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LITERATURE REVIEW

TUBERCULOSIS PREVENTIVE THERAPY AS A STRATEGY TO PREVENT AND CONTROL TUBERCULOSIS INCIDENCE 2010-2024: A BIBLIOMETRIC ANALYSIS

Terapi Pencegahan Tuberkulosis sebagai Strategi Pencegahan dan Pengendalian Kejadian Tuberkulosis 2010-2024: Analisis Bibliometrik

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ABSTRACT

Background: Tuberculosis Preventive Therapy (TPT) is important in TBC control and elimination strategies at the individual and community levels. However, few studies have systematically mapped developing scientific themes and trends related to TPT, primarily through bibliometric analyses. Therefore, a comprehensive bibliometric study is needed to identify key research foci and gaps in the current TPT knowledge pool. **Purpose:** This study aimed to identify global research trends in TPT as a preventive strategy to reduce TBC incidence. **Methods:** This study used a systematic literature review approach and bibliometric analysis using Scopus and PubMed databases through the Publish or Perish (PoP) platform, publications from 2010 to 2024. The initial search yielded 266 articles, which were screened using Mendeley for abstracts and keywords, resulting in 109 relevant publications. Bibliometric analyses were then conducted using VOSviewer version 1.6.20. **Results:** IPT (Isoniazid Preventive Therapy) has a close relationship with Preventive therapy, tuberculosis, child, contact, and HIV. Other results also show that the number of publications discussing TPT from 2020 to 2024 has decreased from 23 to 2, and the latest research topics related to TPT were only found in 2019. **Conclusion:** Publications related to TPT from 2020-2024 continue to decline; therefore, it is necessary to revitalize research related to TPT, especially by exploring issues that have not been widely discussed, such as the implementation of TPT in high-risk groups other than children and PLHIV, such as people

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with chronic diseases, the elderly, and populations with limited access to health services.

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ABSTRAK

Latar Belakang: Terapi Pencegahan Tuberkulosis (TPT) merupakan strategi penting dalam pengendalian dan eliminasi TBC baik pada tingkat individu maupun komunitas. Namun, masih sedikit penelitian yang secara sistematis memetakan tema-tema ilmiah yang berkembang dan tren terkait TPT, terutama melalui analisis bibliometrik. Oleh karena itu, diperlukan studi bibliometrik yang komprehensif untuk mengidentifikasi fokus utama penelitian dan kesenjangan pengetahuan dalam bidang TPT saat ini. **Tujuan:** Penelitian ini bertujuan untuk mengidentifikasi tren penelitian global terkait TPT sebagai strategi pencegahan untuk menurunkan insiden TBC. **Metode:** Penelitian ini menggunakan pendekatan tinjauan pustaka sistematik dan analisis bibliometrik dengan data yang diperoleh dari basis data Scopus dan PubMed melalui platform Publish or Perish (PoP), mencakup publikasi dari tahun 2010 hingga 2024. Pencarian awal menghasilkan 266 artikel yang kemudian diseleksi menggunakan Mendeley berdasarkan abstrak dan kata kunci, menghasilkan 109 publikasi yang relevan. Analisis bibliometrik dilakukan menggunakan perangkat lunak VOSviewer versi 1.6.20. **Hasil:** IPT (Isoniazid Preventive Therapy) memiliki keterkaitan erat dengan terapi pencegahan, tuberkulosis, anak, kontak, dan HIV. Hasil lainnya menunjukkan bahwa jumlah publikasi terkait TPT mengalami penurunan dari 23 publikasi pada tahun 2020 menjadi hanya 2 publikasi pada tahun 2024, dan topik penelitian terbaru mengenai TPT terakhir ditemukan pada tahun 2019. **Simpulan:** Jumlah publikasi terkait TPT dari tahun 2020 hingga 2024 terus mengalami penurunan; oleh karena itu, perlu adanya revitalisasi penelitian mengenai TPT, khususnya dengan menggali isu-isu yang belum banyak dibahas, seperti implementasi TPT pada kelompok berisiko tinggi selain anak-anak dan ODHA, misalnya pada penderita penyakit kronis, lansia, dan populasi dengan akses terbatas terhadap layanan kesehatan.

