Hepatitis B vaccination for adult population in Indonesia: results of a systematic review, quantitative and qualitative study

Thesis

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by Putri Bungsu Machmud

Supervisor: Prof. Dr. Rafael Mikolajczyk
Reviewers:
1. apl. Prof. Dr. Susanne Unverzagt, Halle (Saale)
2. Jun.-Prof. Dr. Ina Danquah, Heidelberg

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Abstract

In 2020, the World Health Organization (WHO) reported that approximately 900,000 deaths are caused each year by hepatitis B virus infection. Therefore, the WHO has encouraged all countries to reduce hepatitis incidence and mortality rates in a mission to eliminate hepatitis viruses as a global threat. One of the targets in achieving this is ensuring universal access to prevention services (vaccination and testing) as well as the treatment of hepatitis in at-risk populations, including healthcare workers.

Indonesia is an intermediate-to-high endemic region for the hepatitis B virus, rated as one of 11 countries carrying almost 50% of the global burden of chronic hepatitis. The Indonesian Ministry of Health reported that approximately 20 million people were diagnosed with chronic hepatitis B in 2013. This work is a cumulative doctoral thesis that integrates four studies. The first included study was a systematic review designed to summarise the available evidence to identify predictors of the levels of knowledge and vaccination status of hepatitis B, as well as why people choose not to be vaccinated against hepatitis B in developing countries. The second was a study that analysed secondary data, which was provided by the 2017 Indonesian Demographic Health Survey to assess the association between media use and children's vaccination status. I also conducted an institutional-based cross-sectional survey Indonesia to assess factors associated with the willingness to be vaccinated against hepatitis B among Indonesia's adult population. Finally, a mixed-methods study was conducted to identify barriers to and facilitators of hepatitis B vaccination programmes. The systematic review identified various essential predictor variables, such as income, education, and health insurance, as influencing hepatitis B knowledge levels and vaccination status across studies. Our survey revealed that 7% more participants from Yogyakarta were willing to accept a hepatitis B vaccination than those from Aceh, which may have a significant effect when extrapolated to a population such as Indonesia's. Finally, as a result of our mixed-methods study, six factors were identified as barriers to and facilitators of vaccine uptake, according to both the general population and government.

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Referat

Die Weltgesundheitsorganisation (WHO) berichtete, dass im Jahr 2020 etwa 90.000 Todesfälle pro Jahr auf eine Infektion mit dem Hepatitis-B-Virus zurückzuführen sind. Aus diesem Grund hat die WHO alle Länder aufgerufen, die Inzidenz und die Sterblichkeitsraten von Hepatitis zu senken, um Hepatitis-Viren als globale Bedrohung zu eliminieren. Eines der Ziele, um dies zu erreichen, ist die Gewährleistung des allgemeinen Zugangs zu Präventionsmaßnahmen (Impfungen und Tests) sowie zur Behandlung von Hepatitis in Risikogruppen, wie Gesundheitswesen. Indonesien ist eine Region mit mittel- bis hoher Endemie für das Hepatitis-B-Virus und gehört zu den 11 Ländern, die fast 50% der weltweiten Belastung durch chronische Hepatitis tragen. Das indonesische Gesundheitsministerium berichtete, dass im Jahr 2013 bei etwa 20 Millionen Menschen mit chronischer Hepatitis B diagnostiziert wurden.

Diese Arbeit ist eine kumulative Doktorarbeit, die vier Studien umfasst. Die erste Studie handelt es sich um eine systematische Übersichtsarbeit, die das verfügbare Evidenzmaterial zusammenfasste, um die Prädiktoren für den Wissensstand und den Hepatitis-B-Impfstatus sowie die Gründe dafür zu identifiziern, warum sich Menschen in Entwicklungsländern nicht gegen Hepatitis B impfen lassen. Die zweite Studie analysierte Sekundärdaten aus dem *2017 Indonesian Demographic Health Survey*, um die Verbindung zwischen Mediennutzung und Impfstatus von Kindern zu untersuchen. Außerdem wurde eine institutionenbasierte Querschnittserhebung durchgeführt in Indonesien analysiert wurden, um Faktoren zu bewerten, die mit der Impfbereitschaft gegen Hepatitis B in der erwachsenen Bevölkerung in Indonesien in Verbindung stehen. Schließlich wurde eine Studie mit gemischten Methoden durchgeführt, um die Hindernisse und die Erleichterungen von Hepatitis-B-Impfprogrammen. Unsere Studie hat verschiedene wesentliche Prädiktorvariablen identifiziert, wie Einkommen, Bildungsstand und Krankenversicherung, die den Wissensstand über Hepatitis B und den Impfstatus beeinflussen. Unsere Umfrage ergab, dass 7% mehr Teilnehmer aus Yogyakarta bereit waren, sich gegen Hepatitis B impfen zu lassen als diejenigen aus Aceh, was bei einer Extrapolation auf eine Bevölkerung wie die indonesische einen erheblichen Einfluss haben könnte. Schließlich haben wir durch unsere Studie mit gemischten Methoden sechs Faktoren identifiziert, die sowohl für die allgemeine Bevölkerung als auch für die Regierung als Hindernisse und Erleichterungen bei der Impfaufnahme gelten.

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1. Introduction and objectives

1.1. Hepatitis B infection

Hepatitis B is an infectious viral disease borne by blood and body fluids, including saliva, as well as menstrual, vaginal, and seminal fluids [1]. The acute hepatitis B virus may be detected last up to 6 months, with or without symptoms [2]. Most people with acute hepatitis B infection have no symptoms, but some people experience mild symptoms that appear 60-150 days after infection such as loss of appetite, joint and muscle pain, low-grade fever, and abdominal pain [2]. Some people also experience more severe symptoms such as nausea, vomiting, jaundice (yellowing of the eyes and skin), and abdominal bloating that require medical treatment and care [2]. Although acute hepatitis B infection is curable through, a rare life-threatening condition known as "fulminant hepatitis" can occur in new acute infections and requires immediate and urgent medical attention as a person can develop sudden liver failure [2].

Hepatitis B attacks the liver and also causes chronic infections, such as chronic hepatic disease and liver cancer [3]. People are diagnosed with chronic hepatitis B infection when their immune system cannot get rid of the hepatitis B virus in the blood and heart, resulting in a positive blood test result showing hepatitis B for more than six months since the first blood test result [2]. The risk of chronic hepatitis B is inversely related to age: 90% of newborns and infants, 50% of children aged 1 to 5 years, and 5 to 10% of adults. [2].

Hepatitis B infection can be transmitted from an infected person to an uninfected person both horizontally and vertically [4]. The vertical transmission of hepatitis B infection occurs from mother to child, which is known as perinatal transmission [5]. Meanwhile, medical activities, sexual activities, and other modes of contamination via infected blood—such as surgical activities, blood transfusions, dental procedures, the reuse of needles and syringes among injecting drug users (IDUs), and tattooing—comprise examples of the horizontal transmission of hepatitis B infection [5]. Therefore, the following groups constitute high-risk populations for hepatitis B infection: healthcare workers and public safety personnel with reasonably anticipated risk for exposure to blood or blood-contaminated body fluids, children with hepatitis-infected mothers, person at risk for infection by sexual exposure (sex partners of persons who test positive for hepatitis B surface antigen, sexually active persons who are not in a long-term, mutually monogamous relationships, persons seeking evaluation or treatment for a sexually transmitted infection, men who have sex with men), people with current or recent injection use, indigenous peoples and minorities, prisoners, migrants, blood donors, individuals with diabetes at the discretion of the treating clinician, persons with hepatitis C virus infection, persons with HIV infection, persons with chronic liver disease, haemodialysis patients

(including in-centre or home haemodialysis and peritoneal dialysis, and persons who are pre-dialysis), residents and staff of facilities for persons with developmental disabilities, and international travellers to country with high or intermediate levels of endemic hepatitis B virus infection (Hepatitis B surface antigen (HbsAg) Prevalence of ≥2%) [6,7].

Currently, hepatitis B infection is widely known as a significant global health challenge, with more than 257 million people worldwide living with chronic hepatitis B infection in 2015, and 1.1 million people being newly infected with chronic hepatitis B infection in 2017 [7,8]. Moreover, approximately 900,000 deaths are caused each year by hepatitis B virus infection [9]. The World Health Organization (WHO) also reported that the South-East Asia region has the fourth-highest burden of hepatitis B infection after the Western Pacific, African, and Eastern Mediterranean regions, accounting for 18 million people with chronic hepatitis B [1].

Indonesia is one of eleven countries carrying almost 50% of the global burden of chronic hepatitis [1] and currently ranks as the country with the second-highest number of hepatitis B infections in the Asia Pacific region after India, contributing up to 74% of global deaths caused by liver cancer [10]. According to the 2013 Indonesian National Health Survey, the prevalence of hepatitis B in Indonesia reached 21.8%, and the country was considered to be a moderate to high endemic area of the hepatitis B virus [10-12]. This percentage also significantly impacts the absolute number of hepatitis B cases, with the population of Indonesia being nearly 250 million people [10,12,13].

Liver cirrhosis due to hepatitis is one of the eight high-cost diseases covered by the Indonesia National Health Insurance during 2014-2016 with a total cost of 151 billion rupiah for the treatment of 151 cases of hepatitis B infection with life-threatening complications or catastrophic diseases and 141,440 cases of chronic hepatitis B; and 43 billion rupiah for promotes and preventive costs in the hepatitis program [13]

Unfortunately, recent data on hepatitis B in Indonesia are limited. For example, the 2013 Indonesian National Health Survey reported the percentage of hepatitis B infection reached 7.1%, with the most common type of hepatitis virus is hepatitis B (21.8%) [14]. Currently, the latest Indonesian National Health Survey (2018) only report the number of hepatitis cases without specifying the type of hepatitis that based on the result of hepatitis diagnose (0.40%)[15]. We believe that these figures remain underestimated given that only 9% (22 million) of the 257 million people living with hepatitis B infection knew about their diagnoses in 2015; furthermore, only 8% (1.7 million) of those diagnosed had received hepatitis B treatment according to the 2017 Global Hepatitis Report [7].

1.2. Hepatitis B programmes

1.2.1. Global hepatitis programmes

Globally, the WHO has aimed to reduce 90% of hepatitis incidence and 65% of the hepatitis mortality rate compared to the baseline data of 2015[1] in the mission to eliminate hepatitis viruses using multiple approaches [16]. First, prevent infection among infant through the vaccination [17], which are given starting at the first 24 hours after the birth of the child and followed by at least 2 additional doses [18]. The complete hepatitis B vaccination series among children induce more than 95% protection and prevention of infection [18].

The second approach includes routine testing and treatment for hepatitis B, HIV, and syphilis among pregnant women to stop vertical transmission [17]. The WHO has reported that hepatitis B transmission from mother to child at the time of birth, shortly after birth, or in early childhood leads to a high rate of chronic hepatitis B [19]. Therefore, since 2020, WHO recommended test positive of hepatitis B infection for pregnant and followed by providing prophylaxis from the 28th week of pregnancy until at least birth under certain conditions [18].

The third approach involves expanding access to testing and treatment to prevent liver cancer and other severe liver conditions [17]. Two crucial components of hepatitis pandemic response are testing and diagnoses due to both of them are the beginning of prevention and treatment. Unfortunately, in 2016, only 10% (27 million) of people whom living with hepatitis B knew their status [16,20]. Testing also influence to reduce transmission related to health care injection, blood safety, hepatitis B vaccination, and harm reduction services [21]. Other than that, a treatment of long-term antiviral with Tenofovir and Entecavir are available for people who are eligible for treatment with chronic hepatitis B infection [22]. This antiviral treatment aims to reduce mortality and risk of related complications such as liver failure and hepatocellular carcinoma [22].

The fourth approach ensures that everyone, including high-risk populations such as healthcare workers, people who inject drugs, people in prisons, and migrants, has access to hepatitis prevention, testing, and treatment services, also called “Leaving No One Behind” [17]. Some studies have claimed that the hepatitis B vaccination rate is low among healthcare workers [23-26]. For instance, our systematic review in developing countries [M1] revealed that the median proportion of having at least one dose and having complete doses of hepatitis B vaccines among

[1] Incidence: between 6 and 10 million infections to be reduced to 0.9 million infections by 2030 (95% decline in hepatitis B virus infections, 80% decline in hepatitis C virus infections); prevalence: 1.4 million deaths reduced to less than 500,000 by 2030 (65% for both viral hepatitis B and C infections).

healthcare workers were less than 60% and 50%, respectively [27]. To ensure vaccination of people at risk of hepatitis B infection, health care providers should offer hepatitis B vaccination to all adults aged 19-59 years visiting health services who have never been vaccinated, and adults aged >60 years who have hepatitis B risk factors or who are not identified as having risk factors but wish to be protected, and provide hepatitis B vaccination to people at risk of hepatitis B infection [28].

The last approach involves preserving the fundamental services for hepatitis patients during the Covid-19 pandemic, such as immunisation, harm-reduction services, and the continuous treatment of chronic hepatitis B. The COVID-19 pandemic in the first quarter of 2020 has had a significant impact on several health programs, including hepatitis B. For example, longer hospitalization days for hepatitis B patients in 2020 compared to the same period in 2019 and an increased risk of death from COVID-19 in patients with a history of chronic liver disease, especially in patients with liver cirrhosis. In addition, in Indonesia, there was a decrease in hepatitis B early detection coverage in January-April 2020, which was only half of the coverage in the same period in 2019 [29].

1.2.2. Hepatitis programmes in Indonesia

As an intermediate-to-high endemic region for hepatitis B, the Indonesian Ministry of Health began a hepatitis B programme strategy reinforced by the issuing of comprehensive hepatitis virus regulations through promotion, prevention, early detection, and sub-management approaches in 2015 [30], followed by the initiation of free hepatitis B vaccinations for children aged 0 to 11 months in 2017 [31]. In addition, a programme that focuses on the elimination of vertical transmission from mother to child was also launched in the same year [32].

The first universal infant hepatitis B immunization project in Indonesia was conducted from 1987 to 1991 and is known as the "Lombok Hepatitis B Model" [33]. The project aimed to integrate the hepatitis B vaccine into the National Immunization Program, including a targeted birth dose to be administered as soon as possible in the first week after birth. The project achieved >90% coverage for hepatitis B vaccine administration and was able to demonstrate a reduction in hepatitis B prevalence among children under four years of age who had received three doses of vaccine [33].

In 1991, routine hepatitis B immunization in Indonesia was implemented in four provinces: West Nusa Tenggara, Bali, Yogyakarta, and five districts in East Java. In the same year, immunization for newborns (hepatitis B zero-dose) was also recommended [33]. Subsequently, during the period 1992-1995, routine immunization programs in Indonesia were conducted, but not all infants born to hepatitis B-infected mothers received hepatitis B immunoglobulin [33].

In 2022, Indonesia began working to develop a strategic roadmap to gradually eliminate viral hepatitis [29]. The roadmap aims to eliminate hepatitis B and hepatitis C in order to reduce public health problems in Indonesia related to hepatitis viruses—by the end of 2030 for hepatitis B and the end of 2040 for hepatitis C [29]. The following seven strategic issues are summarised in this plan: increasing public awareness of the importance of hepatitis viral prevention from an early age, ranging from examinations during pregnancy, giving complete immunization on time, avoiding risky behaviour and finding tests and treatment; the availability of data and strategic information; the availability of high-quality, affordable vaccines, medication, and diagnosis tools; health services for the early detection and management of standard hepatitis; health safety services for patients, including compliance with the application of awareness of standards and safe blood availability; collaboration between hepatitis treatment providers and other sectors or institutions; and the equalisation of hepatitis B and C services in all regions of Indonesia [29].

This strategic direction will be realized in 2020-2024 through the following approaches: providing quality treatment services without stigma and discrimination; expanding access to services and strengthening service referral networks; ensuring the availability of vaccine commodities, hepatitis B immune globulin, reagents, and drugs; expanding hepatitis B and C early detection services; improving the quality of services in health facilities in accordance with the National Guidelines for Medical Practice and Program Management Guidelines; increasing the capacity of health workers to provide quality services without stigma and discrimination [29]. This approach upholds equity, which is a key principle of universal health coverage: everyone gets the services they need, regardless of their socioeconomic circumstances and geographical position, with adequate quality [29].

The strategy to be used refers to the WHO global strategic direction for hepatitis prevention and control, which is based on the Universal Health Coverage Framework [34]. Program planning is based on data obtained through a strategic information system consisting of two main activities, namely surveillance and monitoring and evaluation [29]. Data obtained through these two activities are reviewed in program planning at the national, provincial, and district/city levels to identify needs, design high-impact responses, allocate resources effectively, guide implementation, and strengthen accountability [29].

Interventions for viral hepatitis are part of an important package of high-impact interventions, in addition to interventions for Human Immunodeficiency Virus (HIV) and Sexually Transmitted Infections (STIs) [29]. Impactful interventions for viral hepatitis include what services are needed during prevention, diagnosis, and ongoing treatment, care, and support [29]. One approach in prevention programs is to provide free immunization for health workers to prevent vaccine-preventable diseases and increase the coverage of hepatitis B zero-dose and hepatitis B immune globuline immunization in less than 24 hours in infants born to HBsAg-reactive

mothers [29]. In addition, there are several other approaches related to the prevention of hepatitis B transmission: increasing knowledge through socialization about viral hepatitis to prevent transmission, improving prompt and appropriate treatment-seeking behavior, and reducing stigma and discrimination for high-risk groups and people living with HIV/Acquired Immune Deficiency Syndrome (AIDS); behavior change interventions for high-risk groups; safety of donor blood from blood-borne diseases; and access to a comprehensive package of harm reduction services for IDUs [29].

Meanwhile, strategies on the diagnosis approach include the integration of viral hepatitis testing into program management and technical guidelines, as well as cross-sector policies related to the detection of blood-borne infections; advocacy and technical support to mobilize cross-sector commitment for early detection of hepatitis B and C; and laboratory management for screening and referral for hepatitis B and C diagnosis. In addition, strategies related to treatment, care and support include the development of referral networks between screening services at primary health facilities and treatment services at advanced referral health facilities and other supporting services, and increasing the capacity of health workers in hospitals, especially internal medicine specialists to be able to provide hepatitis B and C management.

Indonesia also plans to provide innovative activities that will be carried out in the 2020-2024 period. One of these innovative activities is the development of operational studies that include the ability of antiviral prophylaxis interventions to strengthen the prevention of mother-to-child transmission of hepatitis B in addition to the administration of hepatitis B vaccine and hepatitis B immune globulin at 1 x 24 hours after birth. In addition, electronic-based active surveillance of hepatitis B and C in at-risk populations integrated with other programs will be developed in this program. However, globally, financing of hepatitis prevention and control programs is still insufficient to achieve program targets. Financing hepatitis elimination programs is expected to add about 1.5% to the total universal health coverage package [29]. This additional investment is predicted to reduce mortality by 5% and result in an additional 9.6% life expectancy [35].

1.3. State of research, objectives, and research questions

According to WHO, there are four main components of achieving high vaccination uptake: what people think and feel (confidence in vaccine benefit and safety, perceived risk, and seeing negative information); social process (influential other support vaccination, vaccination norms, workplace norms, decision and travel autonomy, and trust in vaccine providers); motivation (intention to get vaccine); and practical issues (know where vaccine is available, ease of access, and availability of on-site vaccination) [36].

In addition, Jung et al., claimed that vaccination coverage is strongly associated with individuals' media exposure and seeking out of information, as well as the mediating effects of related knowledge and neighbourhood social capital such as norm and local-culture [37]. This study found that vaccination is not only closely related to exposure to cable television and national television news, but also has a strong relationship with knowledge and social capital in the neighbourhood as significant mediators that positively impact one's willingness to accept vaccination [37]. Kaufman et al. also indicated that social processes influence vaccine uptake motivations and ideas about the need for vaccination form from individuals' exposure to information that impacts their knowledge about the effects of vaccination [38].

We believe several other barriers may pose severe challenges before adult hepatitis B vaccination as a mandatory vaccination can be effectively introduced as a requirement in Indonesia. Therefore, the present thesis explores the issues, barriers, facilitators, and predictor variables affecting adult hepatitis B vaccination uptake in Indonesia.

The following research questions are addressed:

1. What socio-demographic characteristics influence hepatitis B vaccination status among the adult population in Indonesia?
2. How do system information of dissemination, social processes, and practical issues influence knowledge levels and risk perceptions of hepatitis B that impact hepatitis B vaccination status among the adult population in Indonesia

2. Discussion

This thesis discusses adult hepatitis B vaccination in Indonesia based on four previous studies. This chapter discusses the main results and methodological strengths and weaknesses as well as concludes the research.

To prepare the survey in Indonesia, we first conducted a systematic review [M1] aiming to identify predictors of hepatitis B vaccination knowledge levels and status, as well as reasons why people choose not to be vaccinated against hepatitis B in developing countries. The review summarised the results of studies involving developing countries during the last ten years using the following four databases: MEDLINE, Embase, Web of Science, and CINAHL. Eighty-nine that met the eligibility criteria were included, resulting in an overall sample size of 73,988 participants. More than 90% of the studies were conducted in Asia and Africa, and 48.3% were hospital/health facility-based studies. Almost all articles (97.8%) were cross-sectional studies, with the remaining (2.2%) being case-control and retrospective cohort studies. Fifty-eight studies (65.2%) included knowledge of hepatitis B as an outcome and 69 studies (77.5%) assessed the uptake of hepatitis. The systematic review showed various important determinants for the level of knowledge and vaccination status across studies, which monthly income, level of education, and profession as health care worker were known as the strongest predictive factors for hepatitis B knowledge and vaccination status. The strong influence for hepatitis B knowledge was being ever screened for hepatitis B, while health insurance, management's protection at workplace, experience in infection training on hepatitis B, and experience of hepatitis B exposure were strong predictors for vaccine uptake. Other than that, this review found that lack of motivation, lack of information, and lack of money were three major reasons for people to avoiding hepatitis B vaccination in developing countries.

We also analysed secondary data provided by the 2017 Indonesian Demographic Health Survey (2017 IDHS) [M2], which is part of the international DHS program designed to collect fertility, family planning, maternal and child health data, to assess the effects of media use and predictor variables on child vaccine coverage in Indonesia. This study included 7,867 mothers with a child older than one year from all provinces in Indonesia. The outcome of this study was the primary vaccination status for children aged 0 to 11 months, which reported based on mother's recall. While, the media use variable was assessed based on the year before the 2017 IDHS and compiled from two variables: frequency and type of media use. This study found positive associated between media use among mothers and children's vaccination status, which there was some indication of a dose-response pattern, in the sense that irregular media use among mothers increased children's partial immunisation, but had a lesser benefit to ensure the completeness of vaccination. In addition, regular media use by mothers increased partial

immunization compared to no vaccination, and further increased complete immunization compared to no vaccination.

The third study was an institution-based cross-sectional survey [M3] that aimed to assess factors predicting hepatitis B vaccination willingness among the adult population in Indonesia. This conducted in sixteen-selected heath centre from December 2019 to July 2020 in two Indonesian provinces, Aceh and Yogyakarta. These regions were selected according to the results of the Indonesian National Survey conducted in 2018, reported that Yogyakarta Province had the highest vaccination coverage within the existing program (83.7% with complete vaccination, 16.3% with incomplete vaccination, and none without vaccination), while Aceh Province was reported to have the lowest coverage (19.5% with complete vaccination, 16.3% with incomplete vaccination, and 40.9% never vaccinated) [14]. In addition, this survey considered cultural and geographical differences by including rural and urban for each province. This study involved health care workers (a person who works in a health center with both medical and non- medical backgrounds, such as medical doctors, dentists, nurses, midwives, analysts, pharmacy, helpers, administrative personnel, drivers, cleaners, and security personnel) and outpatients (a person who was registered as an outpatient at the health center on the same day that the data were collected) were included in this study. In total, 757 (84.6%) participants: 373 (49.3%) from Aceh and 384 (50.7%) from Yogyakarta were analysed in this study. Our survey identified that 7% more participants from Yogyakarta are willing to accept a hepatitis B vaccination than from Aceh, which may result in a large effect due to applied into a population such as Indonesia's. Some factors associated with the willingness to be vaccinated are a fair and high knowledge of hepatitis B infection and vaccination, being female, and having health insurance covering hepatitis B vaccination costs. In Aceh, health care workers in high-risk units for hepatitis B had a higher willingness to be vaccinated than those who were not high-risk health care workers. In addition, high-risk perception of hepatitis B infection and vaccination was the common factor associated with a high willingness to get vaccinated against hepatitis B both in Yogyakarta and Aceh.

Fourth and finally, we performed an explanatory sequential mixed-methods study [M4]. A cross-sectional survey (December 2019 to July 2020), followed by a qualitative study (May–July 2021) was conducted to investigate the vaccination uptake for hepatitis B among adults in the population and assessed current hepatitis B programmes as well as barriers to and facilitators of hepatitis B vaccination. This study used mixed method design from two different sides: the population and the government that described potential discrepancies and correspondences of barriers and facilitators of adult hepatitis B programmes in Indonesia. The survey aimed to investigate the knowledge, risk-perception, willingness to get vaccinated, and

vaccination status, as well as the reasons for not getting vaccinated in relation to hepatitis B, among the adult population. The data were collected through face- to-face interviews conducted by the interviewers. The qualitative study assessed the current hepatitis B programme as well as barriers to, and facilitators of, hepatitis B vaccination from the government's perspective, through in-depth interviews. We involved informants for qualitative study from the Ministry of Health's three directorates: the Directorate of Communicable Disease Prevention and Control, the Directorate of Immunization, and the Directorate of Health Promotion and Community Empowerment. The findings from the quantitative and the qualitative arm using a matrix joint display technique, which was adapted from the pillar integration process. The multivariable analyses variables that were statistically associated with vaccine uptake involved all respondents (vaccinated or never). These four factors were found to have a statistically significant association with vaccine uptake in the adult population: living in Yogyakarta compared to living in Aceh, having secondary or higher education compared to primary education, working as a health care worker in a low-risk unit or in a high-risk unit compared to being a non-health care worker, and having health insurance that covered hepatitis B vaccination compared to not having such health insurance. The main reasons for not being vaccinated were that respondents had 'never heard about hepatitis B vaccination for an adult before' and 'never felt the need for vaccination (for hepatitis B for an adult). Our qualitative study also identified several barriers to the adult hepatitis B vaccination programme in Indonesia such as the high cost of vaccination, lack of vaccine availability in certain areas, limited human re- sources to implement the hepatitis B vaccination programme, and the ineffective dissemination of hepatitis B vaccination. This study found six factors assessed as barriers to and facilitators of vaccine uptake, according to pillar integration between quantitative and qualitative findings: people's character and cultural norms between regions, the role of the healthcare worker in the population, knowledge of hepatitis B infection and vaccination, accessibility of hepatitis B vaccination, affordability of hepatitis B vaccination, and dissemination of information regarding hepatitis B infection and vaccination.

2.1. Study's main findings in relation to the state of research: Factors associated with adult hepatitis B vaccination in Indonesia

Based on our studies, several factors were found to influence hepatitis B vaccine uptake in the adult population in Indonesia. Correlations between variables are provided in Figure 1. Knowledge and risk perception related to hepatitis B infection and vaccinations are influenced by media exposure and the effectiveness of the information dissemination system. This correlation is considered to affect a person's motivation to receive vaccination. Other variables that also directly affect motivation are social processes: vaccination norms, workplace norms,

local-region norms, and other support such as Halal vaccination certificate. Furthermore, motivation is closely related to a person's decision to vaccinate. However, accessibility, availability and affordability are also major factors affecting vaccine uptake. All of these processes are inseparable from the influence of a person's socio-demographics such as age, economic ability, education, religion, profession, and experience related to hepatitis B infection and vaccination.

Our publications that contribute to the thesis are marked as M1 to M4: Our review found that socio-demographic factors such as age, education, monthly income, and profession are known predictor variables of hepatitis B vaccine uptake [M1][27]. For example, in our study, younger mothers had higher odds of completely vaccinating their children than older mothers [M2][39]. This finding reflects that younger populations tend to be more exposed to the latest technology and to have access to the internet, which positively impacts their access to health literacy on hepatitis B infection and vaccination. This is not surprising—indeed, previous research in Indonesia has reported that the country became the world's sixth-largest internet user in 2014 and was categorised as the country with the most prominent internet users by the end of 2018, with most users being 20 years old [40].

Our systematic review showed that monthly income has been identified as a strong predictor variable for hepatitis B vaccine uptake [M1][27]; however, we could not prove this association in our survey due to missing data [M3,M4][41,42]. In fact, Park et al. have claimed that high income is an essential factor in health service access via the ability to pay for healthcare in South Korea [43]. This finding is reasonable, as, in some countries such as Indonesia, regulations for financing hepatitis B vaccination have not been established [29], meaning people must actively decide to be immunised and bear the costs themselves, including high-risk populations. Therefore, it is not surprising that our study found that one of reason not to be vaccinated is cost of vaccination are high or expensive [M4][42] and there is an association between health insurance covering vaccination and hepatitis B vaccine uptake [M1,M3,M4][27,41,42].

Another strong predictor of hepatitis B vaccination status is education, with several studies showing an association between education level and vaccine coverage [43-45]. Interestingly, our survey in Indonesia [M3] found no association between education level and willingness to receive hepatitis B vaccination in either Aceh or Yogyakarta provinces [41]. In Aceh, this finding is reasonable. As the first area that official implementation of Islamic Sharia Law, the controversy over vaccines not being halal because they contain prohibited ingredients that contradict religious rules makes people may not feel confident to vaccinate, even though they know the benefits of vaccination [M3] [41]. This finding reflects that education level does not guarantee high health literacy regarding hepatitis B infection and vaccination. For instance, our

study found that around 60% of the participants were highly educated, but only 20% had good knowledge about hepatitis B infection and vaccination [M3][41]. Nevertheless, the research explores how through education, one has the ability to access health-related information [M1][27] and can thus prevent negative preconceptions when making fact-based decisions regarding vaccination [M2][39].

Regarding our studies [M1, M3, M4], a participant's profession being healthcare worker was an influence factor for vaccine uptake [27,41,42]. This is reasonable due to the healthcare worker's need to protect themself from hepatitis B infection through vaccination, being a high-risk population [M4][42,45,46]. Mullins et al. have claimed that risk perception is closely related to knowledge, which often becomes more accurate as knowledge increases over time [47]. Thus, some studies have found that people's perceptions about the risk of hepatitis B infection positively impacts vaccination status [M3, M4][41,42,48,49].

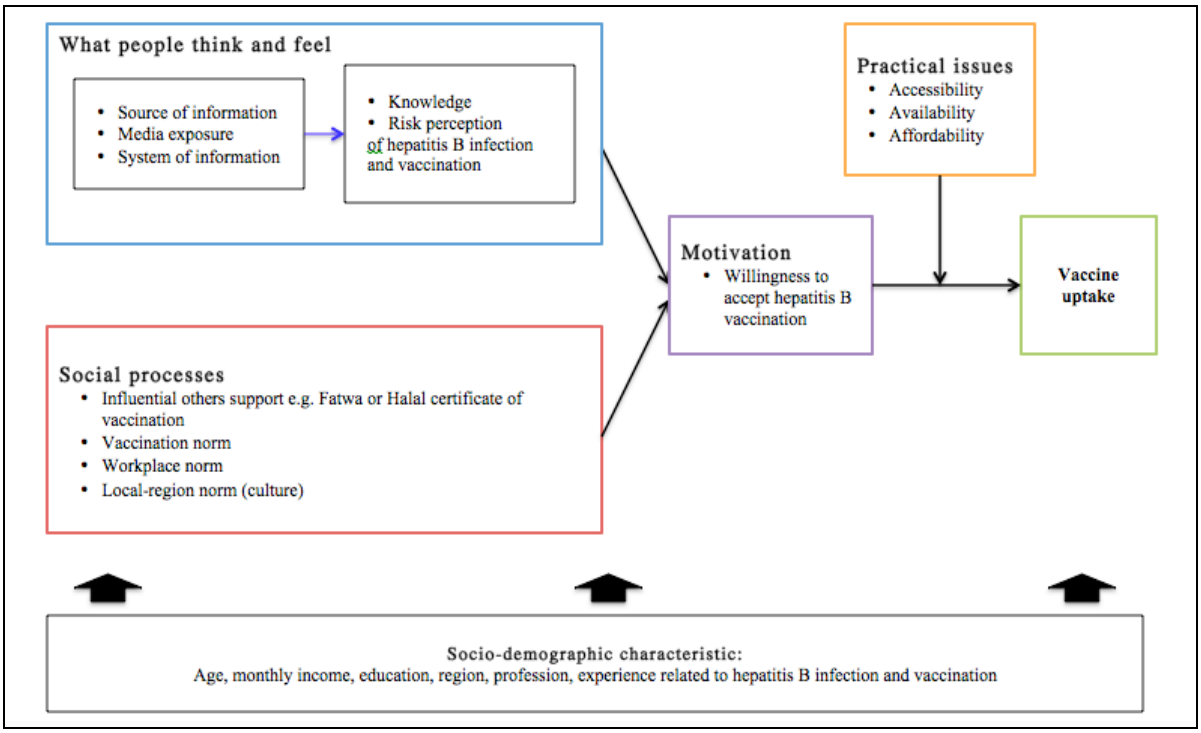

Figure 1. Conceptual framework of hep B vaccination. Illustration modified after Jung et al. (2013) [37] and World Health Organization (2021) [36]

Our study [M2] also found that exposure to accurate information related to hepatitis B infection and the benefits of vaccination had positive impacts on hepatitis B vaccination uptake in Indonesia [39]. Although the receipt of information may not be the same across populations, the reliability of the information source is also an important consideration. For example, a qualitative study in Indonesia found that misinformation about vaccinations, such as

controversy over vaccine ingredients (e.g., halal controversy), belief in natural immunity, and belief in alternative medicine, affected perceptions about immunisation among the population [50]. Our mixed methods study found that the dissemination of hepatitis B information in Indonesia currently mostly uses conventional methods and is considered ineffective because the information delivered does not discuss hepatitis B in detail, but rather talks about the elimination of three diseases - hepatitis in general, AIDS, and syphilis [M4][42]. This study also claimed that information on hepatitis B is disseminated only at specific events, such as the annual World Hepatitis Day [M4][42]. In addition, the Hepatitis B information posters distributed by the Ministry of Health do not reach many people because it used national language (Bahasa), while most of the rural areas population used local languages, so the message of the posters cannot be well understood by the local people [M4][42].

In Indonesia, healthcare providers are not considered to be the main actors in information dissemination regarding vaccinations due to differences in the degree of trust in the public health system across the region, related to local policy and culture [M2,M3,M4][39,41,42]. For instance, our mixed-methods study found differences in the dissemination approaches for vaccination programmes between Aceh and Yogyakarta [M4][42]. In Yogyakarta, local cultural events such as *Wayangan* have become suitable forums for disseminating health information, including about vaccinations [M4][42]. On the other hand, in Aceh, a region of Indonesia that has applied Sharia law, a halal certificate (or *fatwa*) regarding the permissibility of the vaccination from a council of religious scholars in Indonesia (*Ulama*) has been important in reducing vaccine rejection among those who feel uncomfortable with vaccinations due to doubts about their ingredients (i.e., halal controversy) [M3][41,51]. These findings show that there is a need for adjustments in service of local-based approaches to hepatitis B vaccination programmes in Indonesia, as there may be no one-size-fits-all solution for the region [52].

Furthermore, practical issues such as the affordability and accessibility of vaccinations directly influenced the correlation between willingness and hepatitis B vaccine uptake in Indonesia. Our study found the high cost of hepatitis B vaccinations to be a reason not to be vaccinated for hepatitis B, especially for those with low and irregular incomes [M4][42]. Otherwise, some participants claimed that it is not easy to get hepatitis B vaccinations as an adult due to the vaccine being unavailable at health centre facilities near them, especially those living in rural areas [M4][42]. This could be related to geographic conditions. The accessibility of health facilities is an obstacle to various health programmes, including vaccination, in Indonesia, which consists of more than 16,000 islands [53]. For example, in Papua, which is one of the easternmost regions in Indonesia, dosing hepatitis B less than 24 hours after delivery may be difficult due to geographical conditions, so some people dose hepatitis B seven days after delivery [M4][42]. Even if misunderstandings and poor knowledge regarding services have

been well addressed, the situation will not effectively improved without addressing service accessibility [54,55].

Regarding to the 2019 Global Progress Report in the WHO Health Sector estimates that an additional USD 6 billion is needed annually to achieve Sustainable Development Goals (SDGs) targeted by 2030, if only USD 0.5 billion was available in 2016 [56]. Overcoming the challenge of limited financing requires cross-sectoral cooperation to ensure that everyone can get the services they need without causing financial difficulties. Advocacy efforts and partnerships need to be continued to finance hepatitis programs, as well as spending efficiency through collaboration with other health programs in optimizing existing resources, for example by optimizing village fund budgets for prevention and supporting testing and community-based activities [29].

2.2. Study implications: Model target intervention of hepatitis B vaccination among adult population based on the levels of the social ecological model

Global Hepatitis Elimination in 2030 has been established as one of the WHO's seventeen SDGs. In order to achieve this, Indonesia has committed to implementing hepatitis prevention and control programmes through a National Action Plan (for the period of 2020–2024) [29]. There are several strategic issues discussed in this national plan, including increasing public awareness of the importance of prevention of viral hepatitis such as by vaccination [29]. Regarding the social ecological model framework [57], we describe the target intervention for public awareness of an adult hepatitis B vaccination programme based on the result of our studies at five target levels—individual, interpersonal, organisational, community, and society (figure 2).

The individual level relates to knowledge about the disease: how severe it is, how serial it is, and the overall threat of the disease. Increased knowledge has an impact on changes in people's perceptions and behaviours related to vaccine uptake, which was targeted at the individual level [M1][27]. The role of the media is considered important in this stage, including mass media and social media [M2][39]. Jung et al. found that, while media exposure contributes to increased knowledge in individuals; however, health behaviors are more likely to be adopted by groups that are motivated to actively seek information than groups that are passively exposed to media. Therefore, in addition to expanding media coverage to increase vaccination rates, the government needs to conduct strategic communication to attract the attention and increase

public motivation [37]. Vaccination practitioners also needed to modify the delivery of information about hepatitis B infection and vaccination according to local conditions through the media, such as posters using local languages [M4][42] or a particular approach to minimise missed opportunities for vaccination, such as sticker-based reminders of vaccination schedules [58].

