

COVID-19 and male infertility - A review

Roshini Suresh

roshinisureshdepp@gmail.com

UWE Bristol: University of the West of England <https://orcid.org/0009-0009-3808-9876>

Rajesh Kumar

A4 Hospital and Fertility Centre

Systematic Review

Keywords:

Posted Date: October 29th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-11538306/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: The authors declare no competing interests.

Abstract

Background:

Coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2, is a systemic illness capable of influencing the male reproductive system through fever, inflammation, oxidative stress, vascular injury and endocrine disturbance. Because spermatogenesis is temperature-sensitive and spermatozoa are vulnerable to oxidative damage, semen quality may be altered during acute infection and early recovery.

Objective:

This systematic review evaluates the association between COVID-19 and male reproductive function, with a focus on conventional semen parameters, sperm DNA fragmentation and oxidative stress, reproductive hormones, SARS-CoV-2 detection in semen, and the time course of recovery.

Methods:

Published human studies of confirmed or previous SARS-CoV-2 infection were identified through structured searches of electronic literature sources. Eligible observational studies reported at least one male reproductive outcome, including semen quality, sperm functional integrity, reproductive hormones, or viral detection in semen/testicular material. Findings were synthesised qualitatively in accordance with PRISMA 2020 reporting principles (Page et al., 2021).

Results:

Across the available evidence, the clearest pattern is a short-term reduction in sperm concentration, total sperm count and motility after infection, although individual studies differ in magnitude and not all report persistent abnormalities. Longitudinal and pre/post-infection studies indicate improvement over subsequent months in many men (Guo et al., 2021; Hu et al., 2022; Zhao et al., 2025). Sperm DNA fragmentation and seminal oxidative/inflammatory markers may also increase after COVID-19 (Hajizadeh Maleki and Tartibian, 2021; Yuan et al., 2025). Endocrine studies report transient reductions in testosterone or altered gonadotrophin relationships, particularly during symptomatic disease (Ma et al., 2021; Majzoub et al., 2024). SARS-CoV-2 RNA is rarely detected in semen; one early study reported positive samples, whereas most subsequent cohorts did not (Li et al., 2020; Pan et al., 2020; Ruan et al., 2021).

Conclusion:

COVID-19 can act as a temporary reproductive stressor in men, particularly after symptomatic or febrile illness. Current evidence supports predominantly indirect mechanisms such as fever, inflammation, oxidative stress and endocrine disturbance, rather than persistent seminal infection. The evidence is insufficient to conclude that COVID-19 commonly causes permanent infertility. When semen results are abnormal soon after infection, repeat assessment after approximately one spermatogenic cycle may help distinguish transient suppression from persistent dysfunction.

1. Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was initially characterised as a respiratory illness but is now recognised to have multisystem consequences, including cardiovascular, neurological, renal, endocrine and reproductive effects (Collins et al., 2022; Seymen, 2021). Male reproductive function is particularly sensitive to systemic inflammation, febrile illness, oxidative stress and endocrine disruption, providing a biological basis for concern about fertility after infection (Khalili et al., 2020; Dutta and Sengupta, 2021; Agolli et al., 2021).

Male fertility depends on coordinated testicular, endocrine and accessory-gland function. Spermatogenesis requires intact Sertoli-cell support, Leydig-cell testosterone production and a stable testicular microenvironment. Conventional semen analysis remains the first-line laboratory assessment and includes semen volume, sperm concentration, total sperm count, motility, vitality and morphology (World Health Organization, 2021). These parameters therefore provide a clinically relevant framework for examining whether COVID-19 is associated with measurable reproductive change.

Initial concern regarding direct SARS-CoV-2 effects arose from expression of angiotensin-converting enzyme 2 (ACE2) in testicular and reproductive tissues and the requirement for host proteases such as TMPRSS2 during viral entry (Illiano, Trama and Costantini, 2020; Abobaker and Raba, 2021). However, co-expression patterns and clinical detection studies have not established the testis as a consistent reservoir. Most semen studies have failed to identify viral RNA during recovery, including Pan et al. (2020), Song et al. (2020), Ruan et al. (2021), Temiz et al. (2021) and Best et al. (2021). An important exception is Li et al. (2020), who detected SARS-CoV-2 RNA in semen from 6 of 38 men, including men in the acute and recovery phases. This isolated positive finding supports caution but has not been reproduced consistently.

Indirect systemic pathways are therefore central to current mechanistic explanations. Fever may transiently suppress spermatogenesis through testicular heat stress, while inflammatory cytokines and endothelial injury may alter the testicular microenvironment. Oxidative stress is also biologically important because sperm membranes contain high concentrations of polyunsaturated fatty acids and spermatozoa have limited cytoplasmic antioxidant capacity. Excess reactive oxygen species can impair mitochondrial function and motility, damage membranes, and increase sperm DNA fragmentation (Kalfas et al., 2023; Aitken, 2022). In a prospective longitudinal cohort, Hajizadeh Maleki and Tartibian

(2021) reported increased seminal inflammatory and oxidative-stress markers together with impaired semen parameters during follow-up after COVID-19.

Clinical findings are heterogeneous. Several studies have reported reductions in sperm concentration, total count or motility after infection (Gacci et al., 2021; Guo et al., 2021; Koç and Keseroğlu, 2021; Pazir et al., 2021; Ashonibare et al., 2024), whereas other cohorts show little evidence of persistent impairment at later follow-up (Hu et al., 2022; Maruki et al., 2024). The differences are likely to reflect variation in disease severity, fever, timing of semen collection, baseline fertility status, age, comorbidities, vaccination status and study design. Pre-infection semen data are especially valuable because semen parameters have substantial within-person biological variability.

Timing after infection is therefore a key interpretative factor. Guo et al. (2021) observed lower sperm count, concentration and motility at an initial post-recovery assessment, followed by improvement on repeat sampling. More recent longitudinal evidence likewise indicates that the greatest changes may occur in the first weeks to months after infection, with subsequent recovery in many participants (Yuan et al., 2025; Zhao et al., 2025). This time-dependent pattern is compatible with transient disturbance of spermatogenesis rather than irreversible testicular damage.