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INTRODUCTION

Tuberculosis (TBC) is a contagious infectious disease that primarily affects the human lungs and is the world's leading cause of death at all ages (1). TBC generally attacks the lungs in humans but can also attack other organs or systems, such as the bones, brain, etc. The disease is caused by the bacteria *Mycobacterium tuberculosis* (*M. tuberculosis*), which is transmitted to a person through the air by splashing droplets containing germs, usually when a person with TBC coughs, sneezes, or talks (2). *M. tuberculosis* bacterium can survive at room temperature and has a high infectious potential, infecting up to 10-15 individuals through air contaminated with the bacteria (3).

The number of TBC cases globally increased from 2020 to 2023. In 2020, 10.1 million people fell ill with TBC. This number rose to 10.4 million in 2021, then 10.7 million in 2022, and increased to 10.8 million in 2023. The incidence of TBC in 2023 was 134 per 100,000 population. Among all TBC cases in 2023, 6.10% were among people living with HIV. Most TBC cases in 2023 occurred in the WHO regions of Southeast Asia (45.01%), Africa (24.42%), and the Western Pacific (17.03%) (4). The increase in TBC cases is partly attributed to transmission from index cases to other at-risk groups (5).

World Health Organization (WHO) in 2018 organized the first high-level meeting on TBC. During the meeting, all heads of state agreed and reaffirmed that the Sustainable Development Goals (SDGs) target for 2030 is to reduce TBC mortality

by 90.00% and reduce TBC incidence by 80.00%. In addition, four global strategies were established to achieve the SDG targets, one of which is to provide Tuberculosis Preventive Therapy (TPT) to at least 30 million people within 5 years, previously known as isoniazid preventive therapy (IPT) (3). IPT initially focused on the two most at-risk populations, PLHIV and children <5 years of age, who had household contact with active TBC patients who were not proven to be sick with TBC. However, its implementation was still far from the expected target of 40% by 2018, so the program was changed to TPT, provided to all people at risk of TBC (6).

TPT is one of the strategies to control and eradicate TB at the community and individual levels. The provision of TPT aims to prevent the occurrence of TB disease and reduce the burden of TB. According to the Ilbti technical guidelines, TPT is not a stand-alone activity but must be implemented comprehensively in TB services and health systems. In the TPT program, there are several indicators used to assess and evaluate the implementation of TPT, including the coverage of TPT in PLWHA, children under 5 years of age, 5-14 years of age, adolescents, and adults over 15 years of age and other risk groups (6).

Although TPT has been recognized as a key strategy in TBC control, few studies have systematically mapped the development of scientific themes and trends related to TPT, particularly through a bibliometric approach. Therefore, a bibliometric review is needed to identify key foci and limitations of scientific information in the context of TPT research. This study aims to determine trends in TPT research worldwide. TPT research is important to understand the effectiveness of therapy and identify strategies that can improve treatment uptake and adherence. This research objective can be achieved using Bibliometric analysis.

METHODS

Study Design

This study used a systematic literature review approach and analysis bibliometric procedure (Figure 1) based on bibliographic data to explore and analyze research trends related to TBC preventive therapy (TPT) as an effort to prevent and control TBC incidence.

Bibliometric analysis is a quantitative method for evaluating and analyzing research characteristics, be they topic, author, or institution. By measuring elements such as the number of

publications, citations, and collaborations between authors or institutions, this analysis helps identify research trends and academic impact. Bibliometric studies are usually conducted using specialized databases and tools that allow researchers to search, retrieve, and analyze bibliographic data such as article titles, authors, publication dates, and references cited (7,8).

Research time and location

Research data was obtained from the Scopus and PubMed databases, which were accessed through the Publish or Perish (PoP) platform on 24 December 2024. Publish or Perish (PoP) was chosen as a tool in literature data collection because this platform is a reference manager that can collect citations from various reputable scientific sources, including books and journals (9).

Data Search Criteria

Article searches were conducted using the keywords "Tuberculosis Prevention Therapy AND Latent Tuberculosis Infection (LTBI) AND Isoniazid Preventive Therapy (IPT)" in Scopus and Pubmed using the keywords "Tuberculosis Prevention Therapy or Isoniazid Preventive Therapy (IPT) AND cases of Tuberculosis".

Inclusion Criteria

This study involved the selection of articles specifically addressing TBC Preventive Therapy (TPT) or Isoniazid Preventive Therapy (IPT) published globally from 2010-2024. The language of the articles/journals was restricted to English.

