

ORIGINAL RESEARCH

Bibliometric insights into endocrine-disrupting chemicals and male infertility research: global trends from 2000 to 2025

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Abstract

Background: Male infertility has emerged as a major public health challenge, with exposure to endocrine-disrupting chemicals recognized as an important contributor to reproductive dysfunction. **Methods:** We conducted a bibliometric analysis of the scientific literature on male infertility and endocrine-disrupting chemicals published from 2000 to 2025 to characterize the evolution, knowledge structure, and research frontiers of the field. Data were retrieved from the Web of Science Core Collection and analyzed using bibliometric tools, including R software (version 4.3.2), VOSviewer (version 1.6.19), CiteSpace (version 6.2.R6), and GraphPad Prism (version 8.0.2). **Results:** A total of 7083 records were included. Annual publication output increased steadily, reflecting growing attention to this field. The United States and China were the leading contributors. Keyword and reference analyses showed that research on male infertility and endocrine disruptors focused primarily on in utero exposure, heavy metals, and Sertoli cell biology. Emerging research themes included oxidative stress, perfluoroalkyl substances, and molecular pathways involved in reproductive toxicity. **Conclusions:** This study maps the intellectual landscape of research on male infertility and endocrine-disrupting chemicals and identifies major research trajectories, principal contributors, and emerging frontiers. These findings provide a strategic framework for guiding future research in the field.

Keywords

Male infertility; Endocrine-disrupting chemicals; Reproductive toxicity; Semen quality; Bibliometric analysis

1. Introduction

Male infertility is defined as the inability to achieve conception after 12 months of regular, unprotected intercourse [1]. According to the World Health Organization, male factors contribute to approximately 30–50% of infertility cases [2]. Over recent decades, male infertility has attracted increasing global attention. Environmental factors, particularly exposure to endocrine-disrupting chemicals (EDCs), have been recognized as important contributors. Reports from reproductive medicine institutions indicate that chronic diseases, genetic disorders, and other medical conditions explain only a proportion of cases, whereas environmental and occupational factors, especially complex EDC mixtures, may play an important role in reproductive impairment [3]. These compounds are widely distributed in the environment and consumer products; representative examples include bisphenol A (BPA), phthalates, per- and polyfluoroalkyl substances (PFAS), pesticides, and certain heavy metals, such as cadmium. Because of their extensive use in plastics, food packaging, personal care products, industrial materials, and agricultural chemicals, exposure to EDCs is

widespread and occurs primarily through ingestion, inhalation, and dermal contact [4]. These compounds can mimic or interfere with hormone receptor function, disrupt endocrine homeostasis, and impair spermatogenesis and testicular function [5].

Recent studies have advanced understanding of the mechanisms linking EDC exposure to male infertility. Proposed mechanisms include oxidative stress (OS), endocrine disruption, and dysregulated gene expression, all of which may impair sperm development and function [6, 7]. Moreover, EDCs may induce epigenetic modifications with potential transgenerational consequences beyond direct physiological injury. Thus, infertility may reflect not only an individual health problem, but also the legacy of ancestral EDC exposure [8, 9].

Bibliometric analysis enables quantitative evaluation of research trends and knowledge structures [10]. Although publications on male infertility and EDCs have increased rapidly over the past two decades, bibliometric studies focused specifically on this intersection remain scarce. In particular, systematic evaluations of interdisciplinary collaboration networks,

knowledge transfer, and methodological development are lacking. The Web of Science Core Collection (WoSCC) was selected as the primary data source because it provides standardized bibliographic records, detailed citation information, and broad coverage of peer-reviewed journals in environmental health, toxicology, reproductive medicine, and related fields. These characteristics support citation analysis, collaboration mapping, and evaluation of research trends. Although PubMed and Scopus also index relevant literature, the standardized records and citation data available in WoSCC make it suitable for the present analysis. To address this gap, we performed bibliometric and visualization analyses of relevant studies indexed in WoSCC over the past two decades. We aimed to characterize research trajectories, map global collaborations, and identify research hotspots, thereby providing a comprehensive overview of the field.

2. Materials and methods

Data were retrieved from the WoSCC. To minimize bias from ongoing database updates, all searches and exports were performed on 14 June 2025. The search strategy was developed with reference to a prior systematic review [11]. Detailed search terms and retrieval procedures are presented in Table 1. The strategy included both specific EDC-related chemicals and broader EDC-related terminology. Although several environmentally relevant toxicants, such as polychlorinated biphenyls (PCBs), dioxins (TCDD), and mercury, were not specified individually as search terms, broader EDC-related terms were used to improve retrieval sensitivity. Document types were restricted to “Article” and “Review Article”; conference papers, book chapters, editorials, non-peer-reviewed works, and non-English publications were excluded.

To ensure accuracy and reproducibility, two researchers (MG and GD) independently screened all titles and abstracts for relevance. Studies were excluded if they did not specifically investigate any of the listed EDC-related chemicals or evaluate a male reproductive outcome (*e.g.*, sperm quality, testicular function, or a fertility/infertility diagnosis). Disagreements were resolved through discussion with a third investigator (DM). Interrater agreement was assessed using Cohen’s

kappa coefficient ($\kappa = 0.945$), indicating excellent agreement. After sequential screening and consistency assessment, 7083 eligible records were included (Fig. 1). All records were exported in plain-text format with “Full Record and Cited References” for subsequent analysis. Duplicate records were identified and removed using the bibliographic information provided by Web of Science before the bibliometric analyses. Author names, institutional affiliations, and country information were standardized when necessary to minimize inconsistencies arising from differences in spelling, abbreviations, or institutional naming conventions. Records with incomplete bibliographic information were manually reviewed, and missing data were retained or excluded according to their availability and relevance to each analysis.

Data processing, statistical analysis, and visualization were performed using R software (version 4.3.2), VOSviewer (version 1.6.19, Centre for Science and Technology Studies, Leiden, Netherlands), CiteSpace (version 6.2.R6, Drexel University, Philadelphia, PA, USA), and GraphPad Prism (version 8.0.2, GraphPad Software, San Diego, CA, USA). R, with the bibliometrix package, was used for descriptive bibliometric analyses and statistical processing; VOSviewer and CiteSpace were used for network visualization, co-occurrence analysis, co-citation analysis, and the identification of emerging research trends; while GraphPad Prism was employed for generating supplementary statistical graphs and visualizations, such as bar charts and scatter plots, to enhance data presentation. Citation analyses were based on total citation counts recorded in the WoSCC at the time of data extraction (14 June 2025). No adjustments were made for publication age, citation window, or self-citations; citation-based indicators were, therefore, interpreted in light of potential biases related to publication year, exposure time, and citation practices.

3. Results

3.1 Global publication trends

A total of 115 countries/regions worldwide contributed to research on male infertility and EDCs (Fig. 2A). Among the 10 most productive countries, China and the United States (U.S.)

TABLE 1. Electronic literature search strategies.

No.	Search item
#1	“PBDE” OR “brominated” OR “organophosphate” OR “pesticides” OR “chlorpyrifos” OR “POP” OR “phthalate” OR “DEHP” OR “BBP” OR “DBP” OR “DiBP” OR “phenol” OR “bisphenol” OR “BPA” OR “BPS” OR “BPF” OR “triclosan” OR “triclocarban” OR “benzophenone” OR “PFAS” OR “PFOA” OR “perfluor*” OR “pyrethroid” OR “paraben*” OR “cadmium” OR “OPFR” OR “alkylphenols” OR “phytoestrogen” OR “nonylphenol” OR “endocrine disruptor*” OR “EDC” OR “EDCs”
#2	“male reproduct*” OR “sperm” OR “semen” OR “testis” OR “testes” OR “testicular function” OR “male infertility” OR “male fertility” OR “asthenozoospermia” OR “male subfertility” OR “male sterility” OR “oligospermia” OR “oligoasthenozoospermia” OR “asthenospermia” OR “azoospermia”
#3	#1 AND #2

PBDE, polybrominated diphenyl ether; *POP*, persistent organic pollutant; *DEHP*, di(2-ethylhexyl) phthalate; *BBP*, benzyl butyl phthalate; *DBP*, dibutyl phthalate; *DiBP*, diisobutyl phthalate; *BPA*, bisphenol A; *BPS*, bisphenol S; *BPF*, bisphenol F; *PFAS*, per- and polyfluoroalkyl substances; *PFOA*, perfluorooctanoic acid; *OPFR*, organophosphate flame retardants; *EDC*, endocrine-disrupting chemical.

