

Bibliometric and Visual Analysis of the Current Status and Trends of Postoperative Pain in Children from 1950–2021

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Background: Postoperative pain in children has been overlooked for a long time. The knowledge structure, research hotspots and trends related to postoperative pain in children are unclear and have not been systematically summarized.

Purpose: We aimed to analyze the current state of research on postoperative pain in children and to conduct in-depth mining of the knowledge structure.

Methods: The PubMed database for publications on postoperative pain in children between 1950 and 2021 was searched. Bibliographic Item Co-Occurrence Matrix Builder (BICOMB) was performed to obtain the co-word matrix and co-occurrence matrix. The H-index method was used to extract high-frequency main Medical Subject Headings (MeSH) terms/subheadings.

Results: The high-frequency MeSH terms were analyzed by biclustering, strategic diagram and social network analyses. Totally, 4022 publications were retrieved. The analysis showed that 60 countries or regions published relevant documents, with the United States publishing the most significant number of papers. Totally, 811 journals published relevant papers, with Pediatric Anesthesia ranking first. Moreover, we extracted 43 high-frequency main MeSH terms/subheadings and clustered them into five categories: overview, aetiology and epidemiology, pharmacotherapy, opioid administration and dosing, and prevention and control of postoperative pain in children.

Conclusion: Pharmacological treatments, pain prevention and control are the focus of research and are becoming increasingly mature. Opioid stewardship and regional anesthesia is the trend and focus of future research. Our study offers a better understanding of the current status and knowledge structure of postoperative pain in children and provides a reference for improving postoperative pain management in children in the future.

Keywords: bibliometrics, visualization analysis, postoperative pain, children, status, trends

Introduction

Over the past decades, many parents and physicians have been under-aware of postoperative pain in children, with a greater focus on the completion of the surgery, and the pain experienced by children after surgery has been overlooked. The World Health Organization (WHO) states that postoperative pain in children is a public health problem in most countries of the world.¹ Surveys on the incidence of moderate to severe postoperative pain in children are 21% to 64%.^{2,3} However, there are no universally accepted guidelines for the management of perioperative pain in children. Although the WHO has developed guidelines for “persistent pain in children”, they specifically exclude perioperative pain. In recent years, clinicians have become increasingly aware of the need for adequate analgesia for children after surgery.⁴ Adequate analgesia during the first 48 hours after surgery reduces the neuroendocrine stress response of the body, improves the prognosis of the children and reduces medical costs.⁵ However, the management of postoperative pain in children varies greatly around the world.

Management strategies for pain management are influenced by a variety of factors, including geography, culture, infrastructure, etc.⁶ Postoperative pain management involves multiple disciplines, including surgery, anesthesiology, nursing,

addiction science, and parent and child psychology. In this context, it is extremely necessary to define minimum standards for postoperative analgesia in children. The WHO recommends a two-step management approach involving analgesic selection according to the severity of pain, for persistent pain in children and adolescents.¹ Stepwise management is the basic standard for postoperative pain management in children, with a graded approach of primary, secondary, and advanced management according to different types of surgery. Combining multimodal analgesia further optimizes pain management. Enhanced psychological treatment for the child and parents will help to relieve postoperative pain in children.⁷

Bibliometrics and information visualization are important scientific research tools that are widely used in a variety of disciplines. The rapid development of bibliometric analysis software has made it easier for researchers to obtain scientific quantitative analysis, which is an important reference value for exploring the knowledge structure of disciplines, planning the layout of disciplines, and adjusting the direction of disciplines. A large amount of literature on postoperative pain in children has been published in recent years, which mainly includes assessment of postoperative pain in children, treatment with analgesic drugs, multimodal analgesia techniques, and multidisciplinary cooperation. Nevertheless, none of the studies comprehensively analyzed and elaborated the research status, research hotspots, and research trends of postoperative pain in children. Due to the inherent specificity of the pediatric population, such as rapid physical development and high psychological sensitivity and vulnerability, it is difficult to conduct large-scale clinical studies, and the vast majority of current evidence comes from single-center studies and isolated procedures. In this study, we used analytical tools to conduct a bibliometric analysis and mine the knowledge structure of the literature related to postoperative pain in children. These findings may provide a better understanding the field of postoperative pain in children and a reference for future investigations.

Materials and Methods

Data Collection and Retrieval Strategy

The original data for this paper were all obtained from the PubMed database. The PubMed was chosen as the data source for two reasons: (1) PubMed is a national library of medicine with a free authoritative database of medical literature on health and medical information; and (2) Medline, a subset of PubMed, is indexed with Medical Subject Headings (MeSH) terms, which are a set of normalized words that can reflect the content of an article. Co-word clustering analysis can be implemented according to these terms. The search was conducted on December 31, 2021, and was completed within one day to ensure that the results were as up-to-date as possible. There are no language restrictions on the literature search and download process. The search strategy of our study was: pain, postoperative [MeSH terms] AND child [MeSH terms]. There was no time limit, the type of literature was limited to “Journal Article”, and the search results were filtered. A total of 4032 publications were identified from PubMed. The titles and abstracts of the publications were filtered based on relevance and selection criteria. The inclusion criteria were mainly concerned with postoperative pain in children. The exclusion criteria included 1) animal studies, 2) use of sedation in the intensive care unit, 3) including adults, 4) not within the prescribed age range, and 5) retracted articles. Two investigators performed independent reviews and assessments and reached an agreement on inclusion analysis. The 90% of papers were agreed upon by the two investigators, representing strong concordance. Before reaching a consensus, all discrepancies present would be discussed concerning the study objectives, and 4022 relevant articles were finally identified, saving the literature in “.TXT” format.

BICOMB Co-Word Analysis

The documents in.TXT format downloaded from the PubMed database were imported into the Bibliographic Item Co-Occurrence Matrix Builder (BICOMB) software developed by Professor Lei Cui⁸ of the China Medical University to extract the data. The key fields were set as main MeSH terms/subheadings, and the main MeSH terms/subheadings were excavated and investigated to extract and count the frequencies of all the main MeSH terms/subheadings. In this study, the H-index method was used to obtain high-frequency MeSH terms and the information related to year, country and periodical were also counted, and the co-word matrix and co-occurrence matrix of high-frequency MeSH terms were generated.

