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Research Article

Global Research Trends on the Relationship Between Metabolic Syndrome and Mental Health: A Bibliometric and Visual Analysis (2000–2025)

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Background

The bidirectional relationship between metabolic syndrome (MetS) and mental health has emerged as a critical public health concern. However, no comprehensive bibliometric analysis has systematically mapped the knowledge structure and evolutionary trajectory of this interdisciplinary field.

Objective

This study aims to examine the relationship between MetS and mental health through a systematic bibliometric analysis, identifying research hotspots and emerging trends.

Methods

Literature from the Web of Science Core Collection (January 2000 to June 2025) was analyzed using VOSviewer, CiteSpace, and the bibliometrix package in R to examine publication trends, collaboration networks, research hotspots, molecular mechanisms, and disease association patterns.

Results

Analysis of 18,647 publications from 138 countries/regions revealed a 45.7-fold increase in annual publications, from 29 articles in 2000 to 1,324 in 2024, with 46.73% published in the past five years. The United States was ranked first in publication volume (26.75%) and network centrality. Keyword analysis identified 16 thematic clusters, with "inflammation" rising from ninth to fourth position across study periods. "Gut microbiota" emerged prominently post-2016, while "COVID-19" became a burst keyword after 2020. Molecular network analysis identified interleukin-6, insulin, and tumor necrosis factor as central hub proteins. Disease co-occurrence analysis demonstrated strong associations between MetS and depression and between insulin resistance and anxiety.

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Conclusion

This analysis reveals rapid, accelerating growth in MetS–mental health research, with inflammation and the gut–brain axis as pivotal mechanistic links. Future priorities include elucidating the functional mechanisms of the gut microbiome and developing targeted interventions for shared pathological pathways. These findings provide a framework for identifying research priorities in this evolving field.

1. INTRODUCTION

Metabolic syndrome (MetS) represents a constellation of interrelated metabolic abnormalities—including central obesity, hypertension, dyslipidemia, and impaired glucose metabolism—that collectively amplify the risk of Type 2 diabetes and cardiovascular disease.[1] According to the International Diabetes Federation diagnostic criteria, MetS affects approximately 20–25% of the global adult population, with prevalence escalating with age.[2] Concurrently, mental health disorders have emerged as a paramount global health challenge. The World Health Organization reported that depression affects approximately 280 million individuals and anxiety disorders affect 301 million people worldwide.[3] Accumulating evidence reveals a complex bidirectional relationship between MetS and mental health, profoundly impacting quality of life while imposing substantial socioeconomic burdens.[4,5]

The past two decades have witnessed remarkable advances in elucidating the relationship between MetS and mental health. In 2013, Zhang *et al.*[6] published a seminal meta-analysis that reported evidence supporting the bidirectional relationship between depression and MetS. This foundational work catalyzed subsequent large-scale cohort studies that further delineated mechanisms linking psychological factors—including anxiety and chronic stress—with metabolic perturbations.[7,8] The 2017 Lancet Psychiatry Commission consensus report underscored the critical importance of metabolic health management in individuals with mental illness.[9] Recent breakthroughs in understanding biological mechanisms—particularly the gut–brain axis, inflammatory pathways, and oxidative stress—have provided novel perspectives for deciphering this complex relationship.[10,11] The COVID-19 pandemic further intensified scientific focus on the interplay between psychological stress and metabolic dysfunction.[12]

Despite substantial research progress, critical challenges persist. First, the expansive and fragmented literature lacks systematic integration. Preliminary analysis indicates over 10,000 relevant publications in the Web of Science database alone, spanning multiple disciplines and hindering researchers' ability to comprehensively grasp the field's landscape.[13] Second, research hotspots and emerging trends remain inadequately characterized. The relationships between novel topics—such as gut microbiota and epigenetics—and established research themes require further elucidation.[14] Third, collaboration networks among countries, institutions, and research teams, along with their temporal evolution, remain poorly mapped, constraining international cooperation.[15] Finally, the field's knowledge structure, evolutionary trajectory, and future directions lack quantitative analysis and visualization.

Bibliometrics employs mathematical and statistical methods to quantitatively analyze scientific literature, objectively revealing research trajectories, knowledge structures, and field evolution.[12] Through systematic analysis of publication patterns, citation networks, collaboration structures, and thematic distributions, bibliometric approaches can identify research hotspots, track emerging trends, evaluate research impact, and inform scientific decision-making.[16] Recent advances in visualization tools—particularly VOSviewer and CiteSpace—enable transformation of complex bibliometric data into intuitive knowledge maps, substantially enhancing analytical efficiency and depth.[17]

Several bibliometric analyses have examined topics related to metabolism and mental health, yet none have comprehensively addressed the relationship between MetS and the full spectrum of mental health disorders. Chen *et al*.[18] focused specifically on metabolic bariatric surgery outcomes, while Liu *et al*.[19] analyzed sedentary behavior and mental health. Other studies examined antipsychotic-induced metabolic disorders[20] or obesity–depression comorbidity in pediatric populations.[21] These analyses either addressed single interventions, isolated risk factors, reverse causality, or restricted populations. In contrast, the present study provides a comprehensive bibliometric analysis of research on the bidirectional relationship between MetS—as a unified clinical entity—and diverse mental health conditions across all populations over a 25-year period.

This study aims to systematically analyze the literature on the relationship between MetS and mental health from 2000 to 2025 using advanced bibliometric methods. We seek to: (i) construct comprehensive knowledge maps of the field; (ii) identify research hotspots and emerging trends; (iii) delineate collaboration networks and their evolution; and (iv) provide evidence-based guidance for future research directions. This analysis will equip researchers with essential insights for navigating this rapidly evolving interdisciplinary field.

2. METHODS

2.1. DATA SOURCE AND SEARCH STRATEGY

This study utilized the Web of Science Core Collection (WoSCC), recognized as the premier comprehensive database encompassing the world's most influential academic journals and serving as the gold standard for bibliometric research.[22] Data retrieval was conducted on June 11, 2025, including publications from January 01, 2000, to June 11, 2025. This timeframe was strategically selected based on two key considerations: (i) the standardization of MetS diagnostic criteria post-2000,[23] marking a watershed moment in global research focus; and (ii) the emergence of significant academic attention to the MetS–mental health relationship at the dawn of the 21st century.

The search strategy employed topic-based queries (TS) with the following comprehensive search string: TS=("metabolic syndrome" OR "syndrome X" OR "insulin resistance syndrome" OR "cardiometabolic risk") AND TS=("mental health" OR "psychological health" OR "depression" OR "anxiety" OR "stress" OR "psychological stress" OR "mental disorder" OR "psychiatric disorder"). This search algorithm was developed in accordance with the Preferred

Reporting Items for Systematic Reviews and Meta-Analyses Literature Search Extension guidelines for search strategy reporting,[24] which are increasingly adopted in bibliometric studies to ensure reproducibility and comprehensive literature retrieval.

2.2. LITERATURE SELECTION AND QUALITY CONTROL

The inclusion criteria for the literature search were as follows: (i) studies directly addressing the relationship between MetS and mental health, including their bidirectional interactions; (ii) document types limited to research articles and reviews; (iii) publications in English; and (iv) studies fully indexed in WoSCC.

