Environment International 218 (2026) 110604



Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint



Review article

Systematic review and meta-analysis of exposure to glyphosate and glyphosate-based herbicides (GBHs) and male reproductive health in mammalian animal models

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ARTICLE INFO

Keywords:
Glyphosate
Glyphosate-based herbicide (GBH)
Systematic review
Male reproductive health
Sperm
Testosterone
Meta-analysis

ABSTRACT

Glyphosate is a widely used herbicide and the active ingredient in glyphosate-based herbicides (GBHs). Human exposure is primarily to GBHs, with the highest exposures in occupational settings and widespread lower-level exposure through diet and drinking water. To evaluate potential male reproductive toxicity of glyphosate and GBHs, we conducted a systematic review of non-human mammalian studies. Using a prespecified protocol following the OHAT systematic review framework, we searched PubMed, Web of Science, Scopus, CNKI, and Wanfang through April 2026 for studies evaluating glyphosate or GBHs and male reproductive outcomes. After screening studies against predefined eligibility criteria, we assessed study quality, synthesized evidence qualitatively and, when sufficient data were available, quantitatively through meta-analysis, and rated confidence in bodies of evidence. Most of the 55 included studies reported decreased sperm motility and abundance, increased abnormal sperm morphology, and decreased testosterone following glyphosate or GBH exposure. Testosterone reductions were most consistent in juvenile or adult animals and, for GBHs, following exposures of 30 days or longer. Meta-analyses found inverse associations between glyphosate and GBH exposure and sperm motility, count, concentration, and testosterone. There was high confidence that glyphosate and GBHs decrease overall sperm health and sperm abundance, and that GBHs reduce sperm motility and increase abnormal sperm morphology. There was moderate confidence that glyphosate reduces sperm motility and increases abnormal sperm morphology, and that both glyphosate and GBHs reduce testosterone. Overall, these findings provide evidence of adverse effects of glyphosate and GBHs on male reproductive health from data across multiple species and study designs.

1. Introduction

Glyphosate, or N-(phosphonomethyl) glycine, is a broad-spectrum synthetic herbicide used to kill most broadleaf plants and grasses by inhibiting 5-enolpyruvylshikimate-3-phosphate synthase, an enzyme essential for aromatic amino acid synthesis and plant survival (Boocock and Coggins 1983). Plants that naturally express, or are genetically modified to express, a glyphosate-insensitive type of this enzyme are resistant to glyphosate effects. Approximately 280 million pounds of glyphosate were applied annually in U.S. agricultural settings from 2012 to 2018, with nearly 200 million pounds used on soybeans and corn alone (USEPA 2021; USGS 2024). Additionally, over 21 million pounds of glyphosate are applied annually to non-agricultural settings, including residential areas, roadways and forestry sites (USEPA 2021).

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https://doi.org/10.1016/j.envint.2026.110604
Received 4 September 2026; Received in revised form 6 November 2026; Accepted 9 November 2026
Available online 13 November 2026
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Most human exposure occurs through glyphosate-based herbicides (GBHs), with glyphosate as an active ingredient, along with surfactants and other ingredients that enhance herbicidal activity and may contribute to toxicity (Mesnage et al. 2019). GBH formulations vary widely, and exact compositions are typically proprietary. Exposure is highest in occupational settings, primarily via dermal contact, but also through inhalation and incidental ingestion (Connolly et al. 2019). General population exposure is widespread but lower, with food as the main source (Mellor et al. 2024); additional sources include contaminated drinking or surface water (Li and Kannan 2025). National Health and Nutrition Examination Survey data indicate that over 70–80% of the U.S. population aged ≥6 years had detectable urinary glyphosate from 2013 to 2018 (Wu et al. 2025). Glyphosate is readily absorbed through the gastrointestinal and respiratory tracts relative to dermal absorption, which is limited but may be increased by GBH surfactants (ATSDR 2020). Once absorbed, glyphosate is distributed throughout the body, undergoes limited metabolism, and is predominately eliminated unchanged in feces and urine (ATSDR 2020; Li et al. 2025). Human exposure may also include co-exposures to glyphosate metabolites generated by bacteria, fungi, and plants (Zoller et al. 2020).

Previous reviews have raised concerns about glyphosate and male reproductive toxicity. The Agency for Toxic Substances and Disease Registry (ATSDR) reported sperm abnormalities, reduced testosterone, testicular histopathological anomalies, and decreased sperm counts in glyphosate-exposed male animals (ATSDR 2020). Cai et al. (2017) reported reduced sperm concentrations in glyphosate-exposed rats and mice, and Mohammadi et al. (2022) reported decreased testosterone, follicle-stimulating hormone, and luteinizing hormone following exposure to technical-grade glyphosate (the active ingredient alone) or GBHs in rats. These findings provided a scientific rationale for further evaluating male reproductive toxicity associated with glyphosate and GBHs. In response to a request from the U.S. Department of Health and Human Services (HHS), this review was designed as a rapid systematic review, with the scope narrowed to male reproductive health in mammalian animal models to meet the requested timeline (DTT 2026).

The objective of this evaluation was to systematically identify, critically assess, and synthesize evidence from experimental non-human mammalian studies evaluating the effects of glyphosate and GBH exposure on male reproductive health, including sperm characteristics, reproductive hormone levels, reproductive organ weights and histopathology, and developmental outcomes. Specifically, we assessed the internal validity (risk of bias) of individual studies, synthesized evidence across studies, and evaluated confidence in the bodies of evidence separately for glyphosate alone and GBHs.

2. Methods

This review followed a prespecified protocol, with a narrow scope for a rapid workflow. Brief methods are outlined here, with detailed methods provided in **Supplementary materials** and the protocol (DTT 2026; https://doi.org/10.22427/NTP-DATA-500-106-003-000-5).

2.1. Problem formulation and protocol development

This systematic review was initiated in response to a November 2025 HHS request to evaluate the association between glyphosate and GBHs and male reproductive toxicity, with a rapid timeline for completion. The scope of the current evaluation was limited to experimental data from non-human mammals, which represent the most relevant experimental models for evaluating human health, and is presented in this review. To build on the findings of this systematic review, a subsequent review of this topic will include human, mechanistic, and expanded animal data (e.g., non-mammalian vertebrates such as fish and birds). Using the OHAT[2] Handbook (NTP, 2019) for methods guidance, the protocol was developed by a multidisciplinary team of scientists in the Division of Translational Toxicology (DTT) at the National Institute of Environmental Health Sciences (NIEHS), including DTT and contractor experts in public health, toxicology, epidemiology, and systematic review, with input from NIEHS subject matter experts. The evaluation team decided to assess health effects associated with glyphosate alone and GBHs separately given the complexity of formulations. Additional problem formulation details are described in **Supplement Section S1**. The phase 1 protocol was finalized in February 2026, with updates documented in May 2026.

2.2. Assessing male reproductive toxicity

The male reproductive system relies on highly coordinated endocrine and paracrine signaling to regulate the production, maturation, and transport of sperm for fertilization and is primarily regulated by the hypothalamus-pituitary–gonadal (HPG) axis (Dutta et al. 2019). Gonadotropin-releasing hormone (GnRH) secretion from the hypothalamus stimulates the release of follicle stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary to establish the connection between the brain and the testes (Alves et al. 2013). Within the testes, FSH regulates Sertoli cell function and stimulates spermatogenesis, while LH acts on Leydig cells to stimulate the production of testosterone. Sperm effects are commonly measured by assessing the sperm abundance (count, concentration, and production) in the testis, epididymis or ejaculate, sperm function (motility), and morphology (number and type of abnormal sperm). Organ weight measurements (e.g., testis and epididymis) are potential indicators of reproductive toxicity, and histopathology evaluates the microscopic structures to support and inform impacts on stages of sperm maturation (USEPA 1996). Testosterone production and secretion play critical roles in sexual differentiation, regulation of reproductive developmental milestones (e.g., anogenital distance and preputial separation), germ cell development, and is the primary negative feedback signal to downregulate GnRH and LH production (Dutta et al. 2019). Individual endpoints provide measures of reproductive health, and changes in testosterone secretion may serve as an indicator of alterations in the function of components of the HPG axis.

2.3. Literature search and study selection

2.3.1. PECO statement

The PECO (Populations, Exposures, Comparators, Outcomes) statement guided the research questions, search terms, and inclusion/exclusion criteria (see **Supplement Table S1**). The population was restricted to non-human mammals, exposures were glyphosate or GBHs via any route of administration, comparators were vehicle-only or unexposed groups, and outcomes captured male reproductive health effects including organ weights, hormone levels, sperm characteristics, and developmental endpoints.

2.3.2. Literature search strategy

Comprehensive searches based on the ATSDR Toxicological Profile for Glyphosate (ATSDR 2020) search terms were conducted in PubMed, Web of Science, and Scopus (through April 2026), including terms for glyphosate, GBHs, and male reproductive outcomes (see protocol). No restrictions were placed on language or publication year. Supplemental searches targeted GBH commercial product names and glyphosate

[2] OHAT is the abbreviation for Office of Health Assessment and Translation, which has become the Health Assessment and Translation group in the Integrative Health Assessments Branch of DTT at NIEHS.

metabolites, as well as Chinese databases (CNKI, Wanfang) to capture non-English studies. Duplicates were removed and unique publications were reported in Fig. 1. Non-English studies were screened based on English-language titles and abstracts, with translation as needed.

2.3.3. Study selection

Publications had to meet eligibility criteria based on the PECO statements. The protocol provides specific inclusion and exclusion details (e.g., exclusion of non-mammalian animal models, such as fish and birds).

2.3.4. Screening process

Title-and-abstract screening was performed in DistillerSR® (Evidence Partners, Ottawa, CA) by two independent reviewers following pilot screening to train reviewers and refine guidance. Conflicts were resolved by senior team members. References considered eligible or unclear underwent full-text review by two independent reviewers, with conflicts resolved by a senior team member. Reasons for exclusion were reported using PRISMA practices (Page et al. 2021), with only the primary reason recorded following a predefined hierarchy.

2.4. Data extraction and availability

Data were extracted using Dextr (version 3.5.3), a customized version of LASER AI platform (Evidence Prime, Inc.), which combines advanced machine learning with manual verification to ensure accuracy (Walker et al. 2024). Dextr predicted and populated complex data elements—including study design, animal model, exposure, and outcomes, with manual verification. Controlled vocabularies were used to standardize data. Data were exported via a custom Python script to the HAWC (build 9D7A2580, March 2026) systematic review platform, for quality control and risk-of-bias assessment. All extraction elements are documented in the protocol and supporting data are available in HAWC (https://hawcproject.org/assessment/1592/). Third-party tools, including Distiller (2026.2) and Dextr (3.5.3), are licensed applications.

2.5. Quality assessment of individual studies

Risk of bias (RoB) was evaluated using the OHAT RoB tool (NTP, 2015), with each applicable domain rated using one of four response options (definitely low, probably low, probably high, or definitely high RoB) according to prespecified criteria; detailed RoB criteria are provided in the protocol. The domains evaluated included randomization, allocation concealment, consistency of experimental conditions, blinding, completeness of outcome data, exposure characterization, outcome assessment, selective outcome reporting, and other potential sources of bias. Randomization, exposure characterization, and outcome assessment were designated as key domains; for developmental studies, appropriate treatment of litter as the unit of analysis was also considered a key question. Trained assessors independently evaluated studies and resolved discrepancies through discussion and consensus to finalize ratings for all included studies (Fig. 2). When reporting was insufficient, study authors were contacted for clarification; domains with insufficient information remaining after these efforts were rated probably high RoB. For each outcome, studies rated probably high RoB for at least two key domains or definitely high RoB for any domain were classified as high RoB (low quality); all others were classified as low RoB (high quality). Overall RoB classifications could differ across outcomes within the same study. Ratings and justifications were recorded in HAWC (https://hawcproject.org/assessment/1592/).

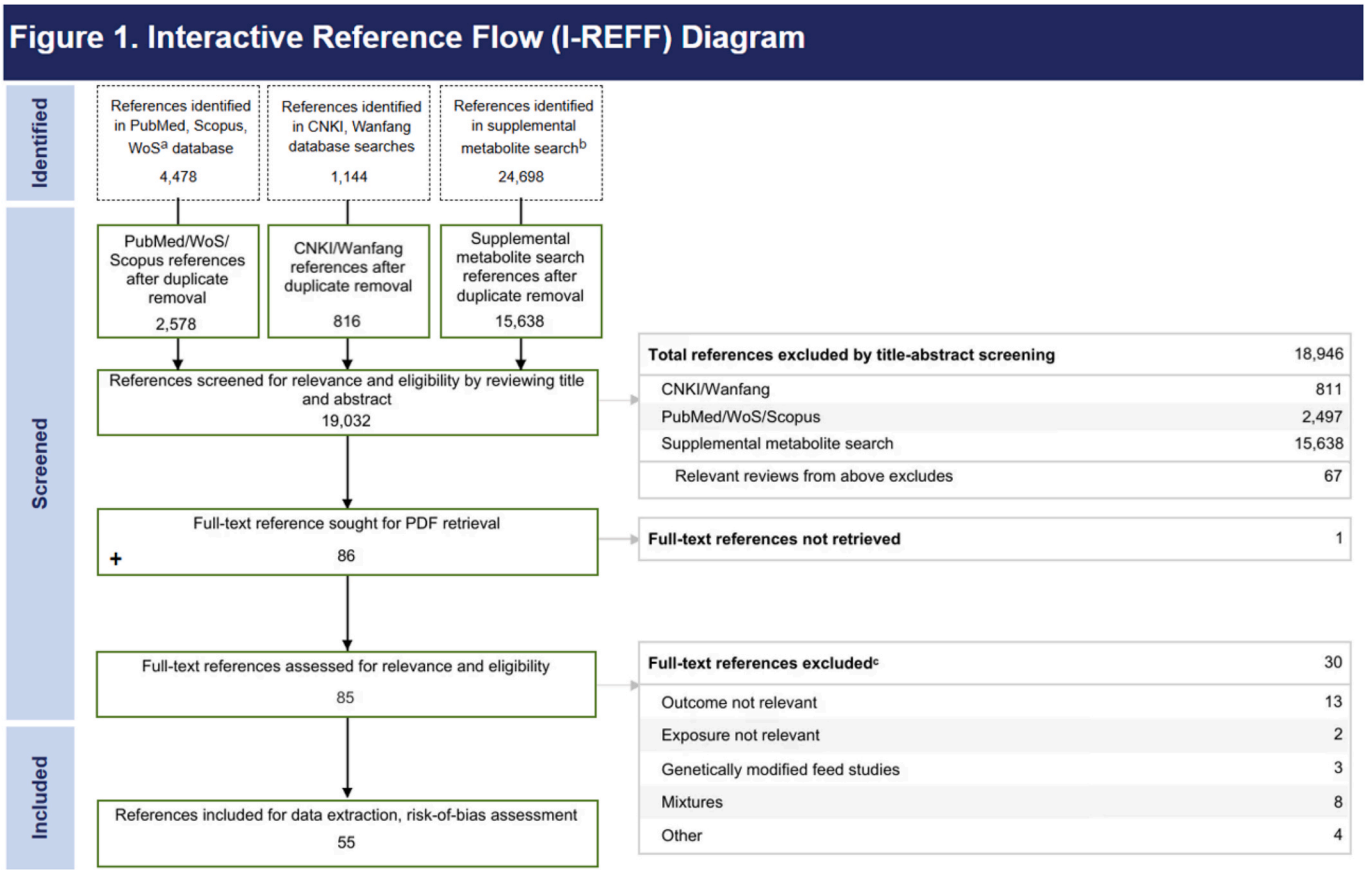


Fig. 1. Study Selection Diagram in Interactive REFerence Flow (I-REFF) Arrangement: An interactive version of the I-REFF is available here: glyphosate HAWC project I-REFF.

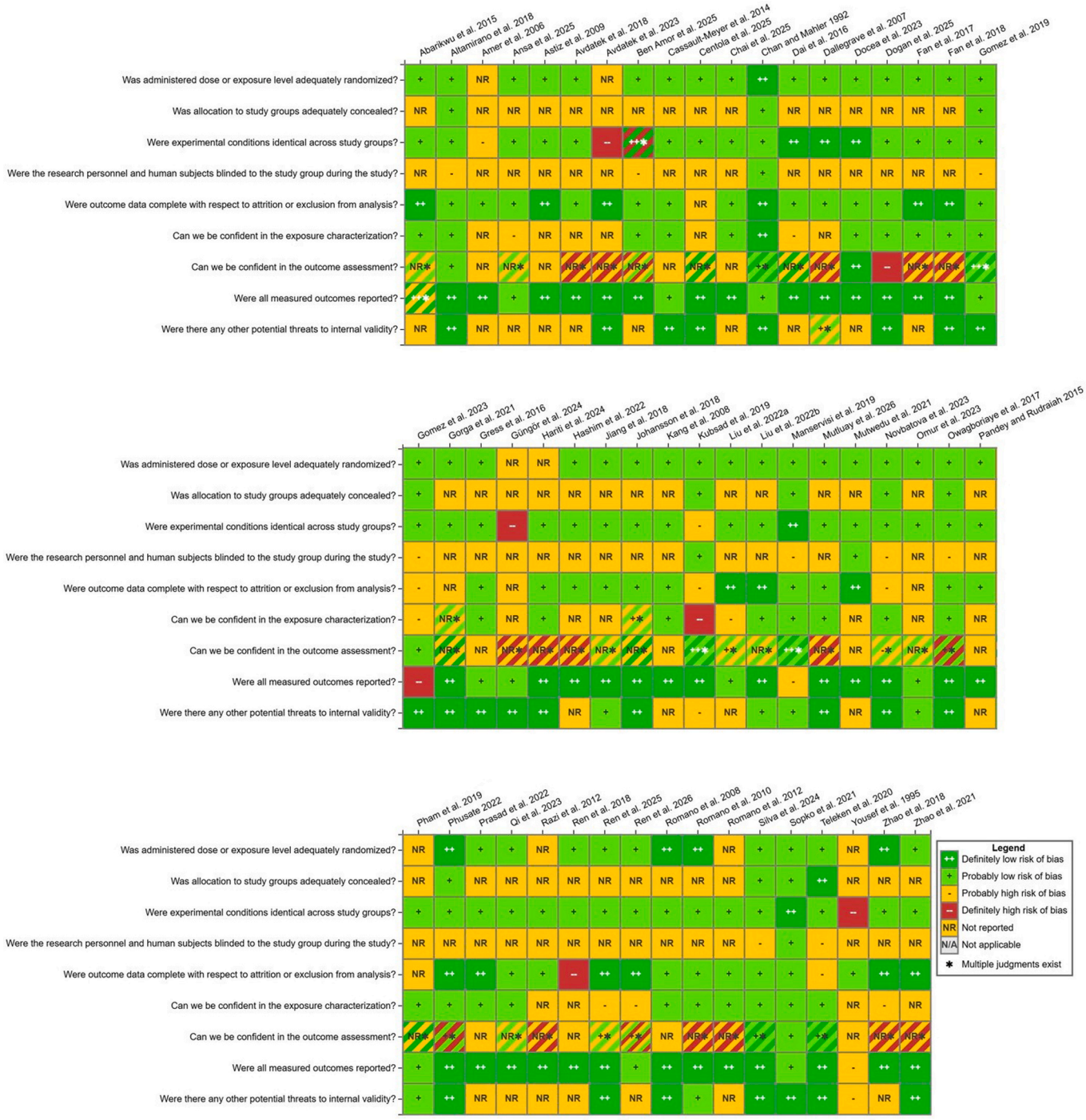


Fig. 2. Risk-of-bias heatmap of all included studies: An interactive version is available at the following link to figure. This plot summarizes the risk-of-bias (RoB) assessment for all 55 included studies across individual bias domains (e.g., selection bias, confounding bias, performance bias, attrition/exclusion bias, detection bias, selective reporting bias, and other sources of bias) using OHAT risk-of-bias tool. Each column represents an individual study, and each row represents a bias domain. Colors in each cell indicate the level of bias for a given domain within each study.

2.6. Meta-analyses

We conducted mean effects meta-analyses separately for glyphosate and GBHs for testosterone, sperm count, sperm concentration, and sperm motility. Studies were included in the meta-analysis if they reported a mean, measure of uncertainty, and sample size for exposed and control groups. Effect estimates were expressed as standardized mean differences (SMDs) calculated using Hedges's *g* to account for small sample sizes (Hedges and Olkin 1985). Pooled SMDs and 95% confidence intervals were estimated using robust variance estimation (RVE) meta-analysis to account for correlations among multiple results reported within the same study (Tanner-Smith and Tipton 2014). Random-effects models with restricted maximum likelihood estimation were also conducted treating results as independent.

Additional analyses evaluated heterogeneity, subgroup differences, influential studies, publication bias, and sensitivity to alternative analytic decisions. Potential publication bias was assessed through visual inspection of funnel plots and Egger's regression and Begg's rank correlation tests, where applicable. Additional methodological details are provided in the protocol and **Supplement Section 1.3**. Statistical

analyses were performed using STATA 18.0 using the *meta*, *robumeta*, *metainf*, *metafunnel*, and *metabias* packages (Palmer and Sterne, 2016; StataCorp 2023).

2.7. Assessment of confidence

Bodies of evidence comprised of studies on the same outcome (e.g., testosterone levels) were evaluated separately for certainty in the evidence for glyphosate and GBH exposures following the OHAT approach described in the protocol. For each outcome and exposure, confidence conclusions were reached by assigning an initial confidence rating based on the presence of the four key study design features (controlled exposure, exposure occurred prior to outcome, individual-based outcomes evaluated, and a comparison group used) and then considering factors that may increase or decrease confidence in each body of evidence.

3. Results

3.1. Literature search results

Literature searches of PubMed, Scopus, and Web of Science databases retrieved 2,578 unique references on glyphosate or GBH exposure and male reproductive outcomes. Supplemental searches added 816 references from Chinese databases and 15,638 references from a metabolite search for a total of 19,032 references. Title-and-abstract screening identified 86 potentially relevant references in non-human mammalian models; 18,946 references were excluded for not meeting PECO criteria. Following full-text review, 55 studies were included for the review: 50 English- and 5 non-English-language studies. These studies underwent data extraction to capture study design, conduct, and endpoints relevant to male reproductive health. Additional screening details are provided in Fig. 1 and in **Supplement Fig. S1**.

3.2. Available non-human mammalian animal data relating to male reproduction

The body of literature consisted of 55 studies reporting data on male reproductive endpoints with most results categorized into three primary areas: sperm parameters, hormones, and developmental milestones. Other outcomes included male reproductive organ weights and histopathology. Thirty-one studies evaluated male reproductive outcomes following GBH exposure, 18 studies evaluated outcomes following glyphosate exposure, and 6 studies evaluated both exposures. The sections below summarize the groups of studies that evaluated the primary endpoints following glyphosate or GBH exposure.

3.3. Sperm parameters

3.3.1. Overview of studies

Thirty-one studies evaluated effects of glyphosate or GBHs on sperm parameters in adult males (Table 1; **Supplement Tables S18–S19**), including 26 of sperm abundance (sperm count, concentration, or daily production), 23 of sperm morphology (percentage abnormal sperm), and 20 of sperm motility. Nineteen studies were conducted using rats, while fewer studies utilized mice (10 studies), rabbits (2 studies), or guinea pigs (1 study). Eight studies evaluated glyphosate alone, 20 evaluated GBHs, and 3 evaluated both exposures. The route of administration of glyphosate or GBH was primarily oral, including gavage (18 studies), diet (7 studies), drinking water (4 studies), and one study each administered the dose via capsule or intraperitoneal injection. Most studies evaluated sperm parameters following exposure to adult males, while five initiated exposure in utero and seven began exposure during the juvenile or peripubertal lifestage.