Biclustering Analysis of High-Frequency Main MeSH Terms/Subheadings

In this study, the graphical clustering toolkit (gCluto) 1.0 developed by Rasmussen from the University of Minnesota was used to import the co-word matrix of high-frequency main MeSH terms/subheadings.⁹ The clustering method was chosen as Repeated Bi-section (RB), the number of clusters was set to 5, and the remaining parameters were chosen as the default values. A biclustering visualization analysis was performed, a mountain visualization and visualization matrix were drawn, and the number of clusters, intra-cluster similarity, and intra-cluster standard deviation (SD) was calculated.¹⁰ The mountain visualization is three-dimensional mountain clustering graphs produced by the multidimensional scaling manner. The color of the mountain peaks is inversely proportional to the intra-cluster SD, with red representing small SD and blue representing large SD. The height of the mountain is proportional to the intra-cluster similarity, the steeper the peak, the greater the intra-cluster similarity. The volume of the mountain is proportional to the number of MeSH terms within the cluster. The distance between the peaks reflects the correlation between clusters, and clusters with strong correlations appear to be gathered and overlapping. The values of the original data of the matrix in the visualization matrix are replaced by colors, and the depth of colors represents the frequency of MeSH terms, the darker the color, the higher the frequency. The rows of the visualization matrix represent the clusters of high-frequency main MeSH terms/subheadings, and the columns represent the PMID clusters corresponding to the source literature.

Strategic Diagram Analysis

The principle of strategic diagram analysis is to visualize the internal and external links between different topics based on co-occurrence matrix and clustering, to quantitatively evaluate the significance and development degree of different topics in a specific field, and to investigate the research hotspots and frontiers and development trends in a specific field.¹¹ The two-dimensional diagram drawn with the parameters of centrality and density is the strategic diagram, with the horizontal axis representing centrality and the vertical axis representing density. Centrality represents the strength of a topic's connection with other topics. A higher value indicates that the topic is more closely associated with other topics and is at the core of the research topic. Density represents the strength of connection within a single topic. The value of density indicates the degree of the topic maturity. The higher value of the density, the higher degree of maturity.

Social Network Analysis

Social networks are social structures composed of individuals (or organizations) called “nodes” that are linked together by one or more specific types of interdependence.¹² The main purpose of social network analysis is to represent the location of research nodes in a multi-relation network and the grid structure containing multiple relations. Network analysis could provide a clear understanding of the role of nodes in the social structure. In the present study, after a co-occurrence matrix of 43 high-frequency main MeSH terms/subheadings was formed by the BICOMB software, a social network analysis was constructed using Ucinet 6.0 software¹³ to interpret the structure of knowledge in the field of postoperative pain in children. Thereafter, the high-frequency main MeSH terms/subheadings network was visualized using NetDraw 2.084 software (Analytic Technologies Co., Lexington, KY, USA) and presented on a two-dimensional map. The high-frequency main MeSH terms/subheadings networks were represented as nodes, and co-occurrence frequencies were represented as line segments. The density of high-frequency main MeSH terms/subheadings is used to measure the closeness of the network. The location of high-frequency main MeSH terms/subheadings was assessed by measuring three centralities (closeness degree, betweenness degree, and degree) of each node to understand the network structure of postoperative pain in children. The diagram process of literature retrieval, study selection and analysis are shown in [Figure 1](#).

Results

Overall Distribution

According to the search strategy, duplicates and literature that did not meet the inclusion criteria were omitted, and a total of 4022 publications were finally identified. Overall, there was an increasing trend in the publication of literature on postoperative pain in children ([Figure 2A](#)). The statistics ([Figure 2B and C](#)) showed that a total of (or only) 60 countries or regions published research papers related to pain in children from 1950 to 2021. In terms of the number of publications,

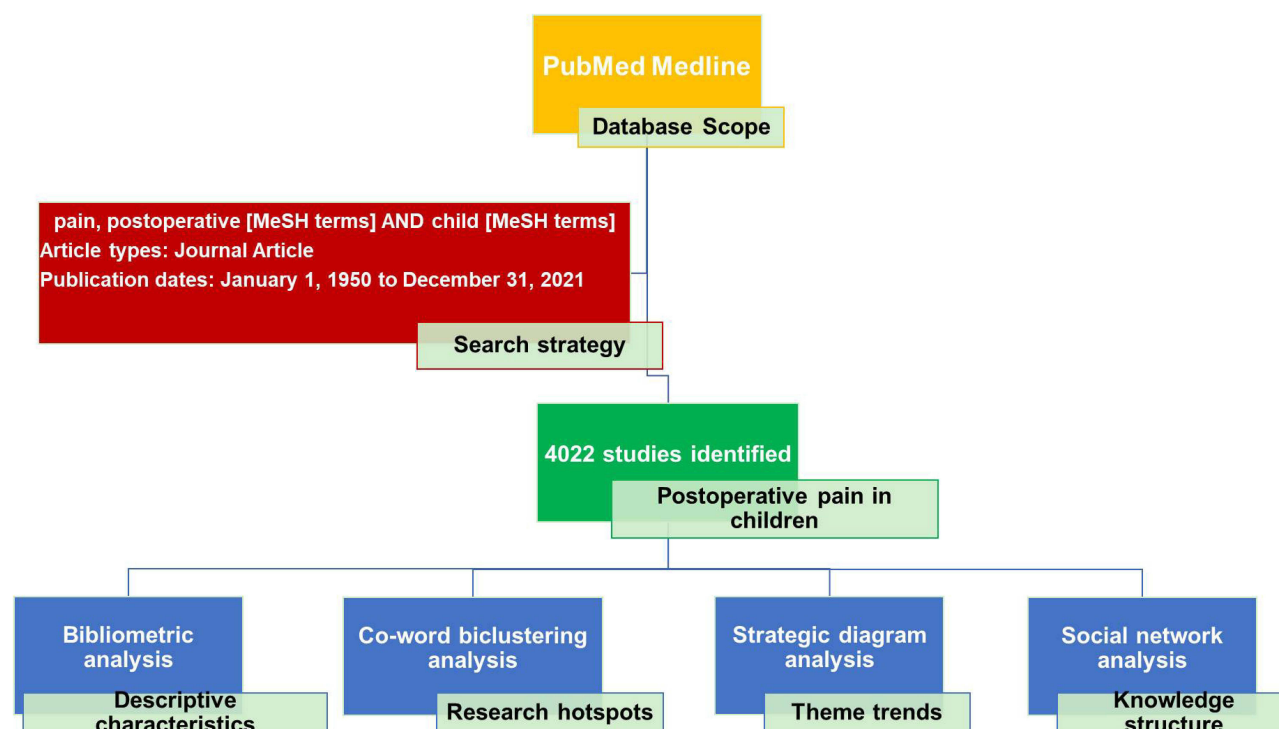


Figure 1 The diagram process of literature retrieval, study selection and analysis. The original data were all obtained from the PubMed database. The search was conducted on from the January 1, 1950 to December 31, 2021 using pain, postoperative [MeSH terms] AND child [MeSH terms] keywords. A total of 4032 publications were identified from PubMed. Thereafter, we performed bibliometric analysis, co-word biclustering analysis, strategic diagram analysis, and social network analysis.

