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Bibliometric Analysis of Vaccine Trends and Novelty to Prevent Human Papillomavirus (HPV) Infection in Pregnant Women

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Abstract

Human papillomavirus (HPV) is the most common viral infection of the genital tract. Human papillomavirus (HPV) is associated with cervical, vulvar, and vaginal cancers in women, penile cancer in men, anal cancer, and oropharyngeal cancer in both. The biomolecular profile of Human Papillomavirus (HPV) has been widely studied in patients treated for HPV-related cervical lesions. Prophylactic vaccination against HPV is recommended as part of the vaccination schedule in many countries. This study aims to determine the trend in the number of publications, visualization of the relationship between the topic of vaccines to prevent human papillomavirus (HPV) infection in pregnant women through bibliometric analysis. The research method used a systematic review with stages following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram. Data on scientific publications related to vaccines to prevent human papillomavirus (HPV) infection in pregnant women were taken through dimensions.ai from 2010 to 2023. The data were then analyzed using Vosviewer. This study produced the following findings. First, the number of publications and citations on the topic of vaccines to prevent human papillomavirus (HPV) infection in pregnant women has increased exponentially from year to year. Second, there are 135 items, 5 clusters, 5463 links, and 14809 link strengths on the topic of vaccines to prevent human papillomavirus (HPV) infection in pregnant women. Third, the suggested research topics related to vaccines to prevent human papillomavirus (HPV) infection in pregnant women are topics that have low density in the low category, namely high prevalence and vaccine hesitancy. The findings of this study can help relevant researchers to recognize trends and novelties in research on vaccines to prevent human papillomavirus (HPV) infection in pregnant women and recommend directions for future research.

Keywords

bibliometric analysis; human papillomavirus (HPV) vaccine; pregnancy; novelty; trend

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Introduction

Nitric oxide (NO) is a molecule commonly produced in mammalian cells. NO synthesis is induced by cytokines and endotoxins in endothelial cells, neurons, fibroblasts, platelets, polymorphonuclear leukocytes, and keratinocytes. Three NO synthases have been reported in the skin (endothelial-eNOS, neural-nNOS, and inducible-iNOS), which synthesize NO in the presence of arginine and O2 (NADPH, FAD, FMH, and BH4-) and citrulline. In epithelial cells, constitutively expressed NOS (eNOS, nNOS) produce small amounts of NO over a relatively short period of time. In contrast, iNOS produces large amounts of NO over a long period of time when oxygen-dependent NO is disrupted. Excessive NO production in the skin is poorly controlled by iNOS, causing tissue damage and promoting the synthesis of bioactive NO-nitrate derivatives (NODs) such as: B. Protein S-nitrosylation (RSNO), N-nitrosamines, nitrosyl metals (RNNO), nitrite (NO 2 -) and nitrate (NO 3 -). NODs contribute to the overall bioavailability of NO under conditions of hypoxia, acidosis, UVA/UVB exposure and changes in oxidative/antioxidant status. In addition to the enzymatic synthesis of NO from L-arginine, it has been found that a large amount of NO in the skin is released non-enzymatically from higher nitrogen oxides such as nitrite and nitrate during photolysis reactions. Current research suggests that high levels of nitrosative stress are present in many skin diseases. It appears to be involved in chronic inflammatory skin diseases such as psoriasis and neurodermatitis. At the site of inflammation, inflammatory cells can release various reactive nitrogen/oxygen species (ROS/RNS), which have a negative effect on the tissue and lead to the development of nitrosative/oxidative stress. RNS/ROS act as second messengers and activate various signaling pathways. NO is essential for various skin functions, including keratinocyte and fibroblast proliferation, collagen production, and immune responses. However, alterations in the NO signaling pathway have important effects on skin homeostasis. (Ene et al., 2023).

