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# Integrative oncology from a bibliometric point of view

# Jenny-Ann Brodin Danell

Department of Sociology, Umeå University, 901 87 Umeå, Sweden



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#### ABSTRACT

*Objectives*: The aim of this article is to analyze the development of integrative oncology from a bibliometric point of view. The publication and citation patterns of publications are analyzed and their contents mapped. *Design*: This study is based on bibliometric methods. The data sets consist of 7 025 respectively 4 990 publications over the time period 1966-2016, shown in PubMed and Web of Science.

Results: The expansion of the numbers of these publications took place in the late 1990s/early 2000s. Research is dominated by authors located in the USA, China and Germany who are working at well-established research universities and university hospitals. The clinical share of publications is relatively small, and few studies are classified according to clinical phase. Content analysis revealed that much of the clinical research is based on surveys, and that content reflects the intersection of complementary therapies and cancer research. The latter aspect is less obvious in pre-clinical research. The most frequent journals in the material show a focus on complementary and alternative therapies or on integrative oncology, although journals focused on oncology or general/internal medicine were well-represented in the material as a whole. The most-cited publications were review articles and surveys.

Conclusions: Integrative oncology has been established as a small, but distinct, research domain. There are several signs of specialization in integrative oncology, but also in its integration into general medical and oncological research.

#### 1. Introduction

In recent years it has become increasingly popular to use concepts such as integrative healthcare and integrative medicine to describe treatments (or general approaches) that brings conventional and complementary medicine together in a coordinated manner (https://nccih. nih.gov/health/integrative-health). In general, integrative healthcare is characterized by holistic ideals, patient centeredness, and a focus on lifestyle and behavioral change. Many conventional health care settings, such as hospitals, have begun to offer integrative health care, 1-3 especially in the treatment of pain and chronic diseases. 4–6 This is often motivated by increased patient demand, although health care professionals and other authorities may promote integrative approaches. Furthermore, a number of studies indicate extensive use of complementary treatments (such as acupuncture, meditation, yoga, dietary supplements and herbs) among specific patients groups - and especially among cancer patients <sup>7–9</sup> and cancer survivors. <sup>10</sup> This development has led to the emerging field of integrative oncology, 11 including integrative health practices as well as the establishment of professional associations (such as the Society for Integrative Oncology), academic conferences and specialized academic journals all focused on the intersection of cancer treatments and integrative healthcare.

What is considered as accepted or trusted knowledge is debated and concepts such as integrative healthcare and complementary medicine indicate underlying tensions and conflicts in relation to the scientific and medical establishments. From a sociological point of view, the establishment of integrative oncology can be understood in terms of a "credibility contest" 12 where different types of actors (researchers, health care professionals, patients or journal editors) negotiate boundaries of trusted knowledge and how this knowledge may - or may not – guide medical practice. In general, the actors enjoy unequal access to relevant resources (for example funding, laboratories or patients). Furthermore, both research and healthcare are governed by norms. In this case, especially ideals of evidence-based medicine  $^{13,14}$  and randomized controlled trials as gold standard are crucial albeit debated.  $^{15-18}$  Although negotiations on credibility take place in a number of contexts, publications in well-reputed peer review journals have been identified as crucial. The establishment of specialized journals is also considered as decisive, since journals and their editorial boards possess the capacity to control access to scientific communication (for example by determining relevant topics or which research designs are to be accepted). 19

E-mail address: Jenny-ann.danell@umu.se.

The aim of this article is to analyze the development of integrative oncology as a research domain during the period 1968–2018. Using bibliometric methods, the publication and citation patterns will be analyzed. Furthermore, the general content of the publications will be mapped.

#### 2. Data

In this study two bibliographic databases have been used, PubMed and Web of Science. PubMed is one of the largest databases for biomedical research and life sciences. One important advantage of this database is that the documents are indexed using Medical Subject Headings (MeSH) - a controlled vocabulary thesaurus published by National Library of Medicine. However, this database has no information concerning citations, and limited information on addresses/organizations of authors. In order to retrieve such information, we have used the Web of Science database.

The initial data set was identified in the PubMed database by combining the MeSH terms *Complementary therapies* (as major topic) and *Oncology* (as major topic) in the advanced search engine. This resulted in 7 025 publications, from 1968 to 2018. For the more detailed analysis the initial dataset was matched with the Web of Science database (Core collection), with PubMed identification numbers. This resulted in 4 990 publications (71 per cent of the initial dataset). All data was retrieved in October 2019.