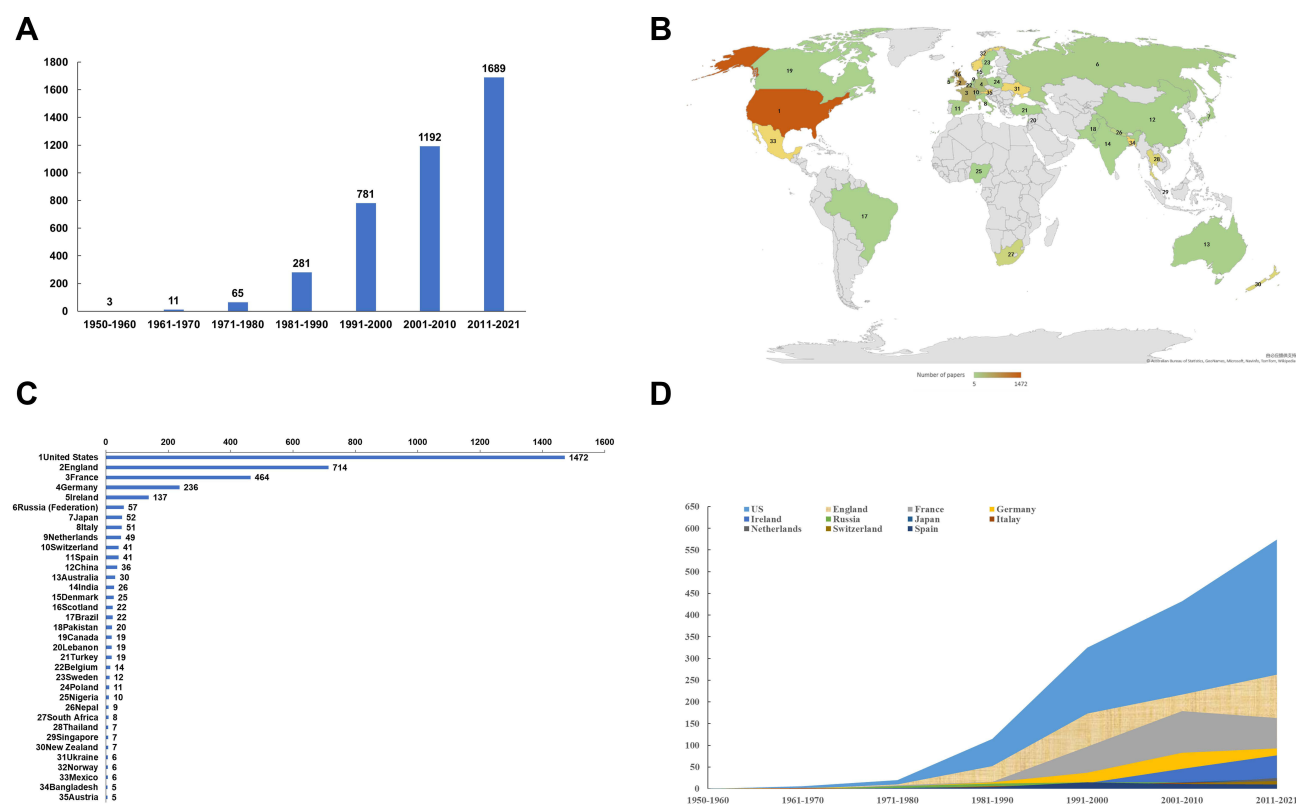


Figure 2 The distribution of published articles on postoperative pain in children from 1950–2021. **(A)** Number of publications on postoperative pain in children from 1950–2021; **(B)** The geographical distribution of the Top 35 countries; **(C)** The number of publications from the Top 35 countries; **(D)** Comparison of the attention level of postoperative pain research in children in different periods in the Top 11 countries.

the United States had the maximum number of publications, with 1472, accounting for 36.60% of the total (1472/4022), and was the most dominant country in the field of pediatric pain research. The countries ranked 2–10 were England, France, Germany, Ireland, Russia, Japan, Italy, Netherlands, and Switzerland, respectively. According to the area chart (Figure 2D), we found that there had been a surge in studies of pain in children in the United States, England, Germany, and Ireland over the last 30 years, indicating that pain in children has gradually become a focus of researchers' attention. Interestingly, France showed an exponential increase from 1980–2010, while the number of studies gradually decreased after 2010. A total of 811 journals published literature related to pediatric pain from 1950 to 2021. This study showed (Table 1) that the top 15 journals in terms of the number of publications published a total of 1324 relevant papers, accounting for 32.92% of the total (1324/4022). Among them, Pediatric Anaesthesia published 366 papers, accounting for 9.1% of the total (366/4022), with the most significant number of publications. The journal is published by Arnette-Blackwell, France Paris.