Exclusion Criteria

The article review examined titles and abstracts using the Mendeley application. Articles that did not include the term "Tuberculosis Prevention Therapy or Isoniazid Preventive Therapy" in the title or abstract were excluded from the analysis. After the article identification process, 109 articles were obtained for analysis.

Statistical analysis

Bibliometric analysis was conducted using the VOSviewer version 1.6.20 application on visualized journal search results from Scopus and PubMed. This research utilizes the application to visualize bibliometric networks in various aspects, such as annual publication trends, a collaboration between keywords, most dominant topics, and keyword Occurrences.

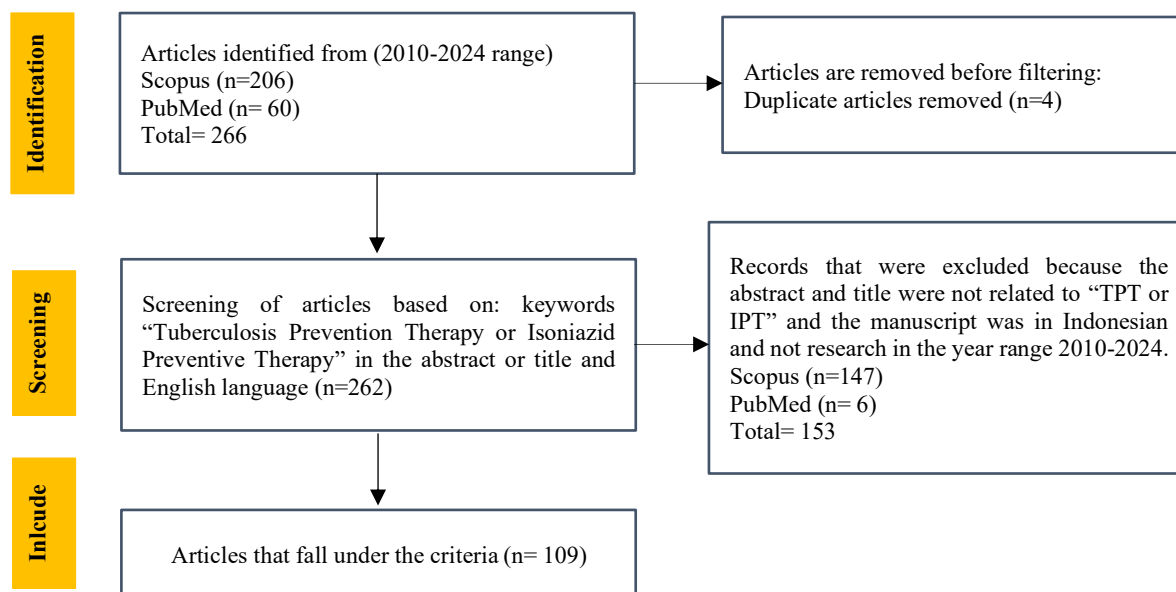


Figure 1. Literature Search Chart from Scopus and PubMed 2010-2024

RESULTS

From the results of the bibliometric analysis conducted using the VOSViewer application, there is some information, namely: 1) Citation data analysis from Publish or Perish (PoP), 2) TPT research trends for the last fourteen years (2010-2024), 3) Network visualization 4) Overlay visualization, 5) Density visualization of the VOSViewer application.

Citation Data Analysis

The results of the analysis of citation data on Publish or Perish (PoP), which have been collected through the Google Scholar, Scopus, and PubMed databases, are presented in Table 1. Based on Table 1, it is known that during the period 2010-2024, there were 109 articles relevant to the keywords displayed in the Scopus and PubMed databases. The total number of citations of all articles is 3,904, with the average number of citations per year being 278.86 and the average per paper being 35.82. Each author's average h-index is 30, with the highest number of citations being 62.

