ACCSCIENCE PUBLISHING

Eurasian Journal of Medicine and Oncology

ORIGINAL RESEARCH ARTICLE

The global research landscape and frontiers of endocrine-disrupting chemicals-induced vascular toxicity: A bibliometric and visualization analysis

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Abstract

Introduction: Endocrine-disrupting chemicals (EDCs) have attracted increasing attention as potential contributors to vascular toxicity.
Objective: This study aimed to characterize the global research landscape, knowledge structure, and emerging trends in this field.
Methods: A total of 911 publications indexed in the Science Citation Index Expanded of the Web of Science Core Collection from 1997 to 2025 were analyzed using bibliometric and visualization methods to map collaboration patterns and knowledge evolution.
Results: The United States leads in both publication output and citation impact. Knowledge mapping indicates that an "exposure–mechanism–endpoint" framework is widely adopted in the literature, with "oxidative stress" appearing as a highly connected keyword linking environmental exposures and vascular outcomes. Trend analysis further suggests a shift in research focus from traditional persistent organic pollutants to emerging contaminants associated with modern lifestyles, alongside an increasing focus on early-life exposures and susceptible populations.
Conclusion: Research on EDC-related vascular toxicity is evolving toward greater emphasis on emerging contaminants, critical exposure windows, and mechanistic exploration. These trends may help inform future research directions and risk assessment strategies.

Keywords: Endocrine-disrupting chemicals; Vascular toxicity; Oxidative stress; Endothelial dysfunction; Atherosclerosis; Bibliometric analysis

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Citation: Kang T, Zhang F, Zheng J, Yong X, Ismail NA. The global research landscape and frontiers of endocrine-disrupting chemicals-induced vascular toxicity: A bibliometric and visualization analysis. *Eurasian J Med Oncol.* 2026;10(3):026050050. doi: 10.36922/EJMO026050050

Received: January 27, 2026

Revised: April 22, 2026

Accepted: April 23, 2026

Published online: May 22, 2026

1. Introduction

Cardiovascular diseases (CVDs) remain the leading cause of mortality worldwide, and their increasing incidence continues to pose a major public health challenge.[1] Although substantial progress has been made in understanding and managing traditional risk factors such as hypertension, hyperlipidemia, diabetes, and smoking, a considerable proportion of CVD risk remains insufficiently explained.[2] In recent years, growing attention has been

directed toward non-traditional risk factors, particularly environmental pollutants, in the pathophysiology of CVD.[3,4] Among these, endocrine-disrupting chemicals (EDCs) have attracted increasing interest due to their widespread presence in the environment and consumer products. EDCs can interfere with endogenous hormonal signaling pathways, potentially leading to adverse physiological effects.[5,6] Accumulating evidence suggests that vascular toxicity represents an important pathway through which EDC exposure may be associated with cardiovascular outcomes, including endothelial dysfunction and the progression of atherosclerosis.[7,8] These vascular alterations are widely considered to be involved in the development and progression of CVDs.

Despite the rapid growth of research in this area, a comprehensive bibliometric evaluation of global research trends and knowledge structures in EDC-induced vascular toxicity remains limited. Therefore, this study applies bibliometric methods to systematically analyze the existing literature, aiming to characterize the research landscape, identify major themes, and explore emerging trends in this field.

2. Literature review

Before presenting the bibliometric results, it is helpful to briefly review the main classes of EDCs, common exposure pathways, and the biological processes discussed in relation to vascular toxicity. This section provides a concise overview of the current evidence on EDC exposure and the mechanisms potentially involved in vascular injury, thereby offering contextual background for the subsequent bibliometric analysis.

2.1. Classes of endocrine-disrupting chemicals and common exposure pathways

Endocrine-disrupting chemicals comprise a diverse group of exogenous substances originating from a wide range of sources. Major categories include bisphenol A (BPA), phthalates (PAEs), parabens (PBs), polychlorinated biphenyls (PCBs), dioxins, per- and polyfluoroalkyl substances (PFAS), and certain pesticides and heavy metals.[9,10] Human exposure to EDCs occurs through multiple pathways in daily life. The use of personal care products (PCPs) represents an important exposure route.[11] Evidence suggests that dermal absorption is a major pathway for PAEs and PBs present in PCPs, as these compounds can penetrate the skin and enter systemic circulation following topical application.[12]

Migration of EDCs from food packaging materials is another relevant source of exposure. Under conditions such as elevated temperature, prolonged storage, or contact with fatty foods, compounds such as PAEs may leach from plastic containers into food and subsequently be ingested.[13,14] In addition, environmental contamination contributes substantially to human exposure. Industrial emissions, including waste gas, wastewater, and solid waste, can introduce EDCs into surrounding environments[15], while agricultural activities may lead to pesticide-related contamination of soil and water bodies. As a result, exposure may occur through drinking water, inhalation of polluted air, and contact with contaminated soil.[16,17]

A growing body of epidemiological and experimental studies suggests that long-term exposure, as well as exposure during critical developmental windows, may be associated with structural and functional alterations in the vascular system.[18,19] The widespread presence of these chemicals results in persistent and complex co-exposure scenarios in human populations.[20] For example, data from the United States Centers for Disease Control and Prevention indicate that a large proportion of the population is simultaneously exposed to multiple EDCs, reflecting a complex internal exposure profile.[21]

2.2. Mechanisms of endocrine-disrupting chemical-induced vascular toxicity

The mechanisms underlying EDC-induced vascular toxicity are complex and involve multiple interacting biological processes. Current evidence suggests that these effects can be interpreted within a framework of interconnected pathways, including receptor-mediated signaling, oxidative stress, inflammation, vascular remodeling, and epigenetic regulation. Oxidative stress-related processes are frequently reported in the literature and are often discussed alongside receptor-mediated signaling, inflammation, vascular remodeling, and epigenetic regulation.

2.2.1. Receptor-mediated triggering pathways

At the upstream level, several receptor-mediated pathways have been investigated. One commonly described mechanism involves activation of the aryl hydrocarbon receptor (AhR). Certain EDCs, such as polycyclic aromatic hydrocarbons, dioxins, and PCBs, can function as AhR ligands, leading to increased expression of downstream enzymes including cytochrome P450 1A1/1A2 and nicotinamide adenine dinucleotide phosphate oxidases.[22,23] These processes are associated with enhanced production of reactive oxygen species (ROS) and oxidative stress in endothelial cells.[24,25] In addition to AhR, EDCs may interact with other nuclear and membrane receptors, such as vascular endothelial growth factor (VEGF)/VEGF receptor, estrogen receptors, and peroxisome proliferator-activated receptors. Alterations in these signaling pathways have

been linked to changes in lipid metabolism, angiogenesis, and endothelial function, which may contribute to vascular dysfunction and atherosclerotic processes.[26,27]

2.2.2. Oxidative stress and inflammatory cascades

A substantial body of evidence indicates that exposure to various EDCs is associated with increased ROS production and activation of oxidative stress-related pathways.[28,29] Mitochondrial dysfunction is considered an important contributing factor, as EDCs may impair the mitochondrial respiratory chain, thereby increasing oxidative burden. Elevated ROS levels are associated with reduced nitric oxide bioavailability, impaired endothelium-dependent vasodilation, and endothelial injury.[8,30] In addition, oxidative stress has been linked to DNA damage, cellular senescence, and apoptosis in vascular cells. ROS can activate transcription factors such as nuclear factor kappa B and activator protein 1[31], leading to increased expression of pro-inflammatory cytokines and adhesion molecules, including monocyte chemoattractant protein-1, interleukin (IL)-1β, IL-6, vascular cell adhesion molecule-1, and E-selectin.[23,32,33] These processes may promote immune cell recruitment and contribute to a pro-inflammatory vascular environment. Some studies further suggest that certain PCBs may induce inflammatory cell death pathways, such as pyroptosis, through ROS-related signaling cascades, thereby contributing to endothelial dysfunction and vascular injury.[34]

2.2.3. Vascular smooth muscle cell phenotypic switching and vascular remodeling

At the cellular level, vascular smooth muscle cells (VSMCs) exhibit phenotypic plasticity in response to environmental and inflammatory stimuli. Under physiological conditions, VSMCs maintain a contractile phenotype; however, exposure to EDCs, together with oxidative and inflammatory signals, has been associated with a shift toward a synthetic phenotype. This transition is characterized by reduced expression of contractile proteins and increased proliferation, migration, and extracellular matrix (ECM) production.[35] Inflammatory mediators such as tumor necrosis factor-α, platelet-derived growth factor-BB, and IL-6 are thought to be involved in this process. In parallel, VSMC apoptosis may occur, potentially affecting vascular structural integrity.[36]

Oxidative stress-related pathways have also been linked to the regulation of matrix metalloproteinases (MMPs), including MMP-2, MMP-9, and MMP-14.[37] These enzymes contribute to ECM degradation and vascular remodeling. In addition, emerging evidence suggests that phenotypically altered VSMCs may contribute to foam cell formation and plaque dynamics, which are relevant to atherosclerosis progression.[38,39]

2.2.4. Epigenetic regulation

Epigenetic mechanisms have gained increasing attention as potential mediators linking EDC exposure to long-term vascular effects. Epigenetic regulation involves heritable changes in gene expression without alterations in DNA sequence, including DNA methylation, histone modifications, and non-coding RNAs.[40–42] These mechanisms are considered to play a role in linking environmental exposures, particularly during early life, with later disease risk.