NO has been defined as a molecular cofactor in HPV infection. In HPV-infected cells, the balance between the beneficial and detrimental effects of NO depends on the type of HPV, the concentration of NO, the cellular microenvironment, and the rate of NO production and degradation. There are more than 200 subtypes of HPV, divided into two major groups based on the likelihood of the virus causing malignant transformation: 4,444 low-risk types (LR - HPV) and high-risk types (HR - HPV). HPV is associated with a variety of benign and malignant skin and mucosal lesions. HR-HPV enhances the inflammatory response, and sustained inflammation and oxidative stress are known to be associated with tumor development. The main mechanisms by which HPV induces the development of oxidative stress-mediated neoplasia include dysregulation of mitochondrial function, ROS-induced DNA alteration, and suppression of antioxidant enzymatic activity. One major outcome is that ROS-induced apoptosis is suppressed in HPV-infected cells. HPV infection persists and can cause cancer by integrating its DNA into the host genome. Two early viral proteins, E6 and E7, have the ability to promote cancer development. In vitro studies have shown that HR-HPV can persist in human keratinocytes in particular. The most common skin lesion associated with HPV infection is the palmoplantar, which is a benign lesion. It is more common in young men and immunocompromised individuals, who are at risk for developing squamous cell carcinoma due to reactivation of latent virus. Transmission of infection occurs through direct contact with micro-lesions at the skin level and, less commonly, indirectly through contaminated objects such as equipment used in nail salons. Safe and effective vaccines are available to prevent HPV-related disease. Bivalent and quadrivalent HPV vaccines have been shown to be significantly effective in preventing HPV infection when incorporated into vacci-

nation programs.(Matei et al., 2024). Human Papilloma Virus (HPV) molecular biology has been extensively studied in patients treated for HPV-associated cervical lesions, as HPV-mRNA testing is more specific and has a higher positive predictive value for CIN2-3 in triage of high-risk (HR) women and in follow-up of women treated for CIN2/3.(Tinelli et al., 2013).

Human papillomavirus (HPV) is a small epitheliotropic DNA virus, of which there are 200 genotypes, 40 of which are known to cause genital infections and are also oncogenic. The clinical picture varies from asymptomatic (identified on routine cervical cancer screening) to large lesions of the vulva, vagina, cervix and some extragenital sites. Its prevalence in pregnancy varies from 5.5% to 65% depending on age, geography and gestational age (increasing with gestational age)(Chilaka et al., 2021). Human papillomavirus (HPV) is the most common viral infection of the genital tract.(Niyibizi et al., 2021) although several infectious processes have been implicated. Objective: To assess whether human papillomavirus (HPV.

Human papillomavirus (HPV) is associated with cervical, vulvar, and vaginal cancers in women, penile cancer in men, anal cancer, and oropharyngeal cancer in both. Prophylactic vaccination against HPV is recommended as part of the vaccination schedule in many countries. Millions of women worldwide receive bivalent vaccines against HPV types 16 and 18, quadrivalent vaccines against types 6, 11, 16, and 18, or 9-valent vaccines against HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58. Although the primary target for HPV vaccination is girls aged 11–13 years, national immunization schedules in many countries recommend vaccination for women up to age 25 or 26 years. Therefore, a significant number of women of childbearing age may be exposed to HPV vaccination.(Wang et al., 2020).

Over time, interest in the topic of human papillomavirus vaccines has increased worldwide.As in(Fauzy & Supandi, 2022) And(Prabowo et al., 2023), this interest data can be searched via Google Trends by typing in the keywords: human papillomavirus vaccine. For example, a search from January 2004 to December 2022 by selecting web search and all categories produces the data presented in Figure 1. This data was taken on November 1, 2024.

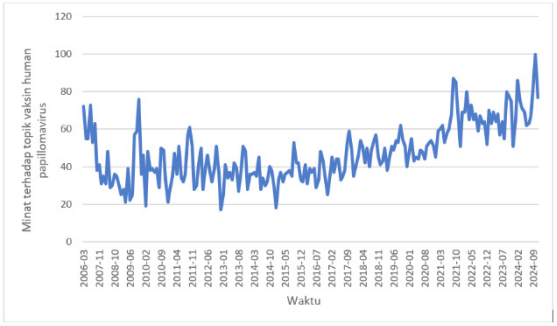

Figure 1. Interest over time in the topic of human papillomavirus vaccine (Data source: Google Trends)

Interest inhuman papillomavirus vaccine topiccan also be reviewed by country. Interest in the topic of vaccineshuman papillomavirusby country is presented in Figure 2. Ethiopia is a country with an interest in the topichuman papillomavirus vaccinehighest followed by Australia.