COVID-19 may additionally affect the hypothalamic-pituitary-testicular axis. Ma et al. (2021) reported higher luteinising hormone and a reduced testosterone-to-luteinising-hormone ratio in reproductive-aged men with COVID-19, while Koç and Keseroğlu (2021) observed lower testosterone in infertile men after infection. Majzoub et al. (2024) found that symptomatic disease was associated with more evident transient endocrine disturbance than asymptomatic infection. These findings suggest that acute systemic illness may influence both spermatogenesis and hormonal regulation.

Despite the expanding literature, uncertainty remains because many studies are observational, relatively small and lack pre-infection semen data. Fertility-clinic populations may also introduce selection bias, and clinically meaningful endpoints such as natural conception, miscarriage, assisted-reproduction success and live birth remain under-reported. Reviews have consequently reached similar broad conclusions while emphasising heterogeneity and the need for longitudinal data (Akhigbe and Hamed, 2020; Malki, 2022; Collins et al., 2022; Wen et al., 2024). The present review therefore focuses on the consistency, timing and biological interpretation of male reproductive changes after COVID-19, while distinguishing semen-quality changes from evidence of permanent infertility.

2. Methods

2.1 Study design

This systematic review was structured and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement, which promotes transparent reporting of study identification, screening, eligibility assessment and inclusion (Page et al., 2021). The review focused on the effect of SARS-CoV-2 infection/COVID-19 on male reproductive function, including

conventional semen parameters, sperm DNA integrity, oxidative stress, reproductive hormones, viral detection and recovery over time.

2.2 Research question

The review addressed the following research question:

What is the effect of COVID-19 on male fertility, semen quality, sperm functional integrity and reproductive hormone profiles, and what mechanisms may explain these changes?

The research question was structured using a PECO framework:

Component	Description
Population	Males of reproductive age assessed for fertility or reproductive parameters
Exposure	Confirmed or clinically diagnosed SARS-CoV-2 infection/COVID-19
Comparator	Healthy controls, pre-COVID semen data, recovered men at different time intervals, or population reference values
Outcomes	Semen parameters, sperm DNA fragmentation, oxidative stress markers, reproductive hormones, viral detection in semen/testis, and recovery over time

2.3 Eligibility criteria

Inclusion criteria

Studies were included if they met the following criteria:

1. Published original research involving human male participants.
2. Participants had confirmed or previous COVID-19/SARS-CoV-2 infection.
3. The study reported at least one male reproductive outcome or SARS-CoV-2 detection in semen or testicular material.
4. Eligible designs included prospective or retrospective cohort studies, cross-sectional studies, case-control studies and other observational clinical studies.
5. Full-text articles were available in English.

Exclusion criteria

Studies were excluded if they met any of the following criteria:

1. Animal-only studies without human reproductive data.
2. In vitro studies without direct clinical male reproductive outcomes.
3. Reviews, editorials, commentaries and opinion articles were excluded from the primary-study synthesis, although relevant reviews were used for contextual interpretation.

4. 4. Studies assessing only female fertility outcomes.
5. 5. Studies focused solely on COVID-19 vaccination without separate infection-related data.
6. 6. Articles with insufficient data on semen, hormonal or reproductive outcomes.

2.4 Information sources

The literature search used PubMed/MEDLINE, Scopus, Web of Science and Google Scholar, with additional relevant articles identified from reference lists of eligible studies and systematic reviews. Searches focused on literature published from the emergence of SARS-CoV-2 onward.

2.5 Search strategy

Search terms combined concepts relating to COVID-19 and male reproduction. Core terms included: (COVID-19 OR SARS-CoV-2 OR coronavirus) AND (male fertility OR male infertility OR semen OR sperm OR spermatogenesis OR testis OR testosterone OR reproductive hormones) AND (semen parameters OR sperm concentration OR sperm count OR sperm motility OR sperm morphology OR sperm DNA fragmentation OR oxidative stress). Database-specific syntax and controlled vocabulary were adapted where appropriate.

2.6 Study selection

Titles and abstracts were screened against the eligibility criteria, followed by full-text assessment of potentially relevant articles. The qualitative synthesis incorporated 18 original human studies addressing semen quality, reproductive hormones, sperm functional integrity and/or viral detection. Figure 1 provides a retrospective reference-based reconstruction using the 35 references retained in the final manuscript: 18 original human studies were included in the qualitative synthesis, while 17 non-primary sources were retained for background, interpretation and methodology. This reconstruction should not be interpreted as the original database-search flow because identification, duplicate-removal and screening counts require the original search exports or screening log.

2.7 Quality assessment

Methodological quality was considered with emphasis on participant selection, comparability of exposed and control groups, outcome measurement, timing of semen collection, availability of pre-infection data and adequacy of follow-up. The Newcastle-Ottawa Scale provides a structured framework for appraising non-randomised cohort and case-control studies (Wells et al., 2000), while ROBINS-I domains provide complementary guidance for considering bias in non-randomised evidence (Sterne et al., 2016). Because the included studies were heterogeneous in design, quality judgements were interpreted alongside study design rather than converted into a single pooled score.

2.8 Ethical considerations

Formal ethical approval was not required for this review because it synthesised previously published data and did not involve participant recruitment or analysis of identifiable patient-level information.

3. Results

3.1 Study selection and general characteristics

The evidence base comprised observational human studies conducted during acute infection or at varying intervals after recovery. Designs included cross-sectional comparisons, prospective cohorts, retrospective pre/post analyses and longitudinal repeated-measure studies. The 18 original studies used in the qualitative synthesis varied considerably in sample size, baseline fertility status, disease severity, fever exposure and timing of semen collection. Table 1 summarises the studies that most directly informed the review.

Table 1
Summary of key original human studies included in the qualitative synthesis.

