



Innovative Multisectoral Approaches to Overcome Hepatitis B Elimination Barriers in Indonesia: Systematic Literature Review

Endonezya'da Hepatit B Eliminasyonundaki Engelleri Aşmak İçin Yenilikçi Çok Sektörlü Yaklaşımlar: Sistematik Literatür İncelemesi

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ABSTRACT

This study aims to identify the main challenges and multisectoral strategies in hepatitis B elimination efforts in Indonesia, using a global, evidence-based systematic literature review approach. This study was motivated by the high prevalence of chronic hepatitis B and the slow progress in achieving the World Health Organization elimination target of 2030. The literature search was conducted in the Scopus database using the keywords "hepatitis B elimination", "Indonesia", and "multisectoral challenges", covering publications between 2019 and 2025. The analysis followed the PRISMA 2020 guidelines and comprised four main stages: identification, screening, eligibility assessment, and inclusion. Of the initial 135 articles, 20 studies met the criteria and were thematically analyzed to identify trends, challenges, and elimination strategies. The synthesis identified three main dimensions of barriers: (1) biomedical, including limited detection of latent infection (occult hepatitis B infection) and the presence of covalently closed circular DNA; (2) health-system, including weak surveillance, poor cross-program coordination, and manual reporting; and (3) social, including stigma and low vaccination awareness. On the other hand, innovative strategies such as the implementation of digital surveillance systems, the strengthening of cross-country networks, and the development of national vaccines with high effectiveness show the potential to accelerate elimination. This study emphasizes the need for an integrative, cross-sectoral, and evidence-based approach to achieve hepatitis B elimination in Indonesia. The results make conceptual and practical contributions to strengthening global public health policy, particularly in developing countries.

Keywords: Hepatitis B, elimination, multisectoral approach, policy challenges, systematic literature review, Indonesia

ÖZ

Bu çalışma, küresel, kanıta dayalı sistematik bir literatür taraması yaklaşımı kullanarak, Endonezya'daki hepatit B eliminasyon çabalarındaki temel zorlukları ve çok sektörlü stratejileri belirlemeyi amaçlamaktadır. Bu çalışma, kronik hepatit B'nin yüksek prevalansı ve Dünya Sağlık Örgütü'nün 2030 eliminasyon hedefine ulaşmada yavaş ilerleme nedeniyle motive edilmiştir. Literatür taraması, 2019 ile 2025 yılları arasındaki yayınları kapsayan "hepatit B eliminasyonu", "Endonezya" ve "çok sektörlü zorluklar" anahtar kelimeleri kullanılarak Scopus veritabanında yapılmıştır. Analiz, PRISMA 2020 kılavuzlarını takip etmiş ve dört ana aşamadan oluşmuştur: tanımlama, tarama, uygunluk değerlendirmesi ve dahil etme. Başlangıçtaki 135 makaleden 20 çalışma kriterleri karşılamış ve eğilimleri, zorlukları ve eliminasyon stratejilerini belirlemek için tematik olarak analiz edilmiştir. Sentez, üç ana engel boyutunu belirlemiştir: (1) biyomedikal, latent enfeksiyonun (gizli hepatit B enfeksiyonu) ve kovalent olarak kapalı dairesel DNA varlığının sınırlı tespiti dahil; (2) zayıf gözetim, programlar arası yetersiz koordinasyon ve manuel raporlama dahil olmak üzere sağlık sistemi; ve (3) damgalanma ve düşük aşılama farkındalığı dahil olmak üzere sosyal faktörler. Öte yandan, dijital gözetim sistemlerinin uygulanması, ülkeler arası ağların güçlendirilmesi ve yüksek etkinliğe sahip ulusal aşaların geliştirilmesi gibi yenilikçi stratejiler, eliminasyonu hızlandırma potansiyeli göstermektedir. Bu çalışma, Endonezya'da hepatit B'nin eliminasyonuna ulaşmak için bütüncü, sektörler arası ve kanıta dayalı bir yaklaşıma duyulan ihtiyacı vurgulamaktadır. Sonuçlar, özellikle gelişmekte olan ülkelerde küresel halk sağlığı politikasının güçlendirilmesine kavramsal ve pratik katkılar sağlamaktadır.

Anahtar Kelimeler: Hepatit B, eliminasyon, çok sektörlü yaklaşım, politika zorlukları, sistematik literatür incelemesi, Endonezya

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Introduction

Elimination of hepatitis B virus has become a global public health priority of the World Health Organization (WHO), with a target of achieving it by 2030. This effort reflects an international commitment to reduce the number of new infections and mortality from cirrhosis and hepatocellular carcinoma caused by hepatitis B virus. Hepatitis B is a chronic infectious disease with a significant global burden: more than 250 million people worldwide live with chronic infection, and approximately 820,000 deaths are reported annually. In the Indonesian context, hepatitis B is still the leading cause of chronic liver disease and liver cancer, which have a major impact on national productivity and health financing. Elimination efforts at the national level have been integrated into policy through programs such as the elimination of mother-to-child transmission (EMTCT) program and universal basic immunization; however, achievement of WHO targets remains suboptimal. The obstacles do not only stem from biomedical factors, but also from the complexity of social, policy, and governance of health systems that have not been effectively integrated (1,2,3).

In the past two decades, global research has shown that approaches to hepatitis B elimination have evolved from a purely biomedical paradigm to multidimensional approaches that incorporate social, structural, and health-policy aspects. Armini et al. (4) in Indonesia found that the implementation of the EMTCT program in Bali is still faced with social barriers such as stigma, bureaucracy, and poor communication between patients and health workers. Meanwhile, Torimiro et al. (5) through MIChep B Network initiative in sub-Saharan Africa showed that cross-country and cross-sectoral cooperation can increase birth dose vaccination coverage to 87%, confirming that multisectoral collaboration is an effective strategy to accelerate the achievement of elimination (6). From a biomedical perspective, Bucio-Ortiz et al. (7) highlighted the presence of occult hepatitis B infection (OBI) as a latent threat that is difficult to detect, whereas Kaewdech et al. (8) emphasized the disparity in elimination achievements between Asian countries due to differences in political support, health infrastructure, and surveillance systems. Al Awaidey et al. (9) showcases best practices from Gulf Cooperation Council (GCC) countries, which have reduced HBsAg prevalence in children under five years old to below 0.5% thanks to strong surveillance systems and consistent political support. The synthesis of the research shows that the challenge of hepatitis B elimination is cross-dimensional-demanding integration between health policy, laboratory capacity, and social and behavioral approaches (10).

