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Original article

UNLOCKING THE TRENDS AND PATTERNS OF MIDAZOLAM RESEARCH: A BIBLIOMETRIC CRITICISM:

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Abstract

Background:

Understanding the research landscape surrounding midazolam is crucial for identifying the current state of knowledge and potential areas for further investigation.

Methodology:

This bibliometric review utilizes various bibliometric indicators to analyze and summarize the body of research on midazolam. A comprehensive search of relevant literature databases is conducted, and the retrieved publications are subjected to data analysis. Bibliometric indicators, such as frequently researched themes, frequently occurring keywords, influential and active journals, relevant and emerging topics, and trends over time, are examined to gain insights into the research landscape.

Results:

The most frequently researched themes include the clinical use of midazolam in anesthesia, sedation, and critical care, as well as its pharmacokinetics and pharmacodynamics. Frequently occurring keywords highlight topics such as adverse effects, drug interactions, and patient outcomes. Influential and active journals in the field are identified, indicating the key sources of research dissemination. Word cloud and trending topic analyses provide visual representations of the data, showcasing the prominent themes and emerging areas of interest.

Conclusion:

This bibliometric review provides a comprehensive overview of midazolam research and its trends and patterns over time. The findings demonstrate the importance of midazolam in clinical practice and research, highlighting the key areas of investigation and emerging topics. The analysis identifies knowledge gaps and potential areas for further research, contributing to the understanding of midazolam's effects, safety, and optimal use.

Recommendations:

Investigations into the long-term outcomes and efficacy of midazolam in different patient populations can provide valuable insights. Furthermore, interdisciplinary collaborations and knowledge exchange between researchers in anesthesia, pharmacology, and critical care can foster innovation and advance the understanding of midazolam. Finally, staying updated with emerging topics and trends in midazolam research is crucial for guiding future investigations and informing clinical practice.

Keywords: Midazolam, Bibliometric, Word cloud, Thematic Evolution, Trending topic, Submitted: 2023-06-19 Accepted: 2023-06-26

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1. Introduction:

Midazolam is a benzodiazepine drug that is commonly used for anaesthesia, sedation, and management of seizures. Its efficacy, safety, and ease of use have made it a popular choice among medical professionals. However, as research in this field continues to grow, it becomes increasingly important to understand the trends and patterns of midazolam research(2). In this bibliometric review, will examine the literature on midazolam and identify pattern that have contributed to its advancement.

The aim of this review is to provide a comprehensive overview of midazolam research and its impact on the medical field. By analysing the research output and impact of midazolam that can gain insights into its current state of development and potential future directions (3). The study will examine the publication trends in midazolam research over the past few decades. This review will also investigate the most frequently studied topics related to midazolam, including its pharmacology, clinical applications, and adverse effects(4).

Moreover, this review will identify the by unlocking the trends and patterns of midazolam research through bibliometric analysis, this review aims to provide a comprehensive and objective assessment of the current state and future direction of midazolam research (1).

2. Objectives:

The objectives of the bibliometric review on midazolam research are:

1. To identify the most frequently researched themes in midazolam research
2. To visualize the most frequently occurring keywords in midazolam research publications through word cloud analysis.
3. To identify the most influential and active journals publishing research on midazolam
4. To identify the most relevant and emerging topics in midazolam research through trending topic analysis.
5. To provide a comprehensive overview of the state of midazolam research and its trends and patterns over time.

3. Materials Methods :

3.1. Study Designing

The study performed a thorough analysis of the literature midazolam found in the PubMed database, utilizing various software tools. Specifically, the study utilized R-Studio version 4.1.3, which was developed by RStudio, PBC, in Boston, Massachusetts, USA, to aid in the analysis. The study also utilized Biblioshiny, a user-friendly web-based application, to assist in the visualization and exploration of bibliometric data. The latest version of Biblioshiny, version 0.4.0, was used, which was released on March 2, 2021 and available on the Comprehensive R Archive Network (CRAN).

3.2. Setting:

This study utilized R-based packages to extract data from the PubMed database. PubMed was chosen due to its widespread use and reputation as a trusted database in the medical and scientific communities. As a specialized database maintained by the National Library of Medicine (NLM), it offers access to an extensive collection of biomedical literature, including research articles, books, and reports. PubMed's indexing system enables researchers and healthcare professionals to easily search and retrieve relevant literature, making it a valuable resource. PubMed is accessible to the public free of charge and provides reliable, up-to-date information for those interested in health-related topics. The database is updated regularly to ensure that the latest research and findings are available to users.

This study provides information about a dataset of 2,622 documents from 943 sources (journals, books, etc) spanning from 2015 to 2022. The data has an annual growth rate of 134.25%, and the average age of the documents is 3.32 years. There is only one reference. The document contents include 3,047 keywords plus and 4,557 author's keywords. There are 13,026 authors listed in the dataset, with 34 authors of single-authored documents. The authors collaborated on 41 single-authored documents, and the average number of co-authors per document

is 6.45. The dataset includes various types of documents, such as case reports, clinical trials, comparative studies, and reviews. The most common document types are journal articles (2,219), comparative studies (123), and clinical trials, phase I (46). There are also a few documents of other types, such as a dataset (1), equivalence trial (1), and historical article (3).