The exclusion criteria included: (i) conference abstracts, editorials, letters, book reviews, corrections, or retractions lacking substantial academic content; (ii) studies without direct relevance to both MetS and mental health; (iii) duplicate publications; (iv) records with incomplete bibliographic information; and (v) studies primarily focused on cardiac syndrome X, which shares the term "syndrome X" but represents a distinct cardiovascular condition unrelated to MetS.

Two independent researchers with 17 and 15 years of bibliometric experience, respectively, conducted the literature selection. Initial screening was performed based on titles and abstracts, followed by a full-text evaluation for potentially eligible articles. Discrepancies were resolved through consensus discussion, with a third researcher consulted when necessary. Inter-rater reliability was assessed using Cohen's kappa coefficient, yielding $\kappa = 0.823$ (95% confidence interval: 0.791–0.855), indicating substantial agreement.

2.3. DATA EXTRACTION AND ANALYTICAL TOOLS

Complete bibliographic records were extracted from WoSCC, encompassing author information, titles, abstracts, keywords, references, publication years, journals, institutional affiliations, and countries/regions. Data were exported in plain text format with "full record and cited references" selected to ensure data completeness.[25] The complete bibliographic dataset of all 18,647 included publications is available in Table S1.

The following specialized bibliometric tools were employed for data processing and visualization:

i. VOSviewer (version 1.6.18, Leiden University, The Netherlands). Utilized for constructing and visualizing bibliometric networks, including collaboration, co-occurrence, and co-citation analyses.[16] Analytical thresholds were established as follows: keywords (⩾25 occurrences), authors (⩾16 publications), institutions (⩾70 publications), and countries (⩾120 publications). The association strength method was applied for normalization, and visualization of similarities clustering algorithms were used for automatic categorization.
ii. CiteSpace (version 6.3.R1, Drexel University, United States). Employed for identifying research frontiers, detecting burst keywords, and constructing dual-map overlays to elucidate knowledge flow across disciplines.[26] Parameters included one-year time slices, node selection based on analysis type, g-index ($k = 25$) selection criterion, and pathfinder network pruning for enhanced visualization clarity.
iii. Scimago Graphica (version 1.0.35, SCImago Research Group S.L., Spain). Applied for geographic distribution mapping and advanced network visualizations, facilitating a comprehensive understanding of global research patterns.
iv. R software (version 4.3.1, R Foundation for Statistical Computing, Austria) with specialized packages. The bibliometrix package enabled descriptive statistical analyses,[27] ggplot2 facilitated the creation of custom visualizations, and dplyr streamlined data processing and management.
v. Online analytical platforms. The Citexs platform (https://www.citexs.com) extracted gene and disease information through text mining. The Search Tool for the Retrieval of Interacting Genes/Proteins (STRING) database (version 12.0, Swiss Institute of Bioinformatics, Switzerland) was employed to construct protein–protein interaction networks,[28] while Cytoscape (version 3.10.0, Institute for Systems Biology, United States) was used to perform network topology analyses.[29]

2.4. DATA ANALYSIS STRATEGY

2.4.1. DESCRIPTIVE ANALYSIS

Descriptive analyses included annual publication volumes, growth rates, and cumulative outputs. A second-order polynomial regression model ($y = ax^2 + bx + c$) was fitted to cumulative growth curves, with model fitness evaluated using the coefficient of determination (R^2). Temporal publication distribution patterns were analyzed, with an emphasis on the proportion of recent publications (2020–2024).[30]

2.4.2. COLLABORATION NETWORK ANALYSIS

Multi-level collaboration networks were constructed for countries/regions and institutions. Inclusion thresholds comprised countries/regions with 120 or more publications and institutions with 70 or more publications. Network metrics calculated included publication volume, percentage contribution, total link strength (TLS), and normalized centrality (0–1 scale). VOSviewer network visualization displayed collaboration patterns.

2.4.3. AUTHOR AND JOURNAL ANALYSIS

Time–density analysis categorized authors by average publication year, identifying active research periods. Author inclusion required ⩾16 publications. CiteSpace's dual-map overlay function analyzed subject distributions of citing and cited journals, revealing interdisciplinary knowledge transfer.[31]

2.4.4. RESEARCH DOMAIN AND KNOWLEDGE BASE ANALYSIS

Literature was classified according to Web of Science Categories. Co-citation analysis constructed knowledge base networks with a minimum citation threshold of 40. Clustering quality was assessed using modularity Q (>0.3 indicating significant clustering) and the mean silhouette S (> 0.5 indicating reasonable clustering).[32]

2.4.5. RESEARCH HOTSPOTS AND THEMATIC EVOLUTION ANALYSIS

Keyword co-occurrence analysis identified research foci (minimum occurrence: 25). The log-likelihood ratio

algorithm generated cluster labels automatically. The study period was divided into five-year phases, with a timeline visualization tracking high-frequency changes in keyword ranking. Kleinberg's burst-detection algorithm identified emerging topics and calculated burst strength values.[33]

2.4.6. MOLECULAR MECHANISM NETWORK ANALYSIS

Gene and protein information were extracted using the Citexs platform. High-frequency genes underwent functional clustering analysis. Proteins with ⩾ 130 occurrences were imported into STRING for protein–protein interaction network construction (confidence threshold: 0.7; species: *Homo sapiens*). Cytoscape was used to calculate network topology parameters. Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses were performed with Benjamini–Hochberg correction (adjusted $p<0.05$).[34]

2.4.7. DISEASE ASSOCIATION PATTERN ANALYSIS

Disease term co-occurrence analysis employed a minimum threshold of 200 occurrences. VOSviewer constructed disease networks with normalized association strength. Disease clusters were identified, and the strengths of inter-disease associations were calculated. Both density and network visualizations presented disease association patterns.[35]

All network visualizations employed proportional node sizing based on relevant metrics, with edge thickness indicating the strength of association. Color coding was used to distinguish different clusters or temporal periods. Data analysis adhered to established bibliometric research procedures and reporting standards.

3. RESULTS

The comprehensive search strategy identified 19,673 records through the WoSCC database. After applying the search period restriction (from January 01, 2000, to June 11, 2025), 19,601 records remained. Further refinement by document types (articles and review articles only) yielded 18,962 records. Language restriction to English resulted in 18,647 records. All 18,647 publications were included in the quantitative and visualization-based bibliometric analyses, encompassing publications per year, countries/regions, institutions, authors, journals, fields, references, keywords, genes, and diseases (Figure 1).