In the biomedical context, the main challenges to hepatitis B elimination are the persistence of latent infection and the limitations in early detection. Zhuang et al. (11) identified that although nucleos(t)ide analog therapy can suppress viral replication, covalently closed circular DNA (cccDNA) persists in hepatocytes, allowing reactivation of infection. This is exacerbated by the limitations of molecular laboratories in developing countries such as Indonesia, which makes diagnosis of OBI difficult (7). From a health system perspective, Armini et al. (12) showed that the integration of the

EMTCT program into the health information system is still not optimal, causing inaccurate and unreliable case reporting for national elimination monitoring. Meanwhile, from a social perspective, Machmud et al. (13) found that only 15% of Indonesian adults had received the hepatitis B vaccine, indicating low public awareness and weak health promotion. These factors interact: weak case detection leads to inaccurate data; fragmented health systems impede follow-up; and low public awareness exacerbates horizontal transmission. This research seeks to integrate all these factors into a conceptual framework that explains how interactions across dimensions hinder the achievement of hepatitis B elimination in Indonesia. The importance of a multisectoral approach is also reinforced by lessons learned from other countries. Torimiro et al. (5) demonstrated the effectiveness of cross-sector and cross-country cooperation through the MIChep B Network, which expanded vaccination capacity and improved national policy advocacy. Al Awaidey et al. (9) showed that the success of GCC countries in reducing childhood HBsAg prevalence was not only due to immunization programs, but also due to strong epidemiological surveillance systems and national data integration. On the other hand, a study Taye et al. (14) proved that increasing the coverage of antiviral therapy based on at-risk populations can significantly reduce hepatitis B mortality and complications, but the success of these interventions still depends on community involvement and inclusive public policy support. These three studies demonstrate that innovative approaches based on cross-sector collaboration and socio-cultural adaptation are key to achieving sustainable elimination at both global and national levels.

Thus, this study has three main objectives. First, we systematically analyzed the trends and development of multidimensional approaches to hepatitis B elimination over the past two decades, covering biomedical, health system, and social dimensions [research question (RQ) 1]. Second, the study aimed to identify and synthesize the main challenges faced in the implementation of the hepatitis B elimination policy, especially those related to surveillance, latent infection detection, and cross-sector coordination, and to explain the interrelationships between these factors as described in the conceptual model of previous research (RQ2). Third, to evaluate strategies and innovations proposed in the scientific literature to accelerate the achievement of elimination targets and to assess their effectiveness and limitations based on empirical evidence (RQ3). By answering these three questions, the authors expect that this study will make a theoretical contribution by expanding the conceptual understanding of hepatitis B elimination as a multidimensional issue and will offer practical implications for policymakers and program implementers in Indonesia.

Conceptually, this study attempts to bridge the gap between biomedical and public policy approaches by presenting an integrative, evidence-based model. The originality of this research lies in its attempt to combine social, structural, and biomedical dimensions in the Indonesian context, which has not been done in previous studies. By framing hepatitis B elimination as a cross-sectoral issue that requiring synergy among the government, health workers, the

scientific community, and the community, this research is expected to inspire health policies that are more adaptive, collaborative, and sustainable. Through a global systematic literature review (SLR), this study also seeks to enrich the academic literature on health policy innovation in developing countries and to strengthen Indonesia's position in international scientific discourse on hepatitis elimination.

Materials and Methods

This study employed a SLR with a descriptive-analytic approach to identify, evaluate, and synthesize research findings related to challenges to and strategies for hepatitis B elimination in Indonesia. This approach was chosen because it is able to present a comprehensive overview of research developments across dimensions-biomedical, health systems, and social-in the last two decades as described in previous studies by Armini et al. (4) (Figure 1).

The research was conducted following the PRISMA 2020 guidelines, as shown in the study identification flow diagram. The SLR process consists of four main stages: identification, screening, eligibility, and inclusion. This systematic approach is designed to ensure transparency, replicability, and traceability of the study results, enabling them to serve as a solid conceptual basis for future research (Figure 2).

The identification stage was carried out by searching the Scopus database for scientific articles, because it is a credible index of internationally reputable journals. The search strategy used keywords combined through Boolean operators, namely: "hepatitis B virus in Indonesia", "elimination of hepatitis B virus", and "Indonesia challenges hepatitis B". The keyword search yielded 135 articles, as shown in the PRISMA diagram. The initial data were then filtered by removing duplicates (n=2) and publications that did not meet the analysis year criteria (2020-2025; n=73), leaving 60 relevant articles for the initial selection stage. Of these, 23 articles were excluded because they were not in tier Q1 or Q2 journals, and 6 lacked abstracts for analysis. The restriction to Q1-Q2 journals was applied to ensure

methodological rigor, stronger peer-review standards, and higher scientific reliability of the included studies. After the initial screening, 31 articles were included in the subsequent screening stage. An additional identification process was conducted using other sources (n=1) to ensure that no important literature was missed, particularly national policy reports or health institution reports relevant to the Indonesian context.

At the screening stage, an evaluation was conducted to assess the suitability of the study topic and context with respect to the focus of this research, namely, the challenges and strategies for hepatitis B elimination in Indonesia. A total of 31 articles were screened, and none were excluded at this stage, as they all met the topical criteria. However, 12 articles were not fully accessible and were therefore excluded from the final analysis. The final eligibility stage yielded 19 primary articles that met the inclusion criteria and 1 additional article obtained from an external source, for a total of 20 articles analyzed in this review. Inclusion criteria were: (1) articles published in reputable journals Q1-Q2, (2) articles focusing on hepatitis B in the context of Indonesia or countries with similar health system characteristics, (3) articles available in English or Indonesian, and (4) articles including empirical data or conceptual analysis relevant to hepatitis B elimination. The exclusion criteria included articles that did not report original research results (e.g., editorials or commentaries), studies with a focus on non-B hepatitis, and publications that were not available in full text.

