

## Review

# Feasibility analysis and development trend of nanomaterials for the treatment of pancreatic cancer

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## Abstract

Pancreatic cancer is a highly aggressive disease that poses a significant threat to human health. Although conventional chemotherapy remains an effective treatment, it is often associated with severe side effects, underscoring the need for more effective cancer therapies. In this study, we analyzed the keywords of past studies, the countries with the highest number of publications, the leading journals, prominent authors, and collaborations between countries, authors, and journals, as well as the impact factors of relevant literature. The aim was to explore the trends in the use of nanomaterials for the treatment of pancreatic cancer, enabling researchers to review past achievements and gain a better understanding of future research directions. Relevant research articles were sourced from core Web of Science databases, and VOSviewer and CiteSpace visualization tools were employed to reveal the intrinsic links between the information. Research on the use of nanomaterials for the therapy of pancreatic cancer has been growing since the twenty-first century, particularly from 2018 to the present. The United States has become a leader in this field, with the highest number of publications and the most published authors. Additionally, a 2018 study published in *Nature* demonstrated that patients with insufficient CD8+ T-cell infiltration in the pancreatic cancer tumor microenvironment (TME) had significantly lower survival rates ( $HR = 2.5$ ,  $p < 0.001$ ). And CSF1R inhibitors combined with a PD-1 antibody resulted in 60% tumor shrinkage in a mouse model. These findings suggest that research on the tumor microenvironment and immunotherapy is poised to be a key focus of future studies, offering new hope for pancreatic cancer patients.

**Keywords** Pancreatic cancer · Nanomaterials · Visual analysis · Past hotspot · Future research trends

## Abbreviations

|       |                                 |
|-------|---------------------------------|
| WoSCC | Web of science core collection  |
| SSCI  | Social science citation index   |
| SCI-E | Science citation index expanded |
| LS    | Link strength                   |
| TLS   | The total link strength         |
| GEM   | Gemcitabine                     |
| OX    | Oxaliplatin                     |
| IND   | Indoximod                       |

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PDAC     Pancreatic ductal adenocarcinoma  
ICD       Immunogenic cell death  
IDO       Indoleamine 2, 3-dioxygenase

## 1 Introduction

Pancreatic cancer is the fourth most common cause of cancer-related deaths globally [1]. It is a highly malignant tumour with an extremely poor prognosis. Despite decades of research and therapeutic advancements, the five-year survival rate for pancreatic cancer patients is 13% [2]. The most recent data reported by the American Cancer Society 2024 shows a gradual improvement in outcomes, with the five-year survival rate rising by one percentage point in the third year [3]. According to relevant statistics patients who undergo resection generally survive for 16 months. The current standard of care involves radical resection and adjuvant chemotherapy [4]. Despite significant improvements in surgical treatment, enhancements in adjuvant therapy, and more aggressive treatment regimens over the past few years, even definitively resectable pancreatic cancer continues to have a poor prognosis and a high risk of recurrence [5]. Early diagnosis and treatment are crucial to improving the prognosis of pancreatic cancer. The use of nanomaterials for the therapy of pancreatic cancer has made significant progress, and indications for their use are expanding.

Nanoparticles offer a promising platform for the safe and efficient therapy of tumors [6, 7]. They are biocompatible and can be used for therapeutic and diagnostic purposes, including precise tumour diagnosis, targeted drug delivery, microenvironmental modulation, and immune system activation [8, 9]. Nanomaterials are a growing research topic in the field of pancreatic cancer, with the aim of improving diagnostic and therapeutic interventions for this disease [10]. Nanomaterials have unique physical and chemical properties that make them potential components in anti-pancreatic cancer therapies. Real-time monitoring and precise assessment of pancreatic cancer progression are vital for optimizing treatment outcomes. Nanomaterials can target fluorescent small molecule chemotherapeutic agents to areas of pancreatic cancer [11]. This design enables the simultaneous release of fluorescent molecules and chemotherapeutic drugs in the specific microenvironment of pancreatic cancer. As a result, it allows for non-invasive and real-time monitoring of treatment, providing a new strategy for accurate diagnosis, rational management, and effective treatment of tumours [12].

Bibliometric analysis transforms large volumes of literature into structured data, offering researchers an objective and global perspective through various quantitative indicators (e.g., h-index, centrality), network topology (e.g., small-world networks), and dynamic models (e.g., trend prediction) [13]. It not only provides insights into historical developments but also aids in forecasting future trends, making it a crucial tool for understanding the academic ecosystem [14]. Algorithms can uncover patterns that are often imperceptible to the human eye, such as 'structural holes' in interdisciplinary collaborations or low-frequency yet high-potential emerging keywords. Additionally, bibliometric analysis identifies key hubs in collaborative networks—such as an organization's role as a bridge in transnational collaborations and helps to avoid unnecessary duplication of resources [15]. Visualization of gaps between thematic clusters can suggest innovative directions for further research. Clinicians are able to expeditiously select highly cited clinical trial literature from our research in order to identify proven treatment options. Researchers are able to pinpoint saturated research areas and explore underdeveloped sub-directions through topic evolution mapping.

The objective of this study is to present a thorough analysis of the evolving role of nanomaterials in the therapy of pancreatic cancer, based on bibliometric data. It is useful for revealing the frontiers and hotspots of research on the use of nanomaterials and pancreatic cancer and provides valuable insights for future research.