3.3. Bias

The study focused on midazolam research found in the PubMed database, utilizing R-Studio and Biblioshiny for data analysis and visualization. The dataset included 2,622 documents from 943 sources, spanning from 2015 to 2022. The study provided insights into document types, keywords, authors, and collaboration patterns, offering a comprehensive overview of the research landscape. However, the analysis might be biased towards literature indexed in PubMed, potentially excluding relevant research from other databases or sources.

3.4. Data analysis and Discussions:

The given figure: 1 shows the top ten sources of research articles in medical science, with the number of articles published in each source. Among these sources, the journal VETERINARY ANAESTHESIA AND ANALGESIA published the highest number of articles, with 43 research articles. This journal focuses on the topics related to veterinary anesthesia, analgesia, and perioperative care(5). The articles published in this journal cover topics related to pharmacological agents, pain management, and anesthesia techniques used in veterinary medicine.

MEDICINE is the second-highest source with 34 articles, and it covers a wide range of topics related to general medicine (6). The articles published in this journal cover topics such as diagnosis, treatment, and prevention of various diseases and disorders. The journal DRUG METABOLISM AND DISPOSITION: THE BIOLOGICAL FATE OF CHEMICALS published 33 articles and focuses on the metabolic pathways of drugs and their fate in the biological system(7).

CLINICAL PHARMACOLOGY AND THERAPEUTICS, BRITISH JOURNAL OF CLINICAL PHARMACOLOGY, and FRONTIERS IN PHARMACOLOGY are the other three sources that have published a significant number of research articles in the field of pharmacology. These journals mainly focus on the pharmacokinetics and pharmacodynamics of drugs, drug interactions, and the clinical applications of drugs(7).

SCIENTIFIC REPORTS, XENOBIOTICA; THE FATE OF FOREIGN COMPOUNDS IN BIOLOGICAL SYSTEMS, PLOS ONE, and JOURNAL OF CLINICAL MEDICINE are the other sources that have contributed to medical science research articles. These sources cover a wide range of topics such as genetics, clinical trials, epidemiology, and public health(8).

3.5. Co-occurrence Network

The figure 2 shows various nodes (e.g. humans, female, hypnotics and sedatives) and their respective values for different measures of centrality in a network, including Betweenness, Closeness, PageRank, and the cluster to which they belong(9).

The nodes belong to only one cluster (cluster 1 or cluster 2 or cluster 3), and their values for each of the measures are as a measure of the node's importance based on the number of shortest paths between pairs of nodes in the network that pass through that node(5). The values range from 67.29 (highest) for humans to 0.05 (lowest) for respiration, artificial. A measure of how quickly a node can access all other nodes in the network(10). The values range from 0.02 (highest) for humans and female to 0.0145 (lowest) for mice. A measure of the importance of a node based on the number and quality of incoming links to that node. The values range from 0.094 (highest) for humans to 0.006 (lowest) for respiration, artificial.The cluster to which the node belongs. Nodes belong to only one cluster, and the values are 1, 2 or 3.

Some notable nodes and their values include:

• Humans have the highest Betweenness (67.29) and PageRank (0.094) values, indicating that they are very important nodes in the network.