Integrative oncology was introduced in MeSH in 2018 as a sub-term to Complementary therapies. Because it is such a new input, it only covers recent publications (at the time for data retrieval it covered 47 publications as major topic), consequently it was not used.

#### 3. Results

## 3.1. Publication pattern and clinical research

In Fig. 1 publications trends identified as integrative oncology in the PubMed database are shown. In the 1970s and 1980s there were very few documents published every year. Some years there were as few as

2-5 publications, others between 40-50. Expansion started in the late 1990s/early 2000s when annual numbers exceeded 100-200. During the last decade there have been an average of 366 publications a year, with a peak in 2012. The drop in numbers in 2017–2018 can, to great extent, be explained by the fact that it takes a couple of years to update bibliographic databases.

Clinical research is crucial to medical practice. <sup>20</sup> Four per cent of the publications in this material were classified as clinical trials according to PubMed. The development of clinical trials has been similar to the general publication pattern, with very few clinical trials in the 1970s and 1980s and substantial growth in the 1990s/early 2000s. During the period 2008–2018, approximately 20 per cent of publications were classified as clinical trials. These numbers, as well as the general growth pattern of publications, are very similar to studies on complementary therapies in general. <sup>21,22</sup> Another similarity is that relatively few of these publications are classified according to clinical phase, which is a sign of small-scale and exploratory studies (for example, see <a href="https://www.cancer.org/treatment/treatments-and-side-effects/clinical-trials/what-you-need-to-know/phases-of-clinical-trials.">httml</a>). In the entire material, 14 publications were classified as Phase 1, 37 as Phase 2, 21 as Phase 3, and none as Phase 4.

### 3.2. Types and sources of publications

In order to retrieve more detailed information about the publications, as indicated above we matched the initial dataset with Web of Science. This subset includes 4 990 publications (71 per cent of the initial dataset). Seventy-eight per cent of these publications were classified as Articles, 10 per cent as Reviews, 6.3 per cent as Editorial material and the remainder as Letters, Proceedings and other document types. These publications were found in 894 sources.

Examining the most frequent sources (Table 1) it is clear that several possess a general scope on complementary and integrative medicine, or on specific complementary therapies. Others are focused on cancer prevention/treatment or, as the most frequent, *Integrative Cancer therapies* and have a specific focus on integrative oncology. There are many more examples of general cancer/oncology journals in the top

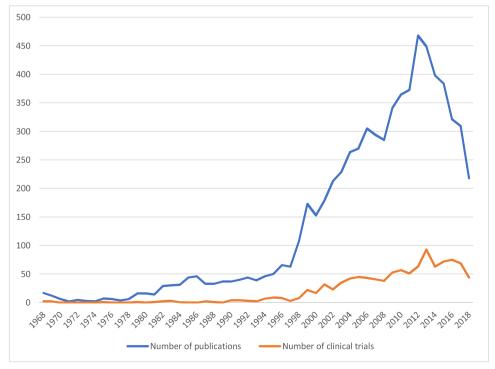


Fig. 1. Publications classified as Integrative Oncology, Web of Science 1968-2018.

**Table 1**Top 10 journals, publications classified as Integrative Oncology, Web of Science, 1968-2018.

Source titles	Number of publications	Percentage (of 4990)	IF*	SNIP***
Integrative Cancer Therapies	176	3.527	2.634	1.02
Supportive Care in Cancer	158	3.166	2.754	1.11
Journal of Alternative and Complementary Medicine	144	2.886	1.868	0.83
BMC Complementary and Alternative Medicine	126	2.525	2.479	1.16
Fitoterapia	87	1.743	2.431	1.33
Asian Pacific Journal of Cancer Prevention	85	1.703	2514**	0.65
American Journal of Chinese Medicine	78	1.563	3.510	0.99
Phytomedicine	78	1.563	4.180	124
Complementary Therapies in Medicine	76	1.523	1.979	0.97
Psycho Oncology	75	1.503	-	-

<sup>\*</sup> IF based on Journal Citation Reports 2018.

100 list, as well as journals in general/internal medicine.