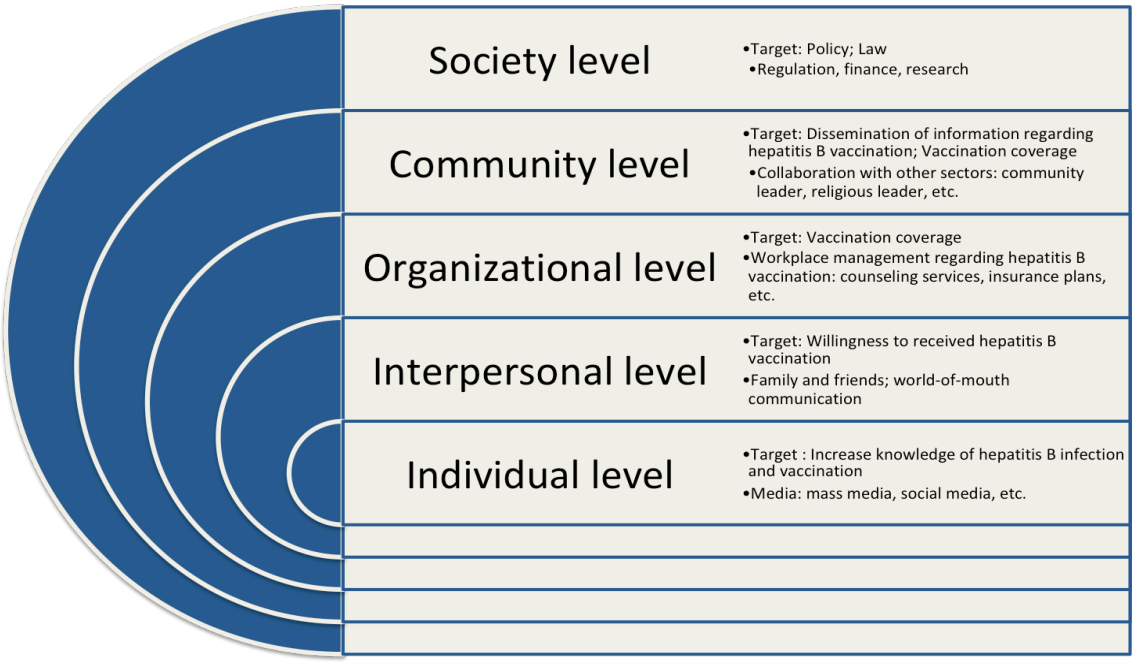

Figure 2. Framework of Model target intervention of hepatitis B vaccination among adult based on level of the social ecological model. Illustration modified after Kolff et al. (2018) [57]

The interpersonal level relates to a person's relationship with other people such as family and friends. At this level, one can provide exposure to information related to hepatitis B vaccination that impacts on people's willingness to receive hepatitis B vaccination. For instance, our systematic review [M1] summarised that the experience of families of friends with hepatitis B infection and vaccination impacted individuals' vaccination status [27]. Eni et al. have revealed that knowing someone who lives with hepatitis B is associated with improved knowledge and awareness regarding hepatitis B infection and vaccination [59]. Previous study support this finding, which found level of knowledge about a disease almost doubles in cases with higher neighbourhood social capital, and correlation between knowledge of disease and neighbourhood social capital results in about a doubling of the likelihood of receiving vaccinations [37]. These results suggest that neighbourhood social capital is linked to trust and strong interactions between neighbours. The main challenge at this level is hoax news about vaccination [60];

therefore, the role of health practices are needed at this level to increase trust about hepatitis B vaccination in the population. Effective collaboration between health providers and other related parties such as local community leaders and religious leaders are needed to counteract negative information that facilitates vaccine hesitancy in Indonesia [M2][39,42,50].

There are opportunities to reach more people in different sectors of society in the organizational level. Organizations such as workplaces can take responsibility for implementing hepatitis B infection prevention for workers such as providing counselling services, immunization, and effective insurance plans for workers. Our study found that workplace management or regulations could have a positive impact on vaccine use [M1][24]. For example, free hepatitis B vaccination provided by an employer [61] or regular training in occupational health or workplace culture [62] emphasise the importance of hepatitis B vaccination. On this level, health providers of hepatitis B programmes might collaborate with companies, such as hospitals and barbershops, that have potentially high transmission rates of hepatitis B infections among employees [63]. For example, the Occupational Safety and Health Administration (OSHA) in the US issued a federal standard in 1991, requiring employers to provide free hepatitis B vaccination for all occupationally exposed employees [64].

Community refers to the culmination of various organizations in an area. There are shared resources and ideas pooled in these organizations that can have a positive impact on public health. Regarding our mixed methods [M4], there are some potential interventions to achieve vaccination coverage of hepatitis B at the community level related to information systems [42]. Through collaboration with other sectors such as local community leaders and religious leaders, the Indonesian Ministry of Health may be able to widely spread reliable information about hepatitis B vaccination to communities [65]. For example, using regular local art events and religious events to disseminate health promotion materials, including information regarding hepatitis B infection and vaccination [M4][42]. Otherwise, collaboration with a council of religious scholars in Indonesia, called the Majelis Ulama Indonesia, has also been essential in providing halal certification or fatwa regarding the permissibility of a given vaccination, which impacts the community acceptance of hepatitis B vaccinations [50,65].

At this final level, governing bodies take responsibility for hepatitis B prevention efforts by establishing agencies and laws at each level of government and finding more effective ways to deal with the problems that arise. This level of the socio-ecological model is important because it affects more of the population than any other level. For example, laws that ensure equity for access to immunization, including financial policies such as insurance for vaccination costs [58]. Park et al. also confirmed that health insurance for vaccinations is an essential factor towards hepatitis B vaccination status, especially for those with lower social-economic status [43]. One way to remove financial barriers and improve vaccination status is to offer free

vaccination, especially for high-risk populations. For instance, a study from China described national and sub-national hepatitis B vaccination policies that provide free vaccination for healthcare workers who are at risk of exposure to infectious materials [61].

2.3. Strengths and limitations

Our systematic review attempted to identify specific patterns in more than 70% of the world's population, which was essential in acquiring background information about relevant variables of hepatitis B knowledge and vaccination status in a variety of countries and cultures with and without the financial ability to run health programmes. We also used data from a large representative population study called the Demographic Health Survey for our second publication. The analyses of media use controlled for a variety of potential confounding variables, increasing the validity of the results. To the best of our knowledge, our survey was the first study in Indonesia to identify predictive factors of willingness to receive hepatitis B vaccination involving provinces with the highest and lowest vaccination program coverage: Aceh and Yogyakarta. In addition, in our mixed methods study, the population (outpatients and health workers) and the government can illustrate potential differences and correspondence of barriers and facilitators from two different sides, helping to increase the validity of the findings.

Apart from the above contributions, there are some limitations to this thesis. First, our systematic review included 77.6% of the studies that considered as unsatisfactory study, as they did not assess outcomes in a multivariable analysis sufficient to identify important predictor variables for knowledge about hepatitis B and vaccination status. In this review, most of studies were based on high-risk population such as health care worker. In addition, the search strategy was restricted to papers that were peer reviewed and written in English, which ten included article were missed due to written in the countries' mother tongues: Mandarin, French, and Turkish. Second, selection bias may occur due to the sequential sampling applied in the Demographic Health Survey and may reduce the generalizability of the results. We also expected confounding variables in this study, as the data from the Demographic Health Survey could not provide all the required variables that have a strong association with child vaccination status, such as religion. Third, the generalizability of our survey results may be reduced because most of the participants in our survey are women. This condition is related to community health centres' support of the Indonesian Ministry of Health's mandate to improve maternal and child health services, which provides health services targeting mothers and children, such as antenatal check-ups and child vaccinations. Some important variables associated with willingness to receive hepatitis B vaccination could not be assessed in this survey, such as economic status and religion, due to high missing data (income might be explained by the fact that many people in

Indonesia consider income very private) and homogeneity of the data (95.9% participants were Muslims). Finally, our qualitative study was limited not only to outpatient and health care workers in selected local health officials in two provinces, with their own specific characteristics in Indonesia, which may differ from the country's other 36 provinces. Nevertheless, these studies' results can inform future vaccination intervention strategies and significantly contribute to public health knowledge, although the findings from our studies may not be generalisable outside Indonesia.

2.4. Conclusion

This thesis has shown that the intention to obtain adult hepatitis B vaccination and vaccine uptake are influenced by several factors, including socio-demographic factors, information exposure related to people's knowledge and risk perceptions of hepatitis B infection and vaccination, social processes such as vaccination norms, local norms/culture, and influential others' support), as well as other practical issues such as accessibility, affordability, and availability related to vaccination. Therefore, there is a need for appropriate and effective media exposure to increase public knowledge and awareness about the importance and benefits of hepatitis B vaccination in preventing hepatitis B infection. Ideally, this dissemination is applied according to the conditions of each region, which has its own regional characteristics. Regarding to implementation of hepatitis B vaccination in Indonesia, health providers should consider further collaboration and exploration with other stakeholders, such as local religious and community leaders or local health offices from other provinces. Policies that support the implementation of hepatitis B vaccination for adults need to be implemented, such as regulations that require companies or workplaces that are at risk of hepatitis B infection to provide protection management in the form of: free vaccination, counselling, and effective insurance plans for workers related to hepatitis B infection. In addition, policies that provided by government related to free vaccination for adult populations with a high risk of hepatitis B infection and adult populations who do not have a history of complete hepatitis B immunization during childhood. Last but not least, health providers should ensure the availability of hepatitis B vaccination for all health facilities in Indonesia to minimize missed opportunities.

3. References

1. World Health Organization. Hepatitis B. https://www.who.int/news-room/fact-sheets/detail/hepatitis-b (13 November 2021).
2. Hepatitis B Foundation. What is hepatitis B. https://www.hepb.org/what-is-hepatitis-b/what-is-hepb/acute-vs-chronic/ (23 April 2023).
3. Sheridan, DA; Robotin, M. Hepatitis b related hepatocellular cacinoma. In All you wanted to know about hepatitis B: a guide for primary care providers, Matthews, G; Robotin, M; Allard, N, Eds. Australasian Society for HIV Medicine (ASHM): Australia, 2014; pp 93-102.
4. Pang, J; Zekry, A. Natural histoy of hepatitis b virus infection. In All you wanted to know about hepatitis B: a guide for primary care providers, Matthews, G; Robotin, M; Allard, N, Eds. Australasian Scoiety for HIV Medicine: Australia, 2014; pp 43-52.
5. World Health Organization. Toward the elimination of hepatitis B and C 2030. 2020.
6. Yano, Y; Utsumi, T; Lusida, MI; Hayashi, Y. Hepatitis B virus infection in indonesia. World J Gastroenterol. 2015; 21 (38): 10714-10720.
7. World Health Organization. Global hepatitis report 2017; World Health Organization: France, 2017.
8. World Health Organization. Progress report on hiv, viral hepatitis and sexually transmitted infections, 2019; World Health Organization: Switzerland, 2019.
9. World Health Organization. World day hepatitis 2020. (https://www.who.int/campaigns/world-hepatitis-day/2020) (10 November 2020).
10. Girawan, D; Judistiani, RTD; Risan, NA; Bestari, MB; Nugraha, ES; Ermaya, YS, et al. The high prevalence of negative hepatitis b surface antibody (anti-hbs) among pregnant women in bandung, indonesia: A community-based study. International Journal of Hepatology. 2020; 2020 1-8.
11. Muljono, DH. Epidemiology of hepatitis b and c in republic of indonesia. Euroasian J Hepatogastroenterol. 2017; 7 (1): 55-59.
12. Lusida, MI; Juniastuti; Yano, Y. Current hepatitis b virus infection situation in indonesia and its genetic diversity. World J Gastroenterol. 2016; 22 (32): 7264-7274.
13. The Indonesian National Health Insurance System (BPJS). Laporan pegelolaan program dan laporan keuangan jaminan sosial kesehatan tahun 2017; The Indonesian National Health Insurance System (BPJS): Jakarta, 2017.
14. The Indonesia Ministry of Health. the Indonesia National Health Survey 2013 (the 2013 Riskesdas); The Indonesia Ministry of Health: Jakarta, 2013.

15. The Indonesia Ministry of Health. the Indonesian Nasional Health Survey 2018 (the 2018 Riskesdas); The Indonesia Ministry of Health: Jakarta, 2018.
16. World Health Organization. Global health sector strategy on viral hepatitis 2016 to 2021; World Health Organization: Geneva, 2016.
17. World Health Organization. Hepatitis-free future. https://www.who.int/campaigns/world-hepatitis-day/2020 (19 April 2021).
18. World Health Organization. Hepatitis b vaccination and prevention of mother-to-child transmission. https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/hepatitis/prevention/mother-to-child-transmission-of-hepatitis-b (19 April 2021).
19. Woldesenbet, S; Jackson, D; Lombard, C; Thu-Ha, D; Puren, A; Sherman, G, et al. Missed opportunities along the prevention of mother-to-child transmission services cascade in south africa: Uptake, determinants, and attributable risk (the sapmtcte). PLoS One. 2015; 10 (7):
20. Centers of Disease Control and Prevention. Access to treatment for hepatitis b virus infection— worldwide, 2016; Centers of Disease Control and Prevention: Atlanta, USA, 2018.
21. World Health Organization. Testing and diagnostics. https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/hepatitis/testing-and-diagnostics (19 April 2021).
22. World Health Organization. Treatment and care https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/hepatitis/treatment-care (19 April 2021).
23. Aaron, D; Nagu, TJ; Rwegasha, J; Komba, E. Hepatitis b vaccination coverage among healthcare workers at national hospital in tanzania: How much, who and why? BMC infectious diseases. 2017; 17 (1): 786-786.
24. Bedaso, A; Duko, B; Fedlu, R. Knowledge on hbv vaccine and vaccination status among health care workers of hawassa university comprehensive specialized hospital, hawassa, southern ethiopia: A cross sectional study. BMC research notes. 2018; 11 (1): 912-912.
25. Mungandi, N; Makasa, M; Musonda, P. Hepatitis b vaccination coverage and the determinants of vaccination among health care workers in selected health facilities in lusaka district, zambia: An exploratory study. Ann Occup Environ Med. 2017; 29 32-32.
26. Zheng, Y-B; Gu, Y-R; Zhang, M; Wang, K; Huang, Z-L; Lin, C-S, et al. Health care workers in pearl river delta area of china are not vaccinated adequately against hepatitis b: A retrospective cohort study. BMC infectious diseases. 2015; 15 542-542.
27. Machmud, PB; Glasauer, S; Gottschick, C; Mikolajczyk, R. Knowledge, vaccination status, and reasons for avoiding vaccinations against hepatitis b in developing countries: A systematic review. Vaccines. 2021; 9 (625): 1-26.
28. Centers of Disease Control and Prevention. Viral hepatitis. (16 May 2022),

29. The Indonesia Ministry of Health. National Action Plan of Hepatitis 2020 to 2024; The Indonesia Ministry of Health: Jakarta, 2020.
30. The Indonesia Ministry of Health. Regulation of hepatitis virus prevention in indonesia no. 53/2015. The Indonesia Ministry of Health: Jakarta, 2015.
31. Purwono, PB; Juniastuti; Amin, M; Bramanthi, R; Nursidah; Resi, EM, et al. Hepatitis b virus infection in indonesia 15 years after adoption of a universal infant vaccination program: Possible impacts of low birth dose coverage and a vaccine-escape mutant. Am J Trop Med Hyg. 2016; 95 (3): 674-679.
32. The Indonesia Ministry of Health. Elimination of human immunodeficiency virus, syphilis, and hepatitis b from mother to children no. 52/2017. The Indonesia Ministry of Health: Jakarta, 2017; Vol. 52/2017.
33. Lusida, MI; Juniastuti; Yano, Y. Current hepatitis b virus infection situation in indonesia and its genetic diversity. World Journal of Gastroenterology. 2016; 22 (32): 7264-7274.
34. World Health Organization. Eliminate hepatitis. (30 March 2022).
35. World Health Organization. Report of the global partner's meeting on hepatitis elimination; World Health Organization: Geneva, Switzerland, 2019.
36. World Health Organization. Data for action: Achieving high uptake of covid-19 vaccines; WHO: Geneva, Switzerland, 2021.
37. Jung, M; Lin, L; Viswanath, K. Associations between health communication behaviors, neighborhood social capital, vaccine knowledge, and parents' h1n1 vaccination of their children. Vaccine. 2013; 31 4860-4866.
38. Kaufman, J; Bagot, KL; Hoq, M; Leask, J; Seale, H; Biezen, R, et al. Factors influencing australian healthcare workers' covid-19 vaccine intentions across settings: A cross-sectional survey. Vaccines. 2021; 10 (3): 1-17.
39. Machmud, PB; Glasauer, S; Gayatri, D; Mikolajczyk, R. Mother's media use and children's vaccination status in indonesia: A community-based cross-sectional study. Global Pediatric Health. 2022; 9 1-10.
40. Muttaqin, M. Internet usage behavior of the ict young workforce in the border region. Jurnal Pekommas. 2019; 4 (1): 11-20.
41. Machmud, PB; Mikolajczyk, R; Gottschick, C. Understanding hepatitis b vaccination willingness in the adult population in indonesia: A survey among outpatient and healthcare workers in community health centers. Journal of Public Health. 2022;
42. 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. 2023; 11 1-17.

43. Park, B; Choi, KS; Lee, HY; Jun, JK; Park, EC. Socioeconomic inequalities in completion of hepatitis b vaccine series among korean women: Results from a nationwide interview survey. Vaccine. 2012; 30 (40): 5844-5848.
44. Assunção, AÁ; Araújo, TMd; Ribeiro, RBN; Oliveira, SVS. [hepatitis b vaccination and occupation exposure in the healthcare sector in belo horizonte, minas gerais]. Revista de Saúde Pública. 2012; 46 (4): 665-673.
45. Adeyemi, AB; Enabor, OO; Ugwu, IA; Bello, FA; Olayemi, OO. Knowledge of hepatitis b virus infection, access to screening and vaccination among pregnant women in ibadan, nigeria. Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology. 2013; 33 (2): 155-159.
46. Ochu, CL; Beynon, CM. Hepatitis b vaccination coverage, knowledge and sociodemographic determinants of uptake in high risk public safety workers in kaduna state, nigeria: A cross sectional survey. BMJ Open. 2017; 7 (5): e015845.
47. Mullins, TLK; Widdice, LE; Rosenthal, SL; Zimet, GD; Kahna, JA. Risk perceptions, sexual attitudes, and sexual behavior after hpv vaccination in 11–12 year-old girls. Vaccine. 2015; 33 3907 - 3912.
48. Chen, IH; Hsu, SM; Wu, JSJ; Wang, YT; Lin, YK; Chung, MH, et al. Determinants of nurses' willingness to receive vaccines: Application of the health belief model. Journal of clinical nursing. 2019; 28 3430-3440.
49. Xiang, H; Tang, X; Xiao, M; Gan, L; Chu, K; Li, S, et al. Study on status and willingness towards hepatitis b vaccination among migrant workers in chongqing, china: A cross-sectional study. International Journal of Environmental Research and Public Health. 2019; 16 1-12.
50. Syiroj, AT; Pardosi, JF; Heywood, AE. Exploring parents' reason for incomplete childhood immunisation in indonesia. Vaccine. 2019; 37 (43): 6486-6493.
51. Harapan, H; Shields, N; Kachoria, AG; Shotwell, A; Wagner, AL. Religion and measles vaccination in indonesia, 1991–2017. American Journal of Prevention Medicine. 2021; 60 (1): 44-52.
52. Hardt, K; Bonanni, P; King, S; Santos, JI; El-Hodhod, M; Zimet, GD, et al. Vaccine strategies: Optimising outcomes. Vaccine. 2016; 34 6691-6699.
53. Johar, M; Soewondo, P; Pujisubekti, R; Satrio, HK; Adji, A. Inequality in access to health care, health insurance and the role of supply t factors. Social Science and Medicine 2018; 2013 134-145.
54. Maina, AN; Bii, LC. Factors affecting hbv vaccination in a medical training college in kenya: A mixed methods study. BMC Public Health. 2020; 20 (48): 1-12.

55. Vedio, A; Liu, EZH; Lee, ACK; Salway, S. Improving access to health care for chronic hepatitis b among migrant chinese populations: A systematic mixed methods review of barriers and enablers. J Viral Hepat. 2016; 24 526-540.
56. World Health Organization. Global progress report on hiv, viral hepatitis and sexually transmitted infections, 2021; World Health Organization: Geneva, Switzerland, 2021.
57. Kolff, CA; Scott, VP; Stockwell, MS. The use of technology to promote vaccination: A social ecological model based framework. Hum Vaccin Immunother. 2018; 14 (7): 1636-1646.
58. Wallace, AS; Peetosutan, K; Untung, A; Ricardo, M; Yosephine, P; Wannemuehler, K, et al. Home-based records and vaccination appointment stickers as parental reminders to reduce vaccination dropout in indonesia: A cluster- randomized controlled trial. Vaccine. 2019; 37 6814-6823.
59. Eni, AO; Soluade, MG; Oshamika, OO; Efekemo, OP; Igwe, TT; Onile-Ere, OA. Knowledge and awareness of hepatitis b virus infection in nigeria. Annals of global health. 2019; 85 (1): 56.
60. Wang, Y; McKee, M; Torbica, A; Stuckler, D. Systematic literature review on the spread of health-related t misinformation on social media. Social Science and Medicine. 2019; 240 1-12.
61. Yuan, Q; Wang, F; Zheng, H; Zhang, G; Miao, N; Sun, X, et al. Hepatitis b vaccination coverage among health care workers in china. PloS one. 2019; 14 (5): 1-12.
62. da Costa, FM; de Barros Lima Martins, AM; Dos Santos Neto, PE; de Pinho Veloso, DN; Magalhaes, VS; Ferreira, RC. Is vaccination against hepatitis b a reality among primary health care workers? Revista latino-americana de enfermagem. 2013; 21 (1): 316-324.
63. Schenkel, K; Radun, D; Bremer, V; Bocter, N; Hamouda, O. Viral hepatitis in germany: Poor vaccination coverage and little knowledge about transmission in target groups. BMC Public Health. 2008; 8 (132): 1-11.
64. Byrd, KK; Lu, P-J; Murphy, TV. Hepatitis b vaccination coverage among health-care personnel in the united states. Public Health Report. 2013; 128
65. Padmawati, RS; Heywood, A; Sitaresmi, MN; Atthobari, J; MacIntyre, CR; Soenarto, Y, et al. Religious and community leaders' acceptance of rotavirus vaccine introduction in yogyakarta, indonesia: A qualitative study. BMC Public Health. 2019; 19 (368): 1-6.

4. Theses

1) In order to achieve Global Hepatitis Elimination by 2030, the World Health Organization has encouraged all countries to reduce hepatitis incidence and mortality rates in the mission to eliminate hepatitis viruses as a global threat; one target is that everyone must have access to prevention services (vaccination and testing) and treatment of hepatitis, including drug users, people in prisons, migrants, and healthcare workers, who are at-risk populations for hepatitis.
2) Indonesia is one of eleven countries carrying almost 50% of the global burden of chronic hepatitis and currently ranks as the country with the second-highest number of hepatitis B infections in the Asia Pacific region after India, contributing up to 74% of global deaths caused by liver cancer.
3) In 2022, Indonesia began work to develop a strategic roadmap for phasing out viral hepatitis that aims to eliminate hepatitis B and hepatitis C by the end of 2030 for hepatitis B and the end of 2040 for hepatitis C.
4) There are four main-factors that influence vaccine uptake—socio-demographic factors, information exposure related to people's knowledge and risk perceptions of hepatitis B infection and vaccination, social processes, and other practical issues related to vaccination.
5) In developing countries, there are various important determinants for levels of knowledge and vaccination status, monthly income, level of education, and profession as a healthcare worker known as the strongest predictive factors for hepatitis B knowledge and vaccination status. Otherwise, strong influences or predictors of vaccine uptake are health insurance, management's protection at the workplace, experience in infection training on hepatitis B, and experience of hepatitis B exposure.
6) There is a positive association between media use and vaccination status, with some indication of a dose-response pattern in the sense that irregular media use among mothers increased children's partial immunisation but had a lesser benefit to ensure the completeness of vaccination.
7) Our survey in Indonesia found no association between education level and willingness to receive hepatitis B vaccination in either Aceh or Yogyakarta provinces, reflecting that education level does not guarantee high health literacy regarding hepatitis B infection and vaccination.
8) In Yogyakarta, local cultural events such as *Wayangan* have become suitable forums for disseminating health information, including about vaccinations. While in Aceh (a region of Indonesia that has applied Sharia law), a halal certificate (or *fatwa*) regarding

the permissibility of the vaccination from a council of religious scholars in Indonesia (*Ulama*) has been important in reducing vaccine rejection among those who feel uncomfortable with vaccinations due to doubts about their ingredients (i.e., halal controversy)

9) There are six factors identified as barriers to and facilitators of hepatitis B vaccine uptake, according to the general population and government, as follows: lack of knowledge about hepatitis B infection and vaccination in the population, high cost of hepatitis B vaccination, lack of hepatitis B vaccine availability in certain areas, limited human resources to implement hepatitis B vaccination programmes, and ineffective dissemination of information regarding hepatitis B vaccination.

5. Publications

List of included publications

1. **Knowledge, Vaccination Status, and Reasons for Avoiding Vaccinations against Hepatitis B in Developing Countries: A Systematic Review [M1]**
   Machmud PB, Glasauer S, Gottschick C, Mikolajczyk R**.** 2021 June 9; 9(6):625. Vaccines. DOI:10.3390/vaccines9060625

2. **Mother's media use and children's vaccination status in Indonesia: a community-based cross-sectional study [M2]**
   Machmud PB, Glasauer S, Gayatri D, Mikolajczyk R. 2022 March 21; 9. Global Pediatric Health. DOI:10.1177?2333794X221092740

3. **Understanding hepatitis B vaccination willingness in the adult population in Indonesia: A survey among outpatient and healthcare workers in Community Health Centres [M3]**
   Machmud PB, Mikolajczyk R, Gottschick C. 2022 November 28; 30. Journal of Public Health. DOI: 10.1007/s10389-022-01775-3

4. **Barriers and facilitators of hepatitis B vaccination among the adult population in Indonesia: A mixed methods study [M4]**
   Machmud PB, Führer A, Gottschick C, Mikolajczyk R. 2023 February 7; 11[66]:398 Vaccines. DOI:10.3390/vaccines11020398

Personal contribution to publications

M1: Machmud PB, Glasauer S, Gottschick C, Mikolajczyk R. 2021

Contribution as an author: I have developed the conception and design of the work, formulation of the review questions, systematic review protocol development and registration, conducting the literature search in all electronic databases, selecting studies per protocol, appraising studies per protocol, extracting data, results analysis, interpretation of results, and writing the manuscript. In addition, I was responsible for the whole submission process until the manuscript was published.

M2: Machmud PB, Glasauer S, Gayatri D, Mikolajczyk R. 2022

Contribution as an author: I have developed the conception and design of the work, formulation of the research questions, register in Demographic Health Survey (DHS) website, submitted a proposal for applied the permission of data access, data management, results interpretation, and wrote the manuscript. Also, I was responsible for the whole submission process until the manuscript was published.

M3: Machmud PB, Mikolajczyk R, Gottschick C. 2022

Contribution as an author: I have developed the conception and design of the work, formulation of the research questions, study questionnaire development, ethical clearance processes, data collection, data dictionary development, data management, results interpretation, and wrote the manuscript.

M4: Machmud PB, Führer A, Gottschick C, Mikolajczyk R. 2023

Contribution as an author: I have developed the conception and design of the work, formulation of the research questions, study questionnaire development, developed in-depth interview guidelines, ethical clearance processes, data collection, data dictionary development, data management, results interpretation, and wrote the manuscript. Also, I was responsible for the whole submission process until the manuscript was published.

Publication 1

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Review

Knowledge, Vaccination Status, and Reasons for Avoiding Vaccinations against Hepatitis B in Developing Countries: A Systematic Review

Putri Bungsu Machmud [1,2], Saskia Glasauer [1], Cornelia Gottschick [1] and Rafael Mikolajczyk [1,*]

[1] Institute of Medical Epidemiology, Biometrics and Informatics (IMEBI), Interdisciplinary Center for Health Sciences, Medical School of the Martin-Luther-University Halle-Wittenberg, Magdeburger Straße 8, 06112 Halle (Saale), Germany; putri.machmud@uk-halle.de (P.B.M.); saskia.glasauer@uk-halle.de (S.G.); cornelia.gottschick@uk-halle.de (C.G.)

[2] Department of Epidemiology, Faculty of Public Health, Universitas Indonesia, Jl. Prof. Dr. Bahder Djohan, Depok 16424, Indonesia

* Correspondence: rafael.mikolajczyk@uk-halle.de; Tel.: +49-(0)345-557-3570

Abstract: (1) Background: The coverage of hepatitis B vaccination remains low in developing countries to date. This systematic review thus analyzes the determinants of people's knowledge and vaccination status as well as the reasons why people in developing countries chose not to receive the hepatitis B vaccination. (2) Methods: We searched four databases to identify all studies from developing countries published within the past 10 years. Both low-risk and high-risk populations aged older than 15 years old were eligible for the study. The quality of studies was assessed by the Newcastle–Ottawa Scale assessment. (3) Results: This study identified 2443 articles, 89 of which were included in the analysis. Monthly income, occupational status, and profession as a health-care worker were the strongest predictive factors for both knowledge of hepatitis B and vaccination status. In addition, strong predictor variables of hepatitis B knowledge were knowing an infected person and level of education, while health insurance, management's protection at workplace, infection training, and experience of hepatitis B exposure were strong influencing factors for vaccine uptake. (4) Conclusions: Exposure to information, support from institutions, and financial support related to vaccination cost have a positive impact on the knowledge about hepatitis B infection and vaccination coverage.

Keywords: developing countries; hepatitis B; knowledge; vaccination status; risk population

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1. Introduction

In 2020, the World Health Organization (WHO) reported that 325 million people worldwide were living with chronic hepatitis B infection and approximately 900,000 people died due to hepatitis B [1]. The majority of cases, 68%, were recorded in the African and Western Pacific regions [2].

Vaccination is considered the most effective way of hepatitis B prevention. Nevertheless, the coverage of hepatitis B vaccination remains low in developing countries [3–6]. The countries' inability to face the hepatitis B burden due to political and financial problems may, thereby, pose a substantial obstacle to prevention [7]. For instance, previous studies found that only 33% of health-care workers (HCW) in Tanzania and 23% of the general population in Korea were fully vaccinated against hepatitis B [3,8]. Potential explanations for these findings include lack of knowledge and awareness of hepatitis B. A systematic review among immigrants and refugees residing in the US, Canada, and Australia by Owiti et al. showed that vaccine acceptance and people's attitude towards hepatitis B was associated with their knowledge about the disease [9]. Furthermore, Abiodun et al. reported that more than 70% of hospital cleaners in Nigeria failed to recognize all ways of

hepatitis B transmission and prevention and named the lack of awareness of hepatitis B as a reason not to be vaccinated [4].

Previous studies from developing countries indicate a variety of factors predicting the level of knowledge and realization of hepatitis B vaccination in adults, but with mixed results. While some conclude that sociodemographic factors, such as age and marital status, are associated with the level of knowledge and vaccination status of hepatitis B [6,10–14], other studies could not find such results [15–20]. As a result, this systematic review aims to summarize the available evidence in order to identify predictors of the level of knowledge and vaccination status of hepatitis B and reasons why people chose not to be vaccinated against hepatitis B in developing countries.

2. Materials and Methods

2.1. Protocol Registration and Reporting Structure

A protocol for this review was registered in the international prospective register of systematic reviews (PROSPERO) with the registration number CDR42020179001 [21]. This manuscript was written using the Preferred Reporting Items for Systematic reviews and Meta-Analyses statement [22,23] (Table S1).

2.2. Eligibility Criteria

Inclusion criteria for this review were determined according to the population, intervention, comparator, outcome, and setting (PICOS) format. The population consists of all adults, including both the population at low and high risk of contracting hepatitis B. People at high risk were defined as people who live and/or work or study closely with hepatitis B patients, including health-care workers (HCW), students in a medical or health-related fields (medicine, dentistry, nursing, and midwifery), pregnant women, barbers, municipal workers, and sex partners and household members of people with hepatitis B. The low-risk population was defined as people from the general population, being >15 years old and not living or working/studying closely with hepatitis B patients. There was no intervention or comparator in this study. Outcomes were the level of knowledge and vaccination status of hepatitis B and the setting was developing countries. We followed the list of developing countries as published in the official report from the United Nations in 2020 [24]. All study designs published within the past 10 years were included. Studies for which the full text was not available in English, abstracts from conferences, and systematic reviews were excluded from this review.

2.3. Databases and Search Strategy

We searched four databases: MEDLINE, Embase, Web of Science and CINAHL [25]. The search began by listing the keywords through MeSH terms: "Health personnel"*, "Healthcare worker"*, "Healthcare provider"*, Patient*, Student*, Person*, Adult*, Knowledge*, Practice*, Vaccine*, Uptake* Vaccination*, Immunization*, Immunisation*, Campaign* and Hepatitis B*. Furthermore, we combined the list of keywords using OR and AND in the advanced search (Table S2). Duplicate articles were checked using the Endnote8 system. Articles were first screened based on the title, followed by abstract und full paper screening (Figure 1).

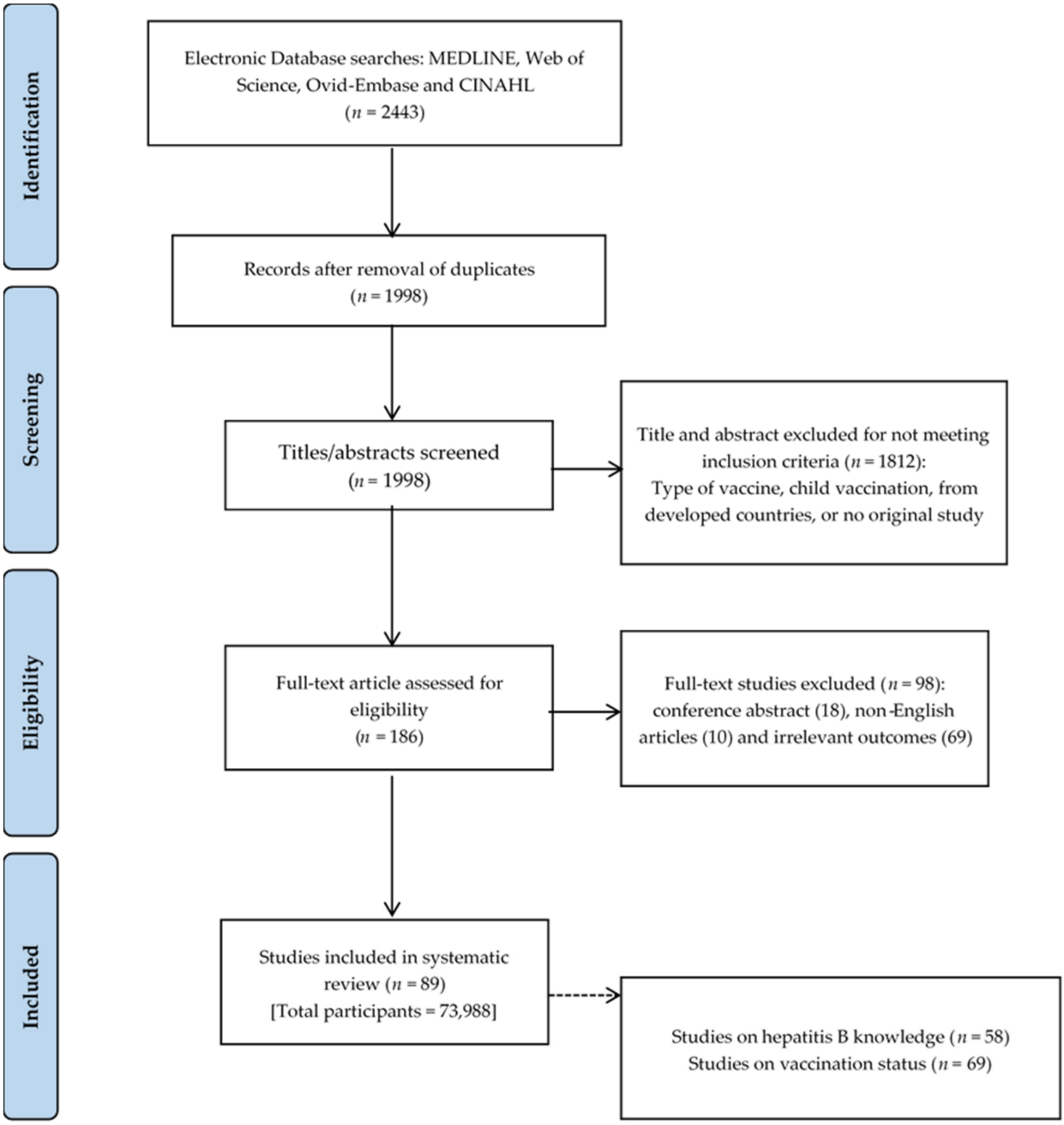

Figure 1. Flowchart of study search (adopted PRISMA: 2009).

2.4. Data Extraction and Management

Selected articles were extracted using a standard table format and entered into Microsoft Excel. The extracted data included information on country and region of study, author and publication year, population under investigation (pregnant women, general population, students and HCW), study design, sample size, percentage of good knowledge, and proportion of vaccine uptake per dose.

2.5. Risk of Bias Assessment

Two independent reviewers (P.B.M. and S.G.) performed quality assessment. Rating and scoring were conducted using the Newcastle–Ottawa Scale (NOS) checklist for quality assessment [26]. Articles were divided into three categories of quality: unsatisfactory,

satisfactory, and good study. Studies were considered unsatisfactory when they had a score of less than five for cross-sectional studies and less than four for cohort/case-control studies. Cross-sectional studies scoring 5 to 7 or cohort/case-control studies scoring 4 to 6 were considered satisfactory. Studies were categorized as good when they reached a score of more than 7 for cross-sectional and more than 6 for cohort/case-control studies (Table S3).