Table 1

Citation Data Matrix of Articles from Scopus and PubMed Databases

Citation Items	Value
<i>Publication years</i>	: 2010-2024
<i>Citation years</i>	: 14 (2010-2024)
<i>Papers</i>	: 109
<i>Citations</i>	: 3,904
<i>Cites/year</i>	: 278,86
<i>Cites/paper</i>	: 35,82
<i>Cites/author</i>	: 3850,40
<i>Papers/author</i>	: 64,65
<i>Author/paper</i>	: 3,86
<i>h-index</i>	: 30
<i>g-index</i>	: 62
<i>hI, norm</i>	: 29
<i>hI, annual</i>	: 2,07
<i>hA-index</i>	: 15
<i>Papers with ACC >=</i>	1,2,5,10,20: 55,53,41,23,12

Source: Publish or Perish, 2024

Trends in TPT Research as a Strategy to Prevent and Control Tuberculosis Incidence (2010-2024)

Figure 2 shows that the research trend from 2010 to 2024 continued to decline, although there was an increase from 2019 to 2020. However, after that, it continued to decline until 2024.

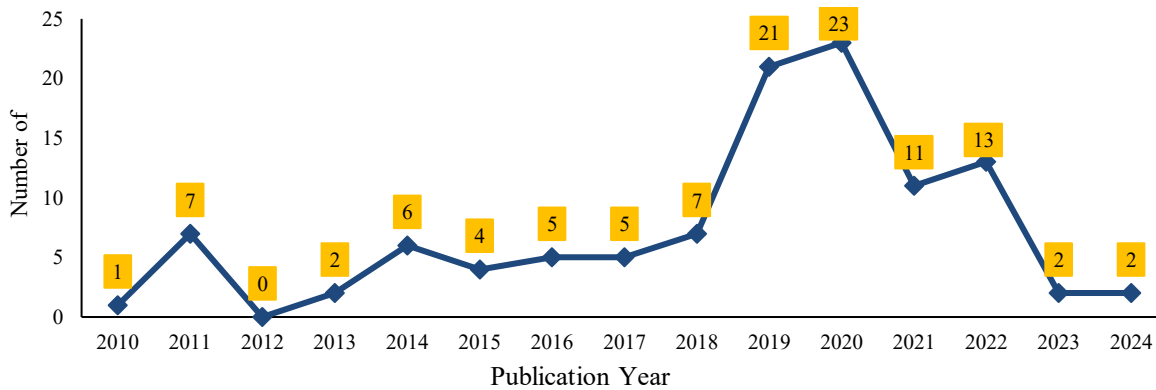


Figure 2. Research Trends in Tuberculosis Preventive Therapy as a Strategy to Prevent and Control Tuberculosis Incidence (2010-2024)

Keyword Analysis Network Visualization

Results on TPT as a Strategy for Tuberculosis Incidence Prevention and Control

The results of the bibliometric analysis in Figure 3 show that there are five keyword clusters, each cluster having a different color. Cluster 1 is marked in red, cluster 2 in green, cluster 3 in blue, cluster 4 in yellow and cluster 5 in purple. The red cluster with the keywords "IPT," "tuberculosis," and "HIV" means that this cluster is related to the administration of IPT in tuberculosis patients with HIV. Green cluster with keywords "child," "month," and "treatment," meaning that this cluster

is concerned with the treatment of childhood tuberculosis. The blue cluster with keywords "contact" and "risk" means that this cluster is associated with the risk of TBC transmission through contact with TBC patients. The Yellow cluster with keywords "adult" and "active TB" means that this cluster is related to active tuberculosis in adults. While in the purple cluster with keywords "tb case" and "data" this means that this cluster deals with reporting, recording, and analyzing TBC case data.