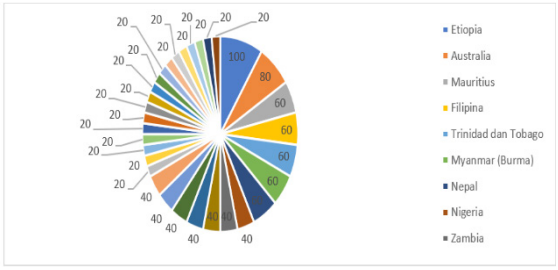

Figure 2. Histogram of interest by country towardshuman papillomavirus vaccine(Data Source: Google Trends)

The data illustrates the interest in the topic of human papillomavirus vaccine which is general in nature. So researchers who want to study the topic of vaccines to prevent human papillomavirus (HPV) infec-

tion in pregnant women need more specific information, such as scientific publications in the form of scientific articles and scientific seminar proceedings on the topic of vaccines to prevent human papillomavirus (HPV) infection in pregnant women.

In the study, researchers need information about trends and novelties for vaccines to prevent human papillomavirus (HPV) infection in pregnant women in the future. This is a problem that arises among researchers. However, bibliometric analysis of publications on vaccines to prevent human papillomavirus (HPV) infection in pregnant women to determine trends and novelties does not yet exist. This study was conducted to answer the following questions:

Question 1. What is the trend in the number of publications on the topic of vaccines to prevent human papillomavirus (HPV) infection in pregnant women?

Question 2. What is the trend in the number of citations on the topic of vaccines to prevent human papillomavirus (HPV) infection in pregnant women?

Question 3. How is the network visualization on the topic of vaccines to prevent human papillomavirus (HPV) infection in pregnant women?

Question 4. How does the visualization overlay on the topic of vaccines to prevent human papillomavirus (HPV) infection in pregnant women?

Question 5. How is the density visualization on the topic of vaccines to prevent human papillomavirus (HPV) infection in pregnant women?

Bibliometric analysis is a scientific and quantitative method for assessing articles thatpublished, which can help researchers to find the development trends and research hotspots of a particular research field, providing future research development for researchers.(Soybeans, 2021). Bibliometric analysis helps researchers to identify emerging areas and future directions of the research domain with the help of visualization tools. (Lam et al., 2022).

This study aims to determine the trend of the number of publications, the trend of the number of citations, network visualization, overlay visualization, and density visualization on the topic of vaccines to prevent human papillomavirus (HPV) infection in pregnant women through bibliometric analysis.

To achieve the objectives of this study, this work is structured as follows. The first section describes the background, problems and objectives of the study. The second section explains the literature study and methods used, data collection, and data analysis. The third section presents the results of the study followed by a discussion. The fourth section provides conclusions, limitations, and recommendations.

Method

There are five types of metric studies available for data analysis, namely: Scientometrics, Bibliometrics, Cybermetrics, Informetrics, and Altmetrics.(Chellappandi Ph Assistant Professor & Vijayakumar, 2018). As in(Murugesu & Khalid, 2022), Bibliometrics analysis is used in the study. Bibliometrics analysis is more suitable for quantitatively analyzing the distribution of research papers, terms, and keywords in determining research trends. (Murugesu & Khalid, 2022). Bibliometric analysis is considered a scientific field that shows a comprehensive map of the structure of knowledge, its evaluation and measurement.(Abuhassna et al., 2022). In addition, bibliometric analysis is a research method used in library and information science to evaluate research performance. (Syros et al., 2022). Bibliometric analysis is very important in assessing the impact of research where studies are ranked based on the citations they receive.(Pahwa et al., 2022).