## 2 Method

### 2.1 Data search

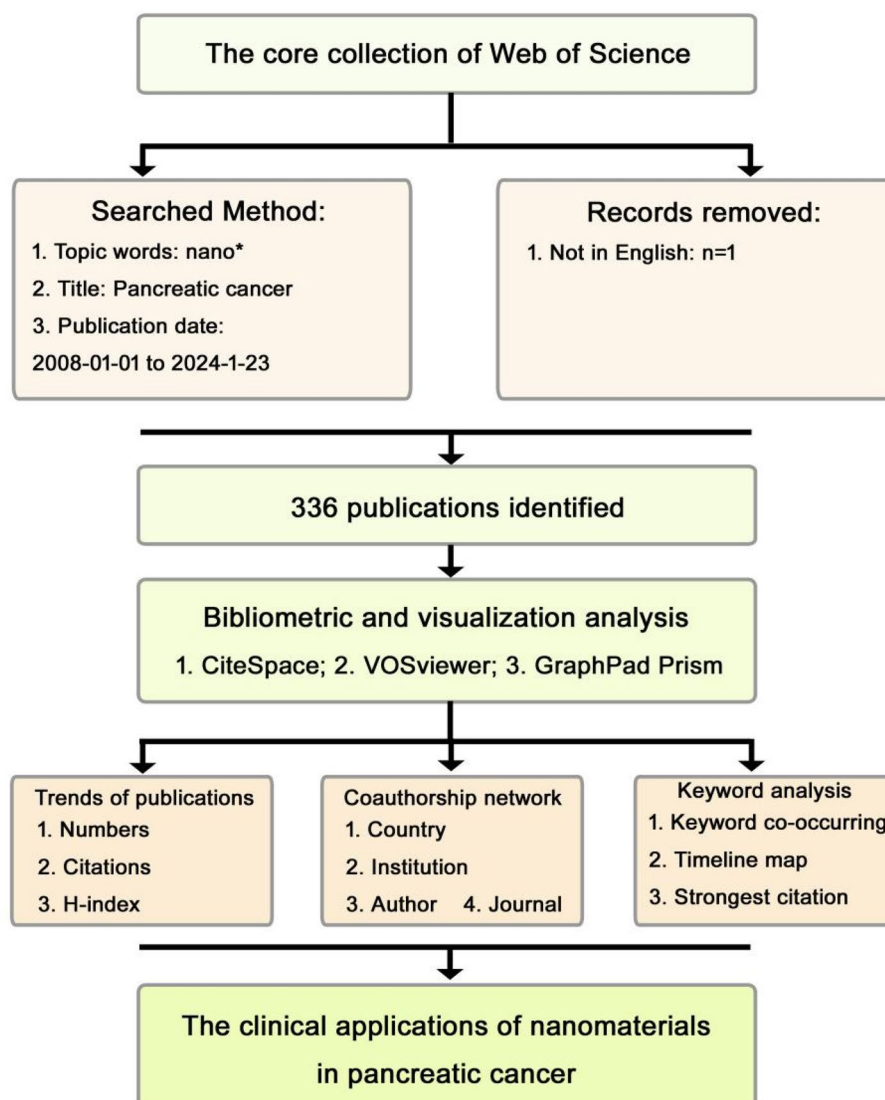
The Web of Science Core Collection's (WoSCC) citation indexing system (e.g., SCI, SSCI) is its main strength. It not only makes literature searches easier but also uses its citation network to track the beginnings and progression of research. WoSCC encompasses a vast array of multidisciplinary content from the scientific sciences, social sciences, and humanities by integrating numerous sub-databases and enabling cross-database searches [16]. Figure 1 illustrates the selection criteria and literature screening process employed in this study. The initial search was conducted using the following

formula: TS = ('nanostructured materials' OR 'nanomaterials' OR 'nanotechnology') AND TS = ('pancreatic cancer') AND TS = ('treatment' OR 'prognosis' OR 'therapy'). Two researchers independently reviewed the search results and excluded ineligible publications based on the following inclusion criteria: (1) Publications were limited to those in English. (2) Conference abstracts and grey literature were excluded. (3) Review papers were included. (4) Only papers sourced from the Web of Science Core Collection (WoSCC), specifically the Science Citation Index Expanded (SCI-E) and Social Science Citation Index (SSCI), were considered. (5) The search covered a 21-year time span, from January 1, 2008, to January 23, 2024. (6) To mitigate bias due to daily updates of the databases, the search and selection of publications were conducted on the same day. All of these criteria can be directly applied via the WoSCC search page.

## 2.2 Analysing data

This study used the visualisation tools VOSviewer and CiteSpace. VOSviewer is a tool used for creating visual charts and analysing the most published/co-authored countries, institutions, authors, as well as the most cited journals and frequently occurring keywords [17]. CiteSpace is another tool used for constructing timeline charts and keyword phrases [18]. Each point on the visual graph represents a country, institution, author, or journal. The dots are divided into groups based on their cooperation. The size of the dots is dependent on the number of publications. Link strength (LS) refers to the thickness of the line connecting the nodes and represents the level of cooperation between

**Fig. 1** Literature screening flow chart



them [19]. Total Link Strength reflects the strength of collaboration between entities based on co-authorships and co-citations [20].