3.1. ANNUAL PUBLICATION TRENDS

Our comprehensive search identified 18,647 articles addressing the bidirectional relationship between MetS and mental health from the WoSCC database (January

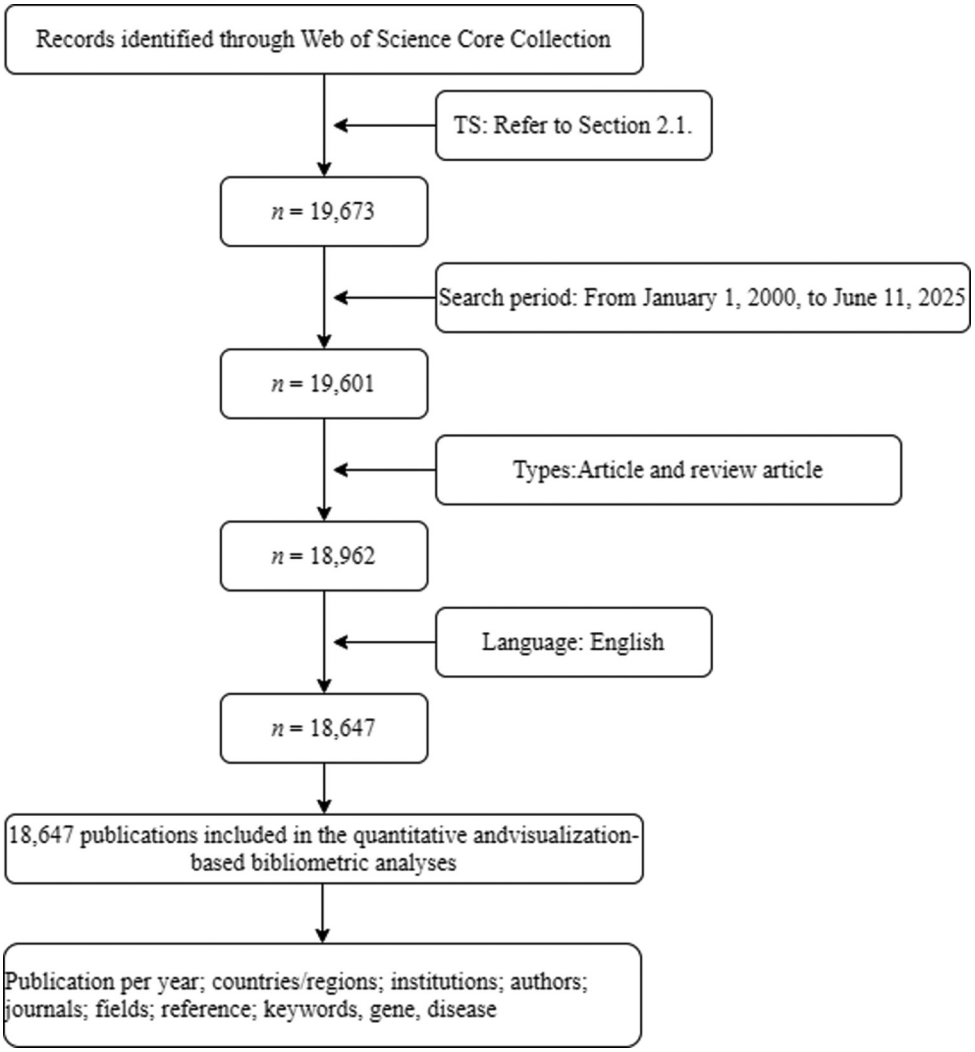

Figure 1. Flow chart of literature search. Image created by the authors
Abbreviation: TS: Topic-based queries.

01, 2000, to June 11, 2025). The annual publication volume demonstrated remarkable growth, increasing 45.7-fold from 29 articles in 2000 to 1,324 articles in 2024. Cumulative publication growth exhibited an excellent fit to a polynomial function ($y = 32.742x^2 - 92.691x - 102.4$; $R^2 = 0.9979$), indicating non-linear (accelerating) growth. The peak annual growth rate of 74.67% occurred in 2006, coinciding with the standardization of MetS diagnostic criteria. Publication output peaked in 2022 (1,398 articles). Notably, publications from the most recent 5-year period (2020–2024) accounted for 46.73% of the total output, underscoring the field's accelerating momentum (Figure 2).

3.2. GEOGRAPHIC DISTRIBUTION AND INSTITUTIONAL COLLABORATION NETWORKS

Research contributions were made by 138 countries/regions and 14,766 institutions worldwide. The United States dominated both publication volume (4,987 articles, 26.75%) and network centrality (0.53), establishing collaborative partnerships with 129 countries. China ranked second in productivity, with 2,555 articles (13.70%), followed by Italy with 1,422 articles (7.62%) (Figure 3A). Institutional analysis revealed University of Michigan as the most collaborative institution based on TLS. Leading institutions by publication volume included São Paulo University (181 articles), Tehran University of Medical Sciences (178 articles), and the University of Toronto (162 articles) (Figure 3B).

3.3. AUTHOR CONTRIBUTIONS AND JOURNAL DISTRIBUTION PATTERNS

The research community comprised 87,194 contributing authors. Time–density analysis revealed distinct generational cohorts: early pioneers (pre-2015), including Sowers and Alfredo Martinez; mid-period contributors (2015–2019), featuring McIntyre and Penninx; and recent leaders (post-2019), including Sahebkar and Marycz (Figure 4A). The dual-map overlay analysis demonstrated that primary publication areas were concentrated in molecular biology/immunology and clinical medicine domains, while cited references predominantly originated from molecular biology/genetics and healthcare/medicine journals (Figure 4B).

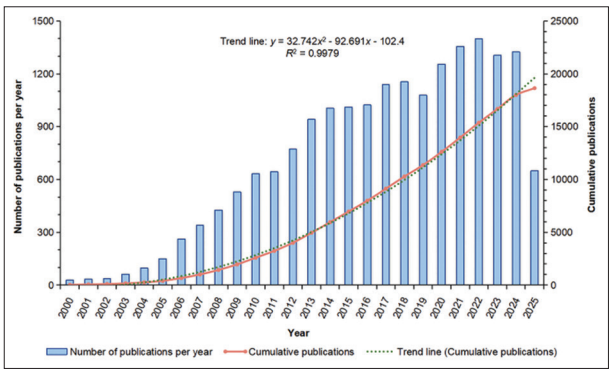

Figure 2. Annual publication trends in metabolic syndrome–mental health research (2000–2025). The bar chart displays annual publication volumes; the curve represents cumulative publications. Inset: polynomial regression model of cumulative growth trajectory

3.4. RESEARCH DOMAIN DISTRIBUTION AND KNOWLEDGE FOUNDATION

Literature analysis revealed five major research domain clusters, with biomedical sciences as the predominant cluster. Core research domains comprised endocrinology and metabolism (4,237 articles, 22.71%), psychiatry (3,856 articles, 20.67%), and biochemistry and molecular biology (2,943 articles, 15.78%) (Figure 5A). Co-citation network analysis yielded robust clustering metrics identifying 279 highly-cited foundational works. Key publications included Saklayen[36] on global MetS epidemiology (279 citations) and Furukawa *et al.*[37] on oxidative stress mechanisms (145 citations), collectively forming the field's knowledge foundation (Figure 5B).

3.5. RESEARCH HOTSPOTS AND THEMATIC EVOLUTION

Keyword co-occurrence analysis ($Q = 0.8497$, $S = 0.9597$) revealed 16 distinct thematic clusters: (i) MetS, (ii) oxidative stress, (iii) chronic kidney disease, (iv) insulin (INS) resistance, and (v) mental health, among others (Figure 6A). Temporal analysis of keyword evolution revealed notable shifts: "inflammation" ascended from the ninth position (2000–2005) to the fourth position (2021–2025), reflecting its growing recognition as a mechanistic link. "Gut microbiota" exhibited rapid emergence post-2016, while "COVID-19" emerged rapidly in the research landscape after 2020 with exceptional strength (burst strength = 6.84) (Figure 6B).