3.3.2. Results by exposure: glyphosate

Abundance: Six of seven studies reported reductions in sperm count following glyphosate exposure (Abarikwu et al. 2015; Chan and Mahler 1992; Dai et al. 2016; Pham et al. 2019; Razi et al. 2012; Ren et al. 2025) (Table 1; Fig. 3). When looking at epididymal sperm count data by the timing of exposure, four studies initiated exposure in the peripubertal period or adulthood in rats including Abarikwu et al. (2015) at 5 mg/kg-day, Chan and Mahler (1992) at 1,678 and 3,393 mg/kg-day, Dai et al. (2016) at 5, 50, 500 mg/kg-day (significant at 500 mg/kg-day), Razi et al. (2012) at 125 mg/kg-day, or in the developmental period in mice reported by Pham et al. (2019) at 0.5, 5, and 50 mg/kg-day (significant at 5 mg/kg-day). Manservisi et al. (2019) reported that exposure to 1.75 mg/kg-day glyphosate for 88 or 140 days beginning during gestation had no effect on epididymal sperm count or testicular spermatids. In contrast to the epididymal data, only one of the three studies that examined testicular sperm reported an effect; Ren et al. (2025) observed reductions in the number of testicular spermatids, spermatogonia, and spermatocytes following 168 days of dietary exposure at 1.75 and 17.5 mg/kg-day. Following a 91-day exposure to peripubertal animals at doses that were substantially higher than other studies (811–3,393 mg/kg-day in rats and 2,273–10,780 mg/kg-day in mice compared to 0.5–500 mg/kg-day in others), Chan and Mahler (1992) reported reduced epididymal sperm count in rats but no effect on testicular spermatids in rats or mice, or epididymal sperm counts in mice.

Three of five studies reported reduced sperm concentration in rats, mice, and rabbits (Liu et al. 2022b; Ren et al. 2025; Yousef et al. 1995) (Table 1; Fig. 5). Dose-dependent reductions in epididymal sperm concentration were observed in mice following adult exposure at 1.75 and 17.5 mg/kg-day for 168 days (Ren et al. 2025) and rats after peripubertal exposure at 2 and 50 mg/kg-day for 120 days (Liu et al. 2022b). In a companion study with a shorter 60-day exposure, Liu et al. (2022a) reported a 10% reduction in sperm concentration at 50 mg/kg-day that was not significant due to wide standard deviations. Sperm concentration was also reduced in ejaculate samples in rabbits following adult exposure at 38 and 380 mg/kg-day, remaining significantly below control levels 6 weeks after exposure ended (Yousef et al. 1995). Chan and Mahler (1992) reported no effect of glyphosate on sperm concentration in mice at doses up to 10,780 mg/kg-day and rats at doses up to 3,393 mg/kg-day following a 91-day exposure.

The only study that evaluated daily sperm production reported no effect of glyphosate exposure (Manservisi et al. 2019).

Motility: Five of six studies reported reduced percentages of motile sperm (Table 1; Fig. 7; **Supplement Table S18**). Decreased sperm motility was observed following exposure of peripubertal mice for 168 days at 1.75 and 17.5 mg/kg-day (Ren et al. 2025) and juvenile rats for 120 days at 2 and 50 mg/kg-day (Liu et al., 2022b) with only the 50 mg/kg-day dose significant in a shorter, 60-day exposure (Liu et al., 2022a). Decreased sperm motility was also observed following glyphosate exposure to adult rats at 0.5 mg/kg-day for 90 days (Ömür et al. 2024) and 125 mg/kg-day for 10 to 40 days with greater percentages of sperm affected in longer exposures (Razi et al. 2012). The remaining study reported no effect in rats or mice after a 91-day exposure to much higher levels of glyphosate (Chan and Mahler 1992).

Morphology: Five of six studies reported higher percentages of abnormal sperm in rats, mice and rabbits (Liu et al. 2022a; Liu et al. 2022b; Razi et al. 2012; Ren et al. 2025; Yousef et al. 1995) (Table 1; Fig. 9; **Supplement Table S19**). An increase in abnormal sperm was reported following exposure of peripubertal mice for 168 days at 1.75 and 17.5 mg/kg-day (Ren et al. 2025) and the percentage of abnormal sperm was increased 40 to 700% following 60 and 120-day exposures of juvenile rats to 2 and 50 mg/kg-day glyphosate (Liu et al. 2022a; Liu et al. 2022b) with evidence of both duration- and dose-dependent effects. Increased percentage of abnormal sperm were also observed following glyphosate exposure to adult rabbits at 38 and 380 mg/kg-day for 42 days (Yousef et al. 1995) and adult rats at 125 mg/kg-day for 10 to 40 days with greater percentage of sperm affected in longer exposures (Razi et al. 2012). The remaining study reported no effect in rats exposed

Table 1
Overview of studies with sperm data Sperm data table The data table below provides a brief description of the studies for each of the main sperm parameters including sperm abundance (count, concentration, production), sperm motility, and sperm morphology. Study descriptions include the exposure (glyphosate or GBH with the glyphosate studies presented first), animal model (species, strain and age at treatment), and treatment details (route, duration, doses), followed by the relevant outcomes measured and a brief summary of the results for each relevant sperm parameters. For sperm motility only the data on percentage of motile sperm or total motile sperm are presented here; additional measures of sperm motility are available in Supplemental Table S18. Similarly for sperm morphology, only the data on common measures of abnormal sperm are presented here; additional measures of abnormal sperm are available in Supplemental Table S19.

Study	Exposure	Model (age at treatment)	Treatment (duration) doses	Outcomes	Summary of Results
Abarikwu et al. (2015)	Glyphosate[1]	Wistar rats (28 – 35 days)	Oral gavage (3x/week for 52 days) 0, 5 mg/kg-day	Sperm per cauda epididymis (10^7)	• Abundance (count): Sperm per cauda epididymis (10^7) significantly decreased 47% relative to controls at 52 days.
Chan and Mahler (1992)	Glyphosate	F344/N rats (43 days) B6C3F1 mice (49 days)	Diet (91 days) Rats: 0, 205, 410, 811, 1,678, 3,393 mg/kg-day Mice: 0, 507, 1,065, 2,273, 4,776, 10,780 mg/kg-day	Percentage of motile sperm Sperm per cauda epididymis (10^6), spermatids per testis (10^7), spermatids per g testis (10^7) Spermatids per testis/mL (10^4) (all sperm outcomes evaluated only at the 3 highest doses)	• Motility: In rats and mice, no change in percentage of motile sperm relative to controls at 91 days. • Abundance (count) at 91 days relative to controls: o In rats, sperm per cauda epididymis (10^6) significantly decreased 20% at the two highest doses. o In rats, no changes in spermatids per testis (10^7) or spermatids per g testis (10^7). o In mice, no changes in sperm per cauda epididymis (10^6), spermatids per testis (10^7), or spermatids per g testis (10^7). • Abundance (concentration): In rats and mice, no changes in spermatids per testis/mL (10^4) relative to controls at 91 days.
Dai et al. (2016)	Glyphosate	SD rats (56 days)	Oral gavage (35 days) 0, 5, 50, 500 mg/kg-day	Sperm per g epididymis (10^7)	• Abundance (count): Sperm per g epididymis (10^7) decreased 22%, 15%, and 29% at the low, mid, and high dose groups relative to controls at 35 days but only the high-dose decrease was statistically significant.
Liu et al. (2022a)	Glyphosate	SD rats (35 days)	Diet (60 days) 0, 2, 50 mg/kg-day	Percentage of total motile sperm[2] Sperm per cauda epididymis/mL (10^6) Percentage of abnormal sperm	• Motility: Significant 14% decrease in percentage of total motile sperm only at the high dose relative to controls at 60 days. • Abundance (concentration): No changes in sperm per cauda epididymis/mL (10^6) relative to controls at 60 days. • Morphology: Percentage of abnormal sperm significantly increased 40% and 233% at the low and high doses relative to controls at 60 days.
Liu et al. (2022b)	Glyphosate	SD rats (35 days)	Diet (120 days) 0, 2, 50 mg/kg-day	Percentage of total motile sperm[2] Sperm per cauda epididymis/mL (10^6) Percentage of abnormal sperm	• Motility: Significant 15% and 19% decreases in percentage of total motile sperm at the low and high doses relative to controls at 120 days. • Abundance (concentration): Sperm per cauda epididymis/mL (10^6) significantly decreased 13% and 18% at the low and high doses relative to controls at 120 days. • Morphology: Percentage of abnormal sperm significantly increased 250% and 700% at the low and high doses relative to controls at 120 days.
Manservisi et al. (2019)	Glyphosate	SD rats (GD6)	Drinking water [gestation, lactation, postweaning] (~88 or 140 days) 0, 1.75 mg/kg-day	Spermatids per g testis (10^6), sperm per cauda epididymis (10^6), sperm per caput-corpus epididymis (10^6) DSP/g testis (10^6) Percentage of abnormal sperm	• Abundance (count): No changes in spermatids per g testis (10^6), sperm per cauda epididymis (10^6), or sperm per caput-corpus epididymis relative to controls at PND73 or PND125. • Abundance (production): No changes in DSP/g testis (10^6) relative to controls at PND73 or PND125. • Morphology: No change in percentage of abnormal sperm relative to controls at PND73 or PND125.
Ömür et al. (2024)	Glyphosate	SD rats (90 days)	Diet (90 days) 0, 0.5 mg/kg-day	Percentage of motile sperm	• Motility: Percentage of motile sperm significantly decreased 39% relative to controls at 90 days.
Pham et al. (2019)	Glyphosate	Swiss mice (GD10.5)	Drinking water [gestation, lactation] (~31 days) 0, 0.5, 5, 50 mg/kg-day	Sperm per epididymis (10^6)	• Abundance (count): Sperm per epididymis (10^6) decreased 56%, 89%, and 30% at the low, mid, and high doses relative to controls at PND35, but only the mid-dose decrease was statistically significant.
Razi et al. (2012)	Glyphosate	Wistar rats (63 days)	Oral gavage (10, 20, 30, or 40 days) 0, 125 mg/kg-day	Percentage of motile sperm Sperm per cauda epididymis (10^6) Percentage of abnormal sperm	• Motility: Percentage of motile sperm significantly decreased 4%, 19%, 49%, and 54% relative to controls at 10, 20, 30, and 40 days.

(*continued on next page*)

Table 1 (*continued*)

Study	Exposure	Model (age at treatment)	Treatment (duration) doses	Outcomes	Summary of Results
					• Abundance (count): Sperm per cauda epididymis (10^6) significantly decreased 13%, 32%, 44%, and 67% relative to controls at 10, 20, 30, and 40 days. • Morphology: Percentage of abnormal sperm significantly increased 17%, 33%, 33%, and 39% relative to controls at 10, 20, 30, and 40 days.
Ren et al. (2025)	Glyphosate	C57BL/6 mice (42 days)	Diet (168 days) 0, 1.75, 17.5 mg/kg-day	Percentage of total motile sperm[2] Number of spermatogonia, number of spermatocytes, number of spermatids Sperm per cauda epididymis/mL (10^6) Proportion of abnormal sperm	• Motility: Significant 26% and 52% decreases in percentage of total motile sperm at the low and high doses relative to controls at 168 days. • Abundance (count) at 168 days relative to controls: o Number of spermatogonia significantly decreased 19% and 44% in the low and high dose groups. o Number of spermatocytes significantly decreased 27% and 49% in the low and high dose groups. o Number of spermatids significantly decreased 14% and 43% in the low and high dose groups. • Abundance (concentration): Sperm per cauda epididymis/mL (10^6) significantly decreased 22% and 46% at the low and high doses relative to controls at 168 days. • Morphology: Qualitative results for sperm morphology were not provided but the authors concluded that glyphosate significantly increased the proportion of abnormal sperm (headless or bent sperm) in the epididymis.
Yousef et al. (1995)	Glyphosate	New Zealand white rabbit (adult)	Oral capsule (42 days) 0, 38, 380 mg/kg-day	Sperm in ejaculate/mL (10^6) Percentage of abnormal sperm	• Abundance (concentration) relative to controls: o Sperm in ejaculate/mL (10^6) significantly decreased 41% and 37% at the low and high doses at 42 days. o Sperm in ejaculate/mL (10^6) significantly decreased 21% and 22% at the low and high doses at 84 days (6 weeks post-exposure). • Morphology relative to controls: o Percentage of abnormal sperm significantly increased 75% and 81% at the low and high doses at 42 days. o Percentage of abnormal sperm significantly increased 26% and 18% at the low and high doses at 84 days (6 weeks post-exposure).
Abarikwu et al. (2015)	GBH[4] (Bretmont Wipeout) [30.38% GAE]	Wistar rats (28 – 35 days)	Oral gavage (3x/week for 52 days) 0, 5 mg/kg-day	Percentage of motile sperm Sperm per cauda epididymis (10^7), spermatids per testis (10^7) DSP (10^6), DSP/g testis (10^6) Percentage of abnormal sperm	• Motility: Percentage of motile sperm significantly decreased 65% relative to controls at 52 days. • Abundance (count) relative to controls at 52 days: o Sperm per cauda epididymis (10^7) significantly decreased 44%. o Spermatids per testis (10^7) significantly decreased 42%. • Abundance (production) relative to controls at 52 days: o DSP (10^6) significantly decreased 40%. o DSP/g testis (10^6) significantly decreased 29%. • Morphology: Percentage of abnormal sperm significantly increased 33% relative to controls at 52 days.
Amer et al. (2006)	GBH (Herbazed) [NR % GAE]	Swiss mice (~63–84 days)	Oral gavage (5 days) 0, 50, 100, 200 mg/kg-day)	Percentage of abnormal sperm[3]	• Morphology: Percentage of sperm abnormalities increased 57%, 105%, and 157% relative to controls at 30 days after first dose, although only the changes at the mid and high doses were statistically significant.
Ansa et al. (2025)	GBH (Force Up®) [NR % GAE]	Composite rabbits (182–210 days)	Diet (84 days) 0, 10 mL/L	Percentage of motile sperm Sperm in ejaculate (10^{12}) Sperm in ejaculate/mL (10^{12}) Percentage of abnormal sperm[3]	• Motility: Percentage of motile sperm significantly decreased 59% relative to controls at 84 days. • Abundance (count): Sperm in ejaculate (10^{12}) significantly decreased 78% relative to controls at 84 days.

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Table 1 (*continued*)

Study	Exposure	Model (age at treatment)	Treatment (duration) doses	Outcomes	Summary of Results
					• Abundance (concentration): Sperm in ejaculate/mL (10^{12}) significantly decreased 60% relative to controls at 84 days. • Morphology: Percentage of abnormal sperm significantly increased 112% relative to controls at 84 days exposure.
Avdatek et al. (2018)	GBH (Knockdown 48 SL) [NR% GAE]	Wistar rats (84 days)	Diet (56 days) 0, 375 mg/kg-day	Percentage of progressive motile sperm Percentage of total abnormal sperm[3]	• Motility: Percentage of progressive motile sperm significantly decreased 39% relative to controls at 56 days. • Morphology relative to controls at 56 days: o Percentage of total abnormal sperm significantly increased 68%.
Avdatek et al. (2023)	GBH (Knockdown 48 SL) [NR% GAE]	Wistar rats (75–90 days)	Oral gavage (56 days) 0, 787.85 mg/kg-day	Percentage of motile sperm Percentage of total abnormal sperm[b]	• Motility: Percentage of motile sperm significantly decreased 11% relative to controls at 56 days. • Morphology: Percentage of total abnormal sperm significantly increased 19% relative to controls at 56 days.
Ben Amor et al. (2025)	GBH (Kalach 360 SL) [30.75% GAE]	Wistar rats (adult)	Oral gavage (48 days) 0, 102.2 mg/kg-day	Percentage of motile sperm[a] Sperm per cauda epididymis/mL (10^6) Percentage of normal spermatozoa forms[3]	• Motility: Percentage of motile sperm significantly decreased 56% and 43% relative to controls at 48 and 96 days (after 48-day recovery). • Abundance (concentration): Sperm per cauda epididymis/mL (10^6) significantly decreased 83% relative to controls at 48 days but showed no change after recovery at 96 days. • Morphology: Percentage of normal spermatozoa forms significantly decreased 61% and 80% at 48 and 96 days.
Cassault-Meyer et al. (2014)	GBH (Roundup Grand Travaux Plus (GT +)) [45% GAE]	SD rats (60 days)	Drinking water (8 days) 0, 172 mg/kg-day	Percentage of total motile sperm[2] (before and after selective motile sperm migration) Sperm per cauda epididymis/mL (10^6) (before and after selective motile sperm migration) Percentage of normal sperm after migration	• Motility: Total motile sperm increased 39% at 8 days and decreased 20% relative to controls at 62 days after selective migration, but neither change was statistically significant. • Abundance (concentration) relative to controls: o No change in sperm per cauda epididymis/mL (10^6) at 8, 27, and 62 days before selective migration. o After selective migration, sperm per cauda epididymis/mL (10^6) increased 38% at 8 and 62 days and decreased 20% at 27 days, but no change was statistically significant. • Morphology: Percentage of normal sperm significantly decreased 20% and 11% relative to controls at 27 and 62 days after selective migration, but no change at 8 days.
Centola et al. (2025)	GBH (Roundup Full II) [NR% GAE]	SD rats (PND3)	Intraperitoneal injection (11 days) 0, 50 mg/kg-day	DSP (10^6), DSP/g testis (10^6)	• Abundance (production): No change in DSP (10^6) or DSP/g testis (10^6) relative to controls at PND90.
Dallegrave et al. (2007)	GBH (Roundup) [NR % GAE]	Wistar rats (GD0)	Oral gavage [gestation, lactation] (~42 days) 0, 50, 150, 450 mg/kg-day	Sperm per cauda epididymis (10^6) DSP (10^6) Percentage of abnormal sperm	• Abundance (count) relative to controls: o Sperm per cauda epididymis (10^6) significantly decreased 27% and 25% in the low and high dose groups at PND140 (~119 post-exposure), but there was no significant change at the mid dose. o Sperm per cauda epididymis (10^6) increased 22%, 52%, and 30% in the low, mid, and high dose groups at PND65 (~34 days post-exposure), but increases were not statistically significant. • Abundance (production) relative to controls: o DSP (10^6) decreased 25%, 4%, and 28% in the low, mid, and high dose groups relative to controls at PND140, although only changes in the low and high dose groups were statistically significant. o There were no changes in DSP any dose group at PND65. • Morphology relative to controls: o Percentage of abnormal sperm increased 94%, 7%, and 35% at the low, mid, and high doses at PND65, although only the low-dose increase was statistically significant.

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Table 1 (*continued*)

Study	Exposure	Model (age at treatment)	Treatment (duration) doses	Outcomes	Summary of Results
					o Percentage of abnormal sperm increased 54%, 56%, and 43% at the low, mid, and high doses at PND140, but no increases were statistically significant.
Fan et al. (2017)	GBH (Roundup) [35% GAE]	BALB/c mice (adult)	Oral gavage (30 days) 0, 20, 200, 2000 mg/kg-day	Percentage of motile sperm Sperm per g testis (10^7)	• Motility: Percentage of motile sperm significantly decreased 23% and 54% in the mid and high dose groups relative to controls at 30 days, but no significant change occurred at the low dose. • Abundance (count): Sperm per g testis (10^7) decreased 20%, 52%, and 50% in the low, mid, and high dose groups relative to controls at 30 days, although only decreases in the mid and high dose groups were statistically significant.
Gorga et al. (2021)	GBH (Roundup) [54% GAE]	SD rats (PND14)	Oral gavage (17 days) 0, 50 mg/kg-day	Percentage of total motile sperm DSP (10^6) Percentage of abnormal sperm	• Motility: No change in percentage of total motile sperm relative to controls at 60 days post-exposure. • Abundance (production): No change in DSP (10^6) relative to controls at PND90. • Morphology: No significant change in sperm morphology was observed relative to controls at PND90.
Güngör et al. (2024)	GBH (Knockdown 48 SL) [NR% GAE]	Wistar rats (75–90 days)	Oral gavage (56 days) 0, 787.85 mg/kg-day	Percentage of motile sperm Percentage of abnormal sperm[3]	• Motility: Percentage of motile sperm significantly decreased 38% relative to controls at 56 days exposure. • Morphology: Percentage of total abnormal sperm significantly increased 87% relative to controls at 56 days.
Hashim et al. (2022)	GBH (Roundup) [NR % GAE]	Albino rats (~56 days)	Oral gavage (42 days) 0, 375 mg/kg-day	Percentage of progressive motile sperm Sperm per epididymis/mL (10^6) Percentage of abnormal sperm	• Motility: Percentage of progressive motile sperm significantly decreased 41% relative to controls at 42 days. • Abundance (concentration): Sperm per epididymis/mL (10^6) significantly decreased 44% relative to controls at 42 days. • Morphology: Percentage of abnormal sperm significantly increased 105% relative to controls at 42 days.
Jiang et al. (2018)	GBH (Roundup) [NR % GAE]	Kunming mice (56 days)	Oral gavage (35 days) 0, 60, 180, 540 mg/kg-day	Percentage of rapid progressive sperm[2] Sperm per cauda epididymis/mL (10^6) Percentages of abnormal sperm[3]	• Motility: Percentage of rapid progressive sperm decreased 22% and 28% at the mid and high doses, but no change occurred at the low dose relative to controls at 35 days. • Abundance (concentration): Sperm per cauda epididymis/mL (10^6) decreased 1%, 27%, and 54% relative to controls at 35 days, but only the change at the high dose was significant. • Morphology: Percentage of abnormal sperm increased 33%, 174%, and 176% relative to controls at 35 days, although only the changes at the mid and high doses were significant.
Kang et al. (2008)	GBH (Roundup) [30.38% GAE]	Kunming mice (adult)	Oral gavage (5 days) 0, 290, 580, 1,160 mg/kg-day	Sperm per testis/mL (10^6) Percentage of abnormal sperm	• Abundance (concentration) relative to controls: o Sperm per testis/mL (10^6) significantly decreased 79% in both the mid and high dose groups at 1 week after treatment, but no significant change occurred at the low dose. o Sperm per testis/mL (10^6) decreased 30%, 31%, and 48% in the low, mid, and high dose groups at 4 weeks after treatment, although only changes at the high dose were statistically significant. • Morphology relative to controls: o Percentage of abnormal sperm significantly increased 113% and 167% in the mid and high dose groups at 1 week after treatment, but no significant change occurred at the low dose. o Percentage of abnormal sperm increased 6%, 66%, and 158% in the low, mid, and high dose groups at 4 weeks after treatment, although only the increase at the high dose was statistically significant.
Manservisi et al. (2019)	GBH (Roundup Bioflow) [36% GAE]	SD rats (GD6)	Drinking water [gestation, lactation,	Spermatids per g testis (10^6), sperm per cauda epididymis (10^6), sperm	• Abundance (count): No changes in spermatids per g testis (10^6), sperm per cauda epididymis

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Table 1 (*continued*)