Analysis of Research Hotspots Based on MeSH Terms Cluster

A total of 3159 main MeSH terms/subheadings were counted using BICOMB, and 43 high-frequency main MeSH terms/subheadings were extracted based on the H-index method (the cumulative percentage was 41.32%) (Table 2). The co-occurrence analysis was performed for the 43 high-frequency main MeSH terms/subheadings to form a co-word matrix with 43 rows \times 2877 columns. Thereafter, the co-word matrix was imported into gCluto software for clustering analysis. According to the actual clustering effect, the 43 high-frequency main MeSH terms/subheadings were finally chosen to be clustered into five categories. The visualization matrix was shown in Figure 3A. The horizontal direction (rows) of the visualization matrix was the clustering of the 43 high-frequency main MeSH terms/subheadings. As revealed from the clustering results, the number of main MeSH terms/subheadings within each cluster had little difference. The vertical

Table 1 Core Published Journals of Postoperative Pain in Children Research from 1950–2021

Rank	Journal	Publication	Percentage%
1	Paediatr Anaesth	366	9.10
2	Int J Pediatr Otorhinolaryngol	137	3.41
3	Anesth Analg	134	3.33
4	Br J Anaesth	101	2.51
5	J Pediatr Surg	90	2.24
6	Anaesthesia	68	1.69
7	Acta Anaesthesiol Scand	58	1.44
8	Can J Anaesth	52	1.29
9	J Pediatr Orthop	50	1.24
10	Anesthesiology	49	1.22
11	Laryngoscope	47	1.17
12	J Laryngol Otol	45	1.12
13	J Clin Anesth	45	1.12
14	Otolaryngol Head Neck Surg	43	1.07
15	Pain	39	0.97
16	Eur J Anaesthesiol	38	0.94
17	Anesteziol Reanimatol	36	0.90
18	Eur Arch Otorhinolaryngol	35	0.87
19	J Pediatr Nurs	33	0.82
20	J Pediatr Urol	33	0.82
21	Anaesthesist	33	0.82
22	Reg Anesth Pain Med	31	0.77
23	Cochrane Database Syst Rev	31	0.77
24	Anaesth Intensive Care	31	0.77
25	J Urol	30	0.75

Abbreviation: MeSH, Medical Subject Headings.

Table 2 High-Frequency MeSh Major Topic/Subheadings from the Included Papers on Postoperative Pain in Children

Rank	MeSh Major Topic/Subheadings	Frequency	Proportion of Frequency (%)	Cumulative Percentage (%)
1	Pain, Postoperative/*drug therapy	988	7.12	7.12
2	Pain, Postoperative/*prevention and control	753	5.43	12.55
3	Pain, Postoperative/*therapy	211	1.52	14.07
4	Analgesics, Opioid/*therapeutic use	210	1.51	15.59
5	Analgesics, Opioid/*administration and dosage	196	1.41	17.00
6	Anesthetics, Local/*administration and dosage	185	1.33	18.34
7	Tonsillectomy/*methods	174	1.25	19.59
8	Nerve Block/*methods	170	1.23	20.82
9	Tonsillectomy/*adverse effects	168	1.21	22.03
10	Analgesics/*therapeutic use	162	1.17	23.20
11	Morphine/*administration and dosage	125	0.90	24.10
12	Pain, Postoperative/*diagnosis	120	0.87	24.96
13	Analgesia/*methods	120	0.87	25.83
14	Bupivacaine/*administration and dosage	119	0.86	26.69
15	Pain Measurement/*methods	117	0.84	27.53
16	Pain, Postoperative/*etiology	111	0.80	28.33
17	Analgesics/*administration and dosage	108	0.78	29.11
18	Pain Management/*methods	90	0.65	29.76
19	Pain, Postoperative/*epidemiology	90	0.65	30.41
20	Hernia, Inguinal/*surgery	90	0.65	31.05
21	Anesthetics, Local/*therapeutic use	89	0.64	31.70
22	Pain, Postoperative/*nursing	87	0.63	32.32
23	Scoliosis/*surgery	81	0.58	32.91
24	Anti-Inflammatory Agents, Non-Steroidal/*therapeutic use	80	0.58	33.48
25	Pain, Postoperative/*psychology	79	0.57	34.05
26	Laparoscopy/*methods	78	0.56	34.62
27	Morphine/*therapeutic use	75	0.54	35.16
28	Analgesics, Non-Narcotic/*therapeutic use	74	0.53	35.69
29	Analgesia, Epidural/*methods	69	0.50	36.19
30	Acetaminophen/*therapeutic use	65	0.47	36.66
31	Anesthesia, Caudal/*methods	61	0.44	37.10
32	Acetaminophen/*administration and dosage	61	0.44	37.54
33	Bupivacaine/*therapeutic use	59	0.43	37.96
34	Funnel Chest/*surgery	51	0.37	38.33
35	Tonsillitis/*surgery	51	0.37	38.70
36	Parents/*psychology	51	0.37	39.07
37	Analgesics, Non-Narcotic/*administration and dosage	49	0.35	39.42
38	Anesthesia, Local/*methods	45	0.32	39.74
39	Anti-Inflammatory Agents, Non-Steroidal/*administration and dosage	44	0.32	40.06
40	Ketamine/*therapeutic use	44	0.32	40.38
41	Ketamine/*administration and dosage	44	0.32	40.70
42	Tramadol/*therapeutic use	43	0.31	41.01
43	Adenoidectomy/*adverse effects	43	0.31	41.32

Notes: The words before “/” mean the subject headings, which are defined as a normalized expression of a natural language. The words after “/” mean the subheadings, which are used to define a specific aspect of a subject. If “*” on the subheadings, such as: Pain, Postoperative/*drug therapy indicates that the article does not discuss all aspects of postoperative pain, but focuses on the effects of drug therapy on postoperative pain. “&” indicates and.

Abbreviation: MeSH, Medical Subject Headings.

direction (columns) was the clustering of 4022 documents, and the PMID numbers of the documents were represented by the corresponding columns at the top of the figure. The visualized mountain map was shown in Figure 3B, and the clustering effect was more satisfactory from the overall layout.

