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Original Article

Early Screening of Pancreatic Cancer: A Bibliometric Study Over the Past Two Decades

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Abstract

Background and objectives: Pancreatic cancer (PC) is a highly malignant tumor of the digestive system with a poor prognosis. The early diagnosis and accurate screening of PC in high-risk populations are warranted to improve the prognosis of patients. The present study aimed to evaluate the global research characteristics, hotspots, and future trends of the early screening of PC.

Methods: A comprehensive search of studies on early screening of PC in the Web of Science core database was performed between 1 January 2003 and 28 December 2022. The information, which included the study population, authorship, journal, contributing institution, country of origin, and keywords, were collected. The Excel, VOSviewer, and Citespace software were used for the bibliometric analytical processing and visualization.

Results: A total of 581 publications were included and analyzed after the screening. For the past 20 years, the annual number of publications exhibited a fluctuating rising trend. The United States contributed more than 40% of the publications. Ralph H. Hruban was the most cited scholar. Pancreas (n = 35), World Journal of Gastroenterology (n = 24), and Pancreatology (n = 18) were the top three journals with the highest number of publications. Keywords related to liquid biopsies, such as "extracellular vesicle", "dna", and "circulating tumor cell", continued to burst until 2022.

Conclusions: Over the past two decades, this area has been gradually gaining attention, with the number of publications rising annually. Liquid biopsy will be the future research trend. These present findings will provide the latest insight into the state of PC early screening, identifying new perspectives for further research.

Keywords: Early-screening; Pancreatic cancer; Bibliometric analysis; Research trends.

Abbreviations: CT, computed tomography; EUS, endoscopic ultrasonography; EUS-FNA, EUS-guided fine-needle aspiration; IF, impact factor; MRCP, endoscopic retrograde cholangiopancreatography; MRI, magnetic resonance imaging; PC, pancreatic cancer.

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Introduction

Pancreatic cancer (PC) is one of the most malignant gastrointestinal tumors, with a 5-year survival rate of less than 9%, and its incident and mortality rates are rising.[1,2] According to the 2020 global cancer statistics, PC has become the 7th leading cause of cancer death in both sexes, and this has become a growing public health concern worldwide.[2] Unfortunately, PC does not typically present with obvious symptoms in its early stages. Thus, this cannot be diagnosed until the advanced stage of the disease, at which point treatment options are limited.[1,3] Therefore, the accurate screening of early-stage PC is urgently needed.

Several international guidelines have illustrated the importance of early screening for PC.[4,5] Since almost 20 years from the appearance of lesions in the pancreas to the development of metastatic PC, a sufficient time window for the early screening of PC was given.[6] A large multicenter study revealed that patients with PC, who received

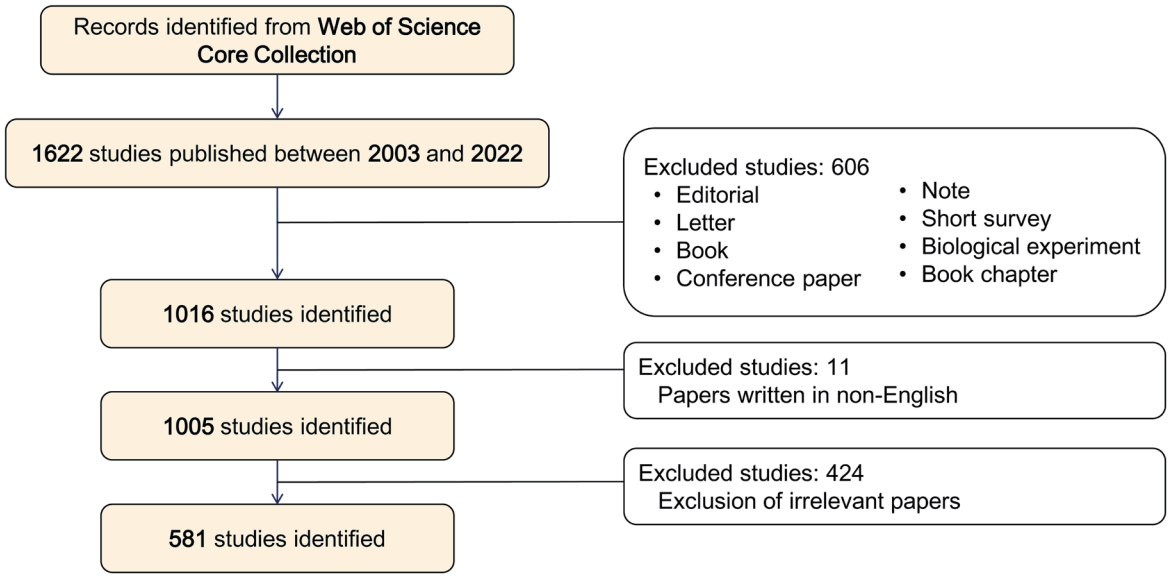


Fig. 1. Flowchart of the literature selection process for pancreatic cancer early screening.

early screening, had a significantly longer median overall survival time, when compared to patients who did not receive early screening (9.8 years vs. 1.5 years).[7] It is presently generally accepted that screening is warranted and cost-effective for individuals who are at high risk for PC. However, the definition of high-risk groups remain controversial.[5,8] For the screening strategies, endoscopic examination, imaging examination, and biomarkers have demonstrated the screening and diagnostic value of PC and precancerous lesions in recent years.[8–10] In general, the establishment of a feasible screening scheme for PC remains at its research and exploration stage, and a broader consensus remains to be formed.[1,8,9,11]

At present, numerous approaches exist to systematically develop an overview of the academic field, in which bibliometric analysis has become a key instrument in assessing research trends and developing guidelines.[12] Bibliometrics can not only analyze the contributions and collaborations of authors, organizations, countries and journals, qualitatively and quantitatively, but also assess the development and new trends of academic research. To date, no bibliometric analysis has focused on the early detection of PC. The present study conducted the most comprehensive search and bibliometric analysis of PC early screening literature over the past 20 years, and explored the present development direction and research hotspots in this field.