2.6. Data Analysis and Synthesis

Data were analyzed separately for the outcomes knowledge of hepatitis B and vaccination status of hepatitis B vaccination. Independent variables were age, gender, education, residency, marital status, monthly income, ethnicity, occupational status, and health insurance for sociodemographics; HCW profession, part-time job, work department, work experience, work regimen, and level of satisfaction with the profession; facility level, management protection at workplace for workers; year of study, and type of facility (university or faculty) for students. In addition to the aforementioned variables, we considered information on exposure to hepatitis B (ever joined in training on infection diseases, and ever heard about hepatitis B before) as well as exposure to hepatitis B, previous hepatitis B screening, and alcohol and tobacco consumption. Other than that, vaccination status of hepatitis B, hepatitis B knowledge and information on the reasons why people chose not to immunize are provided in this review.

3. Results

Of 2443 articles, 445 were removed due to duplication and 1812 were eliminated, as they did not meet the inclusion criteria such as children's immunization, setting in developed countries, and systematic review paper. Furthermore, 98 articles were excluded for the following reasons: 18 were conference abstracts, 10 articles were non-English, and 69 articles had irrelevant outcomes. As a result, 89 articles met the eligibility criteria, resulting in an overall sample size of 73,988 participants (Figure 1).

3.1. Characteristics of Included Studies

More than 90% (N = 83, 93.3%) of the studies were conducted in Asia and Africa, and 48.3% (N = 43) were hospital/health facility-based studies. Furthermore, 80.9% (N = 72) of the studies included high-risk population and 46.1% (N = 41) of studies were about HCW. Most studies (N = 87, 97.8%) were cross-sectional studies, with the remaining (N = 2, 2.2%) being case-control and retrospective cohort studies. Fifty-eight studies (65.2%) included knowledge of hepatitis B as an outcome and 69 studies (77.5%) assessed the uptake of hepatitis B vaccination (Table 1).

Table 1. Summary of studies.

Variable	Categories	Number of Studies (%)
Year of publication	2010	7 (8%)
	2011	7 (8%)
	2012	5 (6%)
	2013	6 (7%)
	2014	10 (11%)
	2015	8 (9%)
	2016	9 (10%)
	2017	10 (11%)
	2018	15 (17%)
	2019	12 (13%)
Region	Central Africa	5 (6%)
	East Africa	8 (9%)
	East Asia	16 (18%)
	North Africa	2 (2%)
	South America	6 (7%)
	South Asia	24 (27%)
	Southern Africa	2 (2%)
	West Africa	19 (21%)
	Western Asia	7 (8%)
Year of study	2004–2008	14 (16%)
	2009–2013	22 (25%)
	2014–2018	38 (43%)
	N/A	15 (17%)
Design study	Cross-sectional	87 (98%)
	Case control	1 (1%)
	Cohort retrospective	1 (1%)
Study sites	Hospital/health facility-based	43 (48%)
	Institution-based	34 (38%)
	Community-based	12 (13%)
Population	High-risk population	72 (81%)
	Low-risk population	16 (18%)
	High- and low-risk population	1 (1%)
Participant *	Health-care worker	41 (46%)
	Student	29 (33%)
	Pregnant women	5 (6%))
	General population >15 years old	9 (10%)
	Others **	5 (6%)
Approached	Interviewed	18 (20%)
	Self-administered	55 (62%)
	Interviewed and self-administered	1 (1%)
	N/A	15 (17%)
Quality grade (knowledge) (n = 58)	Unsatisfactory studies (US)	46 (79%)
	Satisfactory studies (SS)	11(19%)
	Good study (GS)	11(19%)
Quality grade (vaccination status) (n = 69)	Unsatisfactory studies (US)	52 (75%)
	Satisfactory studies (SS)	14 (20%)
	Good study (GS)	3 (4%)
Outcome *	Knowledge	58 (65%)
	Practice of vaccination	69 (78%)

* Some articles have more than one participant/outcome; ** Teacher, household contact, sexual partner, barber, municipal worker, migrant worker, and conference participant.

Forty-seven of the 58 studies (81.0%) analyzing knowledge of hepatitis B included a population at high risk. Among these, 24 studies (51.1%) were on HCW, 18 studies on students in a medical or health-related field (38.3%), 3 studies (6.4%) on pregnant women, and two studies (4.3%) on others. Of the 69 studies that addressed hepatitis B vaccination status, 59 (85.5%) were based on the high-risk population. Again, most were on HCW (N = 35, 59.3%), followed by students in the medical field (*N* = 20, 33.9%).

3.2. Study Quality

Regarding the methodological quality, most of the studies that assessed knowledge of hepatitis B (*N* = 45, 77.6%) were rated as unsatisfactory, and 12 studies (20.7%) were considered satisfactory. Only one study (1.7%) was of good quality. Similarly, 52 studies (75.3%) analyzing the uptake of hepatitis B vaccination were rated to have unsatisfactory quality; 14 studies (20.3%) were considered satisfactory and, again, only three studies (4.3%) were of good quality.

Only four cross-sectional studies stated clearly how risk factors and exposures were ascertained [16,27–29], and that vaccination status was recorded based on personal recall and confirmed by a vaccine registry of hospital or clinic registry. In addition, only 23.0% (*N* = 20) of studies provided information on the proportion of the target sample recruited or a basic summary of non-respondent characteristics. We also found that only 37 studies (42.0%) used statistical tests for analysis, provided a clear description of such, and presented the strength of the association including the confidence interval.

3.3. Hepatitis B Knowledge

Thirty-three studies (56.9%) reported the level of knowledge using percentages of correct answers while ten studies (17.2%) provided means. Five studies (8.6%) reported both percentages and means. Generally, there is a great diversity among the studies in the definition of cutoff points for good knowledge. For example, a survey from Malaysia defined good knowledge about hepatitis B based on the 75% cutoff point (17 or more out of 22 questions correctly answered) [10], while Chung et al. categorized answers into adequate and inadequate knowledge based on a 85% cutoff point [15]. Ahmad et al. used the median as the cutoff point for assessing the level of knowledge [5].

The reported proportion of people with good or adequate knowledge ranged from 1.1% to 83.8% in the high-risk population and from 17.0% to 50.3% in the low-risk population (Table 2). Students were found to have the highest proportion of good or adequate knowledge of hepatitis B among the populations at risk. The median proportion of having good or adequate knowledge was 63.5% (IQR 47.8–77.5%) and 37% (25.5–43.5%) among high- and low-risk populations, respectively (Figure 2).

Table 2. Overview of hepatitis B knowledge and vaccination status.

First Author	Year of Publication	Country	Participants	Sample Size (Participant Rates)	Good Knowledge		Vaccination Status		
					Total Score	NOS Score	At Least One Dose	Complete Dose	NOS Score
High-risk population									
Aaron [3]	2017	Tanzania	HCWs	334 (96%)	-	-	57%	34%	5
Abeje [30]	2015	Ethiopia	HCWs	354 (88%)	62%; 7.6 ± 1.27 [a]	2	10%	5%	2
Abiodun [4]	2019	Nigeria	Cleaner worker in hospital (HCW)	89 (91%)	1.1%; 1.1 ± 1.8 [a]	2	0%	0%	2
Abiola [31]	2016	Nigeria	HCWs	134 (94%)	57%; 72.5 ± 7.6 [a]	4	-	49%	4
Abiola [32]	2013	Nigeria	HCWs	84 (96%)	70%	3	59%	13%	3
Adekanle [11]	2014	Nigeria	HCWs	382 (76%)	-	6	N/A	65%	6
Adenlewo [33]	2017	Nigeria	Medical and dental students	113 (94%)	-		83%	80%	1
Adjei [34]	2018	Ghana	Pregnant women	196 (89%)	6.1 ± 1.2 [a] (physician); 6.1 ± 1.9 [a] (midwife)	5	-	-	-
Adeyemi [17]	2013	Nigeria	Pregnant women	643 (100%)	24%	5	10%	-	5
Akibu [35]	2018	Ethiopia	HCWs	386 (97%)	-	-	-	26%	7
Al-Hazmi [36]	2019	Saudi Arabia	HCWs	41 (85%)	61%	2	58.5%	-	2
Alavian [37]	2011	Iran	Dental students	142 (89%)	-	1	-	-	-
Alese [38]	2016	Nigeria	HCWs	187 (NS)	-	-	16%	-	0
Ali [39]	2017	Pakistan	HCWs	381 (89%)	15.5 ± 3.69 [a]	2	-	-	-
Alqahtani [40]	2014	Saudi Arabia	HCWs and health students	600 (100%)	87%	3	-	-	-
Aniaku [41]	2019	Ghana	Nursing training students	358 (NS)	30%	2	67%	50%	2
Aroke [42]	2018	Cameroon	Medical students	714 (94%)	83%	2	26%	17%	2
Asif [43]	2011	Pakistan	Medical students	375 (95%)	-	-	57%	50%	2
Assuncao [14]	2012	Brazil	HCWs	1770 (NS)	-	-	86%	75%	6
Attaullah [44]	2011	Pakistan	HCWs	824 (NS)	-	-	98%	73%	1
AydemiR [45]	2016	Turkey	HCWs	1359 (NS)	-	-	82%	-	1

Table 2. *Cont.*

First Author	Year of Publication	Country	Participants	Sample Size (Participant Rates)	Good Knowledge		Vaccination Status		
					Total Score	NOS Score	At Least One Dose	Complete Dose	NOS Score
Bedaso [46]	2018	Ethiopia	HCWs	241 (93%)	61%; 6.6 ± 0.9 [a]	4	30%	22%	4
Bekele [47]	2014	Ethiopia	HCWs	98 (75%)	-	-	25%	18%	1
Celikel [48]	2014	Turkey	Pregnant women	198 (NS)	-	-	0.5%	-	2
Chan [13]	2011	Hong Kong	Pregnant women	1697 (85%)	Detailed per-question	4	-	-	-
Chao [49]	2010	China	Others	250 (NS)	13 (4–16) [b]	3	-	-	-
Chingle [50]	2017	Nigeria	Medical students	1200 (NS)	-	-	48%	30%	4
Choudhary [51]	2017	India	Medical students	100 (NS)	82%	0	64%	-	0
da Costa [52]	2013	Brazil	HCWs	762 (96%)	-	-	-	53%	6
de Souza [53]	2014	Brazil	Medical students	675 (79%)	-	-	49%	-	0
Debes [54]	2016	Tanzania	HCWs	114 (NS)	-	1	35%	-	1
Demsis [55]	2018	Ethiopia	Medical students	408 (97%)	81%	6	-	-	-
Dev [56]	2018	India	HCWs	300 (66%)	-	2	34%	7%	2
Ferreira [57]	2012	Brazil	HCWs	292 (88%)	-	-	-	91.2%	5
Ghomraoui [58]	2016	Saudi Arabia	Medical students	444 (93%)	47%	4	88%	60%	4
Guerra [27]	2018	Brazil	Pregnant women	324 (NS)	-	-	26.8%	-	2
Hebo [59]	2019	Ethiopia	HCWs	230 (NS)	74%	4	-	-	-
Ibrahim [60]	2014	Syria	Medical students	128 (NS)	-	1	44%	-	1
Iqbal [61]	2019	India	Medical students	341 (NS)	-	-	55%	37%	0
Jaquet [12]	2017	Senegal	HCWs	127 (NS)	38 (34–44) [b]	4	-	-	-
Joukar [62]	2018	Iran	HCW and others	3391 (58%)	-	4	-	-	-
Kesieme [63]	2011	Nigeria	HCWs	228 (NS)	-	1	27%	-	1
Khan [64]	2010	Pakistan	Medical students	1509 (NS)	10%	1	79%	55%	1
Khandelwa [65]	2018	India	Dental students	240 (NS)	-	2	45%	-	2

Table 2. *Cont.*

First Author	Year of Publication	Country	Participants	Sample Size (Participant Rates)	Good Knowledge		Vaccination Status		
					Total Score	NOS Score	At Least One Dose	Complete Dose	NOS Score
Ko [66]	2017	South Korea	HCWs	242 (44%)	-	-	100%	69%	4
Kouassi [67]	2017	Côte d'Ivoire	HCWs	291 (NS)	-	-	47%	-	4
Li [68]	2015	China	Dental intern students	313 (95%)	83.8%	2	-	-	-
Machiya [69]	2015	Botswana	HCWs	117 (59%)	17%; 7.9 ± 2.3 [a]	4	50%	31%	5
Meriki [70]	2018	Cameroon	HCW and others	265 (NS)	-	-	30%	5%	5
Mirzaei [28]	2019	Iran	HCWs	299 (100%)	-	-	-	58.5%	7
Mungandi [29]	2017	Zambia	HCWs	331 (NS)	78%	-	19%	-	4
Mursy [71]	2016	Sudan	HCWs	110 (73%)	58%	2	73%	41%	2
Mustafa [72]	2015	Sudan	HCWs	372 (NS)	-	2	73%	-	2
Noubiap [73]	2013	Cameroon	Medical students	111 (NS)	83% (risk factor)	1	31%	18%	1
Noubiap [74]	2014	Cameroon	Surgical residents	49 (70%)	Detailed per-question	1	47%	25%	2
Ogoina [75]	2014	Nigeria	HCWs	290 (76%)	-	-	65%	-	3
Okwara [76]	2012	Nigeria	HCWs	169 (NS)	-	2	55%	31%	2
Omotowo [77]	2018	Nigeria	HCWs	3132 (91%)	-	3	51%	-	4
Oyewusi [78]	2015	Nigeria	HCWs	210 (88%)	65%	2	66%	-	-
Pathoumthong [6]	2014	Lao	Health students	961 (NS)	72%	5	31%	21%	6
Ray [79]	2017	India	Dental students	269 (NS)	76%	0	-	52%	0
Resende [80]	2010	Brazil	HCWs	1134 (87%)	-	-	74%	-	7
Rathi [81]	2018	India	Medical students	161 (81%)	-	2	-	-	-
Sandeep [82]	2010	India	HCWs	141 (82%)	7.3 ± 4.4 [a]	3	-	-	-
Shahbaz [83]	2014	India	Medical and dental students	300 (NS)	-	1	40%	8%	1
Shukla [84,85]	2016	India	HCWs	89 (NS)	-	2	37%	-	2

Table 2. *Cont.*

First Author	Year of Publication	Country	Participants	Sample Size (Participant Rates)	Good Knowledge		Vaccination Status		
					Total Score	NOS Score	At Least One Dose	Complete Dose	NOS Score
Singh [86]	2011	India	Dental students	245 (NS)	-	2	39%	-	2
Tatsilong [16]	2016	Cameroon	HCWs	100 (61%)	47%	6	19%	-	5
Usmani [87]	2010	India	HCWs	215 (NS)	-	-	67%	51%	2
Vo [88]	2018	Viet Nam	Healthcare students	2017 (NS)	-	4	69%	-	4
Yamazhan [89]	2011	Turkey	Nursing students	1491 (89%)	-	5	85%	-	5
Yuan [90]	2019	China	HCWs	4168 (86%)	-	-	86%	60%	4
Zheng [91] †	2015	China	HCWs	1420 (NS)	-	-	40%	-	8
Low-risk population									
Ahmad [5]	2016	Malaysia	Students	662 (72%)	50.3%	3	-	14%	3
Chung [15]	2012	Hong Kong	General population >15 years old	1982 (90%)	14.0%; 13.5 ± 2.8 [a]	5	63%	-	5
Eni [92]	2019	Nigeria	Students and general population >15 years old	758 (94%)	-	4	35%	-	3
Lee [93]	2010	South Korea	Students	711 (NS)	1.3 ± 1.7 [a]	4	-	-	3
Moezzi [94]	2016	Iran	General population >15 years old	2956 (99%)	-	-	23%	21%	2
Mustufa [95]	2010	Pakistan	Teacher	200 (NS)	-	-	37%	-	2
Noreen [96]	2015	Pakistan	Women of childbearing age	430 (NS)	-	5	-	-	-
Osei [20]	2019	Ghana	Students	226 (100%)	-	-	56%	14%	30%
Park [19]	2012	South Korea	Women 30+ years old	4350 (NS)	-	-	-	40%	4
Park [18]	2013	South Korea	Men 40+ years old	2174 (NS)	-	-	-	33%	4
Rajamoorthy [10]	2019	Malaysia	General population >15 years old	764 (99%)	37%; 14.9 ± 3.8 [a]	5	-	-	6

Table 2. *Cont.*

First Author	Year of Publication	Country	Participants	Sample Size (Participant Rates)	Good Knowledge		Vaccination Status		
					Total Score	NOS Score	At Least One Dose	Complete Dose	NOS Score
Roushan [97]	2013	Iran	General population >15 years old	13965 (87%)	-	6	-	-	-
Shakeel [98]	2015	Pakistan	General population >15 years old	434 (79%)	-	1	86%	33%	1
Vo [99]	2018	Viet Nam	Students	535 (NS)	3.5 ± 0.2 [a]	6	-	-	-
Yang [100]	2015	China	Migrant worker	2065 (99%)	-	2	-	-	-
Zafrin [101] ††	2018	Bangladesh	General population >15 years old	-	Detailed per-question	6	-	-	-

† = Prospective cohort study; †† = Case-control study; HCWs = Health-care workers; [a] Mean (standard deviation); [b] Median (IQR).

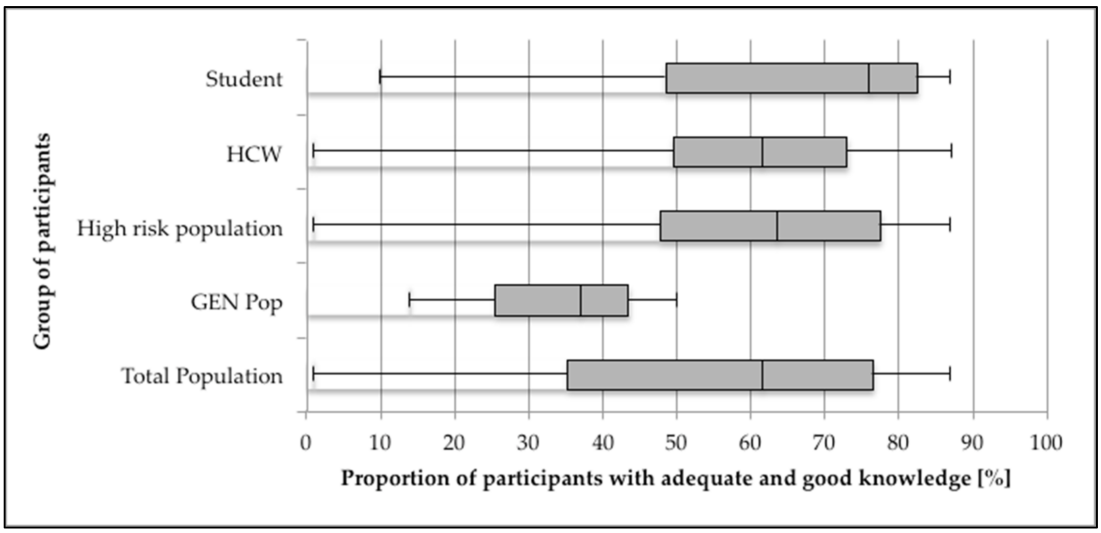

Figure 2. Proportion of participants with good and adequate knowledge combined.

3.4. Hepatitis B Vaccination

The median proportions of getting at least one dose and getting complete doses of hepatitis B vaccination among the high-risk population were 50% (IQR 34.5–73%) and 39% (IQR 21.3–58%), respectively. The median proportion of getting at least one dose and complete doses of hepatitis B vaccination among the low-risk population were 37% (35–74.5%) and 27% (19.3–34.8%), respectively (Figure 3). Therefore, populations at high risk tend to have a higher proportion of complete vaccination (median percentage 39.1% vs. 27%) than the low-risk population. In addition, HCW were found to have the highest proportions of both receiving at least one dose and receiving the complete vaccination among the populations at high risk (Figure 3).

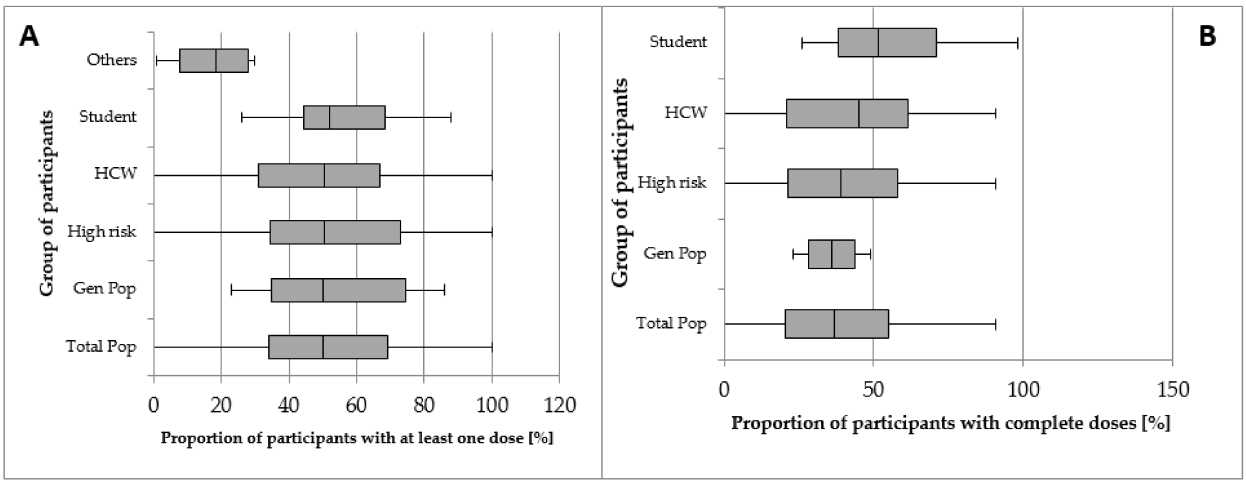

Figure 3. Proportion of participants with (**A**) at least one dose and (**B**) complete doses of hepatitis B vaccination.

3.5. Factors Associated with Knowledge and Vaccination Status

Overall, variables which predicted the knowledge and vaccination status of hepatitis B could be summarized in eight categories: sociodemographic, work related to hepatitis B, student related to hepatitis B, information exposure, exposure experience, vaccination status, knowledge of hepatitis B, and lifestyle in the high- and low-risk populations (Tables 3 and 4).

Table 3. The determinants of hepatitis B knowledge.

No	Factors	High-Risk Population	Low-Risk Population	Number of Studies *
		Sociodemographic factors		
1	Age	Younger age group (positive association; ref = older age group) [11–13]; no association [15–17]	Younger age group (negative association; ref = older age group) [10]; no association [15–17]	4/7
2	Gender	Male sex (positive association; ref = women) [11,16]; no association [10,12,15]	No association [10,12,15]	2/5
3	Ethnic group	-	Malay ethnic group (positive association; ref = Indian ethnic group) [10]	1/1
4	Residency	Urban (positive association; ref = rural) [49,99]; no association [12,15]	No association [12,15].	2/4
5	Occupational status	Health-care worker (positive association; ref = unemployed) [17]	No association [10,15]	1/3
6	Monthly income	Higher income (positive association; ref = lower income) [10,13,15]	Higher income (positive association; ref = lower income) [10,13,15]	3/3
7	Level of education	Higher education (positive association; ref = lower education) [10,16,17,49]	Higher education (positive association; ref = lower education) [10,16,17,49]	4/4
		Work-related factors		
8	Profession of HCW	Physician (positive association; ref = nurse/midwife/pharmacist) [11,49]; general practitioner (positive association; ref = specialist) [12]	-	3/3
9	Part-time job	No part time job (positive association; ref =having part-time job) [99]	-	1/1
		Student-related factors		
10	Year of study	Higher level (positive association; ref = lower level) [99]	-	1/1
11	University/faculty/type of facility	Private facility (positive association; ref = public facility) [99]; no association [17,92]	-	1/3

Table 3. *Cont.*

No	Factors	High-Risk Population	Low-Risk Population	Number of Studies *
		Experience factors		
12	Knowing someone who lives infected	-	Yes (positive association; ref = no) [92]	1/1
13	Screening for Hepatitis B	Yes (positive association; ref = never) [11,49,92]; frequently/systematic (positive association; ref = never) [12]	Yes (positive association; ref = never) [11,49,92]	4/4
		Information exposure factors		
14	Heard about hepatitis B/lecturer on hepatitis B	Yes (positive association; ref = never) [12,92]	Yes (positive association; ref = never) [12,92]	2/2
		Vaccination status		
15	Vaccination status	Yes (positive association; ref = No) [99]; appropriate (positive association; ref = inappropriate) [11]	No association [49,92]	2/4

* Number of studies finding a significant association/number of studies investigating the fact.

Table 4. The determinants of hepatitis B vaccine uptake.

No	Factors	High-Risk Population	Low-Risk Population	Number of Studies *
		Sociodemographic factors		
1	Age	Older age group (positive association; ref = older age group) [15,29,77]; (negative association; ref = older age group) [13,19,52,90]; no association [14,17,18,20,67,70,75,102]	Older age group (positive association; ref = older age group) [15,29,77]; (negative association; ref = older age group) [13,19,52,90]; no association [14,17,18,20,67,70,75,102]	7/15
2	Gender	Female (positive association; ref = women) [20,28,66,80,102]; (Negative association; ref = women) [11]; No association [14,15,29,35,67,70,75,77,90]	Female (positive association; ref = women) [20,28,66,80,102]; no association [14,15,29,35,67,70,75,77,90]	6/15
3	Ethnic group	Lao Soung ethnic group (positive association; ref = Lao Loum ethnic group) [6]	-	1/1

Table 4. *Cont.*

No	Factors	High-Risk Population	Low-Risk Population	Number of Studies *
4	Residency	Giansu (positive association; ref = Fijian) [90]; No association [14,15,19,20,66]	Urban (positive association; ref = metropolitan) [19]; no association [14,15,19,20,66]	2/7
5	Marital status/family status	Married (positive association; ref = single) [6]; with partner (positive association; ref = without partner [14]; single (positive association; ref = married [77]; no association [11,15,17–20]	No association [11,15,17–20]	3/8
6	Monthly income	No association [57]	Higher income (positive association; ref = lower income [15,18,19]	3/4
7	Health insurance	-	Having health insurance (positive association; ref = no [18,19]	2/2
8	Level of education/educational in year	Higher education (positive association; ref = lower education) [14,17–19,52]; no association [15,57,77]	Higher education (positive association; ref = lower education) [14,17–19,52]; no association [15,57,77]	5/8
9	Occupational status	Health worker (positive association; ref = unemployed) [17]	Routine and manual (positive association; ref = professional) [19]; teacher (positive association; ref = housewife) [15]; no association [18]	3/4
		Work-related factors		
10	Profession of HCW	Laboratory staff (positive association; ref = nurse) [29]; internship doctor (positive association; ref = nurse/pharmacist/laboratory staff) [77]; medical technology/nurse (positive association; ref = physician) [90]; physician (positive association; ref = technician) [14]; nurse (positive association; ref = physician) [67]; nurse/consultant/resident (positive association; ref = house office) [75]; no association [11,35,102]	-	6/9
11	Work department	Outpatient department (positive association; ref = medical pediatric) [70]; high-risk department (positive association; ref = low-risk department) [90]; no association [35]	-	2/3

Table 4. *Cont.*

No	Factors	High-Risk Population	Low-Risk Population	Number of Studies *
12	Work experience	10 years or less (positive association; ref = more than 10 years) [70]; less than 5 years (positive association; ref = 5 years and more) [35]; more than 10 years (positive association; ref = less than one year) [77]; no association [14,29,57,66,75,90,102]	-	3/10
13	Work regimen and level of satisfaction with the profession	Fixed (positive association; ref = hired employee) [52]; high satisfaction (positive association; ref = low satisfaction) [57]	-	2/2
14	Facility level	High level (positive association; ref = low level) [29]; tertiary hospital (positive association; ref = non-tertiary [17]; country/township hospital (positive association; ref = municipal) [90]; no association [29,67]	-	3/5
15	Management's protection at workplace	Using personal protective equipment (positive association; ref = no) [14,80]; free hepatitis B vaccination from work (Positive association; ref = no) [90]; regular training in occupational health in the last two years (positive association; ref = no) [52]	-	4/4
		Student-related factors		
16	Faculty	Post-graduation (positive association; ref = medicine); medicine (positive association; ref = basic science/pharmacy/medical technology) [6]	-	1/1
		Information exposure factors		
17	Training infection	Yes (positive association; ref = No) [29,35,67,90,103]; no association [66]	-	5/6
		Experience factors		
18	Exposure experience	Ever had experience of occupational exposure (positive association; ref = No) [35,52,57]; no blood transfusion history (positive association; ref = no) [80]; having positive family/friend of hepatitis B infected (positive association; ref = no) [28] no association [14]	-	5/6

Table 4. *Cont.*

No	Factors	High-Risk Population	Low-Risk Population	Number of Studies *
19	Previous hepatitis B screening/anti-hepatitis B	Ever HBsAg screen test (positive association; ref = never) [11]; anti-hepatitis B status resulted positive (positive association; ref = resulted positive) [70]	-	2/2
		Knowledge		
20	Hepatitis B knowledge	Acceptable knowledge (positive association; ref = unacceptable [90]; no association [20,29,66]	-	1/4
		Lifestyle		
21	Alcohol consumption	Alcohol consumption (negative association; ref = no) [52,57,70]; no association [14,70]	-	3/5
22	Tobacco used	Tobacco used (negative association; ref = no) [57]; no association [14,70]	-	1/3

* Number of studies finding a significant association/number of studies investigating the topic.

Nine of 58 (15.5%) studies addressing knowledge and 22 of 69 (31.8%) studies addressing vaccination status assessed sociodemographic factors as predictor variables. Among these, monthly income and level of education were strong predictors of both hepatitis B knowledge and vaccination status in both the high- and low-risk population.

In the high-risk population, four (6.9%) and 15 (22.1%) studies discussed the association between work-related factors and hepatitis B knowledge and vaccination status, respectively. However, only profession as a HCW influenced hepatitis B knowledge and vaccination status among participants. In addition, management's protection at workplace was a predictor for vaccine uptake. Apart from that, of the four studies assessing the association between being a student and hepatitis B knowledge and vaccination status, only one study found that year of study and type of university or school were predictor variables for hepatitis B knowledge [6,17,92,99].

Two (3.4%) and five (7.4%) studies analyzed the association between exposure to information and hepatitis B knowledge and vaccine uptake, respectively, and found that 'ever heard about hepatitis B' had a positive association with better knowledge in both the high- and low-risk populations [92]. Furthermore, among HCW, four of five studies showed that experience in infection training on hepatitis B was a strong predictor variable for vaccination status [29,35,67,90].

Knowing an infected person, screening for hepatitis B, family history, and exposure to hepatitis B were variables included in twelve studies related to knowledge and vaccination status of hepatitis B. Of those, exposure and previous hepatitis B screening influenced vaccine uptake while knowing an infected person was a strong predictor variable for hepatitis B knowledge in the low-risk population. In addition, in the high-risk population, vaccination status influenced hepatitis B knowledge [11,99], while knowledge of hepatitis B [90] and lifestyle (alcohol and tobacco used) [52,57,70] were predictors for vaccine uptake, albeit on a lower level.

3.6. Reasons for Not Being Immunized

In this systematic review, 32 studies (36%) assessed people's reasons for not being immunized, of which most (N = 29, 90.6%) were conducted in the high-risk population (left side of the red line). Here, among HCW (N = 17, 53.1%), the most common reason for not being vaccinated was vaccine costs (N = 12, 70.6%) [4,16,31,32,35,44,56,66,67,72,77,90], followed by lack of time (N = 10, 58.8%) [11,16,35,44,56,63,66,67,77,90] and lack of motivation (N = 9, 52.9%) [16,35,39,44,56,66,77,80,90], including 'never felt the need for vaccination' or 'having no fear of catching hepatitis B infection'. Slightly different results were found among students of medicine or a health-related field (N = 10, 31.6%) [6,33,50,58,60,65,73,74,83,99]. Here, lack of motivation was the major reason against vaccination (N = 8, 80%) [6,33,50,58,60,65,73,74,83,99], followed by fear of injection or side effects (N = 5, 50%) [6,58,60,65,99], and lack of information (N = 5, 50%) [6,33,73,74,99]. Three studies (9.4%) addressed the low-risk population, which is general population (right side of the red line) and found three major reasons: lack of motivation (N = 2, 66.7%) [19,20], lack of time (N = 3, 100%) [18–20], and lack of information (N = 2, 66.7%) [18,19] (Figure 4).

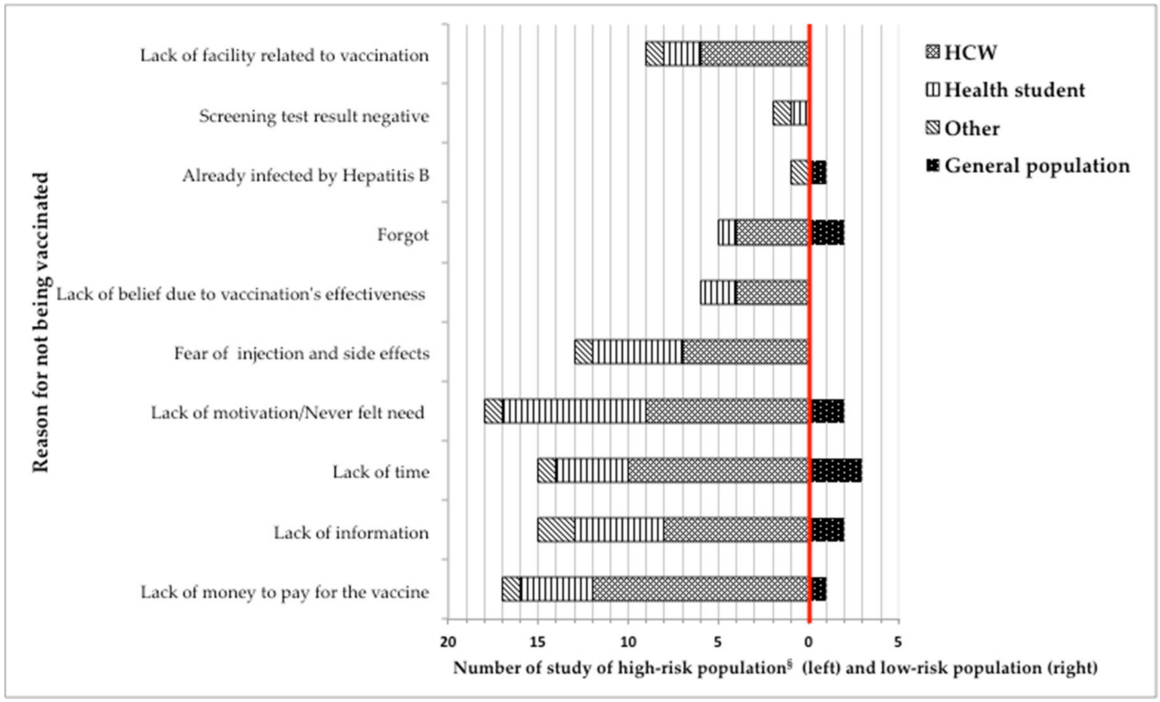

Figure 4. Number of studies addressing reasons for not being vaccinated by high-risk and low-risk populations. § High-risk population consisted of HCW, students, and others.

4. Discussion

We conducted a comprehensive systematic review of hepatitis B knowledge and vaccination status and predicting factors in developing countries that included articles published between 2010 and 2019. Overall, 2443 records were identified and 89 articles were ultimately included. Of these, 58 and 69 studies provided data on knowledge and vaccination status of hepatitis B, respectively.

4.1. Main Findings

We found that important determinants for the level of knowledge and vaccination status varied considerably across studies. However, the strongest predictive factors for hepatitis B knowledge and vaccination status were monthly income, level of education, and profession as HCW in the high- and low-risk populations. Being ever screened for hepatitis B was a strong influence for hepatitis B knowledge, while health insurance, management's protection at workplace, experience in infection training on hepatitis B, and experience of hepatitis B exposure were strong predictors for vaccine uptake.

We also revealed that there are different predictors of the level of knowledge and vaccination status between high-risk and low-risk populations. This is most likely due to a limited number of studies regarding the low-risk population (10%). Among those, only two and three studies assessed the predictor variables of hepatitis B knowledge and vaccination status, respectively. Additionally, some variables were only assessed in a particular population, e.g., variables related to work were only collected among HCW.

Other than that, this study found that lack of motivation, lack of information, and lack of money were three major reasons for people to avoiding hepatitis B vaccination in developing countries.

4.2. Factors Associated with Knowledge and Vaccination Status

Whereas sociodemographic variables such as age, sex, ethnicity, residency, and marital status were still inconclusive predictor variables, monthly income and level of education were found to be strong predictors for hepatitis B knowledge and vaccination status.

A number of articles demonstrated that participants with higher income had better knowledge and vaccination uptake [10,13,15,18,19]. This is reasonable, because income is a driving force behind the health disparities and is directly associated with health literacy. Hence, according to Tang et al., people with lower income are less likely to seek health information or to use health-care professionals as a first source of health information and have greater difficulty understanding information compared to people with higher income [104].

Another strong predictor for hepatitis B knowledge and vaccination status was education. Our review revealed that the higher the level of education, the more likely a person was to have good knowledge and to receive hepatitis B vaccination. This is most likely due to the fact that education affects health through an individual's improved ability to acquire and process health-related knowledge, and improved health behavior [105].

Our findings also indicate that factors related to work, such as profession as HCW, had strong evidence as predictor variables for hepatitis B knowledge and vaccine uptake among the high-risk population. People working in high-risk conditions of hepatitis B transmission were more likely to have good knowledge of the disease and tend to protect themselves from infection through vaccination [15,17]. This is reasonable because HCW have wider access to information which has a substantial impact on both knowledge and vaccination status. Ochu et al., for example, revealed that the higher the perceived risk of contracting hepatitis B, the higher the awareness of the need for vaccination [102].