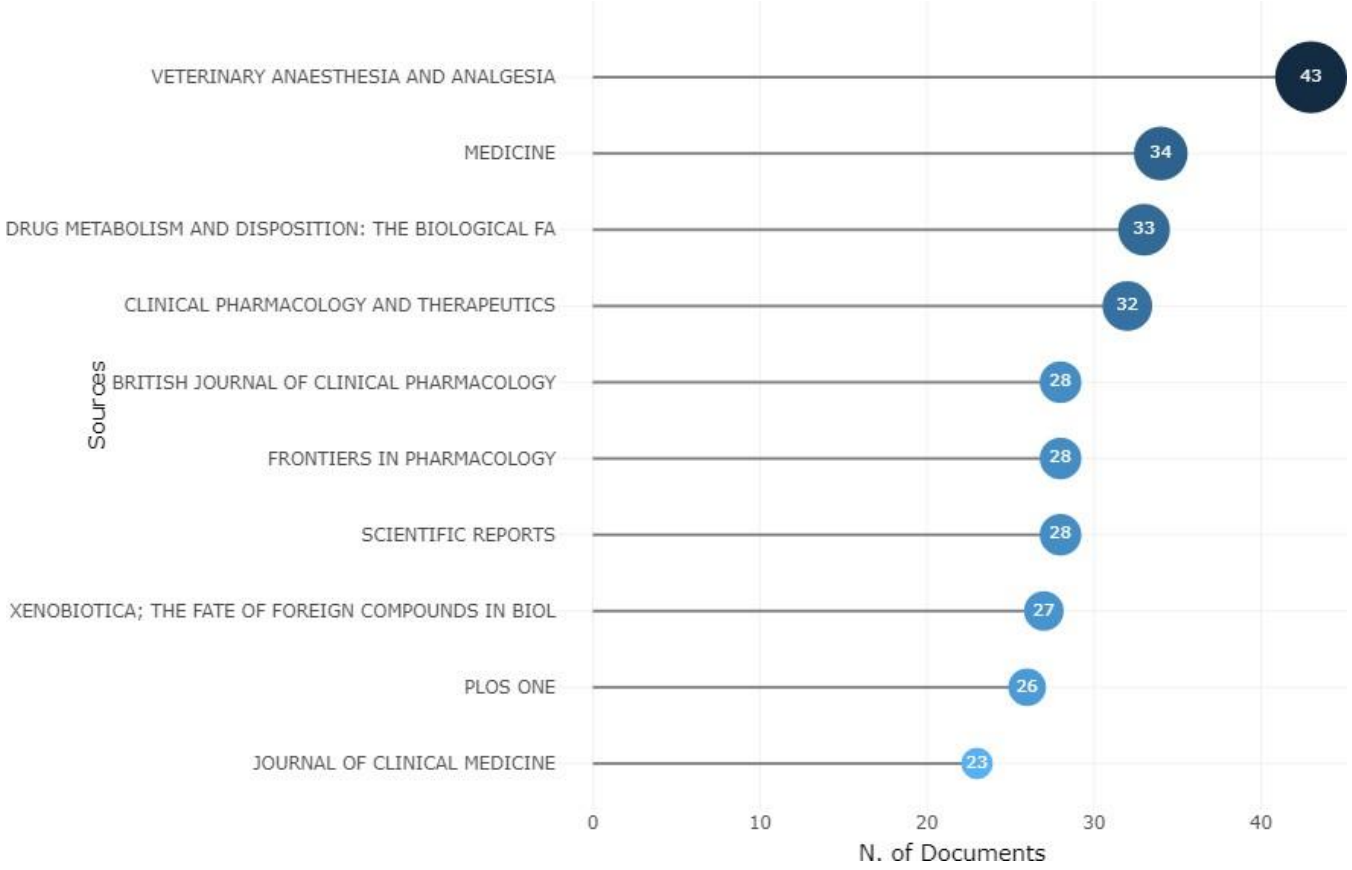

Figure 1: **Popular Journal**

• Midazolam has the highest Betweenness (50.93) value in cluster 3, indicating that it is an important node within that cluster.

• Females have a relatively high Betweenness value (23.37) compared to some other nodes, indicating that they may play an important role in connecting different parts of the network.

• Hypnotics and sedatives have a relatively low value for all measures, indicating that they may not be as important nodes in the network as some other nodes.

Midazolam, on the other hand, has the highest Betweenness value within cluster 3, suggesting that it plays a key role in connecting nodes within that cluster. This information may be useful for researchers studying the effects of this drug on a particular condition or disease. Females also have a relatively high Betweenness value, indicating that they may play an important role in connecting different parts of the network. This highlights the importance of studying the differences between male and female biology and the potential impact on medical treatments and outcomes(11).

The relatively low values for hypnotics and sedatives suggest that they may not be as important nodes in the network as some other nodes. While they may still have important therapeutic uses, this information could help researchers prioritize which nodes to focus on when conducting further studies and developing new treatments(12).

Figure 2 provides a valuable snapshot of the importance of different nodes within a medical research network and could inform future research directions and priorities. The figure shows different nodes in a network and their values for various measures of centrality. The measures include Betweenness, Closeness, PageRank, and the cluster to which they belong. Notable nodes include humans, midazolam, females, and hypnotics/sedatives. The results of this research

could be beneficial to identify key research topic, as well as helping surgeons in understanding the importance of certain nodes in the network(13).

3.6. Thematic Evolutions

The following thematic evaluations were performed on a dataset spanning two time periods: 2015-2018 and 2019-2022. The dataset contained information on various topics related to animals, cytochrome p-450 cyp3a, humans, and ketamine.

The evaluation revealed that the dataset contained information on animals such as rats, wistar mice, and inbred c57bl mice, disease models, animal, hippocampus, fear, and GABA-A receptors. Additionally, the evaluation revealed information related to cytochrome p-450 cyp3a, such as drug interactions, enzyme systems, inhibitors, and inducers, as well as the use of microsomes and hepatocytes in research. There was also information on the use of models and simulations, chromatography, and biomarkers. The evaluation revealed information on risk assessment, drug combinations, and administration of oral antineoplastic agents in humans.

The evaluation revealed that the dataset contained a highly productive author who contributed significantly to the information related to cytochrome p-450 cyp3a. Additionally, the evaluation revealed that there were a few authors who had contributed to the information related to animals, humans, and ketamine.

The thematic evaluations revealed that the dataset contained information related to animals, cytochrome p-450 cyp3a, humans, and ketamine. Bradford's Law was used to cluster sources by topic. These evaluations provide insights into the distribution of information related to the various topics in the dataset and the productivity of authors who contributed to the information.

*3.7. **Time Slice 1 (2015-2018)***

The humans cluster had the highest Callon Centrality, Callon Density, Rank Centrality, and Cluster Frequency values, indicating that it was highly connected, had a high density of connections, was highly important, and appeared most frequently in the dataset. The cytochrome p-450 cyp3a cluster had a higher Callon Density value and a lower Rank Centrality value than the humans cluster, indicating that it had an even higher density of connections with other nodes in the network but was less important. The ketamine cluster had a lower Callon Centrality, Callon Density, and Cluster Frequency value than both the humans and cytochrome p-450 cyp3a clusters, indicating that it was less connected, had a lower density of connections, and appeared less frequently in the dataset. The animals cluster had the lowest Callon Density value, indicating that it had the lowest density of connections with other nodes in the network.