Materials and methods

Data sources and search strategies

All data employed for the present study were retrieved from the Web of Science (WoS) core database from January 2003 to December 2022. The specific screening strategy was, as follows: TS = ((((((AK = (Pancreatic Neoplasm*)) OR AK = (PC*)) OR AK = (Pancreatic tumor*)) OR AK = (Pancreatic carcinoma*)) OR AK = (Pancreatic adenoma*)) OR (((((TI = (Pancreatic Neoplasm*)) OR TI = (PC*)) OR TI = (Pancreatic tumor*)) OR TI = (Pancreatic carcinoma*)) OR TI = (Pancreatic adenoma*))) AND (((((TI = (cancer detect*)) OR TI = (cancer screen*)) OR TI = (early detection of cancer)) OR TI = (early diagnosis of cancer)) OR ((((AK = (cancer detect*)) OR AK = (cancer screen*)) OR AK = (early detection of cancer)) OR AK = (early diagnosis of cancer))) AND publication year = (2003 to 2022).

Studies published in the English language, with the theme, PC early screening, were included. The exclusion criteria were, as follows: (1) editorials, meetings, letters, news, book chapters, and corrections; (2) non-English publications; (3) studies with main topics not related to PC early screening. Two authors (GX M and YC W) independently screened the search results. Any disagreements were resolved by discussion with a third reviewer (WBZ). Figure 1 shows the specific selection process.

Data extraction

Two reviewers (GX M and YC W) independently extracted the following information from the included studies: study title, study type, name of author(s), abstract, keywords, references, journal and the impact factor (IF), citations, country(ies)/region(s), institutions, and address. These were exported in plain text format.

Bibliometric analysis and visualized analysis

An Excel spreadsheet was used to present the bibliometric indicators, which included the following: total number of publications, year of publication, study type, the top journals ranked by IF, the number of publications of each country, institution and scholar, and the citations of the studies. The sum of the citations of all articles published in the same journal were divided by the number of articles, in order to obtain the average number of citations of journals. The IF and quartile rank (Q) were retrieved from the year of publication of the journal from Journal Citation Reports (jcr.clarivate.com).

For the visualized analysis, CiteSpace and VOSviewer were used for the present study. These are widely used in scientific and technical text mining, and information visualization, and have the most important feature of being able to provide a scientific visualization map, in order to understand the structure, pattern and distribution of relevant studies.[13] YL and LH analyzed the data. The obtained data were imported into the CiteSpace (Version 6.1.R6) software, and this was used as the literature visualization applica-

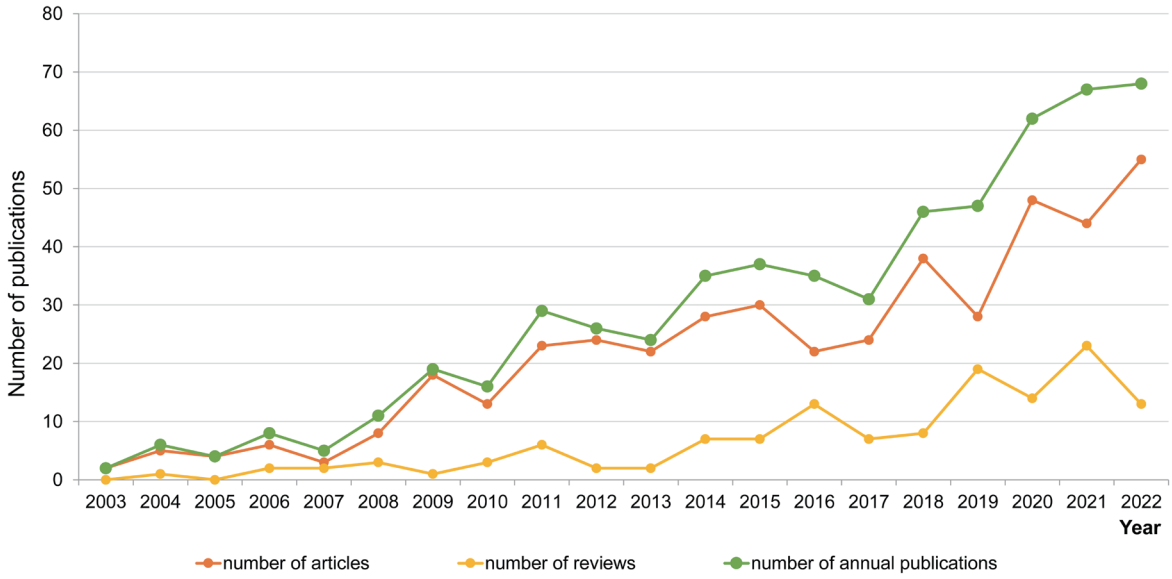


Fig. 2. The number of papers included by year of publication.

tion tool to analyze indicators, such as country, journal, institution, author and reference. Furthermore, CiteSpace was used to analyze the keywords and co-cited references (those that were cited by one or more publications at the same time) with the strongest citation bursts, in order to predict the trends in the field. VOSviewer (version 1.6.16) was used to plot the country collaboration, institutional collaboration, scholar collaboration, keyword co-occurrence, and literature co-citation. The nodes of the network diagram comprised of different scholars, the size of the nodes indicated the richness, the connection between the nodes indicated the degree of association, and the thickness of the connection indicated the strength of the association. The color of the element represented the cluster it belongs to, and different clusters were represented by different colors.