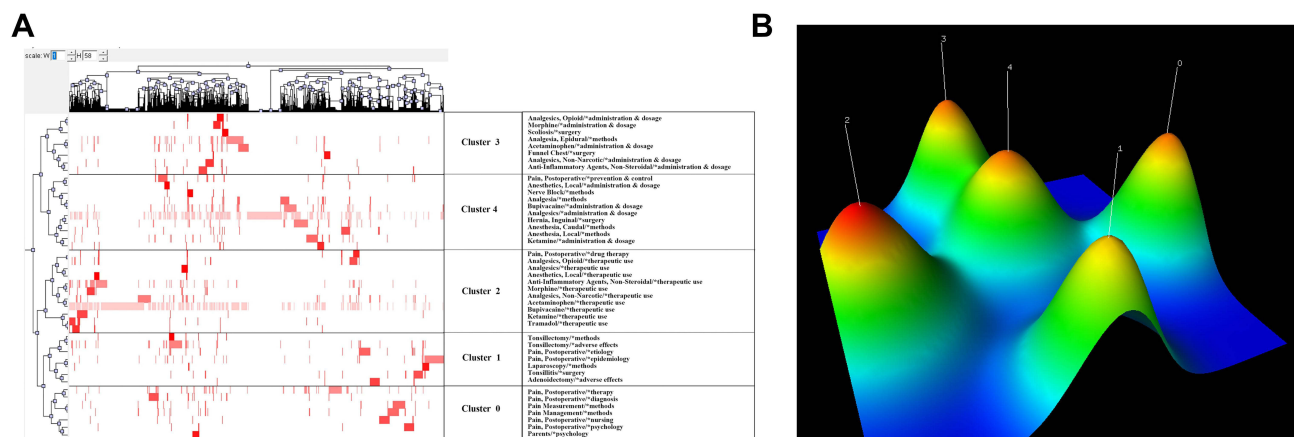


Figure 3 Biclustering analysis of 43 high-frequency main Medical Subject Heading (MeSH) terms/subheadings and articles on postoperative pain in children from 1950–2021. (A) Matrix visualization of biclustering of 43 high-frequency main MeSH terms/subheadings and PubMed Unique Identifiers of the articles; (B) Mountain visualization of biclustering of 43 high-frequency main MeSH terms/subheadings and articles.

Cluster 0 included seven high-frequency main MeSH terms/subheadings with towering peaks and a light red peak color. This cluster was an overview study of pain in children. Cluster 1 included seven high-frequency main MeSH terms/subheadings with medium peak height and yellow peak color, indicating that the topic similarity and the literature distribution were in the middle. This cluster was an etiological and epidemiological study of postoperative pain in children. Cluster 2 included 11 high-frequency main MeSH terms/subheadings, with the most prominent peak volume and a dark red peak color, indicating that the studies were more concentrated. This cluster was a study of pharmacological treatment of postoperative pain in children. Cluster 3 included eight high-frequency main MeSH terms/subheadings, with medium volume and light red peak color, and medium intracluster similarity. Clusters 3 and 4 had a few consecutive peaks, which may overlap with each other. The cluster was mainly focused on opioid administration and dosage studies. Cluster 4 included ten high-frequency main MeSH terms/subheadings with gentle mountains and similar color peaks to cluster 3, indicating looser research and a wider distribution of literature. This cluster was for studies on the prevention and control of postoperative pain in children.

Results of Strategic Diagram Analysis

Based on the results of the co-word clustering analysis and the co-occurrence matrix of high-frequency main MeSH terms/subheadings, the centrality and density of each cluster were calculated. Thereafter, the two-dimensional strategic diagram was plotted using the centrality and density (Figure 4). Clusters 2 and 4 located in Quadrant I had high centrality and density, indicating that the research on pharmacological treatment and prevention and control of postoperative pain in children had a relatively mature level of research. In addition, they also had extensive links with the remaining clusters and belonged to the core themes of postoperative pain in children. Clusters 0 and 1 in Quadrant III had low centrality and density values, indicating that the research of the overview and the study of etiological and epidemiological postoperative pain in children were immature, and the connection with other research themes was not close. Cluster 3 in Quadrant IV had low density and loose internal structure; however, it was relatively concerned in the hot topics of children's postoperative pain research compared with other themes, indicating that the administration and dosage of opioids needed to be further developed and improved.

Results of Social Network Analysis

The density value of the studies related to postoperative pain in children was calculated to be 0.64, indicating that the studies were overall closely connected. Social network analysis knowledge structure was constructed using closeness degree, betweenness degree and degree as centrality parameters (Table 3 and Figure 5). In the 1950–2021 children's postoperative pain network, a total of 18 high-frequency main MeSH terms/subheadings had high centrality above the mean. "Pain, Postoperative/*prevention & control" had the highest degree of centrality.

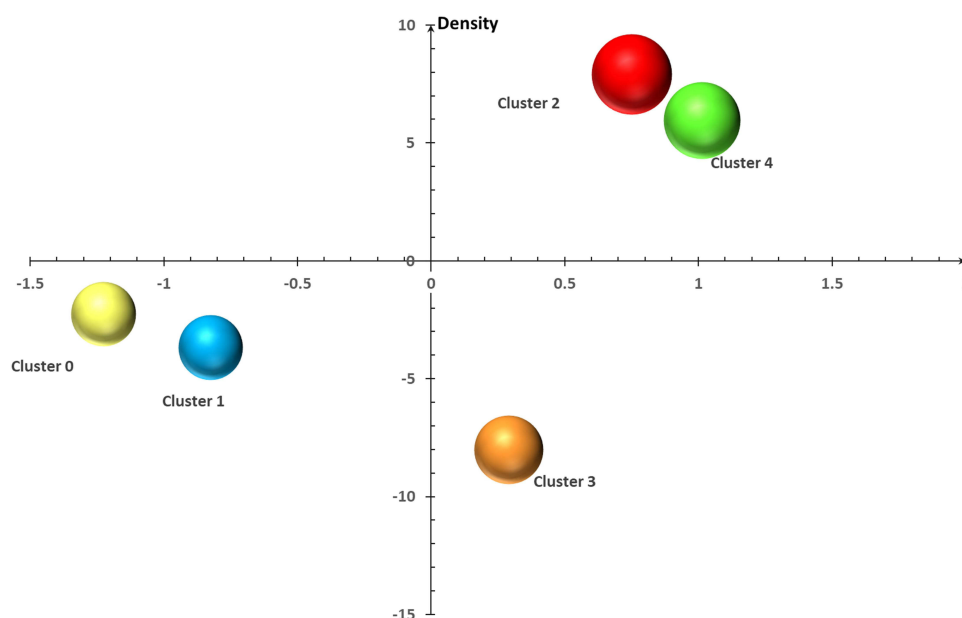


Figure 4 Strategic diagrams for postoperative pain in children related research. The quadrant represents the difference between density and centrality of the node. The size of a signal node represents the number of major Medical Subject Heading (MeSH) terms/subheadings involves in each cluster.