The data used in this study is based on online searches throughhttps://app.dimensions.ai/. Data was taken on November 1, 2024. The research method used a systematic review with stages following the Prefer-

red Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram. (Page et al., 2021).The stages in PRISMA include identification, screening, and included. Stage 1 (Identification) detected 17,879 records fromdimensions.ai, taking into account, for each key search term vaccine for preventing human papillomavirus (HPV) infection in pregnant women, "document type articles and proceedings" and "all data published in the data range from 2010 to 2023.In phase 2 (screening), the option "article title, abstract" was selected in the field of each search term, resulting in 9,572 records being excluded. In phase 3 (including), the final sample yielded 8,307 articles, which were accessible

Data were analyzed using VOSviewer. VOSviewer is a computer program for creating and viewing bibliometric maps.(Van Eck & Waltman, 2010). Type if data is selected, create a map based on text data. In this study, the analysis was reviewed from co-occurrence and co-author.

The procedure for co-occurrence analysis is as follows. The data source is selected reading data from the reference manager file. Select fields are selected fields from which terms will be extracted are the title and abstract fields. The counting method is selected full count. The threshold is selected minimum number of occurrence of a term is 10. Select the number of terms is selected 125.

Results and Discussion

Publication Analysis

The search from 2010 to 2023 yielded scientific article publications. The number of publications on vaccines to prevent human papillomavirus (HPV) infection in pregnant women per year from 2010 to 2023 is presented inFigure 3.The highest increase occurred in 2022 with an increase of 669. Meanwhile, the lowest increase occurred in 2010 and 2011 with an increase of 309.

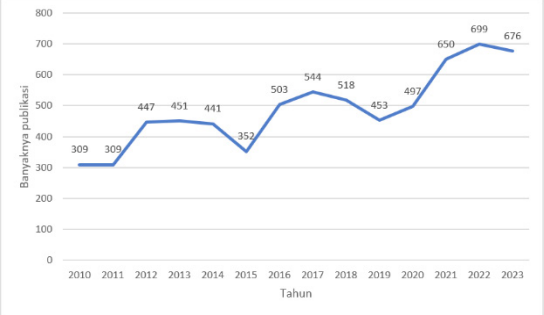

Figure 3. Number of publicationsvaccine to prevent human papillomavirus (HPV) infection in pregnant womenfrom 2010 to 2023 (source):https://app.dimensions.ai/)

Bibliometric analysis has been used in studies on the topic of infection. humanpapillomavirus(HPV) in pregnant womenin the health sector.Bibliometric analysis to determine research outcomes of human papillomavirus (HPV) infection in pregnant women.This study shows that from 2010 to 2023, the number of publications on HIV infectionshuman papillomavirus (HPV) in pregnant womenthe smallest occurred in 2010 and the highest in 2023 with an average of 489 (Figure 4). The number of publications increased exponentially from year to year.

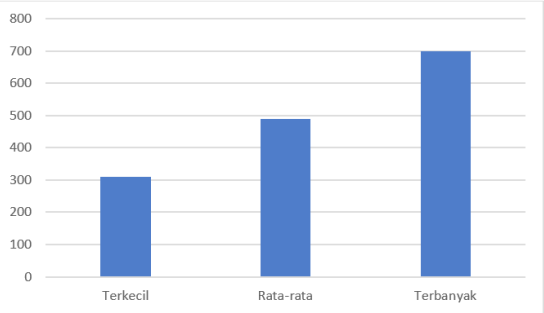

Figure 4. Histogram of the increase in the number of smallest, average, and highest publications for the topic vaccine to prevent human papillomavirus (HPV) infection in pregnant women.

Analysis Quote

The number of vaccine citations to prevent human papillomavirus (HPV) infection in pregnant women per year from 2010 to 2023 is presented in Figure 5. The highest

increase occurred in 2023 with an increase of 35325. While the lowest increase occurred in 2010 with an increase of 246.