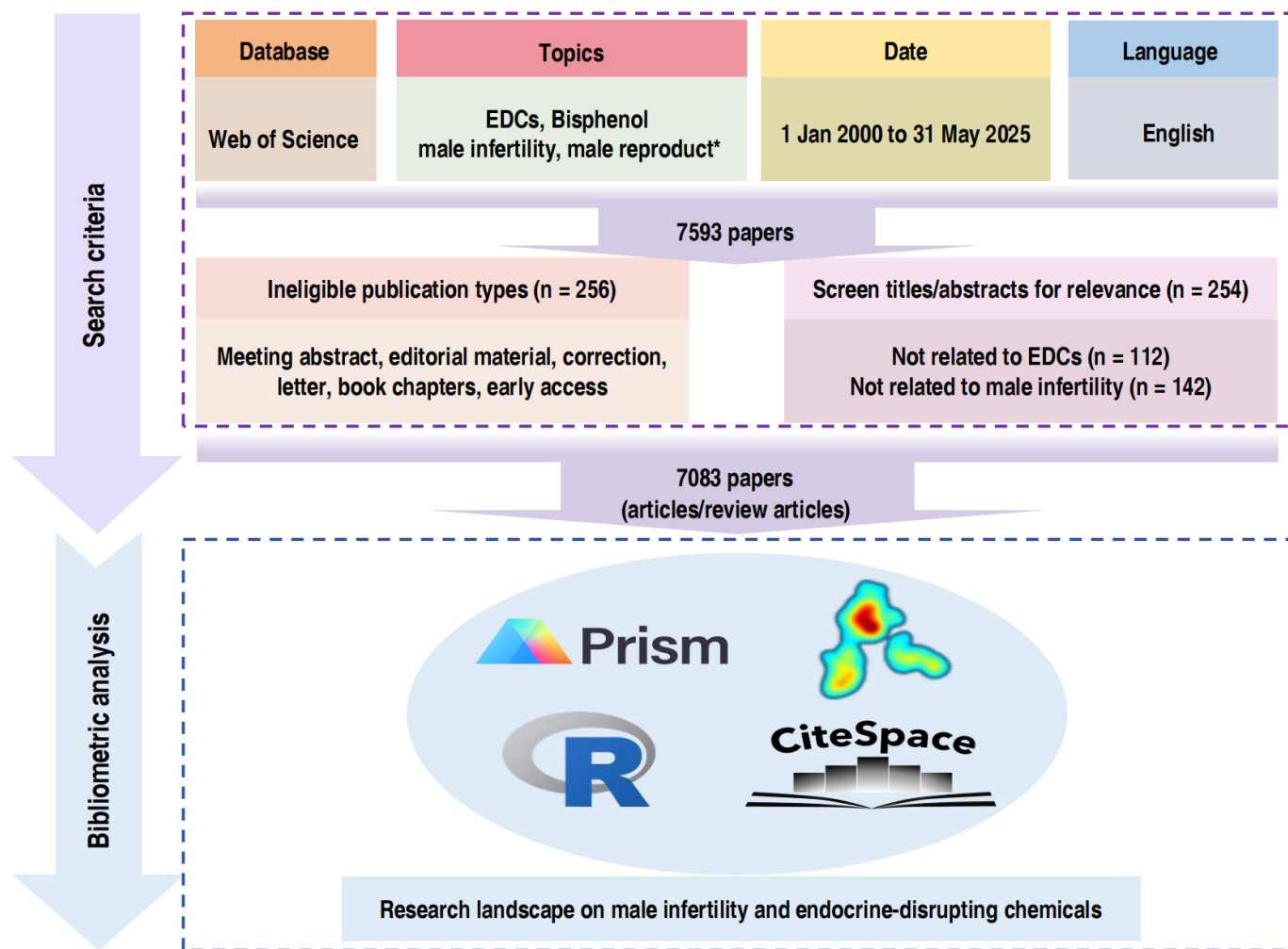


FIGURE 1. Literature search strategy and screening flowchart. EDCs, endocrine-disrupting chemicals. *: the asterisk denotes database truncation to capture terms such as reproduction, reproductive.

led in multiple-country publications, reflecting a highly internationalized research model (Fig. 2B). Italy, Denmark, and the United Kingdom also had high proportions of multiple-country publications, indicating strong international collaboration and cross-border scientific exchange. These countries contributed actively to multicenter research and played important roles in global academic networks and knowledge sharing.

Annual publication output reflects the level of scholarly activity and the development of the field (Fig. 2C). The dataset comprised 7083 publications by 24,063 researchers on male infertility and EDCs from 01 January 2000, to 31 May 2025, including 6272 articles and 811 reviews. Despite year-to-year fluctuations, annual publication output increased markedly over the study period, with an average annual growth rate of 6.91%. The highest annual output was recorded in 2022 (485 publications), and the cumulative citation count for the dataset was 286,313. Because the 2025 data cover only 01 January to 31 May, the publication count for that year is incomplete and likely underestimated (Fig. 2C).

3.2 Analysis of countries/regions and authors

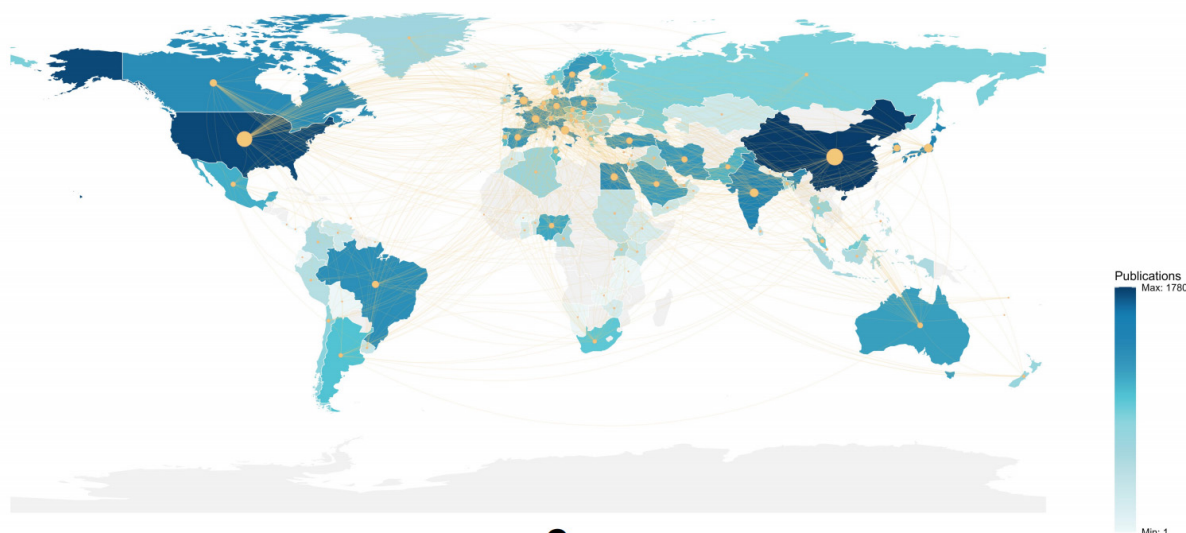
The U.S. and China were the leading contributors to this field. China ranked first in publication output (n = 1780),

whereas the U.S., despite producing fewer publications (n = 1519), had a higher citation total (105,609 vs. 47,158). The remaining countries each produced approximately 200–400 publications, forming a second tier. Some European countries, including Denmark and France, had relatively modest publication output but high citation totals, suggesting substantial scholarly influence (Fig. 3A). The international collaboration network showed a multiteam structure centered on the U.S. and China. China occupied a central position in the network and maintained extensive links with numerous countries, with particularly strong collaboration with the U.S. (Fig. 3B).