Study	Exposure	Model (age at treatment)	Treatment (duration) doses	Outcomes	Summary of Results
			postweaning] (~88 or 140 days) 0, 1.75 mg/kg-day	per caput-corpus epididymis (10^6) DSP/g testis (10^6) Percentage of abnormal sperm	(10^6), or sperm per caput-corpus epididymis (10^6) relative to controls at PND73 or PND125. • Abundance (production): No changes in DSP/g testis (10^6) relative to controls at PND73 or PND125. • Morphology: No change in percentage of abnormal sperm relative to controls at PND73 or PND125.
Mutluay et al. (2026)	GBH (Roundup) [36% GAE]	ICR mice (56–70 days)	Oral gavage (35 days) 0, 500 mg/kg-day	Percentage of motile sperm Sperm per cauda epididymis/mL (10^6) Percentage of abnormal sperm[3]	• Motility: Percentage of motile sperm significantly decreased 30% relative to controls at 36 days (1 day post-exposure). • Abundance (concentration): Sperm per cauda epididymis/mL (10^6) significantly decreased 50% relative to controls at 36 days. • Morphology: Percentage of abnormal sperm significantly increased 75% relative to controls at 36 days.
Mutwedu et al. (2021)	GBH (WILLOSATE) [NR% GAE]	Guinea pig (adult)	Oral gavage (60 days) 0, 67, 103, 202 mg/kg-day	Percentage of motile sperm Sperm per cauda epididymis/mL (10^6) Percentage of sperm major anomalies[3]	• Motility: Percentage of motile sperm significantly decreased 46%, 46%, and 68% relative to controls in the 67-, 103-, and 202_mg/kg-day dose groups at 60 days. • Abundance (concentration): Sperm per cauda epididymis/mL (10^6) decreased 12%, 29%, and 41% relative to controls at 60 days, although only changes at the mid and high doses were significant. • Morphology: Percentages of sperm major anomalies significantly increased 44% and 28% relative to controls at the mid and high doses at 60 days, but no significant change occurred at the low dose.
Owagboriaye et al. (2017)	GBH (Roundup) [36% GAE]	Albino rats (adult)	Oral gavage (84 days) 0, 3.6, 50.4, 248.4 mg/kg-day	Percentage of motile sperm Sperm per epididymis/mL (10^6) Percentages of abnormal sperm[3]	• Motility: Percentage of motile sperm significantly decreased 26%, 41%, and 35% relative to controls in the 3.6-, 50.4-, 248.4-mg/kg-day dose groups at 84 days. • Abundance (concentration): Sperm per epididymis/mL (10^6) significantly decreased 8%, 36%, and 61% relative to controls in the low, mid, and high doses at 84 days. • Morphology: Significant 469%, 868%, and 1123% increases in % of abnormal sperm relative to controls at the low, mid, and high at 84 days.
Pham et al. (2019)	GBH (Roundup 3 Plus) [15.56% GAE]	Swiss mice (GD10.5)	Drinking water [gestation, lactation] (~31 days) 0, 0.5, 5, 50 mg/kg-day	Sperm per epididymis (10^6)	• Abundance (count): Sperm per epididymis (10^6) decreased 85% and 63% at the low and high doses and increased 44% at the mid dose relative to controls at PND35, although only the low-dose decrease was statistically significant.
Qi et al. (2023)	GBH (Roundup) [30.38% GAE]	Kunming mice (56 days)	Oral gavage (30 days) 0, 50, 250, 500 mg/kg-day	Sperm per cauda epididymis/mL (10^6) Percentage of sperm deformities	• Abundance (concentration): No change in sperm per cauda epididymis/mL (10^6) relative to controls at 30 days. • Morphology: Percentage of sperm deformities increased 14%, 279%, and 750% relative to controls at 30 days, although only the changes at the mid and high doses were statistically significant.
Romano et al. (2012)	GBH (Roundup Transorb) [48% GAE]	Wistar rats (GD18)	Oral gavage [gestation, lactation] (~8 days) 0, 50 mg/kg-day	Spermatids per testis (10^6), spermatids per g testis (10^6), sperm per caput-corpus epididymis (10^6), sperm per cauda epididymis (10^6) DSP (10^6), DSP/g testis (10^6)	• Abundance (count) relative to controls at PND60: o Spermatids per testis (10^6) significantly increased 90%. o Spermatids per g testis (10^6) significantly increased 103%. o Sperm per caput-corpus epididymis (10^6) significantly increased 50%. o No change in sperm per cauda epididymis (10^6). • Abundance (production) relative to controls at PND60: o DSP (10^6) significantly increased 92%. o DSP/g testis (10^6) significantly increased 104%.

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Table 1 (*continued*)

Study	Exposure	Model (age at treatment)	Treatment (duration) doses	Outcomes	Summary of Results
Teleken et al. (2020)	GBH (Roundup Original DI) [37% GAE]	C57BL/6 mice (GD4)	Drinking water [gestation, lactation] (~47 days) 0, 420 mg/kg-day	Sperm per cauda epididymis/mL (10^4), sperm per caput-corpus epididymis/mL (10^4)	• Abundance (concentration) relative to controls at PND 150. o Sperm per cauda epididymis/mL (10^4) significantly decreased 70%. o No change in sperm per caput-corpus epididymis/mL (10^4).

[1]Glyphosate doses are reported as mg glyphosate per kg body weight per day. [2]Additional sperm motility measurements are available in **Supplemental Table S18**. [3]Additional abnormal sperm classification data are available in **Supplemental Table S19** and **Supplemental Fig. S18**. [4]GBH doses are reported as mg formulation mass of GBH per kg body weight per day. ALH = amplitude of lateral head displacement; BCF = beat cross frequency; g = grams; DSP = daily sperm production measuring homogenization-resistant spermatids in testis samples; GAE = glyphosate acid equivalent; GBH = glyphosate-based herbicide; GD = gestational day; LIN = linearity; NR = not reported; PND = postnatal day; SD = Sprague-Dawley; STR = straightness; VAP = average path velocity; VCL = curvilinear velocity; VSL = straight-line velocity.

for 88 or 140 days at 1.75 mg/kg-day beginning during gestation (Manservisi et al. 2019). Additional description of glyphosate sperm data by species, strain, dose, duration, and timing of exposure are provided in **Supplement Section 3** with separate sections on count, concentration, production, motility, and morphology.

3.3.2.1. Glyphosate risk-of-bias considerations. Risk of bias was rated on an outcome basis, and six of eleven studies evaluating sperm parameters were high-quality based on low risk-of-bias ratings for at least two of the three key questions of randomization, exposure characterization, and outcome assessment, with minimal concerns in other domains (Fig. 11). The high-quality studies for sperm parameters were: Abarikwu et al. (2015); Chan and Mahler (1992); Liu et al. (2022a); Liu et al. (2022b); Manservisi et al. (2019); Ren et al. (2025). Manservisi et al (2019) was the only high-quality study to report no effect on any sperm measure. All five lower-quality studies reported an adverse effect on at least one measure of sperm health (Dai et al. 2016; Ömür et al. 2024; Pham et al. 2019; Razi et al. 2012; Yousef et al. 1995). Detailed descriptions of the risk-of-bias assessment for glyphosate exposure and each sperm parameter are located in **Supplement Section 3.2.3.1** (motility), **3.3.1.3.1**, **3.3.2.3.1**, **3.3.3.3** (abundance), **3.4.3.1** (morphology), **Supplement Section 1.2** (individual study risk-of-bias details for all high-quality studies), and **Fig. S20** (key risk-of-bias domains for all studies with sperm data).

3.3.3. Results by exposure: GBH

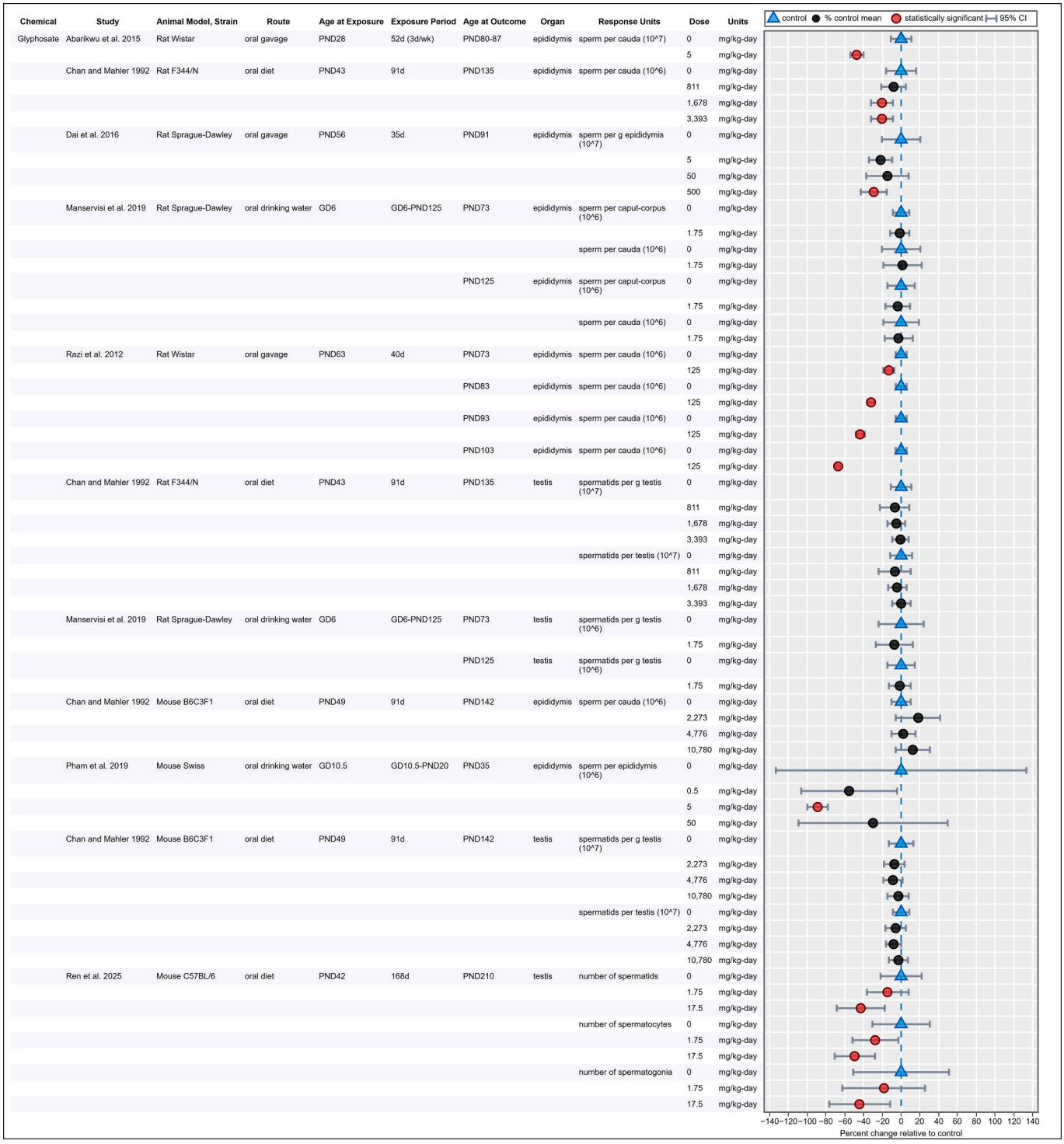
Abundance: Five of seven studies reported reduced sperm count following GBH exposure ranging from 0.5 to 2000 mg/kg-day in rats, mice, and rabbits, with exposure beginning in adulthood (Ansa et al. 2025; Fan et al. 2017), the peripubertal period (Abarikwu et al. 2015), and gestation (Dallegrave et al. 2007; Pham et al. 2019) (Table 1; Fig. 4). Mature sperm counts from epididymis and ejaculate samples were more consistently reduced by GBHs (5 of 7 studies) than spermatid counts in the testis (1 of 3 studies). Most studies with exposure duration of ≥30 days reported reductions in sperm count. In contrast, Romano et al. (2012) reported higher sperm counts in caput-corpus (but not cauda) epididymis and testis in rats at PND 60 following a short 8-day GBH exposure to 50 mg/kg-day starting at GD 18. Manservisi et al (2019) reported no effects in rats after 88- or 140-day exposures at 1.75 mg/kg-day starting during gestation.

Nine of 11 studies reported reduced sperm concentration following GBH exposures ranging from 3.6 to 375 mg/kg-day in rats (Ben Amor et al. 2025; Hashim et al. 2022; Owagboriaye et al. 2017), 60 to 1,160 mg/kg-day in mice (Jiang et al. 2018; Kang et al. 2008; Mutluay et al. 2026; Teleken et al. 2020), 67, 103, and 202 mg/kg-day in guinea pigs (Mutwedu et al. 2021), and 10 mL/L in rabbits (Ansa et al. 2025) (Table 1; Fig. 6). All studies measured epididymal sperm, except Ansa et al. (2025), which evaluated ejaculate samples. Dose-dependent reductions in sperm concentration were observed in four studies (Jiang et al. 2018; Kang et al. 2008; Mutwedu et al. 2021; Owagboriaye et al. 2017). Two studies reported no effect (Cassault-Meyer et al. 2014; Qi et al. 2023). Qi et al. (2023) reported non-statistically significant, dose-dependent reductions at 50, 250, and 500 mg/kg-day following a 30-day exposure in adult mice. Cassault-Meyer et al. (2014) reported no effect in rats following an 8-day exposure at 172 mg/kg-day GBH beginning at PND 60, with assessments through 54 days post-exposure.

Two of six studies that evaluated sperm production reported a reduction in daily testicular production following GBH exposure of peripubertal rats at 5 mg/kg-day for 52 days (Abarikwu et al. 2015) or developmental exposure through gestation and lactation at 50, 150, and 450 mg/kg-day (Dallegrave et al. 2007) (Table 1). One study reported higher daily sperm production in rats at PND 60 following 8-day exposure to 50 mg/kg-day starting at GD 18 (Romano et al. 2012). Manservisi et al (2019) reported no effects in rats after 88- or 140-day exposures at 1.75 mg/kg-day starting during gestation, and the two remaining studies reported no effect of 50 mg/kg-day GBH following relatively short exposure durations via gavage (17 days;Gorga et al. 2021) and intraperitoneal injection (11 days; Centola et al. 2025).

Motility: Twelve of 14 studies reported reduced percentage of motile sperm in rats, mice, rabbits and guinea pigs (Table 1; Fig. 8; **Supplement Table S18**). Effects were reported in seven rat studies following 42 to 84 day GBH exposures ranging from 3.6 to 788 mg/kg-day (Abarikwu et al. 2015; Avdatek et al. 2018; Avdatek et al. 2023; Ben Amor et al. 2025; Güngör et al. 2024; Hashim et al. 2022; Owagboriaye et al. 2017), as well as 30 to 35 day exposures in mice at 180 to 2000 mg/kg-day (Fan et al. 2017; Jiang et al. 2018; Mutluay et al. 2026), 84 day exposure in rabbits (Ansa et al. 2025), and 60 day exposure in guinea pigs at 67, 103, and 202 mg/kg-day (Mutwedu et al. 2021). Dose-dependent responses were observed in three studies (Fan et al. 2017; Jiang et al. 2018; Mutwedu et al. 2021). Two rat studies reported no effect following shorter exposure periods – 172 mg/kg-day for 8 days beginning at PND 60 (Cassault-Meyer et al. 2014), or 50 mg/kg-day for 17 days beginning at PND 14 (Gorga et al. 2021), with motility assessed in adulthood (PND 90).

Morphology: Sixteen of 18 studies reported higher percentages of abnormal sperm (Table 1; Fig. 10; **Supplement Table S19**). Effects were observed in nine studies of rats at GBH exposures from 3.6 to 788 mg/kg-day (Abarikwu et al. 2015; Avdatek et al. 2018; Avdatek et al. 2023; Ben Amor et al. 2025; Cassault-Meyer et al. 2014; Dallegrave et al. 2007; Güngör et al. 2024; Hashim et al. 2022; Owagboriaye et al. 2017), five studies of mice at exposures from 50 to 1,160 mg/kg-day (Amer et al. 2006; Jiang et al. 2018; Kang et al. 2008; Mutluay et al. 2026; Qi et al. 2023), and one study each of guinea pigs at 103 and 202 mg/kg-day (Mutwedu et al. 2021) and rabbits (Ansa et al. 2025). Dose-dependent effects observed in one study in rats (Owagboriaye et al., 2017) and three studies in mice (Amer et al., 2006; Jiang et al., 2018; Kang et al., 2008). Two studies reported no effect, Gorga et al. (2021) in rats exposed to 50 mg/kg-day GBH for 17 days starting on PND 14, and



Chemical	Study	Animal Model, Strain	Route	Age at Exposure	Exposure Period	Age at Outcome	Organ	Response Units	Dose	Units
Glyphosate	Abarikwu et al. 2015	Rat Wistar	oral gavage	PND28	52d (3d/wk)	PND80-87	epididymis	sperm per cauda (10^7)	0	mg/kg-day
									5	mg/kg-day
	Chan and Mahler 1992	Rat F344/N	oral diet	PND43	91d	PND135	epididymis	sperm per cauda (10^6)	0	mg/kg-day
									811	mg/kg-day
									1,678	mg/kg-day
									3,393	mg/kg-day
	Dai et al. 2016	Rat Sprague-Dawley	oral gavage	PND56	35d	PND91	epididymis	sperm per g epididymis (10^7)	0	mg/kg-day
									5	mg/kg-day
									50	mg/kg-day
									500	mg/kg-day
	Manservisi et al. 2019	Rat Sprague-Dawley	oral drinking water	GD6	GD6-PND125	PND73	epididymis	sperm per caput-corpus (10^6)	0	mg/kg-day
									1.75	mg/kg-day
								sperm per cauda (10^6)	0	mg/kg-day
									1.75	mg/kg-day
						PND125	epididymis	sperm per caput-corpus (10^6)	0	mg/kg-day
									1.75	mg/kg-day
								sperm per cauda (10^6)	0	mg/kg-day
									1.75	mg/kg-day
	Razi et al. 2012	Rat Wistar	oral gavage	PND63	40d	PND73	epididymis	sperm per cauda (10^6)	0	mg/kg-day
									125	mg/kg-day
						PND83	epididymis	sperm per cauda (10^6)	0	mg/kg-day
									125	mg/kg-day
						PND93	epididymis	sperm per cauda (10^6)	0	mg/kg-day
									125	mg/kg-day
						PND103	epididymis	sperm per cauda (10^6)	0	mg/kg-day
									125	mg/kg-day
	Chan and Mahler 1992	Rat F344/N	oral diet	PND43	91d	PND135	testis	spermatids per g testis (10^7)	0	mg/kg-day
									811	mg/kg-day
									1,678	mg/kg-day
									3,393	mg/kg-day
								spermatids per testis (10^7)	0	mg/kg-day
									811	mg/kg-day
									1,678	mg/kg-day
									3,393	mg/kg-day
	Manservisi et al. 2019	Rat Sprague-Dawley	oral drinking water	GD6	GD6-PND125	PND73	testis	spermatids per g testis (10^6)	0	mg/kg-day
									1.75	mg/kg-day
						PND125	testis	spermatids per g testis (10^6)	0	mg/kg-day
									1.75	mg/kg-day
	Chan and Mahler 1992	Mouse B6C3F1	oral diet	PND49	91d	PND142	epididymis	sperm per cauda (10^6)	0	mg/kg-day
									2,273	mg/kg-day
									4,776	mg/kg-day
									10,780	mg/kg-day
	Pham et al. 2019	Mouse Swiss	oral drinking water	GD10.5	GD10.5-PND20	PND35	epididymis	sperm per epididymis (10^6)	0	mg/kg-day
									0.5	mg/kg-day
									5	mg/kg-day
									50	mg/kg-day
	Chan and Mahler 1992	Mouse B6C3F1	oral diet	PND49	91d	PND142	testis	spermatids per g testis (10^7)	0	mg/kg-day
									2,273	mg/kg-day
									4,776	mg/kg-day
									10,780	mg/kg-day
								spermatids per testis (10^7)	0	mg/kg-day
									2,273	mg/kg-day
									4,776	mg/kg-day
									10,780	mg/kg-day
	Ren et al. 2025	Mouse C57BL/6	oral diet	PND42	168d	PND210	testis	number of spermatids	0	mg/kg-day
									1.75	mg/kg-day
									17.5	mg/kg-day
								number of spermatocytes	0	mg/kg-day
									1.75	mg/kg-day
									17.5	mg/kg-day
								number of spermatogonia	0	mg/kg-day
									1.75	mg/kg-day
									17.5	mg/kg-day

Fig. 3. Sperm Count Animal Data – Glyphosate: An interactive version is available at the following link to figure. This plot shows percentage change in sperm count in glyphosate-exposed groups as compared to the control groups. The x-axis denotes % change sperm count relative to control with confidence intervals. Control groups are shown as blue triangles; glyphosate groups plotted as circles for the % change relative to control, with statistically significant data points colored red. The 95% confidence interval (95% CI) is shown as a grey bar. Glyphosate doses are reported as mg glyphosate per kg body weight per day. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Manservisi et al. (2019) in rats exposed to 1.75 mg/kg-day GBH for 88 or 140 days starting during gestation.

Additional description of GBH sperm data by species, strain, dose, duration, and timing of exposure are provided in **Supplement Section 3** with separate sections on count, concentration, production, motility, and morphology.

3.3.3.1. GBH risk-of-bias considerations. Eleven of 23 studies of GBH exposure that assessed sperm parameters were high-quality based on low risk-of-bias ratings for at least two of the three key considerations – randomization, exposure characterization, and outcome assessment – with minimal concerns in other domains (Fig. 12); the high quality studies for GBH and sperm parameters were: Abarikwu et al. (2015); Ben

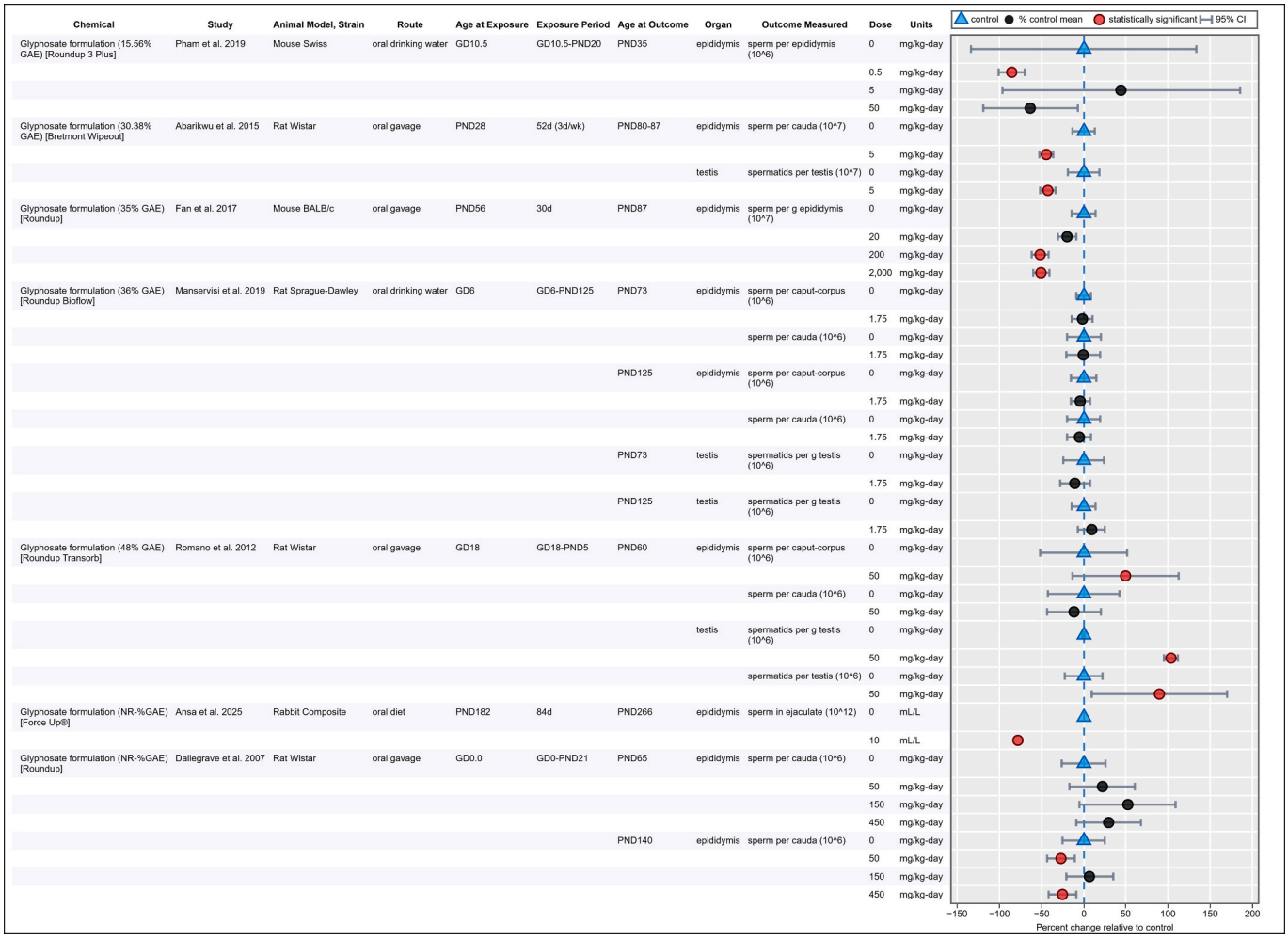


Fig. 4. Sperm Count Animal Data – GBH: An interactive version is available at the following link to figure. This plot shows percentage change in sperm count in GBH-exposed groups as compared to the control groups. The x-axis denotes % change in sperm count relative to control with confidence intervals. Control groups are shown as blue triangles; GBH groups plotted as circles for the % change relative to control, with statistically significant data points colored red. The 95% confidence interval (95% CI) is shown as a grey bar. GBH doses are reported as mg formulation mass of GBH per kg body weight per day. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Amor et al. (2025); Cassault-Meyer et al. (2014); Fan et al. (2017); Gorga et al. (2021); Kang et al. (2008); Manservisi et al. (2019); Mutluay et al. (2026); Owagboriaye et al. (2017); Qi et al. (2023); Teleken et al. (2020). Nine of the 11 high-quality studies reported had an adverse effect on at least one measure of sperm health. Detailed descriptions of the risk-of-bias assessment for studies assessing GBH exposure and each sperm parameter are located in **Supplement Section 3.2.4.1** (sperm motility); **3.3.1.4.1, 3.3.2.4.1**, **3.3.3.3** (sperm abundance); **3.4.4.1** (sperm morphology); **Supplement Section 12** (individual study risk-of-bias details for all high-quality studies), and **Fig. S20** (key risk-of-bias domains for all studies with sperm data).