Furthermore, in the high-risk population, a workplace with good occupational protection measures in place most likely also had higher hepatitis B vaccination coverage among the employees. These protection measures could be in the form of mandatory use of personal protective equipment [14,80], provision of free hepatitis B vaccination for employees [90], and regular safety training for employees, including demonstration of the benefits of hepatitis B vaccination [52].

People with previous experience related to hepatitis B, such as people with family members or friends infected by hepatitis B, or people with a positive hepatitis B screening result, tended to have a better knowledge of the disease and received hepatitis B vaccination for prevention purposes [11,28,70,80]. Therefore, the greater the experience with or exposure to hepatitis B, the better knowledge people had and the greater their willingness to receive vaccination.

Information exposure has a direct association with good knowledge, which in turn, also has an impact on vaccination status in both high-risk and low-risk populations. Eni et al. found that persons who had ever heard about hepatitis B before were more likely to have been vaccinated and have a higher score of knowledge [92]. This finding is supported by Mungandi et al., who found that HCW who were ever trained in infection control were twice as likely to be vaccinated against hepatitis B as those who were not trained before [29].

A study among dentists in Monte Carlo reported that lifestyle factors, such as alcohol consumption and tobacco use, had a negative association with vaccine uptake [57]. The study estimated that non-smokers and people not consuming alcohol were 2.5 and 3.0 times more likely to receive the hepatitis B vaccine, respectively [57]. Correspondingly, a variety of other studies found a lower prevalence of vaccination among people consuming alcohol [52]. This association might be explained by increased health awareness, as people with a healthy lifestyle tend to protect themselves from any potential disease, including hepatitis B.

4.3. Reasons for Not Being Vaccinated

Generally, there were three major reasons for people opposing vaccination: lack of motivation, lack of information, and lack of money. However, some of these reasons were interrelated, as the lack of information and awareness of the vaccination might influence someone's belief regarding its effectiveness. Poor information regarding hepatitis B infection and vaccination reduces people's motivation to vaccinate, as most participants

claimed they never felt the need to vaccinate against hepatitis B infection. Although none of the selected studies reported fear of occult hepatitis B infection after vaccination as a reason not to vaccinate among the adult population, Aghakhani et al. found that hepatitis B vaccine escape mutants had caused infections in vaccinated individuals since 1990s. This issue might be considered as another factor influencing vaccine hesitancy [106–108]. Hence, there is a pressing need for information about hepatitis B infection, benefits of hepatitis B vaccination, and the emergence of vaccine escape mutations through, e.g., participation in infection training on hepatitis B regularly, and increasing risk perception and awareness of hepatitis B vaccination among the adult population, especially for high-risk populations such as HCW.

Furthermore, according to Park et al., the lack of awareness is the main barrier to vaccination in the population [18]. Apart from that, HCW named the costs of the hepatitis B vaccination as the most common reason against it. Given that HCW are a group at high risk of contracting hepatitis B and can also take the role of a vector in the transmission of disease to their patients, health-care systems should advocate health policies for free hepatitis B vaccination for HCW. For example, a system could be implemented in the workplace that provides management protection for staff such as free vaccinations.

4.4. Strength and Limitation of the Review

By focusing on developing countries, this study attempted to identify specific patterns from more than 70% of the world's population. This is considered essential in providing a considerable amount of information about relevant variables of hepatitis B knowledge and vaccination status in a variety of countries with different cultures and financial abilities to run health programs. Apart from that, there are some limitations to this review. First, most studies (77.6%) were considered unsatisfactory, because they did not assess outcomes in a multivariable analysis, identifying important predictor variables for knowledge about hepatitis B and vaccination status. Second, approximately 82% of studies were based on high-risk populations such as HCW. Third, our study did not look at vaccine escape mutations regarding any population criteria due to limited scientific evidence. Therefore, we report the results stratified by population allowing interpretation for both the high- and low-risk populations. Last, the search strategy was restricted to papers that were peer reviewed and written in English and, thus, 10 included articles written in the countries' mother tongues, such as Mandarin, French, and Turkish were missed.

5. Conclusions

Our results suggest that various factors are associated with knowledge and vaccination status relating to hepatitis B. Some of the variables showed a strong and consistent relationship, while findings regarding others were inconclusive. In addition, there were different predictor variables for hepatitis B knowledge and vaccination status in the high-risk and low-risk populations. Exposure to information has an impact on increasing knowledge and awareness of hepatitis B infection and vaccination. In addition, institutional support, i.e., from the workplace, is needed through management protection for employees and especially for those at high risk. Finally, financial support related to vaccination is an important factor in increasing vaccine coverage. Therefore, stakeholders could improve further hepatitis B vaccination programs and research by providing funds for routine monitoring and evaluation of vaccination coverage as well as research funding. For this purpose, our review can act as guideline on important factors for prioritization in vaccination programs. In addition, further studies of good quality are necessary to improve the ascertainment of risk factors, using vaccine records or vaccine registries instead of personal recall only.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/vaccines9060625/s1, Table S1: PRISMA 2020 Checklist, Table S2: Keyword statements and search strategies, Table S3: Evidence quality based on the Newcastle-Ottawa Scale (NOS).

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References

1. World Health Organization. World Day Hepatitis 2020. Available online: https://www.who.int/campaigns/world-hepatitis-day/2020 (accessed on 10 November 2020).
2. World Health Organization. *Global Hepatitis Report, 2017*; World Health Organization: Geneva, Switzerland, 2017.
3. Aaron, D.; Nagu, T.J.; Rwegasha, J.; Komba, E. Hepatitis b vaccination coverage among healthcare workers at national hospital in tanzania: How much, who and why? *BMC Infect. Dis.* **2017**, *17*, 786. [CrossRef] [PubMed]
4. Abiodun, O.; Shobowale, O.; Elikwu, C.; Ogbaro, D.; Omotosho, A.; Mark, B.; Akinbola, A. Risk perception and knowledge of hepatitis b infection among cleaners in a tertiary hospital in Nigeria: A cross-sectional study. *Clin. Epidemiol. Glob. Health* **2019**, *7*, 11–16. [CrossRef]
5. Ahmad, A.; Munn Sann, L.; Abdul Rahman, H. Factors associated with knowledge, attitude and practice related to hepatitis b and c among international students of Universiti Putra Malaysia. *BMC Public Health* **2016**, *16*, 611. [CrossRef] [PubMed]
6. Pathoumthong, K.; Khampanisong, P.; Quet, F.; Latthaphasavang, V.; Souvong, V.; Buisson, Y. Vaccination status, knowledge and awareness towards hepatitis b among students of health professions in Vientiane, Lao Pdr. *Vaccine* **2014**, *32*, 4993–4999. [CrossRef] [PubMed]
7. Zampino, R.; Boemio, A.; Sagnelli, C.; Alessio, L.; Adinolfi, L.E.; Sagnelli, E.; Coppola, N. Hepatitis b virus burden in developing countries. *World J. Gastroenterol.* **2015**, *21*, 11941–11953. [CrossRef] [PubMed]
8. Juon, H.-S.; Choi, K.S.; Park, E.-C.; Kwak, M.-S.; Lee, S. Hepatitis b vaccinations among Koreans: Results from 2005 Korea national cancer screening survey. *BMC Infect. Dis.* **2009**, *9*, 185. [CrossRef]
9. Owiti, J.A.; Greenhalgh, T.; Sweeney, L.; Foster, G.R.; Bhui, K.S. Illness perception and explanatory models of viral hepatitis b and c among immigrants and Ferugees: A narrative systematic review. *BMC Public Health* **2015**, *15*, 151. [CrossRef]
10. Rajamoorthy, Y.; Taib, N.M.; Munusamy, S.; Anwar, S.; Wagner, A.L.; Mudatsir, M.; Müller, R.; Kuch, U.; Groneberg, D.A.; Harapan, H.; et al. Knowledge and awareness of hepatitis b among households in Malaysia: A community-based cross-sectional survey. *BMC Public Health* **2019**, *19*, 47. [CrossRef]
11. Adekanle, O.; Ndububa, D.A.; Olowookere, S.A.; Ijarotimi, O.; Ijadunola, K.T. Knowledge of hepatitis b virus infection, immunization with hepatitis b vaccine, risk perception, and challenges to control hepatitis among hospital workers in a Nigerian tertiary hospital. *Hepat. Res. Treat.* **2015**, *2015*, 439867. [CrossRef]
12. Jaquet, A.; Wandeler, G.; Tine, J.; Diallo, M.B.; Manga, N.M.; Dia, N.M.; Fall, F.; Dabis, F.; Seydi, M. Prevention and care of hepatitis b in Senegal; Awareness and attitudes of medical practitioners. *Am. J. Trop. Med. Hyg.* **2017**, *97*, 389–395. [CrossRef]
13. Chan, O.K.; Lao, T.T.; Suen, S.S.H.; Lau, T.K.; Leung, T.Y. Knowledge on hepatitis b infection among pregnant women in a high endemicity area. *Patient Educ. Couns.* **2011**, *85*, 516–520. [CrossRef]
14. Assunção, A.Á.; de Araújo, T.M.; Ribeiro, R.B.N.; Oliveira, S.V.S. Hepatitis b vaccination and occupation exposure in the healthcare sector in Belo Horizonte, minas Gerais. *Rev. Saúde Pública* **2012**, *46*, 665–673. [CrossRef]
15. Chung, P.W.; Suen, S.H.; Chan, O.K.; Lao, T.H.; Leung, T.Y. Awareness and knowledge of hepatitis b infection and prevention and the use of hepatitis b vaccination in the Hong Kong adult Chinese population. *Chin. Med. J.* **2012**, *125*, 422–427.
16. Tatsilong, H.O.P.; Noubiap, J.J.N.; Nansseu, J.R.N.; Aminde, L.N.; Bigna, J.J.R.; Ndze, V.N.; Moyou, R.S. Hepatitis b infection awareness, vaccine perceptions and uptake, and serological profile of a group of health care workers in Yaoundé, Cameroon. *BMC Public Health* **2016**, *15*, 706. [CrossRef]
17. Adeyemi, A.B.; Enabor, O.O.; Ugwu, I.A.; Bello, F.A.; Olayemi, O.O. Knowledge of hepatitis b virus infection, access to screening and vaccination among pregnant women in Ibadan, Nigeria. *J. Obstet. Gynaecol. J. Inst. Obstet. Gynaecol.* **2013**, *33*, 155–159. [CrossRef]
18. Park, B.; Choi, K.S.; Lee, H.-Y.; Kwak, M.-S.; Jun, J.K.; Park, E.-C. Determinants of suboptimal hepatitis b vaccine uptake among men in the republic of Korea: Where should our efforts be focused: Results from cross-sectional study. *BMC Infect. Dis.* **2013**, *13*, 218. [CrossRef]
19. Park, B.; Choi, K.S.; Lee, H.Y.; Jun, J.K.; Park, E.C. Socioeconomic inequalities in completion of hepatitis b vaccine series among korean women: Results from a nationwide interview survey. *Vaccine* **2012**, *30*, 5844–5848. [CrossRef]

20. Osei, E.; Niyilapah, J.; Kofi Amenuvegbe, G. Hepatitis b knowledge, testing, and vaccination history among undergraduate public health students in Ghana. *Biomed. Res. Int.* **2019**, *2019*, 7645106. [CrossRef]
21. PROSPERO. University of York Centre for Reviews and Dissemination. Available online: http://www.crd.york.ac.uk/PROSPERO/ (accessed on 27 July 2020).
22. Shamseer, L.; Moher, D.; Clarke, M.; Ghersi, D.; Liberati, A.; Petticrew, M.; Shekelle, P.; Stewart, L.A.; Group, P.-P. Preferred reporting items for systematic review and meta-analysis protocols (prisma-p) 2015 statement. *BMJ* **2015**, *349*, 1. [CrossRef]
23. Liberati, A.; Altman, D.G.; Tetzlaff, J.; Mulrow, C.; Gøtzsche, P.C.; Loannidis, J.P.A.; Clarke, M.; Devereaux, P.J.; Kleijnen, J.; Moher, D. The prisma statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: Explanation and elaboration. *BMC Online* **2009**, *339*, 2700. [CrossRef]
24. United Nations. *World Economic Situation and Prospects 2020*; United Nations: New York, NY, USA, 2020.
25. Bramer, W.M.; Rethlefsen, M.L.; Kleijnen, J.; Franco, O.H. Optimal database combination for literature searches in systematic reviews: A prospective explanatory study. *Syst. Rev.* **2017**, *6*, 245. [CrossRef] [PubMed]
26. Wells, G.; Shea, B.; O'Connell, D.; Peterson, J.; Welch, V.; Losos, M.; Tugwell, P. The Newcastle-Ottawa Scale (Nos) for Assessing the Quality of Nonrandomised Studies in Meta-Analysis. Available online: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (accessed on 8 April 2020).
27. Guerra, A.B.; Siravenha, L.Q.; Laurentino, R.V.; Feitosa, R.N.M.; Azevedo, V.N.; Vallinoto, A.C.R.; Ishak, R.; Machado, L.F.A. Seroprevalence of hiv, htlv, cmv, hbv and rubella virus infections in pregnant adolescents who received care in the city of Belem, para, northern brazil. *BMC Pregnancy Childbirth* **2018**, *18*, 169. [CrossRef] [PubMed]
28. Mirzaei Alavijeh, M.; Vaezi, M.; Jalilian, F. Hepatitis b vaccine acceptability among nurses: A theory based conceptualization. *Middle East J. Dig. Dis.* **2019**, *11*, 45–51. [CrossRef] [PubMed]
29. Mungandi, N.; Makasa, M.; Musonda, P. Hepatitis b vaccination coverage and the determinants of vaccination among health care workers in selected health facilities in Lusaka district, Zambia: An exploratory study. *Ann. Occup. Env. Med.* **2017**, *29*, 32. [CrossRef]
30. Abeje, G.; Azage, M. Hepatitis b vaccine knowledge and vaccination status among health care workers of Bahir Dar city administration, northwest ethiopia: A cross sectional study. *BMC Infect. Dis.* **2015**, *15*, 30. [CrossRef]
31. Abiola, A.-H.O.; Agunbiade, A.B.; Badmos, K.B.; Lesi, A.O.; Lawal, A.O.; Alli, Q.O. Prevalence of Hbsag, knowledge, and vaccination practice against viral hepatitis b infection among doctors and nurses in a secondary health care facility in Lagos state, south-western Nigeria. *Pan Afr. Med. J.* **2016**, *23*, 160. [CrossRef]
32. Abiola, A.O.; Omoyeni, O.E.; Akodu, B.A. Knowledge, attitude and practice of hepatitis b vaccination among health workers at the lagos state accident and emergency centre, toll-gate, Alausa, Lagos state. *West Afr. J. Med.* **2013**, *32*, 257–262.
33. Adenlewo, O.J.; Adeosun, P.O.; Fatusi, O.A. Medical and dental students' attitude and practice of prevention strategies against hepatitis b virus infection in a Nigerian university. *Pan Afr. Med. J.* **2017**, *28*, 33. [CrossRef]
34. Adjei, C.A.; Atibila, F.; Apiribu, F.; Ahordzor, F.; Attafuah, P.A.; Ansah-Nyarko, M.; Asamoah, R.; Menkah, W. Hepatitis b infection among parturient women in peri-urban Ghana. *Am. J. Trop. Med. Hyg.* **2018**, *99*, 1469–1474. [CrossRef]
35. Akibu, M.; Nurgi, S.; Tadese, M.; Tsega, W.D. Attitude and vaccination status of healthcare workers against hepatitis b infection in a teaching hospital, ethiopia. *Scientifica* **2018**, *2018*, 6705305. [CrossRef]
36. Al-Hazmi, A. Knowledge, attitudes, and practice of medical students regarding occupational risks of hepatitis b virus in college of medicine, Aljouf University. *Ann. Med. Health Sci. Res.* **2015**, *5*, 13–19. [CrossRef]
37. Alavian, S.M.; Mahboobi, N.; Mahboobi, N.; Savadrudbari, M.M.; Azar, P.S.; Daneshvar, S. Iranian dental students' knowledge of hepatitis b virus infection and its control practices. *J. Dent. Educ.* **2011**, *75*, 1627–1634. [CrossRef]
38. Alese, O.O.; Alese, M.O.; Ohunakin, A.; Oluyide, P.O. Seroprevalence of hepatitis b surface antigen and occupational risk factors among health care workers in Ekiti state, Nigeria. *J. Clin. Diagn. Res.* **2016**, *10*, LC16–LC18. [CrossRef]
39. Ali, A.; Khan, S.; Malik, S.M.; Haris Iqbal, M.; Aadil, M. Comparison of knowledge and attitudes regarding hepatitis b among healthcare professionals in Pakistan. *Cureus* **2017**, *9*, e1049. [CrossRef]
40. Alqahtani, J.M.; Abu-Eshy, S.A.; Mahfouz, A.A.; El-Mekki, A.A.; Asaad, A.M. Seroprevalence of hepatitis b and c virus infections among health students and health care workers in the Najran region, southwestern Saudi Arabia: The need for national guidelines for health students. *BMC Public Health* **2014**, *14*, 577. [CrossRef]
41. Aniaku, J.K.; Amedonu, E.K.; Fusheini, A. Assessment of knowledge, attitude and vaccination status of hepatitis b among nursing training students in Ho, Ghana. *Ann. Glob. Health* **2019**, *85*, 18. [CrossRef]
42. Aroke, D.; Kadia, B.M.; Anutebeh, E.N.; Belanquale, C.A.; Misori, G.M.; Awa, A.; Mbanga, C.M.; Ngek, L.T. Awareness and vaccine coverage of hepatitis b among Cameroonian medical students. *Biomed. Res. Int.* **2018**, *2018*, 3673289. [CrossRef]
43. Asif, M.; Raja, W.; Gorar, Z.A. Hepatitis b vaccination coverage in medical students at a medical college of mIrpurkhas. *J. Pak. Med. Assoc.* **2011**, *61*, 680–682.
44. Attaullah, S.; Khan, S.; Ayaz, S.; Khan, S.N.; Ali, I.; Hoti, N.; Siraj, S. Prevalence of HBV and HBV vaccination coverage in health care workers of tertiary hospitals of Peshawar, Pakistan. *Virol. J.* **2011**, *8*, 275. [CrossRef]
45. Özlem, A.; Köroglu, M.; Yüksel, B.; Öybek, A.; Altindis, S.; Gürkan, F.; Altindis, M.; Lab BioSafety TR Working Group. Hepatitis b virus vaccination rates among medical laboratory workers: A multi-centered assessment. *Viral Hepat. J.* **2016**, *22*, 82–87.

46. Bedaso, A.; Duko, B.; Fedlu, R. Knowledge on hbv vaccine and vaccination status among health care workers of Hawassa university comprehensive specialized hospital, Hawassa, southern Ethiopia: A cross sectional study. *BMC Res. Notes* **2018**, *11*, 912. [CrossRef] [PubMed]
47. Bekele, A.; Tadesse, A. Status of hepatitis b vaccination among surgeons practicing in Ethiopia: A cross sectional study. *Ethiop. Med. J.* **2014**, *52*, 107–112. [PubMed]
48. Celikel, A.; Ustunsoz, A.; Guvenc, G. Determination of vaccination status of pregnant women during pregnancy and the affecting factors. *J. Clin. Nurs.* **2014**, *23*, 2142–2150. [CrossRef] [PubMed]
49. Chao, J.; Chang, E.T.; So, S.K. Hepatitis b and liver cancer knowledge and practices among healthcare and public health professionals in china: A cross-sectional study. *BMC Public Health* **2010**, *10*, 98. [CrossRef]
50. Chingle, M.; Osagie, I.; Adams, H.; Gwomson, D.; Emeribe, N.; Zoakah, A. Risk perception of hepatitis b infection and uptake of hepatitis b vaccine among students of tertiary institution in Jos. *Ann. Afr. Med.* **2017**, *16*, 59–64. [CrossRef]
51. Choudhary, S.K.; Kumar, S.; Sinha, S. Knowledge and vaccination coverage of hepatitis b among first year MBBS students at indira gandhi institute of medical sciences, Patna. *Int. J. Sci. Study* **2017**, *4*, 101–104.
52. Da Costa, F.M.; de Barros Lima Martins, A.M.; Dos Santos Neto, P.E.; de Pinho Veloso, D.N.; Magalhaes, V.S.; Ferreira, R.C. Is vaccination against hepatitis b a reality among primary health care workers? *Rev. Lat. Am. Enferm.* **2013**, *21*, 316–324. [CrossRef]
53. Souza, E.P.d.; Teixeira, M.d.S. Hepatitis b vaccination coverage and post vaccination serologic testing among medical students at a public university in brazil. *Rev. Inst. Med. Trop. São Paulo* **2014**, *56*, 307–311. [CrossRef]
54. Debes, J.D.; Kayandabila, J.; Pogemiller, H. Knowledge of hepatitis b transmission risks among health workers in tanzania. *Am. J. Trop. Med. Hyg.* **2016**, *94*, 1100–1102. [CrossRef]
55. Demsiss, W.; Seid, A.; Fiseha, T. Hepatitis b and c: Seroprevalence, knowledge, practice and associated factors among medicine and health science students in northeast ethiopia. *PLoS ONE* **2018**, *13*, e0196539. [CrossRef]
56. Dev, K.; Sunil, S.K.; Abhay, G.; Gajanan, K.; Akash, S.; Bisure, K. Knowledge and awareness of the health care workers about the hepatitis b infection and their vaccination status in a newly started medical college. *J. Assoc. Physicians India* **2018**, *66*, 27–30.
57. Ferreira, R.C.; Guimarães, A.L.S.; Pereira, R.D.; Andrade, R.M.; Xavier, R.P.; de Barros Lima Martins, A.M.E. Vacinação contra hepatite b e fatores associados entre cirurgiões-dentistas. *Rev. Bras. Epidemiol.* **2012**, *15*, 315–323. [CrossRef]
58. Ghomraoui, F.A.; Alfaqeeh, F.A.; Algadheeb, A.S.; Al-Alsheikh, A.S.; Al-Hamoudi, W.K.; Alswat, K.A. Medical students' awareness of and compliance with the hepatitis b vaccine in a tertiary care academic hospital: An epidemiological study. *J. Infect. Public Health* **2016**, *9*, 60–65. [CrossRef]
59. Hebo, H.J.; Gemeda, D.H.; Abdusemed, K.A. Hepatitis b and c viral infection: Prevalence, knowledge, attitude, practice, and occupational exposure among healthcare workers of Jimma University medical center, southwest Ethiopia. *Sci. World J.* **2019**, *2019*, 9482607. [CrossRef]
60. Ibrahim, N.; Idris, A. Hepatitis b awareness among medical students and their vaccination status at Syrian Private University. *Hepat. Res. Treat.* **2014**, *2014*, 131920. [CrossRef]
61. Iqbal Gul, A.; Asif, M.; Rootaba, S.; Akif, D.; Ali, H.; Shafqat, R. Awareness of hepatitis b infection and its vaccination amongst medical students of different medical colleges in Lahore. *Pak. J. Med. Health Sci.* **2019**, *13*, 783–785.
62. Joukar, F.; Mansour-Ghanaei, F.; Naghipour, M.R.; Hassanipour, S. Knowledge, distribution and risk factors of hepatitis b and c infection in high-risk groups in Guilan province, Iran. *Hepat. Mon.* **2018**, *18*, e65870. [CrossRef]
63. Kesieme, E.B.; Uwakwe, K.; Irekpita, E.; Dongo, A.; Bwala, K.J.; Alegbeleye, B.J. Knowledge of hepatitis b vaccine among operating room personnel in Nigeria and their vaccination status. *Hepat. Res. Treat.* **2011**, *2011*, 157089. [CrossRef]
64. Khan, N.; Ahmed, S.M.; Khalid, M.M.; Siddiqui, S.H.; Merchant, A.A. Effect of gender and age on the knowledge, attitude and practice regarding hepatitis b and c and vaccination status of hepatitis b among medical students of Karachi, Pakistan. *J. Pak. Med. Assoc.* **2010**, *60*, 450–455.
65. Khandelwal, V.; Khandelwal, S.; Gupta, N.; Nayak, U.A.; Kulshreshtha, N.; Baliga, S. Knowledge of hepatitis b virus infection and its control practices among dental students in an Indian city. *Int. J. Adolesc. Med. Health* **2017**, *30*. [CrossRef]
66. Ko, K.; Kim, S.; Kim, S.H.; Son, K.Y.; Lee, J.; Lee, D.R. Knowledge, current status, and barriers toward healthcare worker vaccination among family medicine resident participants in a web-based survey in Korea. *Korean J. Fam. Med.* **2017**, *38*, 21–27. [CrossRef] [PubMed]
67. Kouassi, D.; Angbo-Effi, O.; Aka, L.; Coulibaly, M.B.; Soumahoro, S.; Yao, G.; Soro, N. Perceptions and practice of health care workers regarding hepatitis b vaccination, Bouaké, Côte D'ivoire, 2016. *J. Public Health Afr.* **2017**, *8*, 715. [CrossRef] [PubMed]
68. Li, X.; Kang, H.; Wang, S.; Deng, Z.; Yang, T.; Jia, Y.; Yang, Y. Knowledge, attitude, and behavior of hepatitis b virus infection among chinese dental interns. *Hepat. Mon.* **2015**, *15*, e25079. [CrossRef]
69. Machiya, T.; Burnett, R.J.; Fernandes, L.; Francois, G.; De Schryver, A.; van Sprundel, M.; Mphahlele, M.J. Hepatitis b vaccination of healthcare workers at the princess marina hospital, Botswana. *Int. Health* **2015**, *7*, 256–261. [CrossRef] [PubMed]
70. Meriki, H.D.; Tufon, K.A.; Anong, D.N.; Tony, N.J.; Kwenti, T.E.; Bolimo, A.F.; Kouanou, Y.S.; Nkuo-Akenji, T. Vaccine uptake and immune responses to HBV infection amongst vaccinated and non-vaccinated healthcare workers, household and sexual contacts to chronically infected hbv individuals in the south west region of Cameroon. *PLoS ONE* **2018**, *13*, e0200157. [CrossRef]
71. Mursy, S.M.-e.M.; Mohamed, S.O.O. Knowledge, attitude, and practice towards hepatitis b infection among nurses and midwives in two maternity hospitals in Khartoum, Sudan. *BMC Public Health* **2019**, *19*, 1597. [CrossRef]

72. Mustafa, A.S.M.; Ahmed, A.S.M.; Alamin, T.A.A.; Shaheen, M.T.H.A.; Hilali, A.M.M.A.; Abdelsalam, M.; Abdelrahim, M.A.S.; Elsheikh, M.N.M.A. Knowledge, attitude and practice of hepatitis (b) among healthcare workers in relation to their vaccination status in khartoum, sudan, 2015: A cross-sectional study. *Sudan J. Med. Sci.* **2018**, *13*, 22–32. [CrossRef]
73. Noubiap, J.J.; Nansseu, J.R.; Kengne, K.K.; Tchokfe Ndoula, S.; Agyingi, L.A. Occupational exposure to blood, hepatitis b vaccine knowledge and uptake among medical students in Cameroon. *BMC Med. Educ.* **2013**, *13*, 148. [CrossRef]
74. Noubiap, J.J.N.; Nansseu, J.R.N.; Kengne, K.K.; Wonkam, A.; Wiysonge, C.S. Low hepatitis b vaccine uptake among surgical residents in Cameroon. *Int. Arch. Med.* **2014**, *7*, 11. [CrossRef]
75. Ogoina, D.; Pondei, K.; Adetunji, B.; Chima, G.; Isichei, C.; Gidado, S. Prevalence of hepatitis b vaccination among health care workers in Nigeria in 2011–2012. *Int. J. Occup. Environ. Med.* **2014**, *5*, 51–56.
76. Okwara, E.C.; Enwere, O.O.; Diwe, C.K.; Azike, J.E.; Chukwulebe, A.E. Theatre and laboratory workers' awareness of and safety practices against hepatitis b and c infection in a suburban university teaching hospital in Nigeria. *Pan Afr. Med. J.* **2012**, *13*, 2.
77. Omotowo, I.B.; Meka, I.A.; Ijoma, U.N.; Okoli, V.E.; Obienu, O.; Nwagha, T.; Ndu, A.C.; Onodugo, D.O.; Onyekonwu, L.C.; Ugwu, E.O. Uptake of hepatitis b vaccination and its determinants among health care workers in a tertiary health facility in Enugu, south-east, Nigeria. *BMC Infect. Dis.* **2018**, *18*, 288. [CrossRef]
78. Oyewusi, C.O.; Okanlawon, F.A.; Ndikom, C.M. Knowledge and utilization of hepatitis b infection preventive measures and influencing factors among Helath care workers in Ibahan, Nigeria. *Int. J. Caring Sci.* **2015**, *8*, 164–176.
79. Ray, S.S.; Pattnaik, S.; Sharma, A.K. Hepatitis b—A killer study of awareness and practice among dental students regarding hepatitis b infection and preventive. *J. Evol. Med. Dent* **2017**, *6*, 6460–6463.
80. Resende, V.L.S.; Abreu, M.H.G.; Paiva, S.M.; Teixeira, R.; Pordeus, I.A. Concerns regarding hepatitis b vaccination and post-vaccination test among Brazilian dentists. *Virol. J.* **2010**, *7*, 154. [CrossRef]
81. Rathi, A.; Kumar, V.; Majhi, J.; Jain, S.; Lal, P.; Singh, S. Assessment of knowledge, attitude, and practices toward prevention of hepatitis b infection among medical students in a high-risk setting of a newly established medical institution. *J. Lab. Physicians* **2018**, *10*, 374–379. [CrossRef]
82. Sandeep, S.; Utsuk, D. Level of knowledge regarding hepatitis-b immunization amongst health personnel in Delhi, India. *J. Commun. Dis.* **2010**, *42*, 147–151.
83. Shahbaz, T.; Raza, S.M.; Manzoor, Z.; Jamsid, A. Hepatitis b and c: Knowledge, attitude and perception of medical students at lahore medical and dental college, Lahore. *Pak. J. Med. Health Sci.* **2014**, *8*, 789–793.
84. Shukla, A.; Hillegass, J.M.; MacPherson, M.B.; Beuschel, S.L.; Vacek, P.M.; Pass, H.I.; Carbone, M.; Testa, J.R.; Mossman, B.T. Blocking of erk1 and erk2 sensitizes human mesothelioma cells to doxorubicin. *Mol. Cancer* **2010**, *9*, 314. [CrossRef]
85. Shukla, M.; Tyagi, S.; Gupta, N.K. Knowledge, attitude, and practice concerning hepatitis b infection among the health care personnel in selected primary health care centers in Lucknow. *J. Res. Med. Dent. Sci.* **2016**, *4*, 45–49. [CrossRef]
86. Singh, A.; Purohit, B.M.; Bhambal, A.; Saxena, S.; Singh, A.; Gupta, A. Knowledge, attitudes, and practice regarding infection control measures among dental students in central India. *J. Dent. Educ.* **2011**, *75*, 421–427. [CrossRef] [PubMed]
87. Usmani, R.A.; Rana, M.S.; Wazir, M.S.; Sarwer, H.; Fazli, H.; Pervaiz, M.A.; Tahir, I.; Sajjad, R. Assessment of hepatitis b vaccination status in doctors of services hospital, Lahore. *J. Ayub. Med. Coll. Abbottabad* **2010**, *22*, 36–39. [PubMed]
88. Vo, T.Q.; Do, A.T.N.; Tran, T.T.T. Current status of knowledge about and attitudes toward the hepatitis b virus at a private university in southern vietnam: A cross sectional self-reported study. *Asian J. Pharm.* **2018**, *12*, 99–112.
89. Yamazhan, T.; Durusoy, R.; Tasbakan, M.I.; Tokem, Y.; Pullukcu, H.; Sipahi, O.R.; Ulusoy, S.; Turkish Nursing Hepatitis Study, G. Nursing students' immunisation status and knowledge about viral hepatitis in turkey: A multi-centre cross-sectional study. *Int. Nurs. Rev.* **2011**, *58*, 181–185. [CrossRef]
90. Yuan, Q.; Wang, F.; Zheng, H.; Zhang, G.; Miao, N.; Sun, X.; Woodring, J.; Chan, P.-L.; Cui, F. Hepatitis b vaccination coverage among health care workers in china. *PLoS ONE* **2019**, *14*, e0216598. [CrossRef]
91. Zheng, Y.-B.; Gu, Y.-R.; Zhang, M.; Wang, K.; Huang, Z.-L.; Lin, C.-S.; Gao, Z.-L. Health care workers in pearl river delta area of china are not vaccinated adequately against hepatitis b: A retrospective cohort study. *BMC Infect. Dis.* **2015**, *15*, 542. [CrossRef]
92. Eni, A.O.; Soluade, M.G.; Oshamika, O.O.; Efekemo, O.P.; Igwe, T.T.; Onile-Ere, O.A. Knowledge and awareness of hepatitis b virus infection in Nigeria. *Ann. Glob. Health* **2019**, *85*, 56. [CrossRef]
93. Lee, O.; Hae Ok, L.; Kim, S.; Young Woo, K.; Moo Sik, L.; Su Jeong, H.; Moon Sook, S.; Nam Yeong, Y. Differences in knowledge and attitudes toward hepatitis b infection and vaccination between adolescents in juvenile detention centers and in schools in south korea. *J. Transcult. Nurs.* **2009**, *21*, 65–72. [CrossRef]
94. Moezzi, M.; Imani, R. Protection provided by hepatitis b vaccine in adult population of chaharmahal and bakhtiari province, iran in 2013. *J. Clin. Diagn. Res.* **2016**, *10*, LC01–LC04. [CrossRef]
95. Muhammad Ayaz, M.; Ashfaque Ahmed, M.; Sadia, N.; Anjum, S.; Sobiya Mohiuddin, O. Exposure to risk factors for hepatitis b and c viruses among primary school teachers in Karachi. *J. Infect. Dev. Ctries.* **2010**, *4*, 616–620.
96. Noreen, N.; Kumar, R.; Shaikh, B.T. Knowledge about hepatitis b vaccination among women of childbearing age: A cross-sectional study from a rural district of punjab, pakistan. *East. Mediterr. Health J.* **2015**, *21*, 129–133. [CrossRef]
97. Roushan, N.; Nasiri Toosi, M.; Meysamie, A.; Esteghamati, A.-R.; Hajrassuliha, H. Hepatitis b knowledge among iranian adolescents: A national survey. *Iran. Red Crescent Med. J.* **2013**, *15*, e11558. [CrossRef]
98. Shakeel, S.; Iffat, W.; Rehman, H.; Jamil, N.; Nazeer, F.; Naveed, S.; Ishaq, H. Assessing the level of awareness and vaccination status of hepatitis b among young female community of Pakistan. *Bangladesh J. Med. Sci.* **2015**, *14*, 376–383. [CrossRef]

99. Vo, T.Q.; Nguyen, T.L.H.; Pham, M.N. Exploring knowledge and attitudes toward the hepatitis b virus: An internet-based study among vietnamese healthcare students. *J. Pharm. Pharmacogn. Res.* **2018**, *6*, 458–470.
100. Yang, Y.; Yan, M.; Yue, M.; Wang, X.; Zhang, W.; Li, J.; Li, S. Prevalence of hepatitis b and knowledge about hepatitis b among migrant workers in shandong province, china: A cross-sectional study. *Iran. Red Crescent Med. J.* **2015**, *17*, e26725. [CrossRef]
101. Zafrin, N.; Sarkar, M.A.S.; Rahman, M.M.; Salma, U.; Mahbub, T.; Azhar, H.A. Hepatitis b virus infection: Knowledge and awareness among the patients admitted in a tertiary care hospital in Bangladesh. *Viral Hepat. J.* **2019**, *25*, 6–13. [CrossRef]
102. Ochu, C.L.; Beynon, C.M. Hepatitis b vaccination coverage, knowledge and sociodemographic determinants of uptake in high risk public safety workers in Kaduna state, Nigeria: A cross sectional survey. *BMJ Open* **2017**, *7*, e015845. [CrossRef]
103. Carvalho, M.; Carmo, H.; Costa, V.M.; Capela, J.P.; Pontes, H.; Remião, F.; Carvalho, F.; Bastos, M.D.L. Toxicity of amphetamines: An update. *Arch. Toxicology. Arch. Toxikol.* **2012**, *86*, 1167–1231. [CrossRef]
104. Tanga, A.T.; Teshome, M.A.; Hiko, D.; Fikru, C.; Jilo, G.K. Sero-prevalence of hepatitis b virus and associated factors among pregnant women in Gambella hospital, south western Ethiopia: Facility based cross-sectional study. *BMC Infect. Dis.* **2019**, *19*, 602. [CrossRef]
105. Hoffmann, R.; Lutz, S.U. The health knowledge mechanism: Evidence on the link between education and health lifestyle in the philippines. *Eur. J. Health Econ.* **2018**, *20*, 27–43. [CrossRef]
106. Basuni, A.A.; Butterworth, L.; Cooksley, G.; Locarnini, S.; Carman, W.F. Prevalence of hbsag mutants and impact of hepatitis b infant immunisation in four pacific island countries. *Vaccine* **2004**, *22*, 2791–2799. [CrossRef] [PubMed]
107. Aghakhani, A.; Mohraz, M.; Aghasadeghi, M.R.; Banifazl, M.; Vahabpour, R.; Karami, A.; Foroughi, M.; Ramezani, A. Occult hepatitis b virus infection and s gene escape mutants in HIV-infected patients after hepatitis b virus vaccination. *Int. J. STD AIDS* **2015**, *27*, 967–972. [CrossRef] [PubMed]
108. Mokaya, J.; McNaughton, A.L.; Hadley, M.J.; Beloukas, A.; Geretti, A.-M.; Goedhals, D.; Matthews, P.C. A systematic review of hepatitis b virus (HBV) drug and vaccine escape mutations in Africa: A call for urgent action. *PLoS Negl. Trop. Dis.* **2018**, *12*, e0006629. [CrossRef] [PubMed]

Publication 2

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Putri Bungsu Machmud, PhD (cand.)[1,2], Saskia Glasauer, PhD (cand.)[1], Dwi Gayatri, PhD (cand.)[1,2], and Rafael Mikolajczyk, Prof. Dr.[1]

Abstract

Exposing appropriate information to mothers is a key factor for children's immunization status. This study aims to assess the influence of mothers' media use on their children's vaccination status in Indonesia, using the 2017 Indonesia Demographic Health Survey data. A multilevel multinomial logistic regression model was employed. Mothers who used media irregularly and regularly had higher odds of having partially vaccinated children (vs unvaccinated) than mothers who never used media with adjusted odds ratio (aOR): 1.74; 95% Confidence interval (95% CI): 1.06-2.85 and aOR: 1.48; 95% CI: 1.02-2.16, respectively. Furthermore, they had higher odds of having a fully vaccinated child (vs unvaccinated) (aOR: 1.86; 95% CI: 1.12-3.08 for irregular media use and aOR: 2.41; 95% CI: 1.64-3.53 for regular media use vs. no media use). Our findings suggest that mothers' media use could positively affect their children's vaccination status by increasing mothers' knowledge about children's vaccination.