Study	Design/sample	Timing	Main finding
Li et al. (2020)	Cohort; 38 men with COVID-19	Acute/recovery	SARS-CoV-2 RNA detected in semen in 6/38 men; an early positive finding not consistently reproduced.
Song et al. (2020)	12 recovering men + testicular sample from 1 deceased patient	Recovery/acute tissue	No SARS-CoV-2 RNA detected in semen or testicular tissue.
Pan et al. (2020)	34 recovering men	~ 1 month after diagnosis	No viral RNA detected in semen; questioned efficient ACE2/TMPRSS2-mediated testicular entry.
Holtmann et al. (2020)	Cohort of acute/recovered men	Acute and recovery	No semen viral RNA; semen impairment more evident after moderate than mild disease.
Ma et al. (2021)	12 semen samples; hormones in 119 infected men vs 273 controls	During/after infection	No semen viral RNA; higher LH and lower testosterone: LH ratio in infected men.
Temiz et al. (2021)	Cross-sectional pilot; 30 participants	Before/after treatment and controls	No semen viral RNA; lower morphology and transient hormone differences, potentially related to acute illness/fever.
Ruan et al. (2021)	74 recovered men; 70 semen samples	Median ~ 80 days after last positive swab	No viral RNA in semen/urogenital secretions; concentration, total count and total motility lower than controls.
Best et al. (2021)	Prospective; 30 recovered men	11–64 days after positive test	Lower total sperm number vs controls; no viral RNA in tested semen; small follow-up suggested improvement.
Gacci et al. (2021)	Prospective multicentre cohort after recovery	Early recovery	Substantial semen impairment in a subset despite absence of consistent seminal viral detection.
Guo et al. (2021)	41 recovered men; 22 repeat samples	Median 56 days; repeat ~ 29 days later	Lower count, concentration and motility initially, with significant improvement on repeat sampling.
Hajizadeh Maleki & Tartibian (2021)	Prospective longitudinal; 84 COVID-19 and 105 controls	Repeated 10-day assessments to 60 days	Higher inflammatory/oxidative-stress and apoptotic markers with lower semen quality.
Koç & Keseroğlu (2021)	Pre/post study; 21 infertile men	Before vs after COVID-19	Lower volume, motility, morphology and testosterone after infection.

Study	Design/sample	Timing	Main finding
Pazir et al. (2021)	Prospective pre/post; 24 men with mild COVID-19	Median ~ 112 days	Total motility and total motile sperm count declined; several other parameters were not significantly different.
Hu et al. (2022)	36 recovered men vs 45 controls	Median recovery 177.5 days	No significant overall long-term differences; total sperm number showed time-related recovery.
Majzoub et al. (2024)	Asymptomatic vs symptomatic infection	Short- and long-term follow-up	Symptomatic infection showed clearer transient endocrine disturbance; later semen differences were limited.
Maruki et al. (2024)	Descriptive Japanese post-COVID cohort	Post-COVID conditions	Did not demonstrate a clear sustained reduction in sperm count compared with population data.
Yuan et al. (2025)	Cross-sectional and longitudinal clinical study	Post-infection follow-up	Lower sperm count/motility and higher DNA fragmentation after COVID-19.
Zhao et al. (2025)	Retrospective longitudinal study with pre-infection data	1, 2, 3 and 6 months	Largest decline early after infection, followed by recovery over approximately 3–5 months.

3.2 Effect of COVID-19 on conventional semen parameters

The most consistent clinical signal is reduced sperm number and motility during acute infection or early recovery. Gacci et al. (2021) reported semen impairment in recently recovered men, while Best et al. (2021) found a lower total sperm number in men sampled 11–64 days after infection than in age-matched SARS-CoV-2-negative men. Ruan et al. (2021) similarly observed lower sperm concentration, total sperm count and total motility compared with healthy controls despite overall values frequently remaining above WHO lower reference limits.

Studies with within-person pre-infection data strengthen the evidence because they reduce confounding by baseline semen variability. Koç and Keseroğlu (2021) found significant post-COVID reductions in semen volume, total and progressive motility, normal morphology and testosterone in 21 infertile men. Pazir et al. (2021) observed significant reductions in total motility and total motile sperm count after mild COVID-19, although semen volume, concentration and progressive motility did not change significantly. These differences illustrate that COVID-19 does not affect every semen parameter uniformly.

Guo et al. (2021) found significantly lower total sperm count, sperm concentration and motility at the first post-recovery assessment, followed by improvement in repeat samples. Hajizadeh Maleki and Tartibian (2021) also reported lower semen volume, concentration, progressive motility and morphology in association with inflammatory and oxidative-stress changes. At the evidence-synthesis level,

Ashonibare et al. (2024) and Wen et al. (2024) reported overall adverse associations between SARS-CoV-2 infection and multiple semen outcomes, although heterogeneity between studies was substantial.

Conversely, later follow-up studies do not consistently demonstrate persistent impairment. Hu et al. (2022) found no significant overall difference between recovered men and controls at a median recovery duration of 177.5 days, and Maruki et al. (2024) did not identify a clear sustained reduction in sperm count in a Japanese post-COVID cohort. Collectively, the evidence supports a time-dependent effect rather than uniform long-term deterioration.

3.3 Timing of semen impairment and recovery after infection

Timing is one of the strongest sources of heterogeneity across studies. Semen collected soon after symptomatic infection may reflect fever-related disruption and injury to germ cells that were developing during the acute illness. Because a complete spermatogenic cycle takes several weeks and newly formed sperm must then transit the epididymis, recovery in ejaculate quality is not expected immediately after systemic recovery.

Longitudinal observations support this interpretation. Guo et al. (2021) reported significant improvement in count, concentration and motile sperm number on a second sample obtained after the initial post-recovery assessment. Hu et al. (2022) observed an improving trend in total sperm number with longer recovery. Zhao et al. (2025), using repeated post-infection assessments and pre-infection data, found the greatest reduction around the first month and subsequent recovery, with estimated recovery occurring over approximately three to five months for key parameters. Yuan et al. (2025) likewise found post-COVID deterioration but demonstrated that changes must be interpreted according to follow-up interval.

These studies suggest that a single abnormal semen analysis soon after COVID-19 should not automatically be interpreted as permanent infertility. When clinically appropriate, repeat semen testing after approximately three months provides a more informative assessment of persistence or recovery.

