as exercise gave comparable benefit to liraglutide. Bariatric surgery did not reliably improve semen quality. Sexual-function data remain conflicting. Evidence is limited by small samples and short follow-up.

Conclusions: GLP-1 RAs appear reproductively safe and may improve semen parameters in men with obesity-related functional hypogonadism, offering a fertility-sparing alternative to TRT. Benefit is largely attributable to weight loss; lifestyle intervention remains reasonable first-line. Larger, longer trials, including tirzepatide, are needed.

Keywords: GLP-1, semaglutide, liraglutide, tirzepatide, semen quality, male infertility, obesity, functional hypogonadism, weight loss, physical activity

1. Introduction

The debate over declining semen quality in Western populations has been running for more than three decades. Its starting point was the meta-analysis by Carlsen et al. published in 1992, which suggested a substantial decline in sperm counts during the second half of the twentieth century [1]. The analysis by Levine et al. from 2017, drawing on data from many regions of the world, confirmed a downward trend in populations of North America, Europe, Australia and New Zealand [2]. Regardless of how the methodological dispute over the reliability of these estimates is ultimately resolved, the same period saw an unquestionable epidemiological shift: the global prevalence of obesity increased several-fold [3]. The coincidence of these two phenomena prompted systematic investigation of the relationship between body weight and male reproductive function.

The evidence accumulated over the past fifteen years is fairly unequivocal. The meta-analysis by Sermondade et al., covering data from more than 13,000 men, showed that compared with men of normal body weight the odds ratio for low sperm count rises with BMI — to 1.28 in men with a BMI of 30.0–39.9 kg/m² and to 2.04 above 40.0 kg/m² [4]. The updated meta-

analysis by Salas-Huetos et al. confirmed the association of excess adipose tissue with poorer semen parameters and an unfavorable reproductive hormone profile [5]. The study by Andersen et al. demonstrated impaired semen characteristics and reduced anti-Müllerian hormone concentrations across a wide weight range [6], and Mendelian randomization analyses in the MoBa cohort linked the BMI of both partners with subfertility [7]. The systematic review by Service et al. organized the evidence on the impact of obesity and metabolic health on male fertility [8].

Against this background a drug class has emerged that has transformed obesity treatment within a few years. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) — liraglutide, semaglutide, dulaglutide, exenatide, and in the form of a dual GIP/GLP-1 agonist also tirzepatide (GIP — glucose-dependent insulinotropic polypeptide) — achieve weight reduction previously unattainable by non-surgical means, with documented cardiovascular benefit [9]. A substantial proportion of people taking these drugs are men of reproductive age. This raises a question of direct clinical importance: do GLP-1 RAs improve, impair, or leave unchanged a man's reproductive potential?

The question is not merely academic. Men with obesity and accompanying functional hypogonadism are routinely referred for testosterone replacement therapy (TRT), which — by suppressing the hypothalamic–pituitary–gonadal **(**HPG) axis — inhibits spermatogenesis, sometimes in a manner that is difficult to reverse. If GLP-1 RAs raise testosterone concentrations without shutting down the axis, this would represent a therapeutic option fundamentally different in its reproductive consequences [10].

The aim of this paper is to review the current evidence regarding the potential direct effects of GLP-1 on the male reproductive system, with particular emphasis on its impact on semen parameters and the hypothalamic–pituitary–gonadal (HPG) axis. Furthermore, this review examines the extent to which the observed reproductive effects may be attributable to weight loss itself rather than to GLP-1 receptor agonists per se, and highlights existing gaps in the current literature. Particular attention is devoted to comparing pharmacotherapy with lifestyle interventions, including dietary modification and physical activity, as this distinction has important implications for preconception counseling in men with obesity.

2. Methods

This paper is a narrative literature review. Research articles available in the PubMed, Scopus and Web of Science databases were analyzed. Original studies, review articles, systematic reviews, and meta-analyses concerning the effects of GLP-1 receptor agonists on the male

reproductive system were included, together with reference works on the relationship between obesity, weight reduction and semen quality that were necessary for the interpretation of the findings. The search was conducted using a combination of keywords and Boolean operators, including: "GLP-1", "glucagon-like peptide-1", "semaglutide", "liraglutide", "dulaglutide", "tirzepatide", "semen quality", "sperm parameters", "spermatogenesis", "male fertility", "testosterone", "functional hypogonadism", "obesity", and "weight loss". The search was supplemented by screening the reference lists of the included papers and the ClinicalTrials.gov registry. Studies published in languages other than English and reports without available numerical data were excluded. No time restriction was applied.