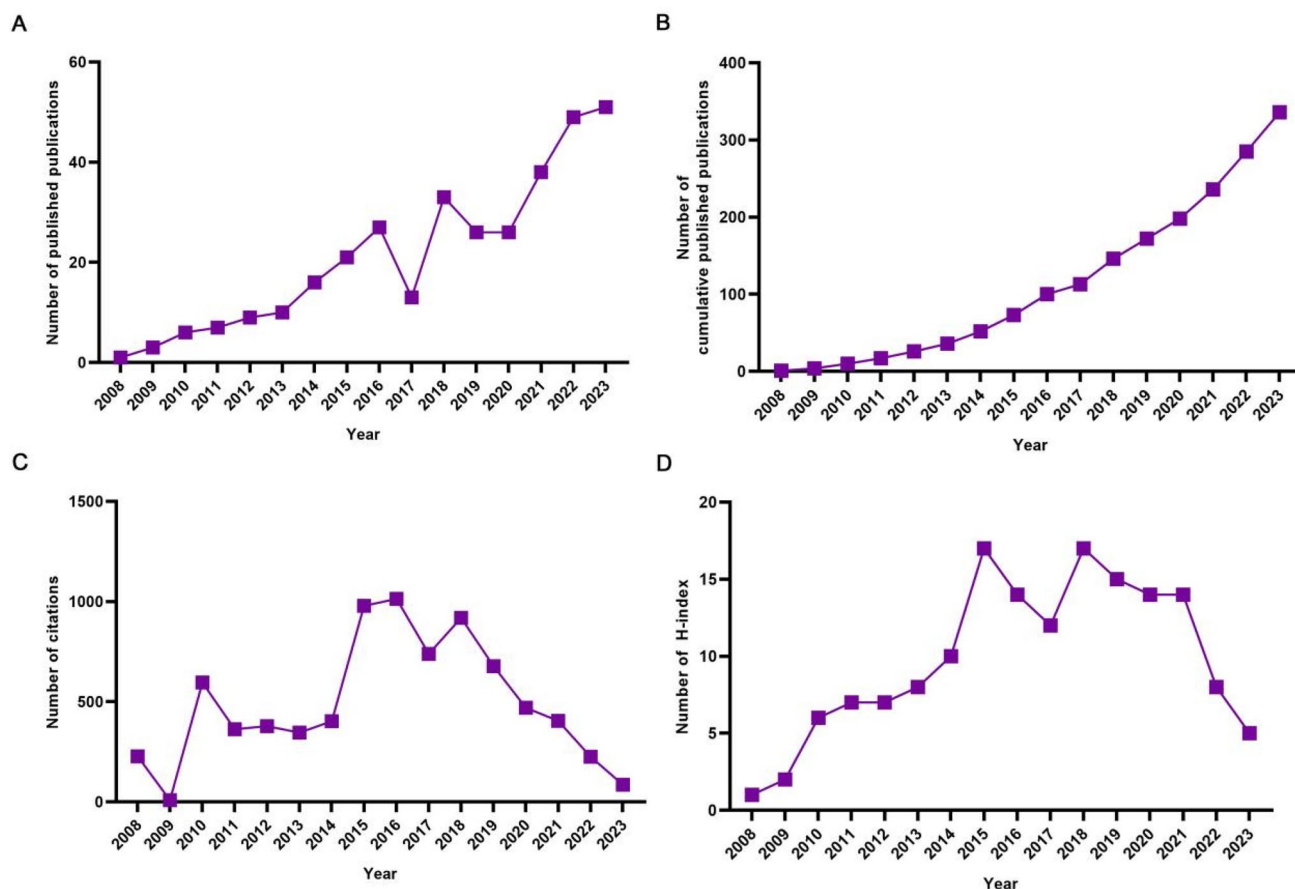
### 2.3 Data extraction

The publications included in the analysis were examined in various file formats. The extracted data from these publications include the title, author, institution, country, journal, impact factor, number of citations in the year of publication, and H-index.

## 3 Result

### 3.1 Annual number of publications and citations

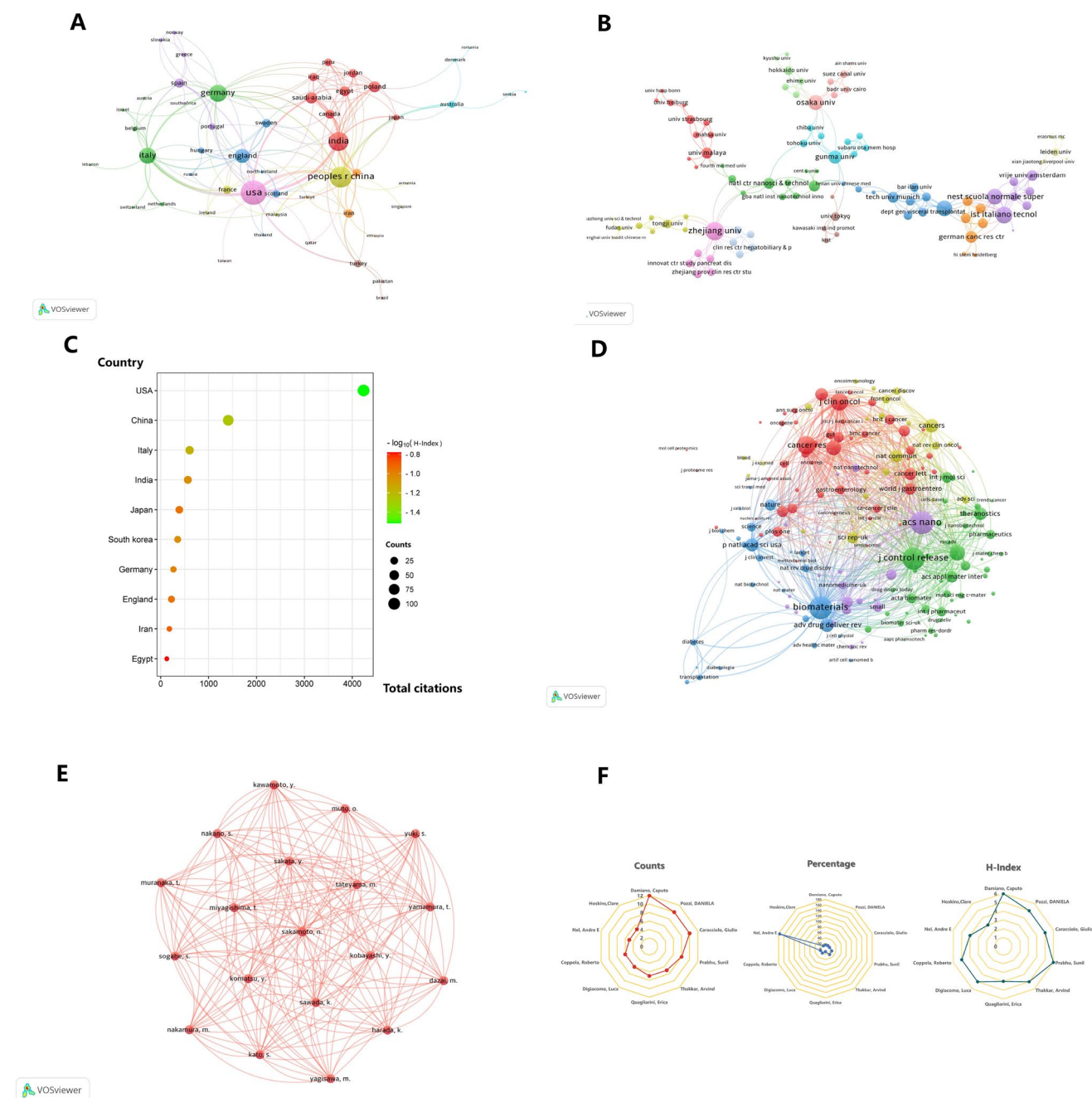
We analysed 336 papers included in the study and tallied the yearly publications and citations. As demonstrated in Fig. 2A–D, both the number of publications and citations increased consistently, with rapid growth commencing in 2018. In 2023, there were 51 publications and 84 citations. The significant increase after 2018 indicates the widespread application of nanomaterials and the general academic interest.