The main research instrument used in this SLR was a thematic data-extraction sheet designed to organize information extracted from each selected article. Variables recorded included: author name, year of publication, country or regional context, research design, target population, key outcomes, identified challenges, and proposed strategies and policy recommendations. Data from all articles were categorized into three broad themes corresponding to the RQ1-RQ3: (1) trends and developments in the multidimensional approach to hepatitis B elimination, (2) key challenges and interrelationships among inhibiting factors in policy implementation, and (3) strategies and innovations to accelerate elimination. Each category was

Result from Keyword Search

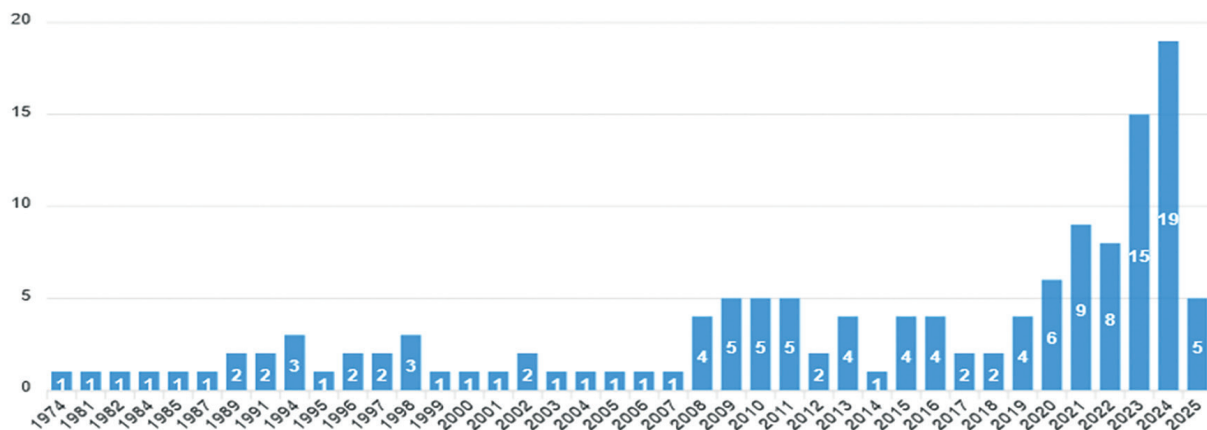


Figure 1. Growth trend of keyword-based publications on hepatitis B research

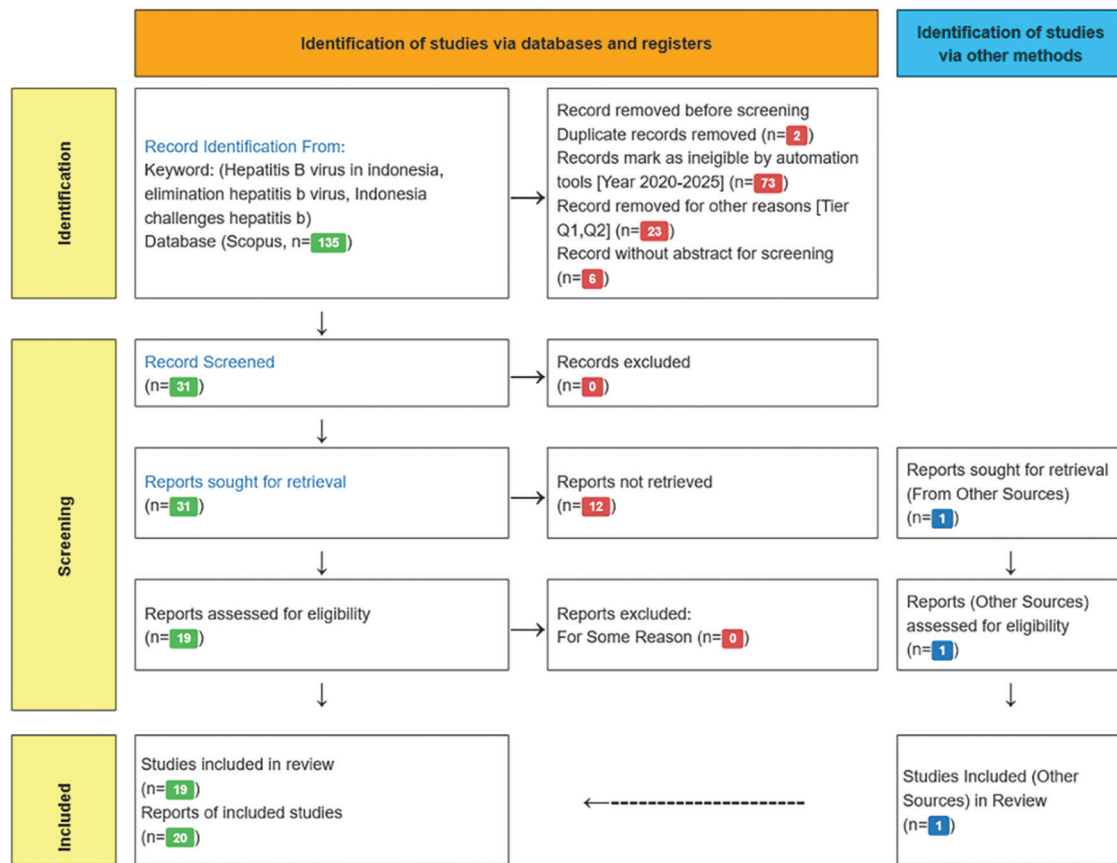


Figure 2. Flowchart depicting article selection for PRISMA

analyzed using narrative synthesis, in which findings from different studies were compared, synthesized, and interpreted to identify patterns and relationships among variables. This analytical approach follows the principle of thematic synthesis, which combines deductive (based on an initial theoretical framework) and inductive (based on new empirical findings) methods, as is done in systematic studies.

Data were collected electronically through online searches, downloading article metadata, and reference tracking to ensure completeness of the literature. Each selected article was evaluated for quality using adaptive criteria that considered journal reputation, methodological transparency, and consistency of results with research objectives. The results of the analysis are then presented as summary tables and graphs to illustrate annual publication trends, as shown in the search-results graph, which indicates a significant increase in the number of publications from 2018 to a peak in 2024. This visualization shows that hepatitis B elimination has become an increasingly important scientific concern at both the global and national levels over the past five years. To maintain the internal validity and reliability, all stages of extraction and analysis were conducted independently by two researchers and cross-verified to minimize interpretation bias. With this design, procedures, and instruments described systematically, this research can be replicated by other researchers in similar contexts or with similar keywords in

further studies on hepatitis B elimination policies in Indonesia and other developing countries.