3. Obesity and Male Reproductive Function — Pathophysiological Background

3.1. Endocrine disturbances

Excess adipose tissue increases aromatase activity, converting testosterone to estradiol. Rising estradiol concentrations intensify negative feedback at the hypothalamic and pituitary level, reducing the pulsatile secretion of GnRH and consequently of LH and FSH [11]. The result is a picture of hypogonadotropic hypogonadism described as functional hypogonadism — functional because it is potentially reversible once the underlying cause, excess adipose tissue, is removed [12]. In parallel, obesity lowers sex hormone-binding globulin (SHBG), which complicates the interpretation of total testosterone and necessitates assessment of the free or bioavailable fraction [12,13].

3.2. Oxidative stress and chronic inflammation

Visceral adipose tissue is an active secretory organ releasing pro-inflammatory cytokines. Chronic low-grade inflammation promotes overproduction of reactive oxygen species (ROS). The spermatozoon is a cell exceptionally susceptible to oxidative damage: its membrane contains a high proportion of polyunsaturated fatty acids, while its cytoplasm — and with it the reserve of antioxidant enzymes — is reduced to a minimum during spermiogenesis. The consequences are membrane lipid peroxidation, reduced motility and sperm DNA fragmentation [8].

3.3. Thermal and mechanical factors

Accumulation of adipose tissue in the suprapubic and scrotal regions and on the inner thighs raises scrotal temperature, disrupting the thermal gradient necessary for spermatogenesis. In a study using 24-hour scrotal temperature monitoring, men with obesity had significantly higher

mean daily temperatures than healthy controls, and this increase was associated with impaired sperm parameters and higher plasma FSH [14]; the heat sensitivity of spermatogenesis is independently confirmed by studies of sauna exposure [15]. The thermal factor is largely independent of hormonal disturbance and helps explain why some men with obesity show impaired semen parameters despite a normal hormonal profile.

3.4. Insulin resistance

Insulin resistance, hyperinsulinemia and hyperglycemia act on Leydig and Sertoli cells, affecting steroidogenesis and the maintenance of the metabolic environment required by maturing germ cells [16]. In vitro data suggest that impaired Leydig cell function in obesity is attributable to the accompanying inflammatory state rather than to hyperinsulinemia as such [17]. This is relevant to the present topic: drugs improving glycemic control and the inflammatory profile could theoretically benefit spermatogenesis independently of any change in body weight.

4. GLP-1 and Its Receptor in the Male Reproductive System

4.1. Pharmacological basis

GLP-1 is an incretin hormone secreted by intestinal L cells in response to a meal. It enhances glucose-dependent insulin secretion, inhibits glucagon secretion, slows gastric emptying and — through central action — reduces appetite. Long-acting analogs (liraglutide, semaglutide, dulaglutide) and the dual GIP/GLP-1 agonist tirzepatide exploit these mechanisms in the treatment of type 2 diabetes and obesity, additionally exhibiting anti-inflammatory activity and a favorable cardiovascular profile [9].

4.2. Expression of the GLP-1 receptor in reproductive tissues

Crucial to any assessment of possible direct action is the question of whether the GLP-1 receptor (GLP-1R) is present in the male reproductive system at all. The answer is affirmative and has been documented in two independent papers from 2020. Caltabiano et al. demonstrated GLP-1R expression in human and rodent testis [18]. Rago et al. showed that the receptor for GLP-1 is present directly on human spermatozoa and that its stimulation affects sperm function and metabolism [19].

This carries important interpretive consequences. If GLP-1R is present on the spermatozoon and in testicular tissue, the effect of therapy need not be solely a derivative of weight reduction

— a local action is possible, encompassing modulation of cellular energy metabolism, Sertoli cell function and the local inflammatory response.

4.3. Acute effects of GLP-1 on the HPG axis in healthy men

Izzi-Engbeaya et al. examined the direct effect of GLP-1 administration on the reproductive axis in healthy men [20]. In a placebo-controlled study using intravenous GLP-1 infusion, acute administration did not significantly alter the number of LH pulses, LH area under the curve, FSH area under the curve, or testosterone area under the curve compared with vehicle, despite a significant reduction in food intake confirming biological activity of the infused peptide. This work has reference value: it shows how the HPG axis behaves under acute receptor stimulation, without any contribution from a change in body weight, and the absence of an effect stands in contrast to preclinical data from animal models. Findings of this kind are indispensable for separating the pharmacological effect from the metabolic one — a distinction that constitutes the principal axis of dispute in this field.

