International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

# Post-treatment azoospermia and utilisation of cryopreserved semen in male cancer survivors: a systematic review and meta-analysis of observational cohorts

INPLASY2026110108
doi: 10.37766/inplasy2026.11.0108
Received: 26 November 2026
Published: 26 November 2026

Wang, Q; Yin, M; Li, M; Zheng, B; Zhao, Z; Zhou, J; Li, L.

**Corresponding author:**
Linxi Li

lilinxi1234@163.com

**Author Affiliation:**
Zhejiang Engineering Research Center for Innovation and Application of Intelligent Radiotherapy Technology, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou 325000, China.

## ADMINISTRATIVE INFORMATION

**Support -** Zhejiang Provincial Natural Science Foundation of China (grant no. LTGY24H040007).

**Review stage at the time of initial registration -** Completed but not published.

**Conflicts of interest -** None declared.

**INPLASY registration number:** INPLASY2026110108

**Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 November 2026 and was last updated on 26 November 2026.

## INTRODUCTION

**Review question / Objective** In male cancer patients and survivors, to estimate after gonadotoxic treatment: (1) the proportion with post-treatment azoospermia; (2) the utilisation rate of cryopreserved semen; (3) the live-birth rate after assisted reproduction, analysed separately per ART cycle and per couple or patient using banked semen; and (4) paternity, oligospermia and post-treatment sperm concentration. We further examine whether cancer type, treatment modality, availability of radiotherapy-specific data, data source and era explain heterogeneity.

**Rationale** Sperm cryopreservation before gonadotoxic cancer treatment is routine, yet three clinically important quantities remain uncertain: how many men become permanently azoospermic, how many banked samples are ever used, and what the chance of a live birth is when they are. Published syntheses address only part of this: the most comparable review reported utilisation and per-cycle delivery but did not report post-treatment azoospermia and excluded paediatric and adolescent patients. In addition, live birth after assisted reproduction is usually treated as a single estimand although per-cycle and per-couple denominators are not interchangeable and answer different clinical questions. We therefore estimate all three quantities in one analysis and report live birth separately by denominator.

**Condition being studied** Impaired gonadal function and compromised fertility in male cancer patients and survivors after gonadotoxic treatment.

## METHODS

**Search strategy** PubMed, Scopus and Web of Science, from inception to 21 November 2025, plus a supplementary search targeting chemotherapy and haematopoietic stem-cell transplantation cohorts.
Core PubMed string:

Wang et al. INPLASY protocol 2026110108. doi:10.37766/inplasy2026.11.0108 Downloaded from https://inplasy.com/inplasy-2026-11-0108/

(testis OR testicular OR "germ cell" OR lymphoma OR leukemia OR cancer OR malignancy OR neoplasm)
AND ("sperm cryopreservation" OR "semen cryopreservation" OR "fertility preservation" OR "semen analysis" OR azoospermia OR oligospermia OR paternity)
AND (male OR men)

Reference lists of included studies were hand-searched and forward citation tracking was performed in Web of Science.

**Participant or population** Male patients with any malignancy who had received or were receiving gonadotoxic treatment (alkylating chemotherapy, pelvic or testicular radiotherapy, haematopoietic stem-cell transplantation, or orchiectomy), of any age including children and adolescents. Exclusion criteria: studies reporting hormone concentrations only; service or administrative data only; prostate-cancer testosterone kinetics; female-only or ovarian outcomes only; animal or in-vitro studies; reviews, editorials and conference abstracts.

**Intervention** Alkylating chemotherapy, pelvic or testicular radiotherapy, haematopoietic stem-cell transplantation conditioning, and orchiectomy.

**Comparator** Not applicable: this is a single-arm proportion meta-analysis without a comparator group. Between-study subgroup comparisons are made at study level by cancer type, treatment modality, availability of radiotherapy-specific data, data source and era.

**Study designs to be included** Prospective and retrospective cohort studies, cross-sectional studies, and case series of at least three patients. Case reports, narrative and systematic reviews, animal and in-vitro studies, and conference abstracts are excluded.