Journal impact factor (IF) is often used as a method of measuring the relative importance of journals in a scientific field. IF reflects the annual average number of citations of publications (usually based on the last two or five years) in a given journal. The assumed logic is that high quality research receives a large number of citations – and that the most prestigious journals (with high IF), in which it is difficult to get published, attract high-quality research.<sup>23,24</sup> However, there is substantial variation both within single journals and within scientific fields,<sup>25</sup> consequently SNIP values have been added for the journals. SNIP is a field-normalized measure of journal impact.<sup>26</sup> The most frequent journals in this dataset have moderate impact factors and SNIP values close to one, which represents the average in the field. There are notable exceptions for publications in high-impact journals. For example, there are 22 publications in The Lancet Oncology (IF 35.386, SNIP 9.24), 18 in New England Journal of Medicine (IF 70.670, SNIP 13.0), 11 in JAMA (IF 51.273, SNIP 9.85), and 11 in The Lancet (IF 59,102, SNIP 16.04).

# 3.3. Citations

One way of measuring the impact of research is to analyze citations, although there are a number of limitations attached to this approach.<sup>2</sup> The basic idea is that citations represent a relationship between cited and citing documents, and that a citation is an acknowledgment that one publication receives from another publication.<sup>28</sup> In general, authors are expected cite the relevant and useful work of others. Furthermore, they are assumed to be honest and well-informed (for example about recent developments in their field). From that, we can expect muchcited publications to be more important or relevant than those with few or no citations at al.<sup>29</sup> However, as many have noted, reasons how and why authors cite – or not cite – are complex. For example, citations may represent specific results, broad theoretical frameworks or research methods.<sup>30</sup> They may be confirmatory or critical and may be guided by reviewers and journal guidelines. Furthermore, different research domains are governed by different citation cultures and individuals have different preferences and writing styles (for an overview, see <sup>31</sup>). In this case is it important to keep in mind that the citations in focus not are normalized.<sup>32</sup> Citations for the entire time period are presented, which means that older publications have more chances to be cited because they have been available for longer. Neither have we gone into detail regarding specific characteristics of research domains, although it is reasonable to assume that both cited and citing publications are related

The publications in focus have been cited 119 399 times (100 593 not including self-citations). On average, they have been cited 23.9 times and the h-index is 123. As in most research domains there is great variation in the dataset. 50 per cent of the publications show 12 citations or less. About 7 per cent (363) of the documents have no citations

at all. In Table 2 we present the ten most-cited publications. As expected, these studies are relatively old, several from the late 1990s/ early 2000s, although still cited frequently. Another pattern is that most of them are review articles or based on survey data. This is also expected, since review articles normally attract more citations in medical research eg <sup>33,34</sup> For medical practice is, as indicated above, clinical research in general and randomized controlled trial in particular of great importance. For this reason, we have identified the five most cited randomized controlled trials in the material. The most cited, "A randomized, wait-list controlled clinical trial: The effect of a mindfulness meditation-based stress reduction program on mood and symptoms of stress in cancer outpatients", 35 is included in Table 2, with 535 citations. This is followed by "Antiemetic effect of delta-9-tetrahydrocannabinol in patients receiving cancer chemotherapy", 36 297 citations, "Randomized controlled trial of mindfulness-based stress reduction (MBSR) for survivors of breast cancer", 37 252 citations, "Psychological adjustment and sleep quality in a randomized trial of the effects of a Tibetan voga intervention in patients with lymphoma", 3 226 citations, and "Hypnosis and nonhypnotic techniques for reduction of pain and anxiety during painful procedures in children and adolescents with cancer", <sup>39</sup> 223 citations. All of these are more than ten years old, and the oldest from 1975.

# 3.4. Countries and organizations

In order to obtain an indication of where research on integrative oncology is carried out, information on the countries/regions (based on reprint addresses) and organizations (based on the Organization enhanced field in Web of Science) is presented. In total there are 84 countries and 4 253 organizations represented in the dataset. Overall there is a dominance of research based in the US (32.3 per cent of the publications), followed by China (14.1 per cent) and Germany (6.8 per cent), England (6.3 per cent), and Canada (5.2 per cent). The pattern is similar to complementary and alternative medicine in general.<sup>40</sup> Among the most frequent organizations we find well-established universities and university systems, such as University of Texas systems (3 per cent of the publications), University of California systems (2.5 per cent), and Harvard University (1.8 percent), but also specialized cancer centers such as UTMD Anderson Cancer Center (2.1 per cent), associated to the University of Texas, and Memorial Sloan Kettering Cancer Center in New York (1.6 per cent), as well as the US National institute of Health (1.5 per cent).

## 3.5. General content of publications

In order to capture the general content of the publications we have used co-word analysis. The basic idea of this method is to identify themes, and relationships between them in research domains based on how pairs of words occur in text corpora.<sup>41</sup> This is based on the

<sup>\*\*</sup> IF 2014.