Results

Publications and journals

A total of 581 publications in the field of early screening of PC was included for the analysis. For study type, 448 (77.11%) were original articles, and 133 (22.89%) were reviews or guidelines. The annual number of publications exhibited a fluctuating rising trend worldwide. Furthermore, 2022 was the year with the highest number of publications (n = 71), and the year with the highest number of articles published (n = 58), while 2021 was the year with the highest number of published reviews/guidelines (n = 23) (Fig. 2). Among these studies, 319 studies had an observational design (251 studies were retrospective studies and 68 studies were prospective studies), 23 studies were meta-analysis studies, 15 studies were systematic reviews, and three studies were randomized controlled studies.

The included studies were published in 272 journals. In the field of PC early screening, the top 10 most prolific journals are listed in Table 1. Among these, the most published journal was Pancreas (n = 35), followed by the World Journal of m, Gastroenterology (n = 24), and Pancreatology (n = 18). Furthermore, among the top 10 journals, Gastroenterology had the highest IF of 33.883. In partitioning according to Journal Citation Reports, among the top 10 journals, 50% were classified as Q1, 10% were classified as Q2,

Table 1. Top 10 journals that published literature related to pancreatic cancer early screening

Rank	Journal	Number	Citations	Average citations	IF_{2021}	Quartile in category
1	*PANCREAS*	35	1,081	30.886	3.243	Q3
2	*WORLD JOURNAL OF GASTROENTEROLOGY*	24	1,125	46.875	5.374	Q2
3	*PANCREATOLOGY*	18	288	16.000	3.977	Q3
4	*CANCERS*	15	98	6.533	6.575	Q1
5	*JOURNAL OF THE PANCREAS*	11	150	13.636	-	Q4
6	*CLINICAL CANCER RESEARCH*	8	801	100.125	13.801	Q1
7	*GASTROENTEROLOGY*	8	837	104.625	33.883	Q1
8	*INTERNATIONAL JOURNAL OF CANCER*	7	319	45.571	7.316	Q1
9	*FAMILIAL CANCER*	7	206	29.429	2.446	Q3
10	*GASTROINTESTINAL ENDOSCOPY*	7	199	28.429	10.396	Q1

and 30% were classified as Q3. The top two journals with the highest average number of citations per article were Gastroenterology (n = 104.625) and Clinical Cancer Research (n = 100.125), indicating the high quality of articles published in these two journals in this field.

Countries, institutions, scholars and cooperation

A total of 49 countries/regions contributed to the field of PC early screening between 2003 and 2022 (Fig. 3a). The four most prolific countries are presented in Figure 3b, and the top 10 countries are detailed in Additional file 1. The United States (n = 245) was the most productive, followed by China (n = 82), Japan (n = 82), and Germany (n = 48). The five most cited countries were the United States (n = 9,700), Japan (n = 2,079), Germany (n = 2,003), Italy (n = 1,945), and China (n = 1,844). For international cooperation, the United States was the center of collaboration. Germany, Italy, France, and the United Kingdom had more intense ties with other countries in the research cooperation network (Fig. 3c). Germany and Canada started their collaborative research earlier, while China, France, and other countries started foreign cooperation in recent years (Fig. 3d).

For the present selected publications, 783 institutions were involved in the study. The top five research institutions with the highest number of publications were all from the United States (detailed in Additional file 2). The institution with the most publications was the University of Texas MD Anderson Cancer Center (n = 41), and the institution with the highest average number of citations for each article was Mayo Clinic (n = 71.33). The close connections between these different units indicate the extensive cooperation among various agencies, and demonstrate the presence of several institutional cooperation clusters. The top three institutions for collaboration were the University of Texas MD Anderson Cancer Center, Johns Hopkins University, and Harvard University. These three institutions had the highest density of cooperative cluster nodes, and were at the center of the relationship graph (Fig. 4a).

In the past 20 years, 3,883 scholars contributed to the research of PC early screening. Among the 10 scholars with the highest number of publications, nine scholars were from the United States, and one scholar was from Germany (detailed in Additional file 3). Furthermore, three scholars were from Johns Hopkins Medicine, and two scholars were from UTMD Anderson Cancer Center. Anirban Maitra was the scholar with the most publications (n = 15), and Ralph H. Hruban was the scholar with the most citations per article on average (n = 125.455). A cluster of 16 academic groups was obtained through the cooperative statistical analysis of scholars who published three or more papers. As presented in Figure 4b, Marcia Irene Canto of Johns Hopkins Medicine and Randall E. Brand of the University of Pittsburgh had a large number of nodes in the whole layer, and were surrounded by several scholars.