Accumulating evidence suggests that EDC exposure may influence epigenetic regulation. For example, alterations in DNA methylation patterns have been associated with dysregulation of genes involved in inflammation and vascular homeostasis.[43–45] EDCs may also affect histone modification processes, potentially through interactions with nuclear receptors and their co-regulators, thereby influencing the transcription of vascular-related genes such as *eNOS* and *ICAM-1*.[46,47] Furthermore, EDC-induced histone modifications may also influence the binding of other transcription factors, which has been associated with altered regulation of vascular endothelial and smooth muscle cell function.[48] In addition, changes in the expression of non-coding RNAs, particularly miRNAs, have been linked to pathways involved in vascular inflammation, apoptosis, and atherosclerosis.[49–51] These findings suggest that epigenetic regulation may represent an additional layer through which EDC exposure is associated with vascular dysfunction.

3. Methods and data collection

This section describes the methodological framework and data source used in the present study. Specifically, it outlines the bibliometric approach and analytical tools, as well as the data retrieval strategy and screening process applied to construct the final dataset.

3.1. Bibliometrics and analytical tools

This study used bibliometric analysis as the primary methodological approach. Bibliometrics is a quantitative method based on mathematical and statistical techniques and is widely used to examine the structure, development, and research trends of a scientific field.[52,53] With the support of visualization tools, including VOSviewer (version 1.6.20, Leiden University, Netherlands), CiteSpace (version 6.4, Drexel University, USA), and R (version 4.5.1, R Foundation for Statistical Computing, Austria), bibliographic data can be transformed into visual knowledge maps, facilitating

the analysis of publication trends, collaborative networks, knowledge bases, and research hotspots.[54,55] Given the growing body of literature on EDCs and vascular toxicity, a bibliometric approach may help provide a structured overview of this research area. Accordingly, this study aims to: (i) characterize the developmental trajectory of the field and the collaboration networks among major countries and institutions; (ii) identify major mechanistic themes and emerging research trends through keyword co-occurrence and burst analyses. The findings are expected to provide a data-based overview of the research landscape of EDC-induced vascular toxicity and may offer useful references for future studies in this area.

3.2. Data acquisition and screening process

The data were retrieved from the Science Citation Index Expanded within the Web of Science Core Collection (WoSCC) database. WoSCC was selected because it is one of the most widely used databases in bibliometric studies and provides standardized bibliographic and citation data compatible with tools such as VOSviewer, CiteSpace, and R-based bibliometric packages. To maintain consistency in data structure and citation links, only WoSCC-indexed records were included in the present analysis.

The search was completed on August 10, 2025, with no restriction on the starting year in order to capture all potentially relevant publications. The search strategy was constructed around two main themes: "endocrine-disrupting chemicals" and "vascular toxicity." The search query was as follows: TS = (("endocrine disrupt*" OR "endocrine-active substance*" OR "Bisphenol A" OR Phthalate* OR Paraben* OR Dioxin* OR "Polychlorinated Biphenyls" OR "organochlorine pesticide*" OR "perfluoroalkyl substance*" OR PFAS OR "heavy metal*" OR "polybrominated diphenyl ether*" OR PBDE*)) AND (TS = (("vascular toxicity" OR "vascular injury" OR "vascular damage" OR Atherosclerosis OR Atherogenesis OR "endothelial dysfunction" OR "endothelial injury")) OR (TS = (("oxidative stress" OR inflammation OR "nitric oxide")) AND TS = (vessel* OR vascular* OR artery OR arterial OR endothelial*)))

The literature screening process followed predefined inclusion and exclusion criteria (Figure 1). The initial search identified 1,129 records. After limiting document types to "Articles" and "Reviews" and language to "English," 1,106 records remained. Two researchers independently screened the titles and abstracts of these records to assess topical relevance. Any disagreements were resolved through discussion, and when necessary, a third senior researcher was consulted to reach a final decision.

Studies were included if they explicitly investigated the toxic effects of, or associations between, one or more exogenous EDCs and the vascular system. Studies with clearly irrelevant topics were excluded. After screening and cross-checking, a final dataset of 911 publications, comprising 752 articles and 159 reviews, was included in the analysis.

4. Results

4.1. Global development trends

The 911 publications included in this study were contributed by 4,839 authors from 1,303 organizations across 72 countries, published in 360 journals, and received 51,235 citations from 7,119 citing journals. To characterize the historical development of this field, annual publication output and annual citation counts were analyzed (Figure 2).

As shown in Figure 2, the annual number of publications increased over time and first exceeded 70 in 2020. During the subsequent period (2021–2024), annual output fluctuated slightly but remained above 60 publications, suggesting relatively sustained research activity. Total citations accrued by documents published in each year also showed an upward trend, peaking at more than 3,800 in 2024.

Overall, these publication and citation patterns suggest that the field experienced a period of growth followed by a relatively stable phase after 2020, with continued accumulation of academic attention and influence.

4.2. Analysis of main research forces and collaboration networks

4.2.1. Country level

A total of 72 countries contributed to research in this field. As shown in Figure 3 and Table 1, the global distribution of research output showed clear differences in publication volume and citation impact. The USA ranked first in both publication count (278) and total citations (18,430), indicating a leading position in this field. China ranked second in publication output (225), followed by Japan and Brazil, with relatively high productivity.

When average citation impact was considered, England stood out with 101.61 citations per document despite a relatively small number of publications (23). The USA (66.29) and Germany (35.35) also showed citation impacts above the overall average. The country collaboration network (Figure 4) further illustrates the structure of international cooperation. The USA and China had the largest nodes, consistent with their leading

publication outputs. The USA occupied a central position in the network and showed extensive collaboration links with multiple countries. China also appeared as a major node, and the link between China and the USA had the highest total link strength (TLS) in the network, indicating particularly strong bilateral collaboration.

In addition to these major hubs, several regional clusters were observed. For example, Brazil, Spain, and France formed a closely connected cluster, while Italy anchored another cluster. Asian countries such as India and South Korea also formed active subgroups. Overall, the country-level collaboration pattern showed features of a core-periphery network, with several major hubs connected to multiple regional clusters.

4.2.2. Institutional level

At the institutional level, the distribution of research output and citation impact also showed marked heterogeneity (Table 2 and Figure 5). The University of Kentucky ranked first with 58 publications, indicating the highest institutional productivity in this field. In contrast, institutions such as the University of California, Davis, New York University, and Uppsala University had lower publication counts but relatively high average citation rates, suggesting strong citation performance per paper.

Between these patterns, several institutions combined relatively high productivity with moderate citation impact, including the Chinese Academy of Sciences, the Federal University of Espirito Santo, and National Taiwan University. Together, these institutions contributed substantially to the field's overall publication output.

The institutional collaboration network (Figure 6) showed multiple collaborative clusters rather than a single centralized structure. The Chinese Academy of Sciences occupied a central position within the mainland China cluster, which showed dense internal collaboration. The University of Kentucky functioned as another major hub and maintained collaboration links with institutions in North America and Europe. A visible connection was observed between these two major institutional nodes.

Additional regional sub-networks were also apparent. For example, the Taiwan region cluster, centered on National Taiwan University, showed close collaboration among member institutions such as National Yang Ming University. Another cluster centered on the Federal University of Espirito Santo linked South American institutions with European collaborators. Overall, institutional collaboration in this field was characterized by several major hubs and multiple coexisting clusters.

4.3. Core author analysis: Temporal evolution of major contributors

To examine the distribution of scientific productivity, Lotka's law was applied to the author dataset (Figure 7). Lotka's law suggests that a small number of highly productive authors account for a substantial proportion of publications, whereas most authors contribute only one or a few papers.[56] As shown in Figure 7, the author distribution in this field broadly followed this pattern: most authors published only one or two papers, whereas a relatively small group showed high productivity.

Based on this distribution, the trajectories of the most productive authors were further examined (Figure 8). The author map suggests a temporal evolution in the field, with some authors being more active during the earlier development stage and others contributing more prominently in later years. Authors such as Hennig B, Toborek M, Kaji T, and Robertson LW were active during the early phase of the field, particularly from approximately 1998 to 2010. Among them, Hennig B and Toborek M, both affiliated with the University of Kentucky, showed sustained productivity and a close collaborative relationship over an extended period. Their work was frequently cited and was mainly associated with early studies on legacy pollutants such as PCBs and oxidative stress-related mechanisms.

From around 2011 onward, another group of highly productive authors became more prominent, including Petriello MC, Su TC, Lin CY, and Morris AJ. These authors showed increased publication activity after 2015. In particular, Petriello MC published several influential papers between 2016 and 2018. This temporal pattern suggests a gradual shift in the core contributor group. It also appears to coincide with a broader shift in research emphasis, from traditional persistent pollutants to newer EDCs, such as PFAS and PAEs, and to susceptible populations.

4.4. Core journal analysis

Analysis of source journals provides insight into the publication structure and disciplinary distribution of this field. The journal distribution exhibited a relatively concentrated pattern consistent with Bradford's law[57,58], as illustrated in the Bradford's law polar chart (Figure 9). A core set of 16 journals accounted for a substantial proportion of the publications, whereas the remaining articles were distributed across 344 journals in Zones 2 and 3. This pattern indicates that the literature in this field is concentrated in a limited number of major publication venues.