3.3.4. *Meta-analyses for glyphosate and GBHs*

Using the RVE approach, meta-analysis of 13 effect estimates from 5 glyphosate studies and 21 effect estimates from 13 GBH studies found inverse associations with sperm motility, although the association was statistically significant only for GBH exposure (SMD[glyphosate] = −1.29, 95%CI: −3.61, 1.02, $p = 0.20$; SMD[GBH] = −2.92, 95%CI: −4.40, −1.43, $p = 0.001$). After excluding potential outlier studies for glyphosate (Razi et al. 2012) and GBH exposure (Owagboriaye et al. 2017) the pooled SMDs were attenuated but remained inverse (SMD [glyphosate] = −0.54, 95%CI: −1.19, 0.11, $p = 0.084$; SMD[GBH] = −2.51, 95%CI: −3.74, −1.28, $p < 0.001$).

For sperm count, RVE meta-analyses of 15 effect estimates from 6 glyphosate studies and 12 effect estimates from 6 GBH studies also showed inverse associations, although neither was statistically significant (SMD[glyphosate] = −1.96, 95%CI: −4.66, 0.75, $p = 0.126$; SMD [GBH] = −1.22, 95%CI: −2.74, 0.31, $p = 0.095$). After excluding potential outlier studies for glyphosate (Abarikwu et al. 2015; Razi et al. 2012) and GBH exposure (Abarikwu et al. 2015; Fan et al. 2017), estimates were attenuated but remained inverse, with the GBH association statistically significant (SMD[glyphosate] = -0.46, 95%CI: −1.35, 0.42, $p = 0.22$; SMD[GBH] = -0.40, 95%CI: −0.67, −0.14, $p = 0.018$).

For sperm concentration, RVE meta-analyses of 12 effect estimates from 4 glyphosate studies and 20 effect estimates from 10 GBH studies showed inverse and statistically significant associations for both exposures (SMD[glyphosate] = −0.57, 95%CI: −0.95, −0.19, $p = 0.015$; SMD[GBH] = -2.92, 95%CI: −4.94, −0.90, $p = 0.01$). After excluding the potential GBH outlier (Owagboriaye et al. 2017), the estimate was attenuated but remained inverse and statistically significant (SMD [GBH] = -2.34, 95%CI: −3.96, −0.72, $p = 0.01$).

At least one of Egger's and Begg's tests (p-values reported in that order) indicated statistically significant funnel plot asymmetry for sperm motility (glyphosate: $p < 0.001$, $p = 0.124$; GBHs: both $p < 0.001$), sperm count (glyphosate: $p < 0.001$, $p = 0.006$; GBHs: $p < 0.001$, $p = 0.016$), and sperm concentration following GBH exposure (both $p <$



Fig. 5. Sperm Concentration Animal Data – Glyphosate: An interactive version is available at the following link to figure. This plot shows percentage change in sperm concentration in glyphosate-exposed groups as compared to the control groups. The x-axis denotes % change in sperm concentration relative to control with confidence intervals. Control groups are shown as blue triangles; glyphosate groups plotted as circles for the % change relative to control, with statistically significant data points colored red. The 95% confidence interval (95% CI) is shown as a grey bar. Glyphosate doses are reported as mg glyphosate per kg body weight per day. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

0.001), but not glyphosate exposure ($p = 0.696$, $p = 0.114$). These findings should be interpreted cautiously given the limited number of independent studies, between-study heterogeneity, and correlations between effect estimates within studies. Detailed results, including sensitivity analyses excluding potential outliers and information on study inclusion in the meta-analyses are provided in **Supplement Section 3.2.5, 3.3.1.5, and 3.3.2.5**.

3.3.5. Confidence: sperm parameters

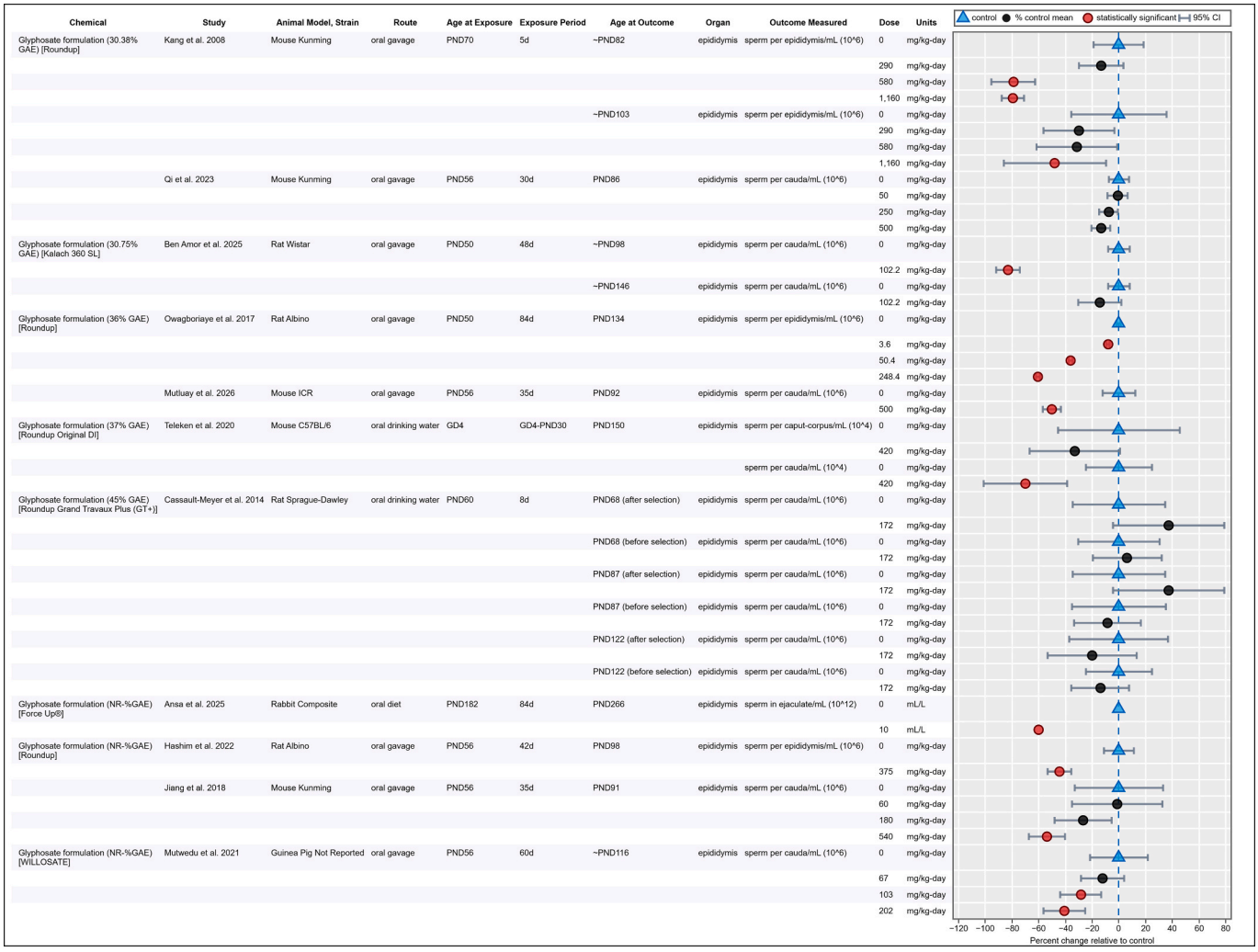
We conclude there is high confidence that exposure to both glyphosate and GBHs adversely affects overall sperm health based on data from rodents and rabbits.

3.3.5.1. Glyphosate. Most studies (10 of 11) across the three major sperm endpoint categories (i.e., 5 of 6 studies of sperm motility (Liu et al. 2022a; Liu et al. 2022b; Ömür et al. 2024; Razi et al. 2012; Ren et al. 2025), 8 of 10 studies of sperm abundance (Abarikwu et al. 2015; Chan and Mahler 1992; Dai et al. 2016; Liu et al. 2022b; Pham et al. 2019; Razi et al. 2012; Ren et al. 2025; Yousef et al. 1995), and 5 of 6 studies of sperm morphology (Liu et al. 2022a; Liu et al. 2022b; Razi et al. 2012; Ren et al. 2025; Yousef et al. 1995) reported impaired sperm health following exposure to glyphosate. These confidence conclusions were driven by the high-quality studies: three of four studies of sperm motility reported decreased motility; four of six studies of sperm abundance reported decreased count or concentration; and one of two studies of sperm morphology reported an increased percentage of abnormal sperm.

Sperm abundance received a final rating of high confidence, whereas two of the individual measures – sperm motility and sperm morphology – received final ratings of moderate confidence. Confidence in sperm motility was downgraded from high to moderate for unexplained inconsistencies; specifically, one of the four high-quality studies (Chan and Mahler 1992) reported no effect of glyphosate at oral doses much higher than those tested in most other studies. Confidence in sperm morphology was downgraded from high to moderate based on the collective consideration of risk-of-bias concerns and unexplained inconsistency between the two high-quality studies. Four of the six studies were rated low quality, and the two high-quality studies reported differing findings: Liu et al. (2022b) reported increased abnormal sperm, whereas Manservisi et al. (2019) reported no effect, despite these studies evaluating comparable doses (2 and 1.75 mg/kg-day, respectively). Although five of the six studies reported increased sperm morphology, with findings consistent across species (rats, mice, and rabbits), as well as some evidence of large magnitudes of effect, and dose response across all sperm parameters, these factors were not considered sufficient to warrant upgrading confidence.

Overall sperm health received a rating of high confidence, despite the endpoint-specific downgrades, due to consistency within and across all sperm measurements and across species. Confidence was further strengthened by evidence of dose response in sperm motility, sperm concentration, and sperm morphology and a large magnitude of effect for sperm motility. Meta-analyses found consistent inverse associations between glyphosate and multiple sperm measures that were statistically significant for sperm count and non-statistically significant for sperm motility and sperm count. Overall, the evidence provides consistent support that glyphosate exposure adversely affects sperm health in non-human mammals.

3.3.5.2. GBH. There was consistent evidence that GBH exposure adversely impacts sperm health in 19 of 23 studies overall, including 9 of 11 high-quality studies. GBH exposure was associated with decreases in sperm motility (12 of 14 studies (Abarikwu et al. 2015; Ansa et al. 2025; Avdatek et al. 2018; Avdatek et al. 2023; Ben Amor et al. 2025; Fan et al. 2017; Güngör et al. 2024; Hashim et al. 2022; Jiang et al. 2018; Mutluay et al. 2026; Mutwedu et al. 2021; Owagboriaye et al. 2017), including 5 of 7 high-quality studies), decreases in sperm abundance determined by sperm count, concentration, or daily sperm production (13 of 19 studies (Abarikwu et al. 2015; Ansa et al. 2025; Ben Amor et al. 2025; Dallegrave et al. 2007; Fan et al. 2017; Hashim et al. 2022; Jiang et al. 2018; Kang et al. 2008; Mutluay et al. 2026; Mutwedu et al. 2021; Owagboriaye et al. 2017; Pham et al. 2019; Teleken et al. 2020), including 7 of 11 high-quality studies), and increases in the percentage of abnormal sperm (16 of 18 studies (Abarikwu et al. 2015; Amer et al. 2006; Ansa et al. 2025; Avdatek et al. 2018; Avdatek et al. 2023; Ben Amor et al. 2025; Cassault-Meyer et al. 2014; Dallegrave et al. 2007; Güngör et al. 2024; Hashim et al. 2022; Jiang et al. 2018; Kang et al. 2008; Mutluay et al. 2026; Mutwedu et al. 2021; Owagboriaye et al. 2017; Qi et al. 2023), including 7 of 9 high-quality studies).



Chemical	Study	Animal Model, Strain	Route	Age at Exposure	Exposure Period	Age at Outcome	Organ	Outcome Measured	Dose	Units
Glyphosate formulation (30.38% GAE) [Roundup]	Kang et al. 2008	Mouse Kunming	oral gavage	PND70	5d	~PND82	epididymis	sperm per epididymis/mL (10^6)	0	mg/kg-day
									290	mg/kg-day
									580	mg/kg-day
									1,160	mg/kg-day
						~PND103	epididymis	sperm per epididymis/mL (10^6)	0	mg/kg-day
									290	mg/kg-day
									580	mg/kg-day
									1,160	mg/kg-day
	Qi et al. 2023	Mouse Kunming	oral gavage	PND56	30d	PND86	epididymis	sperm per cauda/mL (10^6)	0	mg/kg-day
									50	mg/kg-day
									250	mg/kg-day
									500	mg/kg-day
Glyphosate formulation (30.75% GAE) [Kalach 360 SL]	Ben Amor et al. 2025	Rat Wistar	oral gavage	PND50	48d	~PND98	epididymis	sperm per cauda/mL (10^6)	0	mg/kg-day
									102.2	mg/kg-day
						~PND146	epididymis	sperm per cauda/mL (10^6)	0	mg/kg-day
									102.2	mg/kg-day
Glyphosate formulation (36% GAE) [Roundup]	Owagboriaye et al. 2017	Rat Albino	oral gavage	PND50	84d	PND134	epididymis	sperm per epididymis/mL (10^6)	0	mg/kg-day
									3.6	mg/kg-day
									50.4	mg/kg-day
									248.4	mg/kg-day
	Mutluay et al. 2026	Mouse ICR	oral gavage	PND56	35d	PND92	epididymis	sperm per cauda/mL (10^6)	0	mg/kg-day
									500	mg/kg-day
Glyphosate formulation (37% GAE) [Roundup Original DI]	Teleken et al. 2020	Mouse C57BL/6	oral drinking water	GD4	GD4-PND30	PND150	epididymis	sperm per caput-corpus/mL (10^4)	0	mg/kg-day
									420	mg/kg-day
								sperm per cauda/mL (10^4)	0	mg/kg-day
									420	mg/kg-day
Glyphosate formulation (45% GAE) [Roundup Grand Travaux Plus (GT+)]	Cassault-Meyer et al. 2014	Rat Sprague-Dawley	oral drinking water	PND60	8d	PND68 (after selection)	epididymis	sperm per cauda/mL (10^6)	0	mg/kg-day
									172	mg/kg-day
						PND68 (before selection)	epididymis	sperm per cauda/mL (10^6)	0	mg/kg-day
									172	mg/kg-day
						PND87 (after selection)	epididymis	sperm per cauda/mL (10^6)	0	mg/kg-day
									172	mg/kg-day
						PND87 (before selection)	epididymis	sperm per cauda/mL (10^6)	0	mg/kg-day
									172	mg/kg-day
						PND122 (after selection)	epididymis	sperm per cauda/mL (10^6)	0	mg/kg-day
									172	mg/kg-day
						PND122 (before selection)	epididymis	sperm per cauda/mL (10^6)	0	mg/kg-day
									172	mg/kg-day
Glyphosate formulation (NR-%GAE) [Force Up®]	Ansa et al. 2025	Rabbit Composite	oral diet	PND182	84d	PND266	epididymis	sperm in ejaculate/mL (10^12)	0	mL/L
									10	mL/L
Glyphosate formulation (NR-%GAE) [Roundup]	Hashim et al. 2022	Rat Albino	oral gavage	PND56	42d	PND98	epididymis	sperm per epididymis/mL (10^6)	0	mg/kg-day
									375	mg/kg-day
	Jiang et al. 2018	Mouse Kunming	oral gavage	PND56	35d	PND91	epididymis	sperm per cauda/mL (10^6)	0	mg/kg-day
									60	mg/kg-day
									180	mg/kg-day
									540	mg/kg-day
Glyphosate formulation (NR-%GAE) [WILLOSATE]	Mutwedu et al. 2021	Guinea Pig Not Reported	oral gavage	PND56	60d	~PND116	epididymis	sperm per cauda/mL (10^6)	0	mg/kg-day
									67	mg/kg-day
									103	mg/kg-day
									202	mg/kg-day

Fig. 6. Sperm Concentration Animal Data – GBH: An interactive version is available at the following link to figure. This plot shows percentage change in sperm concentration in GBH-exposed groups as compared to the control groups. The x-axis denotes % change in sperm concentration relative to control with confidence intervals. Control groups are shown as blue triangles; GBH groups plotted as circles for the % change relative to control, with statistically significant data points colored red. The 95% confidence interval (95% CI) is shown as a grey bar. GBH doses are reported as mg formulation mass of GBH per kg body weight per day. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

For individual measures, high confidence in sperm abundance was driven by consistent GBH-associated decreases in sperm count and concentration (13 of 17 studies). Confidence conclusions on sperm production could not be reached due to heterogeneity of the data, differences in exposure duration, and dose levels administered.

Overall sperm health received a rating of high confidence due to the consistency of findings within and across different sperm health measures, and across species, with evidence of dose response in sperm concentration, motility, and morphology providing additional support for the conclusions. Meta-analyses found statistically significant inverse associations between GBH exposure and sperm motility, sperm count, and sperm concentration. No downgrades or upgrades applied to the initial confidence rating after considering all factors. Overall, the body of evidence provides robust and consistent support for adverse effects of GBHs on sperm health following GBH exposure.

Detailed explanations of the confidence assessment process for each sperm endpoint for the glyphosate and GBH bodies of evidence are provided in **Supplement Section 3.6** including stepwise discussion of all nine factors considered for potential downgrades or upgrades.

3.4. Testosterone

3.4.1. Overview of studies

Thirty rodent studies evaluated plasma, serum, or intratesticular testosterone following glyphosate or GBH exposure. Twelve studies evaluated glyphosate effects on testosterone and 23 studies evaluated GBHs and testosterone. Most studies evaluated testosterone following oral administration (20 via gavage, 2 via diet, and 6 via drinking water) of glyphosate or GBHs, and two studies administered glyphosate or GBH via subcutaneous or intraperitoneal injection. Exposure occurred directly in adulthood, during the peripubertal or early postnatal stages, or indirectly through the dam during gestation (Table 2).

3.4.2. Results by exposure: glyphosate

Seven of 12 studies reported a decrease in testosterone following glyphosate exposure. Six of the seven studies that reported a treatment-related effect began treatment in juvenile rats following 5 mg/kg-day (Abarikwu et al. 2015) or 200 and 800 mg/kg-day (Zhao et al. 2018) glyphosate or in adult rats or mice (Dai et al. 2016; Prasad et al. 2022; Razi et al. 2012; Zhao et al. 2021) at doses that ranged from 5 to 985 mg/kg-day, and the other study reported effects following 0.5 and 50 mg/kg-

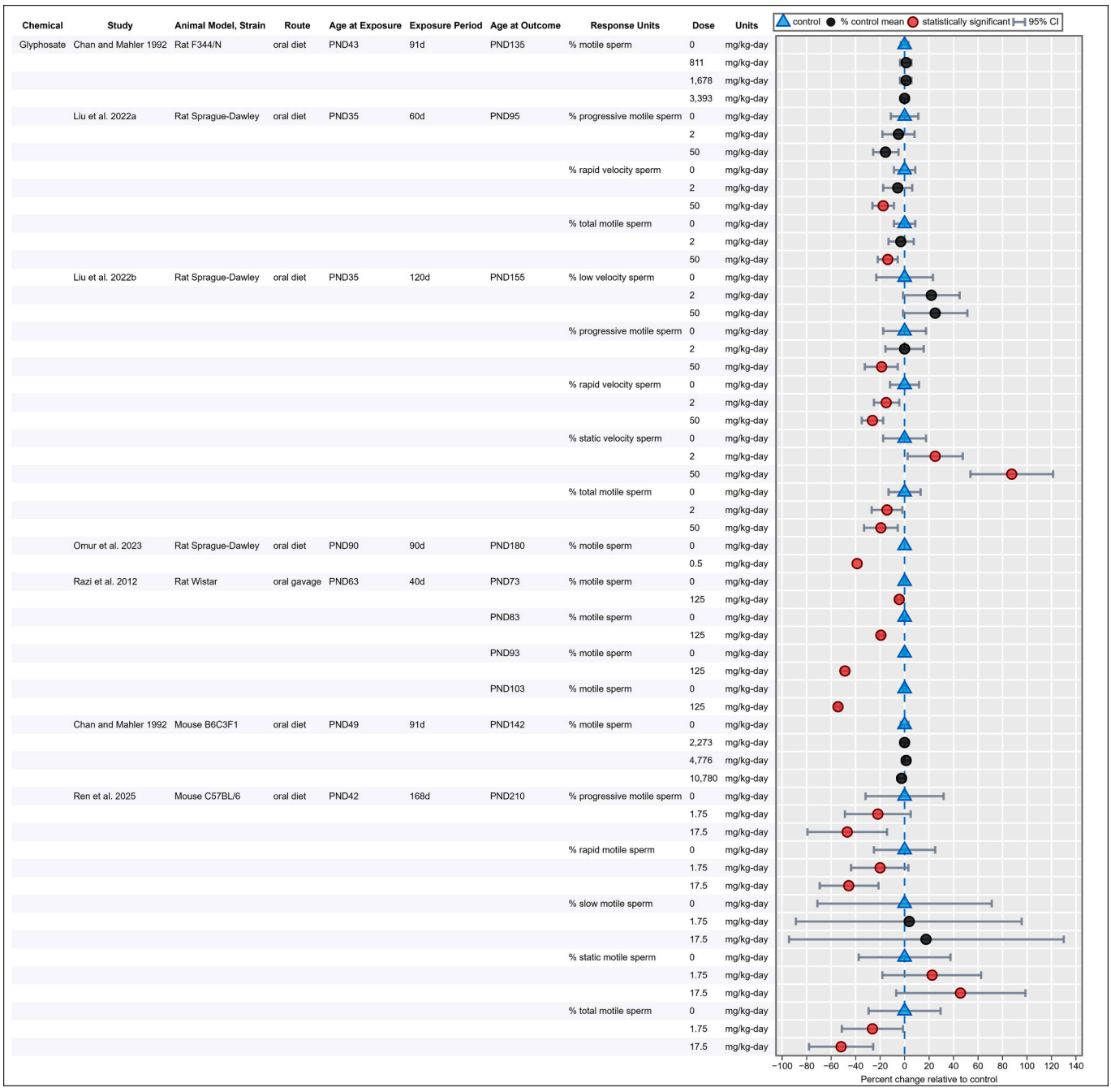


Fig. 7. Sperm Motility Animal Data – Glyphosate: An interactive version is available at the following link to figure. This plot shows percentage change in sperm motility in glyphosate-exposed groups as compared to the control groups. The x-axis denotes % change in sperm motility relative to control with confidence intervals. Control groups are shown as blue triangles; glyphosate groups plotted as circles for the % change relative to control, with statistically significant data points colored red. The 95% confidence interval (95% CI) is shown as a grey bar. Glyphosate doses are reported as mg glyphosate per kg body weight per day. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

day exposures that began during gestation (Pham et al. 2019) (Fig. 13). The remaining five studies did not report a treatment-related change in testosterone, including two gestational exposure studies with both in-direct and direct oral exposures at 1.75 to 3.9 mg/kg-day (Gomez et al. 2023; Manservisi et al. 2019), two short duration (14 to 17 day) oral exposure studies in sexually immature rats at 2 to 50 mg/kg-day (Gorga et al. 2021; Johansson et al. 2018), and one intraperitoneal injection exposure study in adult rats at 10 mg/kg-day (Astiz et al. 2009).