5. Preclinical Data

Animal studies currently constitute the largest body of evidence and point predominantly to beneficial or neutral effects.

In rodent models of obesity and diabetes, GLP-1 RAs (including liraglutide and exenatide) improved sex hormone profiles, fertility indices and sperm function. The postulated signaling pathways include cAMP/PKA and PI3K/Akt — both well characterized in the context of cell metabolism and survival. A summary of these data was presented by Kuchakulla et al. in a review, which identified 16 clinical studies meeting the inclusion criteria along with an extensive preclinical literature [21].

An important complement is the 2025 paper by Yin et al., using murine models and cell lines. The authors found no detrimental effect of GLP-1R agonists on sperm concentration or motility, either in vivo or in vitro; at the same time they observed that absence of the GLP-1R was associated with increased sperm concentration [22]. This latter finding is intriguing and calls for interpretive caution — it suggests that the physiological role of the receptor in spermatogenesis may be more complex than a simple "stimulation equals benefit" schema.

The skeptical perspective should not be overlooked either. Du Plessis, Omolaoye and Cardona Maya published a commentary tellingly entitled "a fable of caution", noting that findings for liraglutide are sometimes divergent and that the direct action of these drugs on sperm function, hormone concentrations and male fertility remains poorly investigated in clinical studies [23].

The authors also pointed out that in some high-fat-diet murine models the administration of GLP-1 RAs did not restore reduced testosterone concentrations.

Limitations of the preclinical data: extrapolation to humans is constrained for at least three reasons: (a) doses used in animal models are often disproportionately high relative to body weight; (b) the duration of the spermatogenic cycle differs between species (approximately 74 days in humans), which complicates transfer of the observation horizon; (c) diet-induced obesity models do not fully reproduce the metabolic phenotype of a human with long-standing obesity.

6. Clinical Data — the Hypothalamic–Pituitary–Gonadal Axis

The systematic review by Deameh et al. covered the effects of liraglutide, semaglutide, dulaglutide and exenatide on reproductive hormones, semen parameters and metabolic outcomes in men. The authors' conclusions are cautiously positive: GLP-1 RAs may raise testosterone concentrations and potentially improve semen quality in men with metabolic disorders, while gonadotropic function is preserved. This last observation is clinically pivotal — it distinguishes GLP-1 RAs from TRT, which switches the gonadotropic axis off.

An increase in total testosterone was most evident in populations with obesity and metabolic dysfunction, that is, where functional hypogonadism was present at baseline. The data suggest that with liraglutide, changes in LH, FSH and SHBG were observed, whereas with semaglutide gonadotropin concentrations remained stable [24].

7. Clinical Data — Semen Parameters

7.1. Randomized trial: semaglutide versus testosterone replacement therapy

A direct comparison of a GLP-1 RA with testosterone replacement therapy is provided by the open-label randomized trial published in *Diabetes, Obesity and Metabolism* in 2025 [25]. It enrolled 25 men with type 2 diabetes (median age 50 years, median BMI 35.9 kg/m²) and functional hypogonadism, randomly assigned to semaglutide 1 mg weekly or to intramuscular testosterone undecanoate 1000 mg every 10–12 weeks. Treatment lasted 24 weeks, and semen analysis and hypogonadism parameters were supplemented by the IIEF-15 and AMS questionnaires. Baseline semen quality in the cohort was poor — parameters fell below the fifth percentile of reference values, which in itself illustrates the andrological status of men with obesity and type 2 diabetes.

Changes in the two arms ran in opposite directions. In the semaglutide group the proportion of morphologically normal spermatozoa rose significantly from baseline (2% [2; 3.5] vs 4% [2;

5.5]; P = 0.012), whereas in the testosterone group sperm concentration and total sperm count fell significantly. In the between-group comparison, semaglutide was significantly superior for all three of these parameters. Importantly, total testosterone rose in both groups — semaglutide therefore achieved the primary endocrine goal of treating functional hypogonadism without the cost of deteriorating semen parameters.