Keywords

children, immunization program, community-based, vaccination, Indonesia

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Introduction

Vaccines are an effective way to prevent deadly vaccine-preventable diseases and, hence, have the potential to save 2 to 3 million lives per year.[1] Yet, 19.4 million infants worldwide were not fully vaccinated in 2019, 13.5 millions of whom did not receive any vaccine.[1] Currently, Indonesia's immunization program for children aged 0 to 11 months is providing free and is commonly known as primary immunization. The program covers the birth dose of hepatitis B (HepB 0) vaccines and Oral polio vaccine/OPV birth dose (OPV 0) vaccines, followed by Bacillus Calmette–Guérin (BCG) vaccines, 3 doses vaccines of Diphtheria-Tetanus-Pertussis (DTP), 3 additional doses vaccines of HepB and OPV, 3 doses vaccines of *Haemophilus influenzae type B* and measles vaccination.[2,3] However, the Indonesian National Health Surveys (INHS) of 2010, 2013, and 2018 show that the primary immunization coverage rates across the country are consistently low,[4-6] with only 57.9% of children being fully vaccinated, 32.9% being partially vaccinated and 9.3% was not vaccinated in 2018.[4] Various factors influence this disparity; however, the most common reasons given by parents for unvaccinated children in Indonesia consisted of 3 themes (belief barriers eg, religious issue that vaccine ingredients contain pork (halal issue), safety concerns and issues of trust, and misinformation (such as the threat of fever following immunization).[7] Mothers' exposure to reliable immunization information from adequate and trustworthy sources is considered a key factor in the success of immunization

[1]Institute of Medical Epidemiology, Biometrics, and Informatics (IMEBI), Medical School of the Martin-Luther-University Halle-Wittenberg, Halle (Saale), Germany
[2]Department of Epidemiology, Faculty of Public Health, Universitas Indonesia, Depok, Indonesia

Corresponding Author:
Putri Bungsu Machmud, University of Indonesia, Jalan Prof Badher Djohan, Depok 16424, Indonesia.
Email: putri.machmud@uk-halle.de

programs for children.[7,8] This approach aims to improve mothers' knowledge of immunization benefits and vaccine safety. Media can be one way to deliver this information. However, there are mixed results in the literatures on the relationship between mothers' media use and children vaccination status.[9-14] Some emphasizes the benefits of mothers' media use to children's immunization status.[10,15] On the other hand, some research report that there is no association between mothers' media use and their children's vaccination status.[9,13,14] However, most of these studies analyzed vaccination status as binary outcomes: complete and incomplete vaccination.[8-10,12,13] The INHS reports that the proportion of Indonesian children who received partial vaccination was still high (32.9%) within the last decade[4.6] This finding indicates that there is a group of mothers who have access to vaccination and are willing to vaccinate their children but could not complete the vaccination schedule. We argue that this group might differ from mothers whose children are unvaccinated, regarding primary vaccination and media use. Therefore, we aim to assess the association between mothers' media use and their children's vaccination status by comparing unvaccinated with partially and fully vaccinated children through data analysis provided by the Demographic Health Survey (DHS) Program.

Methods

Study Design, Data Sources, and Study Area

This study analyzed data from the 2017 Indonesian Demographic Health Survey (2017 IDHS).[16] The 2017 IDHS is part of the international DHS program designed to collect fertility, family planning, maternal and child health data.[16] The 2017 IDHS dataset was obtained with permission from the DHS. The first author (PBM) registered through the DHS website, followed by submitting a proposal and a summary of the study protocol. Since the DHS data have no individual identifiers, the confidentiality of the participants was ensured.

Study Participants

To be included in this study, the following inclusion criteria were to be met: (i) woman of childbearing age of 15 to 49 years, (ii) having a child aged above 1 year (as only for these, the completeness of primary immunization could be judged), and (iii) having complete data on personal media use, information about the immunization status of the child and socio-demographic variables. Mothers who stated that they do not know their child's immunization status were excluded from this study.

Variables

The outcome of this study was the primary vaccination status for children aged 0 to 11 months, which reported based on mother's recall. This variable was categorized into 3 groups: fully vaccinated (the child received all primary vaccines), partially vaccinated (the child received some vaccines) and not vaccinated (the child did not receive any vaccines).

The media use variable was assessed based on the year before the 2017 IDHS and compiled from 2 variables: frequency and type of media use. A score of 1 was given if a mother was exposed to any media of the following: newspaper/magazine, radio, television, and internet less than once a week and a score of 2 if the mother was exposed almost every day. Mothers who claimed that they have never used a given medium were given a zero score. As a result, each subject had an overall media use score ranging from 0 to 8, which was grouped into 3 categories: no media use (never used in the last 12 months) (score 0), irregular media use (score 1) and regular media use (score $\geq$2) as for scores of 2 or more there were little differences (Figure 1).

Potential confounders were identified based on previous studies[8,9,12,13,17-19] and controlled for in the multivariable analysis. We considered the following variables: place of residence (urban versus [vs] rural), parents' age (15 to 19, 20 to 24, 25 to 29, 30 to 34, and 35 to 39 years old vs 40 and more years old), parents' education (primary, secondary and higher education vs. no education), marital status (living with a partner vs. married), child's age (age of 2 and 3 vs 1) and sex (girl vs boy), number of children in the household ($\leq$2 children vs $>$2), health insurance coverage (yes vs no), history of antenatal and postnatal care (yes vs no) and economic status through wealth terciles (middle and high economic status vs low economic status).

Statistical Analysis

Descriptive results are presented as median and interquartile ranges (IQR) for continuous variables and as proportions for categorical variables. The association between media use and vaccination status was analyzed using a multilevel multinomial logistic regression. Random effects were applied to account for data nested within provinces. The analysis was conducted with STATA 16.

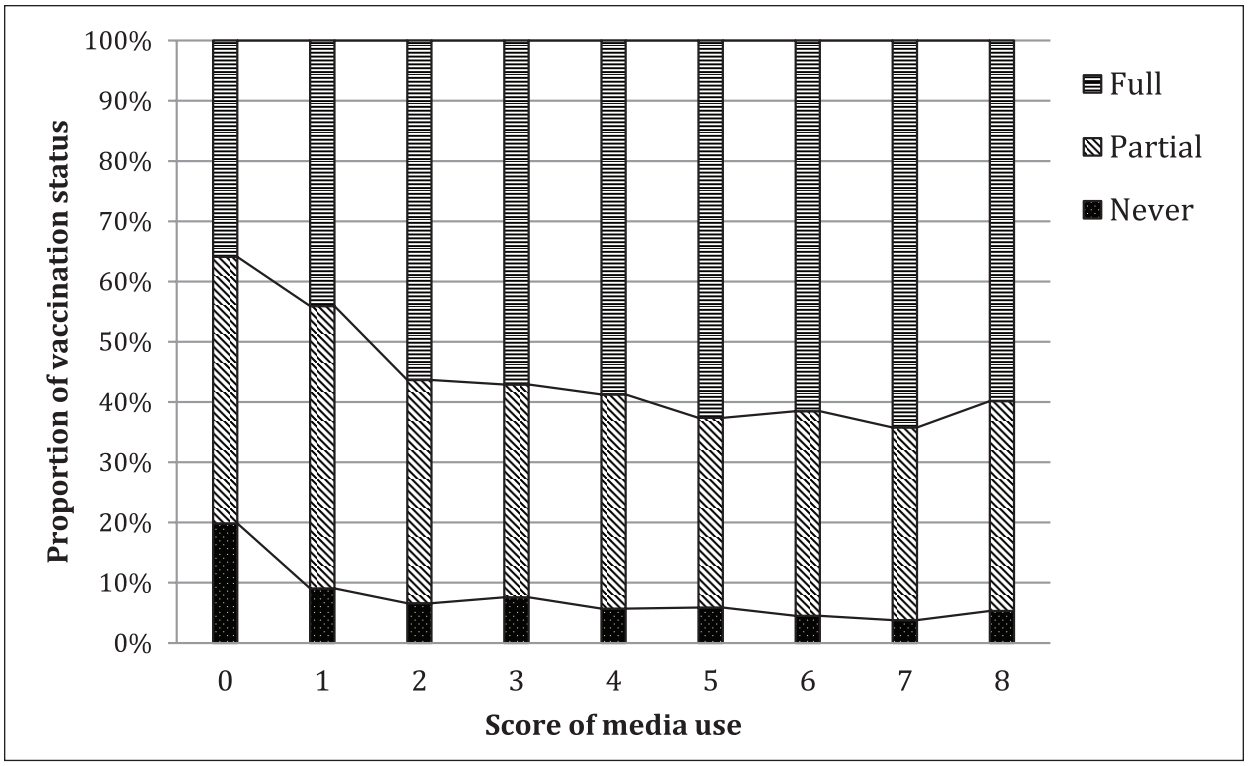

Figure 1. Proportion of children with given vaccination status for each value of the media use score.

Results

Socio-Demographic Characteristics

In total, 7867 women, who met the inclusion criteria, were included in this study. Seven participants who did not know their children's immunization status were excluded (Figure 2). Mothers' and fathers' median age was 30 (IQR 26-35) and 34 (IQR 29-39) years, respectively. A large proportion of mothers had low economic status (46.9%) and half of mothers were residing in a rural area (50.4%) (Table 1).

Mother's Media Use and Children's Immunization Status

Approximately 91% (n=7151) of mothers used media regularly, 5.0% (n=397) used media irregularly, while 4.0% (n=312) did not use media in the last year before survey participation (Table 1). In the sample, 57.0% (n=4506) of children were fully vaccinated, while 36.0% (n=2829) were partially vaccinated and 7.0% (n=525) were not vaccinated (Table 1).

Mothers' media use was associated with their children's vaccination status. Children whose mothers used media irregularly and regularly compared to those who never used media showed 1.74 (95% CI: 1.06-285) and 1.48 (95% CI: 1.02-2.16) times higher odds of being partially vaccinated vs. not vaccinated. Similarly, children of mothers who used media irregularly (aOR: 1.86; 95% CI: 1.12-3.08) and regularly (aOR: 2.41; 95% CI: 1.64-3.53) compared to those who did not use media had higher odds of being fully vaccinated vs. not vaccinated (Table 2).

Variables Associated With Children's Immunization Status

In addition to media use, several variables were associated with children's immunization status: parents' age and education, economic status, child's age and sex, number of children, and health insurance coverage (Table 2).

Compared to children with older fathers (aged ≥ 40 years), children whose fathers were aged 25 to 29 years had higher odds of being partially vaccinated compared to not vaccinated (aOR: 1.57; 95% CI: 1.04-2.38). Mothers with secondary education showed 2 (aOR: 2.00; 95% CI: 1.07-3.74) times higher odds of having partially vaccinated children compared to unvaccinated children than to those without education.

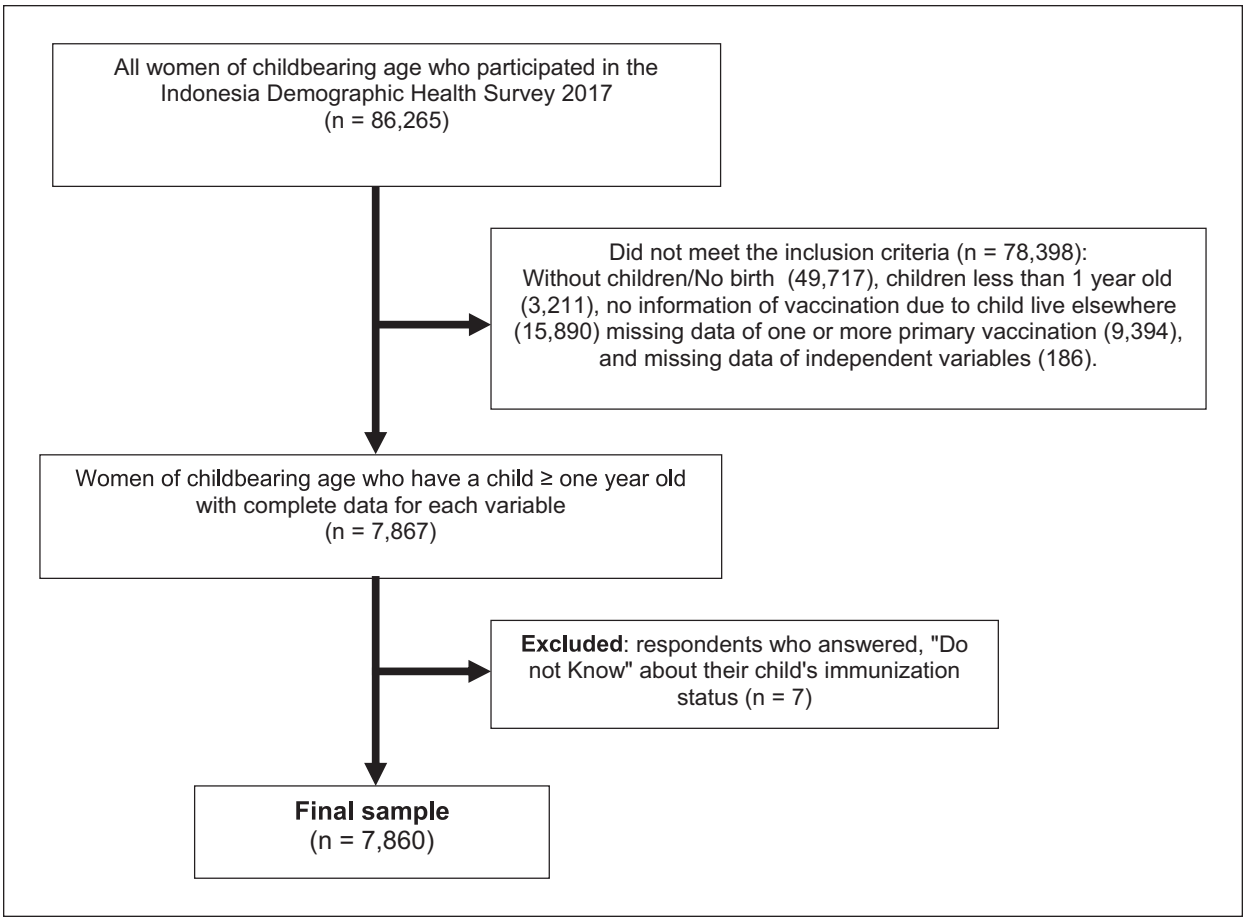

Figure 2. Flow chart of participant selection for the study.

Similarly, fathers with primary (aOR: 2.08; 95% CI: 1.16-3.73), secondary (aOR: 3.21; 95% CI: 1.77-5.79) and higher (aOR: 2.96; 95% CI: 1.51-5.80) education had higher odds of having partially vaccinated compared to not vaccinated children than to fathers without education. Apart from that, the odds of being partially vaccinated compared to not vaccinated was higher among children born to mothers with health insurance than those born to mothers without any health insurance (aOR: 1.31; 95% CI: 1.07-1.60). Mothers who had 2 or fewer children had almost double the odds of having partially vaccinated compared to unvaccinated children than those who had more than 2 children (aOR: 1.46; 95% CI: 1.14-1.87). Compared to boys, girls had lower odds of being partially vaccinated (aOR: 0.78; 95% CI: 0.64-0.94) compared to unvaccinated children. In addition, children aged 2 years had about 30.0% lower odds of being partially vaccinated compared to not vaccinated than those aged 1 year old (aOR: 0.73; 95% CI: 0.59-0.89). Mothers in age groups 15 to 19 years and 20 to 24 years had 55.0% (aOR: 0.45; 95% CI: 0.21-0.98) and 40.0% (aOR: 0.60; 95% CI: 0.36-0.99) lower odds of having fully vaccinated compared to not vaccinate children than those in the older age group (≥40 years old). Children whose mothers had secondary education showed almost 3 (aOR: 2.78; 95% CI: 1.50-5.17) times higher odds of being fully vaccinated compared to not vaccinated than those without education. Correspondingly, fathers with primary (aOR: 1.72; 95% CI: 0.99-2.99), secondary (aOR: 2.32; 95% CI: 1.32-4.08) and higher (aOR: 2.26; 95% CI: 1.18-4.32) education had higher odds of having fully vaccinated compared to not vaccinated children compared to those without education. Compared to low economic status, children with middle (aOR: 1.51; 95% CI: 1.13-2.02) and high (aOR: 1.59; 95% CI: 1.20-2.09) economic status had higher odds of being fully vaccinated compared to unvaccinated children. Children aged 2 (aOR: 1.36; 95% CI: 1.11-1.67) and 3 (aOR: 1.49; 95% CI: 1.10-2.01) were more likely to be fully vaccinated compared to not vaccinated compared to children aged 1 year. The odds of being fully vaccinated compared to not

Table 1. Demographic Characteristic of the Studied Sample.

Variable	Vaccination status (%)			Total n = 7860	
	Not vaccinated n = 525	Partially vaccinated n = 2829	Fully vaccinated n = 4506	Frequency	Percentage
Place of residency					
Rural	61.3	51.7	48.3	3961	50.4
Urban	38.7	48.3	51.7	3899	49.6
Parent's age					
Age of mother (years)					
15-19	2.9	2.8	1.6	166	2.1
20-24	16.6	17.2	15.9	1289	16.4
25-29	25.9	25.0	26.4	2032	25.9
30-34	22.3	26.8	27.9	2132	27.1
35-39	21.9	19.2	19.6	1541	19.6
≥40	10.5	9.0	8.6	700	8.9
Age of father (years)					
15-19	1.0	0.4	0.4	33	0.4
20-24	5.9	7.1	6.0	502	6.4
25-29	15.8	21.5	19.4	1563	19.9
30-34	28.4	26.4	27.0	2113	26.9
35-39	23.2	21.6	23.7	1802	22.9
≥40	25.7	23.0	23.5	1847	23.5
Parent's education					
Mother's education					
No education	5.0	1.4	0.8	103	1.3
Primary	36.6	26.3	20.5	1858	23.6
Secondary	42.5	55.5	58.0	4406	56.1
Higher	16.0	16.8	20.7	1493	19.0
Father's education					
No education	5.1	1.4	1.2	118	1.5
Primary	37.3	27.2	23.4	2021	25.7
Secondary	45.7	57.3	58.8	4509	57.4
Higher	11.8	14.1	16.6	1212	15.4
Marital status					
Married	97.9	98.2	98.2	7718	98.2
Living with a partner	2.1	1.8	1.8	142	1.8
Economic status					
Low	63.8	50.4	42.7	3687	46.9
Middle	13.3	17.7	19.2	1437	18.3
High	22.9	31.8	38.1	2736	34.8
Child's age (years)					
1	45.5	53.8	38.6	3498	44.5
2	42.3	35.2	47.1	3339	42.5
3	12.2	11.1	14.3	1023	13.0
Child's sex					
Boys	48.0	54.0	50.0	4033	51.3
Girls	52.0	46.0	50.0	3827	48.7
Number of children					
>2 children	49.9	38.4	32.9	2829	36.0
≤2 children	50.1	61.6	67.1	5031	64.0

(continued)

Table 1. (continued)

Variable	Vaccination status (%)			Total n = 7860	
	Not vaccinated n = 525	Partially vaccinated n = 2829	Fully vaccinated n = 4506	Frequency	Percentage
Cover by health insurance					
No	44.6	38.1	34.7	2874	36.6
Yes	55.4	61.9	65.3	4986	63.4
Antenatal care history					
No	96.6	97.2	97.4	7646	97.3
Yes	3.4	2.8	2.6	214	2.7
Postnatal care history					
No	73.1	70.5	21.2	5615	71.7
Yes	26.9	29.5	28.8	2245	28.9
Media use					
Never	11.8	4.9	2.5	312	4.0
Irregularly	6.9	6.6	3.9	397	5.0
Regularly	81.3	88.5	93.6	7,151	91.0
Type of media used[a]					
Radio (Yes)	40.6	37.4	41.0	3117	39.7
Newspaper/	37.7	40.1	44.1	3319	42.2
Magazine (Yes)					
Television (Yes)	85.9	93.3	96.3	7430	94.5
Internet (Yes)	29.1	40.9	47.0	3428	43.6

[a]Mothers could use more than 1 type of media.

Table 2. Adjusted Odds Ratios of Partial and Full Vaccination Compared to No Vaccination.

Variable	Partially vaccinated vs. Not vaccinated		Full vaccinated vs. not vaccinated	
	aOR (95% CI)	*P*-value	aOR (95% CI)	*P*-value
Media use (reference: Never)				
Irregular	1.74 (1.06-2.85)	.029	1.86 (1.12-3.08)	.016
Regular	1.48 (1.02-2.16)	.041	2.41 (1.64-3.53)	<0001
Place of residency (reference: Urban)				
Rural	1.01 (0.81-1.27)	.911	1.06 (0.85-1.32)	.614
Parents' Age (reference: ≥ 40 years old)				
Age of mother (age groups)				
15-19	0.68 (0.31-1.48)	.326	0.45 (0.21-0.98)	.046
20-24	0.60 (0.36-1.02)	.058	0.60 (0.36-0.99)	0048
25-29	0.73 (0.46-1.15)	.172	0.78 (0.50 - 1.21)	.267
30-34	1.18 (0.78-1.80)	.431	1.22 (0.81-1.85)	0329
35-39	0.99 (0.68-1.46)	.974	1.05 (0.73-1.53)	0781
Age of father (age groups)				
15-19	0.47 (0.14-1.55)	.216	0.45 (1.14-1.45)	0181
20-24	1.32 (0.75-2.32)	.333	1.04 (0.60-1.81)	.887
25-29	1.57 (1.04-2.38)	.032	1.16 (0.77-1.75)	.467
30-34	0.94 (0.67-1.32)	.719	0.79 (0.56-1.10)	.467
35-39	0.92 (0.68-1.26)	.610	0.90 (0.66-1.21)	.477
Parent's education (reference: No education)				
Mother's education				
Primary	1.39 (0.76-2.55)	.285	1.67 (0.91-3.04)	.095
Secondary	2.00 (1.07-3.74)	.029	2.78 (1.50-5.17)	.001
Higher	1.29 (0.64-2.58)	.473	1.70 (0.86-3.37)	.129

(continued)

Table 2. (continued)

Variable	Partially vaccinated vs. Not vaccinated		Full vaccinated vs. not vaccinated	
	aOR (95% CI)	*P*-value	aOR (95% CI)	*P*-value
Father's education				
Primary	2.08 (1.16-3.73)	.013	1.72 (0.99-2.99)	.056
Secondary	3.21 (1.77-5.79)	<.001	2.32 (1.32-4.08)	.003
Higher	2.96 (1.51-5.80)	.002	2.26 (1.18-4.32)	.013
Marital status (reference: Married)				
Living with partner	0.88 (0.42-1.82)	.725	1.42 (0.73-2.77)	.306
Economic status (reference: Low)				
Middle	1.32 (0.97-1.78)	.075	1.51 (1.13-2.02)	.005
High	1.23 (0.92-1.65)	.156	1.59 (1.20-2.09)	.001
Child's age (years) (reference: 1 years old)				
2	0.73 (0.59-0.89)	.003	1.36 (1.11-1.67)	.003
3	0.82 (0.60-1.11)	.209	1.49 (1.10-2.01)	.010
Child's sex (reference: Boys)				
Girls	0.78 (0.64-0.94)	.010	0.89 (0.74-1.07)	.210
Number of children (reference: > 2 children)				
≤2 children	1.46 (1.14-1.87)	.003	2.00 (1.57-2.55)	<.001
Cover by health insurance (reference: No)				
Yes	1.31 (1.07-1.60)	.009	1.49 (1.22-1.81)	<.001
Antenatal care history (reference: No)				
Yes	0.62 (0.36-1.06)	.082	0.64 (0.38-10.8)	.096
Postnatal care history (reference: No)				
Yes	1.10 (0.89-1.38)	.374	1.09 (0.88-1.35)	.448

aOR, Adjusted Odds Ratio.

vaccinated were 2.00 (95% CI: 1.57-2.55) times higher in children born to mothers who had 2 or fewer children compared to those born to mothers who had more than 2 children. Compared to unvaccinated children, mothers with health insurance had 1.49 (95% CI: 1.22-1.81) times higher odds of having fully vaccinated children compared to mothers without any health insurance.

Discussion

Mother's Media Use and Children's Immunization Status

Our study analyzed the association between mothers' media use and their children's vaccination status and showed that media use among mothers is positively associated with their children's vaccination status. There was some indication of a dose-response pattern, in the sense that irregular media use among mothers increased children's partial immunization, but had a lesser benefit to ensure the completeness of vaccination. Moreover, mothers' regular media use encouraged the partial compared to no vaccination, but even more the full vaccination compared to no vaccination. Our findings are in line with previous studies, which report a positive association between mothers' media use and children's immunization status.[10,20,21] This positive association might be explained by a better understanding of the beneficial role of immunization due to information exposure through the media, thereby, increasing mothers' knowledge.[10,11,19]

Most of the previous studies that investigated determinants of children's vaccination status used a binary outcome, categorized into complete and incomplete vaccination.[8-10,12,13] Children who missed 1 or more doses of vaccination were, then, grouped together with those children, who were never vaccinated, into the group of unvaccinated status.[10,13] This approach seemed to generalizing if both partial and unvaccinated status were similar, but we argued that children in these 2 groups might differ in certain aspects. Therefore, in this study, as well as missed opportunities to vaccinate and geographic barriers. In the perspective of our findings on media use, we believe that mothers with partially vaccinated children need further education and attention regarding the importance of vaccination and vaccine's schedule through the strengthening health promotion and/or literacy in this context.

A qualitative study in Indonesia found that perceptions about immunization were influenced not only by information related to vaccine safety but also by issues of trust and belief barriers, such as controversy of vaccine's ingredient, beliefs in natural immunity and beliefs in alternative medicine.[7] Even if the acceptance of information sources may not be the same across the population, it appears that the perceived reliability of the information source is also a crucial aspect. Tabacchi et al. reported that people who received information related to vaccination from scientific magazines had 8 and 3 times higher odds of having better perceived knowledge (believe about information on vaccines and vaccine preventable disease) and actual knowledge (knowledge about the vaccine, knowledge about the disease, knowledge about the vaccine schedule, knowledge about the national vaccination website, and knowledge about the correct strategy to prevent mentioned disease), respectively, compared to people who did not.[22] Furthermore, Handy et al.[23] found that the health clinic was referred to as the most reliable source of information among caregivers who experienced confusion after receiving some immunization information from news media. However, in Indonesia, health providers are not considered as the main actors in the dissemination of information. As a result, close collaboration between the ministry of health and other related parties, such as religious figures and the communities, is needed to enlighten the negative information facilitating vaccine hesitancy in Indonesia.[7,24] For example, Majelis Ulama Indonesia, who acts as a council of religious scholars in Indonesia, provided a halal certification or fatwa regarding the permissibility of the vaccination, which impacts community acceptance of vaccination.[24,25]

Variables Associated With Children's Immunization Status

Our findings indicate that parents' (age and education), children's (age and sex) and household (number of children, economic status, and health insurance) characteristics can predict children's vaccination status.

It is evident that several parental characteristics, such as age and education, influence the medium of media use. Our study found that younger mothers had higher odds of having vaccinated children in full vaccination compared to older mothers. This is reasonable, given that the younger population tends to have more convenience toward updated technologies and access to the internet, which can positively affect mothers' knowledge and health behavior.[8,26,27] Moreover, in our analyses, higher parental education was associated with better child vaccination status compared to parents with low education. This is in agreement with previous studies, reporting that parents' educational attainment level could prevent negative perceptions and assist parents in making an accurate decision related to their children's vaccination status. In addition, education is also closely related to economic and social status, both of which have a positive impact on vaccination status.[28-34]

Child's age was an important factor in the association between mothers' media use and children's vaccination status. Our study indicated that older children were more likely to be fully vaccinated, even if the vaccinations were recommended for a younger age. A study from Ethiopia found similar results, in which children aged 12 to 18 months had 50.0% lower odds of being vaccinated compared to older children (19-23 months).[35] This situation might be explained by various factors; one of them can be opportunity for a catch-up vaccination at an older age or delay in receiving vaccination.[36,37] In addition, this can be a consequence of misconceptions surrounding vaccination.

Previous studies indicate mixed results concerning the association between the child's female sex and complete vaccination status.[12,13,29] Our analysis revealed that female children were 22.0% less likely to be partially vaccinated vs. not vaccinated compared to male children. However, there was no association between sex and full vaccination vs. no vaccination in our study.

Furthermore, we found that health insurance coverage had an impact on children's vaccination status. Even though primary immunization is available without charges, health insurance ownership was an important factor in increasing vaccination rates in Indonesia. This might be due to the fact that free primary vaccination in Indonesia is only provided in public health facilities through health centers (Puskesmas) and community level-health posts (Posyandu) that only operate in particular days for vaccination services. As a result, a new mechanism of free vaccination services that involve private health care providers is needed in order to increase children vaccination coverage.

Strengths and Limitations

We used data from a large representative population study. The analyses of media use controlled for a variety of potential confounding variables, which increases the validity of the results. However, this study also has some limitations. First, recall bias might have affected mother's reports of information exposure and their child's vaccination status. Yet, we believe that the risk is low because the interviews were conducted by trained personnel who helped mothers remember their child's vaccination history through some probing questions. Furthermore, we

analyzed media use in 2017 while many of the children were vaccinated before; thus, media use could have changed over time and possibly also child's age. Confounding might be present through unobserved variables, such as religion. Finally, selection bias possibly introduced by the consecutive sampling applied in DHS surveys could reduce the generalizability of the study results. Nevertheless, secondary analysis of DHS data is still considered to have a major contribution to public health knowledge.

Conclusion

Our study found that mothers' media use, both irregular and regular use, was positively associated with their children's vaccination status. We also found irregular media use being more strongly associated with partial immunization and regular media use being stronger associated with full vaccination. Thus, further exploration with a more experimental design could be helpful to improve the result.

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Author Contributions

Putri Bungsu Machmud : Conceptualization, Methodology, Data curation, Formal analysis, Writing-original draft, Writing-review & editing
Saskia Glasauer : Conceptualization, Methodology, Data curation, Formal analysis, Writing-review & editing
Dwi Gayatri : Conceptualization, Methodology, Writing-review & editing
Rafael Mikolajczyk : Conceptualization, Methodology, Data curation, Formal analysis, Writing-review & editing, Supervision

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Data Availability Statement

The original contributions presented in the study are included in the article and further inquiries can be directed to the corresponding author.

ORCID iD

Putri Bungsu Machmud https://orcid.org/0000-0002-3322-4006

Supplemental Material

Supplemental material for this article is available online.

Reference

1. World Health Organization/United Nations International Children's Emergency Fund. *Progress and Challenges With Achieving Universal Immunization Coverage*. WHO/UNICEF; 2019.
2. Indonesia Ministry of Health. Program imunisasi ibu hamil, bayi dan batita di Indonesia. Indonesia Ministry of Health; 2019.
3. World Health Organization. Vaccination schedule for Indonesia. WHO; 2020. Accessed December 21, 2021. https://immunizationdata.who.int/pages/schedule-by-country/idn.
4. Indonesia Ministry of Health. *Indonesia National Health Survey Report 2018*. Indonesia Ministry of Health; 2018.
5. Indonesia Ministry of Health. *Indonesia National Health Survey Report 2013*. Indonesia Ministry of Health; 2013.
6. Indonesia Ministry of Health. *Indonesia National Health Survey Report 2010*. Indonesia Ministry of Health; 2010.
7. Syiroj ATR, Pardosi JF, Heywood AE. Exploring parents' reasons for incomplete childhood immunisation in Indonesia. *Vaccine*. 2019;37:6486-6493. doi:10.1016/j.vaccine.2019.08.081
8. Yufika A, Wagner AL, Nawawi Y, et al. Parents' hesitancy towards vaccination in Indonesia: A cross-sectional study in Indonesia. *Vaccine*. 2020;38:2592-2599. doi:10.1016/j.vaccine.2020.01.072
9. Herliana P, Douiri A. Determinants of immunisation coverage of children aged 12-59 months in Indonesia: a cross-sectional study. *BMJ Open*. 2017;7:1-14. doi:10.1136/bmjopen-2016-015790
10. Sarker AR, Akram R, Ali N, Chowdhury ZI, Sultana M. Coverage and determinants of full immunization: vaccination coverage among Senegalese children. *Medicina*. 2019;55:55. doi:10.3390/medicina55080480
11. Priya P K, Pathak VK, Giri AK. Vaccination coverage and vaccine hesitancy among vulnerable population of India. *Hum Vaccin Immunother*. 2020;16:1502-1507. doi:10.1080/21645515.2019.1708164
12. Mbengue MAS, Sarr M, Faye A, et al. Determinants of complete immunization among senegalese children aged 12-23 months: evidence from the demographic and health survey. *BMC Public Health*. 2017;17:630-639. doi:10.1186/s12889-017-4493-3
13. Kinfe Y, Gebre H, Bekele A. Factors associated with full immunization of children 12-23 months of age in Ethiopia: A multilevel analysis using 2016 Ethiopia Demographic and Health Survey. *PLoS One*. 2019;14:e0225639-NaN14. doi:10.1371/journal.pone.0225639
14. Ntenda PAM. Factors associated with non- and under-vaccination among children aged 12–23 months in Malawi. A multinomial analysis of the population-based sample.

Pediatr Neonatol. 2019;60:623-633. doi:10.1016/j.pedneo.2019.03.005
15. Odone A, Ferrari A, Spagnoli F, et al. Effectiveness of interventions that apply new media to improve vaccine uptake and vaccine coverage: a systematic review. *Hum Vaccin Immunother*. 2015;11:72-82.
16. Indonesia Statistic. *Indonesian Demographic Health Survey 2017*. Kementerian Kesehatan RI; 2017.
17. Nozaki I, Hachiya M, Kitamura T. Factors influencing basic vaccination coverage in Myanmar: secondary analysis of 2015 Myanmar demographic and health survey data. *BMC Public Health*. 2019;19:242-248. doi:10.1186/s12889-019-6548-0
18. Acharya P, Kismul H, Mapatano MA, Hatløy A. Correction: Individual- and community-level determinants of child immunization in the Democratic Republic of Congo: a multilevel analysis. *PLoS One*. 2019;14:e0211299-NaN17. doi:10.1371/journal.pone.0211299
19. Jung M, Lin L, Viswanath K. Associations between health communication behaviors, neighborhood social capital, vaccine knowledge, and parents' H1N1 vaccination of their children. *Vaccine*. 2013;31:4860-4866. doi:10.1016/j.vaccine.2013.07.068
20. Catalan-Matamoros D, Peñafiel-Saiz C. Exploring the relationship between newspaper coverage of vaccines and childhood vaccination rates in Spain. *Hum Vaccin Immunother*. 2020;16:1055-1061. doi:10.1080/21645515.2019.1708163
21. Dunn AG, Surian D, Leask J, Dey A, Mandl KD, Coiera E. Mapping information exposure on social media to explain differences in HPV vaccine coverage in the United States. *Vaccine*. 2017;35:3033-3040. doi:10.1016/j.vaccine.2017.04.060
22. Tabacchi G, Costantino C, Cracchiolo M, et al. Information sources and knowledge on vaccination in a population from southern Italy: the ESCULAPIO project. *Hum Vaccin Immunother*. 2017;13:339-345. doi:10.1080/21645515.2017.1264733
23. Handy LK, Maroudi S, Powell M, et al. The impact of access to immunization information on vaccine acceptance in three countries. *PLoS One*. 2017;12:e0180759-NaN16. doi:10.1371/journal.pone.0180759
24. Padmawati RS, Heywood A, Sitaresmi MN, et al. Religious and community leaders' acceptance of rotavirus vaccine introduction in Yogyakarta, Indonesia: a qualitative study. *BMC Public Health*. 2019;19:368-376. doi:10.1186/s12889-019-6706-4
25. Elkalmi RM, Jamshed SQ, Suhaimi AM. Discrepancies and similarities in attitudes, beliefs, and familiarity with vaccination between religious studies and science students in Malaysia: A Comparison Study. *J Relig Health*. 2021;60:2411-2427. doi:10.1007/s10943-021-01212-x
26. Gidado S, Nguku P, Biya O, et al. Determinants of routine immunization coverage in Bungudu, Zamfara State, Northern Nigeria, May 2010. *Pan Afr Med J*. 2014;18 Suppl 1:9-9. doi:10.11694/pamj.supp.2014.18.1.4149
27. Oleribe O, Kumar V, Awosika-Olumo A, Taylor-Robinson SD. Individual and socioeconomic factors associated with childhood immunization coverage in Nigeria. *Pan Afr Med J*. 2017;26:220-221. doi:10.11604/pamj.2017.26.220.11453
28. Mora T, Trapero-Bertran M. The influence of education on the access to childhood immunization: the case of Spain. *BMC Public Health*. 2018;18:1-9. doi:10.1186/s12889-018-5810-1
29. Asif AM, Akbar M, Tahir MR, Arshad IA. Role of maternal education and vaccination coverage: evidence from Pakistan Demographic and Health Survey. *Asia Pac J Public Health*. 2019;31:679-688. doi:10.1177/1010539519889765
30. Kara SS, Polat M, Yayla BC, et al. Parental vaccine knowledge and behaviours: a survey of Turkish families. *Eastern Mediterr Health J*. 2018;24:451-458. doi:10.26719/2018.24.5.451
31. Rammohan A, Awofeso N, Fernandez RC. Paternal education status significantly influences infants' measles vaccination uptake, independent of maternal education status. *BMC Public Health*. 2012;12:336-337. doi:10.1186/1471-2458-12-336
32. Feiring B, Laake I, Molden T, et al. Do parental education and income matter? A nationwide register-based study on HPV vaccine uptake in the school-based immunisation programme in Norway. *BMJ Open*. 2015;5:e006422-NaN10. doi:10.1136/bmjopen-2014-006422
33. Awasthi A, Pandey CM, Singh U, Kumar S, Singh TB. Maternal determinants of immunization status of children aged 12–23 months in urban slums of Varanasi, India. *Clin Epidemiol Glob Health*. 2015;3:110-116. doi:10.1016/j.cegh.2014.07.004
34. Girmay A, Dadi AF. Full immunization coverage and associated factors among children aged 12-23 months in a hard-to-reach areas of Ethiopia. *Int J Pediatr*. 2019;2019:1-8. doi:10.1155/2019/1924941
35. Kindie Yenit M. Factors associated with incomplete childhood vaccination among children 12-23 months of age in Machakel woreda, East Gojjam Zone: A case control study. *J Pregnancy Child Health*. 2015;02:1-6. doi:10.4172/2376-127x.1000180
36. Akmatov MK, Mikolajczyk RT. Timeliness of childhood vaccinations in 31 low and middle-income countries. *J Epidemiol Community Health*. 2012;66:e14. doi:10.1136/jech.2010.124651
37. Masters NB, Wagner AL, Boulton ML. Vaccination timeliness and delay in low- and middle-income countries: a systematic review of the literature, 2007-2017. *Hum Vaccin Immunother*. 2019;15:2790-2805. doi:10.1080/21645515.2019.1616503

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ORIGINAL ARTICLE

Understanding hepatitis B vaccination willingness in the adult population in Indonesia: a survey among outpatient and healthcare workers in community health centers

Putri Bungsu Machmud[1,2] · **Rafael Mikolajczyk**[1] · **Cornelia Gottschick**[1]

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Abstract

Aim This study aimed to assess factors associated with the willingness to be vaccinated against hepatitis B among Indonesia's adult population, considering cultural and geographic differences by analysing the two provinces of Aceh and Yogyakarta.