3.4.2.1. Glyphosate risk-of-bias considerations. Across the key risk-of-bias considerations—randomization, exposure characterization, and outcome assessment—there were three studies that were considered high quality based on low risk-of-bias ratings in at least two out of three key considerations and minimal concerns in other domains (Abarikwu et al. 2015; Manservisi et al. 2019; Prasad et al. 2022) (Fig. 15). These findings, along with five supporting, lower-quality studies in the evidence base (Dai et al. 2016; Pham et al. 2019; Razi et al. 2012; Zhao et al. 2018; Zhao et al. 2021), suggest that glyphosate decreases testosterone levels, particularly following juvenile or adult exposures in rats and mice. Detailed risk of bias information for glyphosate and testosterone studies can be found in **Supplement Section** 4.3.1, detailed risk of bias descriptions for individual high-quality studies can be found

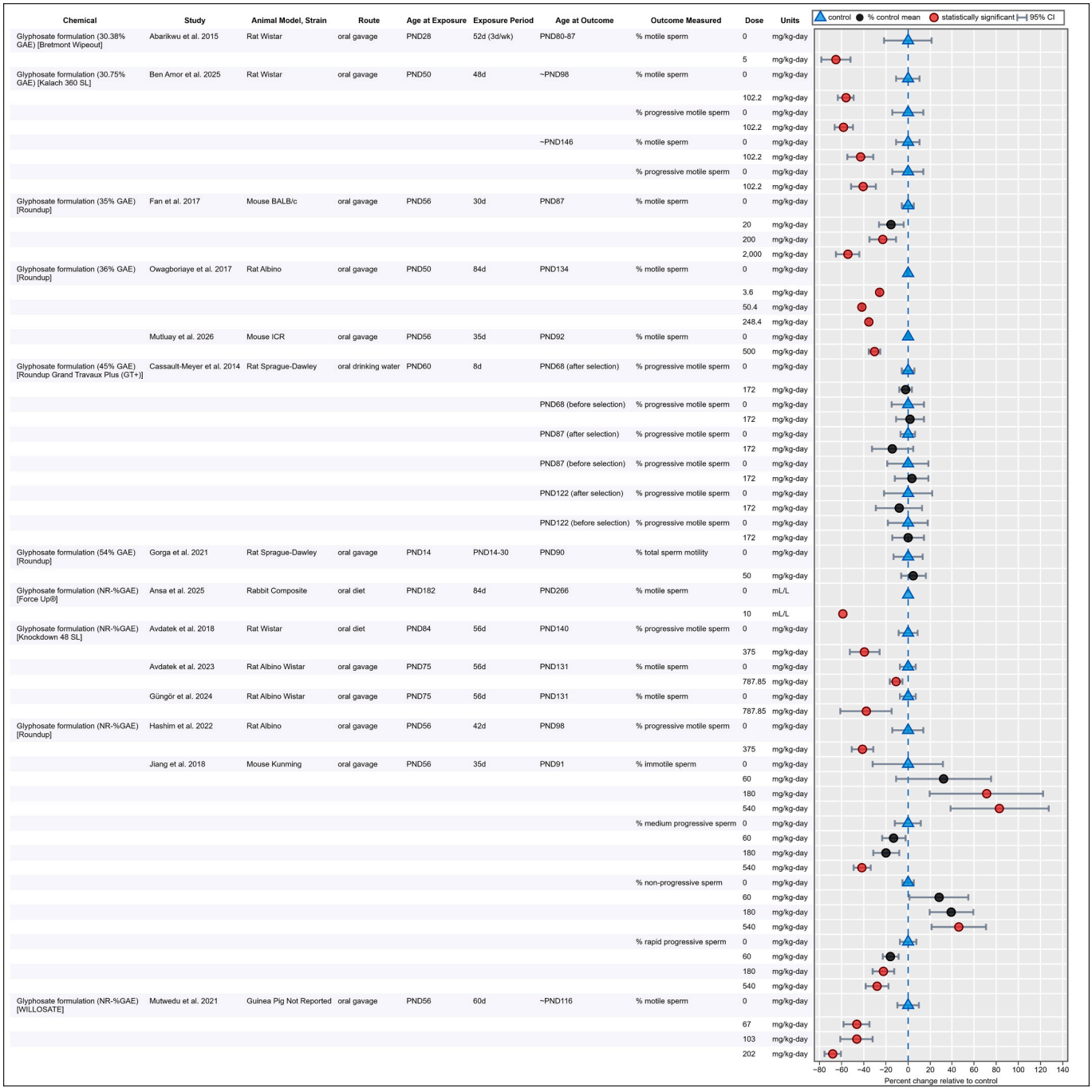


Fig. 8. Sperm Motility Animal Data – GBH: An interactive version is available at the following link to figure. This plot shows percentage change in sperm motility in GBH-exposed groups as compared to the control groups. The x-axis denotes % change in sperm motility relative to control with confidence intervals. Control groups are shown as blue triangles; GBH groups plotted as circles for the % change relative to control, with statistically significant data points colored red. The 95% confidence interval (95% CI) is shown as a grey bar. GBH doses are reported as mg formulation mass of GBH per kg body weight per day. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

in **Supplement Section** 12, and **Fig. S21** (key risk-of-bias domains for all studies with testosterone data).

3.4.3. Results by exposure: GBH

Twenty-three studies evaluated GBHs and testosterone, and 15 of those studies reported a treatment-related effect (Fig. 14). Eight studies reported a decrease in testosterone following adult exposure to GBHs, including studies in rats at exposures that ranged from 3.6 to 787.85 mg/kg-day (Avdatek et al. 2023; Ben Amor et al. 2025; Owagboriaye et al. 2017; Pandey and Rudraiah 2015), in mice following 500 mg/kg-day (Chai et al. 2025; Mutluay et al. 2026) or 20 to 2000 mg/kg-day (Fan et al. 2017) exposures, and gerbils following a 0.17 mg/kg-day exposure (Silva et al. 2024). Three rat studies reported decreases in testosterone following GBH exposures during the peripubertal period (Abarikwu et al. 2015; Phusate 2022; Romano et al. 2010) at doses that ranged from 5 to 250 mg/kg-day, with evidence of a dose response (Romano et al. 2010). Two of four gestational exposure studies reported a decrease in testosterone following a 450 mg/kg-day GBH exposure in rats (Dallegrave et al. 2007) and 5 and 50 mg/kg-day exposures in mice (Pham et al. 2019), and the other two studies reported an increase in

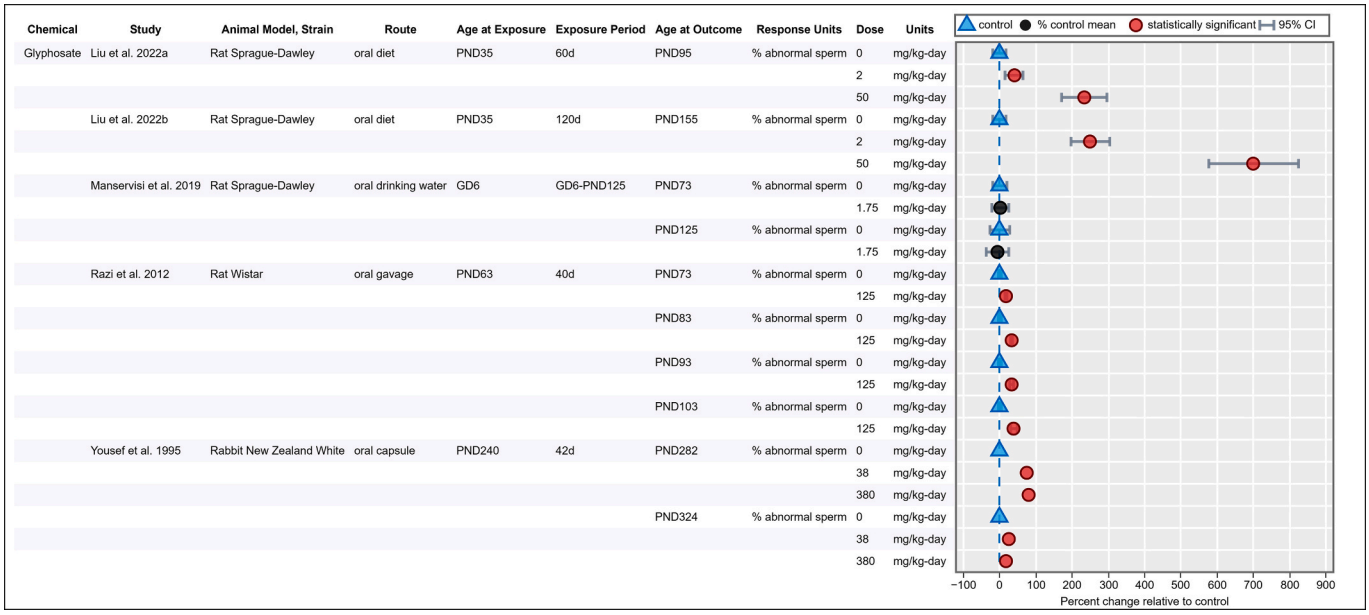


Fig. 9. Sperm Morphology (Common Measures) Animal Data – Glyphosate: An interactive version is available at the following link to figure. This plot shows percentage change in sperm morphology in glyphosate-exposed groups as compared to the control groups. The x-axis denotes % change in sperm morphology relative to control with confidence intervals. Control groups are shown as blue triangles; glyphosate groups plotted as circles for the % change relative to control, with statistically significant data points colored red. The 95% confidence interval (95% CI) is shown as a grey bar. Glyphosate doses are reported as mg glyphosate per kg body weight per day. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

intratesticular testosterone (Teleken et al. 2020) after a 420 mg/kg-day exposure or serum testosterone (Romano et al. 2012) at 50 mg/kg-day exposure. The remaining studies did not report an effect on testosterone levels following GBH exposures ranging from 1.75 to 787.85 mg/kg-day in adult (Gress et al. 2016; Güngör et al. 2024; Hariti et al. 2024), peripubertal (Gorga et al. 2021; Johansson et al. 2018), early postnatal (Altamirano et al. 2018) or gestationally exposed (Gomez et al. 2019; Manservisi et al. 2019) rats.

3.4.3.1. GBH risk-of-bias considerations. Sixteen of 23 studies were high quality based on low risk-of-bias ratings across the key considerations and minimal concerns across other domains (Abarikwu et al. 2015; Altamirano et al. 2018; Ben Amor et al. 2025; Chai et al. 2025; Fan et al. 2017; Gomez et al. 2019; Gorga et al. 2021; Gress et al. 2016; Johansson et al. 2018; Manservisi et al. 2019; Mutluay et al. 2026; Owagboriaye et al. 2017; Phusate 2022; Romano et al. 2010; Silva et al. 2024; Teleken et al. 2020) (Fig. 16). Most studies reported the randomization of animals to treatment groups, and GBH formulations were sufficiently described. Testosterone levels were measured using commercially available kits; however, most studies did not report whether researchers were blinded to dose groups during measurement. Across high-quality studies, six of seven adult (Ben Amor et al. 2025; Chai et al. 2025; Fan et al. 2017; Mutluay et al. 2026; Owagboriaye et al. 2017; Silva et al. 2024), three of six peripubertal/juvenile (Abarikwu et al. 2015; Phusate 2022; Romano et al. 2010), and one of three gestational exposure studies (Teleken et al. 2020) reported effects on testosterone. In adult and peripubertal studies, GBH consistently reduced testosterone when exposures were 30 days or longer. Detailed risk of bias information for glyphosate and testosterone studies can be found in **Supplement Section** 4.4.1, detailed risk of bias descriptions for individual high-quality studies can be found in **Supplement Section 12**, and **Fig. S21** (key risk-of-bias domains for all studies with testosterone data).

3.4.4. Meta-analyses for glyphosate and GBHs

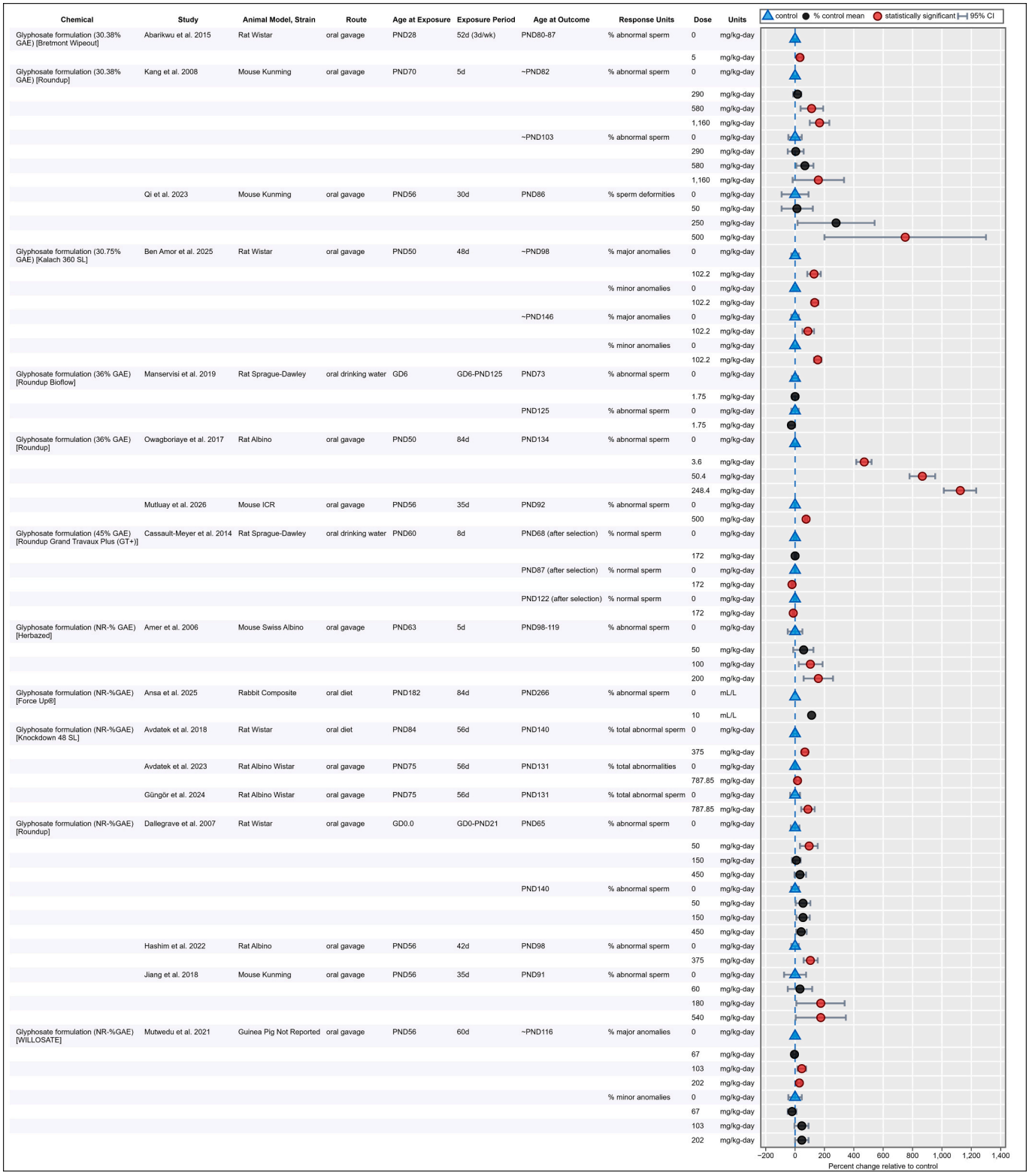
Using the RVE approach, meta-analysis of 18 effect estimates from 10 glyphosate studies, and 38 effect estimates from 22 GBH studies showed a significant inverse association with testosterone (SMD [glyphosate] = −1.77, 95%CI: −3.51, −0.03, $p = 0.047$; SMD[GBH] = -0.76, 95%CI: −1.25, −0.27, $p = 0.004$). Re-estimating the SMDs without the potential outlier studies for glyphosate (Razi et al. 2012) and GBH exposures (Owagboriaye et al. 2017) yielded attenuated results, but inverse associations for the SMDs remained statistically significant (SMD[glyphosate] = −1.18, 95%CI: −2.25, −0.11, $p = 0.04$; SMD[GBH] = −0.64, 95%CI: −1.09, −0.20, $p = 0.007$).

Egger's and Begg's tests (p-values reported in that order) indicated statistically significant funnel plot asymmetry for both glyphosate ($p < 0.001$; $p = 0.0007$) and GBH exposure ($p < 0.001$; $p = 0.006$), suggesting potential small-study effects. However, these findings should be interpreted cautiously given the heterogeneity across studies and potential correlations among multiple effect estimates from the same study. Detailed results, including sensitivity analyses excluding potential outliers and information on study inclusion in the meta-analyses are provided in **Supplement Section 4.6**.

3.4.5. Confidence: Testosterone

We conclude there is **moderate confidence** that exposure to glyphosate or GBHs decreases testosterone based on data from male rodents.

3.4.5.1. Glyphosate. There was consistent evidence that glyphosate exposure decreases testosterone, with a decreasing trend or significant decreases reported in 7 of 12 studies evaluating glyphosate (Abarikwu et al. 2015; Dai et al. 2016; Pham et al. 2019; Prasad et al. 2022; Razi et al. 2012; Zhao et al. 2018; Zhao et al. 2021). Of the three high-quality studies evaluating glyphosate and testosterone, two reported decreases (Abarikwu et al. 2015; Prasad et al. 2022) and one reported no effect (Manservisi et al. 2019). Conclusions were supported by a meta-analysis conducted using the RVE approach, and results remained significant even after removal of an outlier study. Confidence was reduced from high to moderate due to some concern for inconsistencies across gestational exposure studies and some concern for risk-of-bias across the glyphosate body of evidence.



Chemical	Study	Animal Model, Strain	Route	Age at Exposure	Exposure Period	Age at Outcome	Response Units	Dose	Units
Glyphosate formulation (30.38% GAE) [Bretmont Wipeout]	Abarikwu et al. 2015	Rat Wistar	oral gavage	PND28	52d (3d/wk)	PND80-87	% abnormal sperm	0	mg/kg-day
								5	mg/kg-day
Glyphosate formulation (30.38% GAE) [Roundup]	Kang et al. 2008	Mouse Kunming	oral gavage	PND70	5d	~PND82	% abnormal sperm	0	mg/kg-day
								290	mg/kg-day
								580	mg/kg-day
								1,160	mg/kg-day
						~PND103	% abnormal sperm	0	mg/kg-day
								290	mg/kg-day
								580	mg/kg-day
								1,160	mg/kg-day
	Qi et al. 2023	Mouse Kunming	oral gavage	PND56	30d	PND86	% sperm deformities	0	mg/kg-day
								50	mg/kg-day
								250	mg/kg-day
								500	mg/kg-day
Glyphosate formulation (30.75% GAE) [Kalach 360 SL]	Ben Amor et al. 2025	Rat Wistar	oral gavage	PND50	48d	~PND98	% major anomalies	0	mg/kg-day
								102.2	mg/kg-day
							% minor anomalies	0	mg/kg-day
								102.2	mg/kg-day
						~PND146	% major anomalies	0	mg/kg-day
								102.2	mg/kg-day
							% minor anomalies	0	mg/kg-day
								102.2	mg/kg-day
Glyphosate formulation (36% GAE) [Roundup Bioflow]	Manservisi et al. 2019	Rat Sprague-Dawley	oral drinking water	GD6	GD6-PND125	PND73	% abnormal sperm	0	mg/kg-day
								1.75	mg/kg-day
						PND125	% abnormal sperm	0	mg/kg-day
								1.75	mg/kg-day
Glyphosate formulation (36% GAE) [Roundup]	Owagboriaye et al. 2017	Rat Albino	oral gavage	PND50	84d	PND134	% abnormal sperm	0	mg/kg-day
								3.6	mg/kg-day
								50.4	mg/kg-day
								248.4	mg/kg-day
	Mutluay et al. 2026	Mouse ICR	oral gavage	PND56	35d	PND92	% abnormal sperm	0	mg/kg-day
								500	mg/kg-day
Glyphosate formulation (45% GAE) [Roundup Grand Travaux Plus (GT+)]	Cassault-Meyer et al. 2014	Rat Sprague-Dawley	oral drinking water	PND60	8d	PND68 (after selection)	% normal sperm	0	mg/kg-day
								172	mg/kg-day
						PND87 (after selection)	% normal sperm	0	mg/kg-day
								172	mg/kg-day
						PND122 (after selection)	% normal sperm	0	mg/kg-day
								172	mg/kg-day
Glyphosate formulation (NR-% GAE) [Herbazed]	Amer et al. 2006	Mouse Swiss Albino	oral gavage	PND63	5d	PND98-119	% abnormal sperm	0	mg/kg-day
								50	mg/kg-day
								100	mg/kg-day
								200	mg/kg-day
Glyphosate formulation (NR-%GAE) [Force Up®]	Ansa et al. 2025	Rabbit Composite	oral diet	PND182	84d	PND266	% abnormal sperm	0	mL/L
								10	mL/L
Glyphosate formulation (NR-%GAE) [Knockdown 48 SL]	Avdatek et al. 2018	Rat Wistar	oral diet	PND84	56d	PND140	% total abnormal sperm	0	mg/kg-day
								375	mg/kg-day
	Avdatek et al. 2023	Rat Albino Wistar	oral gavage	PND75	56d	PND131	% total abnormalities	0	mg/kg-day
								787.85	mg/kg-day
	Güngör et al. 2024	Rat Albino Wistar	oral gavage	PND75	56d	PND131	% total abnormal sperm	0	mg/kg-day
								787.85	mg/kg-day
Glyphosate formulation (NR-%GAE) [Roundup]	Dallegrave et al. 2007	Rat Wistar	oral gavage	GD0.0	GD0-PND21	PND65	% abnormal sperm	0	mg/kg-day
								50	mg/kg-day
								150	mg/kg-day
								450	mg/kg-day
						PND140	% abnormal sperm	0	mg/kg-day
								50	mg/kg-day
								150	mg/kg-day
								450	mg/kg-day
	Hashim et al. 2022	Rat Albino	oral gavage	PND56	42d	PND98	% abnormal sperm	0	mg/kg-day
								375	mg/kg-day
	Jiang et al. 2018	Mouse Kunming	oral gavage	PND56	35d	PND91	% abnormal sperm	0	mg/kg-day
								60	mg/kg-day
								180	mg/kg-day
								540	mg/kg-day
Glyphosate formulation (NR-%GAE) [WILLOSATE]	Mutwedu et al. 2021	Guinea Pig Not Reported	oral gavage	PND56	60d	~PND116	% major anomalies	0	mg/kg-day
								67	mg/kg-day
								103	mg/kg-day
								202	mg/kg-day
							% minor anomalies	0	mg/kg-day
								67	mg/kg-day
								103	mg/kg-day
								202	mg/kg-day

