

Mapping publication trends in oral anticoagulation in atrial fibrillation: A bibliometric and thematic analysis of 11,039 publications (2006–2025)

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ABSTRACT

OBJECTIVE: This study aimed to systematically map the intellectual evolution, thematic development, and collaborative patterns of oral anticoagulation research in atrial fibrillation (AF) from 2006 to 2025.

METHODS: This bibliometric study analyzed 11,039 documents indexed in the Web of Science Core Collection (2006–2025) using the Bibliometrix R package (version 4.x) within the R statistical environment (version 4.3.1) for comprehensive science mapping. The analytical workflow comprised descriptive performance analysis, collaboration network analysis, keyword co-occurrence analysis, strategic thematic mapping, and latent Dirichlet allocation (LDA) topic modeling.

RESULTS: Publication output increased exponentially from 2 articles per year (2006) to a peak of 960 per year (2021), with subsequent stabilization that may reflect consolidation of the field. The United States produced the highest number of publications (3636; 32.9%). The RE-LY trial received the most citations (n=8788). Thematic mapping revealed two main research clusters: Motor themes (141 keywords), representing direct oral anticoagulant agents, stroke prevention, and clinical outcomes; and emerging/declining themes (43 keywords), including venous thromboembolism and pharmacokinetics. LDA topic modeling identified nine distinct research domains encompassing real-world data, safety reporting, and implementation guidelines.

CONCLUSION: The bibliometric patterns observed are consistent with a maturing research field, characterized by a gradual shift from efficacy-focused randomized trials toward real-world effectiveness studies, implementation science, and personalized anticoagulation strategies. Future research may benefit from increased emphasis on long-term adherence, health-economic outcomes, and personalized approaches integrating genetic, clinical, and patient-centered factors.

Keywords: Anticoagulants; atrial fibrillation; bibliometrics; periodicals as topic; stroke.

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Atrial fibrillation (AF) is the most prevalent sustained cardiac arrhythmia encountered in clinical practice, affecting more than 59 million individuals worldwide and conferring an approximately five-fold increased risk of ischemic stroke [1]. Thromboembolic risk in AF arises from impaired atrial contractility, blood stasis, and endothelial dysfunction, with thrombus formation oc-

curing predominantly within the left atrial appendage [2]. For decades, Vitamin K antagonists (VKAs), particularly warfarin, constituted the cornerstone of stroke prevention in AF; however, their clinical use has been limited by a narrow therapeutic window, frequent drug–food interactions, and the need for continuous coagulation monitoring [3].



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The introduction of direct oral anticoagulants (DOACs) – beginning with dabigatran (Food and Drug Administration approved 2010), followed by rivaroxaban (2011), apixaban (2012), and edoxaban (2015) – fundamentally reshaped anticoagulation therapy by offering predictable pharmacokinetics, fixed dosing regimens, and comparable or superior efficacy relative to warfarin [4–7]. The terms DOAC and non-VKAs oral anticoagulant (NOAC) are used interchangeably in the literature to denote the same drug class; for consistency, the term DOAC is used throughout this article, except where NOAC appears within an indexed author keyword or an original publication title. Large-scale randomized controlled trials – RE-LY, ROCKET-AF, ARISTOTLE, and ENGAGE AF-TIMI 48 [4–7] – collectively enrolled more than 70,000 patients and established DOACs as first-line agents for stroke prevention in contemporary AF management guidelines [8, 9]. These trials marked a pivotal shift in both clinical practice and research activity, triggering rapid expansion of the literature addressing efficacy, safety, and clinical implementation.

Following the publication of these landmark trials, research emphasis progressively extended beyond randomized efficacy studies toward guideline development, post hoc analyses, real-world effectiveness, and special population studies. This expansion is consistent with the growing clinical adoption of oral anticoagulation in AF, which has progressively extended from controlled trial settings to widespread clinical application. Nevertheless, despite the substantial volume of publications generated over the past two decades, the structural evolution of this research domain – including thematic development, collaborative patterns, and shifting research priorities – has not been comprehensively examined through data-driven computational methodologies.

Bibliometric analysis offers quantitative tools for evaluating scientific production, citation impact, authorship networks, and conceptual relationships within a research field [10]. When combined with thematic mapping approaches, bibliometrics enables the identification of core research themes, emerging topics, and declining areas based on keyword co-occurrence and network structure [11]. Thematic analysis classifies research themes according to their centrality (relevance to the broader field) and density (internal development), positioning them within strategic diagrams that reveal driving forces, niche specializations, and emerging frontiers. Such analyses provide insights that extend beyond traditional narrative reviews by elucidating how knowledge domains evolve over time.

Highlight key points

- This study presents the largest bibliometric dataset to date on oral anticoagulation research in atrial fibrillation, including 11,039 publications from 1,351 journals and 48,486 authors.
- Publication output increased markedly from 2006 to 2021, reflecting the rapid expansion and subsequent maturation of the field.
- Landmark randomized trials and major clinical guidelines, including RE-LY, ARISTOTLE, ROCKET-AF, and the 2020 ESC Guidelines, were the most influential publications.
- The United States led in publication output, while Scandinavian countries showed the highest international collaboration rates and citation impact.
- Thematic analyses showed a shift from efficacy and stroke prevention toward real-world evidence, guideline implementation, and personalized anticoagulation strategies.

The present study aims to systematically map the intellectual evolution – defined as the progression of publication trends, thematic developments, and conceptual shifts – of oral anticoagulation research in AF from 2006 to 2025. Specifically, we sought to (i) characterize temporal publication trends and geographic distribution; (ii) identify highly influential publications, authors, institutions, and journals; (iii) analyze international and author-level collaboration networks; (iv) delineate thematic structures using keyword co-occurrence and strategic thematic mapping; and (v) extract latent research domains through topic modeling. By integrating these complementary objectives, this study provides a comprehensive overview of how AF anticoagulation research has transitioned from foundational clinical trials toward a consolidated, multidisciplinary landscape focused on real-world implementation and personalized care.

MATERIALS AND METHODS

Data Source and Search Strategy

Bibliographic data were retrieved from the Web of Science Core Collection (Clarivate Analytics) on 15 November 2025. A structured Topic Search (TS) strategy was applied, targeting titles, abstracts, author keywords, and Keywords Plus fields. The search query was constructed by combining three conceptual domains: (i) AF –related terms (“atrial fibrillation” OR “auricular fibrillation” OR “AF” OR “AFib”), (ii) thromboembolic and stroke-related outcomes (“stroke” OR “thromboembolism” OR “cerebrovascular”), and (iii) oral anticoagulant agents (“anti-

coagula*" OR "warfarin" OR "vitamin K antagonist" OR "VKA" OR "dabigatran" OR "rivaroxaban" OR "apixaban" OR "edoxaban" OR "DOAC" OR "NOAC").

The complete Boolean query executed in the Web of Science Advanced Search interface was:

TS = ((("atrial fibrillation" OR "auricular fibrillation" OR "AF" OR "AFib") AND ("stroke" OR "thromboembolism" OR "cerebrovascular") AND ("anticoagula" OR "warfarin" OR "vitamin K antagonist" OR "VKA" OR "dabigatran" OR "rivaroxaban" OR "apixaban" OR "edoxaban" OR "DOAC" OR "NOAC")) NOT ("pediatric" OR "pediatric" OR "children" OR "valvular"))*

To ensure data specificity and to limit irrelevant records potentially introduced by the non-specific abbreviation "AF" (e.g., amniotic fluid, alcohol fraction, or unrelated biochemical indices), the three conceptual blocks were coupled using the strict logical AND operator. Consequently, a record was retrieved only if it simultaneously contained at least one specific AF descriptor, one stroke/thromboembolism outcome term, and one explicit oral anticoagulant agent. This multi-domain logical filter constrained non-specific "AF" matches to the anticoagulation–stroke context and substantially reduced the retrieval of irrelevant records.