Among authors in this field, 71.4% had published one paper, 14.3% had published two, and 5.7% had published three. The remaining 8.6% comprised authors with four or more publications; among these, 365 scholars had published at least five articles. Fig. 3C presents the 10 most productive authors. Ge RS was the most prolific, with 103 publications, whereas Hauser R (7897 citations), Skinner MK (7214 citations), and Meeker JD (6376 citations) had the highest citation totals. The author collaboration network also revealed several closely connected research communities (Fig. 3D).

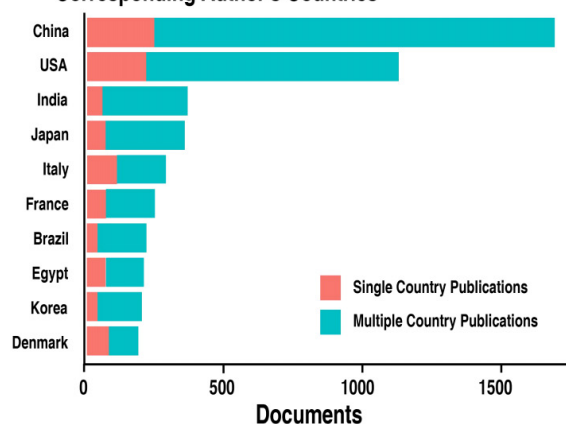
A

Global Scientific Collaboration Network



B

Corresponding Author's Countries



C

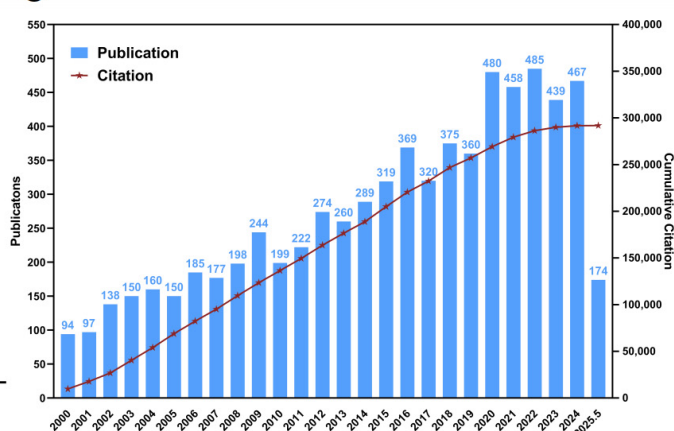


FIGURE 2. International collaboration and annual publication trends. (A) Global network of cross-country research collaborations. Countries/regions are represented by nodes, with node size proportional to publication output and the color gradient indicating output volume; connecting edges denote collaborative relationships, and edge thickness reflects collaboration intensity. The network was constructed from co-authorship data for the included studies and visualized using R software. (B) Single-country and multicounty publications among the 10 most productive countries/regions. Publications are classified according to the corresponding author's affiliation as single-country publications (SCPs) or multicounty publications (MCPs). Bar length represents total output, and the colored segments distinguish SCP and MCP counts. (C) Annual publication output and citation trends. Bars show annual publication output, and the overlaid line shows cumulative citations.

3.3 Analysis of institutions and journals

The 10 most productive institutions showed a broad international distribution, including established research centers in Europe and the U.S., as well as Chinese universities and research institutions (Fig. 4A). The Egyptian Knowledge Bank (EKB) ranked first, with 576 publications. However, EKB is a national library and database consortium rather than an independent research institution. Its leading position, therefore, likely reflects an artifact of Web of Science affiliation indexing rather than research output generated by a single organization. Harvard University ranked second, with 466 publications and 29,982 citations, indicating substantial scholarly influence in this field.

Among Chinese institutions, Wenzhou Medical University, Huazhong University of Science and Technology, Nanjing Medical University, and the Ministry of Education were promi-

nent affiliations, indicating sustained activity in this research area. In the citation network, citation activity for Chinese institutions, including Huazhong University of Science and Technology, the University of Chinese Academy of Sciences, and Jinan University, was concentrated around 2020. By contrast, U.S. institutions, including the Environmental Protection Agency (EPA) and the National Institute of Environmental Health Sciences (NIEHS), showed citation peaks around 2012 (Fig. 4B). This temporal pattern suggests increasing activity among Chinese institutions in recent years, whereas U.S. institutions were more prominent during earlier stages of the field.

The 10 most productive journals spanned toxicology, environmental science, and reproductive health, reflecting the interdisciplinary nature of the field. Reproductive Toxicology led with 331 publications and 16,323 citations, indicating its central role in this research area. Environmental Health Perspectives, despite publishing only 122 articles, had ac-