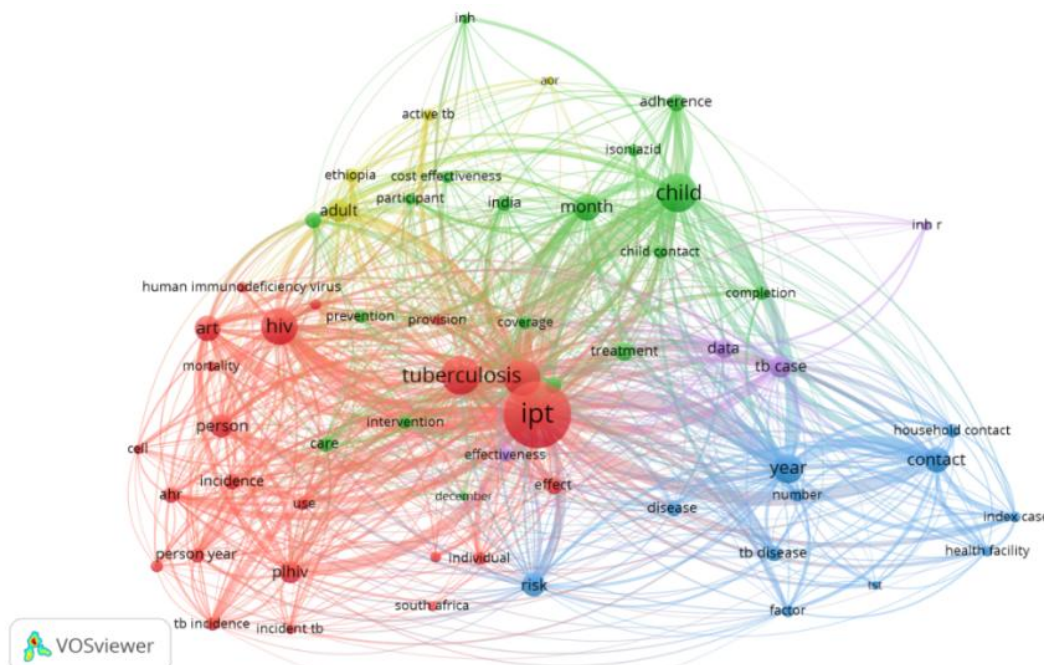


Figure 3. Network Visualization of Tuberculosis Preventive Therapy Research as a Strategy to Prevent and Control Tuberculosis Incidence

Development of TPT Research Trends as a Strategy for Prevention and Control of Tuberculosis Incidence

In addition to network visualization, the results of the bibliometric analysis in the VoSViewer application also have overlay visualization (Figure 4), which shows that yellow circles are keywords that often appear in 2019 research topics, namely "incidence tb," "prevention," and "isoniazid." Green colored circles indicate keywords that

frequently appear in 2018 research topics, namely "treatment," "child contact," and "adherence." The blue colored circles show the keywords that often appear in the 2017 research topics, namely "contact," "HIV," and "active TB." The purple colored circles show the keywords that often appear in the 2016 research topics, namely, "inh," "child," and "household contact."

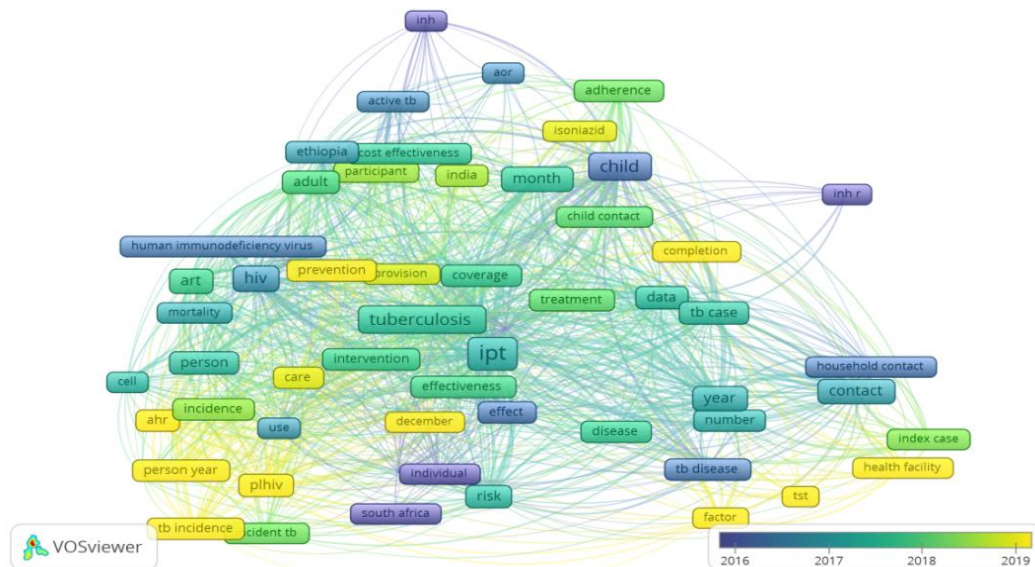


Figure 4. Overlay Visualization of Tuberculosis Preventive Therapy Research as a Strategy for Prevention and Control of Tuberculosis Incidence