The timespan was restricted to 2006–2025 to capture the early developmental phase of DOAC research preceding the publication of pivotal randomized controlled trials, as well as subsequent phases of clinical implementation and real-world investigation. Studies focusing exclusively on pediatric populations or valvular AF were excluded using Boolean NOT operators to ensure clinical homogeneity. All retrieved records were exported in BibTeX format for downstream bibliometric analysis. The search was confined to the Science Citation Index Expanded (SCI-EXPANDED) of the Web of Science Core Collection, and no language or document-type restrictions were applied at the search stage. Because a single database was queried, every record carried a unique Web of Science accession number; the exported dataset therefore contained no within-database duplicate records, and no cross-database deduplication was required. No manual exclusion of records was performed beyond the Boolean NOT criteria specified above, preserving a reproducible, algorithmic workflow. Publications indexed in the most recent years may be partially represented due to indexing delays inherent to the Web of Science database.

Bibliometric Analysis

Bibliometric analyses were conducted using the bibliometrix R package (version 4.x; K-Synth Srl, Naples, Italy) within the R statistical environment (version 4.3.1; R Foundation for Statistical Computing, Vienna, Austria) [10]. The Biblioshiny web interface facilitated the interactive exploration and visualization of bibliometric outputs. The analytical workflow comprised five main components: (a) descriptive performance analysis of publication output, citation metrics, and author productivity; (b) collaboration network analysis at author and country levels; (c) conceptual structure analysis based on keyword co-occurrence networks; (d) strategic thematic mapping using centrality and density metrics; and (e) journal productivity assessment based on Bradford's Law. Co-authorship and country collaboration networks were constructed using full counting methods, and network clustering was performed using the Louvain community detection algorithm. Keyword co-occurrence networks were generated from author keywords (DE), applying association strength normalization to reduce bias from highly frequent terms.

Thematic Mapping and Strategic Diagram Analysis

Thematic mapping was performed using the *thematicMap()* function implemented in the bibliometrix package to identify conceptual structures and their interrelationships within the oral anticoagulation–AF research corpus. Themes were derived from author keyword co-occurrence patterns and positioned on a two-dimensional strategic diagram based on centrality and density measures. Centrality represents the degree of interaction between a theme and other themes within the overall network, reflecting its relevance to the field, whereas density reflects the internal cohesion and developmental maturity of the theme. Based on these parameters, themes were classified into four quadrants: motor themes (high centrality, high density), niche themes (low centrality, high density), emerging or declining themes (low centrality, low density), and basic themes (high centrality, low density). In parallel, a keyword co-occurrence network was constructed to visualize relationships among the 50 most frequent keywords, applying a minimum co-occurrence threshold of three and community detection using the Walktrap algorithm.

Topic Modeling Analysis Latent Dirichlet Allocation (LDA)

LDA, an unsupervised probabilistic generative model, was applied to identify latent thematic structures within

the title and abstract text data of the oral anticoagulation literature related to AF. Before model estimation, textual data were preprocessed by converting all terms to lowercase; removing punctuation, numbers, and common English stop words; and applying sparse-term filtering (removing terms appearing in fewer than 0.5% of documents) to improve the signal-to-noise ratio [11].

The LDA model was implemented using the topicmodels package in R [12]. The optimal number of topics (k) was determined by evaluating candidate models ranging from $k=2$ to $k=20$. Model selection relied on standard statistical criteria implemented in the ldatuning package – specifically maximizing the metric of Griffiths and Steyvers [13] while minimizing the metrics of Cao et al., [14] and Arun et al., [15] – evaluated alongside semantic coherence, interpretability, and clinical relevance. These indices converged on an optimal nine-topic solution ($k=9$), which also exhibited peak semantic coherence and distinct clinical interpretability on qualitative review. Final model estimation was performed using Gibbs sampling with a fixed random seed to ensure full reproducibility, applying the default hyperparameter settings of the topicmodels package (a symmetric document–topic Dirichlet prior of $\alpha=50/k$ and a topic–word prior of $\delta=0.1$) and 2000 sampling iterations. Topic–term probability distributions (β matrix) and document–topic allocations (γ matrix) were extracted to characterize the most representative terms associated with each topic and to summarize thematic prevalence at the field level.

Statistical Analysis

Descriptive statistics were used to summarize publication output, citation metrics, and author productivity. Annual growth rates were calculated as compound annual growth rates (CAGR). Statistical results are reported in accordance with the AMA Manual of Style, 11th edition. p -values are expressed without a leading zero (e.g., $p=0.002$; $p<0.001$ for values <0.001); values near 0.05 are reported to three decimal places (e.g., $p=0.053$). All analyses were performed using the R statistical environment (version 4.3.1; R Foundation for Statistical Computing, Vienna, Austria) and the bibliometrix package (version 4.x; K-Synth Srl, Naples, Italy).

Ethical Considerations

This study was based exclusively on publicly available bibliographic metadata obtained from indexed scientific

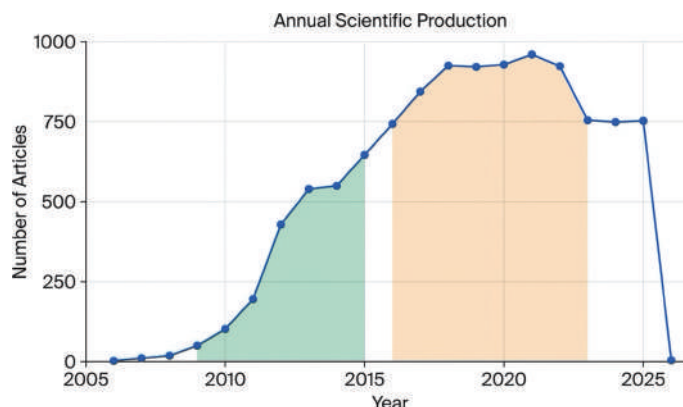


FIGURE 1. Annual scientific production in oral anticoagulation-AF research (2006–2025). The green shaded area indicates the rapid growth phase (2009–2015), and the orange shaded area represents the plateau phase (2016–2023). The decline in 2024–2025 reflects incomplete database indexing at the time of data retrieval.

literature. No human participants, patient-level data, or animal experiments were involved. As this is a bibliometric study utilizing only publicly available data, ethics committee approval was not applicable, and informed consent was not required. The study was conducted in accordance with the principles of the World Medical Association Declaration of Helsinki.

RESULTS

General Characteristics of the Dataset

The bibliometric search yielded a total of 11,039 documents published between 2006 and 2025 across 1351 journals (Table 1). The corpus consisted predominantly of original research articles (7391; 66.9%) and review articles (2304; 20.9%), followed by editorial materials (510; 4.6%), letters (179; 1.6%), and other document types 655 (5.9%). A total of 48,486 unique authors contributed to the dataset. The document-per-author ratio was 0.228, corresponding to an average of 4.39 authors per document, whereas the average number of co-author appearances per document was 11.4, reflecting the contribution of large-scale multicenter collaborations. Internationally co-authored publications accounted for 28.15% of the total output.

The average age of the documents was 6.25 years (mean time since publication), indicating that most articles were published around 2018–2019, with a mean citation count of 26.77 citations per document. The overall citation metrics included an H-index of 195, a G-index

TABLE 1. General characteristics of the bibliometric dataset (Web of Science Core Collection, 2006–2025)

Description	Results
General information	
Timespan	2006–2025
Sources (journals)	1.351
Documents	11.039
Annual growth rate (%)	3.53
Average document age (years)	6.25
Average citations per document	26.77
References	101.838
Citation metrics	
H-index	195
G-index	392
M-index	9.29
Authors	
Total authors	48,486
Documents per author	0.228
Authors per document	4.39
Co-authors per document	11.4
International co-authorships (%)	28.15
Document types	
Articles n (%)	7.391 (66.9)
Reviews	2.304 (20.9)
Editorial material	510 (4.6)
Letters	179 (1.6)
Other types	655 (5.9)
Keywords	
Author keywords (DE)	7.287
Keywords plus (ID)	4.898

DE: Author keywords field (Web of Science); G-index: Cumulative citation impact metric; H-index: Hirsch index (number of papers with ≥H citations); ID: Keywords plus field (Web of Science); M-index: M-quotient (H-index divided by years of academic age).

of 392, and an M-index of 9.29. The dataset contained 7287 author keywords and 4898 Keywords Plus terms, reflecting broad conceptual diversity within the field.