Fig. 10. Sperm Morphology (Common Measures) Animal Data – GBH: An interactive version is available at the following link to figure. This plot shows percentage change in sperm morphology GBH-exposed groups as compared to the control groups. The x-axis denotes % change in sperm morphology relative to control with confidence intervals. Control groups are shown as blue triangles; GBH groups plotted as circles for the % change relative to control, with statistically significant data points colored red. The 95% confidence interval (95% CI) is shown as a grey bar. GBH doses are reported as mg formulation mass of GBH per kg body weight per day. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

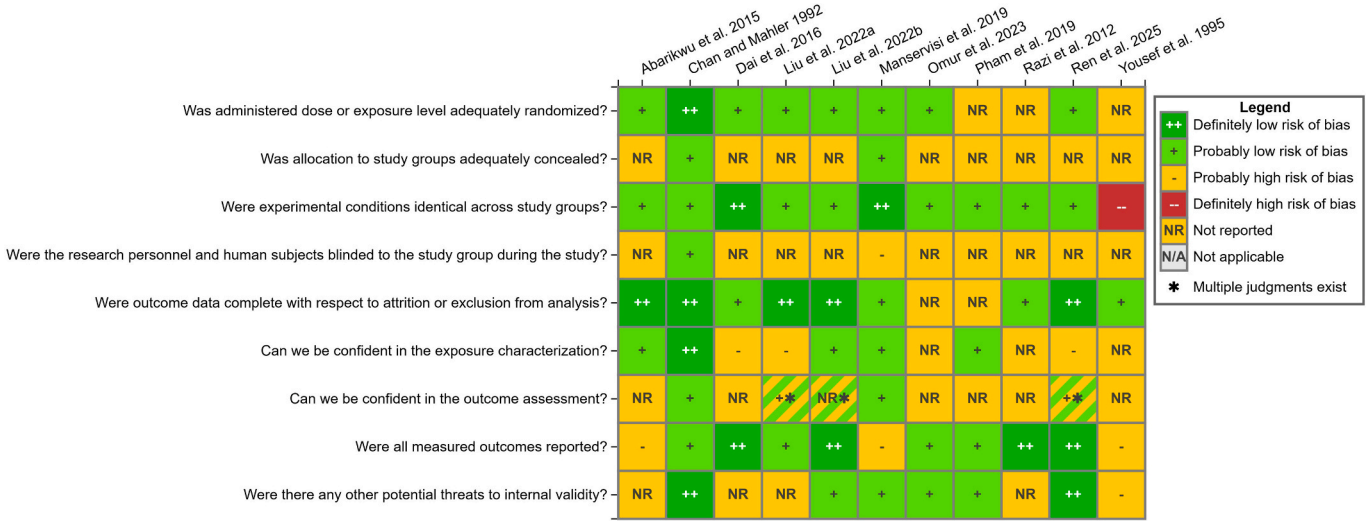


Fig. 11. Risk-of-bias heatmap of studies with sperm data – Glyphosate: An interactive version is available at the following link to figure. This plot summarizes the risk-of-bias (RoB) assessment for studies evaluating the association between glyphosate exposure and sperm-related endpoints (n = 11) across individual bias domains using OHAT risk-of-bias tool. Each column represents an individual study, and each row represents a bias domain. Colors in each cell indicate the level of bias for a given domain within each study.

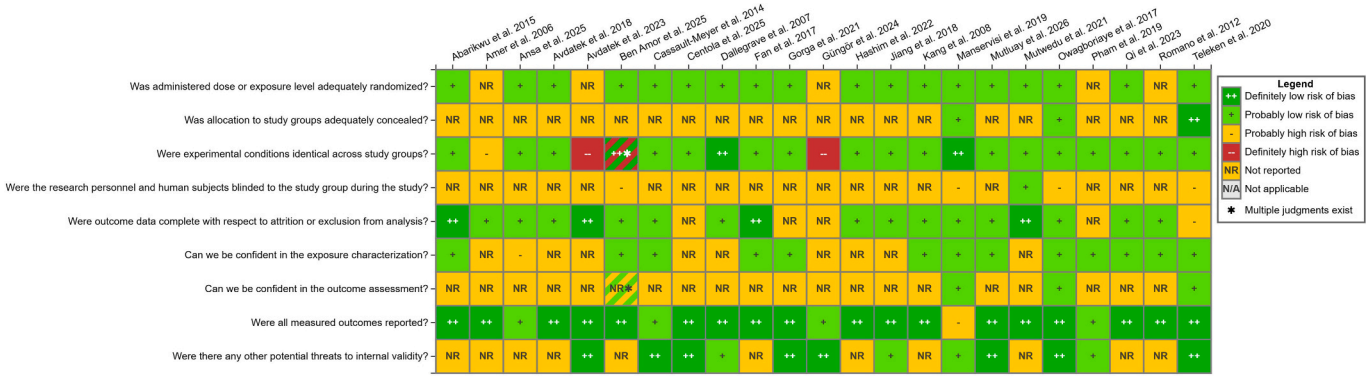


Fig. 12. Risk-of-bias heatmap of studies with sperm data – GBH: An interactive version is available at the following link to figure. This plot summarizes the risk-of-bias (RoB) assessment for studies evaluating the association between GBH exposure and sperm-related endpoints (n = 23) across individual bias domains using OHAT risk-of-bias tool. Each column represents an individual study, and each row represents a bias domain. Colors in each cell indicate the level of bias for a given domain within each study.

3.4.5.2. GBH. Similarly, there was consistent evidence that GBH exposure decreases testosterone with significant decreases reported in 13 of 23 studies (Abarikwu et al. 2015; Avdatek et al. 2023; Ben Amor et al. 2025; Chai et al. 2025; Dallegrave et al. 2007; Fan et al. 2017; Mutluay et al. 2026; Owagboriaye et al. 2017; Pandey and Rudraiah 2015; Pham et al. 2019; Phusate 2022; Romano et al. 2010; Silva et al. 2024). Confidence is largely informed by 16 high-quality studies, with 6 of 7 adult (Ben Amor et al. 2025; Chai et al. 2025; Fan et al. 2017; Mutluay et al. 2026; Owagboriaye et al. 2017; Silva et al. 2024) and 3 of 6 juvenile (Abarikwu et al. 2015; Phusate 2022; Romano et al. 2010) high-quality studies reporting decreased testosterone when GBH was administered for 30 days or longer. GBH effects were observed across adult exposures in rats, mice, and gerbils, with some evidence suggestive of a dose response. Conclusions were supported by a meta-analysis conducted using the RVE approach, and results remained significant even after removal of an outlier study. High-quality studies that did not report an effect consisted of adult (Gress et al. 2016), postnatal (Altamirano et al. 2018), or peripubertal (Gorga et al. 2021; Johansson et al. 2018) studies with exposures of less than 30 days, and gestational exposure studies (Gomez et al. 2019; Manservisi et al. 2019). Confidence was reduced from high to moderate due to some concerns for inconsistencies across studies, particularly gestational exposure studies.

Detailed explanations of the confidence assessment process for testosterone evidence are provided in **Supplement Section 4.6** for glyphosate and GBH, including stepwise discussion of all nine factors considered for potential downgrades or upgrades.

3.5. Sperm measures, other hormones, milestones, histopathology, and organ weight

Additional sperm measures were reported for GBH but not formally evaluated due to the limited number of studies addressing these endpoints including sperm viability, sperm membrane integrity, sperm transit time, ejaculation volume, and semen osmolality (see details in **Supplement Section 3.5**).

The body of evidence was considered inadequate to evaluate glyphosate- or GBH-related effects on other hormones. Five glyphosate and 14 GBH exposure studies evaluated effects on gonadotropins associated with sperm (FSH) or testosterone (LH) production, or other hormones that contribute to male reproduction (dihydrotestosterone, estradiol, progesterone, or prolactin), though all hormones were not evaluated in all studies. The inadequate determination for glyphosate is

Table 2
Overview of studies with testosterone or other hormone data Hormone data table The following data table provides a brief description of the studies that measured reproductive hormones and relevant results including testosterone (T), luteinizing hormone (LH), dihydrotestosterone (DHT), estradiol (E2), follicle stimulating hormone (FSH), prolactin (PRL), progesterone (P4), or 3β − hydroxysteroid dehydrogenase (HSD). Study descriptions include the exposure (glyphosate or GBH with the glyphosate studies presented first), animal model (species, strain and age at treatment), and treatment details (route, duration, doses), followed by the relevant outcomes measured (specific hormones in plasma, serum, or tissues) and a brief summary of the results for each hormone.

Study	Exposure	Model (age at treatment)	Treatment (duration) doses	Outcomes	Summary of Results
Abarikwu et al. (2015)	Glyphosate[1]	Wistar rats (28 − 35 days)	Oral gavage (3x/week for 52 days) 0, 5 mg/kg-day	Plasma T	• Plasma T significantly decreased 55% relative to controls at 52 days.
Astiz et al. (2009)	Glyphosate	Wistar rats (~50 days)[2]	Intraperitoneal injection (3x/week for 35 days) 0, 10 mg/kg-day	Plasma and testicular T, FSH, E2, LH	• No significant changes in plasma T (both bound and free), testicular T, E2, FSH, or LH relative to controls at 5 weeks.
Dai et al. (2016)	Glyphosate	SD rats (56 days)	Oral gavage (35 days) 0, 5, 50, 500 mg/kg-day	Serum T, E2, P4	• Decreasing trend of 20% and 57% in serum T relative to controls in the 50- and 500-mg/kg-day dose groups at 5 weeks, but decreases were not statistically significant. • E2 decreased 83%, 33%, and 84% relative to controls in the 5-, 50-, and 500-mg/kg-day dose groups at 5 weeks, but decreases were not statistically significant. • P4 decreased 28%, 50%, and 44% relative to controls in the 5-, 50-, and 500-mg/kg-day dose groups at 5 weeks, but decreases were not statistically significant.
Gomez et al. (2023)	Glyphosate	Wistar rats (GD9)	Diet [gestation, lactation] (32 − 34 days) 0, 3.9 mg/kg-day	Serum T, E2	• No significant changes in serum T or E2 at PND60.
Gorga et al. (2021)	Glyphosate	SD rats (PND14)	Oral gavage (17 days) 0, 2, 50 mg/kg-day	Intratesticular T	• No significant change in intratesticular T at PND31.
Johansson et al. (2018)	Glyphosate	SD rats (28 days)	Oral gavage (14 days) 0, 2.5, 25 mg/kg-day	Intratesticular T	• Intratesticular T decreased in the 25 mg/kg-day dose group at 2 weeks, but was not statistically significant.
Manservisi et al. (2019)	Glyphosate	SD rats (GD6)	Drinking water [gestation, lactation, postweaning] (~88 or 140 days) 0, 1.75 mg/kg-day	Serum T, DHT, E2, FSH, LH, PRL (PND73)	• Free T was decreased at PND73 and increased at PND125, although neither change was statistically significant. No significant effects were found for total T at either timepoint. • E2 increased at PND73 and decreased at PND125, but did not reach statistical significance. • No change found in DHT, FSH, LH, or PRL.
Pham et al. (2019)	Glyphosate	Swiss mice (GD10.5)	Drinking water [gestation, lactation] (~31 days) 0, 0.5, 5, 50 mg/kg-day	Serum T	• At PND35, serum T significantly decreased 66% and 70% in the 0.5- and 50-mg/kg-day dose groups relative to controls. Serum T decreased 40% in the 5-mg/kg-day dose group, but this decrease was not statistically significant. • At 8 months, serum T decreased in the 5- and 50-mg/kg-day dose groups but did not reach statistical significance.
Prasad et al. (2022)	Glyphosate	Wistar rats (56 days)	Oral gavage (112 days) 0, 50, 100, 250 mg/kg-day	Serum T	• Serum T significantly decreased 29% and 48% relative to controls in the 100- and 250-mg/kg-day dose groups at 16 weeks. Serum T also decreased in the 50-mg/kg-day dose group, but this decrease did not reach statistical significance.
Razi et al. (2012)	Glyphosate	Wistar rats (63 days)	Oral gavage (10, 20, 30, or 40 days) 0, 125 mg/kg-day	Serum T	• Serum T significantly decreased 48%, 70%, 76%, and 82% relative to controls at 10, 20, 30, and 40 days.
Zhao et al. (2018)	Glyphosate	SD rats (~28 − 42 days)[3]	Oral gavage (28, 56, 84 days) 0, 50, 200, 800 mg/kg-day	Serum FSH, LH, T, E2, HSD	• Serum FSH significantly decreased 26% relative to controls in the 800-mg/kg-day dose group at 12 weeks, but no significant changes in other doses or timepoints. • No significant changes in serum LH and E2 at 4, 8, or 12 weeks. • Serum T significantly decreased 21% in the 800-mg/kg-day dose group at 8 weeks and 26% and 32% in the 200- and 800-mg/kg-day dose groups at 12 weeks relative to controls. No significant changes at other doses or timepoints. • Serum HSD decreased in both 200- and 800-mg/kg-day dose groups at 12 weeks, but did not reach statistical significance.
Zhao et al. (2021)	Glyphosate	BALB/c mice (84 − 98 days)	Drinking water (28 days) 0, 985 mg/kg-day	Serum T	• Serum T significantly decreased 88% and 83% relative to controls at 4 weeks during the light and dark phase timepoints.
Abarikwu et al. (2015)	GBH[4] (Bretmont Wipeout) [30.38% GAE]	Wistar rats (28 − 35 days)	Oral gavage (3x/week for 52 days) 0, 5 mg/kg-day	Plasma T, FSH, HSD, LH	• Plasma T significantly decreased 55% relative to controls at 52 days. • No significant changes in FSH level, LH level, or HSD activity at 52 days.

(*continued on next page*)

Table 2 (*continued*)

Study	Exposure	Model (age at treatment)	Treatment (duration) doses	Outcomes	Summary of Results
Altamirano et al. (2018)	GBH (Roundup FULL II) [54% GAE]	Wistar rats (PND1)	Subcutaneous injection (every 48 h for 7 days) 0, 2 mg/kg-day	Serum T, E2	• No significant changes in serum T or E2 levels at PND21 or PND60.
Avdatek et al. (2023)	GBH (Knockdown 48 SL) [NR% GAE]	Wistar rats (~75 – 90 days)	Oral gavage (56 days) 0, 787.85 mg/kg-day	Plasma T	• Plasma T significantly decreased 35% relative to controls at 56 days.
Ben Amor et al. (2025)	GBH (Kalach 360 SL) [30.75% GAE]	Wistar rats (adult)	Oral gavage (48 days) 0, 102.2 mg/kg-day	Serum T, E2	• Serum T significantly decreased 61% at 48 days and significantly increased 35% at 96 days relative to controls. • No significant changes in E2 levels at 48 days or 96 days.
Chai et al. (2025)	GBH (Roundup) [30.38% GAE]	Kunming mice (56 days)	Oral gavage (30 days) 0, 50, 250, 500 mg/kg-day	Serum T	• Serum T significantly decreased 13% relative to controls in the high dose group (500 mg/kg-day) at 30 days.
Dallegrave et al. (2007)	GBH (Roundup) [NR% GAE]	Wistar rats (GD0)	Oral gavage [gestation, lactation] (~42 days) 0, 50, 150, 450 mg/kg-day	Serum T	• Serum T decreased in all dose groups 23%, 38% and 71% relative to controls at PND65, although only the change in the high dose was significant. There were mixed, non-significant results in each dose group at PND140.
Fan et al. (2017)	GBH (Roundup) [35% GAE]	BALB/c mice (adult)	Oral gavage (30 days) 0, 20, 200, 2000 mg/kg-day	Serum T	• Serum T significantly decreased 34%, 44% and 34% in the 20-, 200- and 2000-mg/kg-day dose groups relative to controls at 30 days.
Gomez et al. (2019)	GBH (Magnum Super II) [54% GAE]	Wistar rats (GD9)	Diet [gestation, lactation] (~33 days) 0, 3.7, 352 mg/kg-day	Serum T, E2, PRL (PND60)	• No significant changes in serum T or E2 for any dose group at PND21 or PND60. • PRL significantly increased 142% in the high dose group relative to controls at PND60.
Gorga et al. (2021)	GBH (Roundup) [54% GAE]	SD rats (PND14)	Oral gavage (17 days) 0, 2, 50 mg/kg-day	Intratesticular T (PND31), serum T (PND90)	• Intratesticular T increased in the 2-mg/kg-day and 50-mg/kg-day dose groups at PND31, but did not reach statistical significance. • No significant change in serum T for the 50–mg/kg-day dose group relative to controls at PND90.
Gress et al. (2016)	GBH (Roundup Grand Travaux Plus (GT +)) [45% GAE]	SD rats (PND60)	Drinking water (8 days) 0, 135 mg/kg-day	Plasma T, E2	• No significant change in serum T at 8 days. • E2 significantly decreased 7% relative to controls at 8 days.
Güngör et al. (2024)	GBH (Knockdown 48 SL) [NR% GAE]	Wistar rats (75 – 90 days)	Oral gavage (56 days) 0, 787.85 mg/kg-day	Plasma T	• No significant change in plasma T at 56 days.
Hariti et al. (2024)	GBH (KALASH) [22.97% GAE]	Wistar rats (65 days)	Oral gavage (21 days) 0, 102.5, 200, 400 mg/kg-day	Plasma T, E2	• Plasma T increased in the high dose group at 21 days, although not statistically significant. • No significant changes in E2 for any dose group at 21 days.
Johansson et al. (2018)	GBH (Glyfonova 450 Plus) [45% GAE]	SD rats (28 days)	Oral gavage (14 days) 0, 25 mg/kg-day	Intratesticular T	• No significant change in intratesticular T at 2 weeks.
Manservisi et al. (2019)	GBH (Roundup Bioflow) [36% GAE]	SD rats (GD6)	Drinking water [gestation, lactation, postweaning] (~88 or 140 days) 0, 1.75 mg/kg-day	Serum T, DHT, E2, FSH, LH, PRL (PND73)	• Free T and total T decreased at PND73 and PND125, although neither change was statistically significant. • Significant 87% decrease in DHT relative to controls at PND125 and a non-significant decrease on PND73. • E2 increased at PND73 and at PND125, although neither was statistically significant. • No changes found in FSH, LH, or PRL.
Mutluay et al. (2026)	GBH (Roundup) [36% GAE]	ICR mice (56 – 70 days)	Oral gavage (35 days) 0, 500 mg/kg-day	Serum T, LH	• Serum T significantly decreased 48% relative to controls at 36 days. • LH significantly increased 57% relative to controls at 36 days.
Owagboriaye et al. (2017)	GBH (Roundup) [36% GAE]	Albino rats (adult)	Oral gavage (84 days) 0, 3.6, 50.4, 248.4 mg/kg-day	Serum T, FSH, LH, PRL	• Serum T significantly decreased 13%, 34%, and 66% relative to controls in the 3.6-, 50.4-, and 248.4-mg/kg-day dose groups at 12 weeks. • FSH significantly decreased 17%, 36%, and 66% relative to controls in the 3.6-, 50.4-, and 248.4-mg/kg-day dose groups at 12 weeks. • LH significantly decreased 14%, 35%, and 74% relative to controls in the 3.6-, 50.4-, and 248.4-mg/kg-day dose groups at 12 weeks. • PRL significantly increased 31%, 72%, and 177% relative to controls in the 3.6-, 50.4-, and 248.4-mg/kg-day dose groups at 12 weeks.
Pandey and Rudraiah (2015)	GBH (Roundup) [NR% GAE]	Wistar rats (PND60 – 75)	Oral gavage (14 days) 0, 10, 50 mg/kg-day	Plasma T	• Significant 92% decrease in plasma T relative to controls in the 50-mg/kg-day dose group and a non-significant decrease in the 10-mg/kg-day dose group at 14 days.
Pham et al. (2019)	GBH (Roundup 3 Plus) [15.56% GAE]	Swiss mice (GD10.5)	Drinking water [gestation, lactation]	Serum T	• At PND35, serum T decreased in the 0.5- and 50-mg/kg-day dose groups but neither decrease was statistically significant.

(*continued on next page*)

Table 2 (*continued*)

Study	Exposure	Model (age at treatment)	Treatment (duration) doses	Outcomes	Summary of Results
			(~31 days) 0, 0.5, 5, 50 mg/kg-day		• At 8 months, serum T significantly decreased 90% and 85% in the 5- and 50-mg/kg-day dose groups relative to controls.
Phusate (2022)	GBH (Roundup) [30.38% GAE]	Wistar rats (PND28)	Oral gavage (25 or 60 days) 0, 250 mg/kg-day	Serum T, FSH, LH	• Serum T significantly decreased 31% relative to controls at 60 days. No significant change at 25 days. • No significant changes in FSH or LH at 25 or 60 days.
Romano et al. (2010)	GBH (Roundup Transorb) [48% GAE]	Wistar rats (PND23)	Oral gavage (30 days) 0, 5, 50, 250 mg/kg-day	Serum T, E2	• Serum T significantly decreased 30%, 45%, and 50% relative to controls in the 5-, 50-, and 250-mg/kg-day dose groups at 30 days. • No significant changes in E2 for any dose group relative to controls at 30 days.
Romano et al. (2012)	GBH (Roundup Transorb) [48% GAE]	Wistar rats (GD18)	Oral gavage [gestation, lactation] (~8 days) 0, 50 mg/kg-day	Serum T, E2, FSH, LH	• Serum T significantly increased 127% relative to controls at PND60. • E2 significantly increased 100% relative to controls at PND60. • LH significantly increased 73% relative to controls at PND60. • No significant change in FSH at PND60.
Silva et al. (2024)	GBH (Roundup WG®) [72% GAE]	Mongolian gerbils (~183 days)	Drinking water (90 days) 0, 0.17 mg/kg-day	Serum T, E2	• Serum T significantly decreased 59% relative to controls at 90 days. • E2 decreased at 90 days, but was not statistically significant.
Teleken et al. (2020)	GBH (Roundup Original DI) [37% GAE]	C57BL/6 mice (GD4)	Drinking water [gestation, lactation] (~47 days) 0, 420 mg/kg-day	Intratesticular T, plasma T, FSH, LH	• Intratesticular T significantly increased 195% relative to controls at PND150. No significant change in plasma T relative to controls at PND150. • LH significantly increased 94% relative to controls at PND150. • No significant change in FSH at PND150.