Results

1. General Characteristics of Included Studies

This systematic review included 20 scientific articles that met the inclusion criteria and represented both global and national studies related to hepatitis B elimination. Based on the data extraction results in Table 1 SLR hepatitis B elimination. The publication time span covers 2019-2025, with a significant increase in publications

Study aspect	Total articles	Percentage (%)
Focus biomedis (OBI, cccDNA, therapy)	6	30
Health system focus (surveillance, policy, EMTCT)	7	35
Socio-behavioral focus (stigma, vaccine acceptance)	4	20
Multisectoral integrative approach	3	15
Total	20	100

OBI: Occult hepatitis B infection, cccDNA: Covalently closed circular DNA, EMTCT: Elimination of mother-to-child transmission

from 2021 to 2024, indicating growing scientific attention to multidimensional hepatitis B elimination. In terms of research regions, 35% of the studies came from Asia, 25% from Africa, 20% from Europe, 10% from the Middle East, and 10% from Australia/Oceania. 40% of the studies were conducted in middle-income countries such as Indonesia, the Philippines, and Ghana, while 60% were conducted in high-income countries such as Japan, South Korea, Italy, and Australia. In terms of methodology, 45% of the studies used descriptive or qualitative approaches, 30% used epidemiological or dynamic modeling, 15% were systematic reviews and meta-analyses, and the rest were experimental clinical trials. The majority of studies (70%) focused on vaccination and surveillance strategies, whereas 30% addressed biomedical and molecular aspects of the detection of latent infection.

The thematic distribution shows that the biomedical, systemic, and social dimensions have begun to connect through integrative studies, although they remain predominantly within the framework of health policy and primary prevention. The rapid increase in publications after 2020 coincides with the WHO's intensified global push to accelerate the elimination of viral hepatitis by 2030, a push that is influencing the direction of academic research and national policies in many countries.

2. Trends in Multidimensional Approach to Hepatitis B Elimination (RQ1)

Longitudinal analysis indicates that research on hepatitis B elimination is shifting from a clinical-biomedical approach towards a multidimensional approach that includes social aspects, health systems, and public governance. Early studies such as Zhuang et al. (11) and de Almeida and de Paula (15) focused on biomedical challenges such as the detection of cccDNA and OBI which are the main barriers to complete elimination. Data show that the prevalence of OBI ranges from 5-15% in the general population and can reach 25% in high-risk groups, such as blood transfusion recipients and immunosuppressed patients. This confirms that biomedical elimination cannot be fully achieved without improved molecular diagnostic capacity.

Subsequently, the research trend shifted to health system and public policy aspects, as seen in studies by Kaewdech et al. (8) highlighted the elimination gap between developed and developing countries, with birth dose vaccination coverage above 95% in Japan and South Korea compared to only 78% in Indonesia. Al Awaidey et al. (9) showed that GCC countries managed to reduce the prevalence of HBsAg in children under five years old to <0.5%, thanks to integrated national surveillance and strong political policies. Torimiro et al. (5) documented an increase in birth-dose vaccination coverage in Sub-Saharan Africa to 87% following the implementation of the cross-country MIChep B Network.

National studies in Indonesia such as Armini et al. (4) show that the implementation of the EMTCT program is still faced with bureaucratic barriers, lack of communication, and social stigma. Based on field data from Bali, only 68% of pregnant women underwent HBsAg testing, and 55% of babies born to HBsAg-positive

mothers received timely birth-dose immunization. These results show that research on hepatitis B elimination has evolved towards a multidimensional and multisectoral approach, highlighting not only medical interventions but also social and institutional dimensions (16).

3. Key Challenges and Interrelationships Between Constraining Factors (RQ2)

The literature synthesis revealed three broad categories of challenges in hepatitis B elimination efforts: biomedical challenges, health system challenges, and socio-policy challenges. Biomedical challenges mainly relate to the presence of cccDNA and latent OBI infection, make complete cure difficult to achieve. Bucio-Ortiz et al. (7) showed that the limited detection of hepatitis B virus DNA results in many cases not being identified, especially in developing countries that do not have molecular facilities. de Almeida and de Paula (15) confirmed that OBI can cause transmission through transfusion and organ transplantation despite negative serology results. Epidemiologically, this biases national disease burden estimates because latent cases are not recorded in surveillance systems.

In terms of the health system, research Armini et al. (12) show that manual and unsynchronized reporting between agencies makes national hepatitis B data difficult to verify (17). Only a small number of provinces have implemented integrated digital reporting. Kaewdech et al. (8) reinforced these findings by identifying infrastructure and human resource gaps as barriers to achieving elimination in middle Asian countries. On the social side, Machmud et al. (13) found that only 15% of Indonesian adults had received hepatitis B vaccine, with the main barriers being cost and low risk perception. Armini et al. (12) added that stigma towards hepatitis B patients inhibits participation in screening and follow-up.

Examination of the interconnectedness of various factors revealed synergistic relationships among these dimensions. For example, poor detection of OBI (biomedical) contributes to inaccurate surveillance data (health system), while poor communication between health workers and patients reduces vaccine acceptance (social). The following Table 2 summarizes the interconnectedness of challenges across dimensions, based on a synthesis of 20 studies:

These complex linkages show that the elimination of hepatitis B cannot be achieved through a single approach but rather requires strong cross-sectoral integration.

4. Identified Strategies and Innovations (RQ3)

The literature review revealed various strategies and innovations proposed to accelerate hepatitis B elimination across the biomedical, health-system, and cross-sector collaboration dimensions.