Annual Scientific Production

The annual publication output increased from 2 articles in 2006 to a maximum of 960 articles in 2021 (Fig. 1). Publication growth accelerated markedly after 2009, with sustained high output observed from 2016 onward.

The overall annual growth rate was 3.53%. Based on inflection points in the publication trajectory, two distinct phases were identified: a rapid growth phase (2009–2015), defined as the period when annual publication output exhibited CAGR exceeding 20%, temporally coinciding with DOAC regulatory approvals; and a plateau phase (2016–2023), characterized by sustained high output with annual growth rates below 10%, a pattern often associated with consolidation of a research field. During the plateau phase, publication output remained relatively stable, with approximately 870 articles in 2022 and 790 articles in 2023. The publication counts for the most recent years (2024–2025) were lower, consistent with incomplete indexing at the time of data retrieval.

Most-Cited Publications

Table 2 summarizes the 20 most-cited publications in the field of oral anticoagulation in AF. Randomized controlled trials constituted the majority of highly cited documents (15 of 20). The RE-LY trial [4] received the highest number of citations (n=8788), followed by the ARISTOTLE trial [6] (n=6998), the 2020 ESC Guidelines [1] (n=6958), the ROCKET-AF trial [5] (n=6753), and the ENGAGE AF-TIMI 48 trial [7] (n=3964). Six of the top 20 publications were published in the New England Journal of Medicine, and guideline documents accounted for a substantial proportion of highly cited outputs. Notably, several landmark clinical practice guidelines were simultaneously co-published in more than one journal – for example, the 2016 ESC guideline appeared in both the European Heart Journal and Europace, and the 2019 AHA/ACC/HRS focused update appeared in both Circulation and the Journal of the American College of Cardiology – and were therefore indexed as separate records in the Web of Science. These co-published records are retained as listed in Table 2 but represent the same underlying document and should be interpreted accordingly. The comparatively high citation counts of the most recently published (2023–2024) guidelines reflect the rapid citation accrual that is characteristic of major society guidelines rather than indexing or duplication artifacts.

Geographic Distribution and International Collaboration

The United States was the leading contributor, with 3636 publications (32.9%), followed by the United Kingdom (1666), Germany (1432), Italy (1218), and

TABLE 2. The 20 most-cited publications in oral anticoagulation–atrial fibrillation research (Web of Science Core Collection, 2006–2025)

Rank	First author	Year	Title	Journal	Citations	Study type
1	Connolly et al. [4]	2009	Dabigatran Versus Warfarin in Patients with Atrial Fibrillation	N Engl J Med	8.788	RCT
2	Granger et al. [6]	2011	Apixaban Versus Warfarin in Patients with Atrial Fibrillation	N Engl J Med	6.998	RCT
3	Hindricks et al. [1]	2021	2020 ESC Guidelines for the Diagnosis and Management of Atrial Fibrillation	Eur Heart J	6.958	Guideline
4	Patel et al. [5]	2011	Rivaroxaban Versus Warfarin in Non-valvular Atrial Fibrillation	N Engl J Med	6.753	RCT
5	Giugliano et al. [7]	2013	Edoxaban Versus Warfarin in Patients with Atrial Fibrillation	N Engl J Med	3.964	RCT
6	Ruff et al. [18]	2014	Comparison of Efficacy and Safety of NOACs vs Warfarin in AF: Meta-Analysis	Lancet	3.954	Meta-analysis
7	Kirchhof et al. [9]	2016	2016 ESC Guidelines for the Management of Atrial Fibrillation	Eur Heart J	3.592	Guideline
8	January et al. [8]	2019	2019 AHA/ACC/HRS Focused Update of the 2014 Guideline for Management of AF	Circulation	2.596	Guideline
9	January et al. [8]	2019	2019 AHA/ACC/HRS Focused Update of the 2014 Guideline for Management of AF	J Am Coll Cardiol	2.596	Guideline
10	Schulman et al. [19]	2009	Dabigatran Versus Warfarin in Treatment of Acute Venous Thromboembolism	N Engl J Med	1.982	RCT
11	Connolly et al. [20]	2011	Apixaban in Patients with Atrial Fibrillation	N Engl J Med	1.920	RCT
12	Kirchhof et al. [9]	2016	2016 ESC Guidelines for the Management of AF (Europace)	Europace	1.872	Guideline
13	Steffel et al. [21]	2018	2018 EHRA Practical Guide on NOACs in Patients with AF	Eur Heart J	1.430	Practical guide
14	Holmes et al. [22]	2014	PREVAIL: Watchman LAAC Device vs Long-Term Warfarin in AF	J Am Coll Cardiol	1.374	RCT
15	Joglar et al. [23]	2024	2023 ACC/AHA/ACCP/HRS Guideline for Diagnosis and Management of AF	Circulation	1.254	Guideline
16	Van Gelder et al. [24]	2024	2024 ESC Guidelines for the Management of Atrial Fibrillation	Eur Heart J	1.230	Guideline
17	Camm et al. [25]	2012	2012 Focused Update of the ESC Guidelines for Management of AF	Europace	1.219	Guideline
18	Gibson et al. [26]	2016	Prevention of Bleeding in Patients with AF Undergoing PCI	N Engl J Med	1.214	RCT
19	Kaatz et al. [27]	2015	Definition of Clinically Relevant Non-Major Bleeding in Anticoagulant Studies	J Thromb Haemost	1.127	RCT
20	Van Ryn et al. [28]	2010	Dabigatran Etexilate: Interpretation of Coagulation Assays and Reversal	Thromb Haemost	1.103	Pharmacokinetic

Study types were classified as RCT (randomized controlled trial), guideline, meta-analysis, practical guide, or pharmacokinetic study. ACC: American College of Cardiology; ACCP: American College of Chest Physicians; AF: Atrial fibrillation; AHA: American Heart Association; DOAC: Direct oral anticoagulant; EHRA: European Heart Rhythm Association; ESC: European Society of Cardiology; HRS: Heart Rhythm Society; LAAC: Left atrial appendage closure; NOAC: Non-vitamin K antagonist oral anticoagulant; PCI: Percutaneous coronary intervention; RCT: Randomized controlled trial; VKA: Vitamin K antagonist. Certain landmark guidelines were co-published in more than one journal and are consequently indexed as separate records in the Web of Science (ranks 7 and 12 correspond to the same 2016 ESC guideline; ranks 8 and 9 correspond to the same 2019 AHA/ACC/HRS focused update). These entries are retained as indexed but represent the same underlying document.

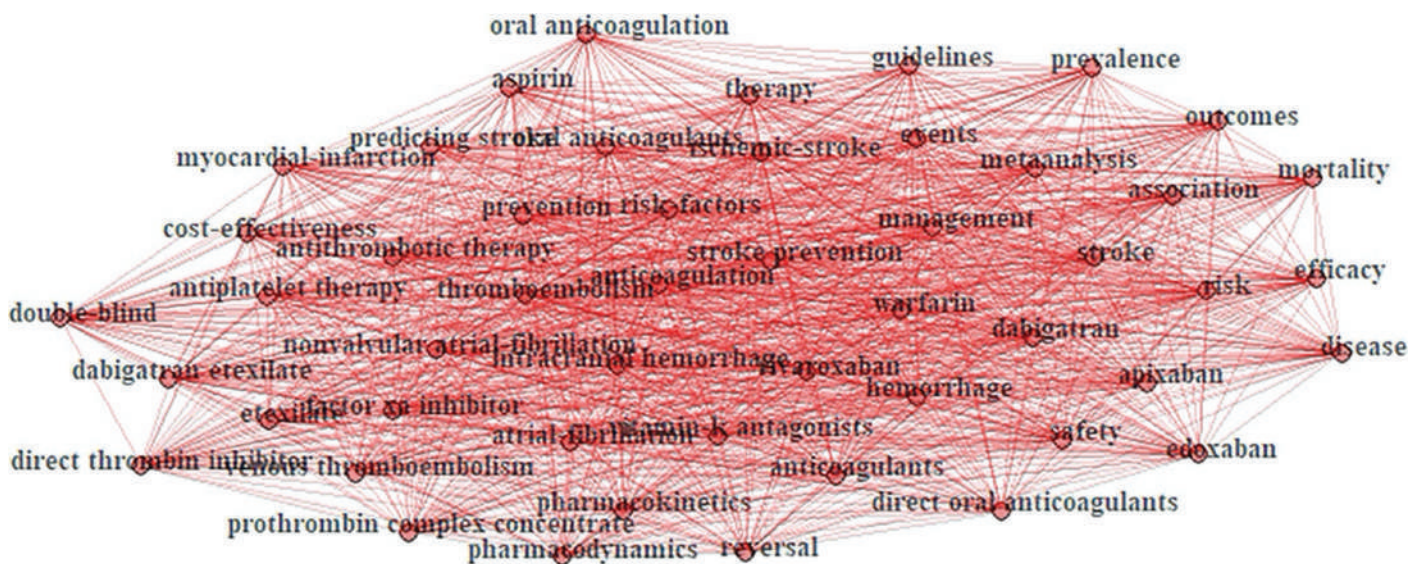


FIGURE 2. Keyword co-occurrence network of the 50 most frequent author keywords (minimum of three co-occurrences). Node size reflects keyword frequency, and edge thickness represents co-occurrence strength. Densely interconnected terms include atrial fibrillation, anticoagulation, stroke, warfarin, and the individual DOAC agents, together with clinical outcome terms such as bleeding, hemorrhage, and mortality.