To further examine the characteristics of the core

journals, their publication output and citation performance were analyzed over time (Figures 10 and 11). In terms of publication volume, the *International Journal of Molecular Sciences* showed a marked increase, particularly after 2020, and became one of the most productive journals in recent years.

In terms of citation performance, *Environmental Health Perspectives* consistently published highly cited papers across different periods of the field's development. *Toxicology and Applied Pharmacology* also showed sustained citation impact across multiple years. In contrast, *PLOS One* appeared to contribute several influential papers during the period around 2010–2015. Taken together, these results suggest that several journals played a stable role in disseminating influential studies, whereas others were more prominent during specific developmental periods. Figures 10 and 11 further indicate that numerous core journals belonged to the Q1 category.

4.5. Core knowledge map: Keyword co-occurrence and burst analysis

4.5.1. Knowledge structure: Three highly connected keyword domains

The keyword co-occurrence network (Figure 12) was used to characterize the overall knowledge structure of research on EDC-induced vascular toxicity. Based on co-occurrence patterns, the network could be broadly divided into three thematic clusters.

The blue cluster was centered on terms such as oxidative stress, heavy metals, cadmium, and lipid peroxidation, reflecting studies on classical pollutants and redox-related injury. The red cluster included terms such as endothelial cells, expression, apoptosis, and nuclear factor kappa B, reflecting research oriented toward cellular and molecular mechanisms. The green cluster was characterized by terms such as exposure, atherosclerosis, EDCs, and CVD, indicating links between exposure assessment and broader disease-related outcomes.

Among all keywords, exposure, oxidative stress, and atherosclerosis were the most prominent nodes in the network, exhibiting high connection density (Figure 13). These co-occurrence patterns indicate that studies in this field frequently connect environmental exposures, mechanistic investigation, and vascular or cardiovascular outcomes. Within this pattern, exposure appeared as a frequent upstream term associated with specific chemicals and population-level studies; oxidative stress occupied a central position and was closely linked to both toxicant-related and cellular mechanism-related terms; and atherosclerosis was a major outcome-related keyword connected to both exposure-related and mechanistic research.

4.5.2. Research frontiers: Increasing attention to novel pollutants and susceptible populations

Keyword burst analysis (Figure 14) was used to identify changes in research emphasis over time. Earlier burst terms included traditional pollutants such as dioxin and PCBs, whereas more recent burst terms include dibutyl PAE (burst strength = 3.65 since 2022) and perfluoroalkyl substances (burst strength = 3.96 since 2021). These patterns indicate increasing recent attention to emerging EDCs.

In addition, children showed a relatively strong recent burst (burst strength = 4.21, since 2021), indicating growing attention to susceptible populations and early-life exposure windows. Mechanism-related terms such as inflammation and endothelial dysfunction also showed recent bursts of activity, suggesting continued interest in mechanistic refinement alongside shifting exposure concerns.

Overall, the burst patterns suggest that the field has broadened from an earlier emphasis on traditional industrial pollutants to increasing interest in newer chemical exposures, mechanism-related processes, and vulnerable populations.

5. Discussion

This study used bibliometric methods to characterize the development, knowledge structure, and emerging trends of research on EDC-induced vascular toxicity. Overall, the findings suggest that the field has expanded from a relatively focused mechanistic literature toward a broader perspective that increasingly incorporates exposure complexity, susceptible populations, and long-term vascular health.

5.1. Deepening the core mechanism: Oxidative stress and emerging oxidative-inflammatory crosstalk

One of the most prominent findings of this study is the central position of oxidative stress in the keyword network. In bibliometric terms, this indicates that oxidative stress has been among the most frequently cited mechanistic concepts in the literature on EDC-induced vascular injury. However, this centrality should be interpreted cautiously: it reflects the structure of published research attention rather than, by itself, definitive biological primacy. Even so, when considered alongside the broader experimental literature, this result is consistent with the view that oxidative stress has served as a major mechanistic entry

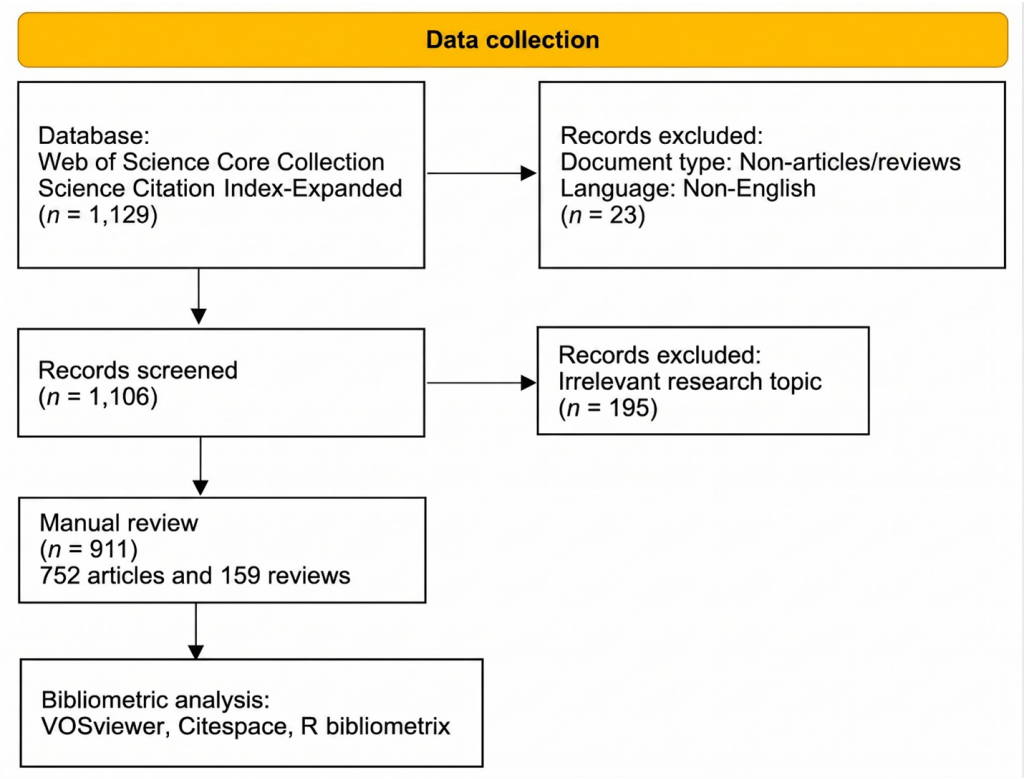


Figure 1. Data collection flowchart. Figure created by the authors.

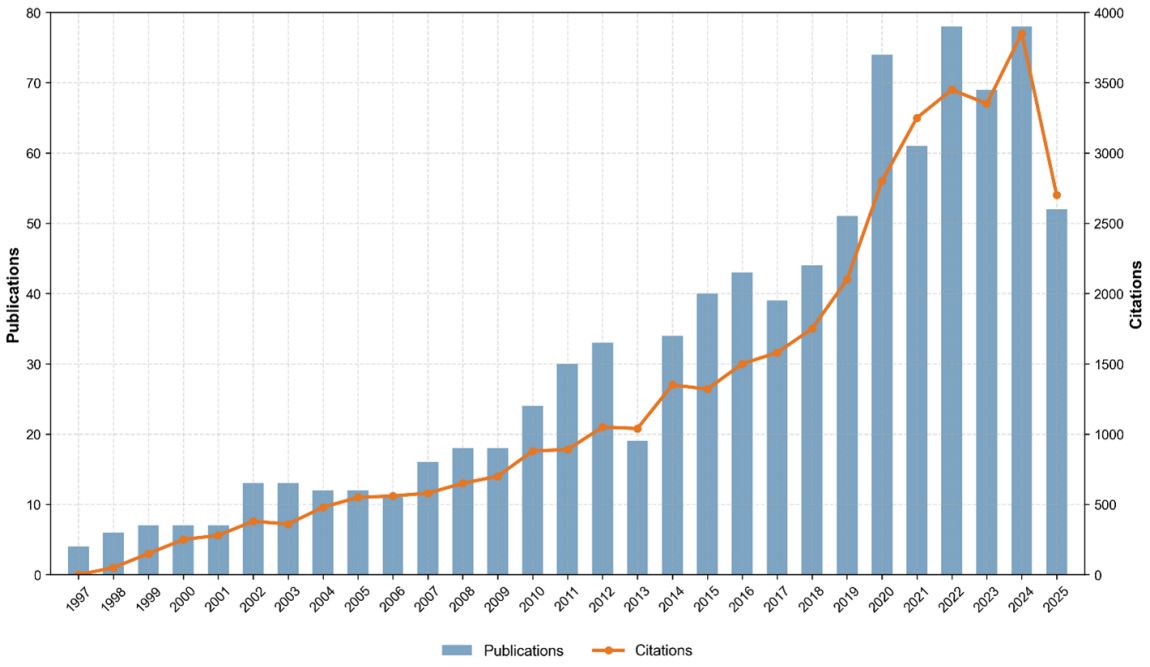


Figure 2. Temporal analysis of publication output and citation impact. The bar chart shows the number of publications per year (left y-axis), and the line chart shows the cumulative number of citations received by the documents published in each year (right y-axis). The decline in recent years, particularly in 2025, is a statistical artifact resulting from the data retrieval date and the inherent time lag required for publications to accumulate citations; it does not indicate a downturn in the field's research momentum. This figure was generated using R based on bibliographic data retrieved from the Web of Science Core Collection.