**Fig. 2** Publication trends in research on the use of nanomaterials for therapy of pancreatic cancer. **A** Number of papers; **B** Cumulative number of papers; publication rate and index trend line for the 15-year period from 2008 to 2023; **C** Total number of citations of publications; **D** H-index values for publications

### 3.2 Analysis of the status of country and institution cooperation

Fifty-four countries are exploring potential applications of nanomaterials in pancreatic cancer treatment (Fig. 3A). The United States contributed the most ( $n = 101$ , 41.94%), followed by China ( $n = 73$ , 19.33%), Italy ( $n = 33$ , 18.30%), India ( $n = 27$ , 21.00%) and Japan ( $n = 24$ , 16.21%) (Table 1). Figure 3B illustrates the main institutions and their co-occurrence in this area. An analysis of the co-occurrence of institutions shows that institutions that publish a large number of papers tend to have close collaborations with each other. Research into the use of nanomaterials for the diagnosis and treatment



**Fig. 3** shows a diagram of the research collaboration network on nanomaterials for therapy of pancreatic cancer. **A** The map displays the coauthorship network between countries. **B** The map displays the coauthorship network of institutions. **C** Top 10 countries (N=336) by volume of publications. **D** The map displays the coauthorship network of journals. **E** The map displays the cocitation network of authors. **F** Top 10 authors with the most publications

**Table 1** Top 10 research institutions by volume of publications

| Rank | Institution                             | Country | Counts | Percentage | Total citations | H-Index |
|------|---|---------|--------|------------|-----------------|---------|
| 1    | University campus bio medico rome Italy | Italy   | 14     | 15.93      | 223             | 7       |
| 2    | Sapienza university rome                | Italy   | 12     | 14.42      | 173             | 6       |
| 3    | University of california system         | USA     | 11     | 94.00      | 1034            | 8       |
| 4    | Chinese academy of sciences             | China   | 10     | 52.80      | 528             | 7       |
| 5    | Egyptian knowledge bank ekb             | Egypt   | 10     | 12.80      | 128             | 6       |
| 6    | University of texas system              | USA     | 8      | 26.13      | 209             | 5       |
| 7    | Mayo clinic                             | USA     | 7      | 117.71     | 824             | 7       |
| 8    | University of california los angeles    | USA     | 7      | 140.14     | 981             | 5       |
| 9    | Westernuniversity of health sciences    | USA     | 7      | 27.57      | 193             | 6       |
| 10   | FuDan university                        | China   | 6      | 48.50      | 291             | 4       |

of pancreatic cancer has been carried out at a number of institutions globally. Table 1 lists the top 10 institutions based on literature output and number of citations. The University Campus of Biomedicine in Rome, Italy, has the highest number of papers (14 or 15.93%), followed by the Sapienza University of Rome (12 or 14.22%).

Centrality is a concept commonly used in network analysis, indicating the degree to which a vertex in a network is at the centre of the whole network. China has the highest degree of centrality (centrality = 0.55) as it has mutually supportive relationships with many countries. The closest collaboration with other countries was with the USA (TLS = 44). The top 10 countries included one North American country, three European countries, and six Asian countries (Fig. 3C). These countries accounted for 97.9% of the total number of publications, totalling 329 papers. Figure 3A illustrates the extensive cooperation between countries. In general, countries with a higher number of publications also collaborate more. The United States of America is the most prominent country in this respect. The primary reason for this is that the United States has long been one of the leading countries in terms of research and development (R&D) expenditures. Both government agencies and the private sector have consistently invested substantial amounts of capital into supporting both basic and applied research. Prestigious universities, such as Harvard, MIT, and Stanford, along with national laboratories, attract some of the world's top talents, thereby fostering a high-output research ecosystem. English serves as the common language in the international scientific community, allowing American scholars to engage in global collaborations without facing language barriers, whereas scholars from other countries must proactively integrate into the English-speaking academic sphere. Additionally, agencies like the NSF have established specialized programs to encourage international collaboration.

### 3.3 Analysing and researching journals

We analysed the top ten journals in terms of number of publications and found that they published 78 papers (Table 2), which accounted for 23.21% of the total number of published papers. The three journals with the highest number of research papers in this field were Cancers, Pharmaceutics and International Journal of Nanomedicine. Acs nano has the

**Table 2** The top 10 most productive journals in terms of the volume of their publications

| Rank | Journal names                                       | Counts | Total citations | H-Index | IF in 2023 | JCR category |
|------|---|--------|-----------------|---------|------------|--------------|
| 1    | Cancers   | 13     | 139             | 7       | 5.2        | Q2           |
| 2    | Pharmaceutics                                       | 12     | 178             | 5       | 5.4        | Q2           |
| 3    | International journal of nanomedicine               | 10     | 271             | 7       | 8.0        | Q2           |
| 4    | Cancer research                                     | 9      | 331             | 3       | 11.2       | Q1           |
| 5    | Journal of controlled release                       | 7      | 288             | 6       | 10.8       | Q1           |
| 6    | Journal of nanobiotechnology                        | 7      | 99              | 5       | 10.2       | Q1           |
| 7    | Biomaterials  | 6      | 232             | 5       | 14.0       | Q1           |
| 8    | Abstracts of papers of the americanchemical society | 5      | /               | /       | /          | /            |
| 9    | Acs nano  | 5      | 667             | 5       | 17.1       | Q1           |
| 10   | Cancer letters                                      | 5      | 65              | 3       | 9.7        | Q1           |



highest number of citations and the highest average number of citations per paper. ACS nano has the highest number of citations and the highest average number of citations per paper. It also has the strongest collaborations with other journals (Fig. 3D). In addition, the IF is an important parameter to assess its value, and ACS nano has the highest IF (17.1).