DHT = dihydrotestosterone; E2 = estradiol; FSH = follicle stimulating hormone; GAE = glyphosate acid equivalent; GD = gestational day; HSD = 3β-hydroxysteroid dehydrogenase; ICR = Institute for Cancer Research; LH = luteinizing hormone; NR = not reported; P4 = progesterone; PND = postnatal day; PRL = prolactin; SD = Sprague-Dawley; T = testosterone. [1]Glyphosate doses are reported as mg glyphosate per kg body weight per day.[2]Rats were assumed to be ~ 50 days at the start of treatment based on their weights reported to be 190 ± 20 g. [3]Rats were assumed to be ~ 28–42 days old at the start of treatment based on their weights reported to be 80–120 g. [4]GBH doses are reported as mg formulation mass of GBH per kg body weight per day.

based on the limited number of studies, different study designs, and lack of effect observed across a small number of studies. Although there were more GBH exposure studies, the inadequate determination is based on different results across studies without a clear pattern by species, dose, duration or other factors in addition to relatively few studies (see details in **Supplement Section 5**).

Two reproductive developmental milestone measures, anogenital distance (AGD) and preputial separation (PPS), were identified in the body of evidence. Four studies evaluated AGD and eight studies evaluated PPS following glyphosate or GBH exposure and reported mixed results across studies that differed in timing of exposure, dose, and species. Given the relatively small body of evidence and heterogeneity in the results, the body of evidence was considered inadequate to determine glyphosate or GBH effects on these endpoints (see details in **Supplement Section 6**).

Histopathology was assessed in 37 studies across the glyphosate and GBH bodies of evidence, with most studies focused on the testis. Although many studies reported testicular changes, most studies were low quality due to concerns related to outcome assessment. Most studies showed inconsistent results, and an expert review noted that many studies had inadequate fixation, incorrect lesion identification, misinterpretation of artifacts, and improper comparisons across spermatogenic stages. Due to the high variability in study methods, doses, durations, and data quality, the body of evidence was considered inadequate to determine whether glyphosate or GBHs alters male reproductive organ histopathology (see details in **Supplement Section 7**).

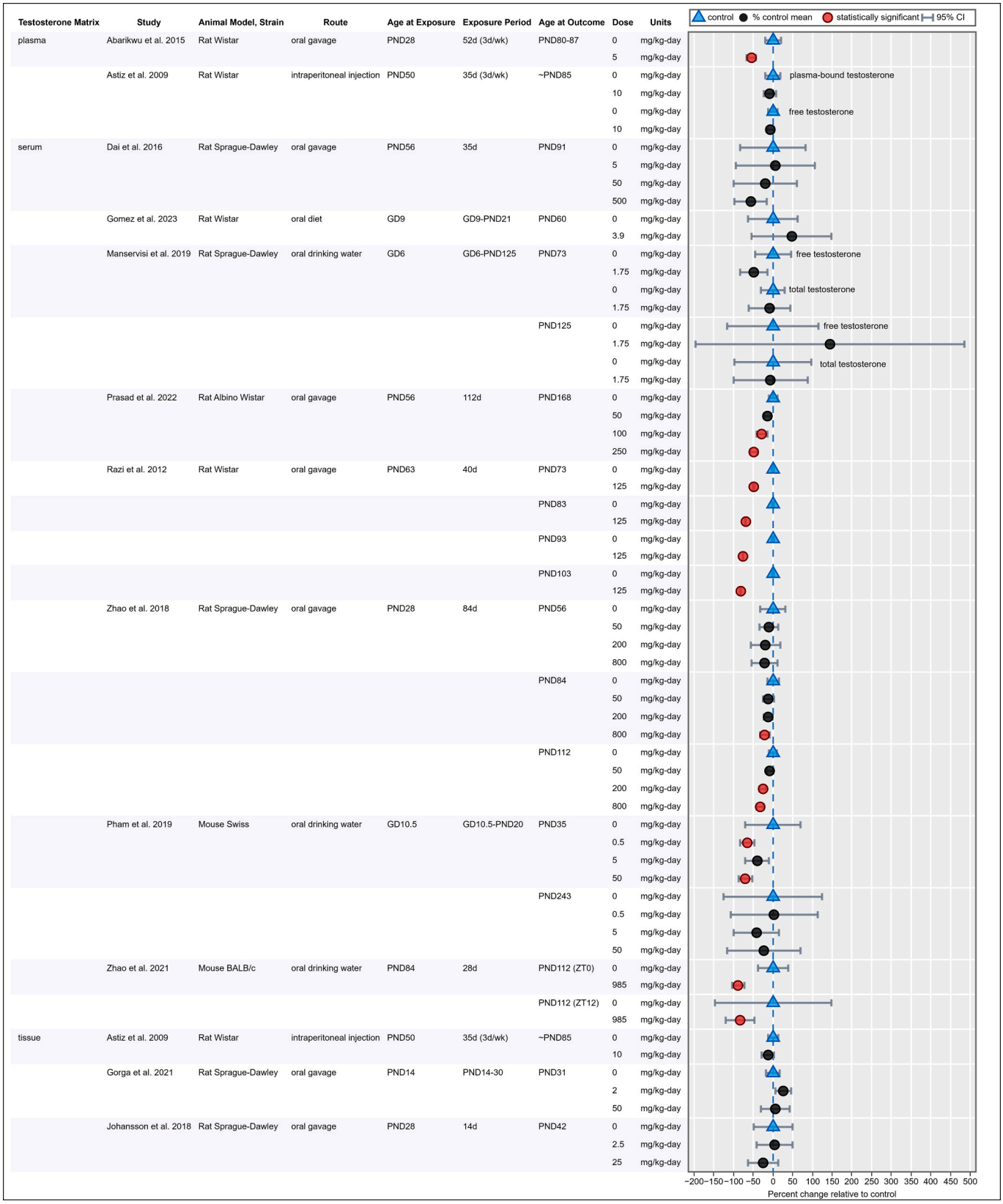
Thirty studies measured testis weight and 21 studies measured epididymis weight following glyphosate or GBH exposure, and results were mixed. The available evidence was unclear for potential effects on testis weight, with 5 of 11 glyphosate and 13 of 22 GBH studies reporting no effect, and multiple studies reporting increased or decreased testis weights. Similarly, all 6 glyphosate studies and 11 of 17 GBH studies reported no effect on epididymis weight, with the remaining studies reporting a decrease and one study reporting increased weight. Taken together, the data were inadequate to determine potential effects on testis or epididymis weights following glyphosate or GBH exposure (see details in **Supplement Section 8**).

4. Discussion

This systematic review evaluated male reproductive effects from glyphosate alone or GBH exposure from in vivo non-human mammalian studies (rodents and rabbits) as the first of two phases of this project, with human epidemiological and mechanistic evidence planned for phase 2. Most references reported sperm parameters, testosterone concentration, or both. Considering all studies on study quality and consistency of results, we developed conclusions for multiple sperm measurements and for testosterone. The conclusions are based primarily on the high-quality, low risk-of-bias studies with support from the other data.

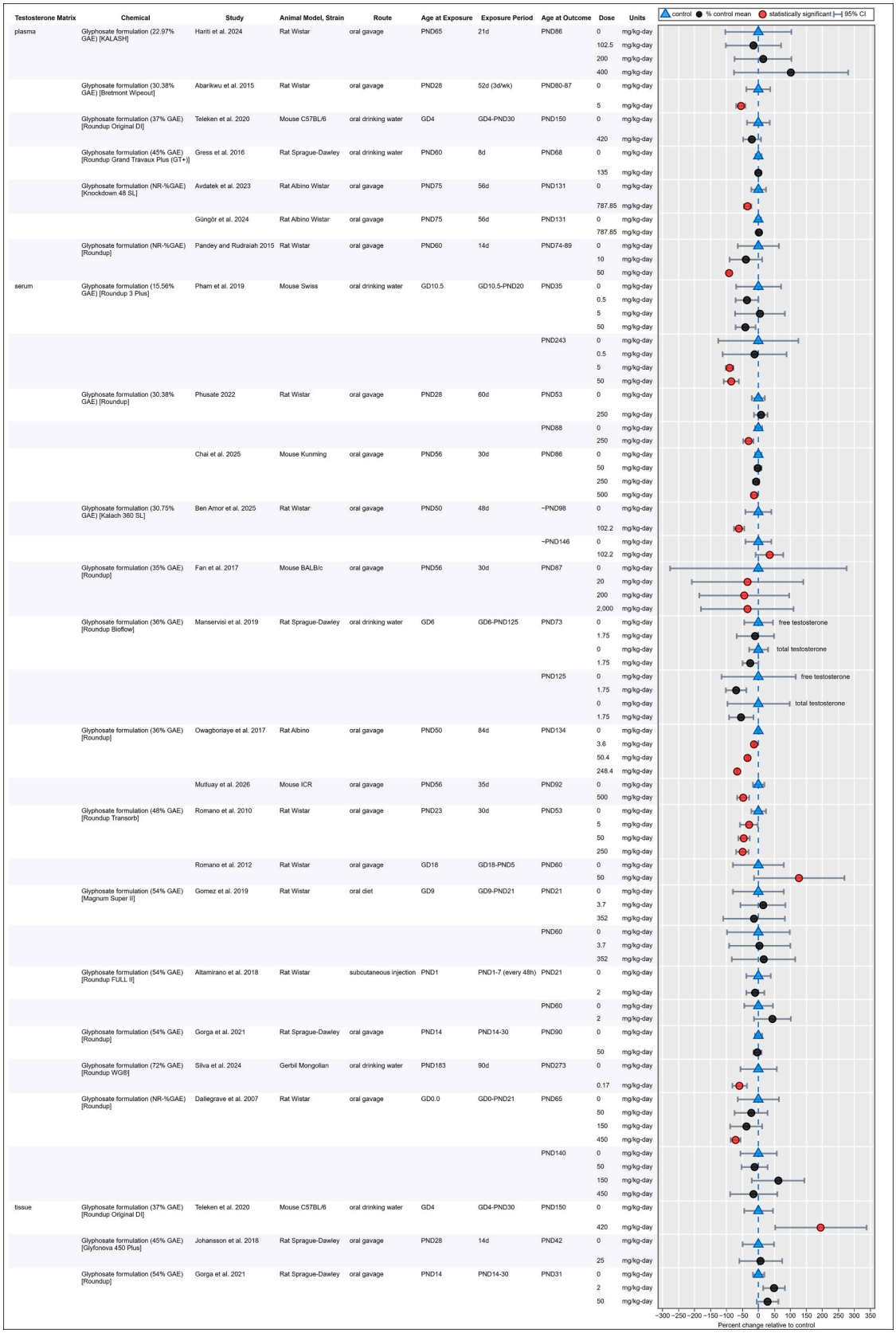
4.1. Sperm outcomes

There was consistent evidence that glyphosate and GBH exposure adversely affect sperm health across multiple sperm-related endpoints, including sperm motility, abundance, and morphology. Findings were most consistent across studies that evaluated exposures initiated in juvenile, *peri*-pubertal or adult males with a duration of ≥30 days exposure. The overall evidence was supported by meta-analyses that observed inverse associations between exposure to glyphosate and GBH and decreases in sperm count, concentration, and motility. Adverse sperm effects were reported in multiple animal models (e.g., rats, mice,



Testosterone Matrix	Study	Animal Model, Strain	Route	Age at Exposure	Exposure Period	Age at Outcome	Dose	Units
plasma	Abarikwu et al. 2015	Rat Wistar	oral gavage	PND28	52d (3d/wk)	PND80-87	0	mg/kg-day
							5	mg/kg-day
	Astiz et al. 2009	Rat Wistar	intraperitoneal injection	PND50	35d (3d/wk)	~PND85	0	mg/kg-day
							10	mg/kg-day
							0	mg/kg-day
							10	mg/kg-day
serum	Dai et al. 2016	Rat Sprague-Dawley	oral gavage	PND56	35d	PND91	0	mg/kg-day
							5	mg/kg-day
							50	mg/kg-day
							500	mg/kg-day
	Gomez et al. 2023	Rat Wistar	oral diet	GD9	GD9-PND21	PND60	0	mg/kg-day
							3.9	mg/kg-day
	Manservisi et al. 2019	Rat Sprague-Dawley	oral drinking water	GD6	GD6-PND125	PND73	0	mg/kg-day
							1.75	mg/kg-day
							0	mg/kg-day
							1.75	mg/kg-day
						PND125	0	mg/kg-day
							1.75	mg/kg-day
							0	mg/kg-day
							1.75	mg/kg-day
	Prasad et al. 2022	Rat Albino Wistar	oral gavage	PND56	112d	PND168	0	mg/kg-day
							50	mg/kg-day
							100	mg/kg-day
							250	mg/kg-day
	Razi et al. 2012	Rat Wistar	oral gavage	PND63	40d	PND73	0	mg/kg-day
							125	mg/kg-day
						PND83	0	mg/kg-day
							125	mg/kg-day
						PND93	0	mg/kg-day
							125	mg/kg-day
						PND103	0	mg/kg-day
							125	mg/kg-day
	Zhao et al. 2018	Rat Sprague-Dawley	oral gavage	PND28	84d	PND56	0	mg/kg-day
							50	mg/kg-day
							200	mg/kg-day
							800	mg/kg-day
						PND84	0	mg/kg-day
							50	mg/kg-day
							200	mg/kg-day
							800	mg/kg-day
						PND112	0	mg/kg-day
							50	mg/kg-day
							200	mg/kg-day
							800	mg/kg-day
	Pham et al. 2019	Mouse Swiss	oral drinking water	GD10.5	GD10.5-PND20	PND35	0	mg/kg-day
							0.5	mg/kg-day
							5	mg/kg-day
							50	mg/kg-day
						PND243	0	mg/kg-day
							0.5	mg/kg-day
							5	mg/kg-day
							50	mg/kg-day
	Zhao et al. 2021	Mouse BALB/c	oral drinking water	PND84	28d	PND112 (ZT0)	0	mg/kg-day
							985	mg/kg-day
						PND112 (ZT12)	0	mg/kg-day
							985	mg/kg-day
tissue	Astiz et al. 2009	Rat Wistar	intraperitoneal injection	PND50	35d (3d/wk)	~PND85	0	mg/kg-day
							10	mg/kg-day
	Gorga et al. 2021	Rat Sprague-Dawley	oral gavage	PND14	PND14-30	PND31	0	mg/kg-day
							2	mg/kg-day
							50	mg/kg-day
	Johansson et al. 2018	Rat Sprague-Dawley	oral gavage	PND28	14d	PND42	0	mg/kg-day
							2.5	mg/kg-day
							25	mg/kg-day

Fig. 13. Testosterone Animal Data – Glyphosate: An interactive version is available at the following link to figure. This plot shows percentage change in testosterone levels in glyphosate-exposed groups as compared to the control groups. The x-axis denotes % change in testosterone level relative to control with confidence intervals. Control groups are shown as blue triangles; glyphosate groups plotted as circles for the % change relative to control, with statistically significant data points colored red. The 95% confidence interval (95% CI) is shown as a grey bar. Glyphosate doses are reported as mg glyphosate per kg body weight per day. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)



Testosterone Matrix	Chemical	Study	Animal Model, Strain	Route	Age at Exposure	Exposure Period	Age at Outcome	Dose	Units
plasma	Glyphosate formulation (22.97% GAE) [KALASH]	Hariti et al. 2024	Rat Wistar	oral gavage	PND65	21d	PND86	0	mg/kg-day
								102.5	mg/kg-day
								200	mg/kg-day
								400	mg/kg-day
	Glyphosate formulation (30.38% GAE) [Bretmont Wipeout]	Abarikwu et al. 2015	Rat Wistar	oral gavage	PND28	52d (3d/wk)	PND80-87	0	mg/kg-day
								5	mg/kg-day
	Glyphosate formulation (37% GAE) [Roundup Original DI]	Teleken et al. 2020	Mouse C57BL/6	oral drinking water	GD4	GD4-PND30	PND150	0	mg/kg-day
								420	mg/kg-day
	Glyphosate formulation (45% GAE) [Roundup Grand Travaux Plus (GT+)]	Gress et al. 2016	Rat Sprague-Dawley	oral drinking water	PND60	8d	PND68	0	mg/kg-day
								135	mg/kg-day
	Glyphosate formulation (NR-%GAE) [Knockdown 48 SL]	Avdatek et al. 2023	Rat Albino Wistar	oral gavage	PND75	56d	PND131	0	mg/kg-day
								787.85	mg/kg-day
		Güngör et al. 2024	Rat Albino Wistar	oral gavage	PND75	56d	PND131	0	mg/kg-day
								787.85	mg/kg-day
	Glyphosate formulation (NR-%GAE) [Roundup]	Pandey and Rudraiah 2015	Rat Wistar	oral gavage	PND60	14d	PND74-89	0	mg/kg-day
								10	mg/kg-day
								50	mg/kg-day
serum	Glyphosate formulation (15.56% GAE) [Roundup 3 Plus]	Pham et al. 2019	Mouse Swiss	oral drinking water	GD10.5	GD10.5-PND20	PND35	0	mg/kg-day
								0.5	mg/kg-day
								5	mg/kg-day
								50	mg/kg-day
							PND243	0	mg/kg-day
								0.5	mg/kg-day
								5	mg/kg-day
								50	mg/kg-day
	Glyphosate formulation (30.38% GAE) [Roundup]	Phusate 2022	Rat Wistar	oral gavage	PND28	60d	PND53	0	mg/kg-day
								250	mg/kg-day
							PND88	0	mg/kg-day
								250	mg/kg-day
		Chai et al. 2025	Mouse Kunming	oral gavage	PND56	30d	PND86	0	mg/kg-day
								50	mg/kg-day
								250	mg/kg-day
								500	mg/kg-day
	Glyphosate formulation (30.75% GAE) [Kalach 360 SL]	Ben Amor et al. 2025	Rat Wistar	oral gavage	PND50	48d	~PND98	0	mg/kg-day
								102.2	mg/kg-day
							~PND146	0	mg/kg-day
								102.2	mg/kg-day
	Glyphosate formulation (35% GAE) [Roundup]	Fan et al. 2017	Mouse BALB/c	oral gavage	PND56	30d	PND87	0	mg/kg-day
								20	mg/kg-day
								200	mg/kg-day
								2,000	mg/kg-day
	Glyphosate formulation (36% GAE) [Roundup Bioflow]	Manservisi et al. 2019	Rat Sprague-Dawley	oral drinking water	GD6	GD6-PND125	PND73	0	mg/kg-day
								1.75	mg/kg-day
								0	mg/kg-day
								1.75	mg/kg-day
							PND125	0	mg/kg-day
								1.75	mg/kg-day
								0	mg/kg-day
								1.75	mg/kg-day
	Glyphosate formulation (36% GAE) [Roundup]	Owagboriaye et al. 2017	Rat Albino	oral gavage	PND50	84d	PND134	0	mg/kg-day
								3.6	mg/kg-day
								50.4	mg/kg-day
								248.4	mg/kg-day
		Mutluay et al. 2026	Mouse ICR	oral gavage	PND56	35d	PND92	0	mg/kg-day
								500	mg/kg-day
	Glyphosate formulation (48% GAE) [Roundup Transorb]	Romano et al. 2010	Rat Wistar	oral gavage	PND23	30d	PND53	0	mg/kg-day
								5	mg/kg-day
								50	mg/kg-day
								250	mg/kg-day
		Romano et al. 2012	Rat Wistar	oral gavage	GD18	GD18-PND5	PND60	0	mg/kg-day
								50	mg/kg-day
	Glyphosate formulation (54% GAE) [Magnum Super II]	Gomez et al. 2019	Rat Wistar	oral diet	GD9	GD9-PND21	PND21	0	mg/kg-day
								3.7	mg/kg-day
								352	mg/kg-day
							PND60	0	mg/kg-day
								3.7	mg/kg-day
								352	mg/kg-day
	Glyphosate formulation (54% GAE) [Roundup FULL II]	Altamirano et al. 2018	Rat Wistar	subcutaneous injection	PND1	PND1-7 (every 48h)	PND21	0	mg/kg-day
								2	mg/kg-day
							PND60	0	mg/kg-day
								2	mg/kg-day
	Glyphosate formulation (54% GAE) [Roundup]	Gorga et al. 2021	Rat Sprague-Dawley	oral gavage	PND14	PND14-30	PND90	0	mg/kg-day
								50	mg/kg-day
	Glyphosate formulation (72% GAE) [Roundup WG®]	Silva et al. 2024	Gerbil Mongolian	oral drinking water	PND183	90d	PND273	0	mg/kg-day
								0.17	mg/kg-day
	Glyphosate formulation (NR-%GAE) [Roundup]	Dallegrave et al. 2007	Rat Wistar	oral gavage	GD0.0	GD0-PND21	PND65	0	mg/kg-day
								50	mg/kg-day
								150	mg/kg-day
								450	mg/kg-day
							PND140	0	mg/kg-day
								50	mg/kg-day
								150	mg/kg-day
								450	mg/kg-day
tissue	Glyphosate formulation (37% GAE) [Roundup Original DI]	Teleken et al. 2020	Mouse C57BL/6	oral drinking water	GD4	GD4-PND30	PND150	0	mg/kg-day
								420	mg/kg-day
	Glyphosate formulation (45% GAE) [Glyfonova 450 Plus]	Johansson et al. 2018	Rat Sprague-Dawley	oral gavage	PND28	14d	PND42	0	mg/kg-day
								25	mg/kg-day
	Glyphosate formulation (54% GAE) [Roundup]	Gorga et al. 2021	Rat Sprague-Dawley	oral gavage	PND14	PND14-30	PND31	0	mg/kg-day
								2	mg/kg-day
								50	mg/kg-day

Fig. 14. Testosterone Animal Data – GBH: An interactive version is available at the following link to figure. This plot shows percentage change in testosterone levels in GBH-exposed groups as compared to the control groups. The x-axis denotes % change in testosterone level relative to control with confidence intervals. Control groups are shown as blue triangles; GBH groups plotted as circles for the % change relative to control, with statistically significant data points colored red. The 95% confidence interval (95% CI) is shown as a grey bar. GBH doses are reported as mg formulation mass of GBH per kg body weight per day. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

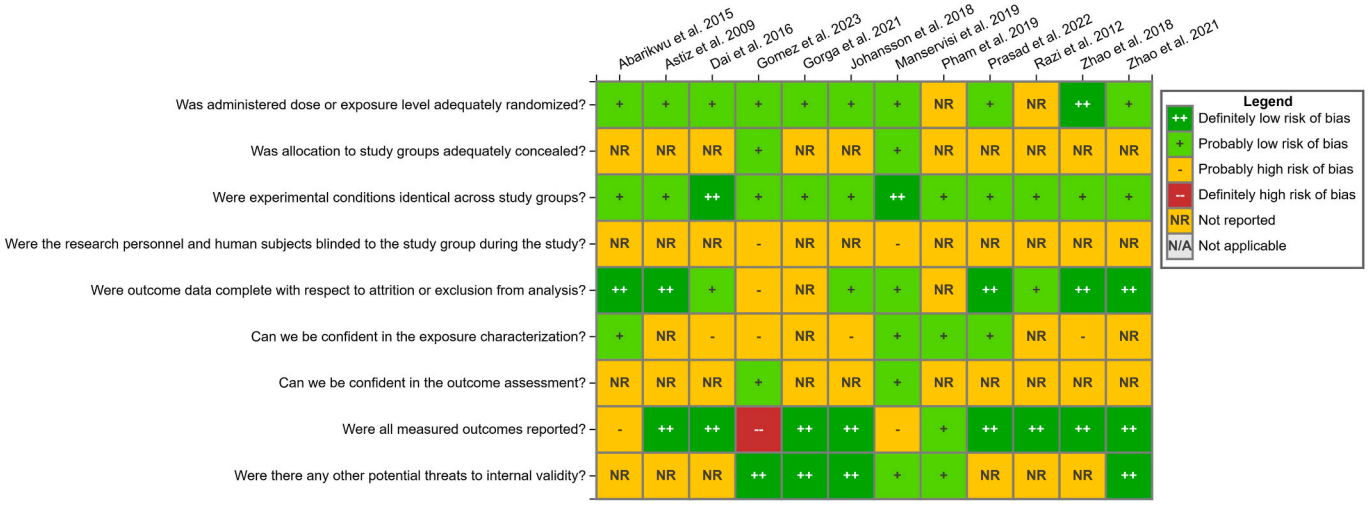


Fig. 15. Risk-of-bias heatmap of studies with hormone data – Glyphosate: An interactive version is available at the following link to figure. This plot summarizes the risk-of-bias (RoB) assessment for studies evaluating the association between glyphosate exposure and hormone-related endpoints (n = 12) across individual bias domains using OHAT risk-of-bias tool. Each column represents an individual study, and each row represents a bias domain. Colors in each cell indicate the level of bias for a given domain within each study.