Discussion

Data on the present trends, research hotspots, and changes in research themes on the postoperative pain in children is limited. In the present study, the trends over the past 70 years in this research were investigated using the PubMed database. Our analysis showed that 60 countries or regions published relevant documents, with the United States publishing the most significant number of papers. Five categories, including overview, aetiology and epidemiology, pharmacotherapy, opioid administration and dosing, and prevention and control of postoperative pain in children, are described based on the 43 high-frequency main MeSH terms/subheadings. After bibliometric analysis, co-word

Table 3 Social Network Analysis of the Studies Related to Postoperative Pain in Children

MeSH Major Topic/ Subheadings	Degree	MeSH Major Topic/ Subheadings	Betweenness	MeSH Major Topic/ Subheadings	Farness
Pain, Postoperative/*prevention and control	42	Pain, Postoperative/*prevention and control	23.728	Pain, Postoperative/*prevention and control	42
Pain, Postoperative/*drug therapy	41	Pain, Postoperative/*drug therapy	23.436	Pain, Postoperative/*drug therapy	43
Analgesics, Opioid/*therapeutic use	38	Analgesics, Opioid/*therapeutic use	16.722	Analgesics, Opioid/*therapeutic use	46
Pain, Postoperative/*therapy	36	Pain, Postoperative/*therapy	16.153	Pain, Postoperative/*therapy	48
Tonsillectomy/*adverse effects	36	Tonsillectomy/*adverse effects	14.943	Tonsillectomy/*adverse effects	48
Anesthetics, Local/ *administration and dosage	34	Analgesics, Opioid/ *administration and dosage	13.491	Anesthetics, Local/ *administration and dosage	50
Analgesics, Opioid/ *administration and dosage	34	Analgesics/*therapeutic use	13.32	Analgesics, Opioid/ *administration and dosage	50
Analgesics/*therapeutic use	33	Anesthetics, Local/ *administration and dosage	12.939	Analgesics/*therapeutic use	51
Analgesia/*methods	32	Scoliosis/*surgery	11.31	Analgesia/*methods	52
Bupivacaine/*administration and dosage	32	Bupivacaine/*administration and dosage	10.181	Bupivacaine/*administration and dosage	52

(Continued)

Table 3 (Continued).

MeSH Major Topic/ Subheadings	Degree	MeSH Major Topic/ Subheadings	Betweenness	MeSH Major Topic/ Subheadings	Farness
Analgesics/*administration and dosage	31	Hernia, Inguinal/*surgery	9.321	Analgesics/*administration and dosage	53
Scoliosis/*surgery	31	Analgesia/*methods	9.09	Scoliosis/*surgery	53
Morphine/*administration and dosage	30	Analgesics/*administration and dosage	8.67	Morphine/*administration and dosage	54
Nerve Block/*methods	30	Nerve Block/*methods	8.18	Nerve Block/*methods	54
Hernia, Inguinal/*surgery	30	Pain, Postoperative/*etiology	8.012	Hernia, Inguinal/*surgery	54
Analgesia, Epidural/*methods	29	Adenoidectomy/*adverse effects	7.964	Analgesia, Epidural/*methods	55
Pain, Postoperative/*etiology	28	Morphine/*administration and dosage	7.579	Pain, Postoperative/*etiology	56
Pain Management/*methods	28			Pain Management/*methods	56
Mean	27.02	Mean	7.488	Mean	56.98
StdDev	6.289	StdDev	5.404	StdDev	6.289
Minimum	15	Minimum	1.103	Minimum	42
Maximum	42	Maximum	23.728	Maximum	69

Notes: The words before “/” mean the subject headings, which are defined as a normalized expression of a natural language. The words after “/” mean the subheadings, which are used to define a specific aspect of a subject. If “*” on the subheadings, such as: Pain, Postoperative/*drug therapy indicates that the article does not discuss all aspects of postoperative pain, but focuses on the effects of drug therapy on postoperative pain. “&” indicates and.

Abbreviations: MeSH, Medical Subject Headings; StdDev, standard deviation.

biclustering analysis, strategic diagram analysis, and social network analysis, we observed that opioid stewardship and regional anesthesia were the trend and focus of future research. Our study may provide a meaningful insight into the current status and knowledge structure of postoperative pain in children and offer an orientation for improving postoperative pain treatment in children in the future investigation.

The issue of pediatric pain received little attention until the first World Congress on Pediatric Pain in Seattle in 1988. However, current practice regarding managing postoperative pain in children varies widely worldwide, and even in more affluent regions, there are no uniform clinical practice guidelines. Clustering is a method to simplify complex data into a few categories, ie, the process of grouping and categorizing a large amount of data to understand the intrinsic structure of a data set based on the qualitative or quantitative characteristics of the data itself, and describing each data set. The classification results are intuitive and more detailed, comprehensive and reasonable than traditional classification methods. Therefore, we investigated the current trends, research hotspots, and changes in research themes on the postoperative pain in children using clustering data analysis. A total of 4022 publications were identified using the high-frequency MeSH terms. These publications were then analyzed by biclustering, strategic diagram and social network analyses. As indicated in our results, we observed that there was an increasing trend in the number of literature published by a total of (or only) 60 countries or regions from 1950 to 2021, with the United States having the maximum number of publications, followed by England, France, Germany, Ireland, Russia, Japan, Italy, Netherlands, and Switzerland. In addition, the results showed that a total of 811 journals published relevant papers, with Pediatric Anesthesia ranking first. These researches are mainly focused on pharmacotherapy, opioid administration and dosing, postoperative pain prevention and control, multimodal analgesia, and pain assessment methods in children.