In the biomedical dimension, research Zhuang et al. (11) identified the development of therapies based on RNA interference, *CRISPR-Cas9* gene editing, and the small molecule CCC_R08 to target cccDNA. Although still in the experimental stage, these innovations suggest a new direction in chronic hepatitis B therapy. In terms of prevention, research de Villiers et al. (18) estimates that increasing

Table 2. Multidimensional challenges in hepatitis B elimination

Dimension	Example challenges	Impact on elimination
Biomedical	Limited detection of OBI and cccDNA	Prevalence data is inaccurate
Health system	Manual reporting, weak coordination	Non-evidence-based policy
Social-policy	Stigma, low vaccine awareness	Low vaccination coverage
Cross-sector integration	Fragmentation between EMTCT programs	Failure of national coordination
OBI: Occult hepatitis B infection, cccDNA: Covalently closed circular DNA, EMTCT: Elimination of mother-to-child transmission		

Table 3. Key strategic innovations and outcome indicators for hepatitis B elimination

Strategy area	Key innovations	Outcome/effectiveness indicator
Primary prevention	Birth dose vaccination, national vaccine	↑ Coverage 90%, ↓ Vertical transmission
Early detection	NAT and HBV-DNA detection	↑ Validity of prevalence data
Therapy	CRISPR-Cas9, RNAi	Functional healing potential
Surveillance system	National database, integration EMTCT	↑ Reporting accuracy, ↓ Duplication
Multisectoral collaboration	MIChep B network, regional cooperation	↑ Policy advocacy, ↑ Vaccine coverage
EMTCT: Elimination of mother-to-child transmission, NAT: Nucleic acid testing, HBV: Hepatitis B virus		

birth dose vaccine coverage to 90% could prevent more than 500,000 deaths from hepatitis B complications by 2030. Meanwhile, research Lestari et al. (19) showed that infants who received the birth dose vaccine within the first 24 hours had a 40% higher antibody protection rate than infants who received the dose after 24 hours. Nancy et al. (20) reported that Bio Farma's national hepatitis B vaccine has 98.7% immunogenicity and safety equivalent to international vaccines, signaling national independence in vaccine supply.

In terms of health systems and policies, Torimiro et al. (5) through the MIChep B Network demonstrated that cross-country and cross-sector collaboration can significantly improve vaccination coverage and national policy advocacy capacity. Al Awaidey et al. (9) documented the success of the GCC surveillance system with an integrated national database that allows verification of case data of HBsAg positive pregnant women in real time. Kaewdech et al. (8) recommended the public health continuum of care model to link prevention, diagnosis and treatment as a continuous system.

The synthesis also showed that there are innovative community-based strategies, such as involving local communities in vaccination campaigns and family-based education to prevent stigma (4,5). Taye et al. (14) added that population-based antiviral therapy interventions can reduce hepatitis B mortality by 35% if therapy coverage reaches 80% of the target population. The following Table 3 summarizes the key strategies identified:

5. Overview of Quantitative Synthesis

Based on the aggregate analysis of the 20 identified studies, the following key numerical patterns can be inferred:

- Average global birth dose vaccination coverage: 84%.
- Average HBsAg prevalence of children <5 years in developed countries: 0.5%.

- Average HBsAg prevalence of children <5 years old in developing countries: 1.9%.
- Indonesia's average vaccination rate (2019-2024): 68%.
- Average HBsAg detection in pregnant women (Indonesian data) was 72%.
- Global antiviral therapy coverage is average, with 4⁵% of the population chronically diagnosed.
- Estimated potential prevention of deaths due to increased vaccination: >500,000 lives (18).

The PRISMA flow diagram shows that, of the initial 135 articles, only 20 met the final inclusion criteria, demonstrating the high selectivity and relevance of this study. Yearly publication trends showed the sharpest increase from 2021 to 2024, consistent with growing scientific urgency toward global viral hepatitis elimination.

Overall, the results show that global and national hepatitis B elimination efforts continue to make progress, but face complex structural, social, and biomedical challenges. A multidimensional approach that integrates vaccine innovation, latent-infection detection, surveillance-system strengthening, and cross-sector collaboration is a dominant theme in the reviewed literature. This synthesis illustrates that hepatitis B elimination in Indonesia is inseparable from global dynamics and requires a national collaboration model that is data-driven, intersectoral, and sustainable.

Discussion

Trends and Developments in Multidimensional Approaches to Hepatitis B Elimination Efforts

Based on the synthesis of 20 articles included in this systematic review, it can be concluded that hepatitis B elimination efforts at the global and national levels have undergone a paradigm shift from a narrow biomedical approach to a multidimensional approach that

emphasizes the interconnection between biomedical, health system, and socio-cultural aspects. This shift is in line with the findings shown by Kaewdech al. (8) and Torimiro et al. (5) who emphasized that the success of hepatitis B elimination is not only determined by the effectiveness of vaccines or antiviral therapy, but also by health system capacity, policy sustainability, and community social participation. In the last two decades, this trend has intensified along with the WHO push towards viral hepatitis elimination targets by 2030, which requires each country to integrate elimination strategies into the national health system. In the Indonesian context, research results Armini et al. (4) show that the multidimensional approach is still at an early stage of implementation. The study shows that the implementation of the hepatitis B EMTCT program still faces social and administrative barriers, such as stigma toward pregnant women who are HBsAg positive and limited communication between health workers and patients. These elements illustrate the social aspects that are often overlooked in the biomedical policy framework. On the other hand, a study Armini et al. (12) reinforced these findings by showing a gap in coordination between programs at the regional level. Non-integrated surveillance data and manual reporting are important barriers to national elimination monitoring. These results suggest that although vaccination programs and elimination policies are in place, implementation remains fragmented across sectors; therefore, a multidimensional approach has not been fully realized in Indonesia.

Comparisons with other countries show that successful elimination is strongly influenced by cross-sectoral integration and political commitment. A study Torimiro et al. (5) in sub-Saharan Africa showed that inter-country and inter-agency collaboration within the MIChep B Network increased birth dose vaccination coverage to 87%, while in GCC countries, strong surveillance systems and political support resulted in a decrease in the prevalence of HBsAg in children under five years old to below 0.5% (9). This suggests that structural and governance elements have the same significance as medical advances in influencing the efficacy of elimination efforts.

The findings of this study confirm that a multidimensional approach to hepatitis B elimination is necessary for Indonesia to adopt. Expanding vaccination is not sufficient; strengthening digital surveillance systems, improving public health communication, and fostering cooperation across ministries and agencies are also required. This approach not only expands the scope of intervention but also connects the micro (biological) and macro (policy) dimensions. The scientific significance of this finding is its contribution to expanding the conceptual framework of hepatitis B elimination from the biomedical domain to a multidimensional model that includes social, structural, and health-political interactions (8).

Key Challenges in Hepatitis B Elimination Policy Implementation and Interrelationships Between Factors

The synthesis shows that the challenges to hepatitis B elimination in Indonesia and other developing countries are complex and interrelated. Based on the study results Bucio-Ortiz et al. (7), the

main biomedical challenge comes from the presence of OBI and cccDNA which makes latent infection difficult to detect and cure. Epidemiologically, the prevalence of OBI reaches 5-15% in the general population and up to 25% in high-risk groups. The presence of latent infection not only poses clinical problems but also impacts the accuracy of national surveillance data, as many cases are not recorded in the conventional HBsAg serology-based reporting system.