Subject and methods An institution-based cross-sectional survey was conducted in 16 community health centres. A multivariable logistic regression model stratified by province was employed to assess variables associated with the willingness to receive hepatitis B vaccination.

Results We found that participants from Yogyakarta more often had a higher knowledge and risk perception of hepatitis B and were more often willing to get vaccinated than participants from Aceh. We also found that a high-risk perception of hepatitis B infection was associated with the willingness to be vaccinated against hepatitis B in participants from both Aceh and Yogyakarta. Furthermore, in Yogyakarta, a fair and high knowledge of hepatitis B infection and vaccination, being female, and having health insurance covering hepatitis B vaccination costs were associated with the willingness to be vaccinated. In Aceh, health care workers in high-risk units for hepatitis B had a higher willingness to be vaccinated than those who were not high-risk health care workers.

Conclusion Given the different factors associated with the willingness to be vaccinated against hepatitis B in Aceh and Yogyakarta, this study also highlights the need of a locally adjusted, culture-based approach to improve the hepatitis B vaccination programme.

Keywords Community health care · Hepatitis B · Health care worker · Outpatient · Vaccination

Introduction

Most people chronically infected with hepatitis B do not know that they are infected; thus, the infection goes unnoticed and undiagnosed until the virus has caused severe liver damage (WHO 2020a). In 2020, the World Health Organization reported that approximately 900,000 deaths are caused by hepatitis B virus infection annually (WHO 2020b). Indonesia is rated as an intermediate-to-high hepatitis B virus endemic region, and it is one of the 11 countries carrying almost 50% of the global burden of chronic hepatitis (WHO 2020a). The Indonesian Ministry of Health estimated that 7% of the population lives with hepatitis B, and approximately 20 million people were diagnosed with chronic hepatitis B in 2013 (The Indonesia Ministry of Health 2013). Moreover, hepatic cirrhosis was categorised as a catastrophic illness, with the

✉ Cornelia Gottschick
cornelia.gottschick@uk-halle.de

Putri Bungsu Machmud
putri.machmud@uk-halle.de

Rafael Mikolajczyk
rafael.mikolajczyk@uk-halle.de

[1] Institute of Medical Epidemiology, Biometrics, and Informatics (IMEBI), Interdisciplinary Center for Health Sciences, Universitätklinikum Halle (Saale), Medical School of the Martin-Luther-University Halle–Wittenberg, Magdeburger Str. 8., 06112 Halle (Saale), Germany

[2] Department of Epidemiology, Public Health Faculty in Universitas Indonesia, Jl. Prof Dr Bahder Djohan, Depok, Jawa Barat, Indonesia

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seventh-highest expenditure of the Indonesian National Health Insurance between 2014 and 2017 (BPJS 2017).

Since 1997, a zero dose of hepatitis B for newborns, followed by three additional doses of hepatitis B for children has been implemented into Indonesia's vaccination strategy (Purwono et al. 2016). However, hepatitis B vaccination coverage was overall low (less than 70% for each dose) with substantial differences between provinces (The Indonesia Ministry of Health 2018). In Yogyakarta, the coverage of hepatitis B vaccination was 97.8% for the first dose and 91% for each of three additional doses. While in Aceh, the coverage among newborns was only 53.9% for the first hepatitis B dose, followed by 26.9%, 24.9%, and 22.0% for three additional doses respectively (The Indonesia Ministry of Health 2018).

This difference may be due to the cultural and political situations in each province and the different histories. For example, Yogyakarta is a monarchy with an ancient sultanate (Harsono 2019), while Aceh is applying the Islamic Sharia Law which may have an indirect impact on the overall health program, including vaccination (Kholiq 2005; Syarkawi 2011; Harapan et al. 2021). Consequently, whereas in some countries, such as USA (Byrd et al. 2013) and Germany (Schenkel et al. 2008; Harder et al. 2013), hepatitis B vaccination is mandatory for health care personnel, many people in Indonesia, including high-risk populations such as health care workers, are unprotected from hepatitis B virus, especially in some provinces.

Although the Indonesian government published regulations about viral hepatitis prevention, recommending that the adult population and especially high-risk groups and people who have never received vaccinations should be vaccinated against hepatitis B (The Indonesia Ministry of Health 2015), currently, Indonesia does not have a compulsory hepatitis B vaccination programme for adults. Thus, people must actively decide to get immunized and bear the costs themselves. However, in order to reach the goals of the Global Hepatitis Elimination 2030 programme (WHO 2016), Indonesia is now preparing a new regulation of hepatitis B vaccination for adults. Starting in 2022, this program will first focus on voluntary vaccinations in health care workers (The Indonesia Ministry of Health 2020).

A study among nurses in Taiwan found that knowledge, the perceived benefit of immunisation, and the perceived barriers to it could predict the willingness to accept a hepatitis B vaccination (Chen et al. 2019). In China it was also found that socio-demographics, such as sex and education level, were the factors impacting the willingness to accept hepatitis B vaccination among migrant workers (Xiang et al. 2019). However, in Indonesia, data on knowledge of hepatitis B infection and vaccination and the community's perception of both is limited.

Therefore, we investigated the willingness of Indonesia's adult population to get vaccinated against hepatitis B in two Indonesian regions (Aceh and Yogyakarta). We determined associated variables, such as knowledge of hepatitis B infection and vaccination, its risk perception, as well as sociodemographic and other characteristics of the respondents. This is a first step in gauging the potential vaccine acceptance and will have large consequences for the upcoming vaccination program and economy (Neumann-Böhme et al. 2020; Yoda and Katsuyama 2021).

Materials and methods

Study design, study site, participants, and sampling procedure

An institution-based (community health centres, Indonesian "Puskesmas"), cross-sectional study was conducted to assess the factors associated with the willingness to accept hepatitis B vaccination among the adult population. In Indonesia, the public primary health care system is decentralized to the district level, with about more than 9,000 community health centres forming the backbone of the country's health system (World Bank 2018). As a result, community health centres are considered to be a suitable setting in which to obtain a sample representing the population. This study was conducted from February to March 2020 at 16 community health centres in two provinces in Indonesia: Aceh and Yogyakarta. Both regions were selected because, according to the results of the Indonesian National Survey conducted in 2018, Yogyakarta Province had the highest vaccination coverage within the existing program (83.7% with complete vaccination, 16.3% with incomplete vaccination, and none without vaccination), while Aceh Province was reported to have the lowest coverage (19.5% with complete vaccination, 16.3% with incomplete vaccination, and 40.9% never vaccinated) (The Indonesia Ministry of Health 2013). This program is aimed at children aged 0 to 11 months and covers the first dose of hepatitis B, followed by three additional doses of hepatitis B, Bacillus Calmette–Guérin (BCG), three doses of diphtheria–tetanus–pertussis, four doses of polio, as well as *Haemophilus influenzae type B*, and measles vaccination (The Indonesia Ministry of Health 2019).

Within the provinces, we selected two regions representing urban and rural areas. For the study purposes, the included urban area was defined as the province's capital city, and the rural regions were randomly selected from the district list in each province. Consequently, we included the cities of Banda Aceh and Yogyakarta as the urban areas and the districts of Takengon and Gunungkidul as rural areas. Data were collected from four health centres that were randomly selected from the health centre list in

each city/district. Only health centres that were accredited by the local health office were included in this study.

Health care workers and outpatients were included in this study. A health care worker was defined as a person who works in a health centre with both medical and non-medical backgrounds, such as medical doctors, dentists, nurses, midwives, analysts, pharmacy, helpers, administrative personnel, drivers, cleaners, and security personnel. An outpatient was a person who was registered as an outpatient at the health centre on the same day that the data were collected. Thereby, outpatients working in other health care centres could later be classified as health care workers. To be included in the study, a participant had to meet the following criteria: older than 15 years of age, in good physical condition, able to answer the questions, willing to participate in the study, and never received hepatitis B vaccination as adults before. Participant who have been infected with hepatitis B or who were already vaccinated against hepatitis B were excluded from this study.

The health care workers were selected through simple random sampling from the centres' employment data. The outpatients were chosen through systematic random sampling, in which the sampling interval referred to the average number of visitors (outpatients) daily in each health centre. At health centres with a small number of health care workers and visitors of outpatients per day, we included all health care workers and outpatients that were eligible and willing to participate during the data collection day. Data collection was achieved through face-to-face interviews conducted by the interviewer. We involved two local enumerators, who were trained and supervised by one field coordinator. The collected data were double-checked by the field coordinator and the principal investigator.

Questionnaire

The questionnaire was based on previous studies (Aaron et al. 2017; Abeje and Azage 2015; Abiodun et al. 2019; Abiye et al. 2019; Ahmad et al. 2016; Akibu et al. 2018; Chao et al. 2010; Pathoumthong et al. 2014; Rajamoorthy et al. 2019) and translated into Bahasa. A pre-test was conducted with 33 participants (health care workers and outpatients) in one of the health centres in West Java, and necessary modification was done after the pre-test. We also improved the data collection technique based on this experience. A structured questionnaire included 15 questions about socio-demographic information, 44 questions about knowledge and risk perception regarding hepatitis B infection, and five questions about the willingness to be vaccinated and pay for hepatitis B vaccination (see supplement 1).

Variables

This study's outcome was the willingness to accept hepatitis B vaccination ("Are you willing to accept a hepatitis B vaccination for adults?"). The socio-demographic variables included in the study were age group (35 to 50 versus (vs) > 50 vs < 35 years old), sex (women vs men), marital status (married vs single/widowed/divorced), religion (Moslem vs Christian and others), residency (urban vs rural), education (secondary and higher education vs primary education), occupational status (employed vs unemployed), profession within the health centre (non health care worker vs high-risk vs low-risk health care worker), monthly income (middle–upper, and upper/high monthly-income vs low monthly-income), and having a health insurance covering hepatitis B vaccination costs (no vs yes). We also considered variables related to exposure to information on hepatitis B: having heard of hepatitis B and knowing someone infected with hepatitis B. In addition, we assessed knowledge of hepatitis B infection and vaccination and risk perceptions of hepatitis B infection. Twenty-nine questions were used to measure knowledge of hepatitis B infection and vaccination. Possible responses to the knowledge questions were "true", "false", and "do not know". Fifteen questions were used to measure the level of risk perception regarding hepatitis B infection. There were two response options for the risk perception questions — "agree" and "disagree" — which measured the extent to which participants believed they could potentially be infected with hepatitis B. A correct answer of knowledge and an agreeing response regarding risk of hepatitis B infection and vaccination was given a score of one; an incorrect answer of knowledge and a disagreeing response of risk perception regarding hepatitis B infection was assigned a score of zero. Consequently, each subject had a total sum of correct and positive answers (see supplements 2 and 3). The total score of knowledge was divided into three categories: poor knowledge (less than 50% correct answers), fair knowledge (50% to 75% correct answers), and good knowledge (more than 75% correct answers). The risk perception was categorised into two groups based on the median cut-off point: low-risk perception and high-risk perception.

Statistical analysis

SPSS version 20 was used for the data analysis. Descriptive analysis ascertained the frequencies of the data, presented as percentages for the categorical variables. We built a multivariable logistic regression to analyse factors associated with the willingness to accept hepatitis B vaccination. First, all independent variables that were associated with the outcome variable based on previous studies were included into univariable logistic regression analyses. This resulted in crude odds ratios of model 1 in

Table 4 (Harapan et al. 2021; Chen et al. 2019; Xiang et al. 2019; Yoda and Katsuyama 2021; Abeje and Azage 2015; Abiodun et al. 2019; Abiye et al. 2019; Pathoumthong et al. 2014; Rajamoorthy et al. 2019; Eilers et al. 2014; Park et al. 2012; Yu et al. 2016; Ghomraoui et al. 2016; Machmud et al. 2021). Then, all variables were included in a multivariable logistic regression model resulting in adjusted odds ratios of model 2 (Table 4). For odds ratios, 95% confidence intervals (CI) are shown. Economic status was not included in this analysis, because more than 80% of the data were missing. Since all participants of the variable "Christian and others" answered that they were willing to accept hepatitis B vaccination (thereby presenting a cell in the data table with the value zero), the odds ratios were obtained from standard contingency table analysis using Haldane's modification of Woolf's method (Ruxton and Neuhäuser 2013) and statistical significance was assessed by a two-tailed Fisher's exact test.

Ethics approval

The Research and Community Engagement Ethical Committee, the Faculty of Public Health, University Indonesia (196/UN2.F10.D11/PPM.00.02/2020), and the ethical committee of the Faculty of Medicine, Martin Luther University Halle–Wittenberg (processing number: 2021-140), approved the study protocol. All participants signed written informed consent forms prior to enrolment. The work was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies that involve humans.

Results

Socio-demographic characteristics

In this study, a total of 1000 participants were approached, of whom 98 refused to participate, seven started and refused to continue the interview, and 138 were excluded due to vaccination or infection with hepatitis B before, leaving a dataset with a total of 757 (84.6%) participants: 373 (49.3%) from Aceh and 384 (50.7%) from Yogyakarta (Fig. 1). Differences in socio-demographic variables between provinces were observed for age group, sex, religion, education level, profession, and health insurance (Table 1). Compared to participants from Yogyakarta, participants from Aceh were more often older than 35 years of age, women, Moslem, more often had a higher education level, and a profession as health care worker; they less often had insurance covering hepatitis B vaccination.

Exposure to information on hepatitis B

In both Aceh and Yogyakarta, around 50% of participants claimed that they had heard information on hepatitis B vaccination for adults. Most of them had heard information on hepatitis B from their health provider, followed by the media. Among the participants who had heard information on hepatitis B information in the media, most used television and social media as the platform to obtain that information (Table 2).

Knowledge and risk perception of hepatitis B and willingness to be vaccinated

Participants from Yogyakarta more often had good knowledge about hepatitis B infection (20.8% vs 8.6% in Aceh, Table 3), vaccination (17.2% vs 12.1% in Aceh) and high risk perceptions of hepatitis B infection (57.8% vs 42.6% in Aceh). In Yogyakarta, they were also more often willing to be vaccinated against hepatitis B (88% vs 81% in Aceh).

Variables associated with the willingness to be vaccinated against hepatitis B

The association between each independent variable and the likelihood of the willingness to take the vaccine was investigated. Crude odds ratios are presented in model 1 (Table 4).

After adjustment, risk perception of hepatitis B was the only variable positively associated with the willingness to accept a hepatitis B vaccination in both provinces. Thereby, the adjusted odds ratio (AOR) for respondents who, based on our questionnaire (see supplement 1), were considered to have a high-risk perception compared to those considered to have a low-risk perception was almost double in Yogyakarta (AOR 5.11; 95% CI: 2.29–11.41, Table 4) compared to Aceh (AOR 2.58; 95% CI: 1.34–4.98).

In Yogyakarta, but not in Aceh, participants with fair and good knowledge of hepatitis B infection and vaccination were 5 times more likely to be willing to get vaccinated against hepatitis B than participants with poor knowledge (AOR 2.48; 95% CI: 1.01–6.14 and AOR 4.77; 95% CI: 1.04–21.83 for fair and good knowledge, respectively). Women in Yogyakarta also had higher odds for the willingness to be vaccinated (AOR 3.92; 95% CI: 1.93–7.96) than men, but not in Aceh. Furthermore, only participants from Yogyakarta with insurance covering vaccination costs were almost 5 times more likely to accept a hepatitis B vaccination compared to those without that kind of insurance (AOR 4.80; 95% CI: 1.01–22.78).

In contrast, only participants from Aceh working as health care workers in hepatitis B high-risk units were 4 times more likely to accept hepatitis B vaccination compared to non health care workers (AOR 4.07; 95% CI: 1.99–8.33). There were no associations in either province between age, residency, marital status, education level, occupational status, heaving heard about hepatitis B, and knowing someone infected with hepatitis B.

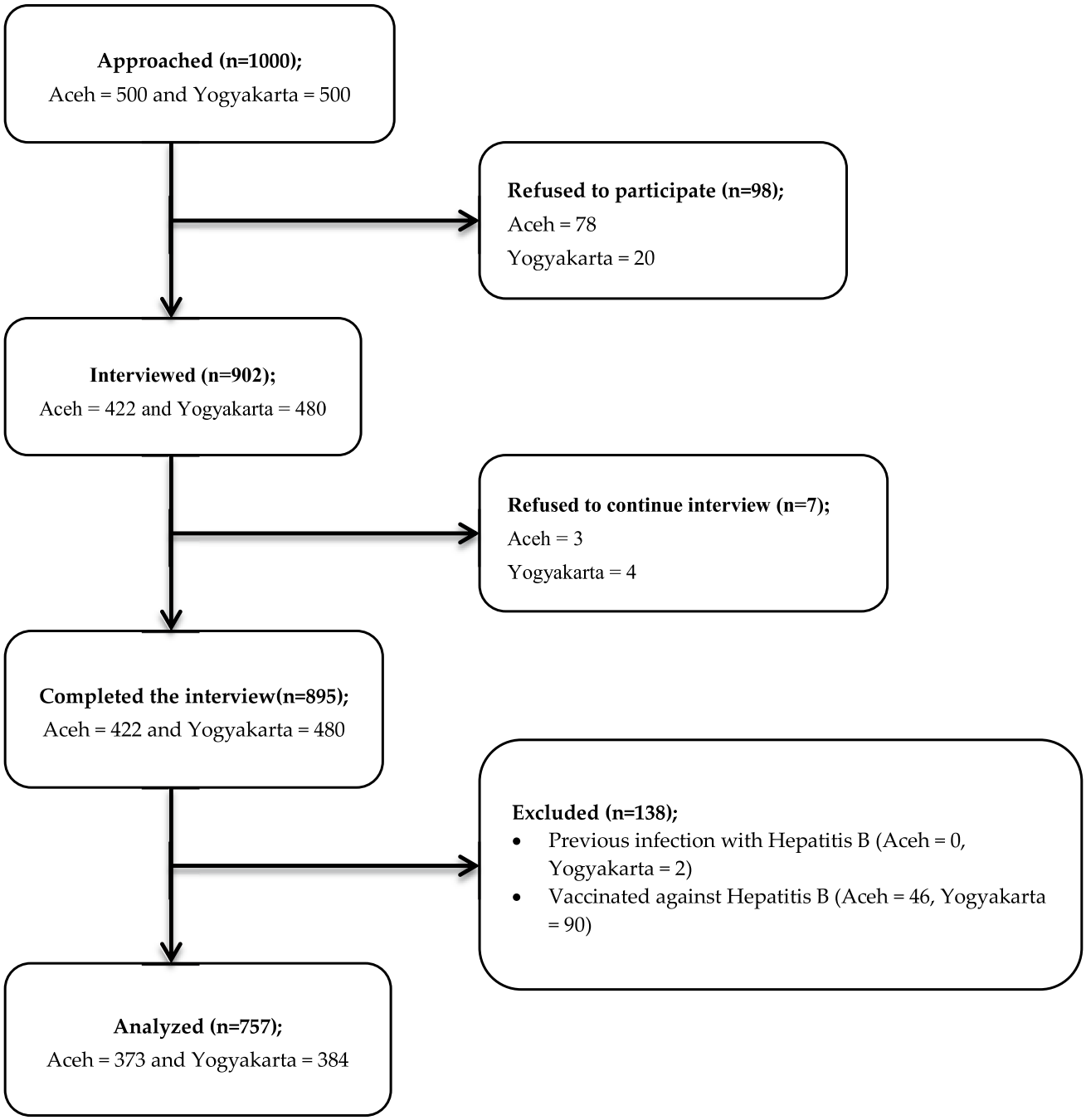

Fig. 1 Sampling scheme

Discussion

We investigated the willingness of Indonesia's adult population to get vaccinated against hepatitis B in two provinces, Aceh and Yogyakarta. Furthermore, we assessed factors associated with the willingness to accept hepatitis B vaccination as a first step in measuring the potential vaccine acceptance among the adult population in Indonesia.

In total, 84.5% of participants were willing to accept hepatitis B vaccination. This result may reflect the fact that most participants understood the benefits of hepatitis B vaccination. In contrast, a previous study in China found that only 30.3% of unvaccinated adults said hepatitis B vaccination was needed (Yu et al. 2016). This difference may be due to the fact that 50.2% of our population are health workers. We also found that 7% more participants from Yogyakarta were willing to accept

Table 1 Demographic characteristics by province

Variable	All participants n =757	Aceh n = 373	Yogyakarta n = 384
Age (years old)			
< 35	392 (51.8)	182 (48.8)	210 (54.7)
35–50	298 (39.4)	170 (45.6)	128 (33.3)
> 50	67 (8.9)	21 (5.6)	46 (12.0)
Sex			
Men	139 (18.4)	46 (12.3)	93 (24.2)
Women	618 (81.6)	327 (87.7)	291 (75.8)
Residency			
Urban	376 (49.7)	190 (50.9)	186 (48.4)
Rural	381 (50.3)	183 (49.1)	198 (51.6)
Marital status			
Single/widowed/divorced	180 (23.8)	91 (24.4)	89 (23.2)
Married	577 (76.2)	282 (75.6)	295 (76.8)
Religion			
Catholic	12 (1.6)	0 (0.0)	12 (3.1)
Moslem	724 (95.6)	369 (98.9)	355 (92.4)
Protestant	16 (2.1)	1 (0.3)	15 (3.4)
Others[†]	5 (0.7)	3 (0.8)	2 (0.5)
Education level			
Primary	137 (18.1)	52 (13.9)	85 (22.1)
Secondary	230 (30.4)	100 (26.8)	130 (33.9)
Higher	390 (51.5)	221 (59.2)	169 (44.0)
Occupational status			
Unemployed	232 (30.6)	113 (30.3)	119 (31.0)
Employed	525 (69.4)	260 (69.7)	265 (69.0)
Profession			
Non-health care worker	377 (49.8)	177 (47.5)	200 (52.1)
Health care worker (low risk)	135 (17.8)	46 (12.3)	89 (23.2)
Health care worker (high risk)	245 (32.4)	150 (40.2)	95 (24.7)
Monthly income (IDR)			
≤ 1 million	43 (5.7)	16 (4.3)	27 (7.0)
> 1 to 2 million	27 (3.6)	15 (4.0)	12 (3.1)
> 2 to 3 million	48 (6.3)	18 (4.8)	30 (7.8)
> 3 million	33 (4.4)	22 (5.9)	11 (2.9)
Missing	606 (80.1)	302 (81.0)	304 (79.2)
Health insurance covering hepatitis B vaccination			
No	663 (87.6)	346 (92.8)	317 (82.6)
Yes	94 (12.4)	27 (7.2)	67 (17.4)

Data presented as number (%)

[†]Buddha, Hindu, and Kong Hu Chu

a hepatitis B vaccination than from Aceh. This may result in a large effect when applied to a population such as Indonesia's (World Bank 2021). Yogyakarta, located in Central Java, and Aceh in the western-most part of Indonesia each have their own decentralized health programmes (BPS 2020b; Nasution 2016). Furthermore, Yogyakarta is one of the provinces in Indonesia with a monarchy system (the kingdom Sultanate of Yogyakarta) (Harsono 2019). It is one of the provinces with a Javanese culture, which is famous for its high harmony, character of self-control, peace, and tolerance (Nashori et al. 2020) and one of the most popular places for education and tourism in Indonesia, with a multi-ethnic population (BPS 2020a). All the above may have valuable impact on the health program including vaccination. Therefore, it is not surprising we found people from Yogyakarta to be more amenable to new ideas or policies, including health programmes.

Table 2 Information exposure regarding hepatitis B by province

Variable	All participants (n =757)	Aceh (n = 373)	Yogyakarta (n = 384)
Heard about hepatitis B vaccination			
No	361 (47.7)	173 (46.4)	188 (49.0)
Yes	396 (52.3)	200 (53.6)	196 (51.0)
Knowing someone infected with hepatitis B			
No	715 (94.5)	353 (94.6)	362 (94.3)
Yes	42 (5.5)	20 (5.4)	22 (5.7)
Source of information[a]	(n = 396)	(n = 173)	(n = 196)
Health provider	320 (80.8)	165 (95.4)	155 (79.1)
Health community	29 (7.3)	18 (10.4)	11 (5.6)
Family/relatives	119 (30.1)	65 (37.6)	54 (27.6)
Community/religious leader	15 (3.8)	9 (5.2)	6 (3.1)
Seminar/training	10 (2.5)	3 (1.7)	7 (3.6)
Media	190 (52.0)	86 (49.7)	104 (53.1)
Media platform[b]	(n = 190)	(n = 86)	(n= 104)
Television	132 (69.5)	61 (70.9)	71 (68.3)
Poster	48 (25.3)	19 (22.1)	29 (27.9)
Newspaper	31 (16.3)	15 (17.4)	16 (15.4)
Radio	18 (9.5)	7 (8.1)	11 (10.6)
Internet	5 (2.6)	1 (1.2)	4 (3.8)
Social media	112 (58.9)	57 (66.3)	55 (52.9)

Data presented as number (%)

[a]Participants had more than one source of information

[b]Participants used more than one media platform

Table 3 Percentage of participant's knowledge, risk perception and willingness to be vaccinated by province

Variable	All participants n =757	Aceh n = 373	Yogyakarta n = 384
Knowledge of hepatitis B			
Hepatitis B infection			
Poor	367 (48.5)	181 (48.5)	186 (48.4)
Fair	278 (36.7)	160 (42.9)	118 (30.7)
Good	112 (14.8)	32 (8.6)	80 (20.8)
Hepatitis B vaccination			
Poor	343 (45.3)	183 (49.1)	160 (41.7)
Fair	303 (40.0)	145 (38.9)	158 (41.1)
Good	111 (14.7)	45 (12.1)	66 (17.2)
Risk perception of hepatitis B infection			
Low	376 (49.7)	214 (57.4)	162 (42.2)
High	381 (50.3)	159 (42.6)	222 (57.8)
Willingness to be vaccinated against hepatitis B			
No	117 (15.5)	71 (19.0)	46 (12.0)
Yes	640 (84.5)	302 (81.0)	338 (88.0)

Data presented as number (%)

The common factor associated with a high willingness to get vaccinated against hepatitis B, in Yogyakarta and Aceh, was a high-risk perception of hepatitis B infection. Thereby, the awareness of risk may be associated with a person's motivation to be vaccinated (Xiang et al. 2019; Chen et al. 2019). A systematic review among immigrants and refugees concluded that health decision-making, such as vaccination, is also influenced by attitude and risk perception (Owiti et al. 2015). Eilers et al. also found that people's attitudes and beliefs regarding immunisation are the most critical factors of vaccine uptake in western societies (Eilers et al. 2014). Moreover, several studies found that one reason for participants not wanting to be vaccinated was that they never felt the need for it or were unaware of it (Park et al. 2012; Yu et al. 2016; Ibrahim and Idris 2014; Ghomraoui et al. 2016; Khandelwal et al. 2017; Machmud et al. 2021). Risk perception is also related to several factors such as education, information exposure, knowledge, and experience of exposure. For example, Mullins et al. found that as knowledge increased over time, risk perception often became more accurate (Mullins et al. 2015).

We also found different factors associated with the willingness to be vaccinated in the different regions, i.e., higher knowledge of hepatitis B infection and vaccination, being female, and having insurance covering hepatitis B

Table 4 Predictive variable of willingness to undergo hepatitis B vaccination by province

Variable	Aceh Province (n = 373)			Yogyakarta Province (n = 384)		
	Willingness to get vaccinated [n (%)]	Model 1 Crude OR (95% CI)	Model 2 Adj. OR (95% CI)	Willingness to get vaccinated [n (%)]	Model 1 Crude OR (95% CI)	Model 2 Adj. OR (95% CI)
Age (years old)						
< 35	139 (46.1)	REF	REF	178 (52.7)	REF	REF
35–50	146 (48.3)	1.88 (1.09–3.26)	1.35 (0.73–2.50)	117 (34.6)	1.91 (0.93–3.94)	1.10 (0.44–2.79)
> 50	17 (5.6)	1.32 (0.42–4.12)	1.26 (0.37–4.29)	43 (12.7)	2.58 (0.75–8.81)	1.49 (0.30–7.36)
Sex						
Men	35 (11.6)	REF	REF	69 (24.2)	REF	REF
Women	267 (88.4)	1.40 (0.67–2.91)	1.34 (0.61–2.95)	269 (79.6)	4.25 (2.25–8.03)	3.92 (1.93–7.96)
Residency						
Urban	153 (50.7)	REF	REF	165 (48.8)	REF	REF
Rural	149 (49.3)	0.94 (0.56–1.58)	0.86 (0.47–1.57)	173 (51.2)	1.14 (0.61–2.11)	1.44 (0.68–3.03)
Marital status						
Single/Widowed/ Divorced	68 (22.5)	REF	REF	75 (22.2)	REF	REF
Married	234 (77.5)	1.65 (0.94–2.90)	0.97 (0.49–2.05)	263 (77.8)	1.53 (0.78–3.02)	0.85 (0.35–2.04)
Religion						
Moslem	298 (98.7)	REF		309 (91.4)	REF	
Christian and others	4 (1.3)	2.16 (0.12–40.53)[†]		29 (8.6)	8.86 (0.53–147.67)[†]	
Educational level						
Primary	41 (13.6)	REF	REF	68 (20.1)	REF	REF
Secondary	67 (22.2)	0.54 (0.25–1.20)	0.52 (0.23–1.15)	114 (33.7)	1.78 (0.85–3.76)	0.97 (0.35–2.69)
Tertiary	194 (64.2)	1.93 (0.89–4.20)	0.62 (0.23–1.71)	156 (46.2)	3.00 (1.38–6.52)	1.95 (0.81–4.68)
Occupational status						
Unemployed	80 (26.5)	REF	REF	104 (30.8)	REF	REF
Employed	222 (73.5)	2.41 (1.42–4.10)	0.85 (0.41–1.78)	234 (69.2)	1.09 (0.56–2.10)	0.94 (0.37–2.41)
Profession						
Non-HCW	124 (41.1)	REF	REF	166 (49.1)	REF	REF
HCW (low risk)	139 (46.0)	2.38 (1.00–5.66)	2.01 (0.83–4.85)	92 (27.2)	1.96 (0.90–4.27)	1.08 (0.35–3.30)
HCW (high risk)	39 (12.9)	5.40 (2.70–10.80)	4.07 (1.99–8.33)	80 (23.7)	5.87 (1.75–19.67)	2.08 (0.38–11.47)
Health insurance covering hepatitis B vaccination						
No	278 (92.1)	REF	REF	273 (80.8)	REF	REF
Yes	24 (7.9)	1.96 (0.57–6.69)	1.13 (0.29–4.43)	65 (19.2)	5.24 (1.24–22.17)	4.80 (1.01–22.78)
Has heard about hepatitis B						
No	126 (41.7)	REF	REF	273 (80.8)	REF	REF
Yes	176 (58.3)	2.74 (1.59–4.71)	1.38 (0.70–2.71)	65 (19.2)	5.95 (2.70–13.14)	1.89 (0.74–4.85)
Knows someone infected with hepatitis B						
No	284 (94.0)	REF	REF	317 (93.8)	REF	
Yes	18 (6.0)	0.94 (0.10–8.54)	1.19 (0.11–12.95)	21 (6.2)	0.01 (0.0006–0.194)[†]	
Knowledge of hepatitis B infection and vaccination						
Poor	138 (45.7)	REF	REF	151 (44.7)	REF	REF
Fair	131(43.4)	3.42 (1.84–6.35)	1.44 (0.59–3.52)	114 (33.7)	3.99 (1.72–9.28)	2.49 (1.01–6.14)
Good	33 (10.9)	6.46 (1.50–27.84)	1.69 (0.30–9.53)	73 (21.6)	8.94 (2.10–38.13)	4.77 (1.04–21.83)
Risk perception of hepatitis B infection						
Low	157 (52.0)	REF	REF	125 (37.0)	REF	REF
High	145 (48.0)	3.76 (2.01–7.04)	2.58 (1.34–4.98)	213 (63.0)	7.01 (3.27–15.00)	5.11 (2.29–11.41)

Model 1: Crude OR

Model 2: Adjusted (Adj.) for all variables

HCW= health care worker

[†]Odds ratio (OR) refers to Woolf–Haldane odds ratios, with 95% Woolf approximation confidence intervals (CI)

vaccination in Yogyakarta and being a high-risk health care worker in Aceh. In Yogyakarta, the influence of the sultanate tradition fully supports the empowerment of women, and encourages women to make independent choices such as health action decisions (Ratnawati and Santoso 2021).

Furthermore, the provincial minimum wage is lower in Yogyakarta than in Aceh (approximately, Rp.1.700.000 vs Rp.3.100.000 or 117 USD vs 213 USD per month in 2021) (Yogyakarta Government 2020). The cost of the adult vaccination in Indonesia reached Rp.255.000 (16.34 USD) per dose (St. Carolus Hospital 2020), which is around 14% of the minimum monthly income in Yogyakarta and 8% of the minimum monthly income in Aceh per dose. Therefore, the coverage of vaccination costs by insurance has a larger effect in Yogyakarta than in Aceh. Furthermore, the inability to afford vaccination is a common reason for adult populations to choose not to be vaccinated (Akibu et al. 2018; Pathoumthong et al. 2014; Yuan et al. 2019; Tatsilong et al. 2016; Noubiap et al. 2013, 2014; Vo et al. 2018; Osei et al. 2019; Omotowo et al. 2018; Park et al. 2012).

As opposed to Yogyakarta, in Aceh, which has a strong history as the first area of the entry of Islam in Indonesia resulting in autonomy (Kholiq 2005) and the official implementation of Islamic Sharia Law (Kholiq 2005; Syarkawi 2011), knowledge of hepatitis B infection and vaccination may not affect someone in their willingness to be vaccinated. This may be due to a controversy of a forbidden ingredient in the vaccine opposing religious rules (the vaccine not being halal) (Harapan et al. 2021). For this reason, in Aceh, people may feel unconfident with regard to vaccination although they know about the benefit of vaccination. A possible motivation for high-risk health care workers in Aceh to be willing to get vaccinated may be self-protection (Adeyemi et al. 2013; Chung et al. 2012; Ochu and Beynon 2017).

Due to small numbers of non-Muslim participants, our analysis can only show a tendency of the association between religion and willingness to be vaccinated. In the literature, there are different reports on this relationship. Several studies show that religious law influences vaccination coverage, i.e., a study by Azizi et al. from Indonesia's neighbour country Malaysia (Harapan et al. 2021; Basharat and Shaikh 2017; Syiroj et al. 2019; Azizi et al. 2017). However, some studies did not find an association between religion and vaccination at all (Osei et al. 2019; Shao et al. 2018). Therefore, further research in this field is needed and could assist strategic planning of vaccination programmes, especially in Muslim-majority countries.

Overall, we can see large differences regarding knowledge and risk perception between the provinces in our data. Thus, we believe that vaccine strategies have to be adapted based on local needs, and they should use culturally appropriate approaches for vaccination programmes since there may be no one-size-fits-all solution for all regions (Hardt et al. 2016; Frew et al. 2014). However, there are grounds for believing that increasing the risk perception of hepatitis B in the general population and adjusting measurements to local religion and culture could have a positive effect in a common Indonesian health programme.

To the best of our knowledge, this study was the first to identify predictive factors of the willingness to accept hepatitis B vaccination involving two regions with different degrees of vaccination coverage in their vaccination programmes. However, this study also has some limitations. Selection bias is one of the limitations. Most of the visitors in the included health centres were women, which might be sufficient to reduce the ability to generalise the study's results. Additionally, some studies have shown that economic factors were one of the factors that had a significant impact on vaccination status (Chung et al. 2012; Park et al. 2013; Park et al. 2012), but that was not included in this study due to a high amount of missing data. This study could also not show a difference between religions because most of the participants were Muslims (95.9%). Lastly, the participants might have provided favourable answers during the interview as a form of social desirability bias. Despite these limitations, this study's results are considered to significantly contribute to public health knowledge.