ACS Nano focuses on nanoscience and technology, particularly cross-disciplinary research. The journal promotes interdisciplinary research, such as the combination of nanotechnology with immunotherapy and drug delivery systems, which has resulted in innovations in pancreatic cancer treatment, and serves as an ideal publication platform for nanoparticles in medicine.

### 3.4 Analytical studies of authors

The analysis of author co-occurrence revealed the existence of multiple research groups and collaborations among researchers in this area (Fig. 3E). The size of each node was positively correlated with the number of publications by a particular author, while the thickness of the lines between nodes represented the frequency of cooperation. The size of each node was positively correlated with the number of publications by a particular author, while the thickness of the lines between nodes represented the frequency of cooperation. Visual analysis showed that Caputo, Damiano, and Caracciolo, Giulio collaborated as much as other authors and had the closest collaboration (TLS = 53). The Fig. 3F presents the top 10 authors with the most publications. Caputo, Damiano had the highest number of publications in this field ( $n = 12$ ), followed by Caracciolo, Giulio ( $n = 10$ ) and Pozzi, Daniela ( $n = 9$ ). Additionally, Caputo, Damiano had the highest number of total citations and the highest H-index among the authors, due to the high quality, innovative and widely influential of research results.

### 3.5 Analysis of the most highly cited literature

Table 3 shows information about the ten most cited papers [21–30]. In 2015, Meng, H published an article in ACS Nano titled “Use of a Lipid-Coated Mesoporous Silica Nanoparticle Platform for Synergistic Gemcitabine and Paclitaxel Delivery to Human Pancreatic Cancer in Mice” was cited 339 times, making it becomes the most cited article [21]. Patra, CR published an article titled “Fabrication of Gold Nanoparticles for Targeted Therapy of Pancreatic Cancer” in Advanced drug delivery reviews in 2010. The article has been cited 335 times [22]. The main reasons these two articles received the most citations were because they established replicable procedures, addressed important issues in the area with state-of-the-art technology, and established scholarly norms using trustworthy data and reputable distribution methods.

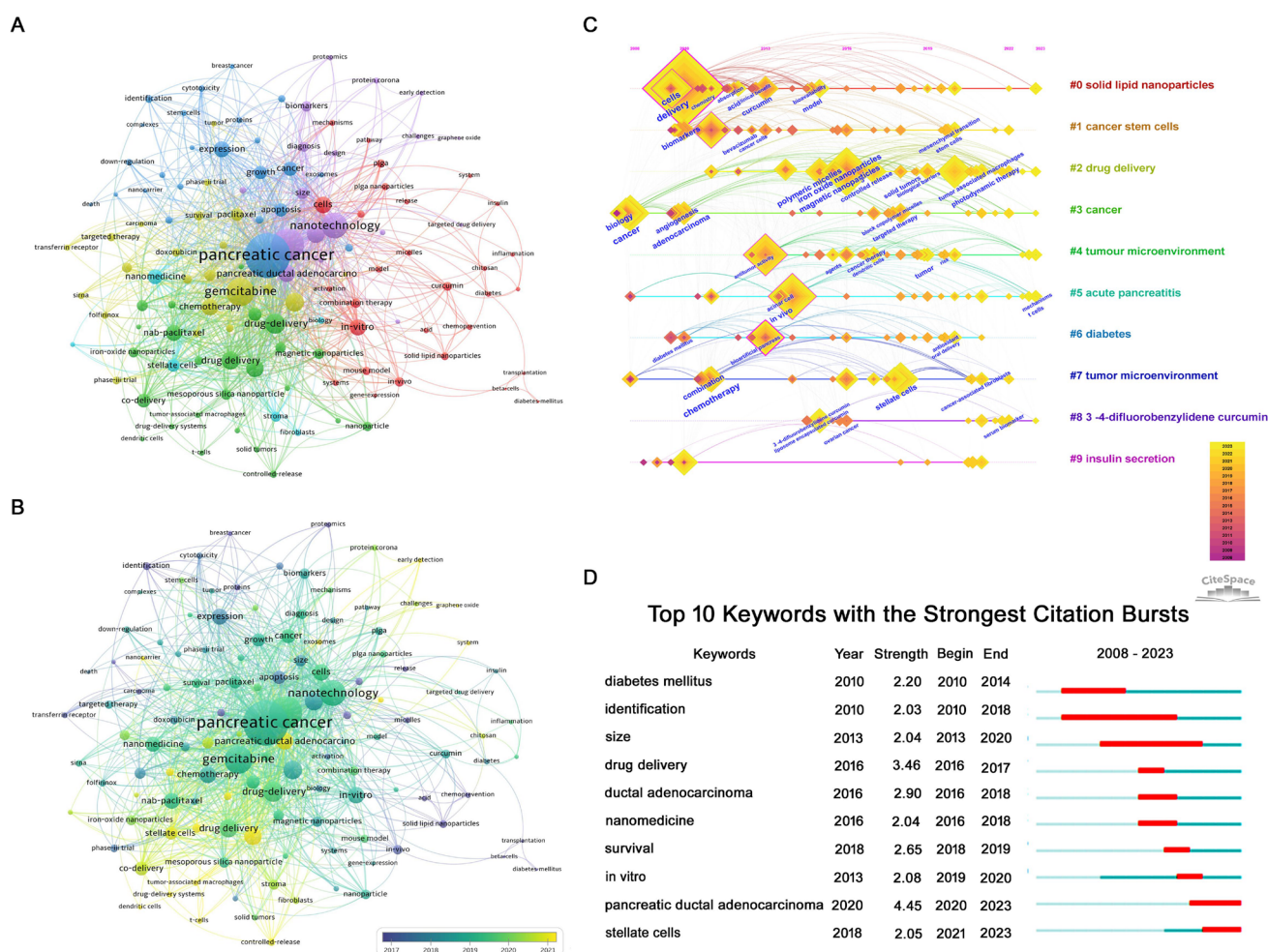
### 3.6 Research and analysis of keywords and hotspots