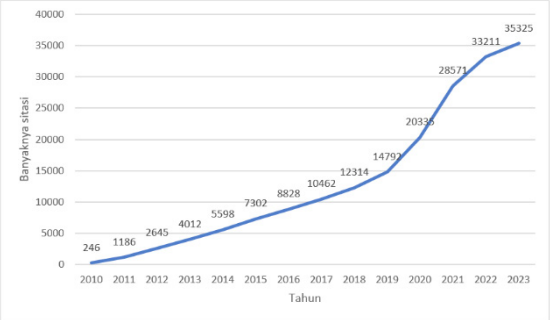

Figure 5. Number of citations for a topicvaccine to prevent human papillomavirus (HPV) infection in pregnant womenfrom 2010 to 2023 (source:https://app.dimensions.ai/)

Increase in the number of citationsvaccine to prevent human papillomavirus (HPV) infection in pregnant womenthe smallest occurred in 2010 and the highest in 2022 with an average of 20610 (Figure 6). The number of citations also increased exponentially from year to year. The most cited article was the article entitled 'Safety of hepatitis E vaccination for pregnancy: a post-hoc analysis of a randomized, double-blind, controlled phase 3 clinical trial'(Zhong et al., 2023).

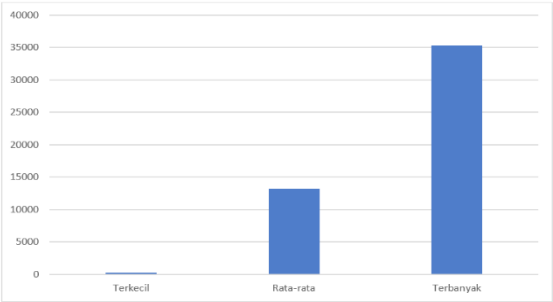

Figure 6. Histogram of the increase in the number of smallest, average, and largest citations for the topic of vaccines to prevent human papillomavirus (HPV) infection in pregnant women.

Analysis Network

Network visualization of125This term is presented in Figure 7.

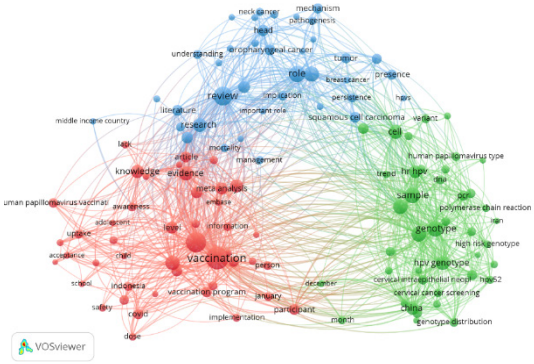

Figure 7. Network visualization (source: VOSviewer)

The selection of the number of terms is 125. Two items connected by a line indicate that the two items appear together in a title and abstract. Conversely, two items not connected by a line indicate that the two items do not appear together in a title and abstract.In Figure 5, there are 125 items, 3 clusters, 4682 links, and a link strength of 14207.

Based on Figure 7, it shows that out of 125 items, there are 3 clusters. Cluster 1 (45 items), cluster 2 (42 items), and cluster 3 (38 items).In more detail, these clusters are presented in Table 1.

The primary goal of human papillomavirus (HPV) vaccination is to reduce morbidity and mortality from HPV-related diseases, especially cervical cancer.(Sucato et al., 2023). From the results of Kjaer's research (2021), it is explained that HPV vaccination is very effective in preventing cervical cancer. The effectiveness of the HPV vaccine against cervical cancer at the population level is high among girls who are vaccinated under the age of 20. The lack of immediate effect in women who are vaccinated at the age of 20-30 years shows the importance of vaccination at an early age(Kjaer et al., 2021).

Overlay Analysis

The overlay visualization is presented in Figure 8.