3.4 Disease severity, fever and semen quality

Disease severity and fever appear to modify reproductive effects. Holtmann et al. (2020) reported that semen impairment was more evident after moderate COVID-19 than after mild disease, while viral RNA was not detected in semen. Temiz et al. (2021) found lower sperm morphology and acute hormone changes and interpreted these cautiously in the context of fever and systemic stress rather than a specific persistent gonadal effect.

Symptomatic illness may also produce stronger endocrine effects. Majzoub et al. (2024) reported lower testosterone and a higher luteinising-hormone-to-testosterone ratio during symptomatic infection, with improvement after recovery. Koç and Keseroğlu (2021) observed a post-infection fall in testosterone alongside semen deterioration in a pre-existing infertility population. Fever is therefore a plausible

mediator because spermatogenesis is highly temperature-sensitive, although available studies do not always record fever duration or maximum temperature consistently.

3.5 Sperm DNA fragmentation and oxidative stress

Conventional semen analysis may not capture all post-COVID reproductive effects. Hajizadeh Maleki and Tartibian (2021) found increased seminal reactive oxygen species, inflammatory cytokines and apoptotic markers together with reduced antioxidant activity and poorer semen parameters during longitudinal follow-up. This provides direct clinical support for oxidative and inflammatory pathways rather than relying only on theoretical mechanisms.

Yuan et al. (2025) reported increased sperm DNA fragmentation after COVID-19 together with lower sperm count and motility. This is potentially clinically relevant because sperm DNA integrity contributes to fertilisation and embryo development, although the available COVID-19 literature has not yet established a consistent relationship with pregnancy or live-birth outcomes. Kalfas et al. (2023) therefore proposed oxidative stress as an important mechanistic target but also emphasised that evidence for COVID-specific antioxidant treatment remains limited.

3.6 Reproductive hormone changes

Several studies suggest transient alteration of the hypothalamic-pituitary-testicular axis. Ma et al. (2021) found higher luteinising hormone and a lower testosterone-to-luteinising-hormone ratio in men with COVID-19 compared with controls, despite no viral RNA in the semen samples examined. This pattern may indicate relative Leydig-cell stress or impaired testicular responsiveness during systemic inflammation.

Koç and Keseroğlu (2021) reported a significant reduction in testosterone after COVID-19 in infertile men, while Majzoub et al. (2024) observed more evident hormonal disturbance during symptomatic than asymptomatic infection, followed by improvement. At the meta-analytic level, Ashonibare et al. (2024) reported reduced testosterone and changes in other reproductive hormones. These findings support temporary endocrine disturbance but do not establish permanent Leydig-cell failure.

3.7 SARS-CoV-2 detection in semen and testicular involvement

Evidence for persistent SARS-CoV-2 in semen is weak. Li et al. (2020) reported viral RNA in 6 of 38 semen samples, including samples collected during acute illness and recovery. This study is important because it demonstrates that seminal detection is possible, but its findings contrast with the majority of subsequent clinical studies.

Pan et al. (2020), Song et al. (2020), Holtmann et al. (2020), Ma et al. (2021), Temiz et al. (2021), Ruan et al. (2021) and Best et al. (2021) did not detect SARS-CoV-2 RNA in semen in their examined cohorts. Ruan et al. (2021) also found no viral RNA in urine or expressed prostatic secretions from recovered

men. Thus, the available literature suggests that persistent seminal shedding is uncommon and is unlikely to account for most observed semen abnormalities.

Broader evidence therefore favours indirect injury pathways such as fever, systemic inflammation, oxidative stress, endothelial dysfunction and endocrine disturbance over persistent infection of semen. Reviews by Dutta and Sengupta (2021), Agolli et al. (2021), Aitken (2022) and Collins et al. (2022) similarly describe a multifactorial model rather than a single direct viral mechanism.

3.8 Summary of main findings

The evidence indicates that COVID-19 can be associated with reduced semen quality, particularly sperm count/concentration and motility, during acute infection and early recovery. Longitudinal data suggest improvement in many men over subsequent months. Oxidative stress, inflammation and transient endocrine disturbance provide plausible mechanisms, while persistent SARS-CoV-2 detection in semen is uncommon. The evidence therefore supports temporary male reproductive impairment in a proportion of infected men but does not establish permanent infertility as a common outcome.

4. Discussion

4.1 Principal findings

This review identifies a coherent pattern across otherwise heterogeneous studies: COVID-19 is most consistently associated with short-term deterioration in semen quality, while the evidence for persistent impairment is weaker. The strongest changes concern sperm concentration/total count and motility, although morphology, vitality, semen volume and DNA integrity are affected in some cohorts. Studies with pre-infection or repeated post-infection data are particularly informative because they show that recovery is possible (Guo et al., 2021; Pazir et al., 2021; Hu et al., 2022; Zhao et al., 2025).

This distinction is clinically important. A decrease in semen quality after COVID-19 does not by itself demonstrate infertility, and an abnormal analysis during early recovery may represent a transient effect of systemic illness. The available evidence is therefore better described as post-infective reproductive dysfunction or temporary subfertility risk rather than proof that SARS-CoV-2 commonly causes permanent male infertility.

4.2 Direct viral injury versus indirect systemic mechanisms

Early hypotheses focused on direct viral invasion because ACE2 is expressed in testicular tissue. However, receptor expression alone does not establish productive infection. The seminal detection literature is dominated by negative studies, with Li et al. (2020) representing the main early positive report and Pan et al. (2020), Song et al. (2020), Holtmann et al. (2020), Ruan et al. (2021), Temiz et al. (2021) and Best et al. (2021) reporting no viral RNA in the semen examined.

Indirect mechanisms therefore provide the more consistent explanation for post-COVID semen changes. Systemic fever, cytokine activation, oxidative stress, vascular/endothelial injury and endocrine disturbance can each impair spermatogenesis without requiring persistent viral infection of the testis. This multifactorial interpretation is consistent with mechanistic reviews (Khalili et al., 2020; Agolli et al., 2021; Malki, 2022; Kalfas et al., 2023) and with clinical studies linking poorer semen quality to inflammatory and oxidative-stress markers (Hajizadeh Maleki and Tartibian, 2021).