We visualised and analysed all the keywords into six different clusters (Fig. 4A). The visualisations indicate that “gemcitabine”, “combination therapy”, “chemotherapy”, and “nanomedicine” have higher densities, highlighting their importance and potential for research in the field of nanomaterials for pancreatic cancer therapy. Our study found that until 2020, the main hotspots were gemcitabine, paclitaxel, chemotherapy and drug delivery. However, in 2021, we observed a gradual shift towards mesoporous silica nanoparticles, tumour-associated macrophages and dendritic cells for the diagnosis and treatment of pancreatic cancer (Fig. 4B, C). In the treatment of pancreatic cancer, the transition from traditional chemotherapeutic agents, such as gemcitabine and paclitaxel, to immunotherapy illustrates a broader trend in pancreatic cancer research. This trend highlights the shift from a singular treatment paradigm to multidisciplinary integrated therapies, with a particular focus on combination therapies that enhance efficacy through multi-mechanism synergy (e.g., chemotherapy + targeted therapy + immunotherapy). This evolution reflects a strategic move from single-agent therapies to multi-drug combinations, as well as a shift from non-specific cytotoxicity to precision targeting and immunomodulation. Precision-targeted therapies reduce damage to healthy tissues by specifically targeting tumor cells or the tumor microenvironment, marking a transition from “broad-spectrum killing” to “precision striking.” Moreover, multidisciplinary comprehensive treatment improves overall efficacy by integrating surgery, chemotherapy, radiotherapy, immunotherapy, and other therapeutic modalities, thus exemplifying the transformation from a “single-discipline” approach to “multidisciplinary collaboration.” This indicates a shift towards nanomaterials and immunotherapy. The core content of article is represented by keywords. To identify active areas of research, keyword co-occurrence analysis can be used. The ten most frequent keywords are “diabetes mellitus”, “identification”, “size”, “drug delivery”, “ductal adenocarcinoma”, “nanomedicine”, “survival”, “in vitro”, “pancreatic ductal adenocarcinoma”, and “stellate cells” (Fig. 4D). We think that the core areas of precision targeting, multimodal therapy, immune modulation, matrix remodeling, etc.,

**Table 3** Top 10 articles in terms of number of citations

| Author                  | Title   | Journal                                | Institution                                   | Year | Citation |
|-------------------------|---|--|---|------|----------|
| <u>Meng, H</u>          | Use of a Lipid-Coated Mesoporous Silica Nanoparticle Platform for Synergistic Gemcitabine and Paclitaxel Delivery to Human Pancreatic Cancer in Mice          | ACS nano                               | Univ Calif Los Angeles, Dept Med, Div NanoMed | 2015 | 339      |
| <u>Patra, CR</u>        | Fabrication of gold nanoparticles for targeted therapy in pancreatic cancer   | Advanced drug delivery reviews         | Mayo Clin,                                    | 2010 | 335      |
| <u>Lu, JQ</u>           | Nano-enabled pancreas cancer immunotherapy using immunogenic cell death and reversing immunosuppression   | Nature communications                  | Univ Calif Los Angeles                        | 2017 | 323      |
| <u>Patra, CR</u>        | Targeted delivery of gemcitabine to pancreatic adenocarcinoma using cetuximab as a targeting agent  | Cancer research                        | Mayo Clin                                     | 2008 | 289      |
| <u>Ye, YQ</u>           | Microneedles Integrated with Pancreatic Cells and Synthetic Glucose-Signal Amplifiers for Smart Insulin Delivery  | Advanced materials                     | Univ N Carolina                               | 2016 | 168      |
| <u>Adisheshaiah, PP</u> | Nanomedicine strategies to overcome the pathophysiological barriers of pancreatic cancer  | Nature reviews clinical oncology       | Leidos Biomed Res Inc                         | 2016 | 164      |
| <u>Li, TD</u>           | An ultrasensitive polydopamine bi-functionalized SERS immunoassay for exosome-based diagnosis and classification of pancreatic cancer                         | Chemical science                       | Fudan Univ                                    | 2018 | 157      |
| <u>Meng, H</u>          | Two-Wave Nanotherapy To Target the Stroma and Optimize Gemcitabine Delivery To a Human Pancreatic Cancer Model in Mice  | ACS nano                               | Univ Calif Los Angeles                        | 2013 | 154      |
| <u>Kesharwani, P</u>    | Hyaluronic acid-conjugated polyamidoamine dendrimers for targeted delivery of 3,4-difluorobenzylidene curcumin to CD44 overexpressing pancreatic cancer cells | Colloids and surfaces B-bio interfaces | Wayne State Univ                              | 2015 | 145      |
| <u>Su, MJ</u>           | Pancreatic Cancer Cell Exosome-Mediated Macrophage Reprogramming and the Role of MicroRNAs 155 and 125b2 Transfection using Nanoparticle Delivery Systems     | Scientific reports                     | Northeastern Univ                             | 2016 | 134      |





**Fig. 4** shows the results of the keyword analysis on research hotspots. **A, B** The keyword co-occurring network A and overlay B. **C** The timeline map shows the co-occurrence of keywords. **D** Top 10 keywords with the strongest citation bursts

will be the focus of nanoparticle therapy for pancreatic cancer in the future. This will involve combining clinical needs and technological innovation, and it will encourage the transition from traditional chemotherapy to high-efficiency, low-toxicity, and personalized treatments for pancreatic cancer.

## 4 Discussion

The software for article analysis enables scientometric analyses. It gathers all literature containing valid information on a given topic within a limited time frame, analyses and quantifies it in an intuitive manner, and summarises this information [31]. The study indicates that chemotherapy and gemcitabine (GEM) have been popular treatments for pancreatic cancer in the past. Regimens such as gemcitabine and FOLFIRINOX remain first-line treatments for pancreatic cancer; however, they exhibit limited efficacy, with a 5-year survival rate of less than 10%, and are prone to the development of drug resistance [32]. Approximately 1–2% of pancreatic cancer patients, or those with high tumor mutation burdens, may respond to PD-1 inhibitors [33]. CXCR4 inhibitors block tumor cell-stroma interactions, and a phase I/II trial combining a PD-1 inhibitor with chemotherapy has demonstrated preliminary efficacy. Tailored mRNA vaccines, based on tumor-specific mutations, show promise in early-phase studies. Additionally, phase I trials targeting KRAS mutations (specifically the G12D/V mutation) are currently underway. The findings outlined above serve to confirm that there is an observable shift in focus towards the tumour microenvironment and immunotherapy as research continues to progress.