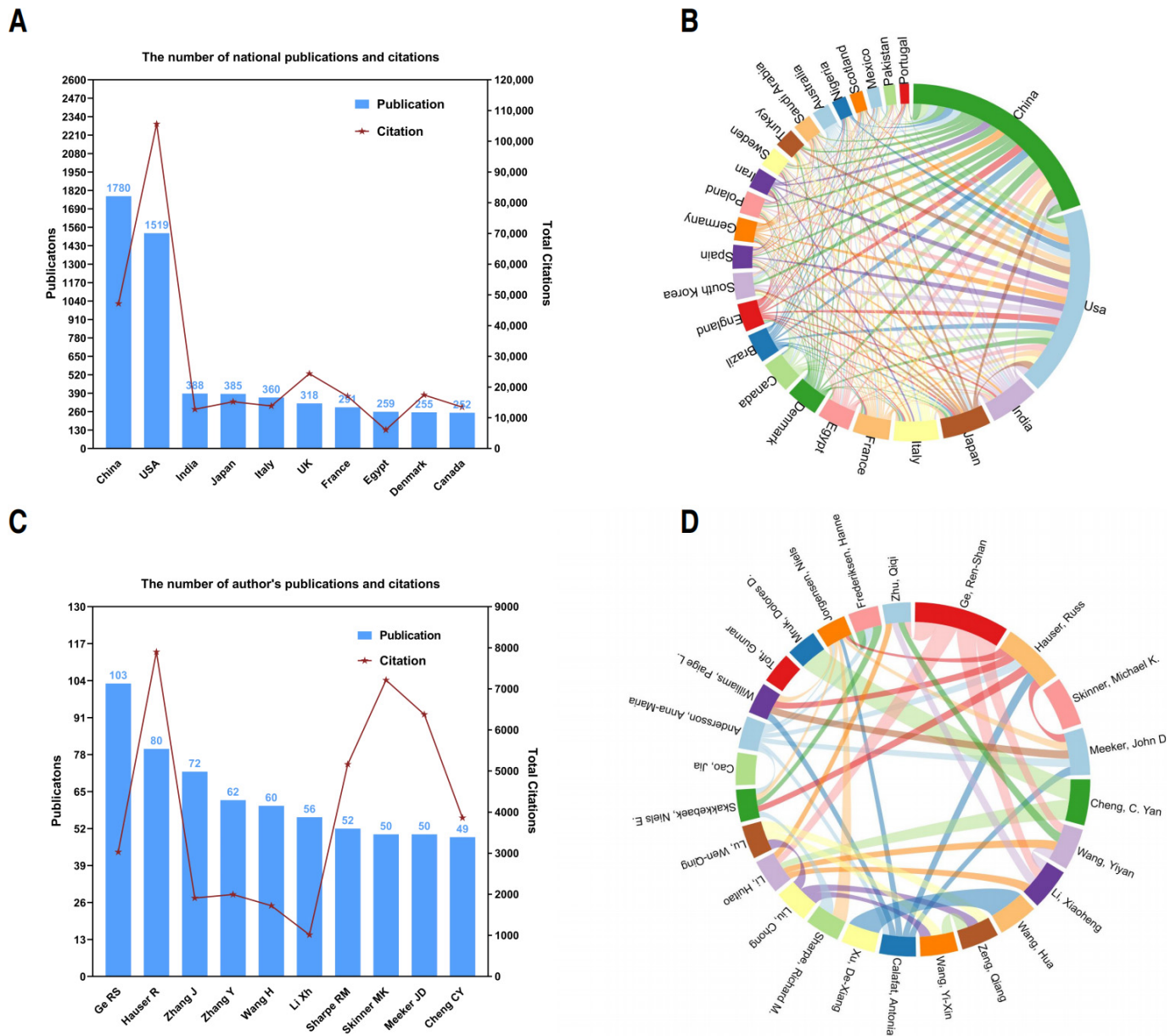


FIGURE 3. Analysis of countries/regions and authors. (A) Publication and citation counts for the 10 most productive countries/regions. (B) Chord diagram of international collaboration. The 25 most productive countries/regions were included in the network; node size corresponds to publication output, connecting chords indicate collaborative relationships, and chord width reflects collaboration intensity. (C) Publication and citation counts for the 10 most productive authors. (D) Chord diagram of author collaboration. The 25 most productive authors were retained for network mapping. Node size indicates publication output, chords represent collaborative links, and chord width denotes collaboration strength.

crued 16,633 citations, highlighting its substantial influence in epidemiologic research on environmental exposures and reproductive health (Fig. 4C).

The journal citation network revealed linkages among journals in male reproductive and EDC research (Fig. 4D). Endocrinology and Environmental Toxicology and Chemistry appeared as blue nodes, indicating that their cited publications were concentrated in earlier years. By contrast, Environmental Pollution, Science of the Total Environment, Environmental Science and Pollution Research, and International Journal of Molecular Sciences appeared as yellow-to-orange nodes, indicating more recent citation activity and increasing attention.

3.4 Keyword analysis

Keywords summarize the core content of the literature and help characterize the evolution of research hotspots. Keyword extraction showed that OS, toxicity, semen quality, *in vitro*, BPA, gene expression, Di(2-ethylhexyl) phthalate (DEHP), dibutyl phthalate, cadmium (Cd), and apoptosis were among the most frequent terms, forming the core knowledge base of the field. In recent years, frequently occurring keywords included DNA damage, DNA methylation, blood–testis barrier, stress, and antioxidants, reflecting increasing interest in molecular mechanisms (Fig. 5A).

Keyword clustering identified two major research themes: (1) exposure during embryonic and neonatal development rep-

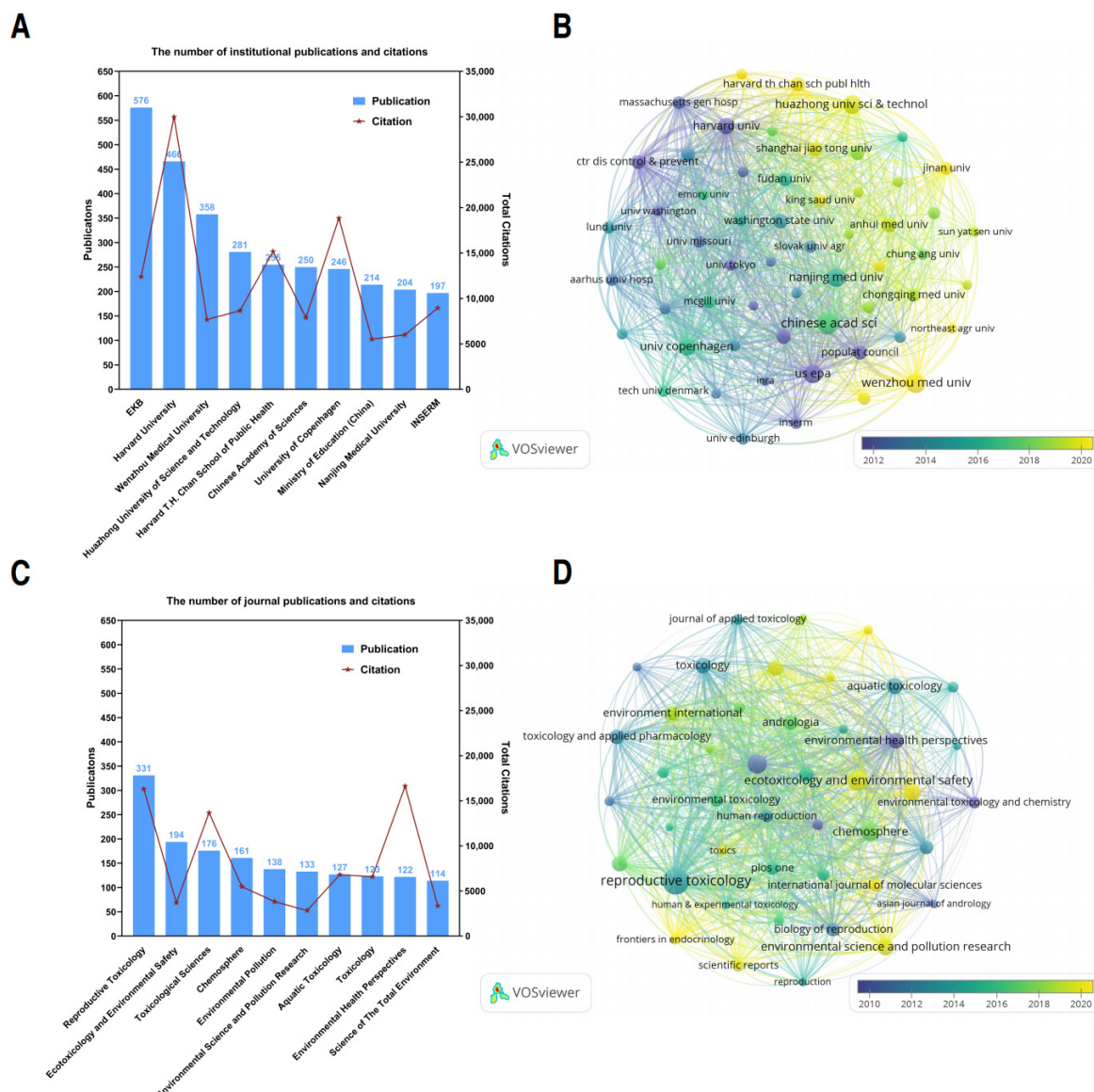


FIGURE 4. Analysis of institutions and journals. (A) Publication and citation counts for the 10 most productive institutions. (B) Institutional citation network. Institutions with at least 30 publications were included, resulting in 58 nodes. Data were normalized using VOSviewer's default association-strength method and clustered using the VOS mapping algorithm, yielding four clusters. Node size denotes institutional publication output; edges represent co-citation relationships, with edge thickness indicating co-citation strength; node colors distinguish clusters. (C) Publication and citation counts for the 10 most productive journals. (D) Journal citation network. Journals with at least 30 publications were included, resulting in 47 nodes. The same normalization and clustering methods were applied, yielding four clusters. Node size represents journal citation frequency; edges denote co-citation relationships, with thickness reflecting co-citation strength; node colors indicate thematic clusters. Abbreviations: EKB, Egyptian Knowledge Bank; HUST, Huazhong University of Science and Technology; INSERM, Institut National de la Santé et de la Recherche Médicale.

resents a critical window of toxicity that can affect male reproductive development and may lead to spermatogenic disorders and transgenerational effects; and (2) EDCs induce OS and DNA damage and impair Sertoli cell function, including disruption of the blood–testis barrier (Fig. 5B).

The thematic map shows the relationships among topics in research on male infertility and EDCs (Fig. 5C). Their distribution according to density and centrality illustrates the structure of the field. Topics in the upper-right quadrant, including OS, BPA, and gene expression, had high centrality and density, indicating mature, well-developed research themes.

By contrast, topics in the lower-left quadrant, including di(2-ethylhexyl) phthalate (DEHP) and in utero exposure, had low centrality and density. Such themes may be emerging or declining and, therefore, require temporal interpretation before they can be classified as prospective research frontiers.