3.6. MOLECULAR MECHANISMS AND SIGNALING NETWORKS

Text mining of 18,647 articles yielded 6,241 genes, with 150 occurrences set as the threshold for visualization. Co-occurrence clustering revealed three distinct gene clusters: red (signaling: *NFKB1, AKT1*, *PPARG*), green (inflammatory: *IL6, TNF*), and blue (metabolic: *INS, CRP, ADIPOQ, LEP*) (Figure 7A). GO enrichment analysis identified significant enrichment in biological processes, including nutrient level response, peptide hormone response, inflammatory regulation, and cytokine production ($p < 0.001$). Cellular components were enriched in the external side of the plasma membrane, vesicle lumens, and secretory granule lumens. Molecular functions showed enrichment in cytokine receptor binding, transcription factor binding, and RNA polymerase II-specific binding (Figure 7B). KEGG pathway analysis revealed significant enrichment in lipid and atherosclerosis, phosphoinositide 3-kinase (PI3K)–protein kinase B (Akt) signaling, fluid shear stress and atherosclerosis, non-alcoholic fatty liver disease, alcoholic liver disease, INS resistance, and tumor necrosis factor (TNF) signaling pathways (Figure 8A). Protein–protein interaction analysis of the top 100 proteins (minimum 131 occurrences) using STRING (confidence: 0.700) generated a network of 100 nodes and 915 edges (average degree: 18.3). Cytoscape analysis identified hub proteins: interleukin (IL) 6, INS, TNF, IL1B, AKT1, albumin, signal transducer and activator of transcription 3, IL10, tumor protein p53, and nuclear factor kappa B subunit 1, representing core regulatory elements in MetS–mental health interactions (Figure 8B).

3.7. DISEASE ASSOCIATION PATTERNS

Analysis identified 3,822 diseases linked to MetS and mental health. Disease co-occurrence analysis revealed three

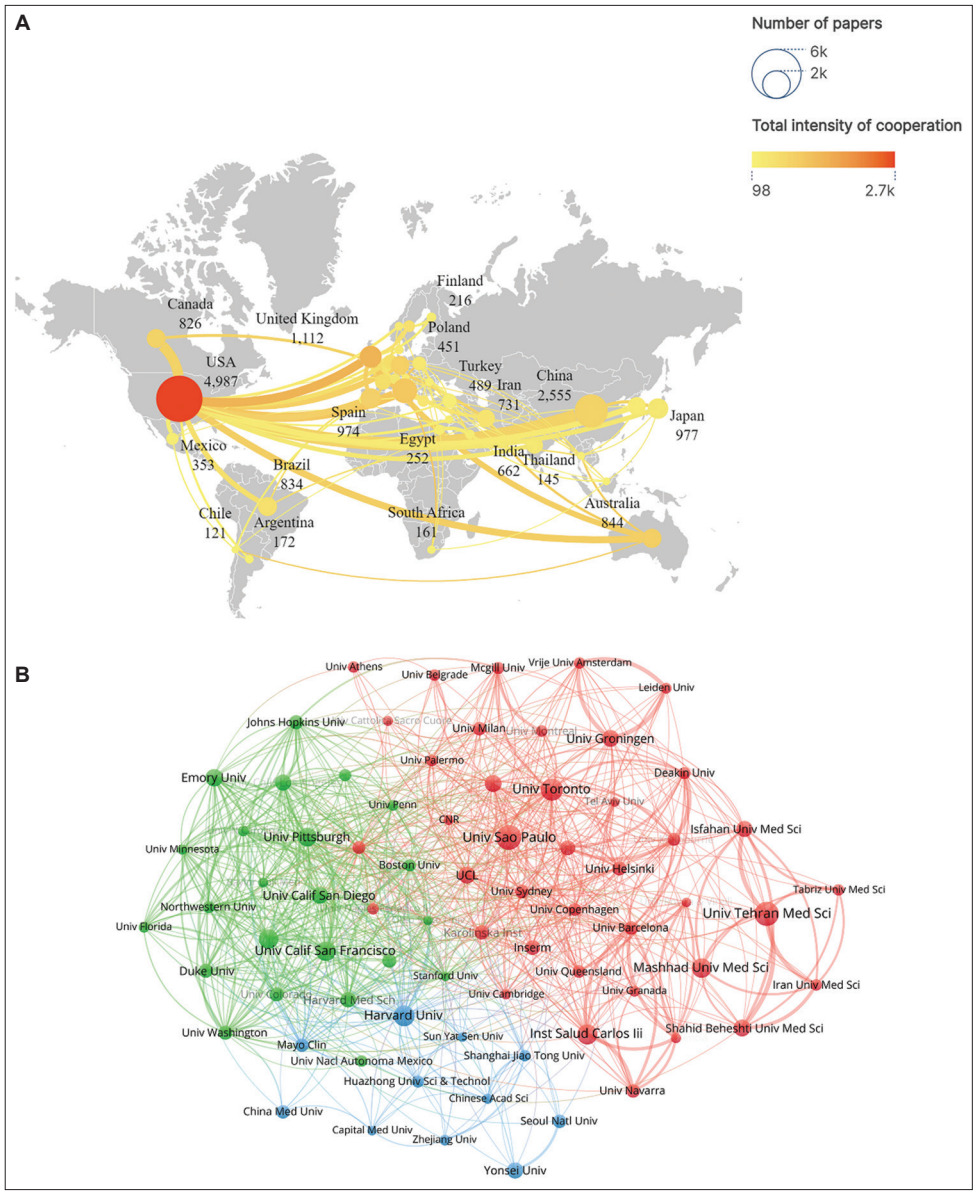

Figure 3. Global research distribution and institutional collaboration networks. (A) Geographic visualization of country/region contributions, with node size proportional to publication volume and edge thickness indicating collaboration intensity. (B) Institutional collaboration network displaying cluster differentiation through color coding, with node size reflecting publication output

major clusters: a metabolic disease cluster (MetS: 54,243 occurrences; INS resistance: 43,668 occurrences), a cardiovascular disease cluster (vascular diseases: 16,722 occurrences; hypertension: 14,893 occurrences), and a psychiatric disease cluster (depression: 12,456 occurrences; anxiety: 9,832 occurrences). Association strength analysis revealed the most robust connections between MetS and depression (link strength = 3,247) and between INS resistance and anxiety (link strength = 2,856) (Figure 9).

4. DISCUSSION

This comprehensive bibliometric analysis of 18,647 articles spanning 2000–2025 provides unprecedented insights into the knowledge architecture, evolutionary trajectory, and emerging frontiers in MetS–mental health research. Our findings reveal exponential growth in research output—a 45.7-fold increase—with nearly half (46.73%) of all publications emerging in the past 5 years. This remarkable expansion reflects the field's transition from nascent exploration to mature investigation. Particularly striking are the rapid ascent of inflammation mechanisms, the emergence of gut microbiota research, the catalytic effect of the COVID-19 pandemic, and the robust association between MetS and depression. These findings offer novel insights into the intricate mechanisms that connect MetS and mental health.