Table 1. Cluster for the topic of vaccines to prevent human papillomavirus (HPV) infection in pregnant women (Source: Vosviewer)

Cluster	Number of items	Cluster member items
1	45	Acceptance, adolescent, article, attitude, awareness, child, country, covid, cross sectional study, mortality, dose, effectiveness, efficacy, embase, ethiopia, evidence, gender, hpv related diseases, hpv vaccine, human papillomavirus vaccination, human papillomavirus vaccine, implementation, indonesia, information, january, knowledge, deficiency, level, male, meta-analysis, order, pandemic, parent, participant, person, pubmed, recommendation, safety, school, systematic review, infectious diseases, uptake, vaccination, vaccination program, vaccine.
2	42	Age group, cell, cervical cancer screening, cervical intraepithelial neoplasia, cervical lesion, china, cin, cytology, december, distribution, dna, frequency, genotype, genotype distribution, genotype, high prevalence, high risk genotype, high risk HPV, high risk human papillomavirus, hpv hdna, hpv genotype, HPV prevalence, HPV testing, HPV16, HPV52, HR HPV, HRHPV, result, human papillomavirus type, infection rate, iran, lineage, month, PCR, polymerase chain reaction, current study, retrospective study, sample, trend, variant, variation.
3	38	Breast cancer, burden, carcinogenesis, challenges, decade, focus, head, hpvs, human papillomavirus, implications, important role, incidence, interaction, light, literature, management, mechanism, middle income countries, mortality, neck cancer, opscc, oral cavity, oropharyngeal cancer, oropharyngeal squamous cell carcinoma, oropharynx, paper, section, pathogenesis, persistence, presence, research, review, role, squamous cell carcinoma, subset, tumor, understanding, virus.

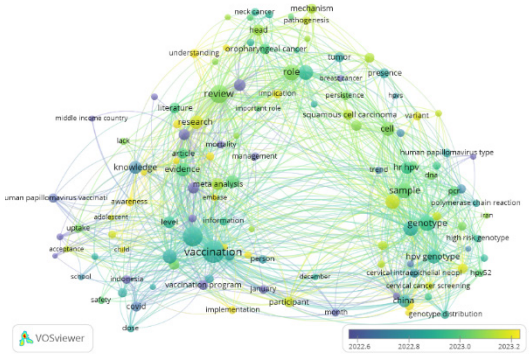

Figure 8. Overlay visualization (source: VOSviewer)

VOSviewer also provides an overlay visualization map. The overlay visualization of these 125 terms is presented in Figure 8.

Overlay visualization provides analysis based on the keywords of human papillomavirus (HPV) infection in women from 2010 to 2023 to observe the trend of research titles related to human papillomavirus (HPV) infection in women. Based on the map overlay visualization in Figure 6, the yellow nodes imply that the keywords are of current research interest. For example, the current research trend in human papillomavirus (HPV) infection in women focuses on infection rate and high risk human papillomavirus.

The different sub-periods in which scientific activity on this topic developed during 2010-2023 represent a rich set of key terms. In the titles, abstracts and keywords of the articles in the sample, VOSviewer has identified different keywords. This allows to validate the breadth of the study axes in the

research activity.

Globally, over the period 2020–2069, nearly two-thirds of cervical cancer cases will occur in low- and middle-income countries. Broad-spectrum HPV vaccination with 80–100% coverage in 2020 could prevent 6.7–7.7 million cases by 2069, but most prevention will occur after 2060. Twice-lifetime HPV-based screening at ages 35 and 45 years with 70% coverage in low- and middle-income countries (LMICs) could prevent 12.5–13.4 million cases over 50 years(Simms et al., 2019).

Density Analysis

Density visualization of125This term is presented in Figure 9.