Three caveats govern the interpretation. First, the trial included 25 participants, which limits statistical power and precludes subgroup analysis. Second, it was open-label and unblinded. Third, the comparator was a therapy known in advance to suppress spermatogenesis, so demonstrating superiority over it is not the same as demonstrating absolute benefit. The appropriate conclusion is rather that semaglutide improves sperm morphology and does not cause the harm the comparator causes. For a man with functional hypogonadism who is planning to have children, that distinction carries direct practical weight.

7.2. A study in healthy men: dulaglutide

Evidence of a different kind comes from the randomized, double-blind, placebo-controlled crossover trial of Lengsfeld et al. [26]. It enrolled healthy, eugonadal, normal-weight men aged 18–50 who received dulaglutide or placebo for 4 weeks; sexual desire, HPG axis hormones and semen parameters were assessed. The authors found no evidence of any negative effect of treatment in any of these three domains — in particular, neither sperm concentration nor progressive motility was impaired relative to placebo.

This result matters for two reasons. First, it argues directly against the hypothesis of a harmful effect of GLP-1 RAs on spermatogenesis advanced after the earlier case reports (see Section 7.4). Second, it bears on the dispute over mechanism: the authors observed the same tendencies in the HPG axis as reported with chronic GLP-1 RA use in patients with obesity, but without statistical significance, which they attribute to the normal BMI and undisturbed HPG axis of their population. The absence of an effect where there is no baseline metabolic dysfunction argues for mediation through improved metabolic status rather than for a direct action of the drug on the testis. The limitation is the short, four-week treatment period — well below the length of the spermatogenic cycle — which can detect only effects acting on spermatozoa already maturing or stored in the epididymis.

7.3. Prospective study: liraglutide versus gonadotropins and testosterone

The largest clinical study with semen assessment published in this area to date is the prospective study by La Vignera et al. from 2023 [27]. It enrolled 110 men of reproductive age

(18–35 years) with metabolic hypogonadism, allocated to three groups according to their reproductive intentions: Group A (men actively seeking fatherhood) received gonadotropins (urofollitropin 150 IU three times weekly and hCG 2000 IU twice weekly), Group B received liraglutide 3 mg daily, and Group C (men with documented paternity) received transdermal testosterone 60 mg daily. Treatment lasted four months.

The results are notable for two reasons. First, the liraglutide group showed significant improvement in conventional semen parameters, both relative to baseline and relative to the gonadotropin-treated group. Second, the same group achieved significantly higher total testosterone and SHBG concentrations after four months than the other arms, together with better erectile function than at baseline and than in Groups A and C. The authors concluded that a GLP-1 analog is effective in the pharmacological treatment of metabolic hypogonadism, with advantages over conventional treatment in reproductive function, sexual function and metabolic protection.

The study has important limitations — it was neither randomized nor blinded, and allocation followed the patient's reproductive plans, introducing a risk of confounding. It nonetheless has a strength the other studies lack: a relatively large sample, a genuinely reproductive-age population, and direct comparison of liraglutide with two real therapeutic alternatives used in this indication.

7.4. Case reports — a warning signal

Historically, the first report to draw attention to this topic was the 2014 case report by Fontoura et al., suggesting an adverse effect of liraglutide on semen parameters [28]. This report is regularly cited, but the dosing context deserves note: the patient received 0.6 mg of liraglutide daily, a dose several times lower than that used in obesity treatment (3.0 mg/day). Later studies using higher doses have not confirmed this signal.

8. Weight Loss as the Principal Mediator — Evidence from the S-LiTE Trial

The study that should constitute the central reference point of this entire discussion is the andrological substudy of the S-LiTE trial, published by Andersen et al. in *Human Reproduction* in 2022 [29]. Its design allows an answer to a question the remaining studies do not pose directly.

8.1. Methods

A total of 56 men with obesity (BMI 32–43 kg/m²) and without diabetes were enrolled. All underwent an eight-week low-calorie diet (800 kcal/day), after which they were randomized 1:1:1:1 for 52 weeks to one of four groups: (i) placebo and habitual activity; (ii) exercise in line with WHO recommendations plus placebo; (iii) liraglutide 3 mg/day plus habitual activity; (iv) liraglutide plus exercise. The exercise program targeted the WHO recommendations (a minimum of 150 minutes per week of moderate-intensity or 75 minutes of vigorous-intensity activity), and adherence was monitored with heart-rate monitors. The trial protocol had been published previously [30], and the results for the primary endpoint — maintenance of weight loss — appeared in the *New England Journal of Medicine* [31].