The extraordinary research growth trajectory stems from multiple converging factors. First, the escalating global burden of both MetS and mental health disorders has mobilized substantial academic attention and funding.[38,39] The 74.67% growth peak in 2006 likely reflects several factors: (i) the American Heart Association's landmark scientific statement on MetS diagnosis and management, which provided standardized diagnostic criteria;[40,41] (ii) increased research funding from major agencies, such as the National Institutes of Health, which expanded chronic disease research portfolios during this period; (iii) growing policy attention to the prevention and management of metabolic and mental health comorbidities; and (iv) the rising global prevalence

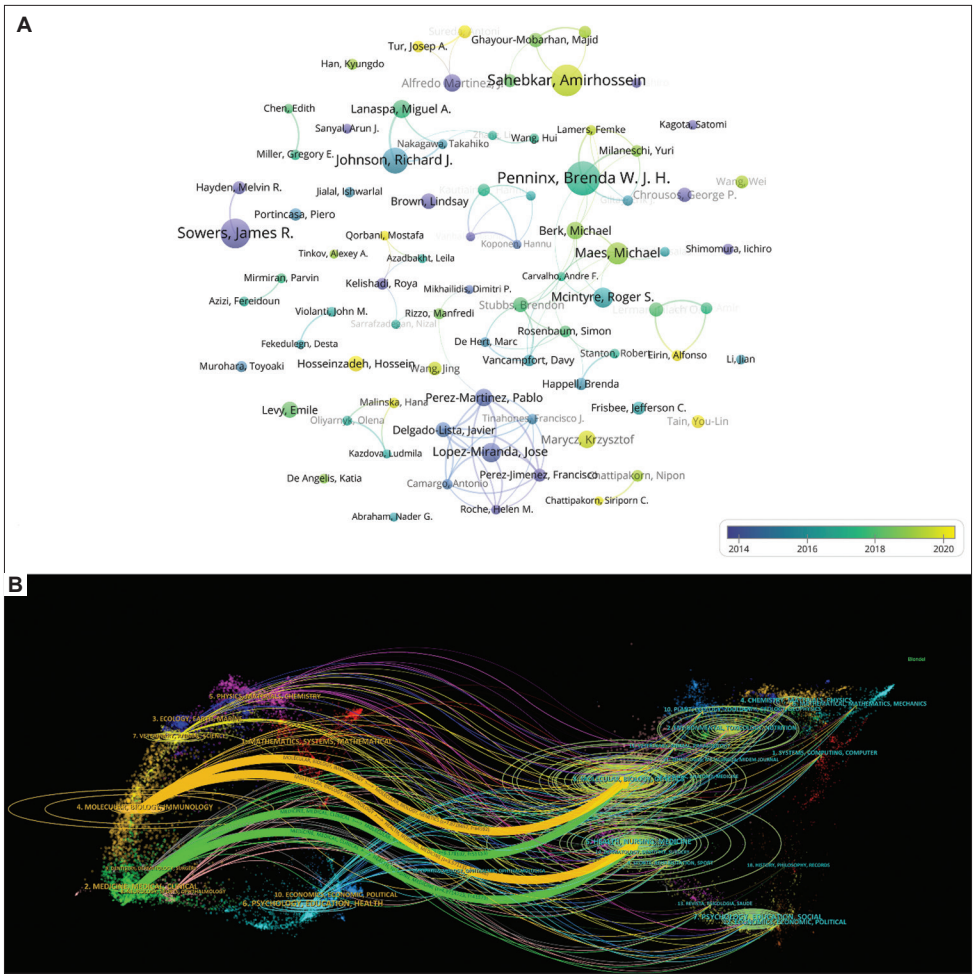

Figure 4. Temporal evolution of author contributions and journal distribution patterns. (A) Author publication time–density visualization with color gradients indicating average publication years. (B) Dual-map overlay illustrating citation flows between citing journals (left) and cited journals (right)

of obesity and MetS, which heightened research urgency. Second, technological advances in molecular biology—particularly high-throughput sequencing and multi-omics platforms—have enabled unprecedented mechanistic exploration of MetS–mental health interactions.[42] Third, the COVID-19 pandemic precipitated an urgent investigation into the interplay between psychological stress and metabolic dysfunction, as evidenced by the emergence of "COVID-19" as a burst keyword (strength = 6.84) post-2020, reflecting acute public health imperatives.[43] However, given the relatively short post-2020 analysis window, the long-term significance of COVID-19 as a sustained research theme in this field requires continued observation in future bibliometric studies.

Geographic collaboration patterns reveal compelling insights into global research dynamics. The United States' dominance—26.75% of publications and 0.53 centrality—reflects not merely quantity but strategic positioning within international networks. This leadership is rooted in a robust research infrastructure, sustained funding from agencies such as the National Institute of Mental Health, and a longstanding commitment to mental health research.[44] China's rapid ascent to second place (13.70%) demonstrates the growing research capacity of emerging economies. However, China's relatively modest network centrality signals opportunities for enhanced international collaboration.[45] São Paulo University's institutional leadership (181 articles) likely reflects both Latin America's high prevalence of MetS and the institution's distinguished reputation in psychiatric research.[46] Notably, international collaboration has substantially increased over the study period. The field expanded to encompass 138 countries/regions, with the United States demonstrating the highest TLS and establishing the strongest bilateral collaboration with China, followed by partnerships with Canada and Italy. The concentration of 46.73% of publications in the last five years reflects growing research activity and collaborative opportunities. However, collaboration remains concentrated among a limited number of countries, suggesting opportunities for broader international engagement.

The evolution of research themes powerfully illustrates conceptual maturation in the field. The progression of inflammation from the ninth position (2000–2005) to the fourth (2021–2025) confirms its recognition as a fundamental mechanistic bridge between metabolic and mental health disorders.[47] Our molecular network analysis reinforces this, positioning pro-inflammatory cytokines IL6 (degree = 76) and TNF (degree = 69) as central nodes in the protein–protein interaction network. This aligns with accumulating evidence that chronic low-grade inflammation represents a shared pathophysiological substrate for both MetS and depression.[48] The post-2016 surge in gut microbiota research reflects a growing appreciation for the gut–brain axis, with compelling evidence that dysbiosis influences bidirectional metabolism and mental health regulation through neurotransmitter synthesis, immune modulation, and the production of microbial metabolites.[49]