This limitation in latent infection detection is closely related to health-system challenges. Research by Armini et al. (12) found that EMTCT data reporting is still done manually, which causes delays and inaccuracies in information. This hinders the government's ability to validate national-level elimination achievements. Similar challenges were also identified by Kaewdech al. (8) which showed that in the Southeast Asian region, many countries including Indonesia still lack reference laboratories capable of conducting molecular tests for hepatitis B virus DNA. These limitations prevent effective monitoring of chronic and latent cases. Thus, biomedical weaknesses (latent detection) interact directly with structural weaknesses (surveillance and reporting), forming a cycle of barriers that is difficult to break.

Social and policy factors exacerbate the challenge. Research Machmud et al. (13) showed that only 15% of the Indonesian adult population had received the hepatitis B vaccine, with the main reasons being low-risk perception and the high cost of vaccination. On the other hand, Armini et al. (4) added that stigma against hepatitis B patients is still strong, especially among pregnant women, which has an impact on low participation in screening. In the socio-ecological framework, as used by Armini et al. (4), individual factors such as perceptions and family support interact with structural factors such as health policies and service infrastructure, resulting in a cumulative effect on the effectiveness of elimination programs.

This multidimensional challenge has major implications for national elimination strategies. First, without effective early detection, vaccination and therapeutic efforts cannot be properly targeted. Second, in the absence of a cohesive surveillance framework, it is impossible to formulate national policies based on reliable data. Third, without community engagement and stigma mitigation, medical interventions are likely to be ineffective due to resistance to behavior change. Consequently, these observations illustrate the complex interconnections between biomedical, health system, and social factors that present significant challenges to Indonesia's hepatitis B eradication efforts.

This study's contribution is mapping the causal relationships among the three dimensions within the context of elimination policy. Previous research by Bucio-Ortiz et al. (7) only highlighted the biomedical aspect, while Kaewdech et al. (8) focused on regional disparities, and Machmud et al. (13) focused on community behavior. This research brings them together into an integrative and contextualized analytical framework for Indonesia. Its significance lies in providing an empirical basis for designing a holistic elimination policy that integrates technical, institutional and social strategies.

Strategies and Innovations to Accelerate Achievement of Hepatitis B Elimination Targets

Strategies and innovations to accelerate hepatitis B elimination can be classified into three main dimensions: biomedical innovations, health system reforms, and socio-multisectoral approaches. In the biomedical dimension, research Zhuang et al. (11) highlights scientific advances in the form of *CRISPR-Cas9-based* gene editing therapy, RNA interference, and the small molecule CCC_R08 targeting cccDNA. Although it has not yet reached the clinical stage in humans, this research suggests a new direction toward a functional cure for chronic hepatitis B. Meanwhile, Nency et al. (20) showed that Indonesia has the capacity to produce its own hepatitis B vaccine with effectiveness and safety equivalent to international vaccines. This is a strategic innovation to strengthen national independence in vaccine supply and ensure the sustainability of the immunization program.

In terms of prevention, studies Lestari et al. (19) showed that timely vaccination of the birth dose has the greatest preventive impact. According to (19), infants who received the vaccine within the first 24 hours had a 40% lower risk of infection than infants who received the vaccine after 24 hours. It was estimated that increasing birth-dose vaccine coverage to 90% could prevent more than 500,000 deaths from hepatitis B by 2030 (18). In Indonesia, birth-dose vaccination coverage has reached only 68%, indicating considerable room for improvement.

In the health system dimension, research Al Awaidy et al. (9) showed that integrated national surveillance systems and databases of pregnant women are key factors for successful elimination in GCC countries. Torimiro et al. (5) reinforced these findings with evidence that cross-sector and cross-country networks such as the MIChep B Network are able to increase vaccination coverage and strengthen policy advocacy. Both studies demonstrate the importance of collaborative and data-driven health governance in accelerating hepatitis B elimination.

In terms of social and policy, emphasized the importance of community-based interventions to reduce stigma and increase vaccination awareness (4,13). Armini et al. (12) showed that family involvement and support from social institutions played an important role in the success of the EMTCT program in Bali. These findings suggest that innovative community-based strategies are as important as medical interventions.

The significance of these results lies in understanding that no single strategy is sufficient to achieve hepatitis B elimination. Successful elimination requires a multi-layered approach: strengthened primary vaccination, improved detection of latent infection, expanded antiviral therapy, and an integrated national surveillance system. This study makes a conceptual contribution by developing an integrative model that explains the synergistic relationship between these strategies in the Indonesian context. It expands scientific understanding of how medical, systemic, and social innovations can interact to accelerate hepatitis B elimination in developing countries.

Scientific Significance and Contribution to Scientific Fields

Conceptually, this study contributes to expanding the hepatitis B elimination paradigm from a biomedical approach to a multidimensional and multisectoral one. The findings of this study reinforce the view that successful elimination cannot be measured only through medical indicators such as vaccination coverage or the number of patients treated, but also through social indicators such as the level of public awareness, data system integration, and cross-agency participation. By integrating the findings of Bucio-Ortiz et al. (7), Kaewdech et al. (8) and Torimiro et al. (5) this study forms a scientific framework that explains that hepatitis B elimination is the result of synergies between technological innovation, institutional reform, and social adaptation (4).

The empirical contribution of this study lies in the synthesis of cross-study findings relevant to the Indonesian context, providing a scientific basis for the formulation of a more comprehensive national elimination policy. In addition, the practical contribution is to provide evidence-based recommendations to strengthen surveillance systems, improve diagnostic capacity, and expand community-based interventions. This study enriches the scientific literature in global public health, chronic infection epidemiology, and health policy in developing countries.

Policy and Practical Implications

The findings of this study have several important policy implications. First, strengthening the integrated surveillance system is a key prerequisite for hepatitis B elimination. The Indonesian Ministry of Health needs to integrate EMTCT reporting into a national digital information system to avoid data redundancy. Second, the involvement of non-health sectors, such as education and media, needs to be expanded in hepatitis B awareness campaigns to reduce social stigma as identified by Armini et al. (4). Third, strengthening molecular diagnostic capacity is needed to detect OBI and ensure accurate prevalence data, as recommended by Bucio-Ortiz et al. (7). Fourth, domestic vaccine production needs to be expanded and subsidized to ensure the sustainability of the birth dose immunization program, as supported by the findings of Nency et al. (20).