The study found that China and the United States accounted for 51.78% of all publications, making them the leading countries. This may be attributed to the strong financial support that both China and the United States provide for

scientific research, particularly in the fields of nanomedicine and cancer research. These two countries are home to world-class universities and research institutes that attract a large number of distinguished scientists. Additionally, both governments likely have targeted support programs to promote research at the intersection of nanotechnology and cancer treatment. Both nations benefit from large patient populations and advanced medical facilities, which facilitate the conduct of clinical trials. It is worth noting that the United States is the most productive and published country globally, with a higher H-index, number of citations, and average number of citations than other countries. But because the United States does not focus on cooperation with other countries, it dominates in terms of influence but not in terms of centrality. The institutional analysis revealed that 50% of the top 10 most productive institutions are based in the United States, indicating a higher number of published papers from US institutions. The University Campus of Biomedicine in Rome, Italy, is a well-established institution in this research field and is significant for further study and collaboration. The analysis of journals indicates that the top 10 journals published 23.2% of the articles, with *oncology-related* journals publishing the highest number of articles, followed by *pharmacology* journals.

The article with the highest number of citations examined the impact of lipid-coated mesoporous silica nanoparticle platforms on the co-delivery of GEM and paclitaxel in mice with human pancreatic cancer [34]. Tumour-associated GEM metabolites were analysed using high-performance liquid chromatography, which confirmed that co-delivery via silica nanoparticles resulted in a 13-fold increase in phosphorylated DNA-interacting GEM metabolites and a fourfold decrease in inactivating and deamidating metabolites. The use of nanoparticles as co-deliverers resulted in a significant reduction in the size of mouse tumours. In vivo imaging of mice showed considerable distribution of particles to the spleen, without systemic toxicity. However, stromal tissues of the group using the carriers were significantly damaged, with a significant decrease in collagen content in the xenografts. Another article with a high number of citations is “Nano-enabled pancreas cancer immunotherapy using immunogenic cell death and reversing immunosuppression” [23]. In this study, the authors developed nanocarriers to improve drug delivery efficiency and enable the host immune system to fight tumours, reducing tumour growth and metastasis (Fig. 5). This study demonstrates the potential of a nano-enabled approach for delivering oxaliplatin (OX) and indoximod (IND) to the pancreatic ductal adenocarcinoma (PDAC) site, resulting in a synergistic immunotherapy response. This is achieved by inducing immunogenic cell death (ICD) and reversing the immune suppressive effects of Indoleamine 2, 3-dioxygenase (IDO). In line with this, a study by Ghazal Mohseni et al. showed that targeting other cells of the immune can also be effective in suppressing pancreatic cancer. Importantly, the combination of radiotherapy