Conclusions

This study found differences in knowledge, risk perception, and the willingness to be vaccination between the Indonesian provinces Yogyakarta and Aceh. Risk perception of hepatitis B infection impacts the willingness to be vaccinated in both provinces, which could provide ground for consideration in a common health care programme. However, other factors are also associated to the willingness to be vaccinated in Aceh and Yogyakarta. Our study shows that cost of hepatitis B is one of the main reasons for not getting vaccinated in Yogyakarta; as a result, the general health insurance could cover costs of hepatitis B vaccination. Furthermore, we identified that a local, culture-based approach may be needed for a successful vaccination programme. Therefore, further studies are necessary to identify the best cultural and local-based approaches, also considering religious rules.

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Author contributions P.B.M. investigated, analysed the data, and wrote the original draft. C.G. and R.M. validated and supervised. All authors

reviewed and edited the manuscript. All authors have read and agreed to the published version of the manuscript.

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Availability of data and material The dataset generated and/or analysed during the current study is not publicly available due to the fact that it constitutes an excerpt of research in progress, but is available from the first author on reasonable request.

Code availability Not applicable

Declarations

Ethical approval statement This study was reviewed and approved by the Research and Community Engagement Ethical Committee, the Faculty of Public Health, University Indonesia (196/UN2.F10.D11/PPM.00.02/2020), and the ethical committee of the Faculty of Medicine, Martin Luther University Halle–Wittenberg (processing number: 2021-140). Informed consent forms and authorization forms were obtained from each eligible participant who volunteered to participate in the study.

Consent to participate Not applicable

Consent for publication Not applicable

Conflict of interest statement The authors declare that they have no conflict of interest.

References

Aaron D, Nagu TJ, Rwegasha J, Komba E (2017) Hepatitis B vaccination coverage among healthcare workers at national hospital in Tanzania: how much, who and why? BMC Infect Dis 17:1–7. https://doi.org/10.1186/s12879-017-2893-8

Abeje G, Azage M (2015) Hepatitis B vaccine knowledge and vaccination status among health care workers of Bahir Dar City Administration, Northwest Ethiopia: a cross-sectional study. BMC Infect Dis 15:1–6. https://doi.org/10.1186/s12879-015-0756-8

Abiodun O, Shobowale O, Elikwu C, Ogbaro D, Omotosho A, Mark B, Akinbole A (2019) Risk perception and knowledge of hepatitis B infection among cleaners in a tertiary hospital in Nigeria: a cross-sectional study. Clin Epidemiol Glob Health 7:11–16. https://doi.org/10.1016/j.cegh.2017.12.001

Abiye S, Yitayal M, Abere G, Adimasu A (2019) Health professionals' acceptance and willingness to pay for hepatitis B virus vaccination in Gondar City Administration governmental health institutions, Northwest Ethiopia. BMC Health Serv Res 19:1–7. https://doi.org/10.1186/s12913-019-4671-3

Adeyemi AB, Enabor OO, Ugwu IA, Bello FA, Olayemi OO (2013) Knowledge of hepatitis B virus infection, access to screening and vaccination among pregnant women in Ibadan, Nigeria. J Obstet Gynaecol 33:155–159. https://doi.org/10.3109/01443615.2012.711389

Ahmad A, Munn Sann L, Abdul Rahman H (2016) Factors associated with knowledge, attitude and practice related to hepatitis B and C among international students of Universiti Putra Malaysia. BMC Public Health 16:1–8. https://doi.org/10.1186/s12889-016-3188-5

Akibu M, Nurgi S, Tadese M, Tsega WD (2018) Attitude and vaccination status of healthcare workers against Hepatitis B Infection in a teaching hospital, Ethiopia. Scientifica 2018:1–8. https://doi.org/10.1155/2018/6705305

Azizi FSM, Kew Y, Moy FM (2017) Vaccine hesitancy among parents in multi-ethnic country, Malaysia. Vaccine 35:2955–2961. https://doi.org/10.1016/j.vaccine.2017.04.010

Basharat S, Shaikh BT (2017) Polio immunization in Pakistan: ethical issues and challenges. Public Health Rev 38:1–6. https://doi.org/10.1186/s40985-017-0049-4

BPS (Statistics Indonesia) (2020a) Kota Yogyakarta dalam angka 2020. BPS-Statistics of Yogyakarta Municipality, Yogyakarta

BPS (Statistics Indonesia) (2020b) Statistical yearbook of Indonesia. BPS-Statistics Indonesia, Jakarta

Byrd KK, Lu PJ, Murphy TV (2013) Hepatitis B vaccination coverage among health-care personnel in the United States. Public Health Rep 128:498–509. https://doi.org/10.1177/003335491312800609

Chao J, Chang ET, So SK (2010) Hepatitis B and liver cancer knowledge and practices among healthcare and public health professionals in China: a cross-sectional study. BMC Public Health 10:1–11. https://doi.org/10.1186/1471-2458-10-98

Chen I, Master SH, Wu JJ, Master YW, Lin Y, Chung M, Huang P, Miao N (2019) Determinants of nurses' willingness to receive vaccines: application of the health belief model. J Clin Nurs 28:3430–3440. https://doi.org/10.1111/jocn.14934

Chung PW, Suen SH, Chan OK, Lao TH, Leung TY (2012) Awareness and knowledge of hepatitis B infection and prevention and the use of hepatitis B vaccination in the Hong Kong adult Chinese population. Chin Med J 125:422–427. https://doi.org/10.3760/cma.j.issn.0366-6999.2012.03.004

Eilers R, Krabbe PFM, de Melker HE (2014) Factors affecting the uptake of vaccination by the elderly in Western society. Prev Med 69:224–234. https://doi.org/10.1016/j.ypmed.2014.10.017

Frew PM, Alhanti B, Vo-Green L, Zhang S, Liu C, Nguyen T, Schamel J, Saint-Victor DS, Nguyen ML (2014) Multilevel factors influencing hepatitis B screening and vaccination among Vietnamese Americans in Atlanta, Georgia. Yale J Biol Med 87:455–471

Ghomraoui FA, Alfaqeeh FA, Algadheeb AS, Al-Alsheikh AS, Al-Hamoudi WK, Alswat KA (2016) Medical students' awareness of and compliance with the hepatitis B vaccine in a tertiary care academic hospital: an epidemiological study. J Infect Public Health 9:60–65. https://doi.org/10.1016/j.jiph.2015.06.008

Harapan H, Shields N, Kachoria AG, Shotwell A, Wagner AL (2021) Religion and measles vaccination in Indonesia, 1991–2017. Am J Prev Med 60:44–52. https://doi.org/10.1016/j.amepre.2020.07.029

Harder T, Remschmidt C, Falkenhorst G, Zimmermann R, Hengel H, Ledig T, Oppermann H, Zeuzem S, Wicker S (2013) Background paper to the revised recommendation for hepatitis B vaccination of persons at particular risk and for hepatitis B postexposure prophylaxis in Germany. Bundesgesundheitsbl

Gesundheitsforsch Gesundheitsschutz 11:1565–1576. https://doi.org/10.1007/s00103-013-1845-8
Hardt K, Bonanni P, King S, Santos JI, El-Hodhod M, Zimet GD, Preiss S (2016) Vaccine strategies: optimising outcomes. Vaccine 34:6691–6699. https://doi.org/10.1016/j.vaccine.2016.10.078
Harsono D (2019) A monarchy without a kingdom: Yogyakarta's exceptional system of government. Dissertation, La Trobe University, Melbourne
Hospital SC (2020) Adult vaccination and promotion. St. Carolus Hospital, Jakarta
Ibrahim N, Idris A (2014) Hepatitis B awareness among medical students and their vaccination status at Syrian Private University. Hepatitis Res Treat 2014:1–7. https://doi.org/10.1155/2014/131920
Khandelwal V, Khandelwal S, Gupta N, Nayak UA, Kulshreshtha N, Baliga S (2017) Knowledge of hepatitis B virus infection and its control practices among dental students in an Indian city. Int J Adolesc Med Health 30(5):/j/ijamh.2018.30.issue-5/ijamh-2016-0103/ijamh-2016-0103.xml. https://doi.org/10.1515/ijamh-2016-0103
Kholiq MA (2005) Pemberlakuan Syari'at islam di Nanggroe Aceh Darussalam (NAD). Jurnal Hukum 12:60–75
Machmud PB, Glasauer S, Gottschick C, Mikolajczyk R (2021) Knowledge, vaccination status, and reasons for avoiding vaccinations against Hepatitis B in developing countries: a systematic review. Vaccines 9:1–26. https://doi.org/10.3390/vaccines9060625
Mullins TLK, Widdice LE, Rosenthal SL, Zimet GD, Kahna JA (2015) Risk perceptions, sexual attitudes, and sexual behavior after HPV vaccination in 11–12 year-old girls. Vaccine 33:3907–3912. https://doi.org/10.1016/j.vaccine.2015.06.060
Nashori F, Iskandar TZ, Setiono K, Siswadi AGP, Andriansyah Y (2020) Religiosity, interpersonal attachment, and forgiveness among the Javanese population in Yogyakarta, Indonesia. Ment Health Relig Cult 23:99–112. https://doi.org/10.1080/13674676.2019.1646233
Nasution A (2016) Government Decentralization Program in Indonesia. ADBI working paper series. Asian Development Bank Institute, Japan
Neumann-Böhme S, Varghese NE, Sabat I, Barros PP, Brouwer W, van Exel J, Schreyögg J, Stargardt T (2020) Once we have it, will we use it? A European survey on willingness to be vaccinated against COVID-19. Eur J Health Econ 21:977–982. https://doi.org/10.1007/s10198-020-01208-6
Noubiap JJ, Nansseu JRN, Kengne KK, Ndoula ST, Agyingi LA (2013) Occupational exposure to blood, hepatitis B vaccine knowledge and uptake among medical students in Cameroon. BMC Med Educ 13:148. https://doi.org/10.1186/1472-6920-13-148
Noubiap JJ, Nansseu JRN, Kengne KK, Wonkam A, Wiysonge CS (2014) Low hepatitis B vaccine uptake among surgical residents in Cameroon. Int Arch Med 7:11–11. https://doi.org/10.1186/1755-7682-7-11
Ochu CL, Beynon CM (2017) Hepatitis B vaccination coverage, knowledge and sociodemographic determinants of uptake in high risk public safety workers in Kaduna State, Nigeria: a cross sectional survey. BMJ Open 7:1–10. https://doi.org/10.1136/bmjopen-2017-015845
Omotowo IB, Meka IA, Ijoma UN, Okoli VE, Obienu O, Nwagha T, Ndu AC, Onodugo OO, Onyekonwu LC, Ugwu EO (2018) Uptake of hepatitis B vaccination and its determinants among health care workers in a tertiary health facility in Enugu, South-East Nigeria. BMC Infect Dis 18:288. https://doi.org/10.1186/s12879-018-3191-9
Osei E, Niyilapah J, Amenuvegbe GK (2019) Hepatitis B knowledge, testing, and vaccination history among undergraduate public health students in Ghana. Biomed Res Int 2019:1–10. https://doi.org/10.1155/2019/7645106
Owiti JA, Greenhalgh T, Sweeney L, Foster GR, Bhui KS (2015) Illness perception and explanatory models of viral hepatitis B and C among immigrants and refugees: a narrative systematic review. BMC Public Health 15:1–17. https://doi.org/10.1186/s12889-015-1476-0
Park B, Choi KS, Lee H, Jun JK, Park E (2012) Socioeconomic inequalities in completion of hepatitis B vaccine series among Korean women: results from a nationwide interview survey. Vaccine 30:5844–5848. https://doi.org/10.1016/j.vaccine.2012.07.022
Park B, Choi KS, Lee H, Kwak M, Jun JK, Park E (2013) Determinants of suboptimal hepatitis B vaccine uptake among men in the Republic of Korea: where should our efforts be focused: results from cross-sectional study. BMC Infect Dis 13:218–218. https://doi.org/10.1186/1471-2334-13-218
Pathoumthong K, Khampanisong P, Quet F, Latthaphasavang V, Souvong V, Buisson Y (2014) Vaccination status, knowledge and awareness towards hepatitis B among students of health professions in Vientiane, Lao PDR. Vaccine 32:4993–4999. https://doi.org/10.1016/j.vaccine.2014.07.022
Purwono PB, Juniastuti, Amin M, Bramanthi R, Nursidah REM, Wahyuni RM, Yano Y, Hotta H, Hayashi Y, Utsumi T, Lusida MI (2016)Hepatitis B virus infection in Indonesia 15 years after adoption of a universal infant vaccination program: possible impacts of low birth dose coverage and a vaccine-escape mutant. Am J Trop Med Hyg 95:674–679. https://doi.org/10.4269/ajtmh.15-0121
Rajamoorthy Y, Taib NM, Munusamy S, Anwar S, Wagner AL, Mudatsir M, Müller R, Kuch U, Groneberg DA, Harapan H, Khin AA (2019) Knowledge and awareness of hepatitis B among households in Malaysia: a community-based cross-sectional survey. BMC Public Health 19:47. https://doi.org/10.1186/s12889-018-6375-8
Ratnawati, Santoso P (2021) Gender politics of Sultan Hamengkubuwono x in the succession of Yogyakarta Palace. Cogent Social Sciences 7:1–10. https://doi.org/10.1080/23311886.2021.1976966
Ruxton GD, Neuhäuser M (2013) Review of alternative approaches to calculation of a confidence interval for the odds ratio of a 2 3 2 contingency table. British Ecol Soc 4:9–13. https://doi.org/10.1111/j.2041-210x.2012.00250.x
Schenkel K, Radun D, Bremer V, Bocter N, Hamouda O (2008) Viral hepatitis in Germany: poor vaccination coverage and little knowledge about transmission in target groups. BMC Public Health 8:1–11. https://doi.org/10.1186/1471-2458-8-132
Shao ER, Mboya IB, Gunda DW, Ruhangisa FG, Temu EM, Nkwama ML, Pyuza JJ, Kilonzo KG, Lyamuya FS, Maro VP (2018) Seroprevalence of hepatitis B virus infection and associated factors among healthcare workers in northern Tanzania. BMC Infect Dis 18:474. https://doi.org/10.1186/s12879-018-3376-2
Syarkawi (2011) Revitalisasi adat istiadat dan pembentukan karakter: Analisis terhadap adat istiadat dan pembentukan karakter Syari'at di Aceh. Lentera 11:40–51
Syiroj AT, Pardosi JF, Heywood AE (2019) Exploring parents' reasons for incomplete childhood immunisation in Indonesia. Vaccine 37:6486–6493. https://doi.org/10.1016/j.vaccine.2019.08.081
Tatsilong HOP, Noubiap JJN, Nansseu JRN, Aminde LN, Bigna JJR, Ndze VN, Moyou RS (2016) Hepatitis B infection awareness, vaccine perceptions and uptake, and serological profile of a group of health care workers in Yaoundé, Cameroon. BMC Public Health 15:706–706. https://doi.org/10.1186/s12889-016-3388-z
The Indonesia Ministry of Health (2013) Indonesia National Health Survey Report 2013. The Indonesia Ministry of Health, Jakarta, Indonesia

The Indonesia Ministry of Health (2015) Regulation of hepatitis virus prevention in Indonesia no. 53/2015. The Indonesian Ministry of Health, Jakarta, Indonesia
The Indonesia Ministry of Health (2018) Indonesia National Health Survey Report 2018. The Indonesia Ministry of Health, Jakarta, Indonesia
The Indonesia Ministry of Health (2019) Program imunisasi ibu hamil, bayi dan batita di Indonesia. The Indonesia Ministry of Health, Jakarta, Indonesia
The Indonesia Ministry of Health (2020) National Action Plan of Hepatitis 2020 to 2024. MoH, Indonesia
The Indonesian National Health Insurance System (BPJS) (2017) Laporan pegelolaan program dan laporan keuangan jaminan sosial kesehatan tahun 2017. The Indonesian National Health Insurance System (BPJS), Jakarta
Vo TQ, Nguyen TLH, Pham MN (2018) Exploring knowledge and attitudes toward the hepatitis B virus: an internet-based study among Vietnamese healthcare students. J Pharm Pharmacogn Res 6:458–470
World Bank (2018) Is Indonesia ready to serve? An analysis of Indonesia's primary health care supply-side readliness. World Bank, Jakarta
World Bank (2021) Data of population: Indonesia. World Bank, Jakarta
World Health Organization (WHO) (2016) Combating Hepatitis B and C to reach elimination by 2030 (Advocacy Brief). WHO, Villars-sous-Yens, Switzerland
World Health Organization (WHO) (2020a) Hepatitis B. WHO, Geneva
World Health Organization (WHO) (2020b) Toward the elimination of Hepatitis B and C 2030. WHO, Geneva
Xiang H, Tang X, Xiao M, Gan L, Chu K, Li S, Tian Y, Lei X (2019) Study on status and willingness towards hepatitis B vaccination among migrant workers in Chongqing, China: a cross-sectional study. Int J Environ Res Public Health 16:1–12. https://doi.org/10.3390/ijerph16204046
Yoda T, Katsuyama H (2021) Willingness to receive COVID-19 vaccination in Japan. Vaccines 9:1–8. https://doi.org/10.3390/vaccines9010048
Yogyakarta Government (2020) Sri Sultan tetapkan UMP DIY 2021 naik 3.54%. Yogyakarta Government, Yogyakarta
Yu L, Wang J, Wangen KR, Chen R, Maitland E, Nicholas S (2016) Factors associated with adults' perceived need to vaccinate against hepatitis B in rural China. Hum Vaccin Immunother 12:1149–1154. https://doi.org/10.1080/21645515.2015.1132964
Yuan Q, Wang F, Zheng H, Zhang G, Miao N, Sun X, Woodring J, Chan P, Cui F (2019) Hepatitis B vaccination coverage among health care workers in China. PLoS One 14:1–12. https://doi.org/10.1371/journal.pone.0216598

Publication 4

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Article

Barriers to and Facilitators of Hepatitis B Vaccination among the Adult Population in Indonesia: A Mixed Methods Study

Putri Bungsu Machmud [1,2], Amand Führer [1], Cornelia Gottschick [1] and Rafael Mikolajczyk [1,*]

[1] Institute of Medical Epidemiology, Biometrics, and Informatics (IMEBI), Interdisciplinary Center for Health Sciences, Medical School of the Martin Luther University Halle-Wittenberg, Magdeburger Str. 8, 06112 Halle (Saale), Germany
[2] Department of Epidemiology, Public Health Faculty, Universitas Indonesia, Jl. Prof Dr Bahder Djohan, Depok 16424, Jawa Barat, Indonesia
* Correspondence: rafael.mikolajczyk@uk-halle.de

Abstract: To reach the goals of the Global Hepatitis Elimination 2030 program, Indonesia is now preparing a new regulation for hepatitis B vaccinations for adult population. This study aimed to determine the factors influencing vaccine uptake for hepatitis B in the adult population, and identify barriers to, and facilitators of, hepatitis B vaccination programmes. An explanatory sequential mixed methods design was implemented in this study. We conducted a survey involving 893 participants in the general population followed by 14 in-depth interviews with health providers. The survey found that only 15% (95% confidence interval 13–18%) of participants received at least one dose of the hepatitis B vaccine. Factors associated with vaccine uptake were, living in Yogyakarta compared to living in Aceh, having secondary and higher education compared to primary education, working as a health worker compared to working in other sectors, and having health insurance that covered hepatitis B vaccination compared to not having such health insurance. Our qualitative study also identified several barriers to the adult hepatitis B vaccination programme in Indonesia such as the high cost of vaccination, lack of vaccine availability in certain areas, limited human resources to implement the hepatitis B vaccination programme, and the ineffective dissemination of hepatitis B vaccination. This study highlights that accessibility and affordability of vaccinations are important determinants of vaccination uptake that should be taken into account when planning vaccination campaigns.

Keywords: adult; hepatitis B; Indonesia; mixed methods; vaccination

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1. Introduction

The World Health Organization states that, in the mission to eliminate hepatitis viruses as a global threat, all countries should aim to reduce hepatitis incidence by 90%, and mortality rates by 65%, compared to the basis data of 2015 [1]. This target is to be achieved through several programmes, one of which is called "Leaving No One Behind". The goal of this programme is to provide access to prevention services (vaccination and testing) and treatment of hepatitis to everyone, including drug users, people in prisons, migrants, and health care workers, which are high-risk populations for hepatitis [2].

Indonesia is one of 11 countries that together carry almost 50% of the global burden of chronic hepatitis, and is rated as an intermediate-to-high hepatitis B virus endemic region [3]. The 2013 Indonesian National Health Survey reported that the percentage of hepatitis infection reached 7.1%, with the most common type of hepatitis virus being hepatitis B (21.8%) [4,5]. The highest incidence of all hepatitis (reported based on diagnoses and symptoms) was in the age group of those 45 to 54 years (1.4%), living in rural areas (1.4%), and people working as farmers/fishers/labourers (2.0%) [4,5].

The country is working to develop a strategic roadmap to gradually eliminate viral hepatitis [6]. The strategy started with a programme that reinforced issuing comprehensive hepatitis virus regulations through health promotion, prevention, early detection, and sub-management approaches in 2015 [7], followed by a comprehensive vaccination schedule for children in 2017 that also includes hepatitis B vaccination (a zero dose of hepatitis B vaccine, followed by three additional doses) [8]. In addition, in the same year, Indonesia's Ministry of Health launched a programme that focuses on the elimination of vertical transmission from mother to child [9]. Furthermore, to meet the goals of the Global Hepatitis Elimination 2030 programme [10], Indonesia is currently preparing a new regulation for hepatitis B vaccinations for adults, which focuses on high-risk populations and aims to gradually offer voluntary vaccinations to health care workers, starting in 2022 [6].

Despite all these activities, no studies have yet assessed the factors that affect vaccine uptake for hepatitis B among the adult population in Indonesia. Some studies from other developing countries have investigated how demographic factors, such as age, sex, education, ethnic group, residency, marital status, monthly income, health insurance, and occupation, are associated with vaccine uptake for hepatitis B [11–16]. In addition, some studies have also found that lifestyle factors [17–19] are also associated with being vaccinated for hepatitis B. However, most of these studies analysed the influences on vaccination status from the receiver side only—that is, the population.

We argue that a population's vaccination status is not influenced by acceptance from the vaccine's receivers alone, but that health care providers, and their ability to deliver accessible and acceptable services, are crucial as well [20]. In addition, there is so far very little research looking at those determinants of vaccination uptake in the Indonesian context. Therefore, we aimed to determine factors influencing vaccine uptake for hepatitis B among the adult population and identify barriers to, and facilitators of, hepatitis B vaccination programmes in two groups, namely those to be vaccinated and vaccination providers, to achieve a deeper understanding of the factors related to vaccination.

2. Materials and Methods

An explanatory sequential mixed methods study was conducted [21]. The quantitative part consisted of a survey that was conducted in 2020 in two provinces in Indonesia: Aceh and Yogyakarta. These provinces were selected to achieve a maximal contrast: Yogyakarta Province had the highest vaccination coverage within the existing programme (83.7% with complete vaccination, 16.3% with incomplete vaccination, and none without vaccination), while Aceh Province was reported to have the lowest coverage (19.5% with complete vaccination, 16.3% with incomplete vaccination, and 40.9% never vaccinated), based on the Indonesia National Health Survey 2018 [5]. In addition, both provinces differ with respect to average income and education, and have very different socio-religious imprints [4].

2.1. Quantitative Study

The survey aimed to investigate the knowledge, risk-perception, willingness to get vaccinated, and vaccination status, as well as the reasons for not getting vaccinated in relation to hepatitis B, among the adult population. The data were collected through face-to-face interviews conducted by the interviewers. We involved two local enumerators, who were trained and supervised by the field coordinator. Details on the methodological approach for the quantitative part have been published elsewhere [22]. In brief, an institution-based cross-sectional survey was conducted from February to March 2020 in Aceh and Yogyakarta. We included staff that worked in a health centre with both medical and non-medical backgrounds, and outpatients who registered at the health centre on the same day that the data were collected.

Staff (N = 508) and outpatients (N = 492) in sixteen selected health centres were randomly sampled from employment data and the patient register, respectively. Participants

who reported in the study questionnaire that they did not get vaccinated because they have already been infected with hepatitis B were retrospectively excluded from the analysis. Participants were asked to respond to the question 'Have you ever received an adult hepatitis B vaccination?' The possible response was dichotomous: yes or no.

Sociodemographic variables included in the study were age group, sex, marital status, religion, residency, education, occupational status, and profession within the health centre, monthly income, and whether the participant had health insurance covering hepatitis B vaccination costs. Furthermore, knowledge about hepatitis B infection and vaccination, risk perceptions, exposure to information regarding hepatitis B, and reasons for not getting vaccinated against hepatitis B were also included in this study. For more details on the questionnaire, see the Tables S1–S3.

The continuous variables were presented as means with their 95% confidence interval (95% CI), while the categorical variables were reported as absolute and relative frequencies. Logistic regression was used to assess the association between the outcome variable (vaccine uptake) and the independent variables (sociodemographics, knowledge, and risk perception regarding hepatitis B infection). First, all independent variables that had an association with the outcome variable based on previous studies [12,15,23–28] were included into a univariable logistic regression model, and crude odds ratios (COR) were obtained (model 1, Table 1). Subsequently, a multivariable logistic regression was applied to calculate mutually adjusted odds ratios (AOR) (model 2, Table 1). In the multivariable model only sociodemographic variables were included. Attitudinal variables were not included, as they are likely in the causal chain for vaccination uptake [29]. We also did not include the variable of monthly income in the multivariable model, due to too many missing responses (>80%). All analyses were performed using the Statistical Package for the Social Sciences software (SPSS version 20, Chicago, IL, USA) and STATA 16.1.

Table 1. Factors associated with hepatitis B vaccination uptake (crude (Model 1) and multivariable logistic regression (Model 2)).

Variables	Vaccination Uptake n (%)	Model 1 COR (95% CI)	Model 2 AOR (95% CI)
Province			
Aceh	46 (33.8)	REF	REF
Yogyakarta	90 (66.2)	1.90 (1.30–2.79)	2.43 (1.56–3.78)
Age (years old)			
<35	54 (39.7)	REF	REF
35–50	59 (43.4)	2.49 (1.43–4.33)	0.96 (0.60–1.53)
>50	23 (16.9)	1.73 (1.00–3.01)	0.69 (0.35–1.35)
Sex			
Men	28 (20.6)	REF	REF
Women	108 (79.4)	0.87 (0.55–1.37)	1.22 (0.72–2.06)
Residency			
Urban	74 (54.4)	REF	REF
Rural	62 (45.6)	1.21 (0.84–1.74)	0.91 (0.59–1.40)
Marital status			
Single/Widowed/Divorced	21 (15.4)	REF	REF
Married	115 (84.6)	1.71 (1.04–2.80)	1.07 (0.57–2.00)
Religion			
Moslem	132 (97.1)	REF	REF
Christian and others	4 (2.9)	1.50 (0.52–4.32)	3.07 (0.94–10.01)
Education level			
Primary	2 (1.5)	REF	REF

Secondary	9 (6.6)	8.19 (4.09–16.43)	3.14 (1.38–7.15)
Tertiary	125 (91.9)	21.96 (5.36–89.97)	8.88 (1.96–40.21)
Occupational status			
Unemployed	5 (3.7)	REF	REF
Employed	131 (96.3)	11.58 (4.68–28.66)	1.04 (0.26–4.14)
Profession			
Non-Health care worker	9 (6.6)	REF	REF
Health care worker (low risk)	25 (18.4)	2.25 (1.48–3.65)	2.84 (1.66–4.86)
Health care worker (high risk)	102 (75.0)	17.44 (8.66–35.13)	5.74 (2.52–13.10)
Health insurance for vaccination			
No	71 (52.2)	REF	REF
Yes	65 (47.8)	6.46 (4.33–9.63)	4.11 (2.63–6.43)
Knowledge of hepatitis B			
Poor	10 (7.4)	REF	
Fair	64 (47.1)	2.79 (1.86–4.21)	
Good	62 (45.5)	34.05 (15.21–76.23)	
Risk perception of hepatitis B			
Low	31 (22.8)	REF	
High	105 (77.2)	3.34 (2.19–5.11)	
Willingness to be vaccinated			
No	5 (3.7)	REF	
Yes	131 (96.3)	4.79 (1.92–11.95)	

Model 1: Crude OR (COR). Model 2: Adjusted OR (AOR), Mutually adjusted for all variables in the table).

2.2. Qualitative Study

The qualitative study assessed the current hepatitis B programme as well as barriers to, and facilitators of, hepatitis B vaccination from the government's perspective, through in-depth interviews. We recruited informants from the local health offices on a city/district level from the same areas as covered in the quantitative study. In these health offices, we targeted employees who were responsible for programmes related to hepatitis B, vaccination, and health promotion. In addition, we recruited informants from the Ministry of Health's three directorates: the Directorate of Communicable Disease Prevention and Control, the Directorate of Immunization, and the Directorate of Health Promotion and Community Empowerment. In total, 49 informants from the Ministry of Health, and four health offices were actively involved with programmes related to this study.

Prior to the interviews, heads of departments received information material introducing the study and signed a memorandum of understanding that they would allow their employees to participate in the study. They then delegated one of their employees to participate in the study, whereby they were asked to choose somebody actively involved as a programme implementer.

In the subsequent step, we sent an invitation letter to the selected informants by an e-mail containing an introductory letter introducing the research topics, detailed research information, and an informed consent form. The interviews were conducted from May 2021 to July 2021. The interviews were conducted in Indonesian (Bahasa) by the first author (PBM), who is Indonesian. Each interview took between 45 and 90 min.

The interviews were video recorded and transcribed verbatim in Bahasa by native speaking research assistants. Then, transcripts were coded by the first author using deductive thematic analysis; that is, the data were categorised based on the 'high-quality health system framework foundations' [30]. Hereby, the researcher made notes on the label codes, which were then classified into themes, based on their five foundations of a high-quality health care system, which is part of the revolution in area of the sustainable

development goals (SDGs) that has appeared in the literature recently. The foundations consist of population, governance and financing, platform, workforce, and tools [30].

Population is defined as a group of people who receive the benefits of the health system. In addition, population also works as an important partner that improves their own health outcomes and the present health care system [30]. In this study, population consists of the people in the communities being studied, including their health needs, knowledge, health literacy, preferences, and cultural norms.

Strong governance and financing are needed in a high-quality health care system to provide regulation, organise care, and institutionalise accountability to the citizens [30]. The component of governance includes leadership (political commitment, change management, and policies), financing (funding, insurance and purchasing, and payment), learning and improvement (institutions for evaluation, measurement, and improvement, learning communities, and trustworthy data), and intersectoral factors (roads, transport, water and sanitation, the electric grid, and higher education) [30].

The third foundation of a high-quality health care system in the era of the SDGs is platform. In this study, a component of platform related to hepatitis B vaccination coverage in Indonesia is the assets that health facilities have, including the number and distribution of health facilities and geographic access to health facilities that provide hepatitis B vaccination [30].

Hepatitis B vaccination coverage in Indonesia also depends on the health workforce. We included an adequate number and distribution of health care workers, the skill and professionalism of health care workers, and the motivation of health care workers, as components of the workforce in this study [30]. Finally, we also included tools, defined as equipment and information systems related to promotion of the hepatitis B programme [30]. All qualitative analyses were performed using MAXQDA Analysis Pro 2020 (version 20.4.2).

2.3. Data Integration

We integrated the findings from the quantitative and the qualitative arm using a matrix joint display technique, which was adapted from the pillar integration process (PIP) concept by combining the findings of the survey and the in-depth interviews [31]. The PIP started by listing all the findings from both the survey and in-depth interviews, followed by a process matching the findings between the population side and government side.

3. Results

3.1. Quantitative Findings

3.1.1. Respondents' Characteristics

In total, 1000 participants were approached, of these, 98 refused to participate from the beginning and seven dropped out during the interview. Two participants who had previously been infected with hepatitis B were excluded retrospectively from the analyses. The participants' median age was 35 (interquartile range (IQR) 26–42) years. Most of the participants were women (n = 726; 81.3%), and the majority (n = 407, 56.8%) were health care workers. For more details on the demographic characteristics of the participants, see Table 2.

Table 2. Demographic characteristics.

Variable	n (%)
Age (years old)	
<35	446 (49.9)
35–50	357 (40.0)
>50	90 (10.1)

Sex	
Men	167 (18.7)
Women	726 (81.3)
Province	
Aceh	419 (46.9)
Yogyakarta	474 (53.1)
Residency	
Urban	443 (49.6)
Rural	450 (50.4)
Marital status	
Single/Widowed/Divorced	201 (22.5)
Married	692 (77.5)
Religion	
Moslem	856 (95.9)
Christian and others	37 (4.1)
Education level	
Primary	139 (15.6)
Secondary	239 (26.8)
Higher	515 (57.7)
Occupational status	
Unemployed	237 (26.5)
Employed	656 (73.5)
Monthly income (IDR)	
≤1 million	43(4.8)
>1 to 2 million	27 (3.0)
>2 to 3 million	59 (6.6)
>3 million	33 (3.7)
Missing	731 (81.9)
Profession	
Non-medical health centre staff	386 (43.2)
Health care worker (low risk) †	160 (17.9)
Health care worker (high risk) ††	347 (38.9)
Health insurance for vaccination	
No	734 (82.2)
Yes	159 (17.8)

† Healthcare workers who work in low-risk unit, such as administrative personnel, pharmacy staff, and driver. †† Healthcare workers who work in high-risk unit, such as medical doctor, nurse, midwife, and analyst.

3.1.2. Knowledge, Risk Perception, and Vaccination Status among Respondents

Table 3 describes the respondents' knowledge and risk perception about hepatitis B infection, as well as their vaccination status. The mean knowledge scores concerning hepatitis B infection and vaccination among health centre staff who worked in high-risk and low-risk units (20.36; 95% confidence intervals (CI): 19.92–20.80 and 18.40; 95% CI: 17.73–19.07, respectively) were higher than the knowledge scores of non health care workers (9.08; 95% CI: 8.46–9.72). Similarly, the mean risk perception scores regarding hepatitis B differed between health centre staff (13.44; 95%CI: 13.26–13.62 in high-risk unit and 13.00; 95%CI: 12.72–13.28 in low-risk units) and non health care workers (11.65; 95%CI: 11.41–11.89). About one sixth (n = 136 of 893, 15.2%) of the participants were vaccinated with at least one dose of the hepatitis B vaccination.

Table 3. Knowledge, risk perception, willingness to pay, and vaccination status.

Variables	All Participants n = 893	HCW in High-Risk Unit n = 347	HCW in Low-Risk Unit n = 160	Non HCW n = 386
Knowledge of hepatitis B				
Score of knowledge related to hepatitis B infection and vaccination (Mean [95% Confidence Interval])	11.01 [10.65–11.37]	20.36 [19.92–20.80]	18.40 [17.73–19.07]	9.08 [8.46–9.72]
Knowledge concerning hepatitis B infection				
Poor	377 (42.2)	30 (8.6)	28 (17.5)	319 (82.6)
Fair	342 (38.3)	189 (54.5)	92 (57.5)	61 (15.8)
Good	174 (19.5)	128 (36.9)	40 (25.0)	6 (1.6)
Knowledge concerning hepatitis B vaccination				
Poor	350 (39.2)	50 (14.4)	38 (23.8)	262 (67.8)
Fair	371 (41.5)	166 (47.8)	87 (54.4)	118 (30.6)
Good	172 (19.3)	131 (37.8)	35 (21.8)	6 (1.6)
Risk perception of hepatitis B infection				
The score of risk perception related to hepatitis B infection (Mean ± 95% Confidence Interval)	12.59 [12.45–12.74]	13.44 [13.26–13.62]	13.00 [12.72–13.28]	11.65 [11.41–11.89]
Low	407 (45.6)	98 (28.8)	67 (41.9)	242 (62.7)
High	486 (54.4)	249 (71.8)	93 (58.1)	144 (37.3)
Willingness to get vaccinated *	(n = 757)	(n = 245)	(n = 135)	(n = 377)
No	117 (15.5)	14 (5.7)	16 (11.9)	87 (23.1)
Yes	640 (84.5)	231 (94.3)	119 (88.1)	296 (76.9)
Vaccination status				
Not vaccinated	757 (84.8)	245 (70.6)	135 (84.4)	377 (97.7)
Vaccinated	136 (15.2)	102 (29.4)	25 (15.6)	9 (2.3)

* Includes only those respondents who were not vaccinated at the time of the survey. HCW = Health Care Worker.

3.1.3. Information Exposure and Reason Not to Be Vaccinated among Respondents

Among the participants who had received hepatitis B information (n = 729, 81.6%), most of them (n = 527, 72.3%) had received information from a health provider; the second source of information was the media (n = 397, 54.5%). Among the participants who had received hepatitis B information from the media, 63.2% (n = 251) and 54.2% (n = 215) reported television and social media as platforms to obtain that information, respectively (Table 4).

The main reasons for not being vaccinated were that respondents had 'never heard about hepatitis B vaccination for an adult before' and 'never felt the need for vaccination (for hepatitis B for an adult)', reported by 45.4% (n = 344) and 24.7% (n = 187) of the unvaccinated participants, respectively. Further reasons for not getting hepatitis B vaccination are illustrated in Figure 1.