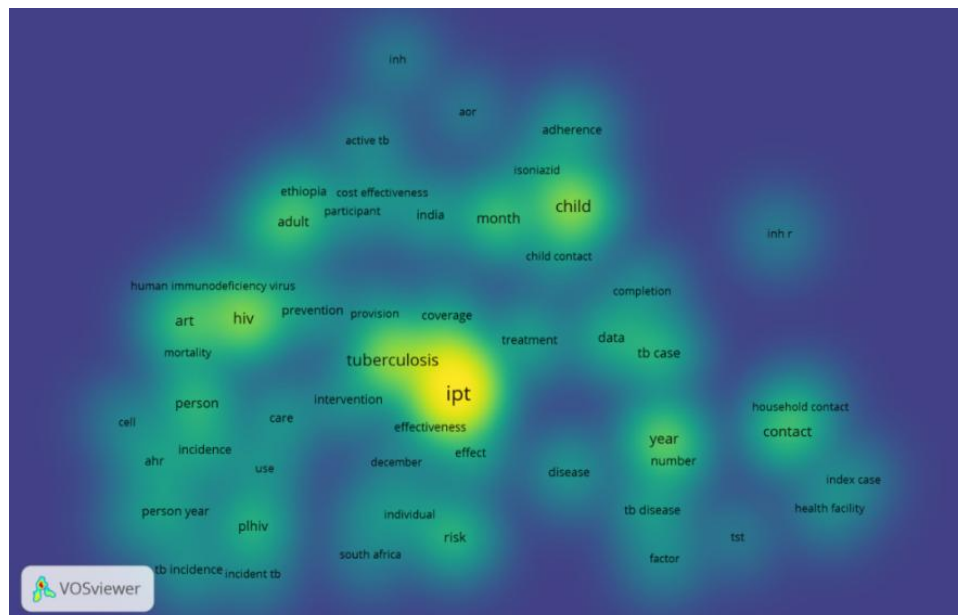


Figure 5. Density Visualisation of Tuberculosis Preventive Therapy Research as a Strategy for Prevention and Control of Tuberculosis Incidence

Visualization of the Analysis Intensity of TPT Research Keywords as a Strategy for Prevention and Control of Tuberculosis Incidence

The visualization result of bibliometric analysis related to literature in the last VoSViewer application is the density visualization (Figure 5), which shows that keywords "IPT," "child," "HIV," and "contact" yellow-colored is a keyword that has a high intensity of occurrence, meaning that it is the most discussed in the research. The green color shows that the keyword has a medium frequency of research, and the blue color is the keyword with the lowest intensity compared to other keywords, meaning that it is the least discussed in the research.

DISCUSSION

TBC is a disease caused by the bacterium *M. tuberculosis* and generally affects the lungs. The disease is transmitted through the air, especially when people with pulmonary tuberculosis cough, sneeze, or spit. Around 10 million people are affected annually by TBC, although the disease is preventable and curable. However, TBC still significantly impacts the lives and development of children and young people (5). One of the prevention efforts for individuals who have close contact or live in the same house with TBC patients is through Tuberculosis Preventive Therapy (TPT). This therapy aims to eradicate latent TB bacteria to reduce the risk of developing active TB. Administering TPT has been shown to reduce the likelihood of someone in contact with a TBC-positive person falling ill by 60-90 % (10).

The trend of research on TPT as a strategy for preventing and controlling TBC incidence, as shown in Figure 2, has decreased from 2020-2024. This means that research related to TPT is getting less and less researched by researchers. Therefore, sources of information related to TPT are lacking, for example, related to the benefits and objectives of TPT, because research journals are media that play an important role in a person's determining attitudes and decisions to act (11). Due to the lack of information, the TPT strategy as an effort to prevent and control TBC is difficult to achieve.

Refusal of the community to conduct TPT can also be caused by the stigma attached to tuberculosis disease. This results is in line by Suratmini et al (12), which states that self-stigma can affect individual self-efficacy in treatment. Self-stigma is a form of internalization of the stigma given to them by the environment. Self-stigma causes psychological distress, decreased social

functioning, and decreased quality of life in individuals.