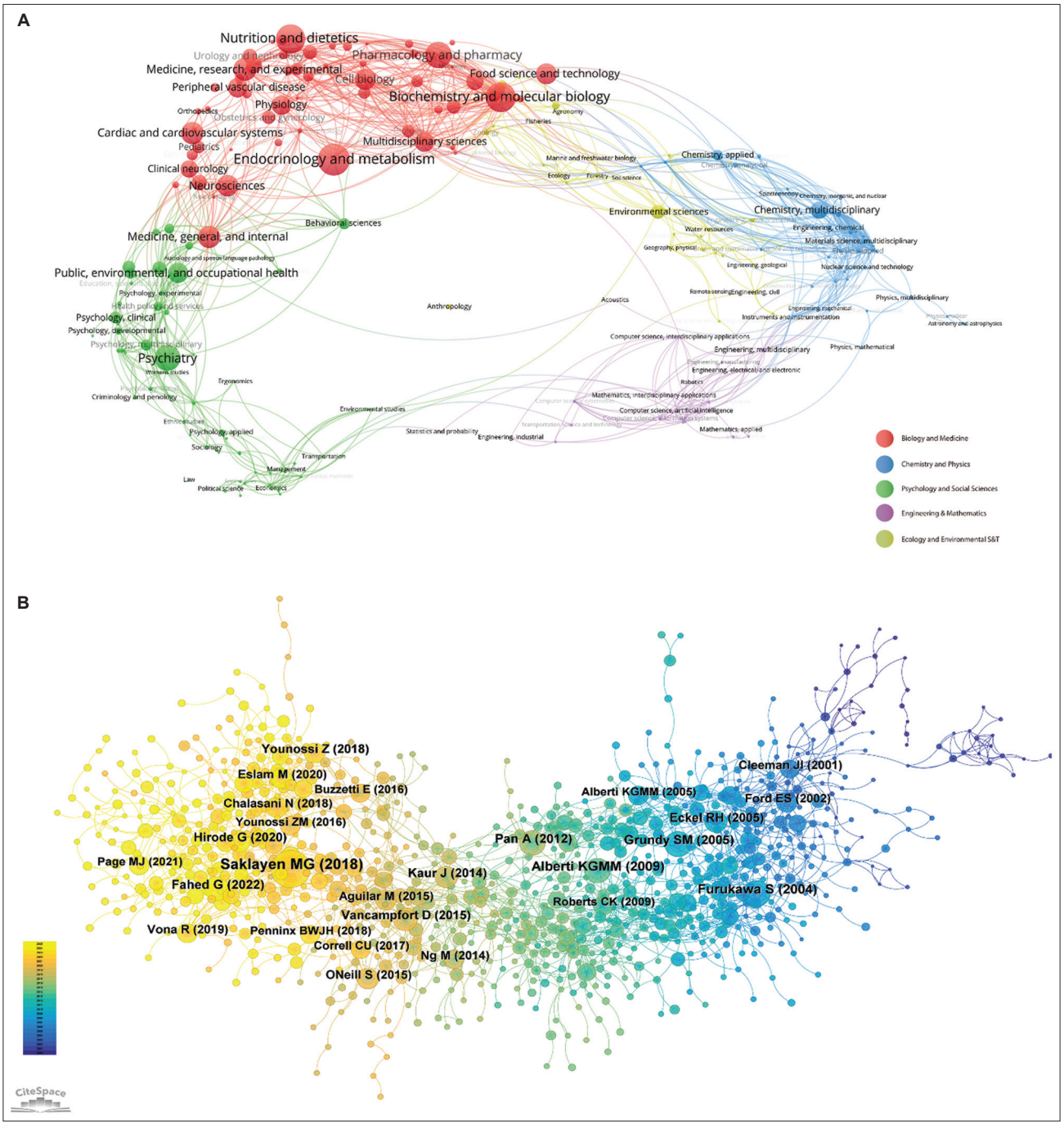

Figure 5. Research domain clustering and knowledge foundation networks. (A) Five major research domain clusters distinguished by different colors. (B) Co-citation network with node size representing citation frequency and color indicating temporal patterns

Molecular mechanism analysis unveiled intricate interaction networks underlying the MetS–mental health interface. GO enrichment highlighting nutrient sensing and peptide hormone responses ($p<0.001$) underscores the critical role of metabolic signaling in mood regulation.[50] KEGG pathway analysis, revealing lipid/atherosclerosis (gene ratio = 0.142) and PI3K–Akt signaling (gene ratio = 0.138) pathways, suggests these cascades not only govern metabolism but also profoundly influence neuroprotection and emotional regulation.[51] INS's network centrality (degree = 72) supports emerging hypotheses that INS resistance serves as a common pathological denominator linking metabolic dysfunction with cognitive-emotional disturbances.[52] These molecular insights provide actionable targets for therapeutic interventions addressing shared pathophysiological mechanisms.

Disease association patterns yield profound clinical implications. The robust MetS–depression link (strength = 3,247) likely operates through multiple interconnected mechanisms: (i) hypothalamic–pituitary–adrenal axis dysregulation driving hypercortisolemia, promoting visceral adiposity and INS resistance;[53] (ii) chronic inflammation activating tryptophan-kynurenine metabolism, depleting serotonin synthesis;[54] and (iii) oxidative stress compromising hippocampal integrity, disrupting mood regulation and cognitive function.[55] The INS resistance–anxiety association (strength = 2,856) suggests metabolic perturbations may precipitate anxiety through disrupted cerebral energy metabolism and neurotransmitter homeostasis.[56] These

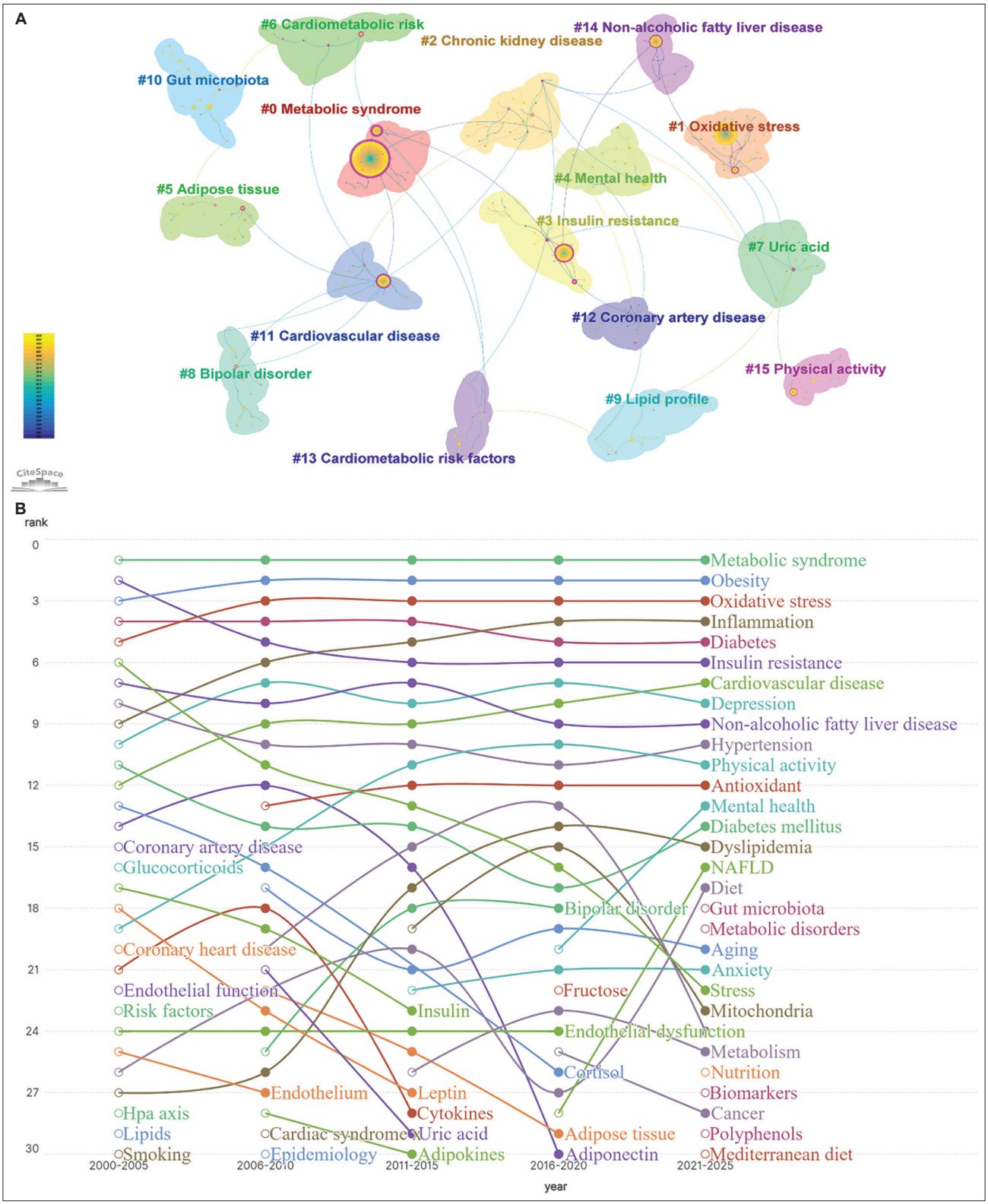

Figure 6. Research hotspot identification and thematic evolution. (A) Keyword co-occurrence network displaying 16 color-differentiated clusters. (B) Temporal heat map illustrating ranking dynamics of top 30 keywords across five-year intervals (2000–2025)

findings support considering routine mental health screening in MetS patients and metabolic monitoring in psychiatric populations.