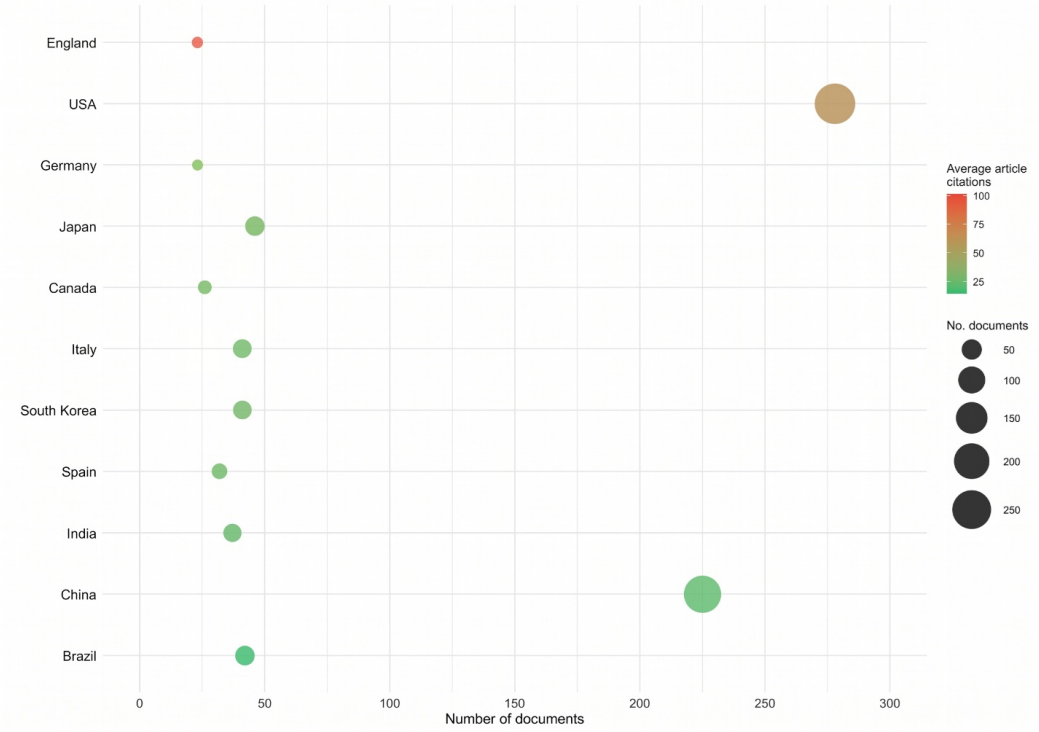


Figure 3. Analysis of scholarly output and citation impact for leading countries. This bubble chart provides a comparative analysis of the most productive countries in the field. Each bubble represents a country. Its position on the x-axis and its size correspond to the total number of documents published, while its color indicates the average article citations. This figure was generated using R based on bibliographic data retrieved from the Web of Science Core Collection.

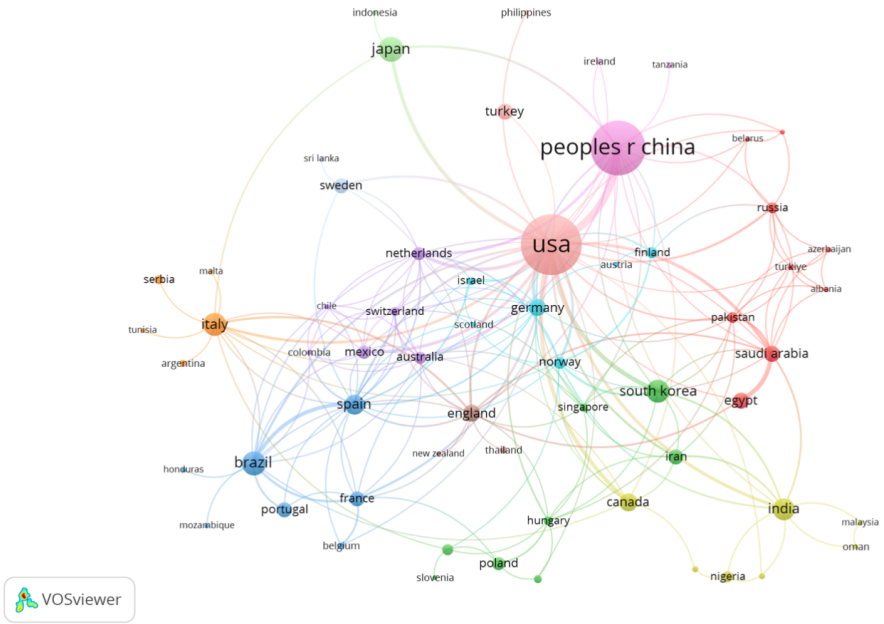
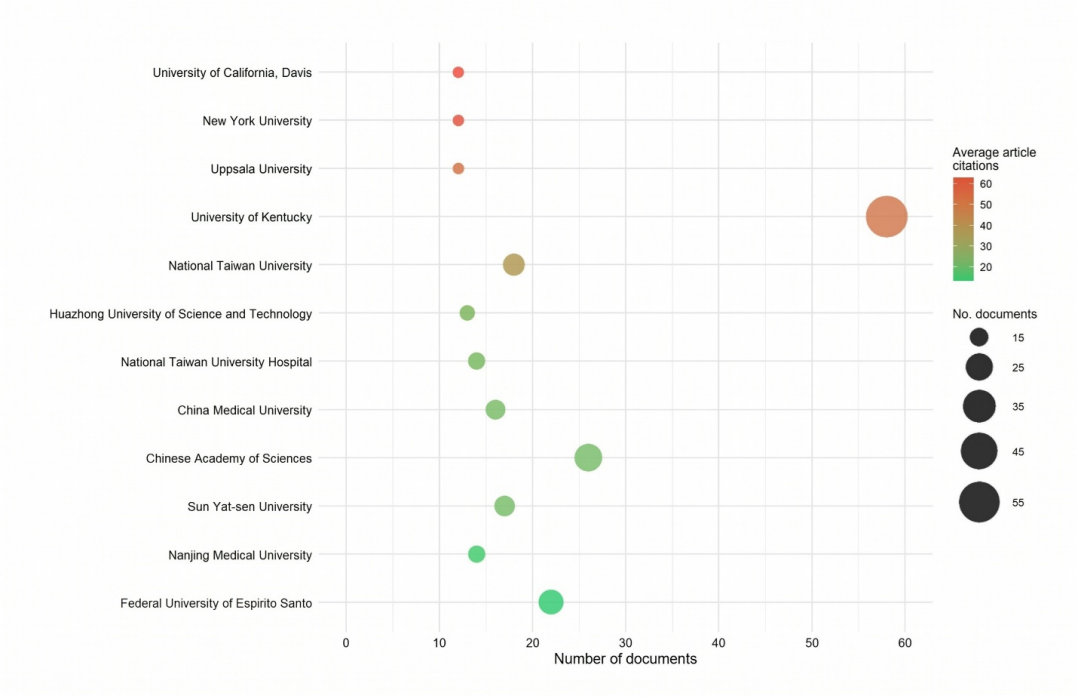


Figure 4. A co-authorship network analysis of countries. This network visualization illustrates the international collaboration patterns among countries in the research field. Each node represents a country, with its size corresponding to its scholarly output (e.g., number of documents). The links between nodes signify co-authorship relationships, and their thickness represents the link strength. This visualization map was generated using VOSviewer based on bibliographic data retrieved from the Web of Science Core Collection.



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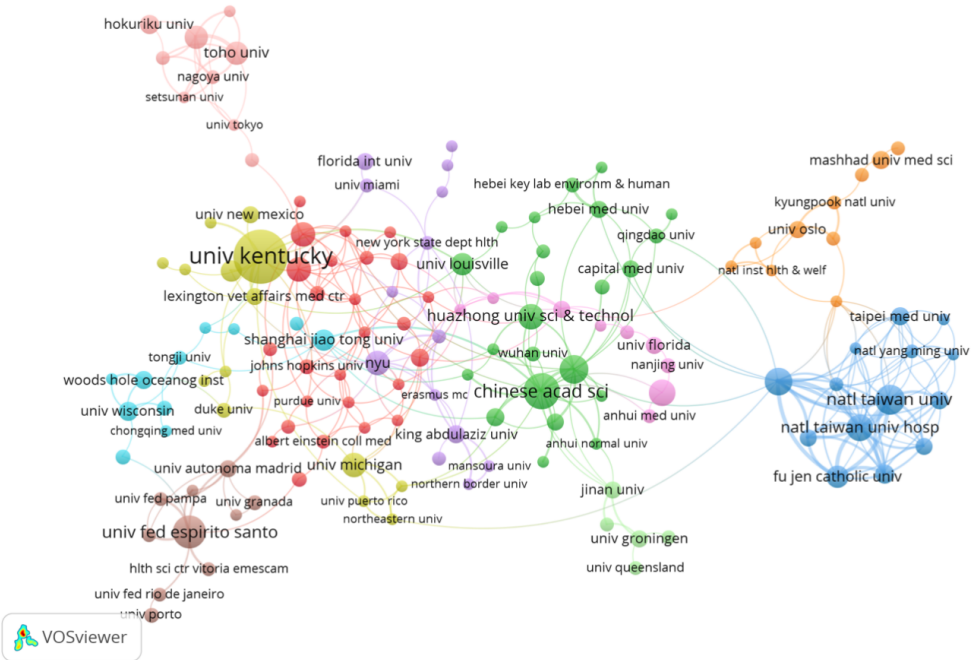

Figure 6. A visualization of the co-authorship network of institutions. This network map illustrates the collaboration patterns among research institutions in this field. Each node represents an institution, with its size corresponding to its scholarly output (e.g., number of documents). The links between nodes signify co-authorship relationships, and their thickness represents the strength of these connections. This visualization map was generated using VOSviewer based on bibliographic data retrieved from the Web of Science Core Collection.