4.3 Role of fever and systemic inflammation

Fever is a credible non-specific contributor to post-COVID semen impairment because spermatogenesis requires a temperature below core body temperature. Febrile illness can disturb germ-cell development, and the effect may only become visible in semen several weeks later. The stronger impairment reported in moderate or symptomatic disease by Holtmann et al. (2020) and the acute changes described by Temiz et al. (2021) are compatible with this mechanism.

Inflammatory pathways may amplify this effect. Hajizadeh Maleki and Tartibian (2021) documented sustained increases in seminal pro-inflammatory cytokines together with oxidative stress and poorer semen quality. Thus, the reproductive effect of COVID-19 probably reflects the intensity and duration of systemic illness rather than a uniform response to SARS-CoV-2 exposure.

4.4 Oxidative stress and sperm DNA fragmentation

Oxidative stress provides a mechanistic bridge between systemic inflammation and sperm dysfunction. Excess reactive oxygen species can impair mitochondrial energy generation and membrane function, reducing motility, while also damaging nuclear and mitochondrial DNA. The longitudinal biomarker findings of Hajizadeh Maleki and Tartibian (2021) support this pathway in COVID-19.

Yuan et al. (2025) further demonstrated increased sperm DNA fragmentation after infection. DNA fragmentation may reveal functional injury that is not apparent from routine semen analysis alone, but its routine use after COVID-19 cannot currently be recommended for all men because evidence linking post-COVID DNA fragmentation to pregnancy and live-birth outcomes remains limited. It may be more relevant in persistent unexplained subfertility or repeated assisted-reproduction failure.

4.5 Endocrine disruption and Leydig cell function

The endocrine findings suggest that acute COVID-19 can temporarily alter testicular or hypothalamic-pituitary regulation. Higher LH with a lower testosterone: LH ratio, as reported by Ma et al. (2021), can indicate reduced Leydig-cell responsiveness. Post-infection reductions in testosterone have also been reported in pre/post data (Koç and Keseroğlu, 2021) and in symptomatic infection (Majzoub et al., 2024).

These changes should nevertheless be interpreted cautiously because testosterone is sensitive to acute illness, inflammation, obesity, medication exposure and time of blood sampling. Current studies support transient gonadal stress more strongly than irreversible endocrine failure.

4.6 Semen impairment appears time-dependent

Time since infection explains part of the apparent conflict between studies. Early-recovery cohorts more frequently report lower sperm number and motility, whereas later cohorts often find attenuated or absent differences. Guo et al. (2021) showed improvement on repeat sampling; Hu et al. (2022) observed recovery trends at longer intervals; and Zhao et al. (2025) demonstrated recovery over approximately three to five months in key parameters.

Accordingly, post-COVID semen results should be interpreted in relation to infection date and fever history. A repeat sample after approximately one spermatogenic cycle can distinguish a temporary post-febrile change from a more persistent abnormality.

4.7 Clinical implications

Men attempting conception or undergoing fertility treatment can be counselled that semen quality may be temporarily reduced after symptomatic or febrile COVID-19. Semen analysis is reasonable when conception is delayed, when there is an unexpected deterioration from previous results, or before assisted reproduction if recent infection may affect interpretation. Standard WHO laboratory methods should be used (World Health Organization, 2021).

If an early post-infection semen analysis is abnormal, repeat testing after approximately three months is often more informative than immediate classification of persistent infertility. Hormonal assessment including testosterone, luteinising hormone, follicle-stimulating hormone and prolactin may be appropriate when there are symptoms of hypogonadism or persistently abnormal semen findings. Clinical decisions about delaying assisted reproduction should remain individualised because current evidence does not support a mandatory delay for all men after COVID-19.

4.8 Recovery strategies and supportive management

No intervention has been proven specifically to reverse COVID-19-related male reproductive impairment. Management should therefore focus on recovery from acute illness and standard modifiable fertility factors: smoking cessation, avoidance of anabolic steroids and excessive heat exposure, healthy body weight, regular physical activity, adequate sleep and management of metabolic disease.

Antioxidants have been proposed because oxidative stress is a plausible mechanism. However, Kalfas et al. (2023) concluded that COVID-specific evidence remains insufficient to establish antioxidant supplementation as a treatment. Any supplementation should therefore be framed as supportive rather than disease-specific therapy, and persistent severe abnormalities should prompt specialist andrological or fertility assessment.

4.9 Implications for public health and fertility counselling

SARS-CoV-2 continues to circulate, making accurate fertility counselling relevant even after the acute pandemic period. Counselling should be balanced: men should be informed that temporary semen and hormonal changes can occur, especially after fever or symptomatic disease, while also being reassured

that available longitudinal evidence shows recovery in many cases. Recording recent infection, fever severity and timing relative to semen collection can improve interpretation in fertility clinics.

4.10 Limitations of the current evidence

The evidence base is limited by observational designs, small samples, inconsistent control groups and substantial variation in the timing of semen collection. Many studies lack pre-infection semen data, making causal attribution difficult because semen parameters vary naturally within individuals. Fertility-clinic recruitment can introduce selection bias, and several studies inadequately report fever duration, medication exposure, abstinence interval, vaccination status, viral variant, body mass index and comorbidity.

Outcome heterogeneity is also important. Some studies report only conventional semen parameters, whereas others assess DNA fragmentation, hormones or seminal biomarkers. Meta-analyses therefore combine studies with different designs and follow-up periods, which contributes to statistical heterogeneity (Ashonibare et al., 2024; Wen et al., 2024). Most importantly, semen quality remains a surrogate endpoint: few studies measure natural conception, miscarriage, assisted-reproduction success or live birth.

A further reporting limitation is that the original database-identification, duplicate-removal, title/abstract exclusion and full-text exclusion counts cannot be reconstructed from the final bibliography. Figure 1 therefore reports only the reference-based classification that can be verified from the manuscript itself.

4.11 Overall interpretation

The most defensible interpretation is that COVID-19 can act as a systemic reproductive stressor capable of transiently impairing spermatogenesis, sperm motility, sperm DNA integrity and reproductive hormone balance. The pattern is strongest soon after symptomatic or febrile disease and appears reversible in many men. Persistent viral shedding in semen is uncommon and does not explain most reported abnormalities. Current evidence therefore supports temporary male reproductive dysfunction after COVID-19 rather than a general conclusion of permanent infertility.

