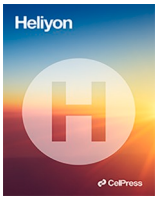
Heliyon 10 (2024) e32114

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Research article

Emerging trends and hotspots in cervical intraepithelial neoplasia research from 2013 to 2023: A bibliometric analysis

Liya Wang [a,b,*,1], Bingying Sun [a,b,1], Ji Xu [c,d,1], Dan Cao [a,b], Yi Chen [a,b], Ying Xu [a,b,**], Dan Wu [a,b,***]

[a] The Center for Cervical Disease, The International Peace Maternity and Child Health Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, 200030, China
[b] Shanghai Key Laboratory of Embryo Original Disease, Shanghai, 200030, China
[c] NMPA Key Laboratory for Research and Evaluation of Narcotic and Psychotropic Drugs, Jiangsu Province Key Laboratory of Anesthesiology, Jiangsu Province Key Laboratory of Anesthesia and Analgesia, Xuzhou Medical University, Xuzhou, China
[d] Key Laboratory of Anesthesiology (Shanghai Jiao Tong University), Ministry of Education, China

ARTICLE INFO

Keywords:
Photodynamic therapy
Human papillomavirus
Cervical intraepithelial neoplasia
Deep learning
Bibliometric analysis
Hotspots
CiteSpace

ABSTRACT

Background: Cervical intraepithelial neoplasia (CIN) encompasses a range of cervical lesions that are closely linked to cervical invasive carcinoma. Early detection and timely treatment of CIN are crucial for preventing the progression of the disease. However, no bibliometric analysis has been conducted in this area. This research aimed to employ bibliometric analysis to summarize the current research hotspots and estimate future research trends in the CIN field.

Methods: Publications related to CIN (2013–2023) were retrieved from the Science-Citation-Index-Expanded-of-Web-of-Science-Core-Collection. CiteSpace, VOSviewer, and the bibliometric-Online-Analysis-Platform-of-Literature-Metrology were employed to analyze the yearly research output, collaborating institutions or countries, leading researchers, principal journals, co-referenced sources, and emerging keywords.

Results: In total, 4677 articles on CIN that were published from 2013 to 2023 and met our criteria were extracted. Major publishing platforms were predominantly USA until 2017 when China emerged as the leading source of publications about CIN. The USA was the leading nation in international collaborations. The National-Cancer-Institute (NCI) was the institution with the most publications. Schiffman Mark produced the highest number of articles, with a total of 92. Ten major clusters were identified through co-cited keyword clustering, including prevalence, human papillomavirus, DNA methylation, p16, methylation, conization, HPV genotyping tests (VALGENT), deep learning, vaginal microbiome, and immunohistochemistry. Keyword burst analysis showed that photodynamic therapy and deep learning emerged as prominent research focal points with significant impact in resent three years.

* Corresponding author. The Center for Cervical Disease, The International Peace Maternity and Child Health Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, 200030, China.
** Corresponding author. The Center for Cervical Disease, The International Peace Maternity and Child Health Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, 200030, China.
*** Corresponding author.The Center for Cervical Disease, The International Peace Maternity and Child Health Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai 200030, China.
E-mail addresses: annya1985010@sina.com (L. Wang), 13621951903@163.com (Y. Xu), danwu202312@163.com (D. Wu).
[1] These authors have contributed equally to this work.

https://doi.org/10.1016/j.heliyon.2024.e32114
Received 19 January 2024; Received in revised form 24 May 2024; Accepted 28 May 2024
Available online 29 May 2024

Conclusion: Global publications on CIN research showed a relatively stable trend over the past eleven years. Current research hotspots are deep learning and photodynamic therapy. This research offered organized data and insightful guidance for future studies, which may help better prevent, screen, and treat CIN.

1. Introduction

Cervical-intraepithelial-neoplasia (CIN) comprises a spectrum of precancerous lesions associated with the development of cervical invasive carcinoma in women. CIN can be divided into 3 grades, namely CIN1, CIN2, and CIN3. Low-grade-intraepithelial-lesions (LSIL) are equivalent to CIN1, and high-grade-intraepithelial-lesions (HSIL) include CIN3 and most of CIN2. Most LSIL resolve naturally, but HSIL may progress into cervical cancer. It ranks as the 4th most frequently diagnosed cancer among women globally, with more than 604,000 new cases worldwide and more than 341,000 deaths [1].

The persistent infection of human-papillomavirus (HPV 16/18/31/33/35/39/45/51/52/56/58/59/68) contributes to the risks of developing cervical cancer and precancerous lesions [2]. Other risk factors include immunosuppression (altered vaginal microbiota, immunosuppressive medications, and HIV infection), experiencing a young age at first pregnancy, having multiple sexual partners, and smoking [3]. HPV genotyping testing combined with cervical exfoliation cytology can be carried out to evaluate the risks of CIN and cervical cancer [2]. Moreover, methylation detection [4], HPV integration detection, HPV DNA load detection, immunocytochemical staining, and artificial intelligence (AI) technology [5] have certain application prospects in screening, but still large-sized prospective studies are needed. Currently, HPV vaccination can achieve primary prevention of CIN [6].

Colposcopy or direct vision cervical histological biopsy is considered the benchmark for diagnosis. Approximately 60 % of LSIL resolve naturally and can be followed up. Cervical conization is a traditional treatment strategy for HSIL, including cold-knife-conization (CKC) and loop-electrosurgical-excision-procedure (LEEP) [7]. Cervical conization may reduce the likelihood of HSIL advancing to invasive cancer. Additionally, ablation therapy, including cryotherapy, laser therapy, and electrocoagulation therapy, can also be applied to some HSIL. However, there is still a long-term risk of persistence, recurrence, or even progression to invasive cancer after resection. Studies have shown that the risk of persistence and recurrence after the treatment of HSIL is also significantly higher than that after the treatment of LSIL [8]. Short-term complications, such as infection [9], bleeding [10], and injury, as well as long-term complications, such as cervical stenosis [11], can occur after treatment, affect pregnancy outcomes [12], and lead to endometriosis [13].

Recently, photodynamic therapy has been gradually popularized as a highly targeted, non-invasive therapy [14]. Although photodynamic therapy offers benefits in maintaining the integrity of normal tissue structures, preserving fertilities, resolving HPV infections, and decreasing recurrence rates compared with conventional therapy [15,16], follow-up management after treating HSIL is pivotal.

The high prevalence of CIN worldwide has put tremendous pressure on women and imposed an economic burden, increasing the need for comprehensive research in this field. Yet, there is presently a deficiency in objective analysis based on big data analytics for the research overview and hotspots of CIN over the past 11 years. Bibliometric analysis refers to a thorough and timely review of publications within a specified timeframe, examining factors such as publication count, geographic distribution, authorship, keywords, references, and other relevant parameters [17–21]. Bibliometric analysis can provide researchers with valuable insights into prevailing research focal points and anticipated future trends [22,23]. The application of bibliometric analysis in the medical field is particularly common, enabling researchers to analyze the research hotspots and development trends of a certain field on macroscopic and microscopic levels [24]. Despite our knowledge, no bibliometric analysis focusing on CIN has been published. Thus, this study aims to bridge this gap by examining publication trends in CIN from 2013 to 2023, with the goal of contributing to the advancement of research in this field.

2. Methods

2.1. Data reservoirs and inquiries methodologies

A detailed literature search was carried out using the Science-Citation-Index-Expanded (SCI-E) of the-Web-of-Science-Core-Collection (WoSCC) database (2013–2023) on March 1, 2024. To mitigate the impact of frequent database updates, we conducted our search and data retrieval within a single day. Relevant publications were obtained from WoSCC by searching TS= ((“cervical intraepithelial neoplasia” or “cervical intraepithelial neoplasm” or “cervical intraepithelial lesion” or “cervical squamous intraepithelial lesion” or “cervical precancerous lesion” or “cervical intraepithelial neoplastic” or “cervical adenocarcinoma in situ” or “cervical glandular intraepithelial neoplasia” or “cervical carcinoma in situ” or “cervical cancer in situ” or “endocervical glandular dysplasia” or “cervical epithelial dysplasia” or “cervical dysplasia”)) AND Language = English AND Document type = Article. To confirm the accuracy of bibliometric analysis, two researchers (Liya Wang and Bingying Sun) examined all articles collected through search strategies based on their publication years, abstracts, and titles. The following exclusion criteria were applied: (i) unrelated to CIN; (ii) non-article document types, such as reviews, meta-analysis, proceeding papers, editorial materials, book chapters, news items, corrections, meeting abstracts, and retracted publications; and (iii) duplicate publications. In total, 4677 articles were identified. The detailed screening process is depicted in Fig. 1.

2.2. Data acquisition

We downloaded all data, comprising full records and cited references of the retrieved articles, from the WoSCC database in TXT format. Subsequently, the data were imported into the bibliometric online analysis platform (https://bibliometric.com), CiteSpace V6.1.R6 (Drexel University, PA, USA), and VOSviewer 1.6.19 (Leiden University, The Netherlands).

2.3. Bibliometric analysis

We performed an extensive bibliometric analysis covering various publication characteristics, such as authors, regions/countries, institutions, co-cited references, journals, and keywords exhibiting the most robust citation bursts. We extracted some bibliometric indicators, including the publication numbers and citation times from the text data downloaded from the WoSCC database. CiteSpace, established by Chen, stands as the most commonly utilized bibliometric analysis software at present [25]. CiteSpace serves as a valuable visual analysis tool utilized to uncover emerging trends and advancements within a research field [26]. We used CiteSpace (V6.1.R6) for analyzing the distribution of journals, authors, institutions, co-cited reference analysis and keyword burst identification to pinpoint current focal points and estimate future research trajectories in CIN. Based on the data exported from CiteSpace, we used Microsoft Office Excel 2019 to create an annual curve of the publication count in the CIN field over the past 11 years and analyze publication trends using an exponential growth function. The VOSviewer software can be used to construct visual bibliometric maps [27] and build networks between countries/regions based on collaborative data. We utilized the bibliometric-online-analysis-platform (https://bibliometric.com) to examine the annual publication count and publication trends of the top 10 regions/countries, as well as to assess the publication count from the top 10 most productive journals. The R package bibliometrix was utilized to generate a keyword cloud consisting of the top 100 most frequently occurring keywords. In addition, in specific cases, H-index is used to evaluate publications of regions/countries, journals, as well as individual academic achievements [28].