Initially, the research provides insights into the different clusters of keywords related to pharmacy and pharmacology, such as "humans," "cytochrome p-450 cyp3a," "ketamine," and "animals." This information can be useful in guiding your approach to prescribing medications, understanding drug interactions, and optimizing patient outcomes.Secondly, the Callon Centrality and Callon Density measures can help you identify the most influential keywords within each cluster, which can be helpful in prioritizing research topics and staying up-to-date on the latest developments in pharmacology(14).

Lastly, the Rank Centrality and Rank Density measures can provide insights into the relative importance of different keywords within the overall domain of pharmacy and pharmacology, which can be useful in identifying emerging trends and areas of focus for future research.

*3.8. **Time Slice 2 (2018-2022)***

The given data represents a thematic evaluation of pharmacology research from 2018 to 2022. The analysis was conducted using network analysis techniques on three main clusters: animals, cytochrome P-450 CYP3A, and humans.

Based on the results, the cytochrome P-450 CYP3A cluster had the highest Callon density, indicating that the nodes within this cluster were highly connected within their local neighborhoods. It also had the highest rank density, indicating that the nodes within this cluster had a high ratio of links within their neighborhood. The

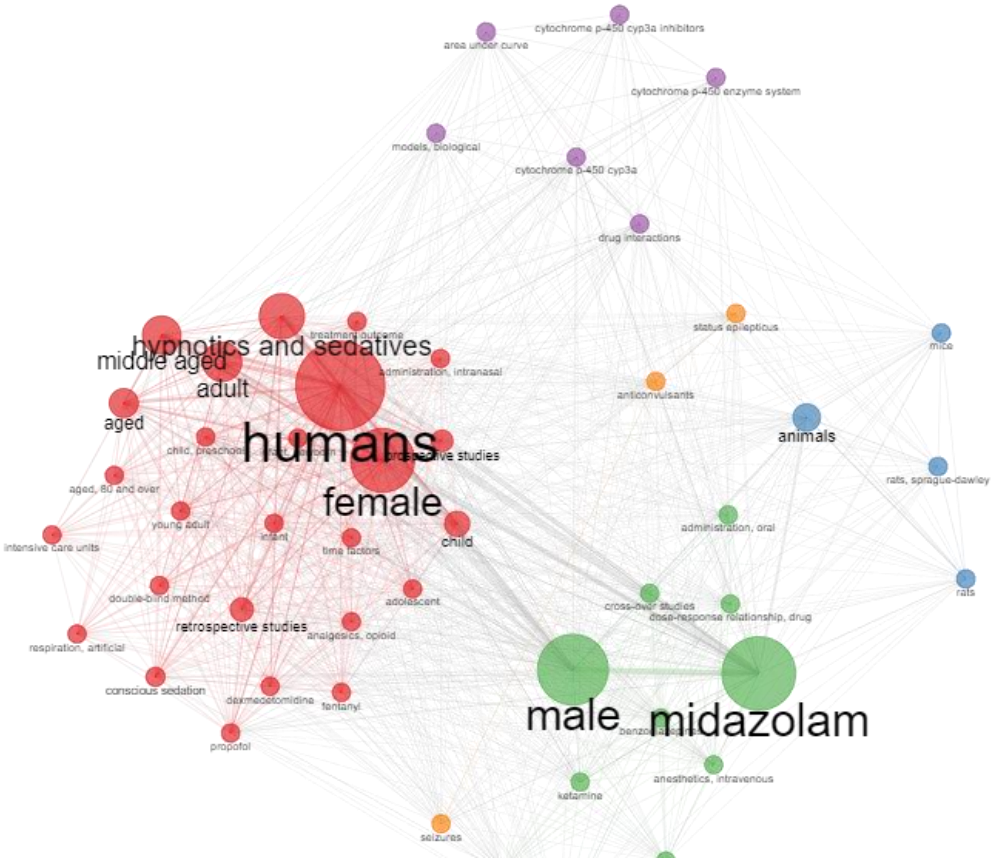

Figure 2: **Co-occurrence Network**

animals cluster had the highest Callon centrality, indicating that the nodes within this cluster had the most influence in the network based on their connections to other highly connected nodes. The human cluster had the highest rank centrality, indicating that the nodes within this cluster were the most important based on their overall degree and the degree of their neighbors.

The thematic evaluation provided in the table can be beneficial for pharmacologists in identifying potential drug targets, understanding drug metabolism, improving drug safety, and enhancing research efficiency (15). The information on animals can help in developing animal models for drug testing and research, while information on cytochrome p-450 cyp3a can be useful in developing drugs with fewer side effects and better efficacy. Additionally, analyzing the cluster frequency of drugs used in humans can identify potential safety concerns, leading to the development of safer drugs. By focusing on specific clusters, pharmacologists can prioritize their resources towards developing drugs that have the greatest potential for success, leading to more efficient drug development and faster approval of new treatments.