5. Future Directions

5.1 Longitudinal Evidence

Future studies should prioritise within-person longitudinal designs with semen data available before infection and repeated testing after recovery. This approach reduces baseline inter-individual variability and allows the trajectory of change to be established more confidently. Zhao et al. (2025) illustrated the value of repeated post-infection assessments, while Guo et al. (2021) demonstrated how a second sample can reveal recovery not apparent at initial follow-up.

5.2 Recovery

Following up at standardised intervals such as one, three, six and twelve months would help define the duration and completeness of recovery and identify a subgroup with persistent abnormalities. Recovery should be analysed according to disease severity and fever exposure rather than reported only as a single overall post-COVID estimate.

5.3 Standardisation

Semen collection and analysis should follow current WHO laboratory guidance, with consistent reporting of abstinence period, collection method, laboratory processing and lower reference limits (World Health Organization, 2021). Studies should also report age, body mass index, smoking, medication exposure, comorbidity, vaccination status, variant/period of infection, fever duration and baseline fertility status to improve comparability.

5.4 Specificity

Future research should distinguish SARS-CoV-2-specific effects from the general reproductive consequences of febrile systemic illness. Comparator groups with non-COVID febrile infections, asymptomatic SARS-CoV-2 infection and symptomatic afebrile infection would help determine whether observed semen changes are driven predominantly by viral-specific mechanisms, fever or broader inflammatory stress.

5.5 Sperm Integrity

Conventional semen parameters should be complemented by validated measures of sperm DNA fragmentation, oxidative stress and mitochondrial function. The biomarker findings of Hajizadeh Maleki and Tartibian (2021) and DNA-fragmentation results of Yuan et al. (2025) indicate that functional injury may extend beyond routine count and motility measurements.

5.6 Endocrine Function

Longitudinal hormone studies should include testosterone, luteinising hormone, follicle-stimulating hormone, prolactin, estradiol, sex hormone-binding globulin and, where feasible, inhibin B. Repeated measurements would clarify whether altered testosterone-to-LH relationships represent temporary Leydig-cell stress or persistent testicular dysfunction.

5.7 Fertility Outcomes

The principal unanswered clinical question is whether laboratory abnormalities translate into reduced fertility. Future studies should measure time to natural conception, fertilisation rates, embryo development, implantation, miscarriage, clinical pregnancy and live birth. These outcomes are necessary before the reproductive significance of transient post-COVID semen changes can be defined.

5.8 Interventions

Controlled trials are required before recommending COVID-specific interventions. Potential strategies including antioxidant supplementation, lifestyle optimisation and treatment of endocrine abnormalities

should be evaluated against standard care using both semen and clinically meaningful reproductive outcomes. Until such data are available, management should remain based on established male-infertility principles rather than unproven post-COVID regimens.

5.9 Evolving Context

Future studies should account for vaccination, reinfection and viral variants because these factors alter disease severity and inflammatory burden. Repeated infections may have different reproductive consequences from a single episode, but cumulative effects on semen quality and endocrine function remain uncertain.

5.10 Summary

Research priorities are to establish within-person trajectories, standardise timing and laboratory methods, separate SARS-CoV-2 effects from febrile illness, expand functional sperm and endocrine assessment, and link laboratory findings to pregnancy and live-birth outcomes. These steps are needed to determine whether persistent reproductive impairment occurs in a definable subgroup and whether targeted intervention is beneficial.

6. Conclusion

COVID-19 is associated with measurable but predominantly time-dependent changes in male reproductive function. The most reproducible findings are reductions in sperm count/concentration and motility during acute infection or early recovery, with morphology, viability and DNA integrity affected in some studies. Longitudinal evidence indicates that these abnormalities improve over subsequent months in many men (Guo et al., 2021; Hu et al., 2022; Zhao et al., 2025).

The mechanism is likely multifactorial. Although seminal SARS-CoV-2 RNA has occasionally been reported (Li et al., 2020), most studies do not detect the virus in semen, making persistent direct infection an unlikely explanation for the majority of reproductive changes (Pan et al., 2020; Song et al., 2020; Ruan et al., 2021). Fever, systemic inflammation, oxidative stress and transient endocrine disturbance provide stronger and more consistent explanatory pathways (Hajizadeh Maleki and Tartibian, 2021; Ma et al., 2021; Kalfas et al., 2023).

The current evidence does not support the conclusion that COVID-19 commonly causes permanent male infertility. In men with fertility concerns after recent symptomatic or febrile infection, semen analysis can be considered, with repeat testing after approximately one spermatogenic cycle when initial findings are abnormal. Future longitudinal studies should prioritise standardised semen testing, sperm DNA integrity, endocrine recovery and clinically meaningful fertility outcomes.

Declarations

Ethics

Ethical approval was not required for this systematic review because the study was based entirely on previously published literature and did not involve recruitment of human participants, collection of identifiable patient data or direct clinical intervention.

Consent

Informed consent was not applicable because this review did not include individual patient-level data, case details, images or identifiable clinical information.

Funding

No specific funding was received for the preparation of this review.

Conflicts of Interest

The author declares no conflict of interest.

Data Availability

No new datasets were generated or analysed for this review. All data discussed in the manuscript were derived from previously published studies cited in the reference list.

Author Contribution

The author was responsible for conceptualisation, literature review, interpretation of findings, manuscript drafting and revision.

Acknowledgements

No acknowledgements are declared at this stage.