Canada (1082) (Appendix Table 1). These five countries accounted for 81.8% of total publications. International collaboration rates varied widely across countries, with Denmark (90.2%), Sweden (87.2%), and France (87.2%) exhibiting the highest proportions of multi-country publications. In terms of citation impact, the United States accumulated the highest total number of citations (160,626), whereas Sweden achieved the highest average citations per article (140.7). Country collaboration network analysis revealed a central cluster dominated by the United States and Western European countries, with additional peripheral clusters involving Southern Europe, Eastern Europe, and Asia (Appendix Fig.1).

Leading Authors and Institutions

Author productivity analysis identified the most prolific contributor with 544 publications and a field-specific h-index of 76 (Appendix Table 3). The second- and third-ranked authors had 160 publications (h-index=56) and 156 publications (h-index=62), respectively. The highest average citation counts per article were 321.6, 251.0, and 227.7 for the three most-cited authors. Institutional analysis revealed the leading institution with 889 publications, followed by the second- (694 publications) and third-ranked institutions (576 publications) (Appendix Table 2). The highest citation impact among leading institutions was an average of 137.5 citations per article.

Co-authorship network analysis of the top 50 authors revealed three major collaborative clusters corresponding to large clinical trial consortia, with several bridge authors connecting multiple research groups (Appendix Fig. 2).

Journal Analysis

The most productive journals included *Circulation* (248 articles), the *Journal of Thrombosis and Thrombolysis* (228), *Thrombosis and Haemostasis* (191), and the *International Journal of Cardiology* (185) (Appendix Table 4). The *European Heart Journal* exhibited the highest citation impact, with an average of 138.8 citations per article. Bradford's Law analysis identified 30 core journals (Zone 1) accounting for 3664 articles (33.2% of total output). These journals spanned cardiology, thrombosis and hemostasis, general clinical medicine, and cerebrovascular research domains.

Keyword Co-Occurrence Network

Keyword co-occurrence analysis of the 50 most frequent author keywords identified three distinct thematic clusters (Fig. 2). The first cluster comprised disease- and classical treatment-related terms, including AF, stroke, anticoagulation, and warfarin. The second cluster consisted of DOAC-specific agent terms such as dabigatran, rivaroxaban, apixaban, edoxaban, and DOACs. The third cluster included clinical outcome-related terms, in-

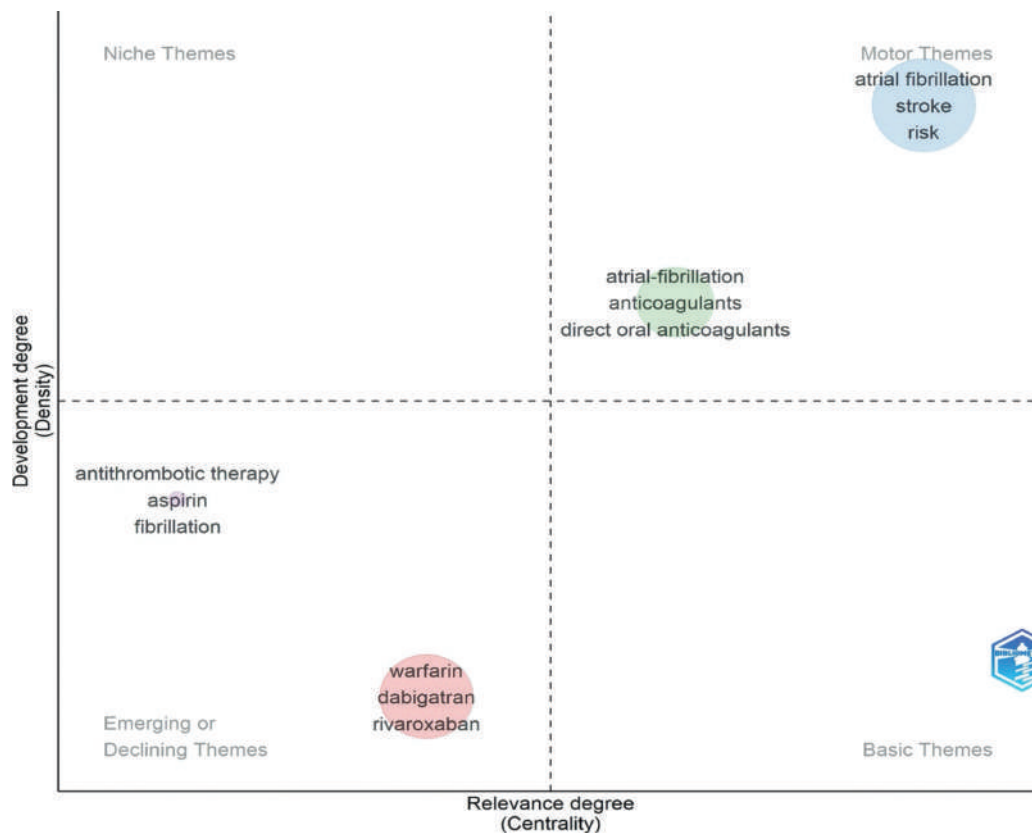


FIGURE 3. Thematic map (strategic diagram). Research themes are positioned based on centrality (x-axis: relevance to the field) and density (y-axis: theme development). Motor themes (atrial fibrillation, stroke, risk) occupy the upper-right quadrant; basic/transversal themes (anticoagulants, direct oral anticoagulants) lie along the central axis; antithrombotic therapy and aspirin appear as niche-leaning themes; and warfarin, dabigatran, and rivaroxaban occupy the emerging or declining lower-left quadrant.

cluding bleeding, hemorrhage, safety, mortality, and major bleeding. Strong co-occurrence links were observed between AF and stroke, as well as among individual DOAC agents and safety endpoints, reflecting the literature's continued focus on balancing ischemic prevention against hemorrhagic risk.

Thematic Map Analysis

Strategic thematic mapping positioned research themes according to centrality and density measures (Fig. 3). Motor themes, characterized by high centrality (0.215) and high density (1.62), comprised 141 keywords with 50,718 total occurrences and included DOAC agents (warfarin, dabigatran, rivaroxaban, apixaban), stroke prevention, and clinical outcomes (risk, stroke, bleeding, and safety-related terms). The positioning of these themes in the upper-right quadrant indicates that DOAC agents and stroke prevention represent the field's driving research forces. Emerging or declining themes consisted of 43 keywords with 10,860 total occurrences and included

pharmacokinetics, venous thromboembolism, and mechanistic concepts in the lower-left quadrant. Additional clusters corresponding to niche themes and basic themes were also identified based on their relative centrality and density positions.