Highly cited literature

The density visualization of the top 100 co-cited literature is presented in Figure 5a. Each literature had 20 or more co-citations. Most of the co-cited literature was from the top journals, and the main disciplines involved were oncology and gastroenterology. The basic information of the 10 most co-cited manuscripts, in the order of total citations and average citations, is listed in Table 2. The highest number of citations was 99, which were published by Canto *et al*. in Clin Gastroenterol Hepatol in 2006, and in Gastroenterology in 2012.[14,15]

After analyzing the 25 co-cited publications with the strongest outbreaks (Fig. 5b), it was found that these publications focused on research advances related to screening technologies, high-risk groups, genetic testing, and cancer morbidity and mortality. The first citation burst in the field began in 2006, and this continued until 2009. Seven literature citation bursts were still in progress. Five of the 25 co-cited publications were from Marcia Irene Canto, with outbreaks in 2006,[16] 2007,[14] 2012,[15] 2014,[17] and 2019.[18] The practice guideline published by Canto *et al*. had the highest outbreak intensity of 20.42.[17]

Keywords

The keywords involved in the selected literature were extracted, and the synonyms were combined. Figure 6a summarizes the top 60 keywords with the highest frequency. Adenocarcinoma was located in the center of the keywords, which is consistent with the present research theme. Adenocarcinoma, biomarkers, family-history, ultrasound endoscopy, and papillary mucinous neoplasms were the keywords that most frequently appeared. For the markers, a table of markers associated with PC, according to the MeSH word frequencies (Additional file 4), was presented. The most frequent marker was CA-19-9 antigen (n = 52), followed by microRNAs (n = 20), proto-oncogene proteins p21 (ras) (n = 17), exosomes (n = 15), and DNA methylation (n = 14). According to the chronological order of keyword occurrences, it was found that extracellular vesicles, cell-free DNA, nanoparticles, microRNA, DNA, blood, and glypican-1 were the emerging keywords (Fig. 6b).

Burst keywords were considered as another important indicator of research frontiers, and these can determine the hot trends in the field. Figure 6c presents the top 15 keywords with the highest number of citation bursts from 2003 to 2022. These keywords were artificially divided into three stages, according to the chronological order of appearance in the outbreak. The first stage was from 2003 to 2009. The earliest keyword burst was “gene expression” (2003–2011), followed by “juice” (2004–2006), “computed tomography” (2006–2009), “brca2 mutation” (2009–2015), “intraepithelial neoplasia” (2009–2014), and “papillary mucinous neoplasm” (2009–2012). The second stage was from 2010 to 2015, in which only one new burst keyword emerged, “differential diagnosis” (2011–2017). There were no new burst keywords during the period of 2012–2015. The third stage was from 2016 to 2022, in which there were eight new burst keywords. Keywords, such as “extracellular vesicle” (2016–2022), “dna” (2019–2022), “circulating tumor cell” (2020–2022), and “blood” (2020–2022), continued to burst with citations until 2022. The keyword that lasted for the longest duration of nine years was “gene expression”, while the keywords that lasted for a long duration were “brca2 mutation”, “cell free dna” (2016–2020), and “cystic neoplasm” (2017–2020). The keywords with a burst strength of >3 were “dna” (n = 4.03), “computed tomography” (n = 3.32), and “extracellular vesicles” (n = 3.15).

Discussion

The present study was the first to use a bibliometric approach to provide the quantitative characterization of the global field of PC early screening at the macro level over the past two decades, which was complemented by qualitative interpretation. The present results suggest that the number of publications in this area remains modest, with fluctuations between years, and an overall increasing trend. The research institutions and scholars in Europe and the United States had a high academic influence in the field of PC early screening. The keywords indicated that the present focus