References

1. Abobaker A, Raba AA (2021) Does COVID-19 affect male fertility? World J Urol 39:975–976. 10.1007/s00345-020-03208-w
2. Agolli A, Yukselen Z, Agolli O, Patel MH, Bhatt KP, Concepcion L, Halpern J, Alvi S, Abreu R (2021) SARS-CoV-2 effect on male infertility and its possible pathophysiological mechanisms. Discoveries 9(2):e131. 10.15190/d.2021.10
3. Aitken RJ (2022) COVID-19 and male infertility: An update. Andrology 10(1):8–10. 10.1111/andr.13098
4. Akhigbe RE, Hamed MA (2020) Possible links between COVID-19 and male fertility. Asian Pac J Reprod 9(5):211–214. 10.4103/2305-0500.294662
5. Ashonibare VJ, Ashonibare PJ, Akhigbe TM, Akhigbe RE (2024) SARS-CoV-2 impairs male fertility by targeting semen quality and testosterone level: A systematic review and meta-analysis. PLoS ONE

- 19(9):e0307396. 10.1371/journal.pone.0307396
6. Best JC, Kuchakulla M, Khodamoradi K, Lima TFN, Frech FS, Achua J et al (2021) Evaluation of SARS-CoV-2 in human semen and effect on total sperm number: A prospective observational study. *World J Men's Health* 39(3):489–495. 10.5534/wjmh.200192
 7. Collins AB, Zhao L, Zhu Z, Givens NT, Bai Q, Wakefield MR, Fang Y (2022) 'Impact of COVID-19 on male fertility', *Urology*, 164, pp. 33–39. 10.1016/j.urology.2021.12.025
 8. Dutta S, Sengupta P (2021) SARS-CoV-2 and male infertility: Possible multifaceted pathology. *Reproductive Sci* 28:23–26. 10.1007/s43032-020-00261-z
 9. Gacci M, Coppi M, Baldi E, Sebastianelli A, Zaccaro C, Morselli S et al (2021) Semen impairment and occurrence of SARS-CoV-2 virus in semen after recovery from COVID-19. *Hum Reprod* 36(6):1520–1529. 10.1093/humrep/deab026
 10. Guo TH, Sang M-Y, Bai S, Ma H, Wan Y-Y, Jiang X-H et al (2021) Semen parameters in men recovered from COVID-19. *Asian J Androl* 23(5):479–483. 10.4103/aja.aja_31_21
 11. Hajizadeh Maleki B, Tartibian B (2021) COVID-19 and male reproductive function: A prospective, longitudinal cohort study. *Reproduction* 161(3):319–331. 10.1530/REP-20-0382
 12. Holtmann N, Edimiris P, Andree M, Doehmen C, Baston-Buest D, Adams O et al (2020) Assessment of SARS-CoV-2 in human semen – A cohort study. *Fertil Steril* 114(2):233–238. 10.1016/j.fertnstert.2020.05.028
 13. Hu B, Liu K, Ruan Y, Wei X, Wu Y, Feng H, Deng Z, Liu J, Wang T (2022) Evaluation of mid- and long-term impact of COVID-19 on male fertility through evaluating semen parameters. *Translational Androl Urol* 11(2):159–167. 10.21037/tau-21-922
 14. Illiano E, Trama F, Costantini E (2020) Could COVID-19 have an impact on male fertility? *Andrologia* 52(6):e13654. 10.1111/and.13654
 15. Kalfas T, Kaltsas A, Symeonidis EN, Symeonidis A, Zikopoulos A, Moustakli E et al (2023) COVID-19 and male infertility: Is there a role for antioxidants? *Antioxidants* 12(8):1483. 10.3390/antiox12081483
 16. Khalili MA, Leisegang K, Majzoub A, Finelli R, Panner Selvam MK, Henkel R, Mojgan M, Agarwal A (2020) Male fertility and the COVID-19 pandemic: Systematic review of the literature. *World J Men's Health* 38(4):506–520. 10.5534/wjmh.200134
 17. Koç E, Keseroğlu BB (2021) Does COVID-19 worsen the semen parameters? Early results of a tertiary healthcare center. *Urol Int* 105(9–10):743–748. 10.1159/000517276
 18. Li D, Jin M, Bao P, Zhao W, Zhang S (2020) Clinical characteristics and results of semen tests among men with coronavirus disease 2019. *JAMA Netw Open* 3(5):e208292. 10.1001/jamanetworkopen.2020.8292
 19. Ma L, Xie W, Li D, Shi L, Ye G, Mao Y et al (2021) Evaluation of sex-related hormones and semen characteristics in reproductive-aged male COVID-19 patients. *J Med Virol* 93(1):456–462. 10.1002/jmv.26259

20. Majzoub A, Khalafalla K, Arafa M, El Ansari W, Nair A, Al Bishawi A et al (2024) COVID-19 and male fertility: Short- and long-term impacts of asymptomatic vs. symptomatic infection on male reproductive potential. *Front Reproductive Health* 6:1403143. 10.3389/frph.2024.1403143
21. Malki MI (2022) COVID-19 and male infertility: An overview of the disease. *Medicine* 101(27):e29401. 10.1097/MD.00000000000029401
22. Maruki T, Morioka S, Miyazato Y, Tsuzuki S, Takezawa K, Kuribayashi S, Kutsuna S, Ohmagari N, Fukuhara S (2024) Association between post-COVID-19 conditions and male semen quality in Japan: A descriptive investigation. *J Infect Chemother* 30(11):1194–1196. 10.1016/j.jiac.2024.06.021
23. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD et al (2021) The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ* 372:n71. 10.1136/bmj.n71
24. Pan F, Xiao X, Guo J, Song Y, Li H, Patel DP et al (2020) No evidence of severe acute respiratory syndrome-coronavirus 2 in semen of males recovering from coronavirus disease 2019. *Fertil Steril* 113(6):1135–1139. 10.1016/j.fertnstert.2020.04.024
25. Pazir Y, Eroglu T, Kose A, Bulut TB, Genc C, Kadihasanoglu M (2021) Impaired semen parameters in patients with confirmed SARS-CoV-2 infection: A prospective cohort study. *Andrologia* 53(9):e14157. 10.1111/and.14157
26. Ruan Y, Hu B, Liu Z, Liu K, Jiang H, Li H et al (2021) No detection of SARS-CoV-2 from urine, expressed prostatic secretions, and semen in 74 recovered COVID-19 male patients: A perspective and urogenital evaluation. *Andrology* 9(1):99–106. 10.1111/andr.12939
27. Seymen CM (2021) The other side of COVID-19 pandemic: Effects on male fertility. *J Med Virol* 93(3):1396–1402. 10.1002/jmv.26667
28. Song C, Wang Y, Li W, Hu B, Chen G, Xia P et al (2020) Absence of 2019 novel coronavirus in semen and testes of COVID-19 patients. *Biol Reprod* 103(1):4–6. 10.1093/biolre/ioaa050
29. Sterne JAC, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M et al (2016) ROBINS-I: A tool for assessing risk of bias in non-randomised studies of interventions', *BMJ*. 355:i4919. 10.1136/bmj.i4919
30. Temiz MZ, Dincer MM, Hacibey I, Yazar RO, Celik C, Kucuk SH et al (2021) 'Investigation of SARS-CoV-2 in semen samples and the effects of COVID-19 on male sexual health by using semen analysis and serum male hormone profile: A cross-sectional, pilot study', *Andrologia*, 53(2), e13912. 10.1111/and.13912
31. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P (2000) The Newcastle-Ottawa Scale for assessing the quality of nonrandomised studies in meta-analyses. *Ottawa Hospital Research Institute, Ottawa*
32. Wen L, Tian H, Huang X, Song T, Tang L, Wei W, Tian S, Huang Y, Zhang X (2024) Effect of SARS-CoV-2 on semen parameters: A meta-analysis of 39 articles from 15 countries. *J Global Health* 14:05021. 10.7189/jogh.14.05021