Thematic Evolution

Temporal thematic evolution analysis was performed across five periods defined on the basis of significant milestones in the field rather than equal time intervals: 2006–2015, 2016–2018, 2019–2020, 2021–2023, and 2024–2025 (Fig. 4). The earliest period was dominated by foundational themes of AF, warfarin, and stroke prevention. Through the middle periods (2016–2020), antithrombotic therapy and aspirin appeared alongside the consolidation of AF as the central theme, while procedural concepts such as catheter ablation became increasingly visible, and risk emerged as a persistent dominant node. In the most recent periods (2021–2025), management, risk stratification, and an-

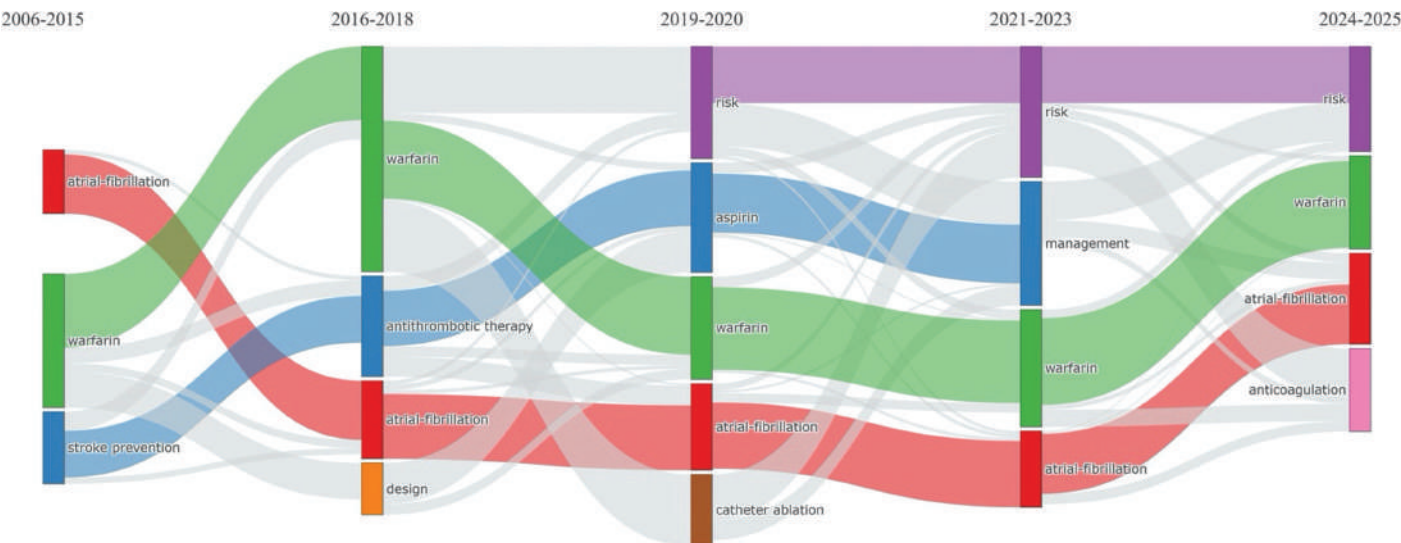


FIGURE 4. Thematic evolution across 5 time periods (2006–2025). Sankey diagram illustrating the temporal evolution of research themes across five periods: 2006–2015, 2016–2018, 2019–2020, 2021–2023, and 2024–2025. Node width represents keyword frequency within each period (wider nodes indicate higher occurrence); connecting flows indicate thematic continuity between consecutive periods, with flow thickness proportional to the strength of thematic linkage.

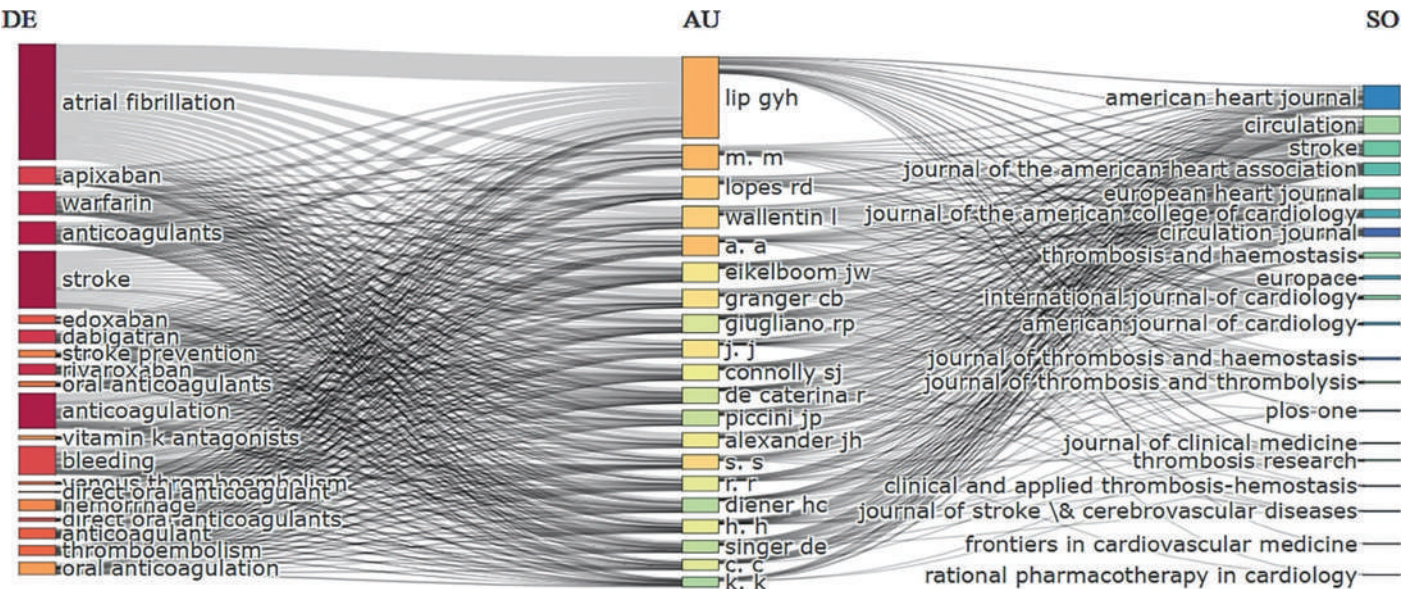


FIGURE 5. Three-field plot: author–keyword–journal relationships. Sankey diagram depicting relationships among the top 20 keywords (left, DE), top 20 authors (center, AU), and top 20 journals (right, SO). Flow width represents the strength of associations based on co-occurrence frequency. The central hub author (Lip GYH) connects multiple keyword clusters to diverse journal outlets, and direct oral anticoagulants-specific keywords demonstrate dual-pathway dissemination through both thrombosis-focused and cardiology-oriented journals.

ticogulation became increasingly prominent, reflecting a shift toward clinical implementation and patient management rather than agent characterization alone. The overall trajectory illustrates a clear conceptual migration from early stroke-prevention and warfarin-centered models toward AF-specific, management-oriented research.

Author–Keyword–Journal Relationships

The three-field plot illustrating relationships among the top 20 authors, top 20 keywords, and top 20 journals demonstrated that Lip GYH occupied the central hub position, connecting multiple keyword clusters to diverse journal outlets (Fig. 5). DOAC-specific keywords exhibited dual-

pathway dissemination through both thrombosis-focused and cardiology-oriented journals, reflecting the multidisciplinary evolution of anticoagulation research in AF.

Topic Modeling Results LDA

LDA analysis identified nine distinct topics within the corpus (Appendix Table 5): (1) bleeding risk and clinical outcomes, (2) stroke prevention and risk stratification, (3) comparative NOAC versus VKA trials, (4) pharmacology and dosing strategies, (5) guideline-oriented management, (6) antithrombotic therapy and complications, (7) mechanistic studies, (8) venous thromboembolism, and (9) real-world data and prescribing patterns. Topic prevalence analysis demonstrated a relatively uniform distribution across topics, with mean document–topic proportions (γ) ranging tightly between 0.105 and 0.119, indicating that the literature maintains integrated, multi-pronged investigation rather than fragmenting into isolated niches.

DISCUSSION

This bibliometric analysis indicates that research on oral anticoagulation in AF has undergone marked quantitative expansion and thematic diversification over the past two decades. The observed publication trajectory highlights a rapid growth phase between 2009 and 2015, temporally aligned with the publication of pivotal randomized trials and subsequent regulatory approvals of DOACs, followed by a phase of sustained high output suggestive of consolidation within the field. The continued prominence of trial investigators such as Wallentin, Lopes, and Granger in author productivity rankings illustrates the enduring influence of landmark clinical trials and their investigators, who have extended their contributions beyond efficacy trials to post hoc analyses, real-world evidence generation, and guideline development.