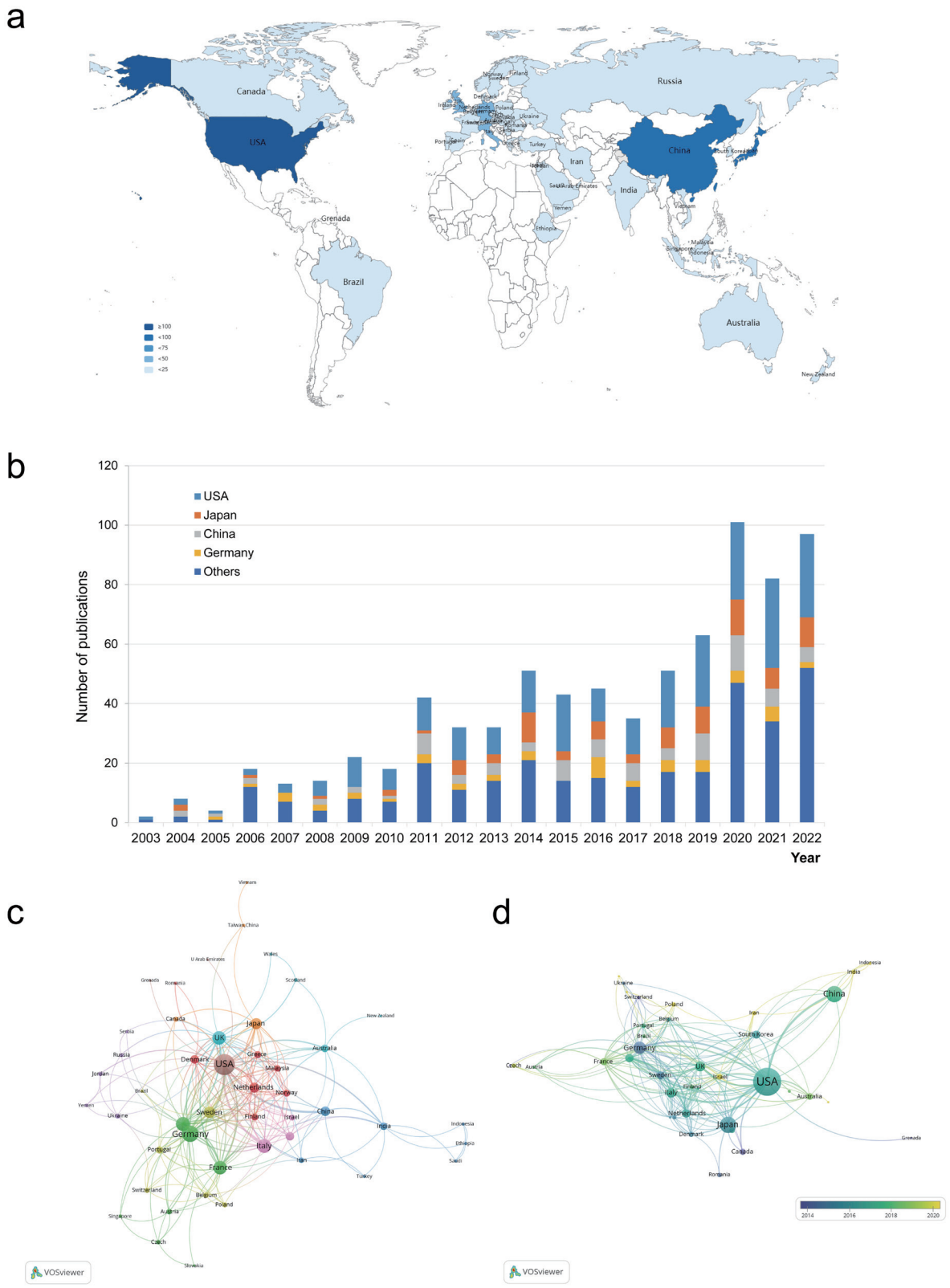


Fig. 3. National publications and cooperation. (a) Global map of countries/regions that contributed to pancreatic cancer early screening. (b) The distribution trend of the top four countries/regions by year. (b) Network visualization map of collaborations among countries/regions. (d) Overlay visualization map of collaborations among countries/regions.

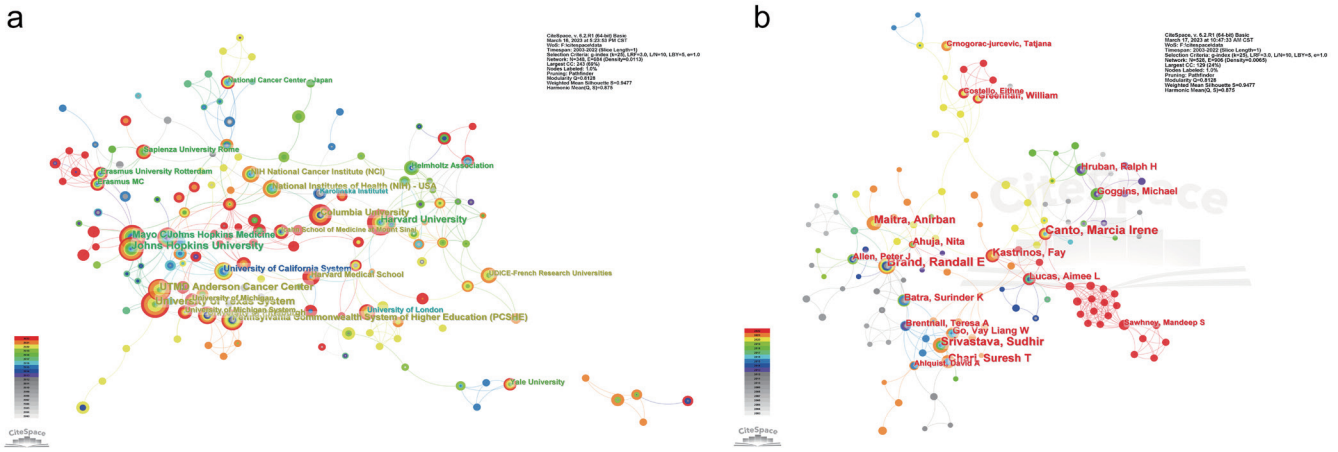
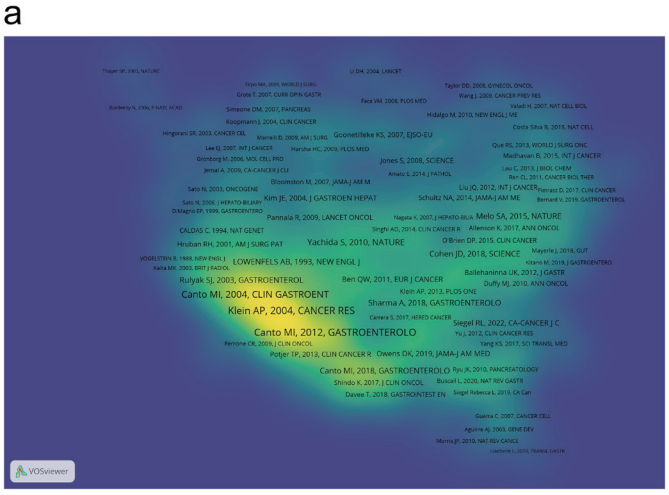


Fig. 4. Cooperation of institutions and scholars. (a) Visualization map of co-authorship between institutions carried on CiteSpace. (b) Visualization map of co-authorship among authors carried on CiteSpace.

on imaging, conventional biomarkers, and liquid biopsy were the three main test methods used in PC early screening, and that circulating tumor cells in the liquid biopsy would lead to new research directions, and provide new vitality.