Another scientific implication is the need for an interdisciplinary research approach that involves biomedical, public health, and social sciences to understand the complexities of hepatitis B elimination in Indonesia.

Study Limitations

This study has several limitations that need to be recognized. This analysis includes only Scopus-indexed articles from 2019-2025 that meet the Q1-Q2 journal criteria; consequently, some relevant literature may be excluded. Secondly, most of the data were derived from secondary reports and systematic reviews that do not always exhibit methodological uniformity. Third, this study did not conduct a quantitative meta-analysis because of heterogeneity in research results and variation in indicators across studies. Fourth, limited access to primary data in Indonesia implies that some conclusions

remain are conceptual and cannot be statistically verified. However, these limitations do not diminish the validity of the findings, as this analysis remains grounded in scientific evidence from credible and relevant literature (Figure 3).

The results of this study confirm that hepatitis B elimination in Indonesia is a multidimensional challenge requiring an integrative, multisectoral approach. This study makes a significant contribution to identifying the linkages among biomedical, health system, and social dimensions and offers a conceptual framework to understand the complex interactions among these factors. By emphasizing vaccination innovation, detection of latent infection, integrated surveillance systems, and strengthened social collaboration, this study contributes to the development of a contextualized and sustainable hepatitis B elimination policy model for Indonesia.

Conclusion

This review demonstrates that hepatitis B elimination in Indonesia remains constrained by interconnected biomedical, health system, and socio-behavioral barriers. Strengthening surveillance systems, expanding birth-dose vaccination, improving molecular diagnostic capacity, and enhancing multisectoral collaboration are essential to

accelerate elimination efforts. These findings provide an evidence-based framework to guide the development of future hepatitis B elimination policies in Indonesia.

Suggestions for Future Research

Further empirical studies using primary data are recommended to test the conceptual model generated in this study. An important focus is the direct measurement of the effectiveness of multisectoral strategies, including inter-ministerial collaboration, the role of local communities, and the impact of surveillance digitization policies. Longitudinal studies assessing the relationship between increased molecular laboratory capacity and reduced prevalence of chronic hepatitis B in Indonesia are also needed. In addition, future studies should integrate a mixed-methods approach to better capture social dynamics and community behavior. Researchers also need to evaluate the economic efficiency of national vaccine innovations and community-based EMTCT programs. Thus, future research will not only strengthen the scientific basis for hepatitis B elimination policies but will also directly contribute to achieving the global target of viral hepatitis elimination by 2030 in the Indonesian context.

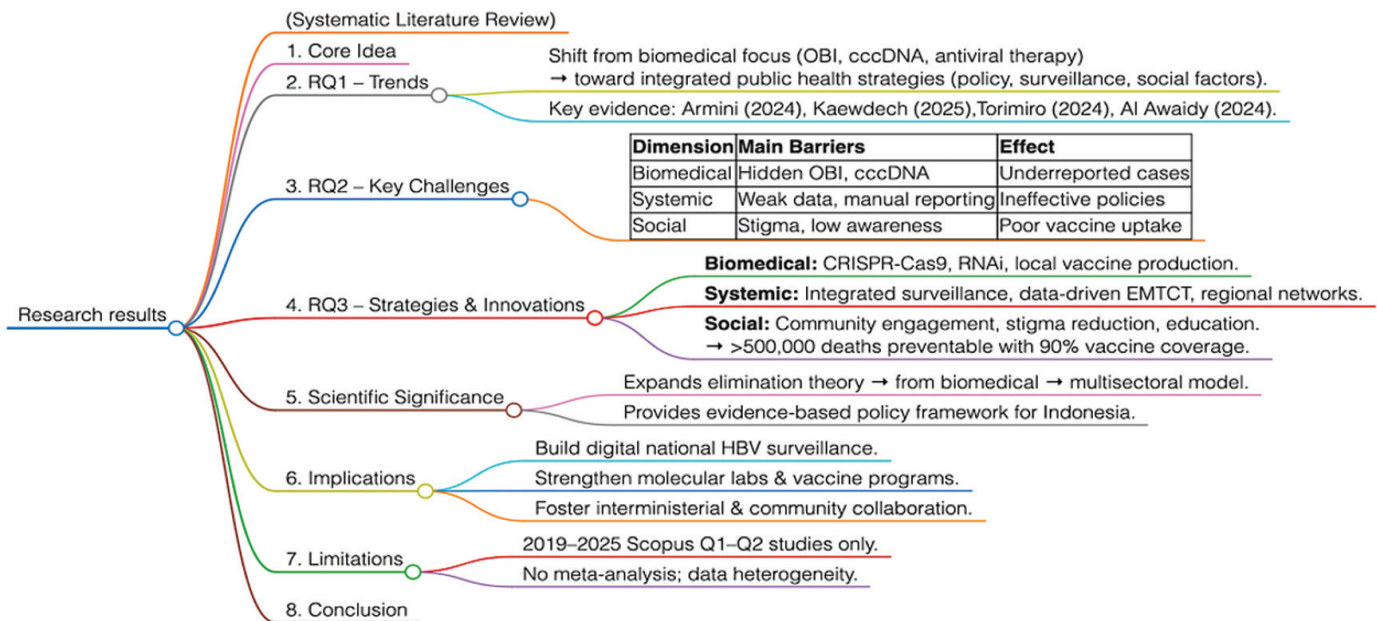


Figure 3. Mind map of research outcomes: trends, barriers, and policy implications for HBV elimination

OBI: Occult hepatitis B infection, cccDNA: Covalently closed circular DNA, HBV: Hepatitis B virus, EMTCT: Elimination of mother-to-child transmission

Footnotes

Authorship Contributions

Concept: N.T., A.A., Design: N.T., A.S.K., Data Collection or Processing: N.T., V.A.R., Analysis or Interpretation: N.T., M.S.J., Literature Search: N.T., A.A., M.S.J., Writing: N.T., V.A.R.