8.2. Results

After the eight-week diet, participants lost an average of 16.5 kg of body weight (95% CI: 15.1–17.8). Sperm concentration increased 1.49-fold (95% CI: 1.18–1.88; $P < 0.01$) and total sperm count 1.41-fold (95% CI: 1.07–1.87; $P < 0.01$). Ejaculate volume, motility and motile sperm count did not change significantly. The proportion of men with oligozoospermia fell from 17% to 13%, and the number with a very low motile sperm count (< 1 million/ejaculate) fell from six to one.

At 52 weeks, the improvement persisted only in men who maintained substantial weight loss (more than 11.7 kg): concentration increased 1.71-fold and sperm count 1.97-fold relative to baseline. In those who regained weight, the effect disappeared. Subgroup analysis indicated maintenance of the increase in sperm concentration in the liraglutide group; no adverse effect of liraglutide on semen parameters was observed.

8.3. Interpretive significance

The conclusions from this study are unequivocal and have an organizing character for the whole field. First, it is weight reduction, and not the particular method by which it is achieved, that improves sperm concentration and count. Second, both liraglutide and physical activity are effective strategies for maintaining that improvement — and in this respect they are alternatives to one another rather than competitors. Third, no additional benefit of liraglutide beyond the effect of weight loss itself was demonstrated, but neither was any harm, which had been feared following earlier case reports.

The authors note an important limitation: randomization into four arms after the dietary phase substantially reduced the size of individual groups, limiting the power of subgroup analyses.

Ejaculate volume was measured by pipette rather than gravimetrically, which may have led to underestimation of absolute values.

9. Comparative Context — Other Routes to Weight Reduction

To judge whether GLP-1 RAs contribute anything distinctive, it is worth setting them against the remaining routes to weight reduction.

9.1. Dietary and behavioral interventions

Håkonsen et al., in a cohort of men with severe obesity, demonstrated improvement in semen parameters and reproductive hormone profile following a fourteen-week program based on a healthy diet and daily activity, with the effect apparent in those who lost more than 12% of body weight [32]. Faure et al., in a case series of subfertile couples, linked reduction of abdominal fat in the man with improved semen quality and achievement of pregnancy [33]. Mir et al. demonstrated a beneficial effect of weight loss on sperm DNA integrity [34]. The systematic review by Best et al. summarized the effectiveness of weight-loss interventions in the fertility context for both sexes [35].

9.2. Physical activity

Rosety et al. demonstrated improved semen quality and hormonal profile in sedentary men with obesity following a training program [36]. Observational data concur: Sun et al., in a cohort of candidate sperm donors in China, linked higher physical activity and less sedentary time with better semen parameters [37], and the ActiART study using accelerometry indicated an association between the frequency of moderate-to-vigorous intensity activity and higher sperm concentration and count [38].

These observations gain further significance alongside the S-LiTE data, in which physical activity and GLP-1 pharmacotherapy served an interchangeable function in maintaining andrological improvement [29]. This raises a practical question about the hierarchy of recommendations — whether, for a man trying to conceive who has obesity but no metabolic indication for pharmacotherapy, a lifestyle intervention remains the more appropriate first line.

9.3. Bariatric surgery — a warning from an adjacent field

Bariatric surgery provides a model of very rapid and very large weight loss, and its andrological outcomes are troublingly equivocal. Lazaros et al. described dramatic deterioration of semen parameters in 2 men after surgery, including azoospermia [39]. The prospective study by

Samavat et al. enrolled 31 men with morbid obesity, 23 of whom underwent laparoscopic Roux-en-Y gastric bypass while 8 formed a non-operated arm; at six months, significant improvement in sex hormones was confirmed in operated patients only [40]. Evidence from meta-analyses is less encouraging: Wei et al. and Lee et al. did not demonstrate unequivocal improvement in semen quality after bariatric procedures [41,42]. The most recent systematic review with meta-analysis, addressing obesity interventions generally in the context of male fertility, confirms the absence of clinically meaningful changes in semen parameters after bariatric surgery and the low certainty of evidence for pharmacotherapy (liraglutide) [43].

10. Sexual Function — an Area of Conflicting Data

Although sexual function is not synonymous with fertility, in clinical practice the two are inseparable and affect time to pregnancy. The data in this area are clearly contradictory.