Several limitations warrant consideration. First, the inherent constraints of bibliometric software present challenges in combining multiple databases for analysis; therefore, this study relied exclusively on the WoSCC database without incorporating other databases, such as Scopus, PubMed, or Embase. Although WoSCC is recognized as the gold standard for bibliometric research due to its comprehensive citation data and compatibility with visualization tools, some influential publications indexed in other databases may have been excluded, potentially introducing coverage bias, particularly for non-English publications and

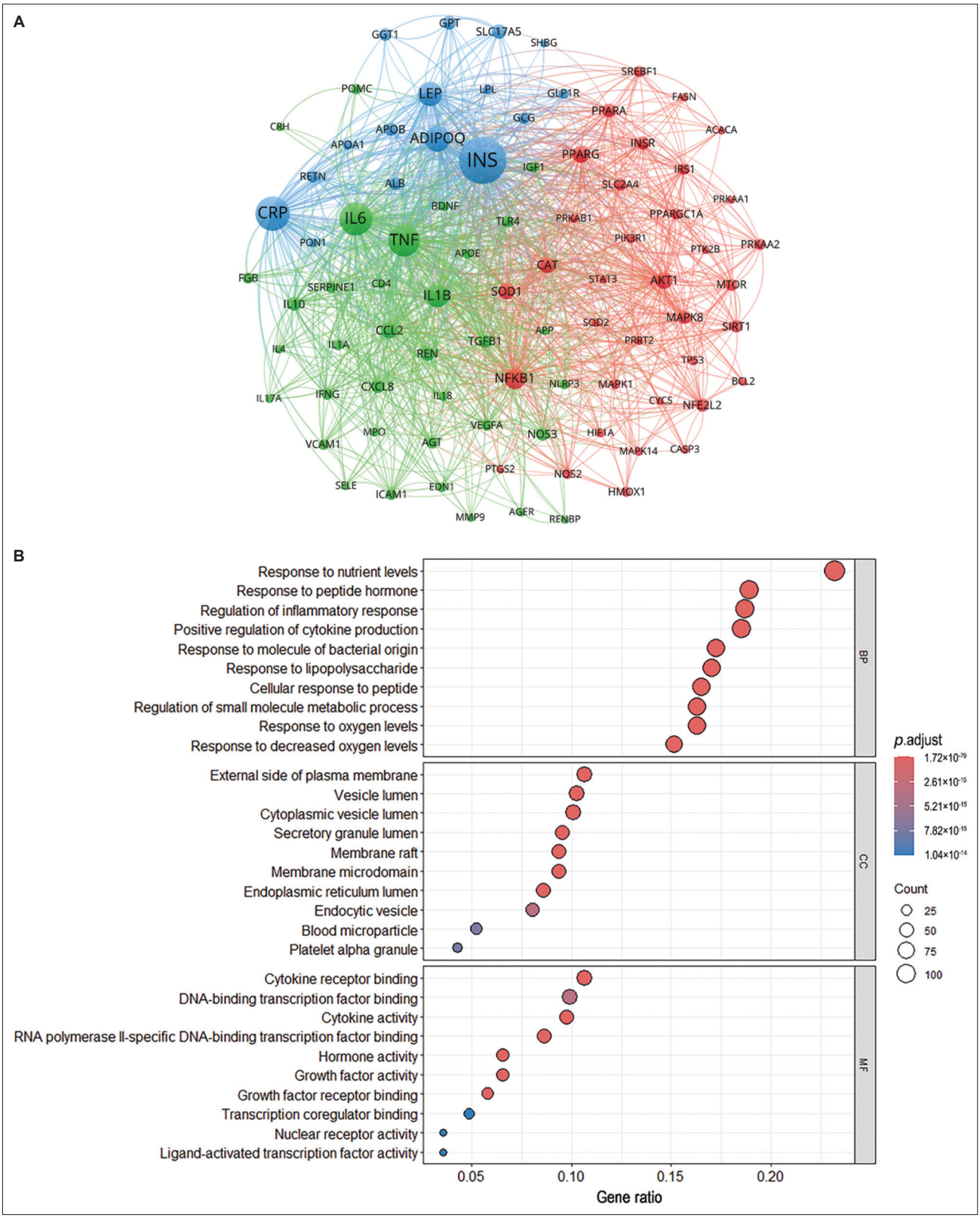

Figure 7. Gene co-occurrence and functional enrichment analysis. (A) Gene clustering network showing signaling (red), inflammatory (green), and metabolic (blue) clusters. (B) Gene ontology enrichment analysis. Bubble size indicates gene count; color represents adjusted *p*-values

Abbreviations: BP: Biological process; CC: Cellular component; MF: Molecular function.

regional journals.[57] Second, English-only inclusion may introduce linguistic bias, underrepresenting research contributions from non-Anglophone regions, particularly studies published in local or regional journals, which could affect the global representativeness of our findings.[58] Third, the bibliometric analysis examined the characteristics of the literature rather than its methodological quality or the validity of the results.[59] Fourth, database updates may alter specific metrics over time. Finally, text-mining approaches for gene/disease extraction may yield false positives or negatives.[60]

Our analysis suggests several future research directions: (i) a mechanistic elucidation of gut–brain axis contributions,