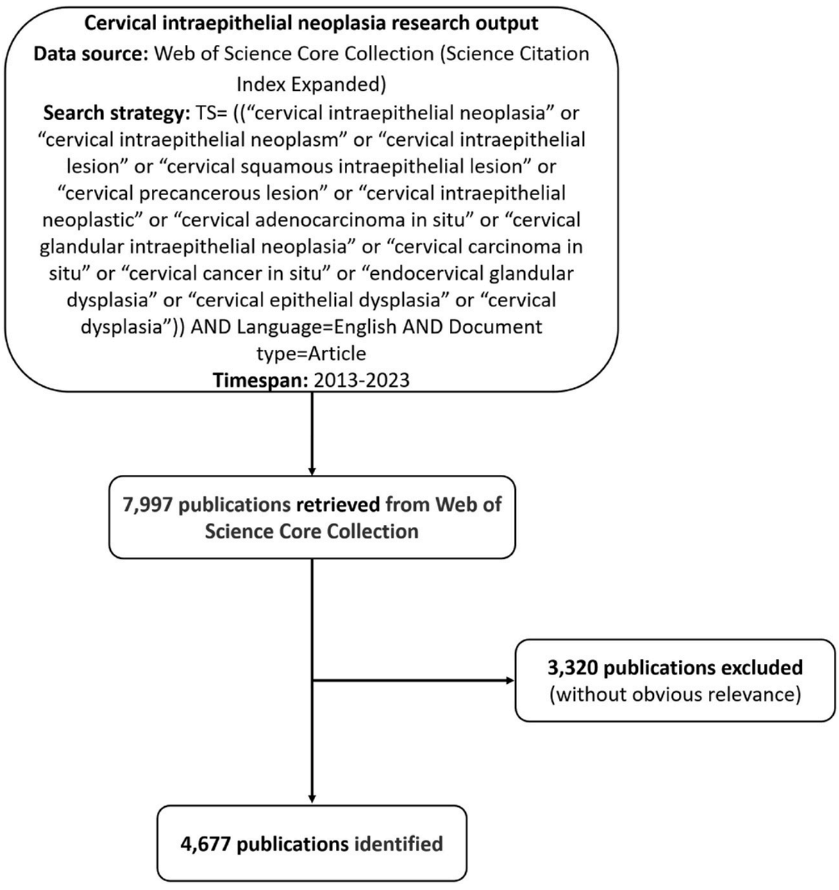


Fig. 1. Flowchart showing the inclusion and exclusion of publications in the CIN research.

3. Results

3.1. Analysis of publication quantity and trends

In this research, 7997 articles published between 2013 and 2023 satisfied the criteria for inclusion. In total, 3320 articles were excluded due to lack of relevance (Fig. 1). Finally, 4677 articles were extracted from WoSCC that were published between 2013 and 2023. The total number of annual publications is shown at the top of each bar (Fig. 2A). The annual publication count serves as an indicator of the pace of research advancement in this field and reflects the level of attention dedicated to CIN research. From 2013 to 2023, the publication count regarding this topic remained at more than 360. The trendline of the total publication count conforms to a quadratic function curve, exhibiting R^2 of 0.935.

The analysis of article publication across various regions/countries was conducted using the bibliometric-online-analysis platform to identify the leading contributors during the last 11 years. In the histogram presented in Fig. 2B, the top 10 regions/countries accounted for the majority of publications during this period. Notably, USA and China have consistently held prominent positions in CIN research. USA maintained its dominance in the field until 2016, after which China surpassed it in publication output from 2017 onward.

3.2. Assessment of partnering regions/countries and institutions

We investigated the cooperation between scholars, institutes, and countries and identified the main collaborative partners using the VOSviewer software. In total, 4677 papers were published in 135 regions/countries from 2013 to 2023. Fig. 3A shows the top 33 cooperating countries in the field of CIN research. We found that USA was the most actively engaged country in international collaboration, and China had the highest publication count. In addition, the USA and China demonstrated the most intimate collaboration.

We utilized CiteSpace software to import TXT files and elucidate the patterns of inter-institutional cooperation. After deduplication by CiteSpace, 4677 publications were included in subsequent analyses. Fig. 3B shows the ten institutions with the highest productivity. The National Cancer Institute (NCI) had the highest publication count (141) and most frequently collaborated with other institutions. Among them, 2 were from USA, including the NCI (141) and Albert Einstein College of Medicine (91). These are prestigious higher education or medical centers in USA with strong scientific research capabilities. Another four institutions were from China, namely the Chinese Academy of Medical Sciences (72), Peking University (62), Zhejiang University (61) and Peking Union Medical College (57). The remaining four institutions with the highest publication numbers were from Sweden, the United Kingdom, the Netherlands and

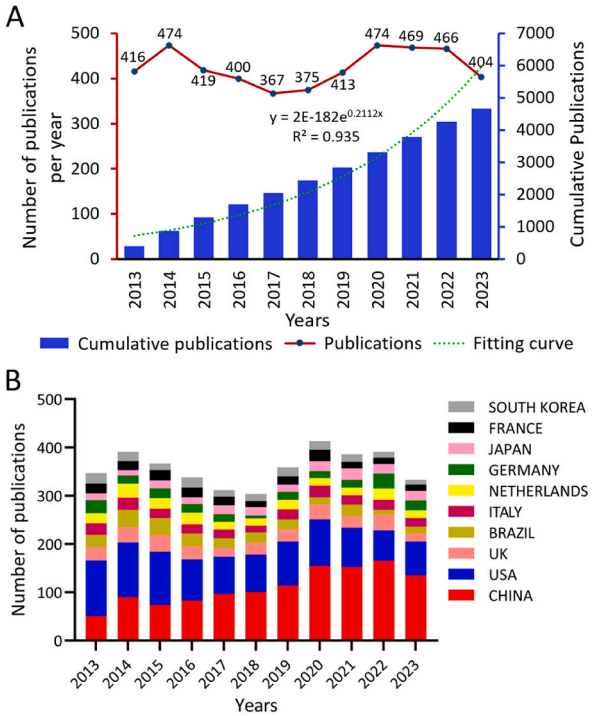


Fig. 2. Analysis of the Volume and Trends of CIN Publications from 2013 to 2023: (A) Examination of Publication Quantity and Trends regarding CIN from 2013 to 2023, results extracted from Web of Science. (B) Assessment of Publication Quantity and Growth Trends among the Top 10 Regions/Countries in the CIN Field from 2013 to 2023.

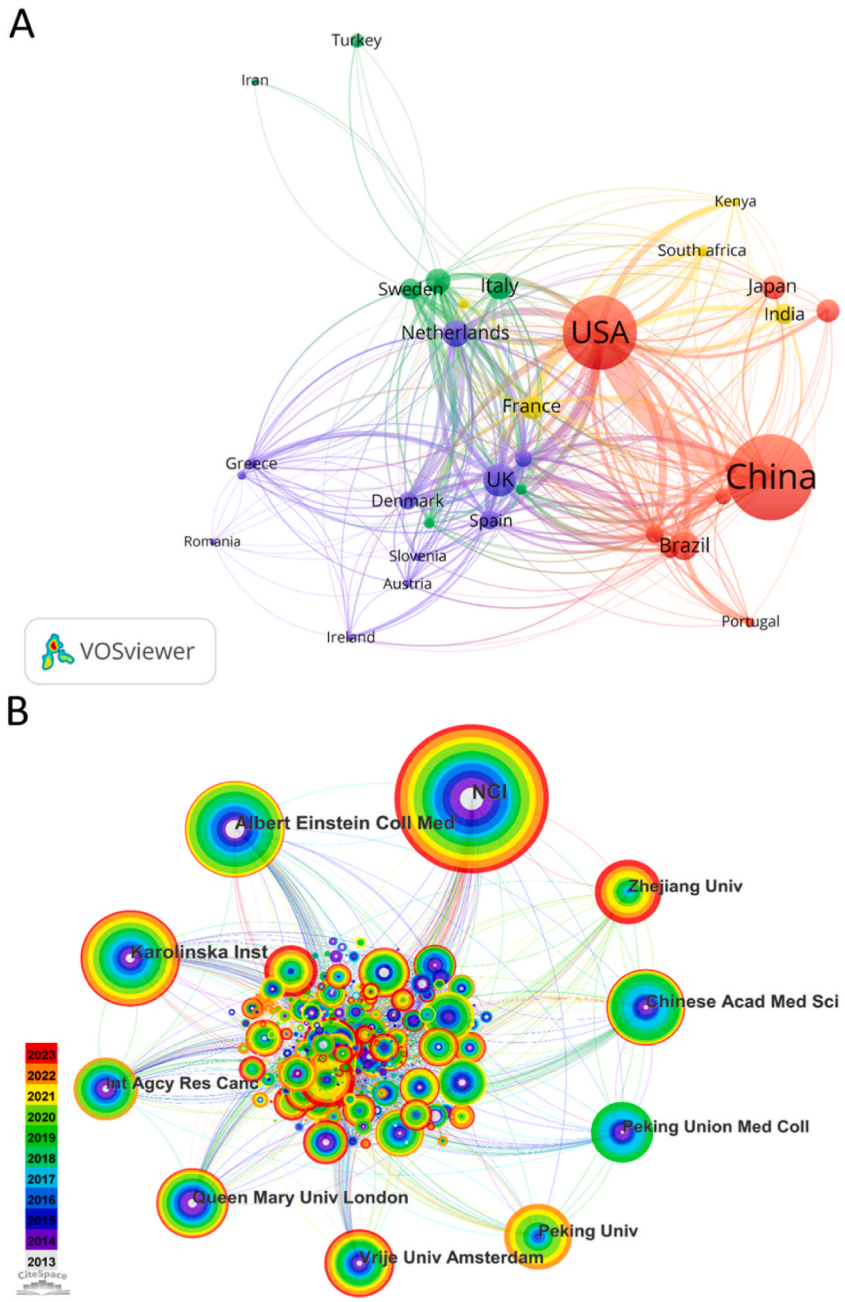


Fig. 3. Collaborative network map of regions/countries and institutions. **(A)** The collaborative efforts of the top 33 countries. **(B)** The Leading 10 Most Prolific Institutions. The circles depict various regions/countries and institutions, with circle size correlating to the number of publications. Link thickness indicates the level of collaboration intensity. Color-coded clusters represent regions/countries and institutions with robust collaborative ties.