33. World Health Organization (2021) WHO laboratory manual for the examination and processing of human semen, 6th edn. World Health Organization, Geneva

34. Yuan L, Sun W, Dong Z, Lu L, Wang X, Du Q, Guo R, Li P, Leng X, Liang H, Pan B (2025) COVID-19 infection was associated with poor sperm quality: A cross-sectional and longitudinal clinical observation study. *Sci Rep* 15:11380. 10.1038/s41598-025-94570-5

35. Zhao X, Zhao Y, Jiang N, Li K, Xu J, Ma R, Luan Z, Xia T (2025) The sperm quality change in 6 months recovery from COVID-19: A retrospective observational study. *Sci Rep* 15:36713. 10.1038/s41598-025-20637-y

Figures

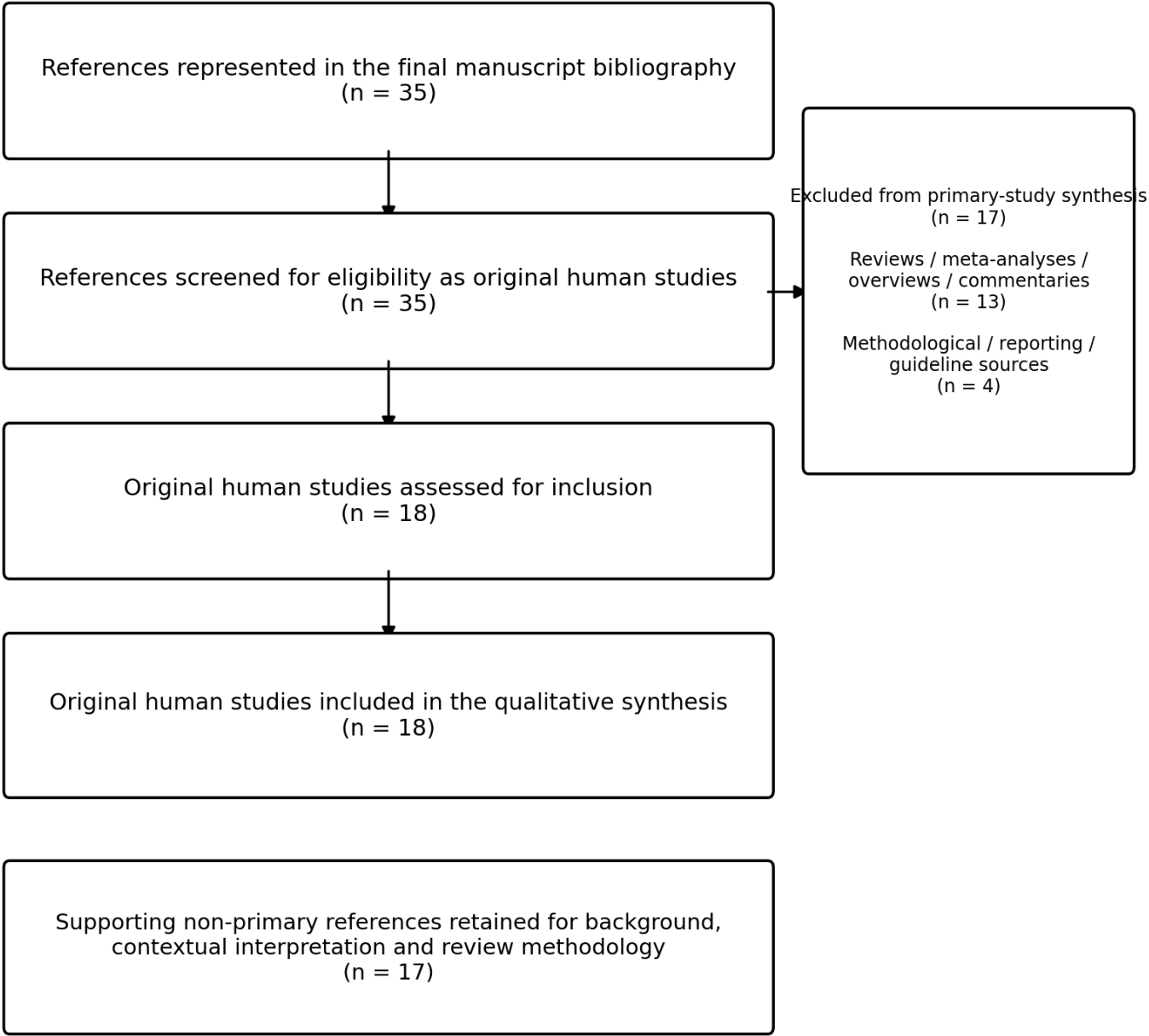


Figure 1

Reference-based PRISMA-style reconstruction of studies and supporting sources retained in the final manuscript.