Burst keyword analysis highlighted the temporal evolution of research themes (Fig. 5D). From 2000 to 2010, the strongest burst keywords included sexual differentiation, induction, diethylstilbestrol, and estrogenic activity, indicating an emphasis on the effects of EDCs on sexual differentiation and hormonal regulation. These studies frequently used model organisms,

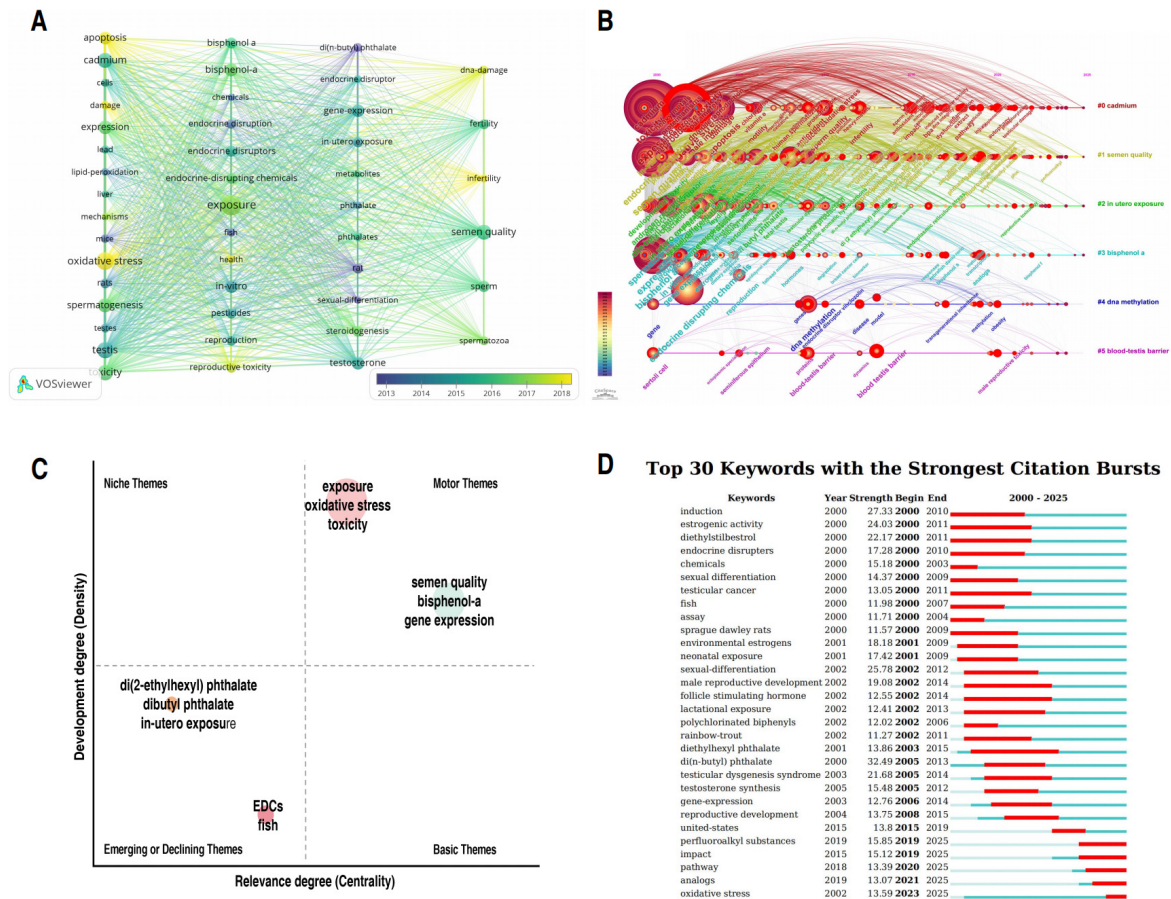


FIGURE 5. Keyword analysis. (A) Keyword co-occurrence network. The network was constructed using VOSviewer with a minimum occurrence threshold of 205, yielding 46 high-frequency keywords. The minimum co-occurrence threshold was set to the default value of 1, retaining all valid links. Data were normalized using the association-strength method to correct for frequency-related size bias. The VOS clustering algorithm identified four thematic clusters from the normalized similarity matrix and generated a two-dimensional visualization. (B) Keyword cluster distribution map. CiteSpace was used for keyword co-occurrence, clustering, and timeline analyses to characterize the knowledge structure and evolution of research hotspots in EDC and male infertility research. Keyword clusters were identified using the log-likelihood ratio (LLR) algorithm. Node size represents keyword frequency, and links indicate co-occurrence relationships. The timeline view illustrates the development of research themes over time. (C) Thematic quadrant map of keywords. The map was generated using the R package bibliometrix from standardized author keywords and co-occurrence networks. Themes were evaluated using Callon centrality (x-axis, thematic relevance/importance) and density (y-axis, thematic development/maturity), with bubble size representing thematic scale. (D) Top 30 keywords with the strongest citation bursts. Bursts were detected using the Kleinberg algorithm in CiteSpace. Burst strength is a dimensionless metric based on deviations from the overall annual mean frequency across the study period and burst duration; higher values indicate sharper increases in research activity. Begin and End indicate the onset and conclusion of each burst interval.

including rainbow trout and Sprague Dawley rats, and emphasized experimental validation of endocrine effects. Since 2019, burst keywords have included perfluoroalkyl substances, impact, and analogs, reflecting growing concern about persistent organic pollutants and their potential effects on male reproduction. Concurrent bursts in OS and pathway suggest a further shift toward molecular pathways and mechanistic studies involving oxidative stress, signal transduction, and epigenetic regulation.

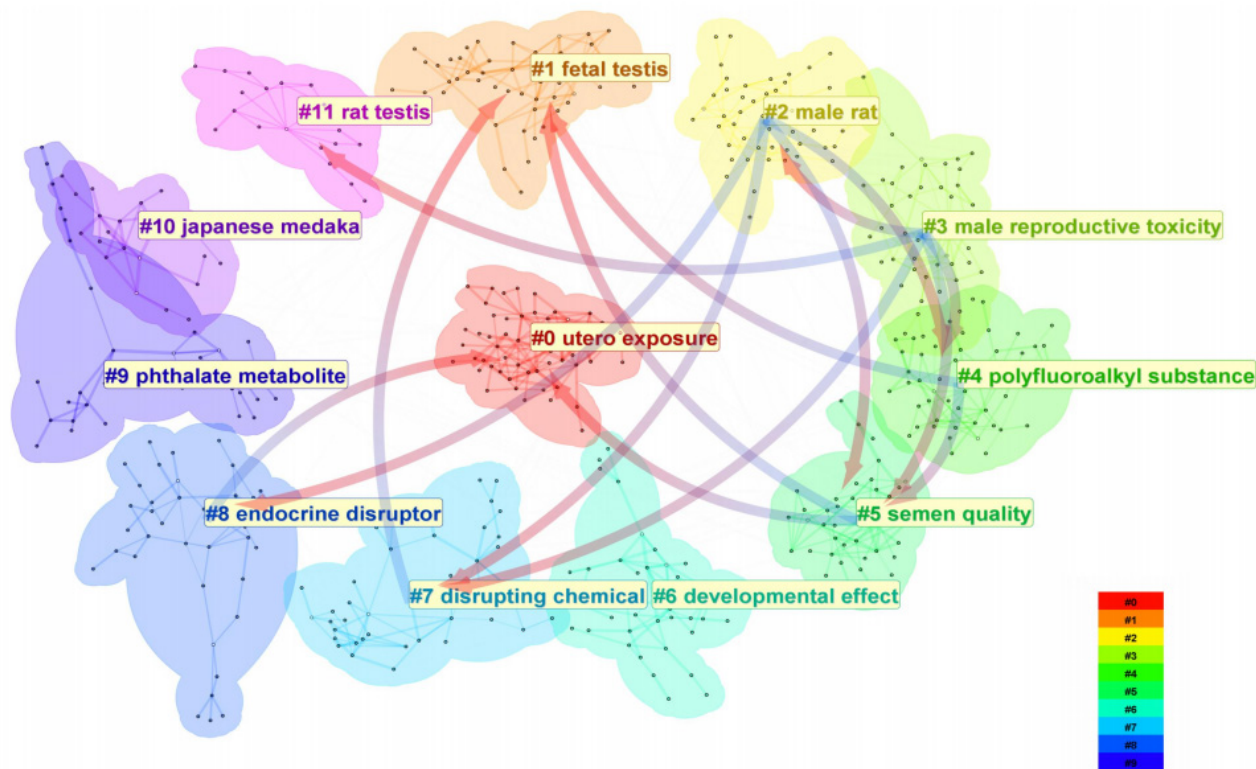
3.5 Co-citation analysis of references

Co-citation analysis helps identify influential and emerging topics within a field. CiteSpace-based clustering of cited references identified several research themes. “In utero ex-