Overall, according to the annual number of publications, the early screening of PC has received increasing attention, but the difficulty of research in related fields remains quite high. The journals that published related articles were dominated by the fields of pancreatic diseases, oncology, and digestive diseases. Researchers would likely prioritize journals with the highest number of published studies that focused on PC early screening. Articles published in journals with higher IF, or in Q1 and Q2, were usually considered to be the more important in the subject area. The analysis of the top 10 journals with the highest number of publications revealed that three journals with an IF of >10, and Q1 and Q2, accounted for 60%. This indicates that PC early screening is valued by top international scientists, while more high-quality articles are still needed in this field.

According to the results for the distribution of publications, a high number of interactions were identified among developed countries, while developing countries had less cooperation with other countries, indicating that the economy may have influenced the degree of research and development in the field of PC early screening between different countries. Although China has published a considerable number of articles in this field (14.11%), the proportion of international cooperative articles was significantly lower than that of the United States or Germany, and there was a lack of authoritative research institutions. All of these show the lack of influence of China in this field. For the outstanding scholars in this research field, Marcia Irene Canto and Randall E. Brand had numerous nodes in the whole layer, indicating that the publications of these scholars are hot topics in this field. Marcia Irene Canto (from Johns Hopkins Medicine) is a core leader in the field of PC early screening, and contributes to the use of endoscopic ultrasonography (EUS) and computed tomography (CT) to detect early PC and its precancerous lesions,[14,16] laying the foundation for a series of subsequent studies. Randall E. Brand (from the University of Pittsburgh) focused on the genetic



b

Top 25 References with the Strongest Citation Bursts

References	Year	Strength	Begin	End	2003 - 2022
Canto MI, 2004, CLIN GASTROENTEROL H, V2, P606, DOI 10.1016/S1542-3565(04)00244-7, DOI	2004	9.84	2006	2009	
Canto MI, 2006, CLIN GASTROENTEROL H, V4, P766, DOI 10.1016/j.cgh.2006.02.005, DOI	2006	15.7	2007	2011	
Brand RE, 2007, GUT, V56, P1460, DOI 10.1136/gut.2006.108456, DOI	2007	13.78	2008	2012	
Langer P, 2009, GUT, V58, P1410, DOI 10.1136/gut.2008.171611, DOI	2009	12.04	2010	2014	
Poley JW, 2009, AM J GASTROENTEROL, V104, P2175, DOI 10.1038/ajg.2009.276, DOI	2009	12.04	2010	2014	
Verna EC, 2010, CLIN CANCER RES, V16, P5028, DOI 10.1158/1078-0432.CCR-09-3209, DOI	2010	12.62	2011	2015	
Jones S, 2009, SCIENCE, V324, P217, DOI 10.1126/science.1171202, DOI	2009	7.89	2011	2014	
Canto MI, 2012, GASTROENTEROLOGY, V142, P796, DOI 10.1053/j.gastro.2012.01.005, DOI	2012	16.2	2012	2017	
Ludwig E, 2011, AM J GASTROENTEROL, V106, P946, DOI 10.1038/ajg.2011.65, DOI	2011	11.89	2012	2016	
Vasen HFA, 2011, GASTROENTEROLOGY, V140, P850, DOI 10.1053/j.gastro.2010.11.048, DOI	2011	11.89	2012	2016	
Al-Sukhni W, 2012, J GASTROINTEST SURG, V16, P771, DOI 10.1007/s11605-011-1781-6, DOI	2012	9.14	2012	2017	
Yachida S, 2010, NATURE, V467, P1114, DOI 10.1038/nature09515, DOI	2010	9.82	2013	2015	
Schneider R, 2011, FAM CANCER, V10, P323, DOI 10.1007/s10689-010-9414-x, DOI	2011	8.54	2013	2016	
Canto MI, 2013, GUT, V62, P339, DOI 10.1136/gutjnl-2012-303108, DOI	2013	20.42	2014	2018	
Rahib L, 2014, CANCER RES, V74, P2913, DOI 10.1158/0008-5472.CAN-14-0155, DOI	2014	14.86	2015	2019	
Melo SA, 2015, NATURE, V523, P177, DOI 10.1038/nature14581, DOI	2015	10.15	2016	2020	
Vasen H, 2016, J CLIN ONCOL, V34, P2010, DOI 10.1200/JCO.2015.64.0730, DOI	2016	8.34	2017	2019	
Siegel RL, 2017, CA-CANCER J CLIN, V67, P7, DOI 10.3322/caac.21387, DOI	2017	8.25	2017	2019	
Canto MI, 2018, GASTROENTEROLOGY, V155, P740, DOI 10.1053/j.gastro.2018.05.035, DOI	2018	11.57	2019	2022	
Klieff J, 2016, NAT REV DIS PRIMERS, V2, P0, DOI 10.1038/nrdp.2016.22, DOI	2016	9.27	2019	2022	
Bray F, 2018, CA-CANCER J CLIN, V68, P394, DOI 10.3322/caac.21492, DOI	2018	8.31	2019	2022	
Cohen JD, 2018, SCIENCE, V359, P926, DOI 10.1126/science.aar3247, DOI	2018	7.99	2019	2022	
Sharma A, 2018, GASTROENTEROLOGY, V155, P730, DOI 10.1053/j.gastro.2018.05.023, DOI	2018	9.29	2020	2022	
Singhi AD, 2019, GASTROENTEROLOGY, V156, P2024, DOI 10.1053/j.gastro.2019.01.259, DOI	2019	8.6	2020	2022	
Owens DK, 2019, JAMA-J AM MED ASSOC, V322, P438, DOI 10.1001/jama.2019.10232, DOI	2019	8.25	2020	2022	

Fig. 5. Co-citation literature of PC screening. (a) Density visualization map of literature with 20 or more co-citations. (b) The top 25 references with the strongest citation bursts. The red bars indicate the duration of the outbreak, while the blue bars represent when the article was published. The burst strength indicates the importance of the article to the field of study.