**Eligibility criteria** In addition to the PICOS criteria above, a study had to report at least one patient-level reproductive outcome with a numerator and denominator: post-treatment azoospermia, utilisation of cryopreserved semen, live birth after assisted reproduction (per cycle or per couple/patient), paternity, oligospermia, or post-treatment sperm concentration with a measure of dispersion. Studies reporting only percentages without a denominator were excluded. Where several post-treatment timepoints were reported, the 12-month value was preferred, then the longest available follow-up.

**Information sources** PubMed, Scopus and Web of Science; reference lists of included studies; forward citation tracking in Web of Science; and a dedicated supplementary search for chemotherapy and haematopoietic stem-cell transplantation cohorts. Last search: 21 November 2025.

**Main outcome(s)** Four primary outcomes, each analysed as a single-arm proportion: (1) post-treatment azoospermia, defined as no spermatozoa in post-treatment semen, with men who underwent post-treatment semen analysis as the denominator; (2) utilisation of cryopreserved semen, defined as a banked sample actually thawed for assisted reproduction, with men who banked as the denominator; (3) live birth per ART cycle; and (4) live birth per couple or patient using banked semen.

Outcomes (3) and (4) are pre-specified as separate estimands and will not be pooled, because the denominators are not interchangeable: a per-cycle rate answers what happens if a couple tries once, whereas a per-couple rate answers the chance of eventually having a child.

**Additional outcome(s)** (5) Paternity, defined as at least one biological child (natural or after assisted reproduction), with survivors followed up as the denominator; (6) post-treatment oligospermia, using each study's own concentration threshold; (7) post-treatment sperm concentration, as mean and standard deviation.

**Data management** Screening and data extraction were performed by a single reviewer at each stage, with a second reviewer resolving uncertain records and adjudicating discordant values. A 35-field extraction form was used. Every outcome data point is recorded as events/total@timepoint together with a verbatim quotation from the source and four provenance fields (data source, inclusion tier, selection flag, and reason for exclusion where applicable), so that the entire analysis set is auditable at the level of the individual data point. All extracted values were subsequently re-checked against the source documents during construction of the analysis set, and discordant values were adjudicated.

To verify the completeness of screening, an independent screener blind to the original decisions re-screened all records that had been passed to full-text assessment and a random 15% sample of excluded records, using titles and abstracts only. No record among the sampled exclusions met the eligibility criteria, corresponding to at most about 25 of the 1,184 excluded records.

Wang et al. INPLASY protocol 2026110108. doi:10.37766/inplasy2026.11.0108 Downloaded from https://inplasy.com/inplasy-2026-11-0108/

Data are held as CSV files; all analysis scripts are retained.

**Quality assessment / Risk of bias analysis** Risk of bias was assessed with the JBI analytical checklists appropriate to each design: prevalence (9 items), cohort (11 items) and case series (10 items). Each item was rated yes, no or unclear, and an overall judgement of low, moderate or high was assigned. Assessments were performed by a single assessor per study following a pre-specified guideline, with a second reviewer adjudicating any study for which the design-appropriate checklist was ambiguous.

Of the 76 studies in the analysis set, 75 were assessed; 15 (20%) were at high, 49 (65%) at moderate and 11 (15%) at low risk of bias. Excluding the high-risk studies did not materially change the principal estimates.

**Strategy of data synthesis** Single-arm proportions were pooled using meta::metaprop in R 4.6.2 (meta 9.0.0), with logit transformation, inverse-variance weighting, DerSimonian-Laird tau-squared, Hartung-Knapp random-effects confidence intervals, and a 0.5 continuity correction for zero cells. Pooled proportions are reported with 95% confidence intervals, I-squared, tau-squared and 95% prediction intervals. Continuous outcomes (sperm concentration) were pooled on the mean-difference scale with the same tau-squared estimator. Certainty of evidence was assessed with GRADE, starting at low for observational evidence.