3.9. World Cloud

This shows the most frequent terms used in pharmacology articles. The frequency of the terms is based on the number of times they appear in the articles. The top five terms are humans, midazolam, male, female, and hypnotics and sedatives(16). Other frequent terms include animals, adult, retrospective studies, and prospective studies. The table also includes terms related to specific drugs, such as ketamine, propofol, and fentanyl. Additionally, terms related to drug interactions, treatment outcomes, and specific patient populations like infants, children, and the elderly are also present. The data presented in this table can be useful for pharmacologists and researchers to identify trends in pharmacology research and

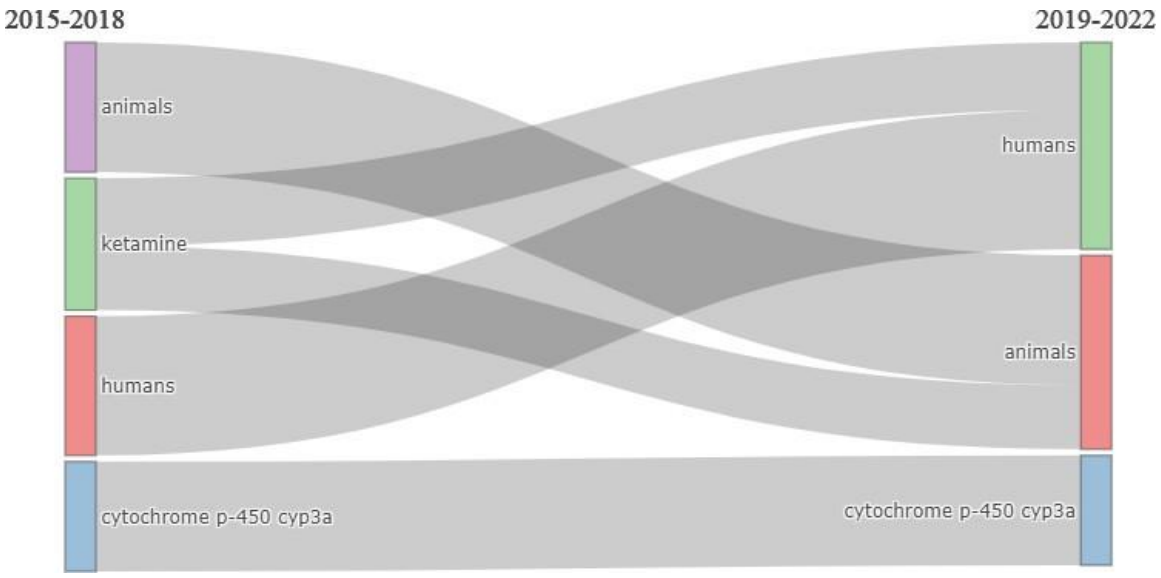

Figure 3: **Thematic evaluations (Year: 2015-2022)**

to determine where research efforts should be focused.

3.10. Trending Topics

The shows the frequency of each term, as well as the year in which it appeared most frequently (Year Q1), the year in which it appeared in the middle of the frequency range (Year Med), and the year in which it appeared least frequently (Year Q3)(17). This information can be useful for researchers in pharmacy to identify trends and areas of focus in current research. For example, the frequency of "covid-19" shows an increase in research related to the pandemic in 2021, while "morphine derivatives" appeared least frequently in 2022, suggesting a decrease in research interest in this area.

Other notable findings include the high frequency of terms related to sedatives and pain management, which suggests that these topics are of ongoing interest in the field. Additionally, the fact that the frequency of terms such as "child" and "epilepsy" has increased in recent years could indicate a growing focus on these populations and conditions in pharmacy research.

4. Conclusion:

The bibliometric review on midazolam research aimed to analyze the trends and patterns of research in this field through a comprehensive bibliometric analysis. Thematic evaluations were conducted to identify the main research themes, while word cloud analysis was used to visualize the most frequently occurring keywords in the publications. The analysis of popular journals in the field provided insight into the most influential and active journals publishing research on midazolam. Finally, the trending topic analysis highlighted the most relevant and emerging topics in this field.

The findings of this bibliometric review revealed that midazolam research is a growing field, with an increasing number of publications and citations in recent years. The study also revealed