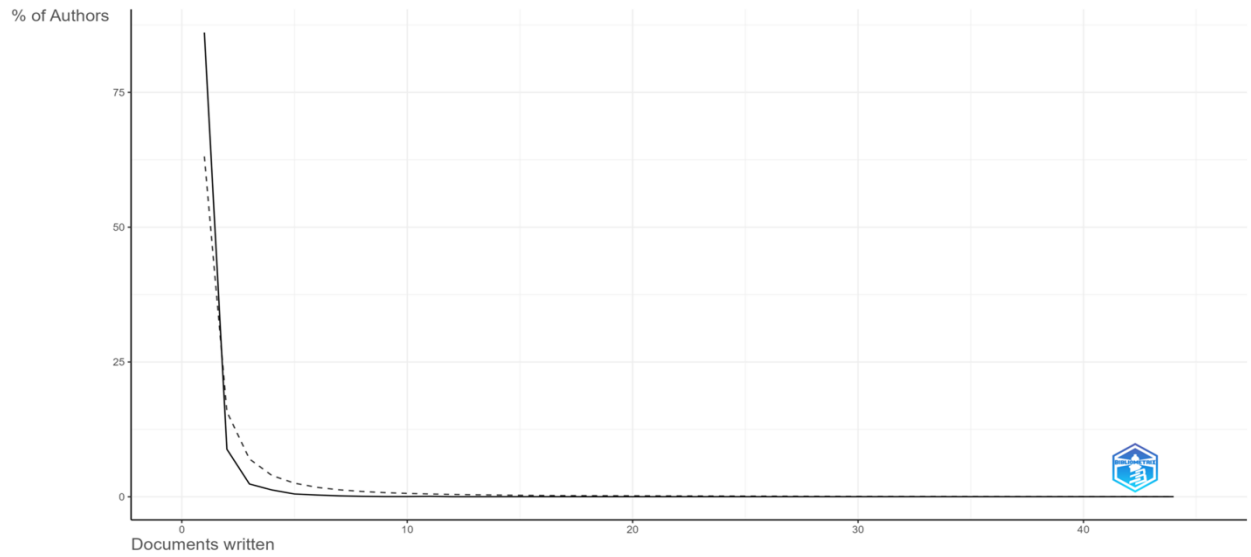

Figure 7. Author productivity distribution according to Lotka's law. The graph illustrates the frequency distribution of author productivity. The solid line represents the observed percentage of authors who have written a specific number of documents (x-axis), while the dashed line shows the theoretical distribution predicted by Lotka's law. The steep curve shows that most authors contribute only one or two papers, whereas a very small number are highly prolific, confirming the presence of a core group of researchers in this field. This figure was generated using R based on bibliographic data retrieved from the Web of Science Core Collection.

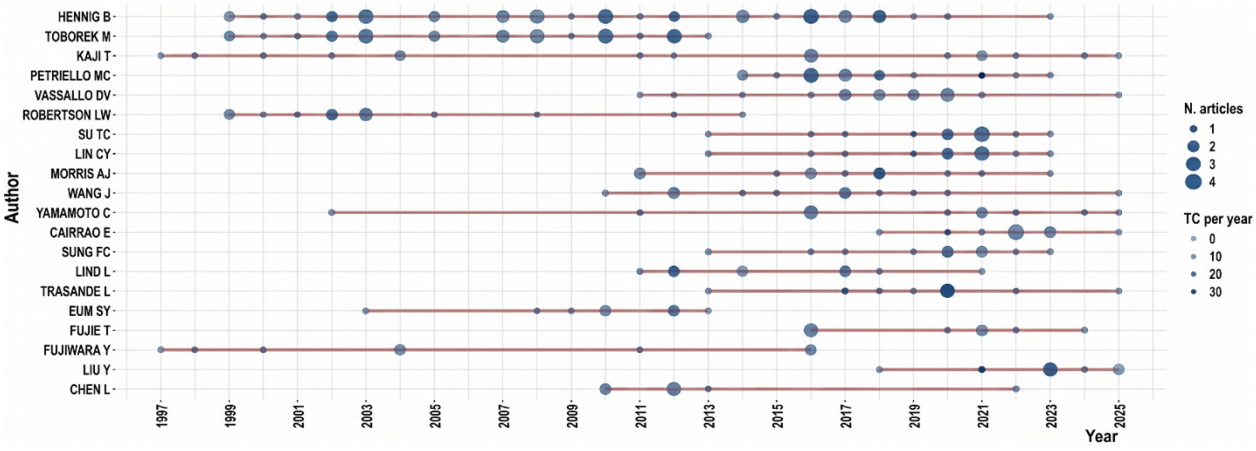

Figure 8. Longitudinal analysis of author productivity and impact. This plot illustrates the temporal distribution of annual publication volume (N. articles) and total citations per year (TC per year) for leading authors in the field. The y-axis lists the authors, and the x-axis represents the year. The size of each data point is proportional to the author's article count for that year, while its color shade is proportional to the TC per year for articles published in that year, indicating scholarly impact. This figure was generated using R based on bibliographic data retrieved from the Web of Science Core Collection.

point for understanding how environmental exposure may translate into vascular dysfunction.

Importantly, the burst analysis further showed that inflammation and endothelial dysfunction have received increased attention in recent years. This pattern suggests that the field may be moving beyond a relatively simple oxidative stress-centered model toward a more integrated framework that incorporates oxidative stress, inflammation, and endothelial injury. Such a shift is meaningful because vascular toxicity is unlikely to be explained solely by ROS generation. Rather, oxidative imbalance may interact with inflammatory signaling, endothelial activation, altered nitric oxide bioavailability, and vascular remodeling, thereby contributing jointly to atherosclerotic progression and broader cardiovascular outcomes. In this sense, the observed bibliometric pattern may reflect a gradual conceptual transition from identifying oxidative stress

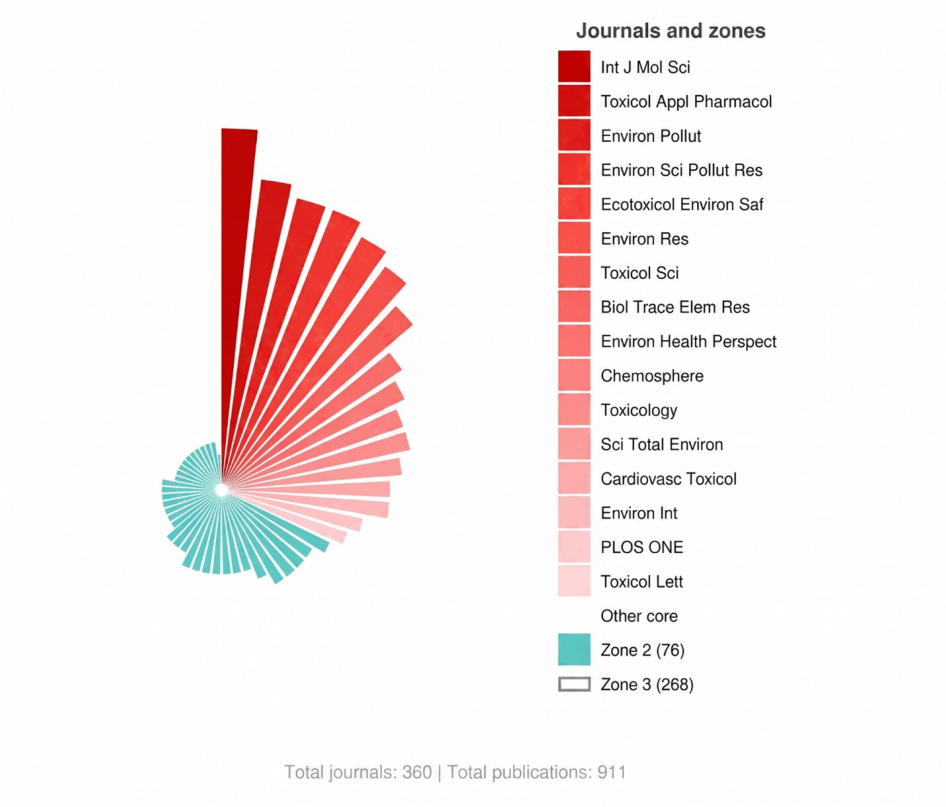

Figure 9. Bradford's law polar chart of the distribution of top 50 journals. This chart visualizes the distribution of journals, sorted by publication frequency, according to Bradford's law. It partitions the 360 total journals into three zones: a "Core" of 16 journals (shown in red segments), Zone 2 (76 journals), and Zone 3 (268 journals). The chart shows a high concentration of literature, with the small core zone accounting for a significant share of all publications. This figure was generated using R based on bibliographic data retrieved from the Web of Science Core Collection.