Table 2. Top 10 publications for pancreatic cancer early screening

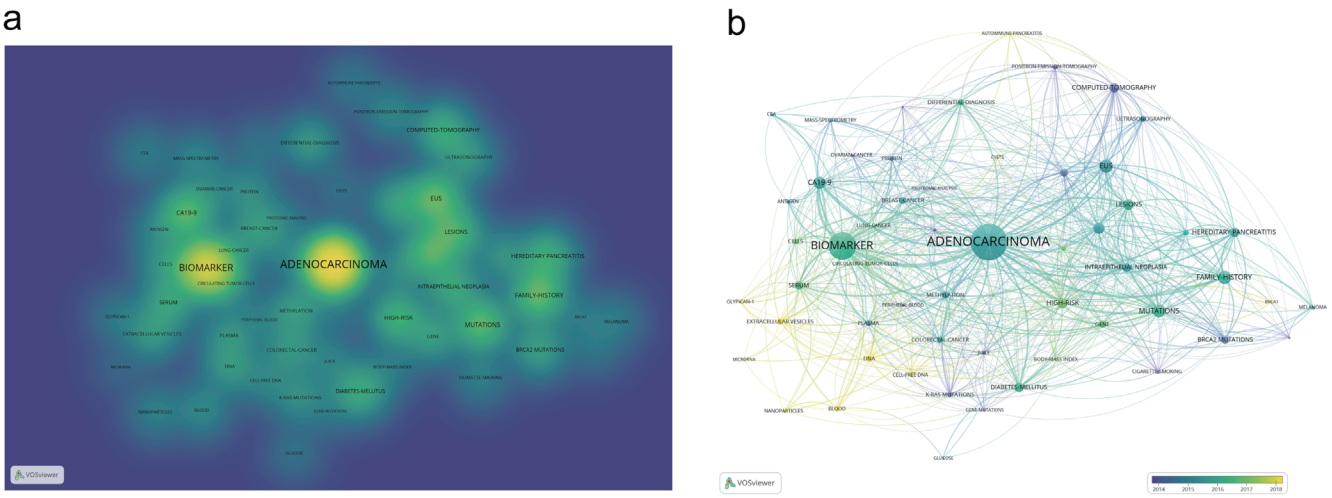
Title	First author	Country	Journal	Year	Total citations	Type
Screening for early pancreatic neoplasia in high-risk individuals: a prospective controlled study	Marcia Irene Canto	USA	*Clin Gastroenterol Hepatol*	2006	99	Article
Frequent detection of pancreatic lesions in asymptomatic high-risk individuals	Marcia Irene Canto	USA	*Gastroenterology*	2012	99	Article
International Cancer of the Pancreas Screening (CAPS) Consortium summit on the management of patients with increased risk for familial pancreatic cancer	Marcia Irene Canto	USA	*Gut*	2013	98	Review/ Guideline
Prospective Risk of Pancreatic Cancer in Familial Pancreatic Cancer Kindreds	Klein AP	USA	*Cancer Res*	2004	95	Article
Screening for pancreatic neoplasia in high-risk individuals: an EUS-based approach	Marcia Irene Canto	USA	*Clin Gastroenterol Hepatol*	2004	88	Article
Projecting cancer incidence and deaths to 2030: the unexpected burden of thyroid, liver, and pancreas cancers in the United States	Lola Rahib	USA	*Cancer Res*	2014	81	Article
Very high risk of cancer in familial Peutz-Jeghers syndrome	F M Giardiello	USA	*Gastroenterology*	2000	73	Article
The yield of first-time endoscopic ultrasonography in screening individuals at a high risk of developing pancreatic cancer	J W Poley	Netherlands	*Am J Gastroenterol*	2009	69	Article
Early diagnosis and treatment of pancreatic dysplasia in patients with a family history of pancreatic cancer.	Brentnall TA	USA	*Ann Intern Med*	1999	68	Article
Pancreatic cancer screening in a prospective cohort of high-risk patients: a comprehensive strategy of imaging and genetics	Elizabeth C Verna	USA	*Clin Cancer Res*	2010	63	Article

research of pancreatic cancer, conducted intensive research in the screening of familial PC, and is one of the major contributors in this field.[19,20]

Literature co-cited for multiple times was considered to constitute the knowledge base of a particular field. A significant proportion of the co-cited articles in this area focused on the exploration of high-risk groups.[15,18,21–25] At present, in addition to patients with a family history of PC and mutation carriers,[17] the recognition of high-risk groups further concentrated on new-onset diabetes,[26] Peutz-Jeghers syndrome,[27] and other groups, such as BRCA2 carriers.[28] However, the need for PC early screening in patients with BRCA2 mutations remains controversial.[8,29] An early study concluded that the screening of this population has little relevance,[30] while the present consensus of the International Consortium for PC Screening suggested that screening should be offered to BRCA2 carriers with at least one first-degree relative, or at least two second-degree relatives.[31] The citation outbreaks of seven pieces of literature remained in progress, and the strongest value was identified in the prediction model published by Sharma *et al*. in 2018, which clearly defined those who warrant the clinical early screening of PC.[26]