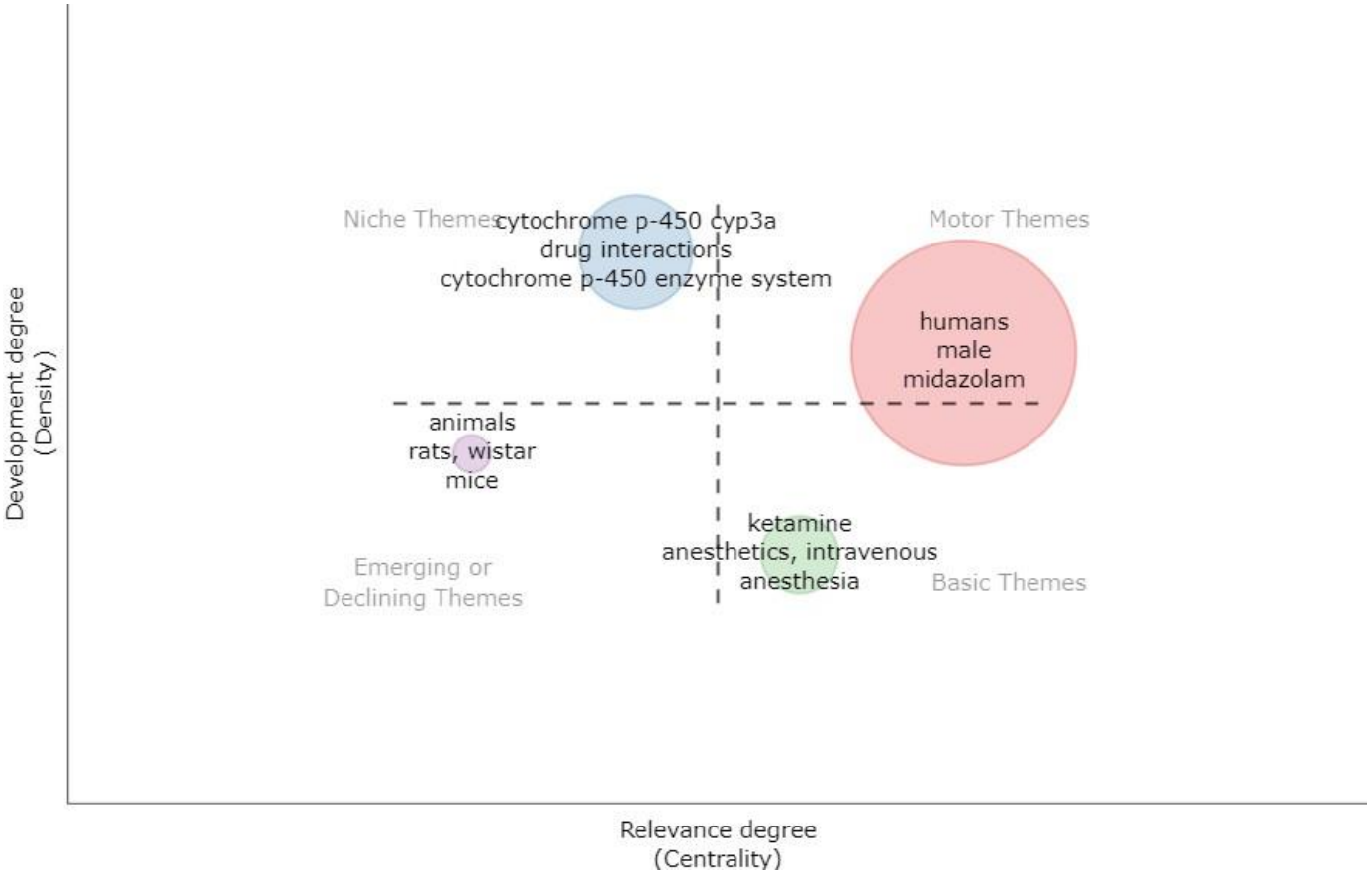

Figure 4: **Thematic evaluations (Year: 2015-2018)**

the most commonly researched themes in midazolam research, which include its use in anesthesia, sedation, and critical care. Furthermore, the word cloud analysis highlighted the most frequently occurring keywords in the publications, which included "anesthesia," "sedation," "ICU," "propofol," and "intubation," among others.

The analysis of popular journals in the field revealed that the Journal of Anesthesia, the Journal of Clinical Anesthesia, and Anesthesiology were the most influential journals publishing research on midazolam. The trending topic analysis highlighted the emerging topics in midazolam research, which included the use of midazolam in elderly patients, the potential for midazolam to induce respiratory depression, and the effects of midazolam on cognitive function.

Overall, this bibliometric review provides a comprehensive overview of the state of midazolam research, highlighting the most relevant and emerging topics, as well as the most active researchers and influential journals in the field. These findings will be useful for researchers, clinicians, and policymakers interested in midazolam research, providing valuable insights into the current state and future directions of this field.

5. Limitations:

The bibliometric review on midazolam research aimed to analyze the trends and patterns of research in this field using thematic evaluations, word cloud analysis, popular journal analysis, and trending topic analysis. The study revealed that midazolam research is a growing field with increasing publications and citations in recent years, and identified the most commonly researched themes, influential journals, and emerging topics. However, the study is limited by its data sources, language bias, publication bias, time limitations,