posure”, “fetal testis”, and “developmental effect” focused on developmental-stage exposures; “male rat”, “rat testis”, and “Japanese medaka” represented commonly used experimental models; “phthalate metabolite” and “polyfluoroalkyl substance” represented major pollutant categories; and “male reproductive toxicity” and “semen quality” represented clinically relevant adverse outcomes (Fig. 6A). Fig. 6B presents the 30 references with the strongest citation bursts, illustrating the intensity and duration of scholarly attention. The strongest burst was observed for Swan SH’s 2005 paper (2006–2010; strength = 44.24), which reported that prenatal phthalate exposure was associated with reduced anogenital distance in male infants [12].

The second- and third-strongest bursts were associated with seminal studies by Skakkebaek NE [13], who examined en-

A



B

Top 30 References with the Strongest Citation Bursts

References	Year	Strength	Begin	End	2000 - 2025
Mylchreest E, 1999, TOXICOL APPL PHARM, V156, P81, DOI 10.1006/taap.1999.8643, DOI	1999	28.97	2000	2004	
Vom Saal FS, 1998, TOXICOL IND HEALTH, V14, P239, DOI 10.1177/074823379801400115, DOI	1998	27.44	2000	2003	
Gray LE, 1999, TOXICOL IND HEALTH, V15, P94, DOI 10.1191/074823399678846664, DOI	1999	25.55	2000	2004	
Mylchreest E, 2000, TOXICOL SCI, V55, P143, DOI 10.1093/toxsci/55.1.143, DOI	2000	26.16	2001	2005	
Parks LG, 2000, TOXICOL SCI, V58, P339, DOI 10.1093/toxsci/58.2.339, DOI	2000	24.49	2001	2005	
Skakkebaek NE, 2001, HUM REPROD, V16, P972, DOI 10.1093/humrep/16.5.972, DOI	2001	29.2	2003	2006	
Wilson VS, 2004, TOXICOL LETT, V146, P207, DOI 10.1016/j.toxlet.2003.09.012, DOI	2004	32.49	2004	2009	
Fisher JS, 2003, HUM REPROD, V18, P1383, DOI 10.1093/humrep/deg273, DOI	2003	26.22	2004	2008	
Barlow NJ, 2003, TOXICOL SCI, V73, P431, DOI 10.1093/toxsci/kfg087, DOI	2003	24.07	2004	2008	
Silva MJ, 2004, ENVIRON HEALTH PERSP, V112, P331, DOI 10.1289/ehp.6723, DOI	2004	29.68	2005	2009	
Lehmann KP, 2004, TOXICOL SCI, V81, P60, DOI 10.1093/toxsci/kfh169, DOI	2004	27.07	2005	2009	
Swan SH, 2005, ENVIRON HEALTH PERSP, V113, P1056, DOI 10.1289/ehp.8100, DOI	2005	44.24	2006	2010	
Anway MD, 2005, SCIENCE, V308, P1466, DOI 10.1126/science.1108190, DOI	2005	25.21	2006	2010	
Foster PMD, 2006, INT J ANDROL, V29, P140, DOI 10.1111/j.1365-2605.2005.00563.x, DOI	2006	24.07	2006	2011	
Main KM, 2006, ENVIRON HEALTH PERSP, V114, P270, DOI 10.1289/ehp.8075, DOI	2006	30.02	2007	2011	
Welsh M, 2008, J CLIN INVEST, V118, P1479, DOI 10.1172/JCI34241, DOI	2008	27.21	2009	2013	
Sharpe Richard M, 2008, FERTIL STERIL, V89, P633, DOI 10.1016/j.fertnstert.2007.12.026, DOI	2008	26.18	2009	2013	
Lambrot R, 2009, ENVIRON HEALTH PERSP, V117, P32, DOI 10.1289/ehp.11146, DOI	2009	26.15	2009	2014	
Diamanti-Kandarakis E, 2009, ENDOCR REV, V30, P293, DOI 10.1210/er.2009-0002, DOI	2009	34.26	2010	2014	
Siu ER, 2009, TOXICOL APPL PHARM, V238, P240, DOI 10.1016/j.taap.2009.01.028, DOI	2009	31.14	2010	2014	
Vandenberg LN, 2012, ENDOCR REV, V33, P378, DOI 10.1210/er.2011-1050, DOI	2012	28.62	2013	2017	
Manikkam M, 2013, PLOS ONE, V8, P0, DOI 10.1371/journal.pone.0055387, DOI	2013	27.78	2014	2018	
Wisniewski P, 2015, TOXICOLOGY, V329, P1, DOI 10.1016/j.tox.2015.01.002, DOI	2015	30.9	2016	2020	
Gore AC, 2015, ENDOCR REV, V36, P1, DOI 10.1210/er.2015-1010, DOI	2015	23.74	2016	2020	
Skakkebaek NE, 2016, PHYSIOL REV, V96, P55, DOI 10.1152/physrev.00017.2015, DOI	2016	40.1	2017	2021	
Levine H, 2017, HUM REPROD UPDATE, V23, P646, DOI 10.1093/humupd/dmx022, DOI	2017	39.91	2018	2022	
de Angelis C, 2017, REPROD TOXICOL, V73, P105, DOI 10.1016/j.reprotox.2017.07.021, DOI	2017	27.84	2019	2022	
Radke EG, 2018, ENVIRON INT, V121, P764, DOI 10.1016/j.envint.2018.07.029, DOI	2018	26.1	2019	2023	
Zhu QQ, 2020, FRONT GENET, V11, P0, DOI 10.3389/fgene.2020.00527, DOI	2020	27.26	2021	2025	
Levine H, 2023, HUM REPROD UPDATE, V29, P157, DOI 10.1093/humupd/dmac035, DOI	2023	27.35	2023	2025	

FIGURE 6. Co-citation analysis of references. (A) Clusters of cited references on EDCs and male infertility. The network was generated using CiteSpace with a time span from January 2000 to May 2025, a 1-year time slice, and “cited references” as the node type. Nodes were selected using the g-index ($k = 25$), with LRF = 3.0, L/N = 10, and LBY = 5. Node size denotes citation frequency; edges indicate co-citation relationships; colors distinguish clusters. (B) Top 30 references with the strongest citation bursts. Bursts were detected using the Kleinberg algorithm in CiteSpace. Burst strength is a dimensionless metric; higher values indicate more pronounced increases in scholarly attention during the burst period. Begin and End indicate the onset and conclusion of each burst, respectively.

environmental influences and genetic susceptibility in male reproductive disorders and fertility trends, and Levine H [14], who analyzed long-term trends in sperm count. A more recent burst involved Radke EG's review of phthalate exposure and male reproductive outcomes in human populations [15]. Ongoing bursts included reviews by Zhu Q and de Angelis C, both of which focused on cadmium as a major heavy metal associated with male infertility [16, 17]. These highly cited references represent milestone contributions and continue to shape emerging research directions, particularly mechanistic and transgenerational studies.