France, which also contributed significantly to the CIN field.

3.3. Evaluation of co-authorship networks and core-author distributions

During the last 11 years, 21,154 researchers have involved in CIN research. Among these authors, 382 researchers published over 10 articles, making major contributions to publication output. Fig. 4 displays the top 11 most prolific authors. Schiffman Mark, from the NIH National Cancer Institute, contributed the highest number of articles (92), followed by Castle Philip E from Duke University (91) and Wentzensen Nicolas from the NCI (63). Interestingly, two authors together occupied the tenth place, namely Heideman

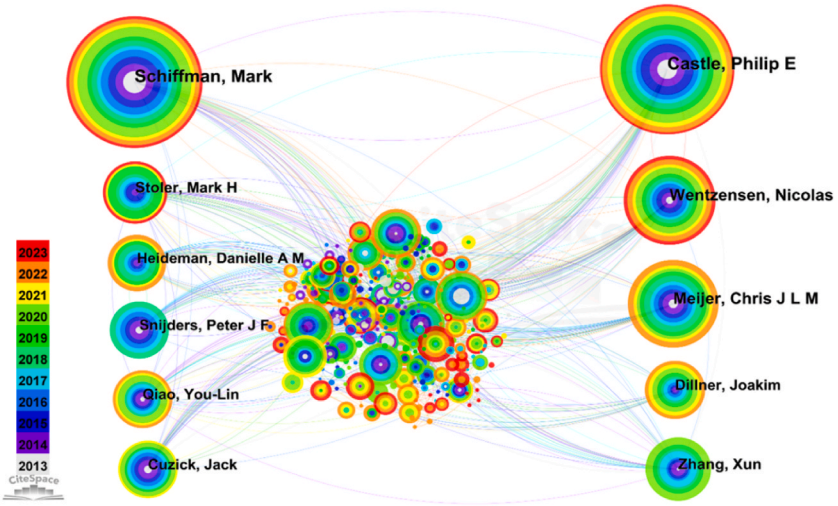


Fig. 4. CiteSpace network illustrating authorship connections in CIN research. The figure displays the top 11 authors with the highest publication count. Circles denote authors, while links among circles depict collaborations among authors.

Danielle and Snijders Peter from Vrije University Amsterdam (Netherlands) (40). The collaborative network diagram of the top 10 prolific authors demonstrated strong cooperative relationships.

3.4. Assessment of journals

We utilized the bibliometric-online-analysis-platform to assess journal impact. Our analysis covered 4677 original articles published across 680 academic journals. The top 10 journals with the highest citation counts are listed in Table 1. Articles published in the *International Journal of Cancer* were cited most frequently in the past 11 years (4357 times), followed by *PLOS One* (4,127), *Gynecologic Oncology* (2,209), *Journal of Lower Genital Tract Disease* (1,820), *BMC Cancer* (1,109), *Journal of Medical Virology* (860), *Oncology Letters* (698), *Archives of Gynecology and Obstetrics* (617), *International Journal of Gynecology & Obstetrics* (*516*), *and Diagnostic Cytopathology* (464). Five journals were from USA, and the others were from Switzerland, the United Kingdom, Greece, Germany, and Netherlands. The *International Journal of Cancer*, based in Switzerland, achieved the highest average citation count per paper at 25.04. There were only 3 Q1 journals based on JCR partitions, among which the *Journal of Medical Virology* had the highest impact factor (12.7). This finding indicates that CIN research still needs improvements.

3.5. Evaluation of article citations

We also identified the ten most cited papers from 4677 articles. Table 2 highlights the most cited article published in *NEJM* in 2015, with 927 citations [29]. The study proposed that the 9-valent-HPV-vaccine (9vHPV) could prevent infections and high-grade vaginal, vulvar, or cervical diseases associated with HPV-31/33/45/52/58 in vulnerable populations and triggers antibody response to HPV-6/11/16/18. The article with the second-highest number of citations was published in *PLOS One* in 2013, accumulating 525 citations [30]. This paper indicated that in addition to screening for and treating CIN, maintaining a healthy BMI through a focus on

Table 1
Ranking of the top 10 most cited journals in the CIN research from 2013 to 2023, arranged by total citations.

Rank	Journal Title	Frequency	Total citations	Average citation per paper	H-index	Impact factor (2022)	JCR	Country
1	*INTERNATIONAL JOURNAL OF CANCER*	174	4357	25.04	38	6.4	Q1	Switzerland
2	*PLOS ONE*	167	4127	24.71	32	3.7	Q2	USA
3	*GYNECOLOGIC ONCOLOGY*	96	2209	23.01	28	4.7	Q1	USA
4	*JOURNAL OF LOWER GENITAL TRACT DISEASE*	185	1820	9.84	20	3.7	Q2	USA
5	*BMC CANCER*	80	1109	13.86	22	3.8	Q2	UK
6	*JOURNAL OF MEDICAL VIROLOGY*	79	860	10.89	18	12.7	Q1	USA
7	*ONCOLOGY LETTERS*	70	698	9.97	15	2.9	Q3	GREECE
8	*ARCHIVES OF GYNECOLOGY AND OBSTETRICS*	88	617	7.01	12	2.9	Q3	Germany
9	*INTERNATIONAL JOURNAL OF GYNECOLOGY & OBSTETRICS*	73	516	7.07	13	2.6	Q3	Netherlands
10	*DIAGNOSTIC CYTOPATHOLOGY*	70	464	6.63	11	3.8	Q2	USA

Table 2
The highest-cited 10 articles among the 4677 retrieved publications on CIN research from 2013 to 2023, arranged by citation frequency.

Rank	Title	First Author	Source	Year	Cited Frequency	DOI
1	A 9-Valent HPV Vaccine against Infection and Intraepithelial Neoplasia in Women	Joura, EA	*NEW ENGLAND JOURNAL OF MEDICINE*	2015	927	10.1056/NEJMoa1405044
2	Mild Obesity, Physical Activity, Calorie Intake, and the Risks of Cervical Intraepithelial Neoplasia and Cervical Cancer	Lee, JK	*PLOS ONE*	2013	525	10.1371/journal.pone.0066555
3	Safety, efficacy, and immunogenicity of VGX-3100, a therapeutic synthetic DNA vaccine targeting human papillomavirus 16 and 18 E6 and E7 proteins for cervical intraepithelial neoplasia 2/3: a randomised, double-blind, placebo-controlled phase 2b trial	Trimble, CL	*LANCET*	2015	436	10.1016/S0140-6736(15)00239-1
4	Genome-wide profiling of HPV integration in cervical cancer identifies clustered genomic hot spots and a potential microhomology-mediated integration mechanism	Hu, Z	*NATURE GENETICS*	2015	329	10.1038/ng.3178
5	Gankyrin Is Frequently Overexpressed in Cervical High Grade Disease and Is Associated with Cervical Carcinogenesis and Metastasis	Liu, Y	*PLOS ONE*	2014	279	10.1371/journal.pone.0095043
6	Cervical intraepithelial neoplasia disease progression is associated with increased vaginal microbiome diversity	Mitra, A	*SCIENTIFIC REPORTS*	2015	273	10.1038/srep16865
7	Final efficacy, immunogenicity, and safety analyses of a nine-valent human papillomavirus vaccine in women aged 16–26 years: a randomised, double-blind trial	Huh, WK	*LANCET*	2017	267	10.1016/S0140-6736(17)31821-4
8	The effects of the national HPV vaccination programme in England, UK, on cervical cancer and grade 3 cervical intraepithelial neoplasia incidence: a register-based observational study	Falcaro, M	*LANCET*	2021	255	10.1016/S0140-6736(21)02178-4
9	Cervical Microbiome and Cytokine Profile at Various Stages of Cervical Cancer: A Pilot Study	Audirac-Chalifour, A	*PLOS ONE*	2016	244	10.1371/journal.pone.0153274
10	An Observational Study of Deep Learning and Automated Evaluation of Cervical Images for Cancer Screening	Hu, LM	*JNCI-JOURNAL OF THE NATIONAL CANCER INSTITUTE*	2019	207	10.1093/jnci/djy225

physical activities can prevent cervical cancer. The third most cited article demonstrated that VGX-3100 can cause histopathological regression of CIN2/3 related to HPV-16/18, serving as a non-surgical therapeutic option for CIN2/3 [31]. Among the ten most cited articles, 3 were published in *Lancet*, 3 were published in *PLOS One*, and the others were published in *NEJM*, *Nature Genetics*, *Scientific Reports*, and *JNCI*.

Furthermore, we computed the total citation number for all papers published by each country and compiled a list of the top ten countries (Fig. 5). During this 11-year period, USA ranked first with 21,451 citations. China and the UK ranked 2nd and 3rd with 14,553 and 8384 citations, respectively. The tenth place was occupied by Japan, with 1739 citations.

We determined the average citations per article per country by dividing each country's total citations by its total publications. Afterwards, we identified the top 3 countries with the highest average citations per article, including the United Kingdom (UK) (28.13), the Netherlands (23.97), and France (23.05) (Table 3). Articles from these countries, except for those from Japan (9.06), had an average of over 10 citations.