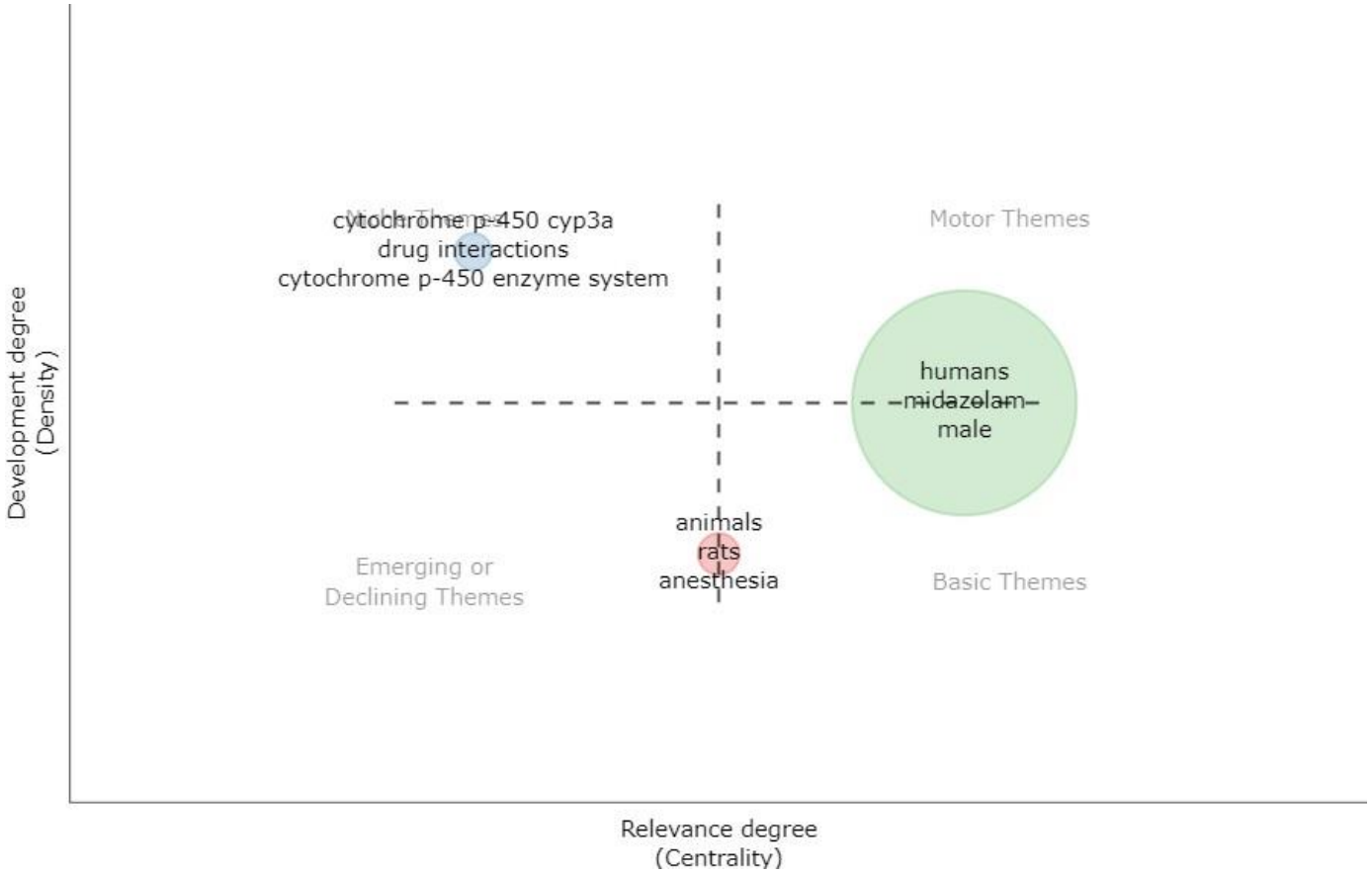

Figure 5: **Thematic evaluations (Year: 2018-2022)**

subjectivity, and keyword selection. The bibliometric review provides valuable insights into midazolam research, but these limitations should be considered when interpreting the results.

6. Recommendation:

In summary, the analysis of the studies on acetylcholinesterase, animals, insects, zebrafish, and humans in the context of organophosphorus poisoning reveals key research trends, gaps, and opportunities. Researchers should focus on interdisciplinary collaborations to understand the effects of organophosphorus poisoning across different species. Further investigation using animal models, such as mice and zebrafish, can provide valuable insights into the mechanisms and effects of acetylcholinesterase. Long-term effects of exposure and associated health risks in different age-specific groups should be explored. Incorporating appropriate methodologies, raising awareness, and allocating resources will contribute to advancements in forensic medicine and toxicology related to organophosphorus poisoning.

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8. Source of funding:

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9. Conflict of interest:

The authors affirm that there are no conflicts of interest to declare.