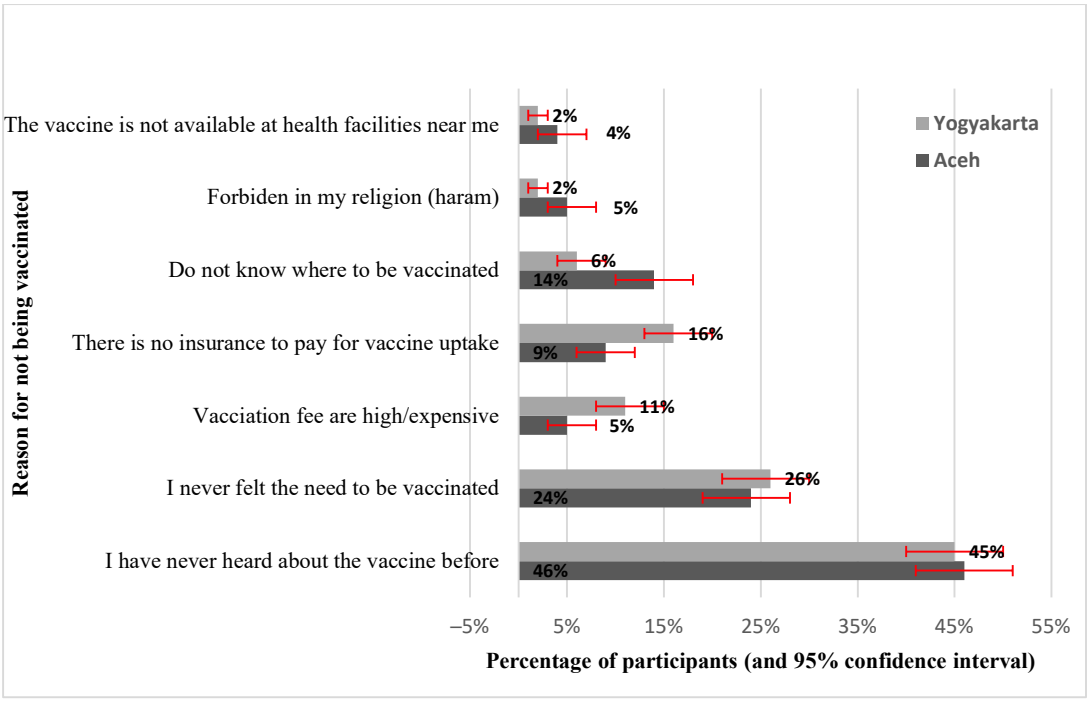

Figure 1. Reasons not to be vaccinated.

Table 4. Exposure to information regarding hepatitis B.

Variables	All Participants n = 893	HCW in High-Risk Unit n = 347	HCW in Low-Risk Unit n = 160	Non HCW n = 386
Heard about hepatitis B vaccination				
Yes	729 (81.6)	340 (98.0)	152 (95.0)	237 (61.4)
No	164 (18.4)	7 (2.0)	8 (5.0)	149 (38.6)
Source of information * [a]	(n = 729)	(n = 340)	(n = 152)	(n = 237)
Health provider	527 (72.3)	289 (85.0)	125 (82.2)	113 (47.7)
Health community	34 (4.7)	11 (3.2)	5 (3.3)	18 (7.6)
Family/relatives	161 (22.1)	93 (27.4)	49 (32.2)	19 (8.0)
Community/Religious leaders	17 (2.3)	10 (2.9)	3 (2.0)	4 (1.7)
Media	397 (54.5)	229 (67.4)	108 (71.1)	60 (25.3)
Seminar/Training	43 (5.9)	25 (7.4)	3 (2.0)	15 (6.3)
Media platform ** [b]	(n = 397)	(n = 229)	(n = 108)	(n = 60)
Television	251 (63.2)	153 (66.8)	73 (67.6)	25 (41.7)
Social media	215 (54.2)	146 (63.8)	59 (54.6)	10 (16.7)
Poster	88 (22.2)	63 (27.5)	18 (16.7)	7 (11.7)
Newspaper	63 (15.9)	41 (17.9)	17 (15.7)	5 (8.3)
Radio	27 (6.8)	22 (9.6)	5 (4.6)	0 (0.0)
Internet	17 (4.3)	8 (3.5)	4 (3.7)	5 (8.3)

HCW = Health Care Worker. * Includes only those respondents who had ever heard about hepatitis B vaccination at the time of the survey. ** Includes only those respondents who received information of hepatitis B vaccination from media platform at the time of the survey. [a] participant had more than one source of information. [b] participant used more than one media platform.

3.1.4. Variables Associated with Vaccine Uptake

The multivariable analyses variables that were statistically associated with vaccine uptake involved all respondents (vaccinated or never). These four factors were found to have a statistically significant association with vaccine uptake in the adult population (Table 1): living in Yogyakarta compared to living in Aceh, having secondary or higher education compared to primary education, working as a health care worker in a low-risk unit or in a high-risk unit compared to being a non-health care worker, and having health insurance that covered hepatitis B vaccination compared to not having such health insurance.

3.2. Qualitative Findings

In total, 14 informants were included in this study. The mean age of the informants was 44.7 (standard deviation = 6.21) years. The following text, and Table 5, describe the qualitative findings, categorised according to the foundations of the high-quality health care system framework.

Table 5. The themes, subthemes, and representative quotes.

Theme	Subthemes	Representative Quote(s)
Population	Knowledge	'For existing programmes (child vaccination), there is a rejection from a particular group. They said vaccination is not important. This is due to a lack of knowledge and awareness about vaccination. In addition, some mothers were afraid of the side effects of vaccination, such as fever' (Transcript 11).
	Cultural norms and vaccine controversy	'There are cultural differences between Aceh and Yogyakarta (which affect the vaccination program). For example, the vaccination (coverage) of children in Aceh is low because of public perceptions. They feel that people health is a gift from God. In addition, the controversy about the issue of Halal and Haram related to vaccine ingredients (containing pork) or Jewish conspiracies. All of these issues impacted vaccination coverage' (Transcript 4). In my opinion, people in Gunungkidul and are still easily driven by certain figures. We still have a king. If the king says, we are still obedient to carry out it. But, I think it's not the same with outside Yogyakarta province. Our society is still easy to move, believe in the leadership, and easy to be directed to in accordance with government programmes (Transcript 7).
Governance	Policies: regulation	'Currently, the hepatitis B vaccination programme provided by the government is still limited to children, and its coverage is still low...where most of the adult population is susceptible to hepatitis B infection. Therefore, further vaccination is needed for the adult population in Indonesia; at least the community knows about hepatitis B vaccination for adults' and can access it' (Transcript 5).
	Financing	'Currently, Indonesia has two vaccination programmes, namely the national and elective programmes. Hepatitis B vaccination for adults is an optional programme. So, for adults who want to receive hepatitis B vaccination, they seek vaccination and pay for it themselves' (Transcript 2).
	Insurance and purchasing	
	Trustworthy data	'Yes indeed, this is some of the homework that we must do. That is true; our data (related to hepatitis B) are still minimal. So that is why there are recommendations in our planning from the committee expert, one our target (has to improve) is reporting' (Transcript 12).

Platforms	Geographic access to facilities	'As far as I know, there are some hard-to-reach areas in Indonesia that we (MoH in Jakarta) might be unable to monitor very well. For example, in Papua, implementing a hepatitis B birth dose (HB0) that should be given less than 24 h might be difficult due to geographic conditions. Some gave HB0 seven days after delivery' (Transcript 2).
Workforce	Managers: number and distribution	'We have a lack of human resources. Most of them handle more than one programme. For example, surveillance and Hajj. In addition, some of our staff have already retired' (Transcript 11).
	Skill	'There is no other staff with a health promotion background in Gunungkidul Regency except me. So, this can be an obstacle to improving our programme. In addition, we only have one staff member for administration and data analysis. We need more staff with the proper skill to achieve our programme' (Transcript 7).
	Teamwork	'We collaborated with other sectors. Usually, we involve the Ministry of Religion, Youth and Sports Office and cadres to educate the community about the benefit of vaccination and vaccine implementation' (Transcript 11).
Tools	Hardware: equipment	'We need a tool for disseminating information that uses the local language so that local people can understand the message' (Transcript 3).
	Information system	'We would like to develop culture-based dissemination, for example, Wayang cakruk. This medium will reach many layers in our community. It still really likes this Wayang segmentation. We believe that the traditions that exist and only exist in Gunungkidul can convey the message from us (health providers). However, this is an expensive medium due to its use of many instruments' (Transcript 7).

3.2.1. Population

The informants' narratives highlighted that knowledge about hepatitis B vaccination, and cultural norms in the population, act as important factors for adult uptake of hepatitis B vaccination. For instance, informants said that one of the common barriers to vaccination programmes is a lack of knowledge concerning the benefits of vaccination, which results in vaccine hesitancy among particular populations in Indonesia. Furthermore, cultural norms, such as the tradition of *manut* (meaning 'obey the command' in Javanese), were also mentioned by informants in the interviews as influencing vaccination uptake among particular populations. For instance, an informant from Yogyakarta and Gunungkidul said that it was not difficult to ask Yogyakarta's people to vaccinate once the king ordered the programme—this statement being related to the culture of Yogyakarta, which is famous for having a population that complies with its king (who is currently also in the role of governor). Thus, it is unsurprising that Yogyakarta achieved almost complete vaccination coverage in recent years. In contrast, informants argued that the suspicion that the vaccine was rumoured to contain pork (the 'halal controversy') was a common reason for the population in Aceh to reject vaccination (Aceh is an Indonesian region where Sharia law is implemented).

3.2.2. Governance and Financing

We found three barriers to hepatitis B vaccination programmes that related to governance and financing in Indonesia. Firstly, some informants indicated that the hepatitis B programme, including hepatitis B vaccination, is 'more unpopular' compared to the other national priority programmes: health insurance, maternal and child health, stunting reduction, tuberculosis, COVID-19, and the healthy living community movement (GERMAS in Indonesian). In fact, one informant confessed that he did not even know that hepatitis B vaccination was available. Secondly, informants believed that the cost of hepatitis

B vaccination is one of the common reasons not to get vaccinated, both for health care workers and the general population, as they have to pay for the vaccination themselves. Finally, informants argued that another barrier to the hepatitis B programme is the lack of data related to hepatitis B. All the informants who were part of the hepatitis B programme said that without accurate data regarding hepatitis B cases, treatment, and adult vaccination in Indonesia, it is difficult for health programmers to analyse hepatitis B-related problems, including assessing the urgency of adult vaccination.

3.2.3. Platforms

In this study, some informants believed that the low availability of the vaccine poses a barrier to vaccination: In some areas in Indonesia, people need to go to urban areas to obtain it. This issue is not restricted to hepatitis B programmes: limited health facilities and geographic access to facilities also impacts the coverage of other vaccination programmes—for example, for children. In this context, one informant, who handles the national vaccination programme, reported that timely birth-dose vaccination coverage was difficult to obtain in hard-to-reach areas in Papua (Indonesia's easternmost region), since not all mothers can give birth in health facilities.

3.2.4. Workforce

Informants expressed the opinion that the ratio between health providers and the population was, at the moment, inadequate. They also reported that almost all health staff members have to handle two or even more different programmes, and are burdened with administrative jobs and field jobs as well, such as vaccination and health promotion. Informants said that the collaboration with other actors, such as community leaders, and religious leaders, is considered a good solution. For instance, some informants said that the health cadre helped to implement a vaccine schedule with reminders for their community. Moreover, informants also reported having limited staff and staff members who do not possess the appropriate competencies—as happens, for example when new staff for a particular programme lack the relevant background and experience. Therefore, they argued that it is necessary to conduct special training for new staff, as well as regular training for all staff.

3.2.5. Tools

Informants in the interview reported that the dissemination of hepatitis B information currently mostly uses conventional tools, such as posters and billboards. However, informants felt that these approaches are ineffective due to the fact that most of the information given talks about the elimination of three diseases—hepatitis, AIDS, and syphilis—instead of discussing hepatitis B in detail. One other informant also said that information about hepatitis B using billboards was disseminated for particular events only, such as World Hepatitis Day, which is celebrated annually. Other than that, informants argued that posters distributed by the Ministry of Health did not reach many people, especially in rural areas, since most of the local population uses a local language instead of Bahasa, Indonesia's national language. As a result, the posters' message was not well understood by local communities.

In general, a variety of methods is used for the dissemination of health information. For instance, some informants reported that health staff directly disseminated information by, for example, using loudspeakers from the mosque or village hall, or even on the road. Health providers also conducted special meetings with religious leaders and community leaders to minimise hoax issues related to vaccination. Informants believed that this information could also be spread through regular community meetings, such as prayer recitations and Friday sermons, with the aim of informing the community about vaccine benefits and reminding it about the different vaccine schedules. They also believed that disseminating information through social media platforms (such as YouTube, Facebook,

Instagram, and Twitter) and local culture-based dissemination, such as *Wayang Cakruk* (a regular traditional-puppets show in Gunungkidul), are also considered a potential medium for disseminating information that can reach different levels within a community.

3.3. Integrated Findings

There are six main pillars from the integrated qualitative and quantitative findings concerning the barriers and facilitators of hepatitis B vaccination on adults in Indonesia. For more details on the figure of Pillar Integration Process (see Table S4).

3.3.1. Theme One: Cultural Norms of the Region

Our survey identified that vaccination coverage for hepatitis B was higher in Yogyakarta than in Aceh. This finding was supported by the qualitative result. For instance, almost all informants said that in Aceh, the halal controversy might be the reason people lack confidence in the vaccine, even when they know about its benefits. In addition, most of the informants said that communication through religious leaders and community leaders was a practical approach to disseminating information on vaccination.

3.3.2. Theme Two: The Role of Health Care Workers

Our integrated findings showed that the role of health care workers was essential in vaccination uptake. In the quantitative arm, we found that most of the participants in our survey reported that they received hepatitis B information from a health provider, and this finding can be seen as a positive result related to health promotion and the dissemination of the hepatitis B vaccination. However, among health care workers in our survey, only 25.0% were vaccinated against hepatitis B. In addition, most informants highlighted that knowledge of hepatitis B infection and vaccination among health care workers is low, with many of them not being able to distinguish hepatitis B from other types of hepatitis, and not realising that they work with a high-risk population. Therefore, most of the informants suggested that regular training regarding hepatitis B infection and vaccination for health care workers is needed, including training on the effective dissemination of information to the community.

3.3.3. Theme Three: Knowledge of Hepatitis B Infection and Vaccination

Findings regarding the knowledge of hepatitis B infection and vaccination converged in the quantitative and qualitative arms of our study. Our survey found that fewer than 20% of the participants had a good knowledge of hepatitis B infection and vaccination. This finding was supported by the qualitative results: Almost all of the informants argued that people's understanding of hepatitis B is low. It is not surprising that some informants said people feel that vaccination is not important due to the fact that they do not know its benefits.

3.3.4. Theme Four: Accessibility of Hepatitis B Vaccination

The integrated results showed that insufficient accessibility of hepatitis B vaccination was one of the barriers to hepatitis B vaccination coverage in Indonesia. In the quantitative arm, 3.2% of unvaccinated survey participants said that the hepatitis B vaccination is unavailable at the nearest health facilities. This finding is supported by the qualitative results, with some informants complaining that obstacles in geographical access impede the implementation of vaccination programmes, especially among participants who live in rural areas, such as mountain areas.

3.3.5. Theme Five: Affordability of Hepatitis B Vaccination

Another obstacle for vaccination coverage is its costs, as the vaccinations are not affordable for some people. In the quantitative arm, our survey identified that only 53.4% of participants were willing to pay for hepatitis B vaccination by themselves. Similarly,

some informants in the qualitative study reported that hepatitis B vaccination was expensive, at IDR 200,000 to IDR 300,000 (USD 14 to 21) per dose. An informant said the price would be unaffordable for some people, especially those with low and irregular incomes. As a result, it is not surprising that 21.0% of unvaccinated survey participants reported that one of the most common reasons to not get vaccinated was the expense.

3.3.6. Theme Six: The Dissemination of Information

Although our survey found that health providers and the media were the common sources of information about hepatitis B infection and vaccination, most informants in the qualitative study admitted that the available information regarding the hepatitis B programme was limited. Some informants reported that health officers provide health information to the community through direct health initiatives in various ways, but have limited human resources. Therefore, most informants suggested several potential interventions to increase public knowledge regarding hepatitis B by optimising information dissemination, such as culture and arts-based dissemination, religion-based dissemination, and an expanded use of social media.

4. Discussion

In this mixed methods study, we established six pillars that act as barriers to, and facilitators of, vaccine uptake: cultural norms of the regions, the role of the health care workers, knowledge of hepatitis B infection and vaccination, accessibility to hepatitis B vaccination, affordability of hepatitis B vaccination, and dissemination of information regarding hepatitis B infection and vaccination.

This study found that vaccination coverage for hepatitis B differs strongly by region, in this case, the province. This finding is associated with both provinces' different histories, cultures, and local regulations. In Aceh, a province that applies Sharia law, vaccine rejection due to a vaccine ingredient that purportedly contains pork, and is therefore considered haram, is a common problem [23]. Meanwhile, Yogyakarta, a region that is defined by Javanese culture, does not have these problems [32], and has the highest vaccination coverage of existing vaccination programmes among children in Indonesia. These findings are in line with the results of a previous systematic review on hepatitis B vaccination in developing countries [30]. A previous study from Indonesia also found that geographic conditions contribute to disparities in the vaccination coverage because each region has its own political situation, religious affiliation, economic potential, and population density that impact the level of development of health programmes [33]. Drawing a conclusion from these findings, we want to highlight that there is no one-size-fits-all solution for all regions; thus, vaccination programmes should use culturally appropriate approaches and should be adapted based on local needs [34,35].

Another barrier is lack of accessibility. The low accessibility is connected to Indonesia's geography, which consists of more than 16,000 islands [36]. Other studies have also found that low awareness of the availability of vaccinations occurs due to limited access to health facilities in some countries [15,37–39]. For instance, 80% of the non-vaccinated population in a hard-to-reach region in the UK declared that they had not been offered the vaccine, suggesting a lack of vaccine availability [40]. Even if misunderstandings and poor knowledge of services are well addressed, the situation will not effectively improve without addressing service accessibility [41,42].

Our study also found that hepatitis B vaccination is associated with exposure to accurate information related to hepatitis B infection, and the benefits of vaccination as one of the most effective preventive methods. Although information about hepatitis B and vaccination is available through the media, such as television, scientific magazines, and the internet [43], Njoroge et al. found that direct information from health providers was most closely associated with being vaccinated for hepatitis B [44]. However, some studies found that knowledge of hepatitis B and vaccination among health care workers is low [28,45–47]. For example, a study among nurses and midwives from Sudan found that the

percentage of respondents with at least an average knowledge of hepatitis B virus was less than 60% [47].

Our survey results showed that most of the participants had a low knowledge about hepatitis B infection and vaccination. This finding was not surprising, considering that a previous study in developing countries reported similar findings [26]. Accurate information is expected to positively impact the relevant knowledge of hepatitis B infection and vaccination [48], and Lee et al. highlighted that missing information about vaccination could reduce people's willingness to carry out hepatitis B vaccinations [39]. Some previous studies have claimed similar findings [26,49,50]. Hence, dissemination of information regarding vaccination also needs other support, such as that of religious leaders and community leaders, especially in reference to this sensitive issue [51–53]. For example, in Indonesia, a halal certification (*fatwa*) regarding the permissibility of the vaccination, provided by a council of religious scholars called *Majelis Ulama Indonesia*, plays an important role in community acceptance of vaccination [23,52]. When it comes to the regions of Indonesia, hepatitis B and vaccination information should also be adapted to the local conditions and culture to make it easier to understand and accept. For instance, reminder stickers positively affected vaccination coverage among children in another study in Indonesia [54].

Finally, this study also identified the vaccination cost as one barrier to hepatitis B vaccine uptake. Since hepatitis B vaccination is not mandatory for adults in Indonesia, people must actively decide to get immunised and privately cover the expenses for the vaccination costs [7]. For instance, informants of our qualitative study claimed that vaccination costs are one of the obstacles to achieving high vaccine coverage in Yogyakarta, which is known as a province with a lower minimum wage compared to Aceh. We calculated that vaccination takes up about 14% and 8% of the minimum monthly income in Yogyakarta and Aceh per dose, respectively [55].

The strengths of this study include the mixed method design, that described potential discrepancies and correspondences of barriers and facilitators from two different sides: the population (outpatient and health care worker) and the government. This method helps to increase the validity of findings. Nonetheless, this study has some limitations. First, more than 80% of the selected participants in the survey were women, which might reduce the generalisability of the study's results. At the same time, the predominance of female participants is representative of the selected health care setting, since the community health centres provide health services targeting mothers and children, such as antenatal care and children's vaccinations, to support the Indonesian Ministry of Health's mandate to improve mother and child health services [56]. Second, due to missing data our survey could not investigate the economic factors that significantly impacted vaccination status in other studies [12,16,57]. The huge percentage of missing data on income might be explained by the fact that many people in Indonesia consider income very private. Lastly, due to time and resource constraints, our study was limited not only to outpatients and health care workers in the sixteen selected local health centers, but also limited to two provinces, with their own specific characteristics, which may differ from the overall population and the other 36 provinces in Indonesia. Although the findings may not be generalisable outside these two provinces, this study's results can inform future vaccination intervention strategies and contribute to public health knowledge.

5. Conclusions

Through integrated findings displaying the population's and the government's perspective, our study found that a lack of information impacted people's knowledge regarding hepatitis B infection and vaccination. Further support from health providers and other stakeholders is needed to achieve high vaccination coverage through culturally appropriate approaches. Beyond that, vaccination access, including the availability and cost of vaccination, also plays an essential role in vaccine uptake. Further studies to explore those aspects among other stakeholders, such as local religious and community leaders or local

health offices from other provinces, could be helpful for improving knowledge on the topic.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/vaccines11020398/s1, Table S1: Questionnaire Survey of Knowledge, awareness, risk perception, attitudes, practice and willingness of Hepatitis B virus infection and vaccination among outpatients and health care workers in Indonesia 2020; Table S2: Question list and proportion of correct answer of knowledge regarding hepatitis B infection and vaccination; Table S3: Question list and proportion of high risk-perception regarding hepatitis B infection and vaccination. Table S4: Pillar integration process.

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References

1. World Health Organization. WHO Releases First-Ever Global Guidance for Country Validation of Viral Hepatitis B and C Elimination. Available online: https://www.who.int/news/item/25-06-2021-who-releases-first-ever-global-guidance-for-country-validation-of-viral-hepatitis-b-and-c-elimination (accessed on 17 February 2021).
2. World Health Organization. A Hepatitis-Free Future is Possible with a United Effort. Available online: https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/hepatitis/overview (accessed on 17 February 2021).
3. World Health Organization. Hepatitis B. Available online: https://www.who.int/news-room/fact-sheets/detail/hepatitis-b (accessed on 13 November 2021).
4. The Indonesian Ministry of Health. *Indonesia National Health Survey Report 2013*; The Indonesian Ministry of Health: Jakarta, Indonesia, 2013.
5. The Indonesian Ministry of Health. *Indonesia National Health Survey Report 2018*; The Indonesia Ministry of Health: Jakarta, Indonesia, 2018.
6. The Indonesian Ministry of Health. *National Action Plan of Hepatitis 2020 to 2024*; The Indonesian Ministry of Health: Jakarta, Indonesia, 2020.
7. The Indonesian Ministry of Health. *Regulation of Hepatitis Virus Prevention in Indonesia No. 53/2015*; The Indonesian Ministry of Health: Jakarta, Indonesia, 2015.
8. Purwono, P.B.; Juniastuti; Amin, M.; Bramanthi, R.; Nursidah; Resi, E.M.; Wahyuni, R.M.; Yano, Y.; Soetjipto; Hotta, H.; Hayashi, Y.; Utsumi, T.; Lusida, M.I. Hepatitis B Virus Infection in Indonesia 15 Years after Adoption of a Universal Infant Vaccination Program: Possible Impacts of Low Birth Dose Coverage and a Vaccine-Escape Mutant. *Am. J. Trop. Med. Hyg.* **2016**, *95*, 674–679.

9. The Indonesian Ministry of Health. *Elimination of Human Immunodeficiency Virus, Syphilis, and Hepatitis B from Mother to Children No. 52/2017*; The Indonesia Ministry of Health: Jakarta, Indonesia, 2017; Volume 52/2017.
10. World Health Organization. *Toward the elimination of Hepatitis B and C 2030*; World Health Organization: Geneva, Switzerland, 2020.
11. Omotowo, I.B.; Meka, I.A.; Ijoma, U.N.; Okoli, V.E.; Obienu, O.; Nwagha, T.; Ndu, A.C.; Onodugo, D.O.; Onyekonwu, L.C.; Ugwu, E.O. Uptake of hepatitis B vaccination and its determinants among health care workers in a tertiary health facility in Enugu, South-East, Nigeria. *BMC Infect. Dis.* **2018**, *18*, 288.
12. Park, B.; Choi, K.S.; Lee, H.Y.; Jun, J.K.; Park, E.C. Socioeconomic inequalities in completion of hepatitis B vaccine series among Korean women: Results from a nationwide interview survey. *Vaccine* **2012**, *30*, 5844–8.
13. Ochu, C.L.; Beynon, C.M. Hepatitis B vaccination coverage, knowledge and sociodemographic determinants of uptake in high risk public safety workers in Kaduna State, Nigeria: A cross sectional survey. *BMJ Open* **2017**, *7*, e015845.
14. Assunção, A.Á.; Araújo, T.M. d.; Ribeiro, R.B.N.; Oliveira, S.V.S. Hepatitis B vaccination and occupation exposure in the healthcare sector in Belo Horizonte, Minas Gerais. *Rev. Saúde Pública* **2012**, *46*, 665–673.
15. Pathoumthong, K.; Khampanisong, P.; Quet, F.; Latthaphasavang, V.; Souvong, V.; Buisson, Y. Vaccination status, knowledge and awareness towards hepatitis B among students of health professions in Vientiane, Lao PDR. *Vaccine* **2014**, *32*, 4993–9.
16. Chung, P.W.; Suen, S.H.; Chan, O.K.; Lao, T.H.; Leung, T.Y. Awareness and knowledge of hepatitis B infection and prevention and the use of hepatitis B vaccination in the Hong Kong adult Chinese population. *Chin. Med. J. Engl.* **2012**, *125*, 422–7.
17. Mungandi, N.; Makasa, M.; Musonda, P. Hepatitis B vaccination coverage and the determinants of vaccination among health care workers in selected health facilities in Lusaka district, Zambia: An exploratory study. *Ann. Occup. Environ. Med.* **2017**, *29*, 32–32.
18. Yuan, Q.; Wang, F.; Zheng, H.; Zhang, G.; Miao, N.; Sun, X.; Woodring, J.; Chan, P.-L.; Cui, F. Hepatitis B vaccination coverage among health care workers in China. *PLoS ONE* **2019**, *14*, e0216598.
19. Kouassi, D.; Angbo-Effi, O.; Aka, L.; Coulibaly, M.B.; Soumahoro, S.; Yao, G.; Soro, N. Perceptions and practice of health care workers regarding hepatitis B vaccination, Bouaké, Côte d'Ivoire, 2016. *J. Public Health Afr.* **2017**, *8*, 715–715.
20. Hennessey, K.; Mendoza-Aldana, J.; Bayutas, B.; Lorenzo-Mariano, K.M.; Diorditsa, S. Hepatitis B control in the World Health Organization's Western Pacific Region: Targets, strategies, status. *Vaccine* **2013**, *31*, J85–J92.
21. Fetters, M.D.; Curry, L.A.; Creswell, J.W. Achieving integration in mixed methods designs-principles and practices. *Health Serv. Res.* **2013**, *48*, 2134–2156.
22. Machmud, P.B.; Mikolajczyk, R.; Gottschick, C. Understanding hepatitis B vaccination willingness in the adult population in Indonesia: A survey among outpatient and healthcare workers in Community Health Centers. *J. Public Health* **2022**. *30*, 1–12, https://doi.org/10.1007/s10389-022-01775-3.
23. Harapan, H.; Shields, N.; Kachoria, A.G.; Shotwell, A.; Wagner, A.L. Religion and measles vaccination in Indonesia, 1991–2017. *Am. J. Prev. Med.* **2021**, *60*, 44–52.
24. Rajamoorthy, Y.; Taib, N.M.; Munusamy, S.; Anwar, S.; Wagner, A.L.; Mudatsir, M.; Müller, R.; Kuch, U.; Groneberg, D.A.; Harapan, H.; et al. Knowledge and awareness of hepatitis B among households in Malaysia: A community-based cross-sectional survey. *BMC Public Health* **2019**, *19*, 47.
25. Park, B.; Liu, G.Y. Targeting the host-pathogen interface for treatment of Staphylococcus aureus infection. *Semin. Immunopathol.* **2012**, *34*, 299–315.
26. Machmud, P.B.; Glasauer, S.; Gottschick, C.; Mikolajczyk, R. Knowledge, Vaccination Status, and Reasons for Avoiding Vaccinations against Hepatitis B in Developing Countries: A Systematic Review. *Vaccines* **2021**, *9*, 625.
27. Yu, L.; Wang, J.; Wangen, K.R.; Chen, R.; Maitland, E.; Nicholas, S. Factors associated with adults' perceived need to vaccinate against hepatitis B in rural China. *Hum. Vaccines Immunotheraupect.* **2016**, *12*, 1149–1154.
28. Ghomraoui, F.A.; Alfaqeeh, F.A.; Algadheeb, A.S.; Al-Alsheikh, A.S.; Al-Hamoudi, W.K.; Alswat, K.A. Medical students' awareness of and compliance with the hepatitis B vaccine in a tertiary care academic hospital: An epidemiological study. *J. Infect. Public Health* **2016**, *9*, 60–65.
29. Richiardi, L.; Bellocco, R.; Zugna, D. Mediation analysis in epidemiology: Methods, interpretation and bias. *Int. J. Epidemiol.* **2013**, *42*, 1151–1519.
30. Kruk, M.E.; Gage, A.D.; Arsenault, C.; Jordan, K.; Leslie, H.H.; Roder-DeWan, S.; Adeyi, O.; Barker, P.; Daelmans, B.; Doubova, S.V.; et al. High-quality health systems in the Sustainable Development Goals era: Time for a revolution. *Lancet Glob. Health Comm.* **2018**, *6*, 1196–1252.
31. Johnson, R.E.; Grove, A.L.; Clarke, A. Pillar Integration Process: A Joint Display Technique to Integrate Data in Mixed Methods Research. *J. Mix. Methods Res.* **2017**, *13*, 301–320.
32. Nashori, F.; Iskandar, T.Z.; Setiono, K.; Siswadi, A.G.P.; Andriansyah, Y. Religiosity, interpersonal attachment, and forgiveness among the Javanese population in Yogyakarta, Indonesia. *Ment. Health Relig. Cult.* **2020**, *23*, 99–112.
33. Herliana, P.; Douiri, A. Determinants of immunisation coverage of children aged 12–59 months in Indonesia: A cross-sectional study. *BMJ Open* **2016**, *7*, 1–14.
34. Hardt, K.; Bonanni, P.; King, S.; Santos, J.I.; El-Hodhod, M.; Zimet, G.D.; Preiss, S. Vaccine strategies: Optimising outcomes. *Vaccine* **2016**, *34*, 6691–6699.

35. Frew, P.M.; Alhanti, B.; Vo-Green, L.; Zhang, S.; Liu, C.; Nguyen, T.; Schamel, J.; Saint-Victor, D.S.; Nguyen, M.L. Multilevel Factors Influencing Hepatitis B Screening and Vaccination among Vietnamese Americans in Atlanta, Georgia. *Yale J. Biol. Med.* **2014**, *87*, 455–471.
36. Johar, M.; Soewondo, P.; Pujisubekti, R.; Satrio, H.K.; Adji, A. Inequality in access to health care, health insurance and the role of supply T factors. *Soc. Sci. Med.* **2018**, *2013*, 134–145.
37. Vo, T.Q.; Nguyen, T.L.H.; Pham, M.N. Exploring knowledge and attitudes toward the hepatitis B virus: An internet-based study among Vietnamese healthcare students. *J. Pharm. Pharmacogn. Res.* **2018**, *6*, 458–470.
38. Adenlewo, O.J.; Adeosun, P.O.; Fatusi, O.A. Medical and dental students' attitude and practice of prevention strategies against hepatitis B virus infection in a Nigerian university. *Pan Afr. Med. J.* **2017**, *28*, 33–33.
39. Lee, A.C.K.; Vedio, A.; Liu, E.Z.H.; Horsley, J.; Jesurasa, A.; Salway, S. Determinants of uptake of hepatitis B testing and healthcare access by migrant Chinese in the England: A qualitative study. *BMC Public Health* **2017**, *17*, 747.
40. Taylor, J.E.B.; Surey, J.; MacLellan, J.; Francis, M.; Abubakar, I.; Stagg, H.R. Hepatitis B vaccination uptake in hard-to-reach populations in London: A cross-sectional study. *BMC Infect. Dis.* **2019**, *19*, 372.
41. Maina, A.N.; Bii, L.C. Factors affecting HBV vaccination in a Medical training College in Kenya: A mixed methods Study. *BMC Public Health* **2020**, *20*, 48.
42. Vedio, A.; Liu, E.Z.H.; Lee, A.C.K.; Salway, S. Improving access to health care for chronic hepatitis B among migrant Chinese populations: A systematic mixed methods review of barriers and enablers. *J. Viral Hepat.* **2016**, *24*, 526–540.
43. Tabacchi, G.; Costantino, C.; Cracchiolo, M.; Ferro, A.; Marchese, V.; Napoli, G.; Palmeri, S.; Raia, D.; Restivo, V.; Siddu, A.; et al. Information sources and knowledge on vaccination in a population from southern Italy: The ESCULAPIO project. *Hum. Vaccines Immunother.* **2017**, *13*, 339–345.
44. Njoroge, J.; Hope, V.D.; O'Halloran, C.; Edmundson, C.; Glass, R.; Parry, J.V.; Ncube, F. Are there missed opportunities for vaccinating against hepatitis B among people who inject drugs in the UK? *Epidemiol. Infect.* **2019**, *147*, e244.
45. Jaquet, A.; Wandeler, G.; Tine, J.; Diallo, M.B.; Manga, N.M.; Dia, N.M.; Fall, F.; Dabis, F.; Seydi, M. Prevention and Care of Hepatitis B in Senegal; Awareness and Attitudes of Medical Practitioners. *Am. J. Trop. Med .Hyg.* **2017**, *97*, 389–395.
46. Machiya, T.; Burnett, R.J.; Fernandes, L.; Francois, G.; De Schryver, A.; van Sprundel, M.; Mphahlele, M.J. Hepatitis B vaccination of healthcare workers at the Princess Marina Hospital, Botswana. *Int. Health* **2015**, *7*, 256–61.
47. Mursy, S.M.-e. M.; Mohamed, S.O.O. Knowledge, attitude, and practice towards Hepatitis B infection among nurses and midwives in two maternity hospitals in Khartoum, Sudan. *BMC Public Health* **2019**, *19*, 1597.
48. Jung, M.; Lin, L.; Viswanath, K. Associations between health communication behaviors, neighborhood social capital, vaccine knowledge, and parents' H1N1 vaccination of their children. *Vaccine* **2013**, *31*, 4860–4866.
49. Pham, T.T.H.; Le, T.X.; Nguyen, D.T.; Luu, C.M.; Truong, B.D.; Tran, P.D.; Toy, M.; So, S. Knowledge, attitudes and practices of hepatitis B prevention and immunization of pregnant women and mothers in northern Vietnam. *PLoS ONE* **2019**, *14*, e0208154.
50. Strong, C.; Lee, S.; Tanaka, M.; Juon, H.-S. Ethnic Differences in Prevalence and Barriers of HBV Screening and Vaccination Among Asian Americans. *J. Community Health* **2012**, *37*, 1071–1080.
51. Seale, H.; Sitaresmi, M.N.; Atthobari, J.; Heywood, A.E.; Kaur, R.; MacIntyre, R.C.; Soenarto, Y.; Padmawati, R.S. Knowledge and attitudes towards rotavirus diarrhea and the vaccine amongst healthcare providers in Yogyakarta Indonesia. *BMC Health Serv. Res.* **2015**, *15*, 528.
52. Padmawati, R.S.; Heywood, A.; Sitaresmi, M.N.; Atthobari, J.; MacIntyre, C.R.; Soenarto, Y.; Seale, H. Religious and community leaders' acceptance of rotavirus vaccine introduction in Yogyakarta, Indonesia: A qualitative study. *BMC Public Health* **2019**, *19*, 368.
53. Syiroj, A.T.; Pardosi, J.F.; Heywood, A.E. Exploring parents' reason for incomplete childhood immunisation in Indonesia. *Vaccine* **2019**, *37*, 6486–6493.
54. Wallace, A.S.; Peetosutan, K.; Untung, A.; Ricardo, M.; Yosephine, P.; Wannemuehler, K.; Brown, D.W.; McFarland, D.A.; Orenstein, W.A.; Rosenberg, E.S.; et al. Home-based records and vaccination appointment stickers as parental reminders to reduce vaccination dropout in Indonesia: A cluster- randomized controlled trial. *Vaccine* **2019**, *37*, 6814–6823.
55. The St. Carolus Hospital. Adult Vaciination. Available online: http://www.rscarolus.or.id/event/vaksinasi-dewasa (accessed on 22 April 2021).
56. Hyre, A.; Caiola, N.; Amelia, D.; Gandawidjaja, T.; Markus, S.; Baharuddin, M. Expanding Maternal and Neonatal Survival in Indonesia: A program overview. *Int. J. Gynecol. Obstet.* **2019**, *144*, 7–12.
57. Park, B.; Choi, K.S.; Lee, H.-Y.; Kwak, M.-S.; Jun, J.K.; Park, E.-C. Determinants of suboptimal hepatitis B vaccine uptake among men in the Republic of Korea: Where should our efforts be focused: Results from cross-sectional study. *BMC Infect. Dis.* **2013**, *13*, 218–218.

Declarations of previous doctoral attempts

(1) I declare that I have not undergone a doctoral procedure or started a doctorate at any other university.

(2) I declare that the information I have provided is true and that I have not submitted the scientific work to any other scientific institution in order to obtain an academic degree.

Halle (Saale),

(Putri Bungsu Machmud)

Declaration of independence

I declare in lieu of on oath that I have written this thesis independently and without outside help. All rules of good scientific practice were observed; no sources and aids other than those indicated by me were used and the passages taken verbatim or in terms of content from the works used have been identified as such. I assure that I have not used the paid help of mediation and consulting services (doctoral/PhD advisors or other persons) for the preparation of the content of this thesis. No one directly or indirectly received monetary benefits from me for work related to the content of the submitted dissertation.

Halle (Saale),

(Putri Bungsu Machmud)

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For indeed, with hardship [will be] ease
Indeed, with hardship [will be] ease
Also, wahrlich, mit der Drangsal geht Erleichterung einher
wahrlich, mit der Drangsal geht Erleichterung (einher)
Al-Inshirah 94:5-6