4. Discussion

4.1 General information

The number of publications on male infertility and EDCs has increased steadily, reflecting growing research attention that is likely to continue. However, the 2025 count ($n = 174$) is incomplete because of the 31 May cutoff and, therefore, does not indicate a true decline. Although researchers from 115 countries and regions contributed to the field, publication output remained concentrated in a small number of countries. The U.S. had the greatest citation impact, whereas China ranked first in publication output. The strongest international collaboration link was between China and the U.S. China's rapid publication growth may reflect increased research investment, supportive national policies, and innovation-oriented strategies.

Institutional patterns broadly mirrored national trends. Harvard University, a major center for reproductive medicine and environmental science, was prominent in both publication output and citations. The University of Copenhagen, the U.S. National Institutes of Health (NIH), and the EPA were also influential. Collaboration remained predominantly domestic, underscoring the need for stronger international partnerships to address global challenges in this field.

The literature on male infertility and EDCs was concentrated in high-impact journals. Reproductive Toxicology published the largest number of articles in this area, and its high co-citation count reflected its influence on research into toxic mechanisms, impaired gametogenesis, and transgenerational effects. Environmental Health Perspectives had the highest citation total and h-index and contributed prominently to research on mixed exposures, emerging biomarkers, and global disparities in exposure. Other influential journals included Toxicological Sciences and Aquatic Toxicology.

Author and co-authorship analyses showed that Ge RS, Hauser R, and Zhang J were among the most productive researchers in the field, whereas Hauser R, Skinner MK, and Meeker JD were the most cited, indicating substantial scholarly influence. Stable research teams had formed, but collaboration remained largely confined to the same countries or institutions. Stronger international and cross-institutional collaboration could provide broader perspectives and support more comprehensive approaches to male infertility.

4.2 Key research themes in male infertility and EDCs

Keyword and reference analyses identified the core themes of research on male infertility and EDCs: exposure, OS, toxicity, semen quality, BPA, and gene expression. BPA is a ubiquitous EDC to which humans are exposed through food, consumer products, and environmental media. Its adverse effects on semen quality are thought to be mediated largely through oxidative stress and altered gene expression.

Other prominent EDC categories associated with male reproductive impairment include phthalates, PFAS, and heavy metals. Phthalates are widely used as plasticizers in food packaging, medical devices, and personal care products [18]. Their metabolites, particularly mono(2-ethylhexyl) phthalate (MEHP) and mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), have been associated with reduced sperm concentration, impaired progressive motility, abnormal sperm morphology, and disrupted testosterone synthesis [19]. PFAS, including perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS), have attracted considerable attention because of their environmental persistence, bioaccumulation potential, and widespread distribution, which have led to restrictions on their use in many countries [20]. PFAS may exert long-term adverse effects on the male reproductive system through mitochondrial dysfunction, inflammatory and immune activation, and epigenetic regulation [21]. Cadmium is among the earliest identified and most extensively studied heavy metals associated with male reproductive toxicity [22]. Its adverse effects involve oxidative stress, mitochondrial damage, apoptosis, and disruption of the blood–testis barrier [23].

Current evidence indicates that EDCs affect male reproductive health through complex molecular networks. However, the effects of combined exposure to multiple pollutants, long-term low-dose exposure, and critical windows of susceptibility remain insufficiently understood. Future priorities include improved exposure assessment, characterization of dose–response relationships and critical windows, and systematic mapping of gene regulatory networks to inform clinical interventions.

CiteSpace keyword clustering suggested that research on male infertility and EDCs is converging around an exposure–damage–reproductive outcome framework. The initial focus on representative EDCs, such as cadmium and BPA, has progressed from descriptive toxicology toward mechanistic investigation of impaired semen quality, including changes in sperm concentration, motility, and morphology. The emergence of the *in utero* exposure cluster has drawn attention to transgenerational risk and fetal male reproductive development as a critical window. Epigenetic mechanisms, particularly DNA methylation, are frequently implicated, suggesting that EDCs may induce persistent reproductive effects by reprogramming gene expression in embryonic or adult testes. The blood–testis barrier is increasingly recognized as structurally and functionally vulnerable to EDC-induced disruption, which may impair spermatogenesis [24].

Several highly cited publications between 2005 and 2008

marked an important advance in the field. Early landmark studies examined individual EDCs, including the association between prenatal phthalate exposure and reduced anogenital distance in male infants [12] and pesticide-induced transgenerational epigenetic effects [25]. Later studies addressed multifactorial interactions, linking environmental pollution to the epidemiology of reproductive disorders and refining risk-assessment frameworks [13]. More recent work has emphasized evidence synthesis and clinical translation, including reports of a global decline in sperm count of 1.6% per year [14], reviews of the reproductive effects of phthalate exposure [15], and assessments of regional trends in sperm parameters.

4.3 Emerging hotspots and frontiers

Research has shifted from simple exposure–outcome associations toward multilayered mechanistic networks. BPA, phthalates, PFAS, and certain heavy metals can impair the spermatogenic microenvironment through oxidative stress, disrupted steroidogenesis, and altered hormonal signaling, thereby compromising semen quality and increasing sperm DNA fragmentation and functional abnormalities [23, 26]. Embryonic and perinatal exposures may reprogram sperm epigenetic profiles, potentially transmitting adverse effects across generations and directing attention toward “paternal epigenetic memory” and its causal role in reproductive outcomes [27].

At the cellular and tissue levels, EDCs can disrupt Sertoli cells and blood–testis barrier integrity, activate apoptotic, ferroptotic, and inflammatory pathways, and impair the spermatogenic microenvironment and steroid hormone synthesis (Fig. 7). These findings identify protection of Sertoli cells and the blood–testis barrier as potential intervention targets [28]. Biomarkers may capture different levels of this molecular and cellular injury. The DNA fragmentation index (DFI) primarily reflects genomic damage associated with oxidative stress and apoptosis, whereas miRNA and DNA methylation profiles may capture broader changes in transcriptional regulation and transgenerational epigenetic reprogramming. DFI has shown dose–response associations with EDC exposure in population-based studies and is used clinically to evaluate sperm DNA integrity in male infertility [29, 30]. Epigenetic biomarkers, particularly miRNAs in seminal plasma exosomes, such as miR-34a, miR-15b, and miR-141, have also been implicated in EDC-related reproductive toxicity. For example, triclosan has been reported to modulate miR-20a-5p and thereby affect spermatogonial proliferation [31, 32]. Seminal plasma extracellular vesicles, including prostasomes and epididymosomes, transfer proteins and small RNAs as bioactive signals. This intercellular communication system may support the development of noninvasive, liquid biopsy-based biomarkers for male reproductive dysfunction [33].

Clinically, growing evidence suggests that antioxidant, lifestyle, and nutritional interventions may mitigate EDC-associated sperm dysfunction, although their efficacy remains heterogeneous [34]. Future research should prioritize mechanism-informed randomized controlled trials and precision intervention strategies.

4.4 Implications for future research, policy, and exposure-reduction strategies

The findings of this bibliometric analysis provide insights into future research priorities, environmental health policy, and strategies to reduce exposure to EDCs.

BPA, phthalates, PFAS, and heavy metals are the most extensively studied EDCs; however, research remains unevenly distributed across pollutants. Toxicologic and epidemiologic evidence on BPA and phthalates is relatively well developed, whereas emerging contaminants, including bisphenol analogs, alternative plasticizers, and chemical mixtures, remain insufficiently investigated. Because humans are typically exposed simultaneously to complex chemical mixtures in real-world settings, future studies should move beyond single-chemical animal models and account for combined exposures and cumulative exposure across different life stages.

The analysis also indicated a broader transition from descriptive epidemiologic studies toward molecular mechanistic research. Future work should identify critical windows of susceptibility, including fetal development, adolescence, and reproductive age. Longitudinal birth cohort studies with repeated exposure assessments are needed to clarify the relationships between lifelong EDC exposure and adverse reproductive outcomes. Integrating multi-omics approaches may further elucidate the molecular pathways through which environmental chemicals disrupt spermatogenesis and facilitate the identification of biomarkers for early prediction of reproductive impairment.