**Subgroup analysis** Pre-specified subgroups, each tested with a between-group test: cancer type (testicular, lymphoma/haematological, mixed or paediatric, other solid); treatment modality (chemotherapy with radiotherapy, chemotherapy alone, radiotherapy alone, mixed whole-cohort); availability of radiotherapy-specific data; data source (primary PubMed/Scopus set, Web of Science, supplementary chemotherapy/HSCT search); and era of publication by decade.

**Sensitivity analysis** Leave-one-out analysis; exclusion of studies at high risk of bias; main analysis set versus the set additionally including studies rated sensitivity-only; Egger's test for small-study effects where k >= 10; meta-regression on log sample size and on year of publication; and trim-and-fill.

**Language restriction** No language restriction.

**Country(ies) involved** China.

**Other relevant information** RETROSPECTIVE REGISTRATION. This protocol was registered after data extraction and analysis had been completed. To enhance transparency we state the status of each review step at registration and list all post-registration amendments. Status at registration: preliminary searches, piloting of selection, formal screening, data extraction (248 of 264 eligible studies, 93.9%), risk-of-bias assessment (75 of 76 analysis-set studies) and data analysis were complete; manuscript preparation was in progress.

SCREENING VERIFICATION. Because screening was performed by a single reviewer, its completeness was verified by an independent screener blind to the original decisions, who re-screened all 304 records passed to full-text assessment and a random 15% sample (n = 178) of the 1,184 excluded records. No record among the sampled exclusions met the eligibility criteria (0%; 95% CI 0-2.1%). This verification is reported in the manuscript.

EXISTING REVIEWS ON THE SAME TOPIC. Li et al. (Hum Reprod Open 2024; PMID 38389980) pooled 69 studies and reported a cryopreserved-sperm use rate of 9% (95% CI 8-10) and a delivery rate of 20% (15-25) per ART cycle, but did not report post-treatment azoospermia and excluded paediatric and adolescent patients. Pape et al. (Andrology 2024; doi:10.1111/andr.13741), restricted to testicular cancer, reported azoospermia of 8% (6-12). Ferrari et al. (Reprod Biomed Online 2016; PMID 27156003) and Kerr et al. (J Adolesc Young Adult Oncol 2020; PMID 32255696) provide earlier narrative or paternity-focused syntheses.

No existing review reports post-treatment azoospermia, cryopreserved-semen utilisation and denominator-stratified ART live birth within a single analysis, nor examines cancer type as a moderator across tumour types. The present review therefore extends and validates rather than duplicates the existing evidence; the utilisation and per-cycle live-birth estimates are expected to agree with prior work.

**Keywords** cancer survivorship; azoospermia; semen cryopreservation; fertility preservation; male infertility; meta-analysis.

**Dissemination plans** Publication in a peer-reviewed journal (target: Journal of Assisted Reproduction and Genetics); conference presentation; and a practice-oriented summary for sperm banks and oncofertility services.

Wang et al. INPLASY protocol 2026110108. doi:10.37766/inplasy2026.11.0108 Downloaded from https://inplasy.com/inplasy-2026-11-0108/

## Contributions of each author

Author 1 - Qianyu Wang - Conceived the study; performed screening, data extraction and statistical analysis; drafted the manuscript
Email: wqy1231029@163.com
Author 2 - Mengyao Yin - Performed screening, data extraction and risk-of-bias assessment
Email: ymy18253409270@163.com
Author 3 - Mingzheng Li - Performed screening, data extraction and risk-of-bias assessment
Email: 18660968396@163.com
Author 4 - Bin Zheng - Performed data extraction and risk-of-bias assessment
Email: czzl8100@163.com
Author 5 - Zihan Zhao - Performed data extraction and risk-of-bias assessment
Email: 18656179591@163.com
Author 6 - Jiahui Zhou - Performed data extraction; prepared figures
Email: zhoujiahui2129@126.com
Author 7 - Linxi Li - Supervised the study; revised the manuscript critically for intellectual content; guarantor
Email: lilinxi1234@163.com

Wang et al. INPLASY protocol 2026110108. doi:10.37766/inplasy2026.11.0108 Downloaded from https://inplasy.com/inplasy-2026-11-0108/