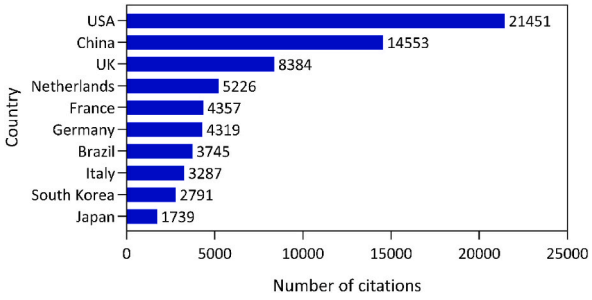
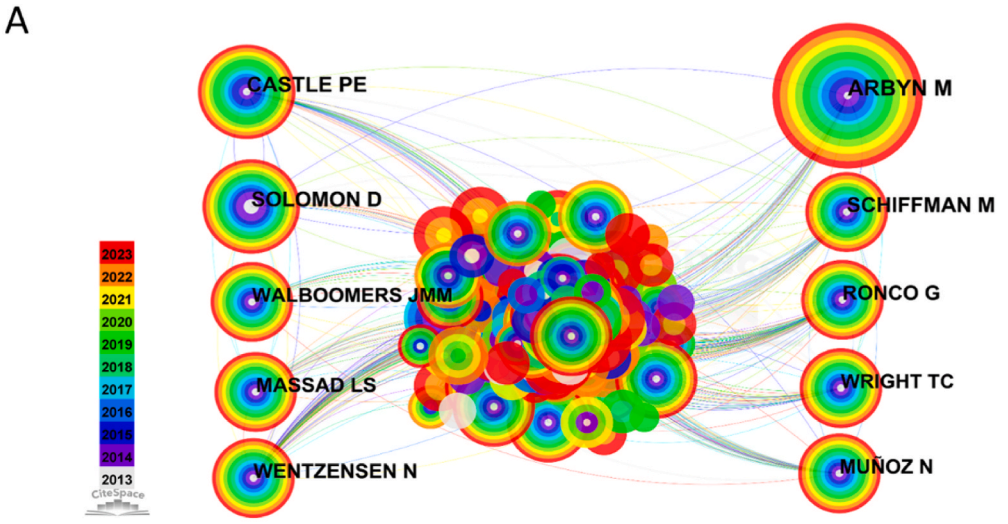


Fig. 5. Bar graph depicting the total publication count from 4677 papers published from countries between 2013 and 2023. This figure displays the top ten countries with the highest total citation number. Bar represent countries, with its length directly proportional to the total citation number.

Table 3
The leading 10 nations with the most significant aggregate citation count in CIN research from 2013 to 2023, ordered by the average citation number.

Rank	Country	Number of Publications	Total number of citations	H-index	Average number of citations
1	UK	298	8384	45	28.13
2	Netherlands	218	5226	40	23.97
3	France	189	4357	35	23.05
4	USA	977	21451	66	21.96
5	Germany	201	4319	34	21.49
6	South Korea	180	2791	24	15.51
7	Brazil	245	3745	25	15.29
8	Italy	222	3287	28	14.81
9	China	1219	14553	43	11.94
10	Japan	192	1739	21	9.06



B

Top 20 References with the Strongest Citation Bursts

References	Strength	Begin	End	2013-2023
de Sanjose S, 2010, LANCET ONCOL, V11, P1048, DOI 10.1016/S1470-2045(10)70230-8	48.15	2013	2015	
Ferlay J, 2010, INT J CANCER, V127, P2893, DOI 10.1002/ijc.25516	32.77	2013	2015	
Ronco G, 2010, LANCET ONCOL, V11, P249, DOI 10.1016/S1470-2045(09)70360-2	30.75	2013	2015	
Saslow D, 2012, AM J CLIN PATHOL, V137, P516, DOI 10.1309/AJCPTGD94EVRSJCG	23.63	2013	2017	
Rijkaart DC, 2012, LANCET ONCOL, V13, P78, DOI 10.1016/S1470-2045(11)70296-0	21.94	2013	2017	
Arbyn M, 2012, VACCINE, V30, PF88, DOI 10.1016/j.vaccine.2012.06.095	24.5	2014	2017	
Massad LS, 2013, J LOW GENIT TRACT DI, V17, PS1, DOI 10.1097/LGT.0b013e318287d329	35.32	2015	2018	
Massad LS, 2013, OBSTET GYNECOL, V121, P829, DOI 10.1097/AOG.0b013e3182883a34	30.7	2015	2018	
Ronco G, 2014, LANCET, V383, P524, DOI 10.1016/S0140-6736(13)62218-7	52.79	2016	2019	
Torre LA, 2015, CA-CANCER J CLIN, V65, P87, DOI 10.3322/caac.21262	22.93	2016	2019	
Wright TC, 2015, GYNECOL ONCOL, V136, P189, DOI 10.1016/j.ygyno.2014.11.076	26.59	2016	2020	
Huh WK, 2015, GYNECOL ONCOL, V136, P178, DOI 10.1016/j.ygyno.2014.12.022	23.26	2016	2020	
Ferlay J, 2015, INT J CANCER, V136, PE359, DOI 10.1002/ijc.29210	33.94	2017	2020	
Chen WQ, 2016, CA-CANCER J CLIN, V66, P115, DOI 10.3322/caac.21338	24.42	2017	2022	
Tainio K, 2018, BMJ-BRIT MED J, V360, P0, DOI 10.1136/bmj.k499	22.02	2020	2023	
Koliopoulos G, 2017, COCHRANE DB SYST REV, V0, P0, DOI 10.1002/14651858.CD008587.pub2	20.28	2020	2023	
Cohen PA, 2019, LANCET, V393, P169, DOI 10.1016/S0140-6736(18)32470-X	20.25	2020	2023	
Perkins RB, 2020, J LOW GENIT TRACT DI, V24, P102, DOI 10.1097/LGT.0000000000000525	83.07	2021	2023	
Fontham ETH, 2020, CA-CANCER J CLIN, V70, P321, DOI 10.3322/caac.21628	29.33	2021	2023	
Arbyn M, 2020, LANCET GLOB HEALTH, V8, PE191, DOI 10.1016/S2214-109X(19)30482-6	47.56	2021	2023	

Fig. 6. Network Analysis of Citations in CIN Research between 2013 and 2023: (A) Visualization of co-citation patterns using CiteSpace, encompassing 60,666 references related to CIN research. Each node denotes an author, and links between nodes signify that the authors' publications were cited as references in the same article. Node size correlates with citation frequency, with denser red nodes indicating top-cited papers recently, and denser purple nodes indicating top-cited references in previous years. The figure highlights the top 10 most cited authors in CIN research. (B) Identification of the top 20 references with the most notable citation bursts in CIN research publication from 2013 to 2023. References highlighted in red experienced a rapid surge in citation frequency during this period, while blue denotes comparatively less cited periods.

3.6. Assessment of article co-citations and clustering networks

CiteSpace was used to analyze 4677 papers retrieved from WoSCC and their 60666 references (excluding self-citations) to assess the association between 2 articles by visualizing their co-citation patterns. Fig. 6A presents the map of co-citation authors for CIN research in CiteSpace. Specifically, the figure shows the authors with the highest co-citation frequency, listed in the top 10.

Table 4 shows the top ten references, ranked by the co-citation frequency. The most cited reference was published by *JAMA* in 2002 [32]. This article updated the Bethesda System terminology concerning the reporting of cervical cytology findings. The 2001 Bethesda System terminology represents significant progress in our biological comprehension of cervical neoplasia and advancements in cervical screening technology. The second most cited article, published in the *Journal of Pathology* in 1999, emphasized the importance of HPV testing alongside, or as a potential substitute for, cervical cytology in routine cervical screening [33]. The highly cited papers listed in Table 4 are widely acknowledged as seminal contributions to CIN research.

Furthermore, we conducted an analysis of strong citation bursts among references in this field to identify research hotspots. Fig. 6B lists the top 20 references exhibiting the most pronounced citation bursts between 2013 and 2023. 'Begin' indicates the year when the references were initially cited, while 'End' signifies the year of its last citation. Six of the articles continued to receive significant citations. A worldwide analysis published by Marc Arbyn et al. was the most recent reference burst occurred in 2021 and extended until the conclusion of 2023 [34]. The researchers described the incidence pattern and mortality rates of cervical cancer alongside HPV prevalence data from 185 countries in 2018, enabling a thorough initial evaluation of the global burden of cervical cancer. Chen WD et al. published a multicenter study in *CA-Cancer J Clin* in 2017 with the longest citation duration [35]. The authors estimated the incidence of new cases and mortality rates from cancer from 72 regions of China in 2015 and found that while developed countries witnessed declining incidence trends, China experienced a significant rise in cervical cancer incidence due to deficiencies in Pap screening tests. The highest strength was 83.07 in a consensus on risk-based management guidelines, published in the *Journal of Lower Genital Tract Disease* by Perkins RB et al. in 2020, which burst in 2021 [36]. In this study, the American-Society-of-Colposcopy-and-Cervical-Pathology (ASCCP) recommended incorporating HPV testing into risk stratification for managing abnormal cervical cancer screening results and pre-cancerous lesions.

Table 4
The top 10 references with the highest citation count among the 4677 papers in CIN research between 2013 and 2023, organized by citation frequency.