Our findings extend and contextualize previous bibliometric work in the anticoagulation field. Earlier bibliometric analyses of AF and anticoagulation, such as those examining NOACs in cardiovascular disease or specific aspects like bleeding complications, typically focused on narrower time windows or specific drug classes. In contrast, the present analysis encompasses the complete DOAC era (2006–2025) and employs an integrated strategic thematic and probabilistic topic-modeling workflow, enabling identification of both established motor themes and emerging research frontiers. While confirming the volume dominance of North American and Western European institutions, our data reveal that international collabora-

tion networks – particularly those involving Scandinavian countries – generate disproportionately high citation impact relative to publication volume. Conversely, the comparatively lower international collaboration profile observed in Japan may reflect region-specific regulatory frameworks, healthcare systems, and prescribing practices. Furthermore, whereas prior bibliometric reviews predominantly relied on citation analysis, our integration of LDA topic modeling maps the steady rise of implementation science, real-world data tracking, and health-systems research as increasingly prominent domains.

Two recent bibliometric analyses published in *The Anatolian Journal of Cardiology* provide important methodological parallels. Yang et al., [16] conducted a bibliometric investigation of cryoablation for AF (2002–2022) using Web of Science Core Collection data and CiteSpace visualization, identifying the USA as the leading contributor and demonstrating progressive growth in annual publications, consistent with the trajectory observed in the present study. Similarly, Ekenoglu Merdan and Aydogan [17] applied VOSviewer-based keyword mapping to infective endocarditis literature spanning 130 years (1892–2022) through Scopus, confirming that North American and Western European institutions dominate bibliometric output across cardiovascular subspecialties. Both studies highlight the value of periodic bibliometric repetition and keyword visualization in guiding future research priorities – a principle that directly motivated the methodological design of the present work.

The predominance of the four pivotal DOAC trials – RE-LY, ARISTOTLE, ROCKET-AF, and ENGAGE AF–TIMI 48 – among the most highly cited publications underscores the central role of high-level evidence in shaping contemporary anticoagulation practice; these trials established non-inferiority or superiority of DOACs compared with warfarin for stroke prevention in AF while consistently demonstrating favorable safety profiles, particularly with respect to intracranial hemorrhage [4–7, 18]. The concurrent strong citation impact of clinical practice guidelines reflects an emphasis on translating trial-based evidence into standardized clinical decision-making. Strategic mapping positioned real-world effectiveness and guideline-oriented management as highly central but comparatively less dense themes; this suggests substantial relevance to the field alongside opportunities for further methodological refinement, particularly regarding data heterogeneity across diverse healthcare systems. Collectively, these findings indicate a research landscape that has expanded beyond foundational efficacy trials toward

broader clinical, population-based, and health-system-oriented investigations, while maintaining strong integration across pharmacological and clinical domains.

Study Limitations

Several limitations of this study should be acknowledged alongside potential approaches for their mitigation in future research. First, reliance on the Web of Science Core Collection may have resulted in underrepresentation of studies indexed exclusively in other databases such as PubMed or Scopus; future bibliometric analyses could employ multi-database searches with deduplication algorithms to achieve more comprehensive coverage. Second, although no language restrictions were applied, the predominance of English-language publications in the Web of Science Core Collection may limit the visibility of research conducted in non-English-speaking regions; incorporating region-specific databases such as CNKI (China) or LILACS (Latin America) could address this limitation. Third, citation-based metrics do not distinguish between supportive and critical citations and may be influenced by publication age and journal visibility; emerging approaches such as citation context analysis and altmetrics could provide more nuanced assessments of research impact. Fourth, bibliometric indicators reflect research activity and influence rather than clinical efficacy or patient-level outcomes; future studies integrating bibliometric findings with clinical registry data could bridge this gap. Finally, the LDA approach assumes relative independence between topics, which may oversimplify the interconnected nature of research themes within this field; alternative approaches such as structural topic modeling or dynamic topic models could better capture thematic interdependencies and temporal evolution.

Conclusion

This bibliometric and thematic analysis illustrates the progressive evolution of oral anticoagulation research in AF, with a clear shift from efficacy-focused randomized trials toward real-world effectiveness studies, implementation science, and guideline-oriented clinical practice. The literature demonstrates sustained attention to key domains, including bleeding risk assessment, stroke prevention strategies, drug-specific pharmacology, and prescribing patterns across diverse patient populations. Future research may benefit from increased emphasis on long-term adherence, health-economic outcomes across healthcare systems, and personalized anticoagulation approaches integrating genetic, clinical, and patient-centered factors.

Ethics Committee Approval: This study is a bibliometric analysis based exclusively on publicly available bibliographic data and does not involve human participants, animal subjects, or identifiable personal information. Ethics committee approval was not required.

Informed Consent: Informed consent was not required, as this study did not involve human participants.

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APPENDIX TABLE 1. Top 20 countries by scientific production (2006–2025)

Country	Articles	SCP	MCP	MCP_ratio	Total citations	TC per article
USA	3636	2090	1546	42.5	160626	44.2
United Kingdom	1666	292	1374	82.5	108514	65.1
Germany	1432	498	934	65.2	100471	70.2
Italy	1218	620	598	49.1	47551	39
Canada	1082	326	756	69.9	79244	73.2
China	1048	692	356	34	41556	39.7
Japan	873	651	222	25	~35531	40.7
Denmark	664	65	599	90.2	37354	56.3
Spain	584	308	276	47.3	34201	58.6
Netherlands	581	135	446	76.8	58082	100
France	546	207	339	87.2	62752	66
Sweden	446	57	389	87.2	62752	140.7
Australia	435	165	270	62.1	46991	108
Switzerland	363	80	283	78	31480	86.7
Korea	314	176	138	43.9	14698	46.8
Belgium	296	49	247	83.4	31763	107.3
Poland	287	129	158	55.1	15128	52.7
Russia	232	178	54	23	17746	~76.5
Austria	227	88	139	61.2	8237	36.3
Greece	225	76	149	66.2	19155	85.1

Geographic distribution of publications showing country name, total publications (TP), single-country publications (SCP), multi-country publications (MCP), MCP ratio (%), total citations (TC), and average citations per article (TC per Article). The United States led productivity with 3,636 publications (32.9% of total), followed by the United Kingdom (1,666 publications, 15.1%) and Germany (1,432 publications, 13.0%). Denmark demonstrated the highest international collaboration ratio (MCP ratio: 90.2%), whereas China showed a relatively lower collaboration ratio (MCP ratio: 34.0%), indicating a higher prevalence of single-country publications. Citation impact varied substantially across countries; the United States exhibited high citation impact, reflecting its central role in global oral anticoagulation research, with additional strong impact observed for several high-income countries (e.g., the United Kingdom and Canada). Data Source: Web of Science Core Collection; Analysis Period: 2006-2025; Minimum threshold: Countries with ≥100 publications.

APPENDIX TABLE 2. Top 20 most productive institutions (2006–2025)

Institution	Articles	Total_citations	TC_per_article
McMaster Univ	889	79068	88.9
Univ Birmingham	694	61569	88.7
Duke Univ	576	79208	137.5
Aalborg Univ	554	27297	49.3
Harvard Med Sch	507	25849	51.0
Univ Liverpool	477	19103	40.0
Uppsala Univ	449	52422	116.8
Liverpool Heart and Chest Hosp	361	16125	44.7
Univ Toronto	357	15616	43.7
Brigham and Womens Hosp	316	36609	115.9
Natl Cerebral and Cardiovasc Ctr	248	9223	37.2
Chang Gung Univ	236	7661	32.5
Duke Clin Res Inst	234	17897	76.5
Mayo Clin	233	25081	107.6
Heidelberg Univ	222	18011	81.1
Taipei Vet Gen Hosp	220	13323	60.6
Mcgill Univ	208	8231	39.6
Stanford Univ	203	15173	74.7
Capital Med Univ	196	8098	41.3
Univ Michigan	196	12604	64.3

Institutional productivity ranking showing institution name, total articles, total citations, and average citations per article. McMaster University (Canada) emerged as the most productive institution with 889 articles and 79,068 total citations (88.9 citations per article), serving as the coordination center for the ARISTOTLE and RE-LY trials. The University of Birmingham (UK) ranked second with 694 articles and 61,569 citations (88.7 citations per article). Duke University (USA) demonstrated the highest citation impact among top institutions (137.5 citations per article) despite moderate publication volume (576 articles). Data Source: Web of Science institutional affiliations; Analysis method: Full counting (each institution counted once per publication).