On the favorable side: the retrospective cohort of Lisco et al. indicated improved erectile function in men with type 2 diabetes treated with long-acting GLP-1 RAs [44], and an exploratory analysis of the REWIND trial (dulaglutide) provided data from a placebo-controlled randomized trial [45]. The prospective study of La Vignera et al. likewise reported better erectile function in the liraglutide arm than at baseline and than in the comparator arms [27]. Mechanistically this is consistent with improved endothelial function, glycemic control and reduced inflammation.

On the unfavorable side: the TriNetX database analysis by Able et al. indicated an increased risk of erectile dysfunction among men without diabetes taking semaglutide for weight reduction [46], and the FAERS analysis by Pourabhari Langroudi et al. described reports of male sexual dysfunction associated with GLP-1 RAs [47]. Both sources carry substantial limitations — reporting and registry databases are subject to selection bias, reporting bias and confounding by indication.

The data on sexual function therefore remain too heterogeneous to support unequivocal recommendations. It would, however, be valuable for future fertility studies to routinely incorporate validated sexual function questionnaires, since potential erectile dysfunction or reduced libido may affect a couple's fertility independently of semen parameters.

11. Discussion

The evidence reviewed points to a two-layer model. The dominant layer is metabolic: weight loss itself, by whatever means, improves the hormonal, inflammatory and thermal environment for spermatogenesis [11–14]. The S-LiTE substudy is the key dataset here, since its design

separates drug from behavior — liraglutide and structured exercise maintained a comparable gain in sperm concentration, with no added benefit of the drug once weight loss was accounted for [29]. A thinner, second layer suggests a possible direct, receptor-mediated effect: GLP-1R is expressed on human spermatozoa and testis [18,19], acute GLP-1 infusion does not suppress the HPG axis [20], and clinical benefit is most apparent in men with baseline metabolic dysfunction [25,27], while healthy, eugonadal men show no measurable effect [26]. This pattern favors metabolic mediation as the primary mechanism, without excluding a modest direct contribution in men with obesity.

Clinically, the most actionable finding is the contrast with TRT: GLP-1 RAs raise testosterone while preserving gonadotropic drive, whereas TRT achieves the same endocrine goal by suppressing spermatogenesis — demonstrated head-to-head in the semaglutide-versus-testosterone trial [24,25]. This makes GLP-1 RAs a mechanistically distinct, fertility-sparing alternative to TRT in men with obesity-related functional hypogonadism. Bariatric surgery complicates the picture: despite larger and faster weight loss, it has not reliably improved semen parameters and has occasionally caused severe deterioration [39–43], suggesting that the pace and context of weight loss matter, not just its magnitude. Data on sexual function remain frankly contradictory [27,44–47] and warrant routine assessment (e.g., IIEF-15) in future trials.

Overall, the evidence base is limited by small samples, open-label or non-randomized designs, treatment durations often shorter than the ~74-day spermatogenic cycle, heterogeneous populations, and near-total reliance on liraglutide and semaglutide — dulaglutide has only short-term data in healthy men, and tirzepatide essentially none [25–27,29,39,40].

12. Conclusions

Obesity impairs semen quality through endocrine, inflammatory, thermal and metabolic pathways, and weight loss generally improves it [4–8,29,32–38]. GLP-1 receptor agonists have not shown harm to semen parameters in adequately dosed studies [23,28], and — unlike TRT — raise testosterone while preserving gonadotropic function [24,25]. This benefit appears attributable mainly to weight loss itself rather than a drug-specific effect [29], though a smaller direct action cannot be excluded.

Practically, lifestyle intervention remains a reasonable first-line approach; GLP-1 RAs are a safer pharmacological alternative to TRT for men with obesity-related functional hypogonadism who wish to preserve fertility; and TRT should generally be avoided in men still planning fatherhood. Bariatric surgery should not be assumed to confer andrological

benefit and warrants separate fertility counseling. Priority research needs include adequately powered randomized trials lasting at least one spermatogenic cycle, dedicated data for tirzepatide and longer-term dulaglutide, routine sexual-function assessment, and mechanistic studies in men with obesity designed to isolate any direct receptor effect from that of weight loss.

Disclosures

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Funding: This research did not receive external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgements: Not applicable

Conflicts of Interest: The authors declare no conflicts of interest.

All authors have read and agreed with the published version of the manuscript.

Declaration of generative AI and AI-assisted technologies in the writing process: In preparing this work, the authors used ChatGPT (OpenAI) for the purpose of language editing and grammar correction only. After using this tool, the authors reviewed and edited the text as needed and accept full responsibility for the substantive content of the publication.

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