Rank	Title	First Author	Source	Year	Cited Frequency	DOI
1	The 2001 Bethesda System - Terminology for reporting results of cervical cytology	Solomon, D	*JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION*	2002	557	10.1001/jama.287.16.2114
2	Human papillomavirus is a necessary cause of invasive cervical cancer worldwide	Walboomers, JMM	*JOURNAL OF PATHOLOGY*	1999	528	10.1002/(SICI)1096–9896 (199909)189:1 < 12:AID-PATH431 > 3.0.CO; 2-F
3	Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study	de Sanjose, S	*LANCET ONCOLOGY*	2010	393	10.1016/S1470-2045(10)70230-8
4	Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four European randomised controlled trials	Ronco, G	*LANCET*	2014	359	10.1016/s0140-6736(13)62218-7
5	Epidemiologic classification of human papillomavirus types associated with cervical cancer	Muñoz, N	*NEW ENGLAND JOURNAL OF MEDICINE*	2003	351	10.1056/NEJMoa021641
6	2012 Updated Consensus Guidelines for the Management of Abnormal Cervical Cancer Screening Tests and Cancer Precursors	Massad, LS	*JOURNAL OF LOWER GENITAL TRACT DISEASE*	2013	284	10.1097/LGT.0b013e318287d329
7	Human papillomavirus and cervical cancer	Schiffman, M	*LANCET*	2007	281	10.1016/S0140-6736(07)61416-0
8	American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology Screening Guidelines for the Prevention and Early Detection of Cervical Cancer	Saslow, D	*AMERICAN JOURNAL OF CLINICAL PATHOLOGY*	2012	237	10.1309/AJCPTGD94EVRSJCG
9	2019 ASCCP Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors	Perkins, RB	*JOURNAL OF LOWER GENITAL TRACT DISEASE*	2020	232	10.1097/LGT.0000000000000525
10	Evidence Regarding Human Papillomavirus Testing in Secondary Prevention of Cervical Cancer	Arbyn, M	*VACCINE*	2012	231	10.1016/j.vaccine.2012.06.095

The CiteSpace graph depicting co-citations was clustered based on keywords derived from the references of 4677 papers (Fig. 7A). The investigation into co-citation clusters indicated the most significant terms for CIN research based on hierarchical cluster labels were # 0 prevalence, # 1 human papillomavirus, # 2 DNA methylation, # 3 p16, # 4 methylation, # 5 conization, # 6 VALGENT, # 7 deep learning, # 8 vaginal microbiome, and # 9 immunohistochemistry. A negative correlation was observed between the number of cluster labels and the number of articles included in each cluster. Alternatively, the cluster labeled as #0 encompassed the highest publication count among the 60666 references. A summary of clusters is provided in Table 5.

3.7. Evaluation of research trends and burst detections

A timeline perspective is displayed in Fig. 7B to clearly describe the shift of hotspots over the past 11 years. We found that the focus of research on CIN shifted from prevalence, human papillomavirus, methylation, and immunohistochemistry to DNA methylation, p16, conization, deep learning, and vaginal microbiome.

A word cloud was produced for the top 100 most frequently occurring keywords in CIN researches (Fig. 8A). The font size denotes the frequency of using keywords. After filtering out keywords deemed irrelevant for our research trend analysis, cancer, risk, human-papillomavirus, intraepithelial neoplasia, prevalence, cytology, lesions, infection, management, and neoplasia were the top ten highest frequency keywords.

Keyword burst detection facilitates the swift identification of emerging research hotspots within a specific field. Fig. 8B displays the top 15 references with the most robust keyword bursts in CIN research between 2013 and 2023. “PCR” was the most robust burst keyword (strength 10.66) from 2013 to 2023, followed by “photodynamic therapy” (strength 9.58), “deep learning” (strength 8.55), and “metaanalysis” (strength 7.82). “machine learning”, “treatment failure”, “vaginal microbiota”, “early detection of cancer”, “deep

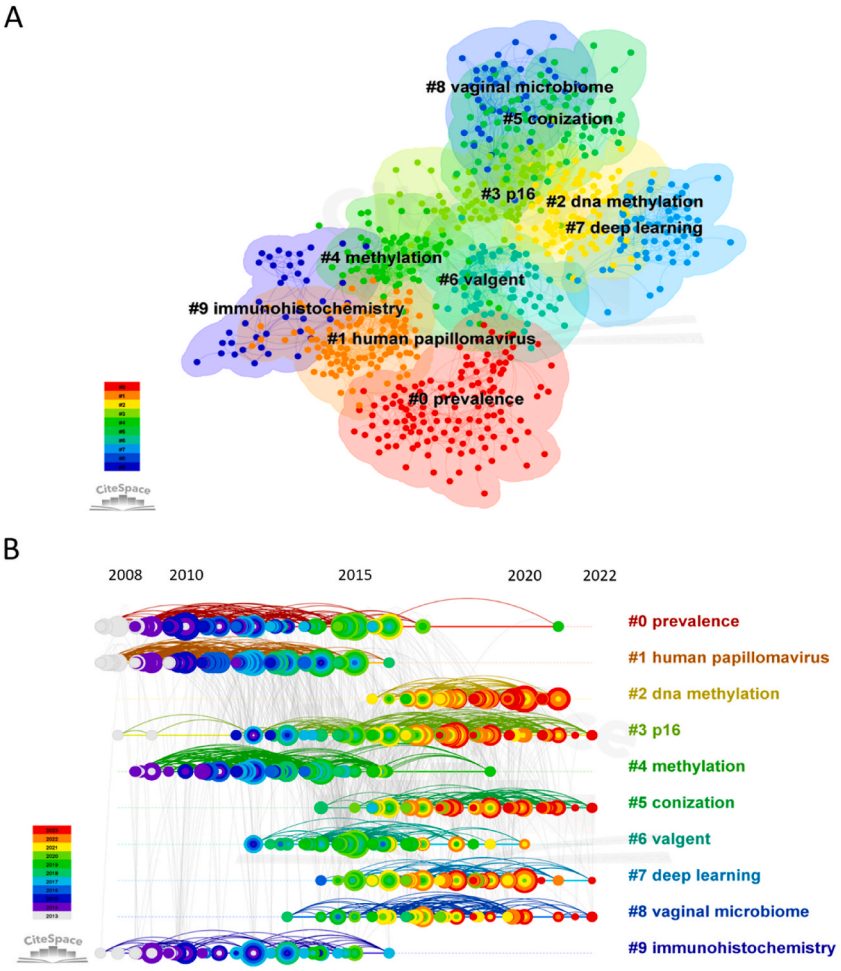


Fig. 7. Analysis of Clustered Network of CIN Publications from 2013 to 2023: (A) Visual representation of the clustering network of co-citations using CiteSpace. The figure highlights the top 10 largest citation clusters. (B) Timeline view of co-cited references pertaining to CIN. Each horizontal line denotes a cluster, with smaller label numbers indicating larger clusters. Node size corresponds to co-citation frequency, and links represent co-citation relationship. The colors of lines and nodes denote the different years cited. Cluster labels are displayed on the right side.

Table 5
Overview of 10 clusters of cited works in CIN research.

Cluster ID	Term	Size	Silhouette[a]
0	prevalence	130	0.824
1	human papillomavirus	123	0.774
2	dna methylation	93	0.754
3	p16	86	0.829
4	methylation	77	0.895
5	conization	71	0.82
6	valgent	69	0.821
7	deep learning	61	0.908
8	vaginal microbiome	44	0.862
9	immunohistochemistry	41	0.893

[a] The silhouette value greater than 0.5 suggests that the clustering outcomes are reliable.

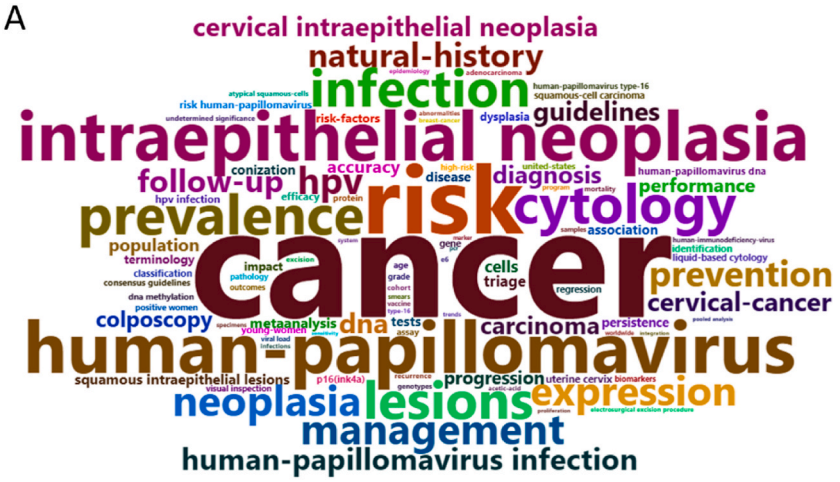


Fig. 8. Examination of Keyword Patterns and Publication Bursts in CIN Studies from 2013 to 2023: (A) Visualization of the top 100 most frequently keywords in CIN research via word cloud analysis. (B) Identification of the top 15 keywords with the most notable citation bursts, organized by starting year. Keywords highlighted in red experienced a sudden surge in their usage frequency during that period, while blue indicates comparatively less popular times.

learning", "photodynamic therapy", "cancer screening test", and "excision" were found as the emerging research focal points.

4. Discussion

This research represents the inaugural bibliometric and visual exploration of CIN. Currently, the research hotspots in the field of CIN mainly focus on deep learning, machine learning, and photodynamic therapy, representing new technologies in diagnosing and treating CIN. Through our bibliometric analysis, scholars interested in CIN can gain a comprehensive overview of the field and swiftly identify the most recent research trends.

4.1. Overall trends in the CIN field

Global publication on CIN during the past 11 years exhibited a relatively stable trend. The USA demonstrated the highest level of international collaboration, whereas China had the highest publication count. Our results showed that USA maintains a leading role, totalling 21,451 citations in 977 articles. USA also has two of the top 10 most productive research organizations, with the NCI being the most productive institution worldwide. In addition, four of the top eleven authors in this field were American, including Schiffman Mark, Castle Philip E, Wentzensen Nicolas, and Stoler Mark H. The publication count in China has surpassed USA since 2017, and four of the top ten institutions ranked by publication output were from China. These findings highlight the significant contributions and potential scientific innovations from Chinese efforts in CIN research. Articles from the United Kingdom (UK) had the highest average number of citations, followed by the Netherlands and France, highlighting the excellence of publications from European countries. Although China ranked 1st regarding the total publication count, the average number of citations per article was only 11.94. Moreover, there were only two Chinese authors among the top 10 authors, including Xun Zhang who occupied the fifth position and You-Lin Qiao who occupied the ninth position. These findings indicate that China still has a long way to go in the field of CIN research.