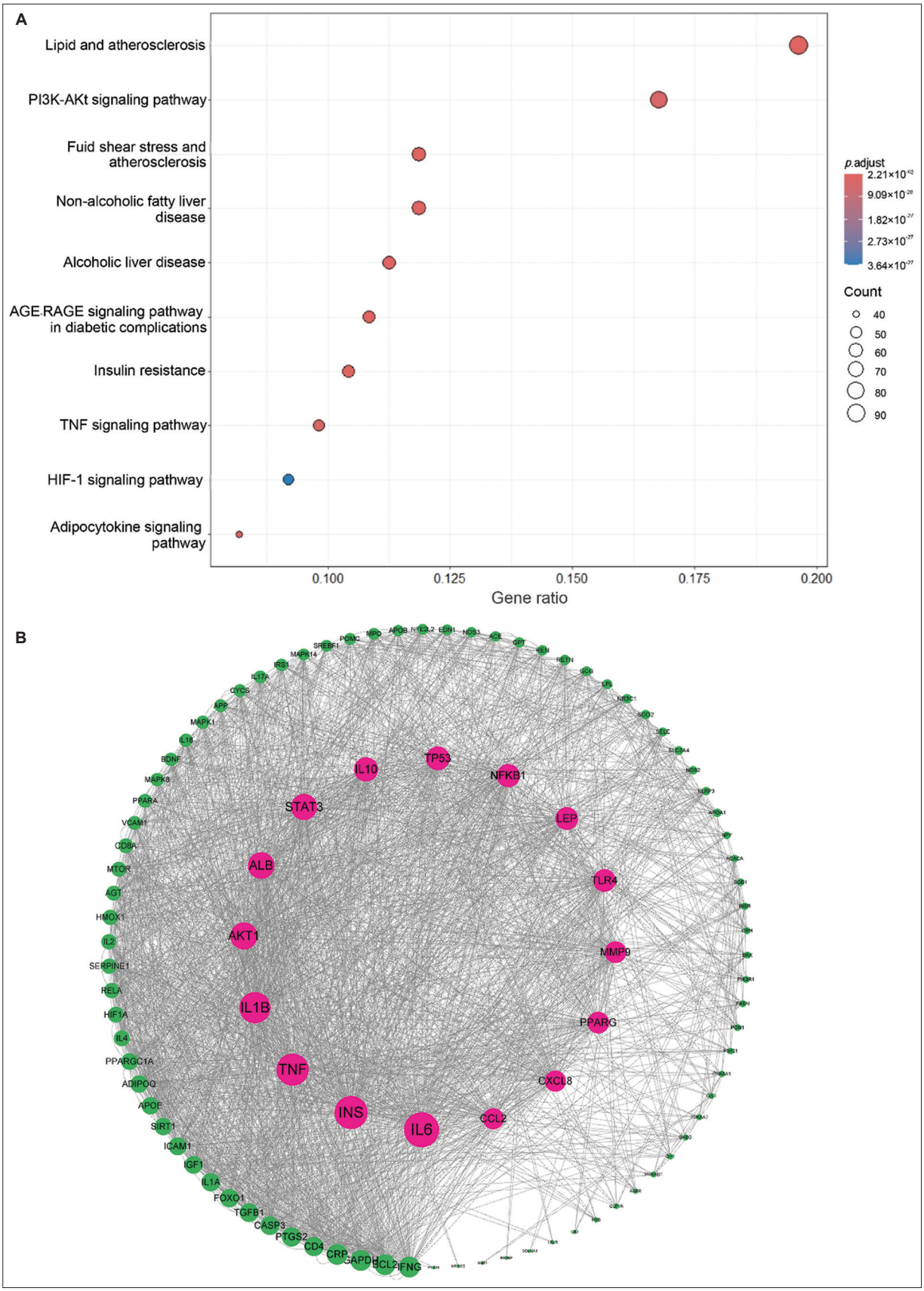

Figure 8. Pathway and protein interaction analysis. (A) Kyoto Encyclopedia of Genes and Genomes pathway enrichment analysis. (B) Protein–protein interaction network with hub proteins (magenta), including interleukin-6, insulin, TNF, and AKT. Node size indicates degree centrality

Abbreviations: AGE–RAGE: Advanced glycation end-product–receptor for advanced glycation end-products; HIF-1: Hypoxia-inducible factor; PI3K–Akt: Phosphoinositide 3-kinase–protein kinase B; TNF: Tumor necrosis factor

particularly specific microbiota strains and their bioactive metabolites;[61] (ii) the development of targeted interventions addressing shared pathological cascades—inflammation, oxidative stress, and metabolic dysfunction;[62] (iii) high-quality

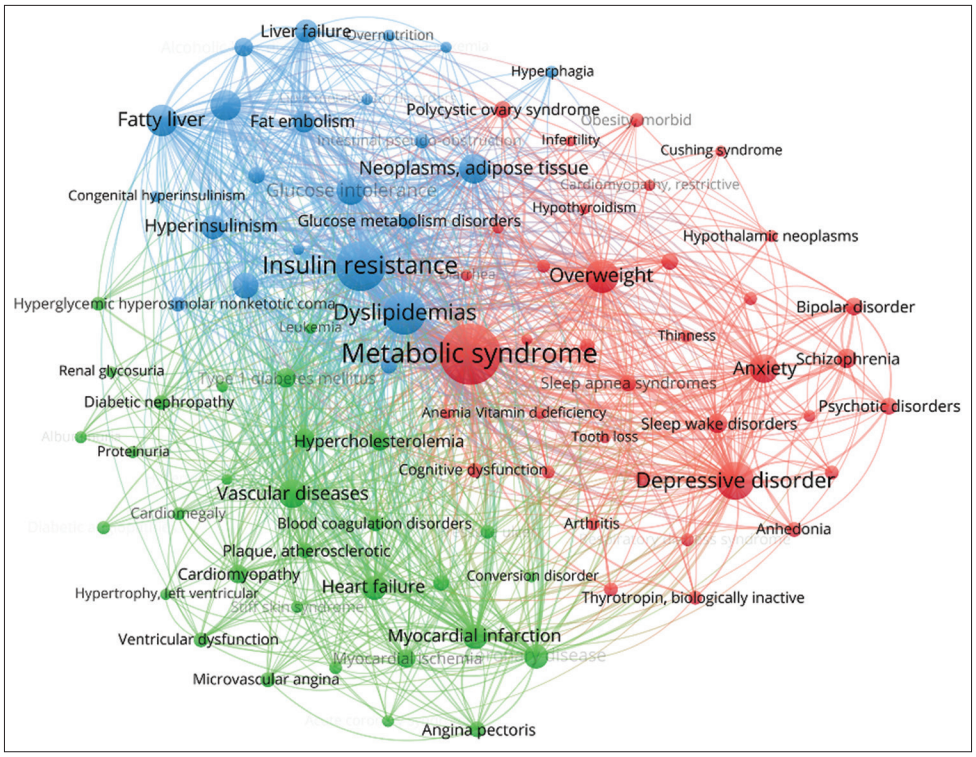

Figure 9. Disease association network analysis. Node size represents disease occurrence frequency, edge thickness indicates co-occurrence strength, and colors distinguish three major disease clusters

longitudinal cohort studies to establish causal directionality;[63] and (iv) enhanced international collaboration to generate globally representative evidence.[64]

5. CONCLUSION

This pioneering bibliometric analysis of 18,647 publications (2000–2025) reveals the exponential growth of MetS–mental health research, with a 45.7-fold increase in annual output. The United States led global research (26.75% of publications, centrality = 0.53), while inflammation (IL6, TNF) and the gut–brain axis emerged as central mechanistic paradigms. The robust associations between MetS–depression (link strength = 3,247) and INS resistance–anxiety (link strength = 2,856) underscore the urgent need for integrated clinical approaches. From a clinical perspective, these findings support the implementation of routine mental health screening in patients with MetS and systematic metabolic monitoring in psychiatric populations. The strong disease associations identified in our analysis reinforce the need for integrated care models that address both metabolic and mental health simultaneously.

Our findings highlight three critical research priorities: elucidating the functional mechanisms of gut microbiota, developing interventions that target shared inflammatory pathways, and conducting longitudinal studies to establish causal relationships.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

CONSENT FOR PUBLICATION

Not applicable.

DATA AVAILABILITY STATEMENT

The datasets generated and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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