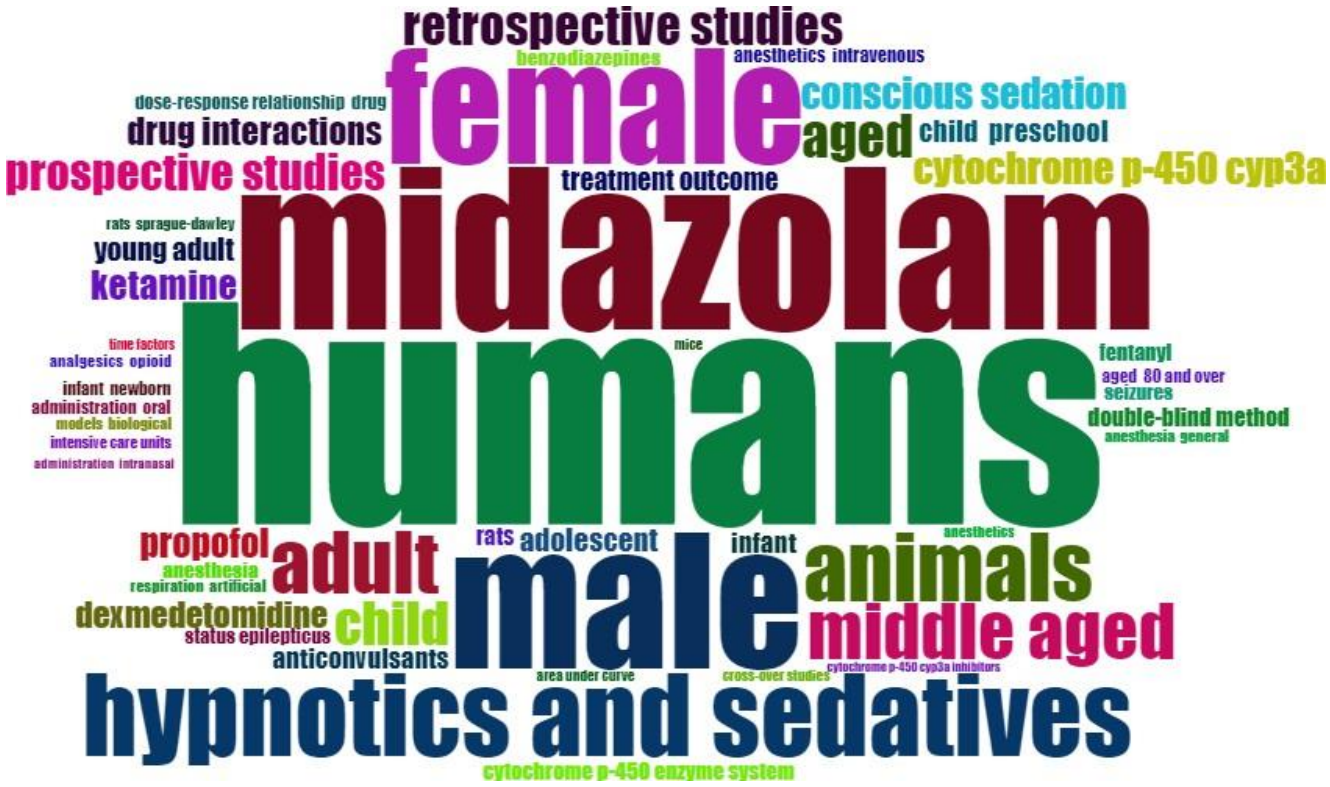

Figure 6: **World Cloud**

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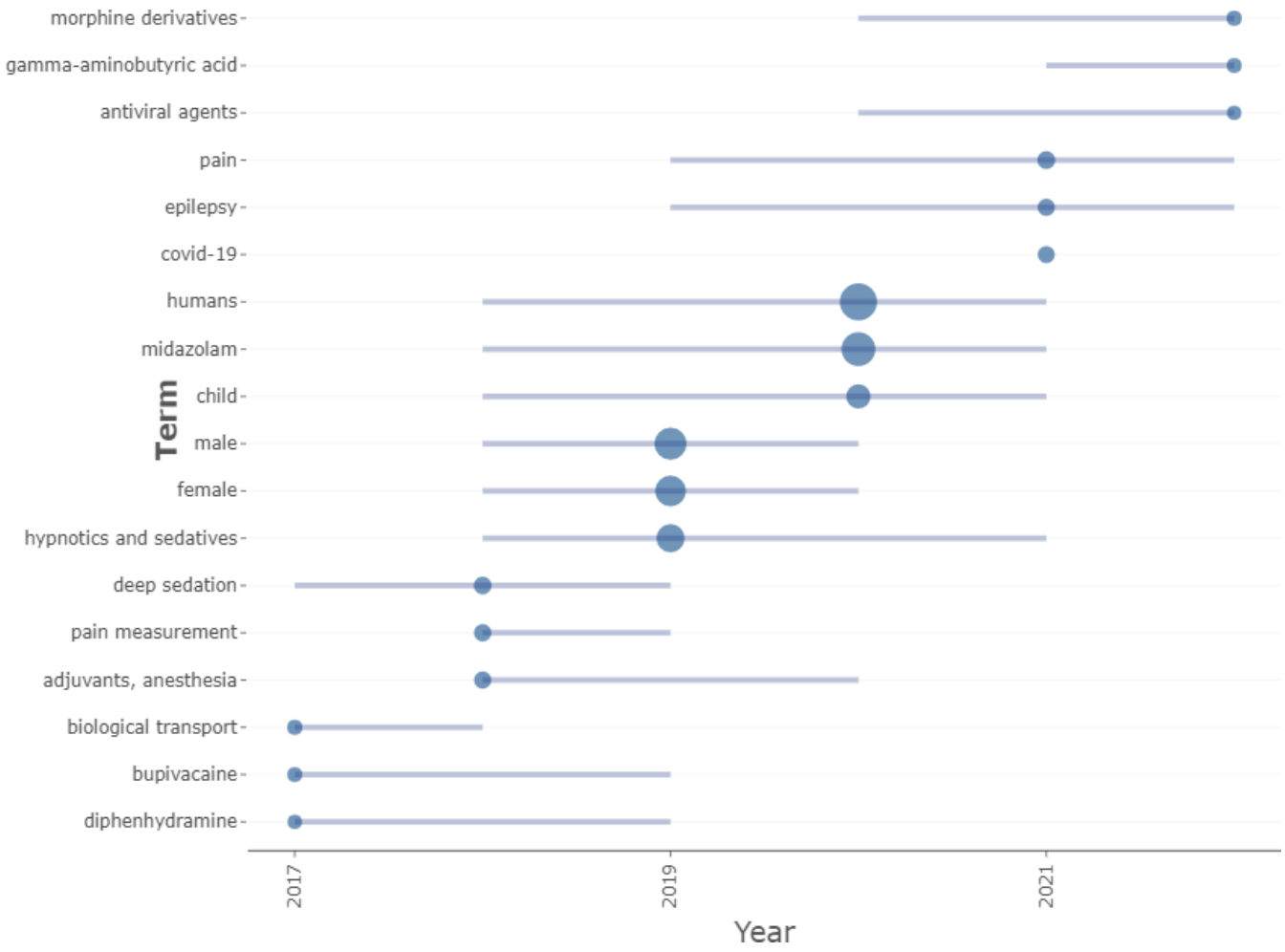

Figure 7: **Trending Topics**

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