As the most productive institution worldwide, NCI conducted a large-scale study and illuminated that the risk of precancerous lesion progression differed substantially by 13 different high-risk HPV subtypes, with HPV16 inducing uniquely elevated risk. For all infections caused by HPV subtypes, annual rates of progression dramatically decreased over the first three years. By year five, the annual rates of progression were less than 0.1 % for most HPV subtypes (except HPV18) and remained low in the following years [37]. Over the past 11 years, Schiffman Mark from the NCI contributed the highest number of articles focusing on cervical smear screening and HPV infection-related screening. His article published in the *International Journal of Cancer* was a cohort study on partial HPV typing and cytological classification for cervical cancer screening [38]. His latest study measured the effect of HPV16 E7 nucleotide variants on E7 protein expression and transformation in cancer-free subjects [39]. The second most productive researcher, Castle Philip E, recommended that screening intervals of every 5 years or more might be feasible and safe after one or more negative HPV and cytology co-testing against cervical cancer [40]. He also compared differences in the risk of HSIL in women with or without human immunodeficiency virus (HIV) in combination with co-testing [40].

4.2. Research hotspots and frontier exploration in the CIN field

Co-cited cluster analysis can provide valuable insights into the cutting-edge developments in scientific works. We found that "prevalence", "human papillomavirus", "methylation", and "immunohistochemistry" were the early main focuses in CIN research. As early as 1894, research has demonstrated that HPV-16 is strongly associated with CIN, which has considerable clinical significance in the differential diagnosis, prognosis, and management of early cervical cancer [41]. In the early days, scholars paid more attention to the risk of CIN associated with HPV infection [42–44]. The main research themes have been "DNA methylation", "deep learning", "p16", "vaginal microbiome", and "conization" in recent years. Methylation has always been a research hotspot in the past 11 years. DNA methylation is a common occurrence in the progression from HPV infection to cervical precancerous lesions [45]. Previous studies have shown that cytosine methylation in CpG dinucleotides, also known as CpG sites, is an important cellular mechanism regulating gene expression. Increased methylation of multiple CpG sites in various regions of the HPV-16 genome correlated with the presence of CIN3 [46]. FAM19A4/miR124-2 DNA methylation tests combined with HPV genotyping can be utilized to support a wait-and-see follow-up approach for female patients with CIN2/3 and avoid overtreatment [47]. With the development of artificial intelligence (AI), disease models based on histological images and machine deep learning are increasingly used to diagnose various tumors. Researchers began to develop a computerized reading system to evaluate cervical cytological specimens for diagnosis [48,49]. Since 2015, more studies founded that vaginal microbiome diversity was closely related with the progression of CIN [50–52].

Keyword bursts represent keywords extensively cited in publications, aiding in the recognition of trends and focal points within a specific research domain. Our results showed that the strongest keyword has been polymerase chain reaction (PCR) in the CIN research field over the past 11 years. It is a key technology for early diagnosis of HPV infection and has been widely valued by scholars. As early as 1989, PCR was used to identify HPV in CIN [53]. A study compared the clinical performance of 4 low-cost HR-HPV assays on the basis of real-time PCR. The study applied the Cobas test for detecting CIN2+ lesions and accelerating the control of cervical cancer in low-resource settings [54].

The second keyword, "photodynamic therapy", began in 2020 with a strength of 9.58, persisting until the conclusion of 2023. Despite large loop, cold knife conization, cryotherapy, and laser surgery are typical treatments of high-grade CIN, several severe side effects cannot be ignored. Thus, more researchers pay attention to a non-invasive treatment intervention that reduces the advancement of the disease. Photodynamic therapy (PDT) is a non-invasive technique based on the interaction of light, photosensitizer, and oxygen. It selectively destroys abnormal tissues through photodynamic reactions. Most studies reported the use of PDT for treating CIN1/2

[55–57]. Compared with other invasive treatments, photodynamic therapy can preserve cervical function [16] and has advantages in eliminating HPV infection and mitigating the recurrence rate [15]. Prior studies have shown the effect of PDT on local immune responses, eradicating pathogenic microorganisms of CIN1/2 [58,59]. In addition, PDT presented the best results two years after treatment of CIN1/2, preventing the progression of CIN [56]. The keywords "deep learning", "machine learning", "vaginal microbiota", "cancer screening test", and "treatment failure" are also current research hotspots. Recent studies have focused on HR-HPV genotype distribution and screening in CIN [60–62] and predictors of treatment failure (residual or recurrent CIN) [63,64]. With the rapid advancement of computer simulation technology, deep learning has been increasingly applied to the diagnosis of CIN. The application of this technology in cervical cytology can replace some repetitive human labor [65]. Deep learning technology can help colposcopists identify cervical lesions and reduce the rate of missed diagnosis [66].

4.3. Limitations

Our study possesses certain limitations. Firstly, owing to constraints within the CiteSpace software, only data extracted from the SCI-E of the WoSCC database were subject to visual analysis, and other databases, such as PubMed and Embase, were not searched, which might have increased the risk of bias. Second, owing to the limited search strategies, literature types, and language limitations, this research only concentrated on papers published in English. English remains the predominant language for academic journals. Consequently, there is a possibility of overlooking articles that do not adhere to these criteria. Third, due to the manual exclusion of articles unrelated to CIN, there may be some bias in accuracy. Therefore, in order to ensure the accuracy of exclusion and reduce bias, we have adopted a strategy of two researchers excluding the retrieved articles separately. If there are any questions about certain articles, a third researcher will be asked to make the final judgment. Finally, bibliometric analysis may introduce a possible time-effect bias, as older articles tend to accumulate more citations. Additionally, factors like self-citation can influence citation rates. To mitigate such errors, we conducted a comprehensive review of the included papers.

5. Conclusion

In summary, this represents the inaugural bibliometric and visual analysis of previous studies on CIN. Using bibliometric atlas, we analyzed the studies on CIN from 2013 to 2023. In the past 11 years, the publications of CIN have been in a relatively steady trend. USA and China have made the most significant contribution to the CIN research field. USA dominated international collaboration, while China has published more articles since 2017. Recent studies have focused on photodynamic therapy and deep learning. Photodynamic therapy may be an effective technology for treating CIN. Deep learning suggests that computer-related technology may be an important method for diagnosing CIN in the future. Researchers and CIN related clinicians can utilize our findings to enhance their comprehension of the research hotspots and development trends in CIN field over the past 11 years. Additionally, this study can help CIN related clinicians to understand the advanced technologies for screening and treating CIN, and then apply them to clinical practice.

Funding statement

This work was supported by the Shanghai Jiao Tong University Medicine Engineering Fund (No. YG2022QN111) and the Application of minimally noninvasive screening program in standardized diagnosis and treatment of gynecological tumors during pregnancy (No. SHDC12023119).

Data availability statement

Data will be provided upon request.

Ethics statement

Informed consent was not necessary for this study as all data utilized were obtained from the WoSCC database and did not involve any animal or human subjects.

CRediT authorship contribution statement

Liya Wang: Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Data curation, Conceptualization. **Bingying Sun:** Writing – original draft, Validation, Resources, Methodology, Data curation. **Ji Xu:** Writing – original draft, Visualization, Resources, Methodology, Data curation. **Dan Cao:** Writing – review & editing, Resources, Funding acquisition. **Yi Chen:** Writing – review & editing, Visualization, Resources, Methodology. **Ying Xu:** Writing – review & editing, Supervision, Project administration, Investigation, Conceptualization. **Dan Wu:** Writing – review & editing, Supervision, Project administration, Investigation, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to

influence the work reported in this paper.

Acknowledgements

We would like to express our gratitude to EditSprings (https://www.editsprings.cn) for the expert linguistic services provided.