Cluster 0 is an overview of postoperative pain in children. It mainly covers several aspects of postoperative pain management and treatment, the psychology of the child and parents, postoperative care, etc. Pain assessment in children is known to be very difficult and is influenced by numerous factors such as the child’s cognitive level, language skills, and cultural background.^{14,15} Pain assessment in children mainly relies on the subjective assessment of the nursing team and the parents.¹⁶ The main pain grading tools include physiological measures, observational and behavioral measures, self-reports, and parental reports.¹⁷ Some studies have demonstrated that physiological measures are usually not associated with self-reported pain, and behavioral measures usually reflect fear and anxiety rather than pain.¹⁸

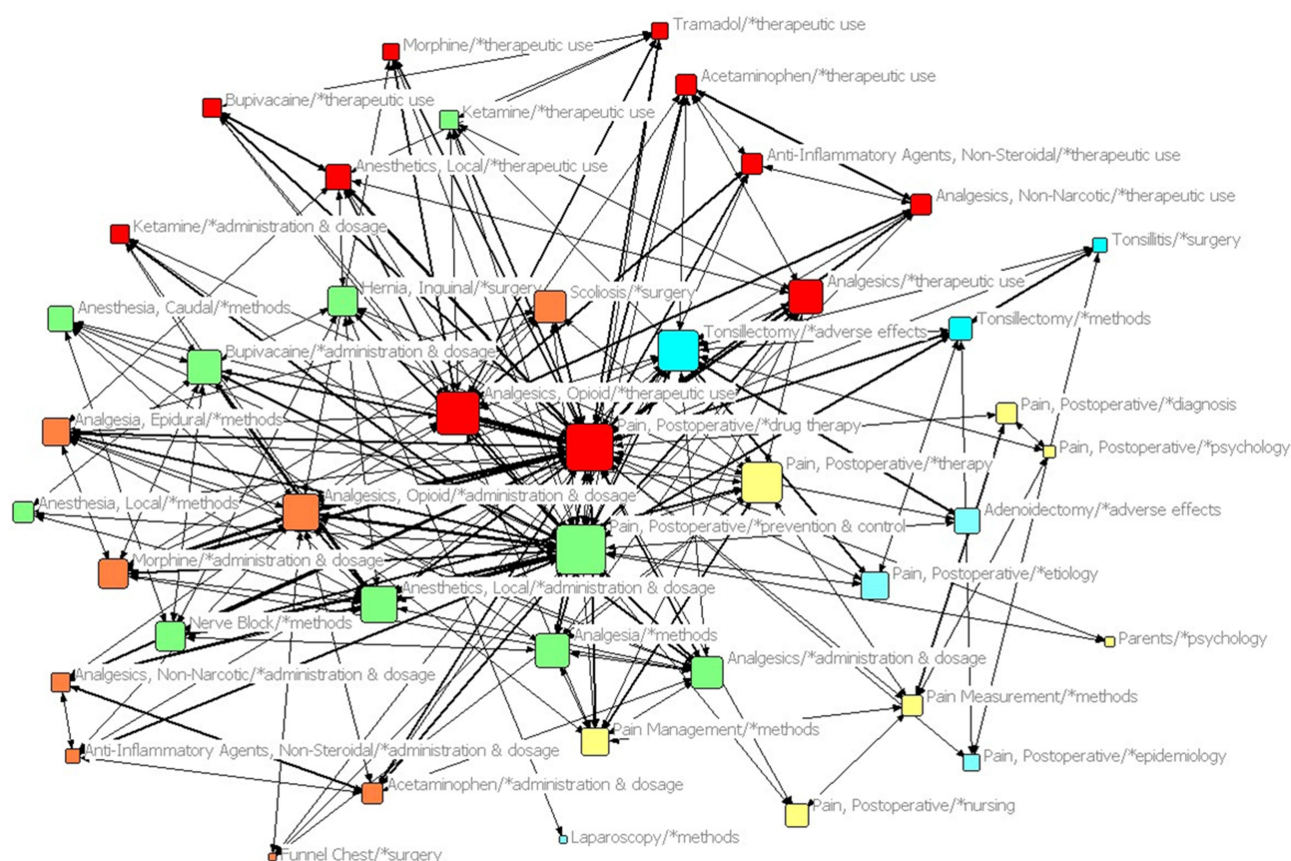


Figure 5 Social network structure map for main Medical Subject Heading (MeSH) terms/subheadings for postoperative pain in Children related research. Social network analysis for 43 main MeSH terms/subheadings from 1950–2021. Nodes represent MeSH terms/subheadings, while node size and location indicate the centrality of a word in the social network analysis map. Links represent the connection between two main MeSH terms/subheadings, and the number or thickness of the lines indicates the co-occurrence frequency of the main MeSH terms/subheadings pairs.

Therefore, self-report is recommended as the gold standard for pain assessment in children older than age 6 years.¹⁹ However, self-assessment is not as reliable in preschool children, and needs to be combined with an observational assessment method.¹⁹ This showed that no single factor assessment was reliable and a combination of multiple measures was usually used in clinical practice. Birnie et al recommended the use of the following eight scales, including the Numerical Rating Scale (NRS)-11, the Color Analog Scale (CAS), the Facial Pain Scale-Revised (FPS-R), the Pieces of Hurt, the Oucher Photographic Scale and Numeric scales, the Visual Analog Scale (VAS) and the Wong-Baker faces scale.²⁰ Parental influence is critical in the developmental pattern of children's pain memory,²¹ as children's memories are most susceptible to distortion due to hint effects. Conducting individualized instruction for children and parents can improve postoperative pain in children. Parents are encouraged to use non-pharmacological therapies, such as distraction and psychoeducation, to reduce the child's pain perception.⁶ Non-pharmacological treatment of postoperative pain in children may be one of the hot spots for future research.

Cluster 1 is an etiologic and epidemiologic study of postoperative pain in children. This part was relatively independent and immature, and we speculated that this part was likely to be a future research trend. Postoperative pain has been reported to occur in 44–93% of children.^{2,22} Poor postoperative pain control can have long-term adverse psychological and cognitive effects on children. A variety of factors, including age, gender, and family, can influence the experience of postoperative pain.²³ Among them, the size of the surgical trauma and the length of the surgery is closely related to the level of pain; therefore, the type of surgery is a key factor in postoperative pain.²⁴ Tonsillectomy and adenoidectomy are the most common pediatric surgery with a higher incidence and longer duration of pain.²⁵ These types of surgery have the largest number of publications. Notably, children with tonsil and adenoidal hypertrophy are often associated with obstructive sleep apnea-hypopnea syndrome (OSAHS),²⁶ and analgesic medications should be

chosen more carefully. Based on the available evidence, a combination of acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs) is recommended for the relief of postoperative pain in children. Debate continues regarding the risk of bleeding with NSAIDs, but most evidence supports their safety and efficacy. Several studies have shown that improvements in surgical techniques can alleviate postoperative pain. For example, intracapsular tonsillectomy²⁷ and laparoendoscopic single-site surgery (LESS) have been shown to reduce the severity and duration of pain.²⁸