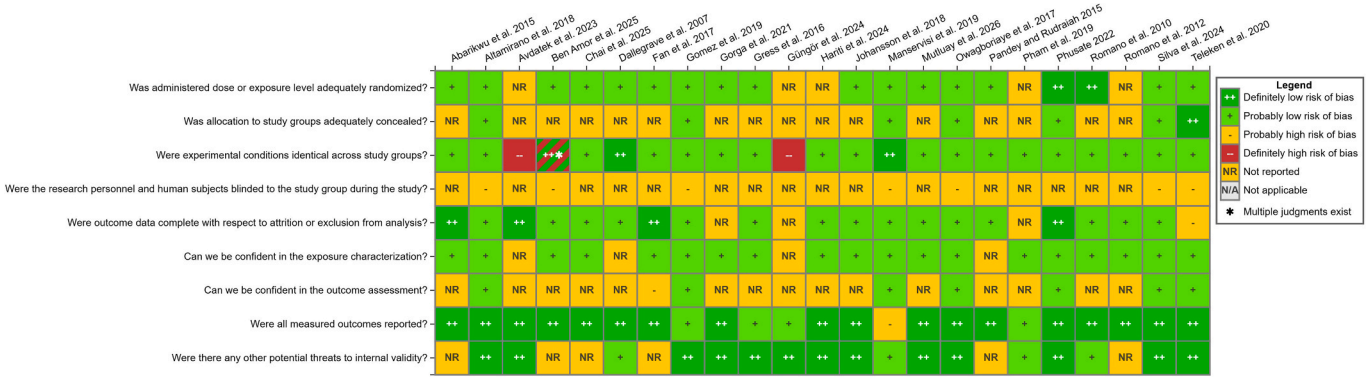


Fig. 16. Risk-of-bias heatmap of studies with hormone data – GBH: An interactive version is available at the following link to figure. This plot summarizes the risk-of-bias (RoB) assessment for studies evaluating the association between GBH exposure and hormone-related endpoints (n = 23) across individual bias domains using OHAT risk-of-bias tool. Each column represents an individual study, and each row represents a bias domain. Colors in each cell indicate the level of bias for a given domain within each study.

guinea pigs, and rabbits) and some studies reported dose-dependent responses for sperm motility, sperm concentration, and sperm morphology.

There is a biological rationale that exposure durations of ≥30 days are more likely to impact sperm parameters, given that spermatogenic cycles in non-human mammalian models are approximately 30 days or longer; for example, a full cycle of spermatogenesis is 27–52 days in rats and 25–35 days in mice (reviewed in Clermont 1972). Studies that utilized a shorter duration of exposures to GBH had more variable results and were less likely to affect sperm parameters (e.g., Centola et al. 2025; Gorga et al. 2021), although there were a few exceptions (Cassault-Meyer et al. 2014; Kang et al. 2008; Romano et al. 2012). For example, Romano et al. (2012) reported an increase in sperm count and production following an approximately 8-day exposure beginning on GD 18; these results were in the opposite direction of effects observed in other studies and may involve imprinting of the developing HPG axis.

Histopathology is generally considered the most sensitive endpoint for the detection of testicular toxicity (Lanning et al. 2002; Vidal et al. 2025) and can add confidence to the results of other sperm measures. In the current review, 37 studies included histopathology; however, the body of evidence was inadequate to reach confidence conclusions due to methodological issues including poor fixation, poor interpretation of artifacts, misidentification of testes and spermatogenesis features, and lack of consideration of seminiferous tubule staging. Few studies evaluated both the epididymis and testis, although features such as exfoliated germ cells in the epididymis duct lumen are a sensitive effect of testicular toxicity (Vidal et al. 2025) that could corroborate testicular findings. In addition, most studies used nonstandard diagnostic descriptions, which limited the ability to compare the data across studies.

4.2. Testosterone

There was consistent evidence that glyphosate exposure decreased testosterone levels, particularly in studies where exposure began during juvenile or adult life stages, whereas findings were more variable following exposures that began during gestation. Similarly, GBH exposure reduced testosterone levels in studies that exposed juvenile or adult animals for 30 days or longer, with effects observed across rats, mice, and gerbils. Meta-analyses supported these findings which showed inverse associations between both glyphosate and GBH exposure and circulating testosterone levels.

Timing and duration of exposure appear to influence glyphosate and GBH effects on circulating testosterone. Reductions in testosterone were most consistently observed when animals were exposed directly as

adults or juveniles, whereas gestational exposure studies produced inconsistent results. Across the studies (three glyphosate and six GBH) that measured circulating testosterone after gestational exposures, one glyphosate (Pham et al. 2019) and two GBH (Dallegrave et al. 2007; Pham et al. 2019) studies reported a decrease in circulating testosterone, and one GBH study reported an increase (Romano et al. 2012). Notably, studies that reported decreased circulating testosterone began exposure before full development of the HPG axis (~GD 18 in rats) (Bidlingmaier et al. 1982), while the study that reported an increase in testosterone began exposure at GD 18, coinciding with HPG axis development (Romano et al. 2012). The HPG axis plays an important role in testicular function, and additional studies are needed to determine if there are critical periods during gestation in which testosterone is more sensitive to glyphosate or GBH action. In addition, reductions in circulating testosterone were more consistently observed following exposures of 30 days or longer. While mechanistic studies were outside the scope of this evaluation, future efforts to understand how glyphosate and GBHs affect key enzymes, receptors, and processes over time would provide insights on how exposure duration affects testosterone levels.

4.3. Consideration of glyphosate and GBH effects across endpoints

Hormone levels and sperm parameters are key indicators of testicular function, with spermatogenesis dependent on adequate testosterone in the testis (Walker 2011). Across the evidence base, glyphosate and GBHs reduce circulating testosterone and adversely impact multiple sperm measures, including motility, abundance, and morphology. Reductions in circulating testosterone levels suggest alterations in signaling of the HPG axis. Testosterone's negative feedback effect on the hypothalamus and pituitary, along with other sex steroids and peptides produced by Sertoli cells, regulates the HPG axis through feedback loops to limit the production of GnRH, LH, and FSH. Testosterone was significantly reduced following glyphosate or GBH exposures across multiple studies; however, the evidence was inadequate to assess effects on other hormones due to the limited number of studies that evaluated other hormones and the inconsistent effects that were reported. A reduction in testosterone should result in the secretion of GnRH, which should stimulate the release of LH and subsequent production of more testosterone by Leydig cells. Of the studies that evaluated LH following glyphosate (three studies) or GBH (seven studies) exposures, there was only one study that reported a decrease (Owagboriaye et al. 2017) and three studies that reported an increase (Mutluay et al. 2026; Romano et al. 2012; Teleken et al. 2020) in LH following GBH exposure. There were no glyphosate exposure studies that reported an effect on LH.

The coordinated endocrine action of the HPG axis regulates germ cell differentiation in addition to proliferation and function of the somatic cells necessary for testis development. While endpoints were evaluated separately in this report, several studies within the glyphosate and GBH evidence bases evaluated both sperm measures and hormones to better understand how these chemicals may affect testicular function. In the glyphosate exposure studies, Abarikwu et al. (2015), Dai et al. (2016), and Pham et al. (2019) evaluated testosterone and sperm counts; Manservisi et al. (2019) evaluated testosterone, sperm count and sperm morphology; and Razi et al. (2012) evaluated testosterone, sperm motility, sperm count, and sperm morphology. The pattern of effects was consistent across endpoints within studies; if a study reported a decrease or decreasing trend in testosterone and also measured sperm parameters, those sperm parameters were also affected (i.e., decreased motility, abundance; increased abnormal sperm). Within the GBH evidence, there were 13 studies that evaluated testosterone and sperm parameters (Abarikwu et al. 2015; Avdatek et al. 2023; Ben Amor et al. 2025; Dallegrave et al. 2007; Fan et al. 2017; Gorga et al. 2021; Güngör et al. 2024; Manservisi et al. 2019; Mutluay et al. 2026; Owagboriaye et al. 2017; Pham et al. 2019; Romano et al. 2012; Teleken et al. 2020). Consistent with the glyphosate evidence base, effects on sperm parameters corresponded with effects on testosterone for most studies. Spermatogenesis is highly regulated by endocrine action, and the effects in this report reflect an association between testosterone levels and sperm parameters. There were three studies that reported a different pattern of effects following GBH exposure. Güngör et al. (2024) did not report effects on circulating testosterone but reported a decrease in sperm motility and an increase in abnormal sperm after exposure to 788 mg/kg-day GBH for 56 days. Teleken et al. (2020) reported an increase in intratesticular testosterone, no effect on circulating testosterone, and a decrease in sperm concentration following exposure to 420 mg/kg-day GBH for 47 days. Finally, Romano et al. (2012) reported an increase in testosterone, sperm count, and sperm production following a short, 8-day exposure at 50 mg/kg-day that began at GD 18, suggesting developmental exposure that impacted HPG axis set points or imprinting. Mechanistic studies are needed to determine whether glyphosate or GBH affects testicular function through direct or indirect actions on hormone production, Leydig cell and Sertoli cell development or function, or other mechanisms.

Glyphosate and GBH doses varied widely across studies, ranging from 0.5 to 10,780 mg/kg-day for glyphosate and 0.17 to 2000 mg/kg-day for GBHs. While meta-regression analyses for testosterone and sperm parameters suggest some evidence of a dose response, many studies only evaluated single doses. More studies evaluating multiple doses would be required to confirm dose response relationships for glyphosate and GBH effects. Although a dose–response analysis and identification of low-dose effect level are beyond the scope of this evaluation, the body of evidence includes several studies that reported effects in the range of 0.5–2 mg/kg-day and others that did not find effects at those levels.

Differences in exposure level/dose alone do not explain inconsistency observed for some of the findings across studies. For example, among four studies evaluating sperm morphology following glyphosate exposure at approximately 1.75–2 mg/kg-day, Liu et al. (2022a; 2022b) and Ren et al. (2025) reported increased abnormal sperm morphology, whereas Manservisi et al. (2019) reported no effect. The results may be explained by differences between the internal dose; however, few studies reported internal dose metrics to allow comparison. In one of the only studies with serum and testes level measurements, Liu et al. (2022b) reported glyphosate residues of 0.035 and 0.023 μg/ml serum and 0.002 and 0.016 μg/g testes following dietary exposure at 10 and 250 mg/kg feed (2 and 50 mg/kg body weight per day). Differences are unlikely to be explained fully by glyphosate purity, as most studies used comparable purity levels (e.g., > 95% in Liu et al. (2022a); 96% in Ren et al. (2025); 98% in Liu et al. (2022b); 99.5% in Manservisi et al. (2019)). Although results for sperm morphology and other endpoints were observed across multiple species and strains, species differences may have contributed to some of the inconsistency, along with differences in exposure window, duration, and route of administration. Manservisi et al. (2019) administered glyphosate in drinking water beginning during gestation, whereas Liu et al. (2022a; 2022b) and Ren et al. (2025) evaluated dietary exposures beginning in the juvenile or *peri*-pubertal periods. Across all sperm parameters, differences in sperm assessment methods, endpoint definitions, and statistical power may also contribute to the variability across studies; however, the extent to which these factors explain the inconsistent findings remains unclear.

Another source of uncertainty is that glyphosate absorption from the gut in rodents is considered poor, with one study estimating absorption of about 23% following a single 400 mg/kg dose in rats (Anadón et al. 2009). However, limited information is available on how absorption varies with dose, particularly at higher doses (up to 10,780 mg/kg-day) used by Chan and Mahler (1992). Additional studies targeting potential mechanisms for disrupting the HPG axis or spermatogenesis may provide insight into the variability in findings across studies, and internal dose metrics would help clarify relationships between administered dose and reproductive effects.

4.4. Consideration of glyphosate in relation to GBH exposure

The consistency of effects observed for multiple sperm parameters and testosterone after exposure to glyphosate or to GBHs is notable and supports the hypothesis that the effects of GBHs on these endpoints are driven, at least in part, by glyphosate. However, lack of information on GBH composition prevented investigation of how much toxicity was affected by chemicals other than glyphosate in GBHs, either directly or through influencing other chemicals (e.g., surfactants may increase glyphosate uptake). GBHs are heterogeneous mixtures that can differ in glyphosate salts and concentrations, surfactants, and other co-formulations. Chemical ingredients and exact composition of GBHs are considered confidential business information (CBI) and can vary widely by intended product use and even geographical region. GBH formulations have also changed over time, sometimes resulting in products with different chemical compositions being sold under the same brand name. Therefore, formulations evaluated in older studies may not be representative of products currently on the market.

When the 37 GBH studies (31 GBH only studies and 6 with data on both GBH and glyphosate) were considered collectively, there was consistent evidence of adverse effects of GBHs on testosterone and sperm health supported by statistically significant meta-analyses for decreases in sperm count, concentration, and motility despite likely differences in surfactants, glyphosate salts, and other ingredients of the GBH mixtures across the body of evidence. However, this heterogeneity in GBH composition limits the interpretation of pooled estimates and their generalizability to specific formulations. The confidence in the conclusions of adverse impact of GBHs is further supported by the consistency of effects of GBHs in a database with significant heterogeneity in timing and duration of exposure, species, strain, and experimental design. For future investigation, evaluating reproductive toxicity from glyphosate alone alongside simulated or commercial GBHs with known composition can better illustrate the effects of each chemical, and might inform less harmful substitution in future herbicides.

4.5. Limitations of the systematic review

To be completed in a shortened timeframe than a standard systematic review, rapid systematic reviews typically narrow the scope and/or use streamlined methods through modifying select elements of a standard systematic review (e.g., single-database search). This rapid systematic review only restricted the scope. All systematic review methods were retained, including an expert-reviewed protocol, comprehensive literature searches in multiple databases, two independent reviewers for study selection and risk-of-bias evaluation, and multiple quality assurance/quality control procedures.

The internal report with draft conclusions developed for HHS is not publicly available; however, this document, **Supplement File**, and web-based project data in HAWC represent a complete presentation of all data and analysis. Because this project was initially developed as an internal deliberative report, the protocol could not be posted publicly; therefore, it was finalized, signed, and locked before the risk-of-bias assessment began, but not added to a public website at that stage. Earlier public posting of the protocol would have improved transparency and facilitate additional scientific input before completion of the assessment.

4.5.1. Limitations of the scope and evidence considered

The evaluation was restricted to male reproductive effects in non-human mammals, precluding consideration of biologically or mechanistically related data across sexes, and fertility was not evaluated. Other research models, including zebrafish and avian species, may provide additional information on reproductive effects, hormones, or endocrine disruption. Although mechanistic data were not evaluated in this review, evidence from the literature suggest that glyphosate and GBH may disrupt pathways related to germ or somatic cell development or function (Serra et al. 2021), hormone or receptor production or function (Branco et al. 2025), oxidative stress (Payne and Pool 2026), and/or inflammation (Maddalon et al. 2021).

To build on the findings of this systematic review, a subsequent review will expand the evidence base to include human epidemiological studies, mechanistic data, and all vertebrate animal studies (including fish and birds). Integration of these data with the rodent and rabbit data from the current evaluation will provide a more comprehensive assessment of potential human health impacts, biological plausibility, sensitive or susceptible subpopulations, and potential opportunities to mitigate adverse effects beyond exposure reduction, such as through interrupting intermediate events in pathways leading to toxicity.

4.5.2. Limitations of the evidence base

There were several limitations of the evidence base. Unpublished pesticide registration data were not available to DTT, although confidential guideline studies of glyphosate or GBHs with male reproductive health endpoints exist. Data provided in pesticide registrations are incomplete summaries and do not allow the critical assessment of methods, study conduct, and results (e.g., risk of bias) necessary to include these studies in a systematic review. No mammalian studies of glyphosate metabolites were identified, although AMPA has been reported to affect sperm and testosterone in zebrafish (Yu et al. 2025).

Although conclusions in this evaluation were based on the entire body of evidence for each endpoint and were driven by the high-quality studies, for some endpoints study quality and or reporting quality presented limitations. Common limitations included inadequate reporting of randomization, blinding, and incomplete exposure characterization. Endpoint-specific limitations included inadequate histopathological methods that limited the utility of the histopathology from most studies. Timing of sperm assessment also presented a limitation for studies that evaluated sperm in peripubertal animals or after short exposure durations, because the greater variability of these conditions reduced the sensitivity to detect effects. For testosterone, sensitive exposure windows, time course, and dose–response relationships need to be further investigated. The number of studies available for other reproductive hormones and reproductive and developmental milestones also presented limitations.

4.5.3. Hazard identification goals and exposure context

This systematic review critically assessed published research from mammalian animal models on glyphosate or GBH exposures and male reproductive health to reach confidence conclusions for hazard identification and therefore a formal dose–response assessment was not conducted. Hazard assessment to characterize both the health effects evidence and the exposure level that is likely to cause health effects is beyond the scope of this evaluation. However, this evaluation may be useful to put effect levels reported in the available studies in context of human exposure levels. Across the body of evidence, studies reported effects on testosterone and/or sperm parameters at glyphosate doses from 0.5-3,393 mg/kg-day and GBH doses of 0.17–2,000 mg/kg-day. The lower effect levels in several studies overlap with the acceptable daily intake of 0.5 mg/kg body weight per day set by EFSA (EFSA 2023) and reference dose of 1.75 mg/kg body weight per day set by US EPA (USEPA 2017). Exposure levels in the United States are typically in the μg/L range, with surface water ranging from 0.02-427 μg/L (ATSDR 2020) and geometric mean of 0.411 μg/L and 95th percentile urinary glyphosate concentration of 1.58 μg/L in the 2013–2014 U.S. National Health and Nutrition Examination Survey (NHANES) (Ospina et al. 2022).

5. Conclusions

Overall, these findings provide evidence of adverse effects of glyphosate and GBHs on male reproductive health across multiple species and study designs. There was *high confidence* from non-human

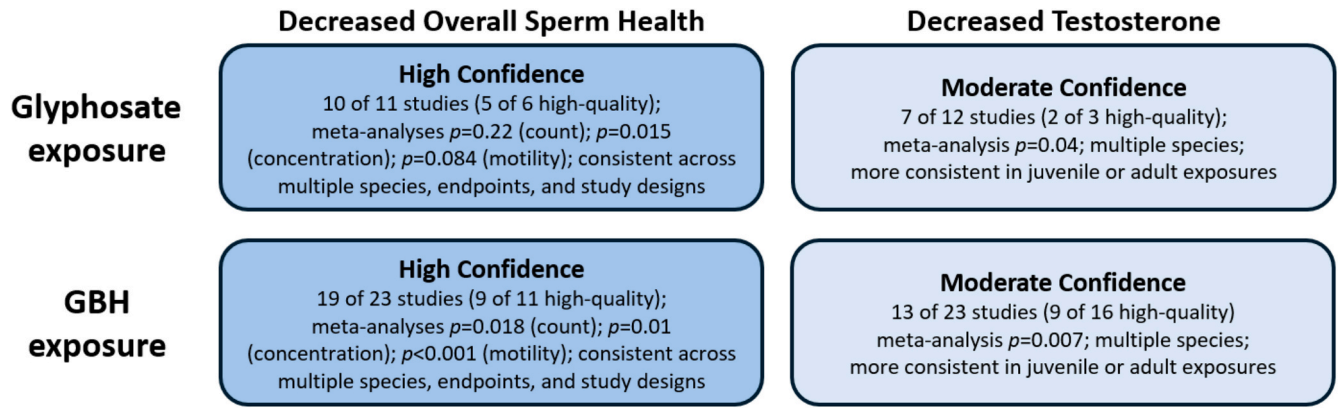


Fig. 17. Confidence conclusions based on the totality of the evidence on male reproductive endpoints for glyphosate and GBH. Conclusions were developed for overall sperm health based on multiple individual measures and for testosterone because the bodies of evidence for these endpoints were considered sufficiently robust in the number of studies, quality of studies, and consistency of the results reported to support informative conclusions. The confidence ratings are on a 4-point scale: high, moderate, low, or very low/no evidence available.

mammal data that glyphosate and GBHs adversely affect overall sperm health and decrease sperm abundance, and that GBHs reduce sperm motility and increase abnormal morphology (Fig. 17). There was *moderate confidence* that glyphosate reduces sperm motility and increases abnormal morphology, and that both glyphosate and GBHs reduce testosterone. These data provide a biologically plausible hypothesis that glyphosate and GBH might affect male reproductive health of humans; the next phase of this project will better inform human health impacts by considering the totality of the evidence across animal studies, epidemiological studies, and mechanistic data.

CRediT authorship contribution statement

Brandiese E.J. Beverly: Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Kembra L. Howdeshell:** Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Kyla W. Taylor:** Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Vickie R. Walker:** Writing – original draft, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Amy Wang:** Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Anisha Singh:** Writing – original draft, Visualization, Validation, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Caitlin G. Niven:** Writing – original draft, Visualization, Validation, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Amlan Talukder:** Writing – review & editing, Visualization, Validation, Software, Methodology, Data curation, Conceptualization. **Robyn B. Blain:** Writing – review & editing, Visualization, Validation, Methodology, Investigation, Data curation. **Pamela A. Hartman:** Writing – review & editing, Visualization, Validation, Methodology, Investigation, Data curation. **Katherine R. Helmick:** Writing – review & editing, Visualization, Validation, Project administration, Methodology, Investigation, Data curation. **Kristen Magnuson:** Writing – review & editing, Visualization, Validation, Project administration, Methodology, Investigation, Data curation. **Nicole Vetter:** Methodology, Investigation, Data curation. **Meredith Clemons:** Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation. **Sorina E. Eftim:** Writing – review & editing, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation. **Angelina Winnett:** Visualization. **Christopher A. Sibrizzi:** Supervision. **Jeanne Luh:** Supervision, Project administration. **Andrew A. Rooney:** Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

We thank Stephanie Smith-Roe for technical review of the protocol, along with Abee Boyles and Chad Blystone for review of both the protocol and a draft report on which this manuscript was based. We also thank Marcos Morgan, Michael Wyde, and Humphrey Yao for review of the draft report. We thank the team at ICF international that contributed to the literature search, literature screen, data extraction, risk of bias assessment, development of visuals, meta-analysis, and project management (see **Supplement Section 14** for details). We greatly appreciate Kelly Shipkowski for her coordination of the ICF contract. Finally, we thank John Bucher for feedback on a draft of this manuscript. Funding for Anisha Singh and Caitlin Niven was supported through NIEHS fellowships. ICF support was provided by the Intramural Research Program (ES103379-01) at NIEHS, National Institutes of Health, and was performed for NIEHS under contract GS00Q14OADU417 (Order No. HHSN273201600015U). This research was supported by the Intramural Research Program of the NIH, National Institute of Environmental Health Sciences. The contributions of the NIH authors are considered Works of the United States Government. The findings and conclusions presented in this paper are those of the authors and do not necessarily reflect the views of the NIH or the U.S. Department of Health and Human Services.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2026.110604.

Data availability

All assessment data and interactive visuals are available in the

HAWC project: https://hawcproject.org/assessment/1592/

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