References

[1] H. Sung, J. Ferlay, R.L. Siegel, M. Laversanne, I. Soerjomataram, A. Jemal, et al., Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, CA Cancer J Clin 71 (3) (2021) 209–249, https://doi.org/10.3322/caac.21660.
[2] R.B. Perkins, N. Wentzensen, R.S. Guido, M. Schiffman, Cervical cancer screening: a review, JAMA 330 (6) (2023) 547–558, https://doi.org/10.1001/jama.2023.13174.
[3] S.J. Bowden, T. Doulgeraki, E. Bouras, G. Markozannes, A. Athanasiou, H. Grout-Smith, et al., Risk factors for human papillomavirus infection, cervical intraepithelial neoplasia and cervical cancer: an umbrella review and follow-up Mendelian randomisation studies, BMC Med. 21 (1) (2023) 274, https://doi.org/10.1186/s12916-023-02965-w.
[4] A. Dovnik, M. Poljak, The role of methylation of Host and/or human papillomavirus (HPV) DNA in management of cervical intraepithelial neoplasia Grade 2 (CIN2) lesions, Int. J. Mol. Sci. 24 (7) (2023), https://doi.org/10.3390/ijms24076479.
[5] J. Jiang, W.L. Chao, S. Culp, S.G. Krishna, Artificial intelligence in the diagnosis and treatment of Pancreatic Cystic lesions and adenocarcinoma, Cancers 15 (9) (2023), https://doi.org/10.3390/cancers15092410.
[6] S.E. Oliver, E.R. Unger, R. Lewis, D. McDaniel, J.W. Gargano, M. Steinau, et al., Prevalence of human papillomavirus among females after vaccine Introduction-national health and nutrition examination survey, United States, 2003-2014, J. Infect. Dis. 216 (5) (2017) 594–603, https://doi.org/10.1093/infdis/jix244.
[7] J. Grubman, S.S. Meinhardt, A. Nambiar, J.S. Lea, Specimen fragmentation and loop electrosurgical excision procedure and cold knife cone biopsy outcomes, J. Low. Genit. Tract Dis. 24 (1) (2020) 27–33, https://doi.org/10.1097/LGT.0000000000000509.
[8] H.A. Katki, M. Schiffman, P.E. Castle, B. Fetterman, N.E. Poitras, T. Lorey, et al., Five-year risk of recurrence after treatment of CIN 2, CIN 3, or AIS: performance of HPV and Pap cotesting in posttreatment management, J. Low. Genit. Tract Dis. 17 (5 Suppl 1) (2013) S78–S84, https://doi.org/10.1097/LGT.0b013e31828543c5.
[9] C. Kietpeerakool, B. Chumworathayi, J. Thinkhamrop, B. Ussahgij, P. Lumbiganon, Antibiotics for infection prevention after excision of the cervical transformation zone, Cochrane Database Syst. Rev. 1 (1) (2017) CD009957, https://doi.org/10.1002/14651858.CD009957.pub2.
[10] L. Giannella, G. D'Ippolito, Cervical ripening balloon: an off-label but effective use to manage massive hemorrhage during outpatient cervical conization, Int. J. Gynaecol. Obstet. 147 (1) (2019) 126–127, https://doi.org/10.1002/ijgo.12910.
[11] Y. Tanaka, Y. Ueda, M. Kakuda, S. Kubota, S. Matsuzaki, T. Iwamiya, et al., Predictors for recurrent/persistent high-grade intraepithelial lesions and cervical stenosis after therapeutic conization: a retrospective analysis of 522 cases, Int. J. Clin. Oncol. 22 (5) (2017) 921–926, https://doi.org/10.1007/s10147-017-1124-z.
[12] M. Kyrgiou, A. Mitra, M. Arbyn, S.M. Stasinou, P. Martin-Hirsch, P. Bennett, et al., Fertility and early pregnancy outcomes after treatment for cervical intraepithelial neoplasia: systematic review and meta-analysis, BMJ 349 (2014) g6192, https://doi.org/10.1136/bmj.g6192.
[13] A. Audebert, [Iatrogenic endometriosis during reproductive age: main issues?], Gynecol. Obstet. Fertil. 41 (5) (2013) 322–327, https://doi.org/10.1016/j.gyobfe.2012.06.001.
[14] S. Kwiatkowski, B. Knap, D. Przystupski, J. Saczko, E. Kedzierska, K. Knap-Czop, et al., Photodynamic therapy - mechanisms, photosensitizers and combinations, Biomed. Pharmacother. 106 (2018) 1098–1107, https://doi.org/10.1016/j.biopha.2018.07.049.
[15] A. Wu, Q. Li, J. Ling, L. Gu, Z. Hong, W. Di, et al., Effectiveness of photodynamic therapy in women of reproductive age with cervical high-grade squamous intraepithelial lesions (HSIL/CIN2), Photodiagnosis Photodyn. Ther. 36 (2021) 102517, https://doi.org/10.1016/j.pdpdt.2021.102517.
[16] T. Muroya, Y. Suehiro, K. Umayahara, T. Akiya, H. Iwabuchi, H. Sakunaga, et al., [Photodynamic therapy (PDT) for early cervical cancer], Gan To Kagaku Ryoho 23 (1) (1996) 47–56.
[17] X. Lin, Y. Zhou, L. Ye, B. Wang, Y. Jiao, W. Yu, et al., A bibliometric and visualized analysis of hepatic ischemia-reperfusion injury (HIRI) from 2002 to 2021, Heliyon 9 (11) (2023) e22644, https://doi.org/10.1016/j.heliyon.2023.e22644.
[18] Y. Liao, L. Wang, F. Liu, Y. Zhou, X. Lin, Z. Zhao, et al., Emerging trends and hotspots in metabolic dysfunction-associated fatty liver disease (MAFLD) research from 2012 to 2021: a bibliometric analysis, Front. Endocrinol. 14 (2023) 1078149, https://doi.org/10.3389/fendo.2023.1078149.
[19] J. Li, L. Wang, S. Yin, S. Yu, Y. Zhou, X. Lin, et al., Emerging trends and hotspots of the itch research: a bibliometric and visualized analysis, CNS Neurosci. Ther. (2023), https://doi.org/10.1111/cns.14514.
[20] P. Kokol, M. Kokol, S. Zagoranski, Machine learning on small size samples: a synthetic knowledge synthesis, Sci. Prog. 105 (1) (2022) 368504211029777, https://doi.org/10.1177/00368504211029777.
[21] D. Suran, H. Blazun Vosner, J. Zavrsnik, P. Kokol, A. Sinkovic, V. Kanic, et al., Lipoprotein(a) in cardiovascular diseases: insight from a bibliometric study, Front. Public Health 10 (2022) 923797, https://doi.org/10.3389/fpubh.2022.923797.
[22] Y. Zhou, X. Lin, S. Yin, L. Zhu, Y. Yang, Y. Li, et al., Emerging trends and hot spots in hepatic glycolipid metabolism research from 2002 to 2021: a bibliometric analysis, Front. Nutr. 9 (2022) 933211, https://doi.org/10.3389/fnut.2022.933211.
[23] Y. Li, Y. Zhou, L. Wang, X. Lin, M. Mao, S. Yin, et al., Emerging trends and hotspots in the links between the gut microbiota and MAFLD from 2002 to 2021: a bibliometric analysis, Front. Endocrinol. 13 (2022) 990953, https://doi.org/10.3389/fendo.2022.990953.
[24] P. Kokol, H. Blazun Vosner, J. Zavrsnik, Application of bibliometrics in medicine: a historical bibliometrics analysis, Health Inf. Libr. J. 38 (2) (2021) 125–138, https://doi.org/10.1111/hir.12295.
[25] C. Chen, CiteSpace II: detecting and visualizing emerging trends and transient patterns in scientific literature, J. Am. Soc. Inf. Sci. Technol. 57 (3) (2006) 359–377, https://doi.org/10.1002/asi.20317.
[26] C. Chen, Searching for intellectual turning points: progressive knowledge domain visualization, Proc. Natl. Acad. Sci. U.S.A. 101 (Suppl 1) (2004) 5303–5310, https://doi.org/10.1073/pnas.0307513100. Suppl 1.
[27] N.J. van Eck, L. Waltman, Software survey: VOSviewer, a computer program for bibliometric mapping, Scientometrics 84 (2) (2010) 523–538, https://doi.org/10.1007/s11192-009-0146-3.
[28] J.E. Hirsch, An index to quantify an individual's scientific research output, Proc. Natl. Acad. Sci. U. S. A 102 (46) (2005) 16569–16572, https://doi.org/10.1073/pnas.0507655102.
[29] E.A. Joura, A.R. Giuliano, O.E. Iversen, C. Bouchard, C. Mao, J. Mehlsen, et al., A 9-valent HPV vaccine against infection and intraepithelial neoplasia in women, N. Engl. J. Med. 372 (8) (2015) 711–723, https://doi.org/10.1056/NEJMoa1405044.
[30] J.K. Lee, K.A. So, C.J. Piyathilake, M.K. Kim, Mild obesity, physical activity, calorie intake, and the risks of cervical intraepithelial neoplasia and cervical cancer, PLoS One 8 (6) (2013) e66555, https://doi.org/10.1371/journal.pone.0066555.
[31] C.L. Trimble, M.P. Morrow, K.A. Kraynyak, X. Shen, M. Dallas, J. Yan, et al., Safety, efficacy, and immunogenicity of VGX-3100, a therapeutic synthetic DNA vaccine targeting human papillomavirus 16 and 18 E6 and E7 proteins for cervical intraepithelial neoplasia 2/3: a randomised, double-blind, placebo-controlled phase 2b trial, Lancet 386 (10008) (2015) 2078–2088, https://doi.org/10.1016/S0140-6736(15)00239-1.
[32] D. Solomon, D. Davey, R. Kurman, A. Moriarty, D. O'Connor, M. Prey, et al., The 2001 Bethesda System: terminology for reporting results of cervical cytology, JAMA 287 (16) (2002) 2114–2119, https://doi.org/10.1001/jama.287.16.2114.