APPENDIX TABLE 3. Top 20 most productive authors with h-index (2006–2025)

Rank	Authors	Articles	Total_citations	TC_per_article	h_index
1	Lip Gregory Y H	544	33304	61.2	76
2	Lopes Renato D	160	18080	113	56
3	Wallentin Lars	156	30692	196.7	62
4	Granger Christopher B	138	16582	120.2	50
5	Eikelboom John W	124	7767	62.6	44
6	Alexander John H	111	14756	132.9	45
7	Giugliano Robert P	103	12726	123.6	38
8	Singer Daniel E	100	14273	142.7	41
9	Piccini Jonathan P	99	16436	166	46
10	Connolly Stuart J	97	20908	215.5	50
11	Halperin Jonathan L	89	22338	251	38
12	Mahaffey Kenneth W	89	14138	158.9	41
13	De Caterina Raffaele	88	6410	72.8	28
14	Hohnloser Stefan H	85	19355	227.7	38
15	Oldgren Jonas	85	27340	321.6	42
16	Okumura Ken	82	2371	28.9	21
17	Ruff Christian T	82	12735	155.3	36
18	Yamashita Takeshi	82	5846	71.3	19
19	Chao Tze-Fan	79	2882	36.5	26
20	Kirchhof Paulus	78	12819	164.3	31

Author productivity ranking including author name, total articles, total citations, average citations per article, and field-specific h-index calculated exclusively for AF anticoagulation publications. Lip Gregory Y.H. emerged as the most prolific author with 544 articles and h-index of 76, reflecting sustained contributions across stroke risk stratification, bleeding risk assessment, and real-world evidence generation. Lopes Renato D. and Wallentin Lars ranked second and third with 160 and 156 articles respectively, both serving as principal investigators for ARISTOTLE. Data Source: Web of Science author metadata; h-index: Field-specific, computed exclusively for AF anticoagulation corpus.

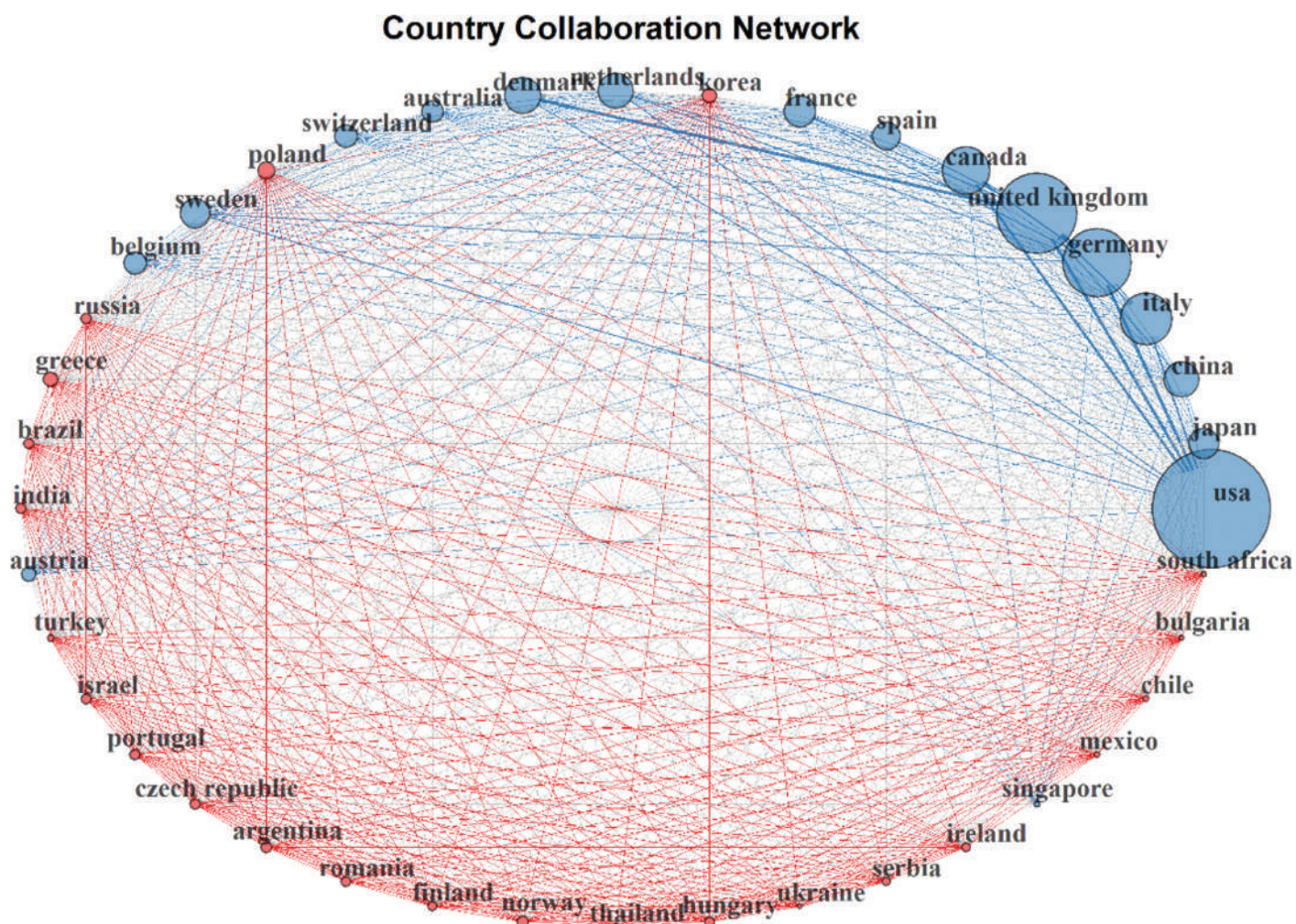
APPENDIX TABLE 4. Top 20 most productive journals with impact factor and bradford zone (2006–2025)

Rank	Journal	Articles	Total_citations	TC_per_article	IF_2023	Quartile	Zone
1	Circulation	248	18223	73.5	37.8	Q1	Zone 1
2	Journal of Thrombosis and Thrombolysis	228	3676	16.1	3.4	Q2	Zone 1
3	Thrombosis and Haemostasis	191	11095	58.1	6.7	Q1	Zone 1
4	International Journal of Cardiology	185	3154	17	3.2	Q2	Zone 1
5	Thrombosis Research	177	3013	17	3.7	Q2	Zone 1
6	Stroke	176	6962	39.6	10.2	Q1	Zone 1
7	European Heart Journal	163	22631	138.8	39.3	Q1	Zone 1
8	Journal of the American Heart Association	150	5669	37.8	5.4	Q1	Zone 1
9	Journal of Clinical Medicine	148	1017	6.9	3.9	Q2	Zone 1
10	Journal of the American College of Cardiology	138	14323	103.8	24	Q1	Zone 1
11	Europace	137	9469	69.1	8.4	Q1	Zone 1
12	American Journal of Cardiology	135	3502	25.9	2.5	Q3	Zone 1
13	Plos One	127	2193	17.3	3.7	Q2	Zone 1
14	American Heart Journal	118	5767	48.9	3.7	Q2	Zone 1
15	Journal of Stroke & Cerebrovascular Diseases	105	1377	13.1	2	Q3	Zone 1
16	Journal of Thrombosis and Haemostasis	99	4345	43.9	6.1	Q1	Zone 1
17	Circulation Journal	98	2778	28.3	3.1	Q2	Zone 1
18	Clinical and Applied Thrombosis-Hemostasis	97	1247	12.9	2.3	Q3	Zone 1
19	Rational Pharmacotherapy in Cardiology	91	83	0.9	0.5	Q4	Zone 1
20	Frontiers in Cardiovascular Medicine	90	667	7.4	3.6	Q2	Zone 1

Journal productivity ranking showing journal name, total articles, total citations, average citations per article, 2023 Impact Factor, quartile classification (Q1-Q4), and Bradford Zone. Circulation published the most articles (248, IF=37.8, Q1, Zone 1), followed by Journal of Thrombosis and Thrombolysis (228, IF=3.4, Q2, Zone 1). Bradford's Law analysis identified 30 journals in Zone 1 (core journals), 296 in Zone 2, and 1,025 in Zone 3 (peripheral journals). All top 20 journals belong to Bradford Zone 1. Data Source: Web of Science; Impact Factors: 2023 Journal Citation Reports; Bradford zones: Calculated by ranking journals by productivity.