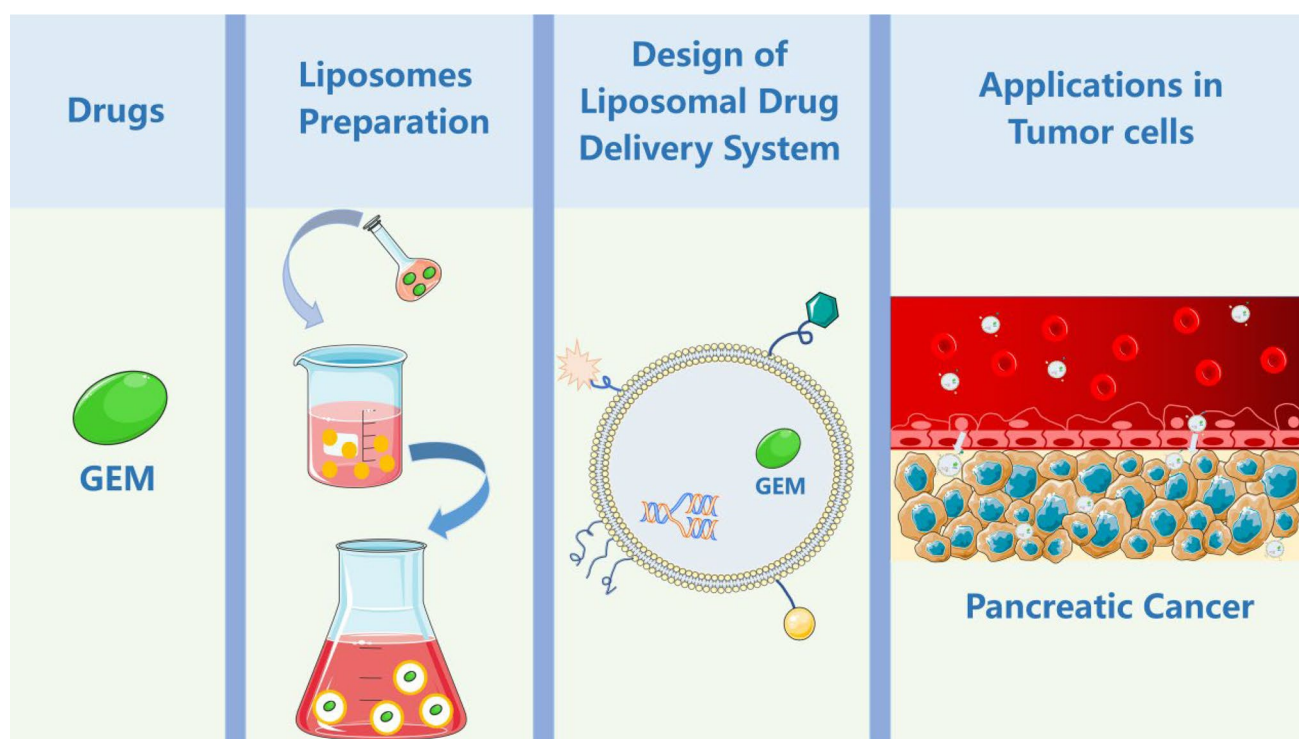


Fig. 5 Increased vascular permeability of gemcitabine after drug encapsulation

and chemotherapy (gemcitabine) was evaluated in the locally advanced pancreatic cancer (LAPC) phase I/II trial (NCT04484935). Early data showed improved local tumour control but no improvement in systemic metastases [35]. A phase III trial (NCT00844649) comparing Abraxane in combination with gemcitabine versus gemcitabine alone showed a median overall survival (OS) of 8.5 months in the combination arm versus 6.7 months in the single-agent arm ( $P < 0.001$ ), establishing it as the standard first-line regimen [36]. The NAPOLI-1 trial (NCT01494506), which evaluated the efficacy of onivudine in combination with 5-FU/folinic acid versus 5-FU/folinic acid alone in the treatment of gemcitabine-resistant pancreatic cancer, demonstrated that the median OS in the combination therapy group was 6.1 months versus 4.2 months in the monotherapy group ( $P = 0.012$ ), and the combination therapy was approved for second-line treatment [37]. The findings of the aforementioned study suggest that the utilisation of nanomaterials has the potential to enhance the efficacy of pancreatic cancer treatment.

Subsequent analyses of literature and keywords for the years 2002–2023 confirmed the strong link between "pancreatic cancer" and "nanotechnology". "Tumour-associated macrophages" and "iron oxide nanoparticles" are also current hot topics. Based on the keyword clustering analysis, keyword time zone map, and keyword burst analysis, the exploration of nanomaterials for pancreatic cancer therapy has remained at a relatively macroscopic and shallow stage from 2002 to 2019. However, in the mid-term (2019–2021), the research direction has expanded to the immune level, which has helped to clarify the interaction between nanomaterials and pancreatic cancer diagnosis and treatment to a certain extent. Research in this area has primarily focused on drug delivery and combination therapies over the past decade. It is expected that future research will concentrate on immune cells, such as tumour-associated macrophages, T cells, and other immune cells, as well as more comprehensive immunotherapy research. Bibliometric analyses provide a dynamic map of immunotherapy clinical practice, helping to identify priority directions, avoid risks and facilitate personalised treatment [38]. In addition, nanomaterials can be designed to target tumour cells, thereby reducing damage to healthy tissue and improving therapeutic efficacy [39, 40]. Nanomaterials can be used as carriers for drugs to improve stability and bioavailability and prolong the duration of drug action in the body [41–43]. Nanomaterials can be adjusted in structure and function to achieve multiple therapeutic mechanisms, such as combination therapy with chemotherapy, photothermal therapy and immunotherapy. Some nanomaterials possess intrinsic imaging properties that can be employed for tumour localisation and the monitoring of therapeutic effects, thereby enhancing the precision and safety of treatment [44].

Notably, nanomaterials provide new hope because they can enhance drug delivery, facilitate targeted drug delivery, and are non-toxic, for many pancreatic cancer patients. Polymeric nanoparticles, such as polylactic acid (PLA) and polylactic acid-hydroxyglycolic acid copolymers (PLGA), are degraded to lactic acid and hydroxyglycolic acid by hydrolysis or enzymatic processes, and subsequently metabolised to carbon dioxide and water [45]. Metal nanoparticles, such as iron oxide, are degraded in vivo by redox reactions. Light- or heat-sensitive materials, such as gold nanoparticles, are degraded under specific conditions, such as near-infrared irradiation. Serum proteins (including complement and immunoglobulin) adsorb to the surface of the nanoparticles, forming a 'protein corona' that promotes recognition and phagocytosis by macrophages [46]. Currently, liposomes and polymer nanoparticles are most promising for short-term application in pancreatic cancer therapy due to their solid clinical foundation and modifiability, while exosomes and multifunctional metal nanoparticles may become future breakthroughs. Ultimate success will need to rely on interdisciplinary collaboration to address tumour microenvironmental barriers and scale-up production challenges.

## 4.1 Limitations

The present study is subject to a number of limitations. In the context of nanomaterials, a potential impediment to clinical translation is the inability of conventional liposomal or polymeric nanoparticles (e.g. gemcitabine nanoparticles) to penetrate the stroma, resulting in inadequate drug concentration in the tumour. Nanoparticles loaded with immune checkpoint inhibitors may fail due to phagocytosis by immunosuppressive cells in the interstitium of the tumour tissue. Furthermore, the efficacy of nanoparticles modified with anti-epidermal growth factor receptor antibodies can be compromised in certain subtypes of pancreatic cancer with low epidermal growth factor receptor expression. When nanomaterials are used as drug carriers, the rate and location of drug release may be difficult to regulate, which may lead to erratic therapeutic effects [47]. Furthermore, the Web of Science Core Collection of Journals (WoSCC) was the exclusive database utilised in this study, and the temporal discrepancy is a salient concern, as it may result in an inadequate representation of emerging research domains, consequently causing delays in the analysis of evolving trends.

## 5 Conclusion

Nanomaterials have become an essential tool in the treatment of pancreatic cancer. However, a multidisciplinary approach integrating nanotechnology, immunotherapy, and precision medicine is essential for advancing pancreatic cancer treatment [48]. Advances in fields such as genetics and drug discovery are playing a pivotal role in the development of more effective anticancer drugs. Effective cancer treatments require targeted drug delivery to specific tumor sites, and nanostructures are particularly well-suited to achieve this goal. Over the past 16 years, research into the use of nanomaterials for pancreatic cancer treatment has grown significantly, especially in the period from 2018 onward. The United States leads in this research area, with a substantial number of publications, institutions, and contributors. Key areas of focus in this field include the tumor microenvironment and immunotherapy, which are central to the development of more effective therapeutic strategies. However, it is crucial for experts to also consider the biodegradation, immune clearance, and long-term toxicity of nanoparticles in vivo, as these factors play a critical role in the safety and efficacy of nanomaterial-based therapies.

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**Data availability** No datasets were generated or analysed during the current study.

## Declarations

**Ethics approval and consent to participate** Not applicable.

**Consent for publication** Not applicable.

**Competing interests** The authors declare no competing interests.

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