[33] J.M. Walboomers, M.V. Jacobs, M.M. Manos, F.X. Bosch, J.A. Kummer, K.V. Shah, et al., Human papillomavirus is a necessary cause of invasive cervical cancer worldwide, J. Pathol. 189 (1) (1999) 12–19, https://doi.org/10.1002/(SICI)1096-9896(199909)189:1<12::AID-PATH431>3.0.CO;2-F.
[34] M. Arbyn, E. Weiderpass, L. Bruni, S. de Sanjose, M. Saraiya, J. Ferlay, et al., Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis, Lancet Global Health 8 (2) (2020) e191–e203, https://doi.org/10.1016/S2214-109X(19)30482-6.
[35] W. Chen, R. Zheng, P.D. Baade, S. Zhang, H. Zeng, F. Bray, et al., Cancer statistics in China, 2015, CA Cancer J Clin 66 (2) (2016) 115–132, https://doi.org/10.3322/caac.21338.
[36] R.B. Perkins, R.S. Guido, P.E. Castle, D. Chelmow, M.H. Einstein, F. Garcia, et al., 2019 ASCCP risk-based management consensus guidelines for abnormal cervical cancer screening tests and cancer precursors, J Low Genit Tract Di 24 (2) (2020) 102–131, https://doi.org/10.1097/Lgt.0000000000000525.
[37] M. Demarco, N. Hyun, O. Carter-Pokras, T.R. Raine-Bennett, L. Cheung, X. Chen, et al., A study of type-specific HPV natural history and implications for contemporary cervical cancer screening programs, EClinicalMedicine 22 (2020) 100293, https://doi.org/10.1016/j.eclinm.2020.100293.
[38] M. Schiffman, N. Hyun, T.R. Raine-Bennett, H. Katki, B. Fetterman, J.C. Gage, et al., A cohort study of cervical screening using partial HPV typing and cytology triage, Int. J. Cancer 139 (11) (2016) 2606–2615, https://doi.org/10.1002/ijc.30375.
[39] H. Lou, J.F. Boland, H. Li, R. Burk, M. Yeager, S.K. Anderson, et al., HPV16 E7 nucleotide variants found in cancer-free subjects affect E7 protein expression and transformation, Cancers 14 (19) (2022), https://doi.org/10.3390/cancers14194895.
[40] P.E. Castle, W.K. Kinney, X. Xue, L.C. Cheung, J.C. Gage, F.H. Zhao, et al., Effect of several negative rounds of human papillomavirus and cytology Co-testing on safety against cervical cancer: an observational cohort study, Ann. Intern. Med. 168 (1) (2018) 20–29, https://doi.org/10.7326/M17-1609.
[41] D. Wagner, H. Ikenberg, N. Boehm, L. Gissmann, Identification of human papillomavirus in cervical swabs by deoxyribonucleic acid in situ hybridization, Obstet. Gynecol. 64 (6) (1984) 767–772.
[42] A.C. Rodriguez, M. Schiffman, R. Herrero, S. Wacholder, A. Hildesheim, P.E. Castle, et al., Rapid clearance of human papillomavirus and implications for clinical focus on persistent infections, J. Natl. Cancer Inst. 100 (7) (2008) 513–517, https://doi.org/10.1093/jnci/djn044.
[43] H. Trottier, S. Mahmud, M.C. Costa, J.P. Sobrinho, E. Duarte-Franco, T.E. Rohan, et al., Human papillomavirus infections with multiple types and risk of cervical neoplasia, Cancer Epidemiol. Biomarkers Prev. 15 (7) (2006) 1274–1280, https://doi.org/10.1158/1055-9965.EPI-06-0129.
[44] F.H. Zhao, A.K. Lewkowitz, S.Y. Hu, F. Chen, L.Y. Li, Q.M. Zhang, et al., Prevalence of human papillomavirus and cervical intraepithelial neoplasia in China: a pooled analysis of 17 population-based studies, Int. J. Cancer 131 (12) (2012) 2929–2938, https://doi.org/10.1002/ijc.27571.
[45] M.A. Clarke, A. Gradissimo, M. Schiffman, J. Lam, C.C. Sollecito, B. Fetterman, et al., Human papillomavirus DNA methylation as a biomarker for cervical precancer: consistency across 12 genotypes and potential impact on management of HPV-positive women, Clin. Cancer Res. 24 (9) (2018) 2194–2202, https://doi.org/10.1158/1078-0432.CCR-17-3251.
[46] L. Mirabello, C. Sun, A. Ghosh, A.C. Rodriguez, M. Schiffman, N. Wentzensen, et al., Methylation of human papillomavirus type 16 genome and risk of cervical precancer in a Costa Rican population, J. Natl. Cancer Inst. 104 (7) (2012) 556–565, https://doi.org/10.1093/jnci/djs135.
[47] W.W. Kremer, S. Dick, D.A.M. Heideman, R.D.M. Steenbergen, M.C.G. Bleeker, H.R. Verhoeve, et al., Clinical regression of high-grade cervical intraepithelial neoplasia is associated with absence of fam19a4/miR124-2 DNA methylation (CONCERVE study), J. Clin. Oncol. 40 (26) (2022) 3037–3046, https://doi.org/10.1200/JCO.21.02433.
[48] M.S. Landau, L. Pantanowitz, Artificial intelligence in cytopathology: a review of the literature and overview of commercial landscape, J Am Soc Cytopathol 8 (4) (2019) 230–241, https://doi.org/10.1016/j.jasc.2019.03.003.
[49] J. Park, H. Yang, H.J. Roh, W. Jung, G.J. Jang, Encoder-weighted W-net for unsupervised segmentation of cervix region in colposcopy images, Cancers 14 (14) (2022), https://doi.org/10.3390/cancers14143400.
[50] Y. Chen, X. Qiu, W. Wang, D. Li, A. Wu, Z. Hong, et al., Human papillomavirus infection and cervical intraepithelial neoplasia progression are associated with increased vaginal microbiome diversity in a Chinese cohort, BMC Infect. Dis. 20 (1) (2020) 629, https://doi.org/10.1186/s12879-020-05324-9.
[51] G. Curty, P.S. de Carvalho, M.A. Soares, The role of the cervicovaginal microbiome on the genesis and as a biomarker of premalignant cervical intraepithelial neoplasia and invasive cervical cancer, Int. J. Mol. Sci. 21 (1) (2019), https://doi.org/10.3390/ijms21010222.
[52] A. Mitra, D.A. MacIntyre, Y.S. Lee, A. Smith, J.R. Marchesi, B. Lehne, et al., Cervical intraepithelial neoplasia disease progression is associated with increased vaginal microbiome diversity, Sci. Rep. 5 (2015) 16865, https://doi.org/10.1038/srep16865.
[53] M.T. Cornelissen, J.G. van den Tweel, A.P. Struyk, M.F. Jebbink, M. Briet, J. van der Noordaa, et al., Localization of human papillomavirus type 16 DNA using the polymerase chain reaction in the cervix uteri of women with cervical intraepithelial neoplasia, J. Gen. Virol. 70 (Pt 10) (1989) 2555–2562, https://doi.org/10.1099/0022-1317-70-10-2555.
[54] P. Xue, L.L. Gao, J. Yin, L.L. Han, J. Zhao, L. Li, et al., A direct comparison of four high-risk human papillomavirus tests versus the cobas test: detecting CIN2+ in low-resource settings, J. Med. Virol. 91 (7) (2019) 1342–1350, https://doi.org/10.1002/jmv.25451.
[55] P. Hillemanns, F. Garcia, K.U. Petry, V. Dvorak, O. Sadovsky, O.E. Iversen, et al., A randomized study of hexaminolevulinate photodynamic therapy in patients with cervical intraepithelial neoplasia 1/2, Am. J. Obstet. Gynecol. 212 (4) (2015) 465 e1–e7, https://doi.org/10.1016/j.ajog.2014.10.1107.
[56] N.M. Inada, H.H. Buzza, M.F.M. Leite, C. Kurachi, J.R. Trujillo, C.A. de Castro, et al., Long term effectiveness of photodynamic therapy for CIN treatment, Pharmaceuticals 12 (3) (2019), https://doi.org/10.3390/ph12030107.
[57] E. Maldonado Alvarado, M.O. Osorio Peralta, A. Moreno Vazquez, L.A. Martinez Guzman, M.E. Melo Petrone, Mar ZI. Enriquez, et al., Effectiveness of photodynamic therapy in elimination of HPV-16 and HPV-18 associated with CIN I in Mexican women, Photochem. Photobiol. 93 (5) (2017) 1269–1275, https://doi.org/10.1111/php.12769.
[58] M.T. Lopez-Cardenas, A. Jimenez, A. Espinosa-Montesinos, E. Maldonado-Alvarado, M.O. Osorio-Peralta, A. Martinez-Escobar, et al., Elimination of human papillomavirus and cervical pathological microbiota with photodynamic therapy in women from Mexico City with cervical intraepithelial neoplasia I, Photochem. Photobiol. 99 (6) (2023) 1468–1475, https://doi.org/10.1111/php.13791.
[59] A. Wu, J. Niu, Z. Hong, L. Gu, Y. Huang, L. Qiu, The effects of 5-aminolevulinic acid photodynamic therapy on the local immune response of women with cervical intraepithelial neoplasia grade 2, Front. Immunol. 14 (2023) 1211114, https://doi.org/10.3389/fimmu.2023.1211114.
[60] A. Bukowski, C. Hoyo, M.G. Hudgens, W.R. Brewster, F. Valea, R.C. Bentley, et al., Extended human papillomavirus genotyping to predict progression to high-grade cervical precancer: a prospective cohort study in the southeastern United States, Cancer Epidemiol. Biomarkers Prev. 31 (8) (2022) 1564–1571, https://doi.org/10.1158/1055-9965.EPI-22-0054.
[61] M.H. Stoler, E. Baker, S. Boyle, S. Aslam, R. Ridder, W.K. Huh, et al., Approaches to triage optimization in HPV primary screening: extended genotyping and p16/Ki-67 dual-stained cytology-Retrospective insights from ATHENA, Int. J. Cancer 146 (9) (2020) 2599–2607, https://doi.org/10.1002/ijc.32669.
[62] J. Zhang, Y. Zhao, Y. Dai, L. Dang, L. Ma, C. Yang, et al., Effectiveness of high-risk human papillomavirus testing for cervical cancer screening in China: a multicenter, open-label, randomized clinical trial, JAMA Oncol. 7 (2) (2021) 263–270, https://doi.org/10.1001/jamaoncol.2020.6575.
[63] S. Alder, D. Megyessi, K. Sundstrom, E. Ostensson, M. Mints, K. Belkic, et al., Incomplete excision of cervical intraepithelial neoplasia as a predictor of the risk of recurrent disease-a 16-year follow-up study, Am. J. Obstet. Gynecol. 222 (2) (2020) 172 e1–e12, https://doi.org/10.1016/j.ajog.2019.08.042.
[64] M.E. Fernandez-Montoli, S. Tous, G. Medina, M. Castellarnau, A. Garcia-Tejedor, S. de Sanjose, Long-term predictors of residual or recurrent cervical intraepithelial neoplasia 2-3 after treatment with a large loop excision of the transformation zone: a retrospective study, BJOG 127 (3) (2020) 377–387, https://doi.org/10.1111/1471-0528.15996.
[65] X. Zhu, X. Li, K. Ong, W. Zhang, W. Li, L. Li, et al., Hybrid AI-assistive diagnostic model permits rapid TBS classification of cervical liquid-based thin-layer cell smears, Nat. Commun. 12 (1) (2021) 3541, https://doi.org/10.1038/s41467-021-23913-3.
[66] D. Brenes, C.J. Barberan, B. Hunt, S.G. Parra, M.P. Salcedo, J.C. Possati-Resende, et al., Multi-task network for automated analysis of high-resolution endomicroscopy images to detect cervical precancer and cancer, Comput Med Imaging Graph 97 (2022) 102052, https://doi.org/10.1016/j.compmedimag.2022.102052.