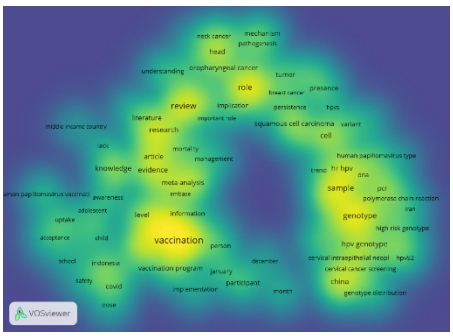

Figure 9. Density visualization (source: VOSviewer)

Figure 9 shows a visualization of density with the number of items that are found in several items, including:HPV and high risk human papillomavirus infections. Some items with yellow nodes mean that they have been widely used as topics in previous journal publications. Thus, the research topics related tovaccine to prevent human papillomavirus (HPV) infection in pregnant womenRecommended topics are those that have low category density visualizations, for example HPV infection and genotype.

Based on Figure 9, it shows that researchers, institutions, countries, and journals with the largest number of papers or citation frequencies come from developed countries. The increasing trend in the growth of publications on the topic of vaccines to prevent human papillomavirus (HPV) infection in pregnant women(Vyankandondera et al., 2019)demonstrates the importance of research on the topic of vaccines to prevent human papillomavirus (HPV) infection in pregnant women and is of international concern and has reached epidemic proportions in developing countries.(Niyibizi et al., 2020). The human papillomavirus (HPV) vaccine, introduced in many countries in the last decade, has shown promising results in reducing HPV infections and related diseases, such as cervical and precancerous lesions.(Suryoadji et al., 2022). The results of Ikeda's study (2021), a nationwide case-control study in Japan, showed a substantial risk reduction in abnormal cytology and CIN among women who received HPV vaccination compared to those who did not.(Ikeda et al., 2021). The results of Tan's (2019) study explain that the relationship between periconceptional or pregnancy HPV vaccine exposure and spontaneous abortion is still uncertain, and additional research is needed to assess the impact of HPV vaccination exposure on spontaneous abortion.(Tan et al., 2019).

Some suggested research topics related to vaccines to prevent human papillomavirus (HPV) infection in pregnant women are:high prevalence and vaccine hesitancy. This topic has great potential for research related to vaccines to prevent human papillomavirus (HPV) infection in pregnant women. (Cheng et al., 2020). The scope of the research is very broad and involves a lot of research content which results in the research being unfocused. The research methods used can include qualitative, quantitative, and mixed research.(Yuill et al., 2021).

This study will help readers understand the dynamics of the development trend of research topics from research results. It will help researchers quickly identify the hot spots and focus of research problems, guide them to find the most influential references, and choose the most influential or relevant researchers and institutions to cooperate. Through the analysis of the results, it will help researchers to find the contribution of key journals, direct and promote the deve-

lopment of further research achievements in scientific research institutions.

Conclusion

This study conducted a bibliometric analysis of publications.vaccine to prevent human papillomavirus (HPV) infection in pregnant womenvia app.dimension.ai from 2010 to 2023. This study shows several results. Among the many publications on the topicvaccine to prevent human papillomavirus (HPV) infection in pregnant womenhas an upward trend, many citations on the topicvaccine to prevent human papillomavirus (HPV) infection in pregnant womenexperienced an increase, Topic relevancevaccine to prevent human papillomavirus (HPV) infection in pregnant womenwith several other topics that can be analyzed using VOSviewer, namely network visualization, overlay visualization, density visualization.

This research shows themes, trends, productive authors, core journals, leading ranking countries and collaborations, and research groups.vaccine to prevent human papillomavirus (HPV) infection in pregnant women. This study provides a systematic review ofvaccine to prevent human papillomavirus (HPV) infection in pregnant womenfrom time to time.

Although this study has contributed to providing insight into the development of vaccine publications to prevent human papillomavirus (HPV) infection in pregnant women from 2010 to 2023 through app.dimension.ai, this study has limitations. The app.dimension.ai database continues to update new publications from time to time. Therefore, the bibliometric analysis of vaccines to prevent human papillomavirus (HPV) infection in pregnant women can be reviewed again in the next few years. In addition, this bibliometric analysis only extracts scientific article data from the app.dimension.ai database. Further research should add other databases for a broader understanding of vaccines to prevent human papillomavirus (HPV) infection in pregnant women.

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