The topic of pharmacological treatment of postoperative pain has been continuously studied throughout the research field. Pharmacotherapy is located at the center of the entire network and is intensively and increasingly studied. Pharmacotherapy for postoperative pain plays a crucial role in the overall knowledge structure, representing the overall direction of this research field. To be precise, the overall and ultimate goal is to reduce the incidence of postoperative pain in children through pharmacotherapy, namely Cluster 2. Studies on the safety and efficacy of analgesic drugs have focused on opioids, local anesthetics, NSAIDs, acetaminophen, ketamine, and tramadol.²⁹ Opioids are the most widely used and definitive effect for postoperative pain in children,³⁰ which have the highest number of publications. The Food and Drug Administration (FDA) suggested restricting the use of codeine and tramadol in pediatric patients under 12 years of age.³¹ NSAIDs can be used for moderate-to-severe pain and reduce the use of opioids. However, at the same time, NSAIDs may cause bleeding.³² Acetaminophen is the most commonly used analgesic for acute pain. The main advantage of acetaminophen over NSAIDs is the lesser effect on coagulation.³³ Ketamine is often used as an adjuvant in pediatric sacral nerve blocks to enhance the effect of the sacral block. Nevertheless, due to its potential to cause neuronal apoptosis and current guidelines recommend a conservative dose of 0.5 mg/kg.³⁴

In recent years, there has been a gradual rise in the number of publications about the administration and dosing of opioids, suggesting that perioperative opioid use will be a research trend and hotspot for postoperative pain in children, regarded as Cluster 3. Opioids are effective in controlling perioperative pain in children. However, due to the pharmacokinetic and pharmacodynamic characteristics of opioids, dose adjustment based on age, weight and individual response is required to optimize analgesia and minimize adverse effects.³⁵ Given the iatrogenic risk factors of opioids, the use of opioids should be minimized after many routine pediatric surgical procedures.³⁶ The incidence of adverse events for opioid prescriptions in the pediatric population has been estimated at 38.3/per 100,000, and the number of children hospitalized for opioid overdose has increased by 200% in recent years.³⁷ In the United States, one in five deaths among young people is linked to opioids.³⁸ The American College of Surgeons (ACS) has called on physicians to change their opioid use habits to prevent opioid overdoses and abuse while providing pain relief.³⁹ Studies have shown that opioids do not need to be prescribed for children after inguinal hernia repair, appendectomy, or adenoidectomy/tonsillectomy because those non-opioid analgesics can meet analgesic needs.⁴⁰ Opioid-induced hyperalgesia (OIH) has been widely demonstrated in scoliosis surgery and may lead to prolonged opioid use after surgery (POUS) and chronic postoperative pain. The use of epidural analgesia in scoliosis surgery is safe and effective, providing not only intraoperative anesthesia with somatosensory evoked potential (SSEP) monitoring capabilities but also better postoperative pain control and minimizing opioid overdose and abuse.⁴¹ Thoracic segmental epidural analgesia is also indicated for children undergoing funnel chest surgery. A recent meta-analysis reported that the postoperative use of acetaminophen or NSAIDs in children reduces opioid dose requirements.⁴² Therefore, multimodal analgesia is recommended for postoperative pain management in children,⁴³ while reducing the dose requirement of a single drug through different analgesic mechanisms, thus minimizing dose-dependent adverse effects.

With the spread of ultrasound technology, the development of multimodal analgesic protocols, and the accumulation of experience, the prevention and control of postoperative pain in children have matured, categorized as Cluster 4. The safety and effectiveness of local anesthetic techniques administered to children have been demonstrated.⁴⁴ Nerve blocks have become an important part of modern postoperative analgesic practice in children. Studies have displayed that nerve blocks not only reduce postoperative pain in children but also reduce the use of opioids and non-opioid analgesics.^{45,46} Before the widespread use of ultrasound guidance, larger doses of local anesthetics were usually required to achieve a reliable block by stimulating the nerve, which might cause an increased incidence of vascular

puncture and local anesthetic systemic toxicity. In recent years, the development of ultrasound-guided peripheral nerve block (UGPNB) has facilitated the widespread use of local anesthetic techniques in children.⁴⁷ The tissue structure

can be displayed under ultrasound guidance, and the delivery of local anesthetic drugs can be more precise. Pharmacokinetic and pharmacodynamic guidelines for the safe administration of local anesthetics have also contributed to the development of local anesthesia practice in children, with bupivacaine receiving significant attention and the most relevant literature reports. Furthermore, there is intermediate evidence that local anesthesia reduces the risk of persistent postoperative pain.⁴⁸ Despite the significant advantages of ultrasound-guided administration of regional anesthesia, significant variation has been reported in the use of regional anesthesia in children.⁴⁹ As we can see from the results of social network analysis, nodes “Pain, Postoperative/*prevention & control” had the highest degree of centrality. This indicated that they were popular keywords in this field. In addition, nodes “Pain, Postoperative/*prevention and control” belonged to Cluster 4. From the analysis of strategic coordinates, it can be seen that this part of research is in the research center and relatively mature. Because the main content in Cluster 4 is “The safety and effectiveness of regional anesthetic techniques and local anesthetics”, therefore, we predicted that there might be a huge potential for the development of regional anesthesia.

However, some limitations should be noted. First, our data were only collected from the PubMed, and thus, other studies from other databases were not included and analyzed in the research. Second, only articles were included in the present study, and other investigation hotspots may have been missed. Third, biclustering analysis was implemented according to the highly frequent keywords, which may lead to some novel but less frequent subjects being overlooked. Last, visualization software, such as gCLUTO and Ucinet, can only process data from one database at a time, which may result in biased outcomes. Therefore, we should improve the search strategy, include more article types, identify new frequent keywords, and apply more advanced visualization software in the further research.

Conclusion

This study is the first time to analyze postoperative pain in children using a co-word clustering approach. The pharmacological treatment of postoperative pain in children and the prevention and control of pain are currently at the core of this research field and are becoming increasingly mature. Opioid overdose and abuse in the pediatric population have attracted significant international attention, and opioid stewardship is a priority for future research. In addition, it is extremely necessary to develop consensus guidelines for opioid prescribing. Regional anesthesia has great potential for development. Nonpharmacologic intervention for the treatment of postoperative pain in children is an emerging topic. The aetiology and epidemiology of postoperative pain in children are still immature, and future research should be strengthened and intensified.

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Disclosure

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