Associations between environmental pollutant exposure and impaired male reproductive function highlight the need to incorporate reproductive health indicators into population-level environmental risk-assessment frameworks. Policy priorities include strengthening routine monitoring of high-risk chemicals, establishing safety criteria for chemical alternatives, and progressively phasing out products with high persistence and bioaccumulation potential. At the individual level, reducing avoidable use of plastic products that may contain EDCs may help limit daily exposure. Given the increasing complexity of human exposure patterns, interdisciplinary collaboration is needed to develop more accurate reproductive-risk prediction models and practical, comprehensive strategies for population-level pollution prevention and control.

4.5 Strengths and limitations

This study analyzed 7083 publications using complementary bibliometric and visualization methods to map the knowledge structure of research on male infertility and EDCs and to characterize changes over the past two decades. The analysis encompassed collaboration networks across countries, institutions, authors, and journals, providing a useful resource for identifying potential collaborators, tracking research hotspots, and exploring emerging directions. Several limitations should be acknowledged. First, the analysis was restricted to the WoSCC, which may have introduced selection bias relative to broader databases such as PubMed and Scopus. Second, although the search strategy combined specific EDC-related chemicals with broader EDC-related terms, relevant studies may have been missed because of variation in chemical

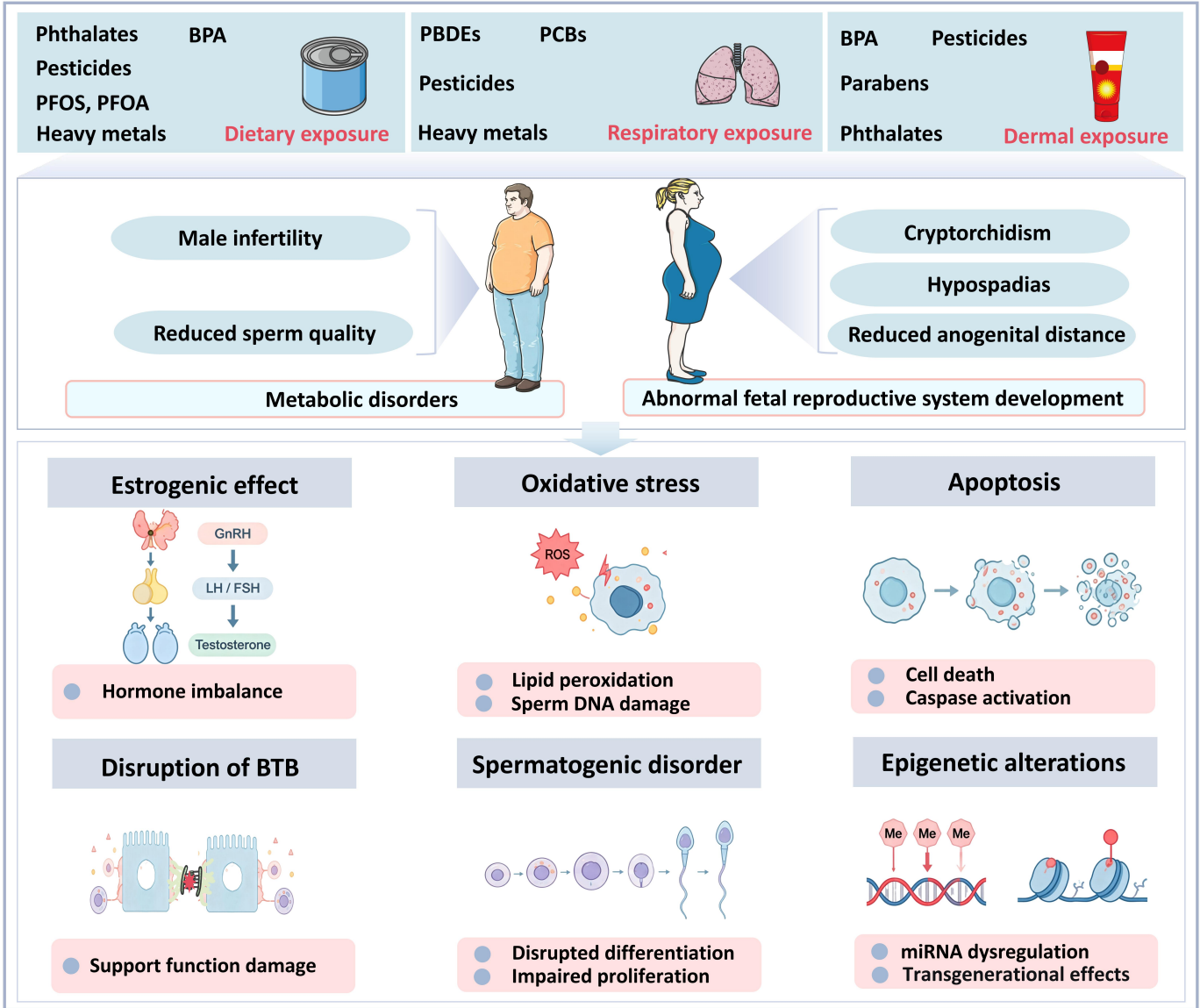


FIGURE 7. Pathways of EDC-induced damage to the male reproductive system. This original illustration was created by the authors and was not adapted from a previously published source. BPA, bisphenol A; PFOS, perfluorooctanesulfonic acid; PFOA, perfluorooctanoic acid; PCBs, polychlorinated biphenyls; GnRH, gonadotropin-releasing hormone; LH, luteinizing hormone; FSH, follicle-stimulating hormone; ROS, reactive oxygen species; BTB, blood–testis barrier; PBDEs, polybrominated diphenyl ethers.

nomenclature and indexing practices. Only English-language publications were included, which may have introduced language bias and underrepresented non-English research, including Chinese-language studies despite China’s substantial contribution to the field. Third, bibliometric results may be influenced by algorithm-dependent methods, including CiteSpace parameter settings, and by potential errors in data cleaning and text processing. Finally, citation-based indicators were not adjusted for publication age, citation windows, or self-citations and should, therefore, be interpreted cautiously.

5. Conclusions

This bibliometric study mapped the development of research on male infertility and EDCs over the past two decades, highlighting sustained growth in publication output, expanding

international collaboration, and the roles of influential researchers and journals. Major research themes included exposure effects, transgenerational inheritance, and molecular mechanisms. Future work should emphasize interdisciplinary integration, standardized evaluation frameworks, and the identification and validation of novel biomarkers. These findings may support future research, clinical translation, and the development of reproductive health prevention and intervention strategies.

AVAILABILITY OF DATA AND MATERIALS

The data that support the findings of this study are available on request from the corresponding author.

AUTHOR CONTRIBUTIONS

MHG—writing—original draft. GCD—writing—review & editing, validation, funding acquisition. DYM—writing—review & editing, software, methodology, formal analysis. All authors read and approved the final manuscript at the end.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable. This study is a bibliometric analysis based solely on publicly available publication data retrieved from the Web of Science Core Collection. It does not involve human participants, animal experiments, or any personal or clinical data; therefore, ethical approval and informed consent are not required.

ACKNOWLEDGMENT

Not applicable.

FUNDING

This study was supported by the Hospital Capacity Enhancement Project of Xiyuan Hospital, China Academy of Chinese Medical Sciences (Grant No. XYZX0304-01), the Major Research Program of the Science and Technology Innovation Project of the China Academy of Chinese Medical Sciences (Grant No. CI2026A02217) and the Fundamental Research Funds for the China Academy of Chinese Medical Sciences (Grant No. ZZ16-XRZ-014).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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How to cite this article: Minghui Gou, Guanchao Du, Dongyue Ma. Bibliometric insights into endocrine-disrupting chemicals and male infertility research: global trends from 2000 to 2025. *Journal of Men's Health*. 2026; 22(10): 57-69. doi: 10.22514/jomh.2026.084.