The present keywords analysis revealed that imaging, conventional biomarkers, and liquid biopsies are predominant in the early screening of PC. Imaging techniques, including CT, magnetic resonance imaging (MRI) and EUS, play important roles in PC early screening for high-risk people.[8] Pancreatic CT is a low-cost technique, and is easy to operate, but the resolution of CT is inferior to MRI and EUS, in terms of small lesions of the pancreas, and its radiation is a disadvantage.[9,11] With the characteristics of absence of ionizing radiation and better soft tissue resolution, MRI combined with endoscopic retrograde cholangiopancreatography (MRCP) contributes to better detect tumors at the early stage.[32–35] EUS can provide high-resolution images of the pancreas, and is important for detecting small pancreatic lesions.[36] It is noteworthy that EUS-guided fine-needle aspiration (EUS-FNA) has high sensitivity and specificity, and is considered as the gold standard for PC diagnosis.[11,37] However, as an invasive procedure, EUS-FNA may lead to pancreatitis or bleeding, and is not recommended for routine screening.[7,8] Due to the different pathological staging of PC, the sensitivity and specificity of different imaging techniques lead to great differences, and the combined application of multiple methods can significantly improve diagnostic accuracy.[36,38]

There is a lack of biomarkers for early stage PC.[8,11] Among the single marker tests, the serum CA19-9 test has sensitivity (approximately 70%), and is the only biological marker presently used in PC early screening, but this lacks sufficient accuracy and specificity in screening for early stage PC.[39–41] The combination of CA19-9 with other biomarkers (such as CEA, CA125 and CA242) can increase the sensitivity to 85–90%, and specificity to more than 90%, presenting as a good application prospect.[42,43] The use of metabonomics to discover differential metabolites as new tumor markers for the early diagnosis of PC has become a research approach.[44] Meanwhile, proteomics has made considerable progress



c

Top 15 Keywords with the Strongest Citation Bursts

Keywords	Year	Strength	Begin	End	2003 - 2022
gene expression	2003	2.14	**2003**	2011	
juice	2004	2.25	**2004**	2006	
computed tomography	2004	3.32	**2006**	2009	
brca2 mutation	2004	2.17	**2009**	2015	
intraepithelial neoplasia	2006	2.13	**2009**	2014	
papillary mucinous neoplasm	2006	2.11	**2009**	2012	
differential diagnosis	2011	1.99	**2011**	2017	
extracellular vesicle	2016	3.15	**2016**	2022	
cell free dna	2016	2.17	**2016**	2020	
cystic neoplasm	2012	2.27	**2017**	2020	
peutz jeghers syndrome	2007	2	**2017**	2018	
lesion	2005	2.79	**2018**	2019	
dna	2005	4.03	**2019**	2022	
circulating tumor cell	2012	2.5	**2020**	2022	
blood	2006	2.3	**2020**	2022	

Fig. 6. Keywords of PC screening. (a) Keywords density visualization for PC early screening. (b) Overlay visualization map of keywords. (c) The top 15 keywords with the strongest citation bursts.

in PC early screening. Some recent studies have revealed that the tumor-specific variants of protein glycosylation may contribute to the early diagnosis of PC.[45,46] The application of omics techniques has facilitated the rapid increase in the number of biomarkers, which accelerate the entry of effective markers in clinical practice, as soon as possible.

Liquid biopsy has become a research focus in recent years. This is minimally invasive, rapid, and suitable for dynamic surveillance, and is represented by extracellular vesicle and circulating tumor cells. Sonia *et al*. reported that $GPC1^{+}$ crExos can be a pathway for the detection and isolation of exosomes in the circulation of cancer patients for further study.[47] A research team from China identified that plasma EV-long RNA analysis may be a new marker for the detection of PC.[48] The Moores Cancer Center research team developed a blood biomarker classifier based on EV, which can detect 95.5% of stage I PCs.[49] However, existing studies on a single marker have not provided the high sensitivity and specificity required for the early detection of PC.[50] Thus, combining multiple biomarkers for the early screening of PC may be the direction of development in this field.[1,51]

There were some limitations in the present study. First, merely WoS was selected as the database, and several relevant articles might have been missed. Second, this may have omitted important non-English articles, leading to bias, and the reduction of its credibility. Finally, since the literature selection focused on the period of 2003-2022, some high-quality articles published earlier in the field may have not been included, which may lead to missing hot terms, and the underestimated number of citations of recently published high-quality articles.

Conclusion

The present study presents a multi-dimensional view of recent research findings in the field of PC early screening by systematically analyzing literature on the early screening for PC obtained from the WoS core database. There was a geographical variation, which reflected that the United States and Europe were advanced in the general practice research of PC early screening. Furthermore, the scientific cooperation network revealed that the cooperation between countries and institutions is calling for further enhancement. For the screening strategies, liquid biopsy will become the key foci in the future. This bibliometric analysis would provide insights into the state of PC early screening research, and identify new perspectives for future research.

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Conflict of interest

Prof. Zhao-Shen Li has been the general editor-in-chief of *Cancer Screening and Prevention* since August 2021. The other authors declare no conflict of interests.

Author contributions

WBZ and LH: study design; GXM and YCW: collected the data and wrote the manuscript; GXM and YL: analyzed the data; XTM, SHM and SHX: participated in the screening of publications; ZSL: provided financial support and supervision for the study. All authors interpreted the data, revised the text, and approved the final draft of the manuscript.

Ethical statement

There was no need for ethics approval, because the data for the bibliometric research were directly extracted from the database, and did not undergo further human intervention.

Data sharing statement

The data sets generated and/or analyzed in the study are available upon reasonable request from the corresponding authors.

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