Visualization results of the bibliometric analysis in Figure 3 show that (IPT) besides being closely related to keywords "child," "preventive therapy," and "tuberculosis," has a close relationship with HIV as well. This is consistent with the research (13), which showed that IPT is one of the most important treatments to be adhered to by TBC patients, especially children and people living with HIV, as they are highly susceptible to TBC. The incidence of tuberculosis infection among HIV-exposed infants ranges from 4.04% to 14.00% using the interferon- γ release assay (IGRA) and 9.01% to 36.03% using the tuberculin skin test. Children infected with TBC have a 10.00% chance of developing TBC disease throughout their lives, with 83.00% of them developing the disease within the first three months after exposure. Timely administration of TPT can reduce the risk of developing TBC by 63.01% in children exposed to active TBC patients and up to 85.04% in children identified with TBC infection (14).

Additionally, IPT deals with topics such as "preventive therapy" and "child". In India, for two decades, Isoniazid Preventive Therapy (IPT) has been used as part of TBC prevention for children living in the same household as TBC patients (15). Tuberculosis Preventive Therapy (TPT) is given to individuals at risk of contracting the disease, such as household contacts and other close contacts (16).

Transmission of TBC disease occurs through sputum droplets from patients with positive sputum test results of Acid Resistant Bacilli (BTA), which spread into the air when coughing or sneezing. When this happens, the *M. tuberculosis* bacteria in the patient's body are released and dispersed in the surrounding environment, allowing the bacteria to survive in the air (17). Transmission of *M. tuberculosis* is influenced by several factors, such as droplets containing bacteria, duration of exposure to particles, close contact with infected individuals, and enclosed and densely populated environments, which increase the risk of spreading the infection to be much higher (18).

The increase in TBC cases is because the *M. tuberculosis* germ infects many people, so there is an urgency to quickly resolve or prevent it so that TBC does not continue to increase over time. The condition of LTBI is a threat of spreading unnoticed because people infected with TBC bacteria do not show symptoms of the disease. In preventing the development of LTBI into TB disease, TPT with antibiotics is one of the most effective interventions the WHO recommends in achieving the End TB

Strategy goals. At the High-Level Meeting on TBC in 2018, a target was set to provide TPT to 30 million people between 2018 and 2022. However, by the end of 2022, only 15.5 million people, or about 52.04% of the target, will have received TPT (19).

Children have a close relationship with IPT. Therefore, children under five years of age who are in contact with bacteriological TBC patients are the primary target for TPT. Research by Shanbag et al (20) also showed that 55.01% of the sick contacts were under six. The association between contact age and disease progression was insignificant (p -value=0.31). In addition, all individuals who have household contact with BTA-positive TBC patients should be screened for TBC disease. Isoniazid Preventive Therapy (IPT) is administered for six months to children under six years old to reduce the incidence of TBC in this age group. In addition to isoniazid, children under six are given rifampicin and rifapentine for TPT (6).

The analysis results in Figure 5 show that in addition to the keywords "ipt," "tuberculosis," and "preventive therapy," the most frequently discussed keyword in the research topic is Human Immunodeficiency Virus (HIV). The association of IPT with TBC incidence in HIV patients was statistically significant (RR: 2.05; 95.01% IK 1.78-2.37; p =0.02) (21). The WHO recommends that IPT should be given to HIV patients with positive tuberculin test results to reduce the incidence of TBC in this group. The use of IPT for six months is known to reduce the risk of TBC in HIV patients by 33.00% (22). Meanwhile, based on the technical guidelines for providing TPT to PLWHA, it is done by screening for TB symptoms without having to do a TST, IGRA examination, or thorax X-ray (6). IPT use is a protective factor against TBC incidence in HIV patients with up to 3 years of protective effect. IPT combined with ART reduces the risk of TBC in HIV-infected individuals, and the combination is significantly more protective than ART monotherapy alone (23).

CONCLUSION

The results of bibliometric analysis related to TB preventive therapy as a strategy to prevent and control TB incidence showed a decline from 2010 to 2024, and the latest research topics related to TPT were only found in 2019. Therefore, it is necessary to revitalize research related to TPT, especially by exploring issues that have not been widely discussed, such as the implementation of TPT in high-risk groups other than children and PLWHA,

such as patients with chronic diseases, the elderly, and populations with limited access to health services.

CONFLICT OF INTEREST

In this study, no conflict of interest occurred.

AUTHOR CONTRIBUTIONS

YS: designing research concepts, analyzing data, and compiling data. ACH, FS, and NSL: Provide direction and suggestions for improvement.

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