<sup>\*\*\*</sup> SNIP based on Scopus.

	Title	Source (incl. IF*)	Modality**	Vear of	Times cited
			(ampour	publication	
Surh, YJ	Cancer chemoprevention with dietary phytochemicals	Nature Reviews Cancer (51.848)	Phytotherapy	2003	1875
Yang, Chung S.; Wang, Xin; Lu, C Gang; et al.	Cancer prevention by tea: animal studies, molecular mechanisms and human relevance	Nature Reviews Cancer (51.848)	Phytotherapy, Plant extracts	2009	652
Richardson, MA; Sanders, T; C Palmer, JL; et al.	Complementary/alternative medicine use in a comprehensive cancer center and the Journal of Clinical Oncology (28.349) implications for oncology	Journal of Clinical Oncology (28.349)	Complementary therapies	2000	613
Ernst, E; Cassileth, BR T	The prevalence of complementary/alternative medicine in cancer - A systematic review	Cancer (6.102)	Complementary therapies	1998	597
Molassiotis, A; Fernandez-Ortega, UP; Pud, D; et al.	Use of complementary and alternative medicine in cancer patients: a European survey	Annals of Oncology (14.196)	Complementary therapies	2005	561
E; Goodey, E;	A randomized, wait-list controlled clinical trial: The effect of a mindfulness meditation-based stress reduction program on mood and symptoms of stress in cancer outpatients	Psychosomatic Medicine (3.937)	Meditation	2000	535
Li-Weber, Min	New therapeutic aspects of flavones: The anticancer properties of Scutellaria and its Cancer Treatment Reviews (8.332) main active constituents Wogonin, Baicalein and Baicalin	Cancer Treatment Reviews (8.332)	Phytotherapy, Plant extracts	2009	499
Messina, MJ	Legumes and soybeans: overview of their nutritional profiles and health effects	American Journal of Clinical Nutrition (6.568)	Phytotherapy, Plants medicinal	1999	467
Wang, Lan; Zhou, Guang-Biao; Liu, I Ping; et al.	Wang, Lan; Zhou, Guang-Biao; Liu, Dissection of mechanisms of Chinese medicinal formula Realgar-Indigo naturalis as Ping; et al.	Proceedings of the National Academy of Sciences of the United States of America (9.580)	Medicine, Chinese Traditional	2008	459
Craig, WJ	Health-promoting properties of common herbs	American Journal of Clinical Nutrition (6.568)	Phytotherapy	1999	444

IF based on Journal Citation Reports 2018. Modality based on main MeSH term(s)

assumption that researchers write their texts intentionally and try to convince the audience of their legitimacy. Words in texts are linked together in phrases which, in turn, are linked together in larger networks of research problems, results, methods, interpretations etc. 42 Some words, which can be labelled as macro terms, are almost impossible to circumvent and have the capacity to synthesize entire research domains. 43 In practice we have analyzed the abstracts of the 4 990 publications (exported from PubMed, as text files), using the VOSviewer software (for more details on the different steps in the procedure, see 44).

In Fig. 2 an overview of the co-word analysis is shown. One striking pattern is that the words form two distinct clusters, with very few connections between. The red cluster, to the left, is characterized by words (such as Participant or Questionnaire) associated with clinical research. This cluster also include terms associated with complementary and alternative medicine, CAM (such as Alternative medicine or Acupuncture). The green cluster, to the right, is characterized by words/concepts associated to pre-clinical or laboratory research (for example, Cell, Extract, Mouse). The few words in-between indicate gynecological research and research on hormones.

In Figs. 3 and 4 we present close-up visualizations of the two dominating networks. At the top of Fig. 2 Fig. 3 is it possible to detect a large number of words indicating CAM (e.g. CAM, Alternative medicine, Alternative treatment, Complementary, CAM therapy), surveys and questionnaires (e.g. Participant, Questionnaire, Respondent, Attitude, Demographic characteristics), various kind of experiences (e.g. CAM use, User, Care, Experience, Perception, Choice), and cancer (e.g. Cancer diagnosis, Cancer care, Oncology department). At the bottom of Fig. 3 there are a number of words indicating specific treatments and therapies related to CAM (e.g. Acupuncture, Yoga, Music therapy, Mindfulness, Meditation, Art therapy, Relaxation) connected to words signaling clinical studies (e.g. Randomized trial, RCT, Intervention group. Outcome measure) and various kind of health issues (e.g. Stress. Fatigue, Anxiety, Pain management). Yet other word, at the bottom right, are associated with meta analyses and systematic reviews (e.g. Meta-analysis, Cochrane library, Database, Pubmed).