Figure 10. Temporal analysis of core journals' productivity and impact. This bubble chart maps the performance of the top 16 core journals over time. For each journal, its publication output per year is represented by the size of the bubbles, and the scholarly impact is indicated by the color of the bubbles (darker blue signifies higher average citations). Average citations per article were calculated as of the retrieval date and were not field-normalized. The background shading categorizes journals by their 2024 impact factor: dark gray (>8), light gray (4–8), and white (<4), providing a direct measure of journal prestige. This figure was generated using R based on bibliographic data retrieved from the Web of Science Core Collection.

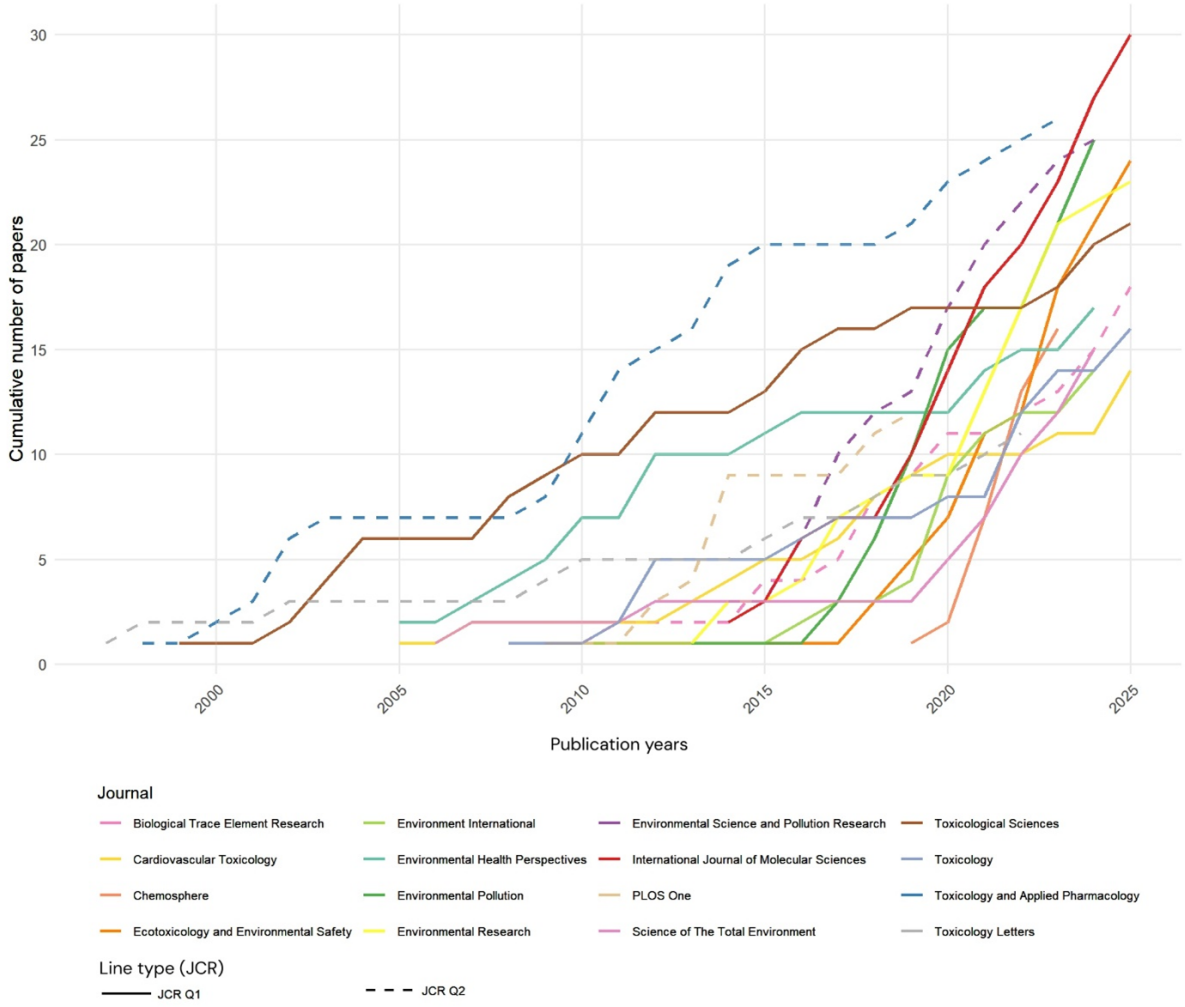

Figure 11. Cumulative publication growth and quality of core journals. This line chart shows the cumulative number of publications over time for each core journal, illustrating their growth trajectories. The line style distinguishes the journals based on their Journal Citation Reports (JCR) quartile ranking: a solid line for Q1 and a dashed line for Q2. This visualization highlights both the field's early contributors and the journals driving its more recent acceleration, while also underscoring the sustained high quality of the primary publication venues. This figure was generated using R based on bibliographic data retrieved from the Web of Science Core Collection.

as a common toxicological response to examining how it participates in a broader pathogenic network.

This interpretation also helps explain why oxidative stress remains highly visible in the literature while newer mechanistic terms are beginning to emerge. Oxidative stress may still function as a shared mechanistic language across different pollutant classes, experimental models, and disease contexts, whereas inflammation and endothelial dysfunction increasingly provide the next level of biological refinement. Therefore, the present findings do not suggest that oxidative stress should be replaced as a key concept, but rather that its interpretation in this field may need to become more relational and system-oriented.

5.2. Blind spots in the knowledge map: Neglected genotoxicity and the "hidden" epigenetic-omics axis

Although oxidative stress appeared as a central node in the keyword network, the knowledge map also suggests that some biologically relevant downstream mechanisms remain insufficiently integrated at the bibliometric level. A notable example is genotoxicity-related injury. ROS generated during oxidative stress are not only functional disruptors of endothelial signaling but may also act as endogenous DNA-damaging agents. Mechanistically, ROS-induced nuclear DNA strand breaks can trigger overactivation of poly(ADP-ribose) polymerase-1 (PARP-1), leading to rapid depletion of nicotinamide adenine

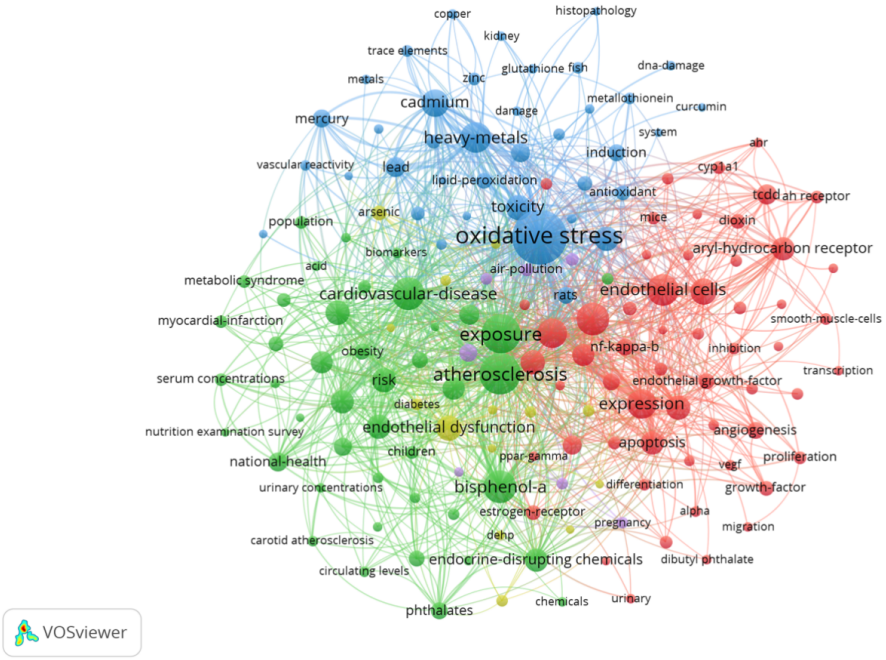

Figure 12. Keyword co-occurrence network in research on endocrine-disrupting chemical-induced vascular toxicity. This network visualization illustrates the thematic structure of the field based on keyword co-occurrence. Each node represents a high-frequency keyword, node size reflects occurrence frequency, and links between nodes indicate co-occurrence relationships. Link thickness reflects the strength of co-occurrence, and colors represent different thematic clusters. This visualization map was generated using VOSviewer based on bibliographic data retrieved from the Web of Science Core Collection.