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References

- Haering C, McMahon B, Harris A, Weis N, Lundberg Ederth J, Axelsson M, Olafsson S, Osiowy C, Tomas K, Bollrup S, Liitsola K, Archibald C, Blystad H, Bruce M, Nolen L. Hepatitis B virus elimination status and strategies in circumpolar countries, 2020. *Int J Circumpolar Health*. 2021;80:1986975.
- Tang J, Luo YQ, Zhou YH. Elimination of hepatitis B virus infection in children: experience and challenge in China. *Chin Med J (Engl)*. 2021;134:2818-2824.
- Zheng H, Walsh N, Lesi O, Cui F. New progress towards elimination of mother-to-child transmission of hepatitis B virus in China. *Hepatol Int*. 2022;16:1273-1281.
- Armini LN, Setiawati EP, Arisanti N, Hilmanto D. Patient perspective on the elimination mother-to-child transmission of HIV, syphilis, and hepatitis B in Bali, Indonesia: a qualitative study. *BMC Public Health*. 2024;24:2258.
- Torimiro JNE, Duri K, Gourmkwa NM, Atah SM, Ndzie Ondigui JL, Lobe C, Bouyou M, Ndeboko B, Mahamat Moussa A, Police C, Awoumou P, Peyonga P, Djivida PV, Felix A, Nchinda GW, Wandji B, Simo RK, Agnès Moudourou S, Gutierrez A, Garcia R, Fernandez I, Mah E, Rowland-Jones S, Mbu R. Toward the elimination of hepatitis B: networking to promote the prevention of vertical transmission of hepatitis B virus through population-based interventions and multidisciplinary groups in Africa. *Front Public Health*. 2024;12:1283350.
- Cohn J, Owiredun MN, Taylor MM, Easterbrook P, Lesi O, Francoise B, Broyles LN, Mushavi A, Van Holten J, Ngugi C, Cui F, Zachary D, Hailu S, Tsiouris F, Andersson M, Mbori-Ngacha D, Jallow W, Essajee S, Ross AL, Bailey R, Shah J, Doherty MM. Eliminating mother-to-child transmission of human immunodeficiency virus, syphilis and hepatitis B in sub-Saharan Africa. *Bull World Health Organ*. 2021;99:287-295.
- Bucio-Ortiz L, Enriquez-Navarro K, Maldonado-Rodríguez A, Torres-Flores JM, Cevallos AM, Salcedo M, Lira R. Occult hepatitis B virus infection in hepatic diseases and its significance for the WHO's elimination plan of viral hepatitis. *Pathogens*. 2024;13:662.
- Kaewdech A, Charatcharoenwitthaya P, Piratvisuth T. Asian perspective on hepatitis B virus and hepatitis C virus elimination. *Viruses*. 2024;17:34.
- Al Awaidey S, Tohme RA, Al Romaihi HE, Ezzikouri S, Mahomed O. Elimination of mother-to-child transmission of hepatitis B virus in gulf cooperation council countries: current status and future prospects. *Am J Trop Med Hyg*. 2023;110:32-35.
- Lu FT, Ni YH. Elimination of mother-to-infant transmission of hepatitis B virus: 35 years of experience. *Pediatr Gastroenterol Hepatol Nutr*. 2020;23:311-318.
- Zhuang AQ, Chen Y, Chen SM, Liu WC, Li Y, Zhang WJ, Wu YH. Current status and challenges in anti-hepatitis B virus agents based on inactivation/inhibition or elimination of hepatitis B virus covalently closed circular DNA. *Viruses*. 2023;15:2315.
- Armini LN, Setiawati EP, Arisanti N, Hilmanto D. Evaluation of process indicators and challenges of the elimination of mother-to-child transmission of HIV, syphilis, and hepatitis B in Bali province, Indonesia (2019-2022): a mixed methods study. *Trop Med Infect Dis*. 2023;8:492.
- Machmud PB, Führer A, Gottschick C, Mikolajczyk R. Barriers to and facilitators of hepatitis B vaccination among the adult population in Indonesia: a mixed methods study. *Vaccines (Basel)*. 2023;11:398.
- Taye BW, Valery PC, Clark PJ. Targeted antiviral treatment of hepatitis B virus in culturally and linguistically diverse populations to achieve elimination targets in Australia. *J Viral Hepat*. 2022;29:868-878.
- de Almeida NAA, de Paula VS. Occult hepatitis B virus (HBV) infection and challenges for hepatitis elimination: a literature review. *J Appl Microbiol*. 2022;132:1616-1635.
- Hui Z, Nayagam S, Chan P, Fuzhen W, Thursz M, Zundong Y, Ning M, Xiaojin S, Cui F, Guomin Z, Hallett TB. Progress towards elimination of mother-to-child transmission of hepatitis B virus infection in China: a modelling analysis. *Bull World Health Organ*. 2021;99:10-18.
- Brancaccio G, Coco B, Nardi A, Quaranta MG, Tosti ME, Ferrigno L, Cacciola I, Messina V, Chessa L, Morisco F, Milella M, Barbaro F, Ciancio A, Russo FP, Coppola N, Blanc P, Claar E, Verucchi G, Puoti M, Zignego AL, Chemello L, Madonia S, Fagioli S, Marzano A, Ferrari C, Lampertico P, Di Marco V, Craxi A, Santantonio TA, Raimondo G, Brunetto MR, Gaeta GB, Kondili LA; PITER collaborating investigators. Trends in chronic hepatitis B virus infection in Italy over a 10-year period: clues from the nationwide PITER and MASTER cohorts toward elimination. *Int J Infect Dis*. 2023;129:266-273.
- de Villiers MJ, Nayagam S, Hallett TB. The impact of the timely birth dose vaccine on the global elimination of hepatitis B. *Nat Commun*. 2021;12:6223.
- Lestari CSW, Dewi RM, Sunarno S, Hasugian AR, Handayani S, Maha MS, Panjaitan NSD, Ningrum N, Sari M, Fairuza F. The effectiveness of hepatitis B vaccine in toddlers based on the five-year period national basic health research (Riskesdas 2007, 2013 and 2018) in Indonesia. *PeerJ*. 2023;11:e15199.
- Nency YM, Rahmadi FA, Mulyono, Anantyo DT, Farhanah N, Hapsari R, Farida H, Sadhana U, Djagat H, Kristina TN, Juniarto AZ, Puspita M, Sari RM, Bachtiar NS. Protectivity and safety following recombinant hepatitis B vaccine with different source of bulk compared to hepatitis B (Bio Farma) vaccine in Indonesia. *Clin Exp Vaccine Res*. 2022;11:43-52.