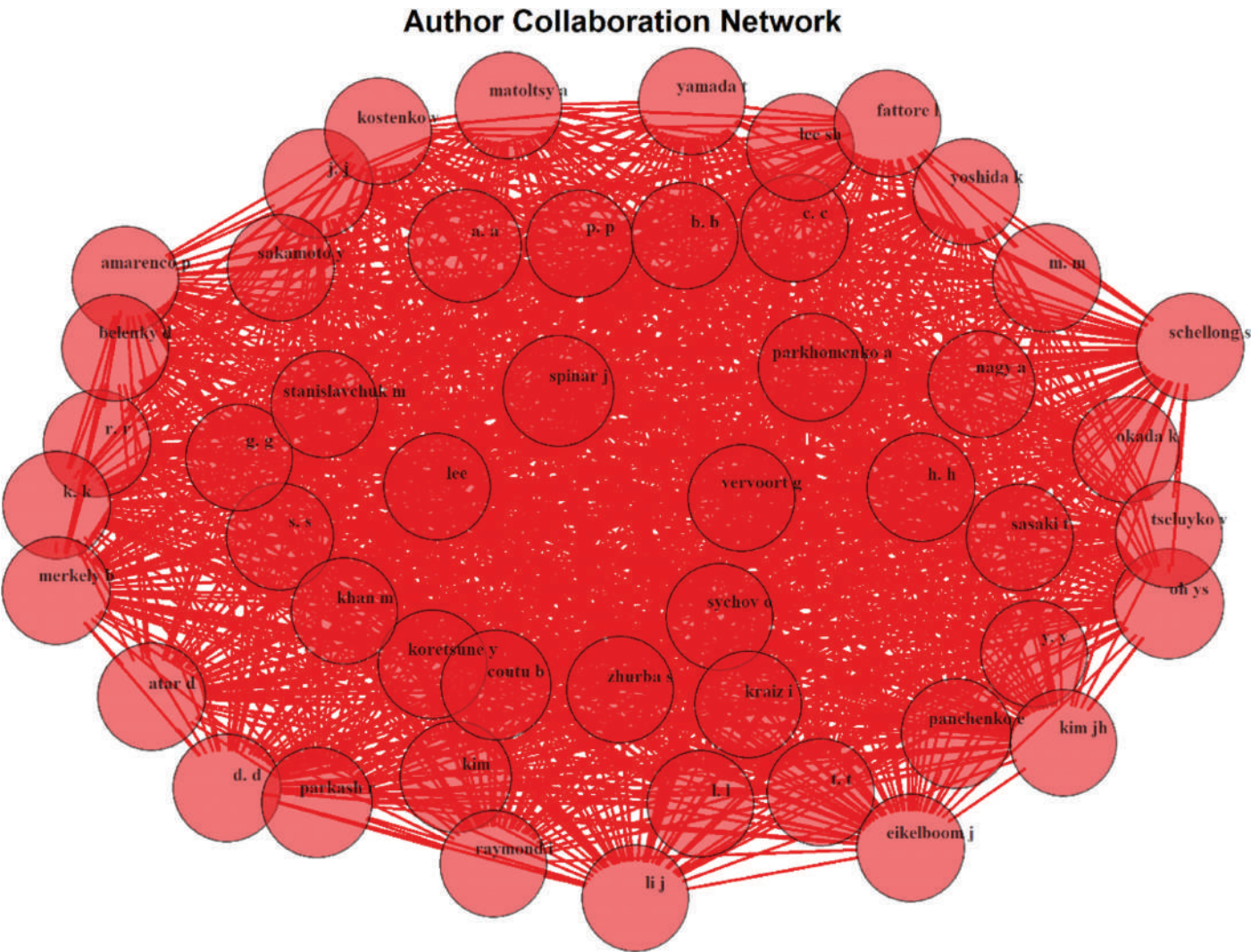
APPENDIX TABLE 5. Latent Dirichlet Allocation (LDA)–derived topics and representative keywords

Topic no	Proposed topic label	Top representative keywords	Conceptual interpretation
Topic 1	Bleeding Risk and Clinical Outcomes	bleed, risk, major, outcome, event, mortal	Focuses on major bleeding events, mortality, and adverse clinical outcomes associated with anticoagulant therapy.
Topic 2	Stroke and Atrial Fibrillation Risk Stratification	stroke, atrial, fibril, ischem, renal, prevent	Represents studies on ischemic stroke prevention and risk assessment in patients with atrial fibrillation.
Topic 3	NOAC vs VKA Comparative Safety and Trials	noac, vka, antagonist, trial, safety, vitamin	Encompasses randomized trials and comparative analyses evaluating safety and efficacy of NOACs versus vitamin K antagonists.
Topic 4	DOAC Pharmacology and Dosing Strategies	warfarin, rivaroxaban, apixaban, dabigatran, dose	Covers pharmacological characteristics, dosing strategies, and drug-specific considerations of oral anticoagulants.
Topic 5	Clinical Practice and Guideline-Oriented Management	clinic, manage, practice, recommend, review	Reflects guideline-based recommendations, clinical management strategies, and real-world practice reviews.
Topic 6	Antithrombotic Therapy and Clinical Complications	therapy, antithrombotic, antiplatelet, complication, coronary	Focuses on antithrombotic and antiplatelet therapies, including associated complications and coronary disease contexts.
Topic 7	Mechanisms of Action and Drug Monitoring	factor, dabigatran, inhibitor, drug, monitor	Represents mechanistic studies on anticoagulant drugs, including factor inhibition and therapeutic monitoring.
Topic 8	Oral Anticoagulation in Venous Thromboembolism	oral, doac, thromboembol, venous, treatment	Addresses the use of oral anticoagulants in venous thromboembolism treatment and prevention strategies.
Topic 9	Real-World Data and Prescribing Patterns	age, score, hospital, prescribe, initiate, year	Captures observational studies focusing on prescribing behavior, risk scores, age-related patterns, and real-world data.



APPENDIX FIGURE 1. Country collaboration network.

Geographic collaboration network visualization (minimum 5 international collaborations) demonstrating international research partnerships. The network comprises 40 countries with node size proportional to publication volume and edge thickness representing collaboration frequency. Two distinct clusters emerged: Cluster 1 (Blue, Core Group) comprises USA, UK, Germany, Canada, Netherlands, and Denmark with dense transatlantic connections. Cluster 2 (Red, Peripheral Group) includes Turkey, Greece, Brazil, India, and Eastern European countries with more limited intercontinental collaborations. The USA occupies the central hub position serving as the primary bridge between European and Asian research groups. Methodology: bibliometrix R package; Minimum 5 collaborations; Louvain community detection; Fruchterman-Reingold layout



APPENDIX FIGURE 2. Co-authorship network (top 50 authors).

Author collaboration network (top 50 authors, minimum 2 joint publications) revealing major trial consortia as organizing structures. Three main clusters identified: Cluster 1 (Lip Gregory Y.H. cluster, Red) focuses on stroke risk stratification and real-world studies. Cluster 2 (ARISTOTLE/Duke cluster, Blue) comprises trial investigators from Duke Clinical Research Institute. Cluster 3 (RE-LY/McMaster cluster, Green) centers at McMaster University. Bridge authors (Connolly SJ, Wallentin L) connect multiple research groups, facilitating cross-trial knowledge transfer. Methodology: bibliometrix; Minimum 2 collaborations; Louvain algorithm; Network metrics: 50 nodes, 187 edges, density 0.153.