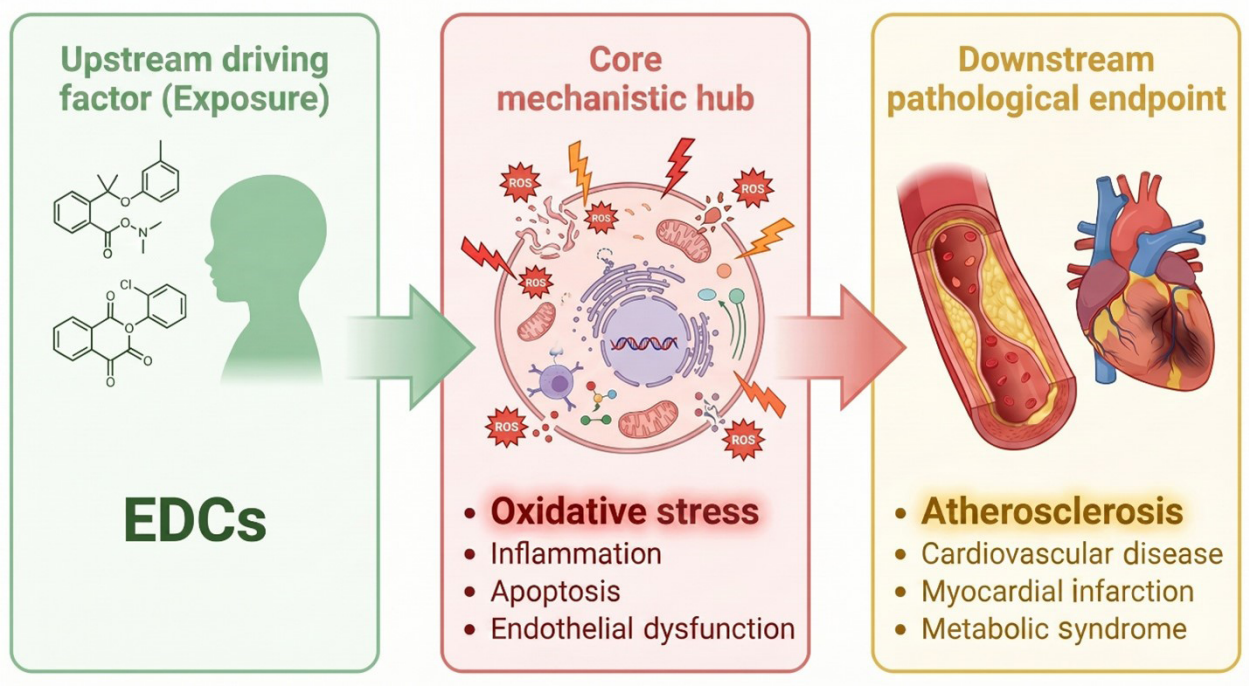

Figure 13. Schematic summary of recurrent keyword relationships in the literature. This schematic summarizes the recurrent pattern identified by the keyword co-occurrence analysis, linking exposure-related, mechanistic, and vascular outcome-related terms. The figure was created by the authors based on the keyword structure observed in the Web of Science Core Collection dataset.

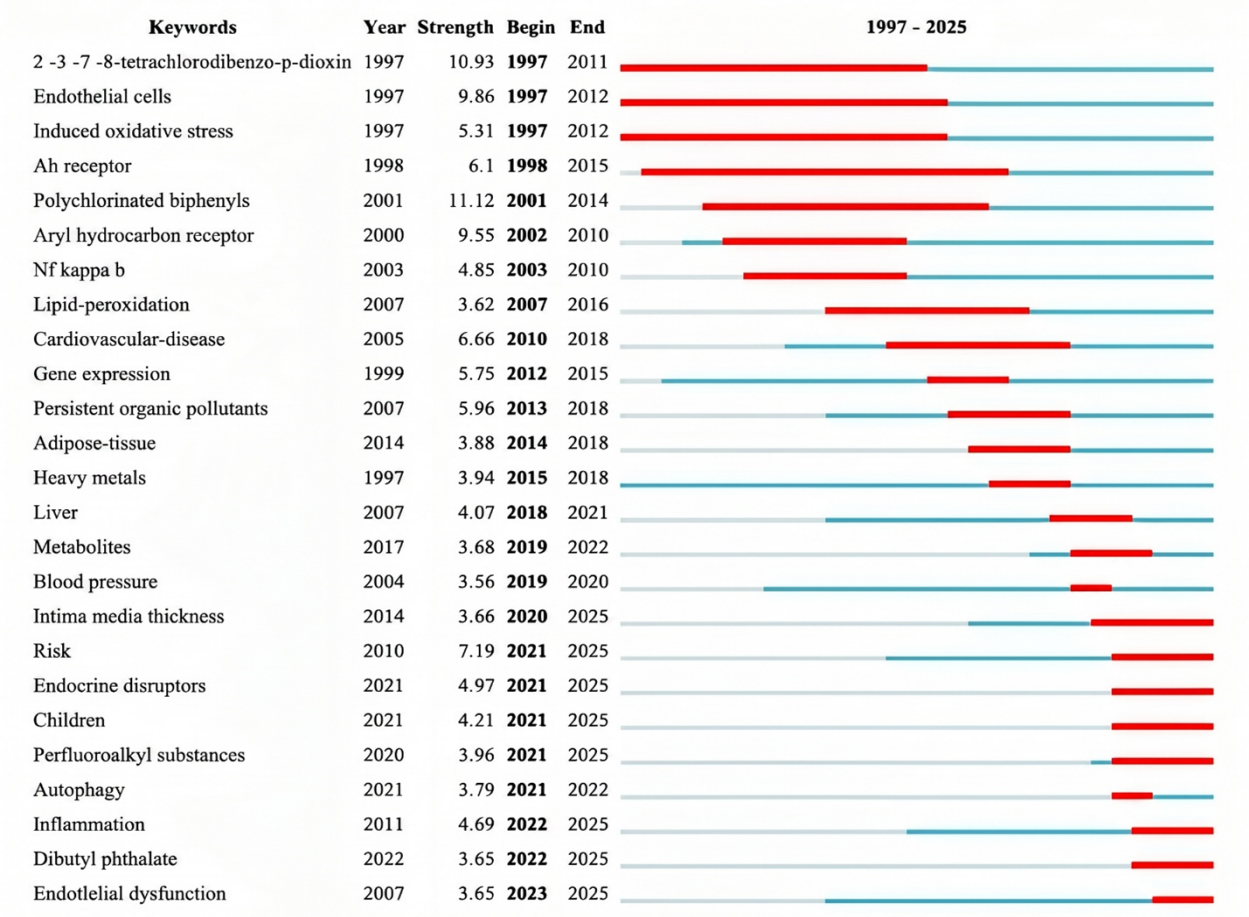

Figure 14. Top 25 keywords with the strongest citation bursts. This figure identifies keywords showing a marked increase in attention between 1997 and 2025. The red bars indicate the burst period for each keyword, and the corresponding start year, end year, and burst strength are shown alongside each term. This figure was generated using CiteSpace based on bibliographic data retrieved from the Web of Science Core Collection.

Table 1. Top 10 most productive countries/regions in endocrine-disrupting chemical-induced vascular toxicity research

Rank	Country	Documents	Total citations	Average citations/document
1	USA	278	18,430	66.29
2	China	225	4,981	22.14
3	Japan	46	1,609	35.00
4	Brazil	42	607	14.45
5 (tie)	Italy	41	1,329	32.41
5 (tie)	South Korea	41	1,222	29.80
7	India	37	865	23.38
8	Spain	32	887	27.72
9	Canada	26	900	34.62
10 (tie)	England	23	2,337	101.61
10 (tie)	Germany	23	813	35.35

Table 2. Top 10 most productive institutions in endocrine-disrupting chemical-induced vascular toxicity research

Rank	Organization	Documents	Total citations	Average citations/document
1	University of Kentucky (USA)	58	2,989	51.53
2	Chinese Academy of Sciences (China)	26	567	21.81
3	Federal University of Espirito Santo (Brazil)	22	294	13.36
4	National Taiwan University (Taiwan, China)	18	699	38.83
5	Sun Yat-sen University (China)	17	366	21.53
6	China Medical University (China)	16	362	22.63
7 (tie)	National Taiwan University Hospital (Taiwan, China)	14	330	23.57
7 (tie)	Nanjing Medical University (China)	14	206	14.71
9	Huazhong University of Science and Technology (China)	13	316	24.31
10 (tie)	University of California, Davis (USA)	12	754	62.83
10 (tie)	New York University (USA)	12	745	62.08
10 (tie)	Uppsala University (Sweden)	12	628	52.33

dinucleotide (oxidized form) and ATP, which may in turn contribute to endothelial necrosis and plaque instability.[59,60] In parallel, oxidative stress has been linked to reduced activity of sirtuins (SIRT) such as SIRT1 and SIRT6, as well as telomere damage, thereby promoting endothelial senescence and the development of a senescence-associated secretory phenotype.[61–63] In addition, mitochondrial DNA (mtDNA) is particularly vulnerable to oxidative injury, and accumulating evidence suggests that mtDNA damage may accelerate atherosclerosis by impairing respiratory chain function, even without further ROS amplification.[64–66] Importantly, some EDCs, including BPA and PAEs, have been reported to act as mitochondrial toxicants by altering membrane potential, impairing ATP generation, and disturbing mtDNA copy number and biogenesis.[67]

Yet, in the present bibliometric analysis, terms such as PARP-1, mtDNA damage, senescence, DNA methylation, and miRNA regulation did not emerge as prominent core nodes. This absence should not be interpreted as evidence that these mechanisms are unimportant. More plausibly, it may reflect terminological dispersion, model heterogeneity, or the fact that these topics are often embedded within narrower mechanistic studies rather than forming highly standardized bibliometric clusters. In other words, the literature may already contain these signals, but they have not yet converged into dominant keywords within the field-level map.