Fig. 4 includes a number of words indicating pre-clinical and laboratory research (e.g. Cell, Apoptosis, Compound, Assay, Extract, Inhibition), studies of effects and mechanisms (e.g. Mechanism, Dose, Growth), proteins and enzymes (e.g. Nf kappa b, Cyclin, Caspase, Alkaline phosphatase, Kinase), and various kinds of cancer (e.g. Colon cancer, Oral cancer, Cancer prevention, Carcinoma, Hcc, Melanoma cell). Some words (such as Plant extract, Herb, Natural product, Black tea) can be associated with CAM, and more particularly with herbal/ natural medicine.

# 4. Conclusions

From a bibliometric point of view, integrative oncology was established as a small - but distinct - medical sub-field from the 1990s forwards. The expansion of publications began with very small numbers in the late 1990s/early 2000s. During the last decade there has been an average of 366 publications a year. There is a dominance of authors located in the USA, followed by China and Germany, at well-established universities, university hospitals and specialized cancer centers.

The clinical research share of publications is growing, but there are very few studies classified according to clinical phase which supports the idea of a young research domain, characterized by small, exploratory studies. The co-word analysis of the abstracts of the publications showed that the research is divided into two distinct clusters, one clinically oriented and one pre-clinical. Surveys and questionnaires are salient in the clinical cluster, and they seem to show a general focus on personal experience, complementary therapies (in general and specific therapies) and cancer treatments, reflecting the intersection of research in/about complementary or integrative therapies and cancer. Furthermore, there are signs of clinical trials and systematic reviews.



**♣** VOSviewer

Fig. 2. Overview map of co-word analysis of documents classified as Integrative Oncology.

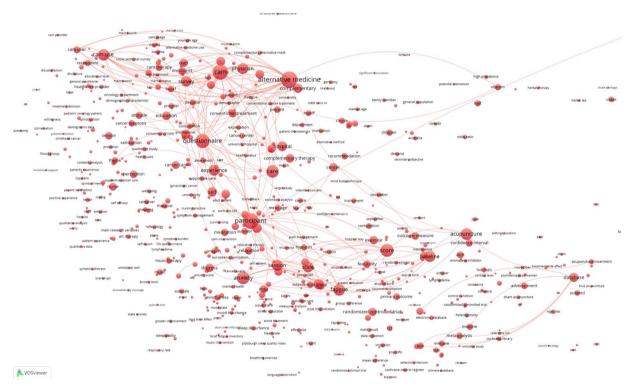


Fig. 3. Close up on clinical cluster in documents classified as Integrative Oncology.

The pre-clinical cluster is less clearly connected to complementary or integrative therapies, although there are examples of herbal and natural medicines.

When examining the sources of the publications, some interesting aspects appear. Among the most frequent journals, the majority show a general focus on CAM (or on specific therapies such as acupuncture) or are even more specialized on integrative oncology. This could be a sign that authors in this emerging domain primarily intend to communicate their results with an audience who have an interest in such therapies – or that it is difficult to get this research published in more conventional medical journals. By broadening the scope, many of the top 100 journals are general cancer/oncology journals or cover general/internal medicine which indicates that this research is well-integrated into medical research. The most-cited publications were, as expected, review articles and surveys.

### **Author declaration**

The single author (Jenny-Ann Brodin Danell) is responsible for conceptualization, theoretical framework, methodology, data retrieval, data analysis, visualizations, writing, review and editing, and project administration of the study.

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### Availability of data and material

Main data is publicly available in the PubMed and Web of Science databases. Supplementary data is publicly available in Journal Citations

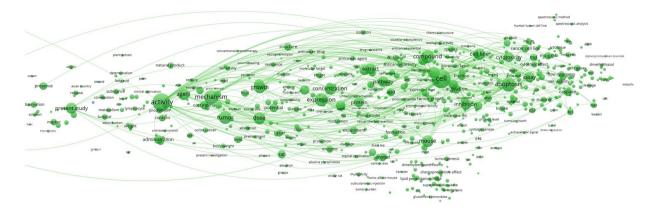


Fig. 4. Close up on pre-clinical cluster in in documents classified as Integrative Oncology.

Reports and Scopus databases.

## **Declaration of Competing Interest**

No conflict of interest.

# Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ctim.2020.102477.

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