This point is important because it highlights a potential mismatch between bibliometric visibility and mechanistic depth. The current keyword structure captures what is most commonly emphasized across the literature, but it may underrepresent slower, cumulative, or less uniformly labeled processes that contribute substantially to long-term vascular injury. From this perspective, epigenetic regulation may represent a particularly important hidden axis. Oxidative stress may act upstream of epigenetic change by altering methyl donor availability, chromatin state, non-coding RNA expression, and other regulatory processes, thereby helping to translate transient exposure events into more persistent vascular consequences. Such mechanisms are especially relevant in the context of chronic low-dose exposure, where overt toxicity may be less evident than long-term molecular reprogramming.

Accordingly, one meaningful future direction is not simply to add more mechanistic detail, but to better integrate these dispersed processes into the broader exposure-mechanism-endpoint framework. Multi-omics approaches may be particularly useful in this regard. Metabolomics could help identify early systemic signatures of exposure and vascular stress, whereas transcriptomics and epigenomics may help map the regulatory pathways linking oxidative imbalance to durable endothelial dysfunction. In this sense, the bibliometric "blind spots" identified here may be valuable precisely because they point to areas where the field remains conceptually fragmented despite substantial biological plausibility.

5.3. The shifting research frontier: Public health implications and a life-course perspective

The burst analysis suggests that the research frontier is shifting in two related directions: toward newer pollutants and toward more exposure-sensitive populations. The increasing prominence of terms such as perfluoroalkyl

substances and dibutyl PAE indicates that the field is no longer centered primarily on traditional persistent pollutants such as dioxins and PCBs. This change may reflect both shifts in the composition of real-world chemical exposure and growing scientific concern about contaminants widespread in contemporary consumer environments. Compared with many legacy pollutants, these newer EDCs are often associated with more diffuse, continuous, and low-dose exposure scenarios, which may partly explain why they are attracting increasing attention in vascular toxicity research.

At the same time, the emergence of children as a recent burst keyword suggests that the field is increasingly incorporating a life-course perspective. Early-life exposure to EDCs may alter vascular developmental programming through epigenetic mechanisms, including DNA methylation and histone modification, thereby increasing susceptibility to CVD in adulthood.[50,68] Within this framework, childhood is not simply another demographic subgroup, but a biologically sensitive period during which environmental perturbation may have disproportionate and long-lasting effects. This may help explain why recent research has become more attentive to critical windows of exposure rather than focusing only on adult toxicological outcomes.

Importantly, these two shifts are conceptually connected. The turn toward emerging pollutants is not only a change in chemical objects of study; it also coincides with increased concern about long-term, cumulative, and population-wide exposure patterns. Similarly, the turn toward children and early-life exposure is not merely an expansion of study populations, but a shift in how vascular risk is framed—from immediate toxicity to developmental susceptibility and delayed health consequences. In that sense, the field may be moving from a model dominated by mechanistic demonstration in conventional systems toward one that increasingly engages with vulnerability, timing, and prevention.

That said, bibliometric findings alone cannot determine regulatory priorities or quantify actual population risk. What they can show is how scientific attention is being redistributed. In the present study, that redistribution points toward a growing convergence between mechanistic vascular toxicology and broader environmental health concerns. Future work may therefore need to place greater emphasis on low-dose chronic exposure, mixture effects, maternal-child exposure pathways, and the translation of experimental findings into epidemiological and preventive frameworks.

5.4. Global research landscape: A data-driven perspective on collaboration and field development

The country- and institution-level analyses indicate that research on EDC-induced vascular toxicity is distributed across multiple regions but remains shaped by several prominent hubs. The United States ranked first in both publication output and total citations, and it occupied a central position in the collaboration network. China ranked second in publication volume and also showed strong network connectivity. In addition, the collaboration link between the United States and China had the highest TLS in the network. These results suggest that the field is shaped to a considerable extent by the activity of a limited number of highly productive national centers and strong bilateral or multilateral collaboration among them.

However, these collaboration patterns should be interpreted carefully. Co-authorship networks reflect patterns of documented research collaboration, not direct evidence of knowledge hierarchy, causal information flow, or strategic dominance. Even so, the observed network structure does suggest that some countries and institutions play disproportionately important roles in sustaining research output, shaping collaborative visibility, and linking otherwise more regionally bounded clusters. The institutional map similarly showed that the field is not organized around a single unified center, but rather around several coexisting hubs, including the University of Kentucky, the Chinese Academy of Sciences, and other regionally influential institutions.

This pattern of "concentrated leadership with clustered expansion" may help explain how the field has developed over time. Early highly productive authors and institutions appear to have established much of the initial mechanistic foundation, especially around legacy pollutants and oxidative stress-related pathways, whereas newer contributors have become increasingly active in studies of PFAS, PAEs, and susceptible populations. Thus, the global landscape is shaped not only by geography, but also by a temporal layering of expertise: foundational groups appear to have helped define the early mechanistic agenda, while emerging networks are broadening the field toward new exposure scenarios and public health questions.

More broadly, the coexistence of central hubs and regional subnetworks may have both advantages and limitations. On the one hand, concentrated hubs can promote continuity, the accumulation of expertise, and international visibility. On the other hand, regionally clustered collaboration may also be associated with uneven research capacity, fragmented data systems, and differences in pollutant regulation or exposure monitoring.

For this reason, stronger cross-regional collaboration may be important not merely as a matter of network expansion, but as a way to improve comparability across exposure contexts, harmonize methodological approaches, and strengthen the global relevance of future vascular toxicity research.

6. Limitations

Although this study sought to provide a comprehensive and objective overview, several limitations should be acknowledged. First, the dataset was derived exclusively from the WoSCC. Although WoSCC is widely used in bibliometric research because of its relatively standardized indexing and citation information, reliance on a single database may have affected the representativeness of the retrieved literature. Relevant studies indexed in other databases, such as Scopus or PubMed, may not have been captured, particularly those published in regional or interdisciplinary journals or in sources with different indexing policies. This may have led to the underrepresentation of certain countries, institutions, research communities, or topic areas. As a result, the observed publication trends, citation performance, collaboration patterns, and the apparent prominence of specific themes may partly reflect the coverage characteristics of WoSCC rather than the complete global research landscape.

Second, only English-language publications were included. This may have introduced language bias and further contributed to the underrepresentation of research from non-English-speaking regions, thereby influencing country-level productivity rankings, collaboration network structures, and the visibility of region-specific research topics.

Third, bibliometric analysis relies primarily on titles, abstracts, author keywords, and citation records rather than full-text evaluation. Consequently, the identified keyword clusters and thematic structures may emphasize standardized terms while underestimating mechanistic details that are less consistently described across studies. This may partly explain why some biologically relevant pathways do not appear as prominent nodes in the bibliometric network.

Fourth, although the literature screening was conducted independently by two researchers and disagreements were resolved through discussion or consultation with a third senior researcher, a formal inter-reviewer agreement statistic was not calculated. This may affect the transparency and reproducibility of the screening process.

Finally, citation-based indicators are subject to a time-lag effect. Recently published studies, particularly those addressing emerging EDCs or newly developing mechanisms, may not yet have accumulated sufficient citations to be fully represented in co-citation networks or burst analyses. As a result, the latest research frontiers may be underestimated to some extent.

7. Conclusion

This study used bibliometric and visualization methods to provide a structured overview of global research on EDC-induced vascular toxicity. The findings show that this field has expanded steadily over time, with the United States and China emerging as major contributors and important hubs for collaboration. Keyword-based analyses indicate that the published literature frequently connects environmental exposure, oxidative stress, and vascular outcomes, while recent research attention has increasingly shifted toward emerging contaminants, inflammation-related mechanisms, endothelial dysfunction, and vulnerable populations, particularly children.

Overall, these patterns suggest that research in this field is moving from a relatively focused mechanistic literature toward a broader perspective that incorporates exposure complexity, developmental vulnerability, and long-term vascular health. At the same time, some biologically relevant processes, including epigenetic regulation and other less standardized mechanistic pathways, appear less visible in the bibliometric map, which may reflect conceptual fragmentation rather than lack of importance.

Future research may benefit from stronger cross-regional and interdisciplinary collaboration, as well as closer integration of bibliometric, experimental, epidemiological, and multi-omics evidence. Greater attention to low-dose chronic exposure, mixture effects, and critical early-life windows may help improve the mechanistic resolution and public health relevance of this field, thereby providing a more robust basis for risk assessment and preventive strategies.

Acknowledgments

The authors acknowledge the Web of Science Core Collection database for providing the bibliometric data used in this study.

Funding

None.

Conflict of 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.

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Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data

Data for this study were retrieved from the Science Citation Index Expanded within the Web of Science Core Collection database (https://webofscience.clarivate.cn).

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