A scoping review on the factors influencing the general acceptance of Southeast Asians towards HPV vaccination

DOI: 10.52629/jamsa.v10i1.190

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Abstract:

Background Southeast Asia is known to have one of the highest Human Papillomavirus (HPV) prevalence rates globally. HPV vaccination has been shown to be successful in the prevention of infection.

Objective This study aims to perform a scoping review of the factors influencing HPV acceptance in Southeast Asia, extract dominant themes, identify factors, describe subgroup representation, and suggest considerations in the creation of interventional and delivery strategies to increase vaccine uptake.

Methods PubMed was used to identify papers discussing vaccine acceptance, published from January 2009 to March 2020. After review, 41 studies were included in qualitative synthesis.

Findings The following outcomes were measured in the included studies: knowledge of HPV, attitudes towards vaccination, factors influencing attitudes towards vaccination, and the effectiveness of interventions and strategies in increasing vaccine uptake. There was an overall level of low to moderate knowledge, with generally high vaccine acceptance. Literacy was found to have a direct relationship with uptake, although limited by one's resources and capability to get vaccinated. Price was noted to be the most crucial factor behind accessibility. Among delivery strategies, school-based and national immunization programs were found to be the most effective.

Conclusions Factors influencing attitudes towards vaccination include economic, personal, social, and cultural factors. Culturally-specific research and interventions that would better grasp the contexts of target communities are recommended.

Keywords: vaccine acceptance, vaccine hesitancy, vaccine uptake, health literacy, HPV

Introduction

Health Literacy & Vaccine Hesitancy

Health literacy is defined by the World Health Organization (WHO) as "the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand and use information in ways which promote and maintain good health[1]." It goes beyond the dissemination and communication of health information and involves health education that calls for individual and collective action that would modify the determinants of health, in order to promote both personal and social benefit[1].

Achieving health literacy implies the need for "interaction, participation, and critical analysis[1]," leading to effective community action. One area of health care that is heavily influenced by this collective involvement is immunization. This can be observed in the context of Cuba, wherein the public's strong trust in the vaccine system is owed to the education provided for all, which results in high levels of health literacy[2].

On the other hand, poor health literacy can reduce the willingness to engage in protective behaviors, such as immunization[3]. This is termed as vaccine hesitancy, which is defined as the "delay in acceptance or refusal of vaccination despite availability of vaccination services[4]." The context-specific and complex nature of vaccine hesitancy is influenced by various factors such as complacency, convenience, and confidence[4].

Vaccination complacency results from low awareness of the risks brought by vaccine-preventable diseases; this means that underestimating the consequences of the spread of infectious diseases can contribute to vaccine hesitancy. Convenience refers to the availability, affordability, and accessibility of the vaccine, as well as the appeal of deciding to get vaccinated. Lastly, vaccination confidence relies on trust towards the vaccine itself, its delivery system, and the motivations of the policies deciding which vaccines are needed.[4]

Considering these factors and the complexity of possible reasons for vaccine hesitancy, the study directs its focus to a specific vaccine and specific region, which are human papillomavirus (HPV) and Southeast Asia, respectively.

Human Papillomavirus (HPV)

According to the WHO, human papillomavirus (HPV) is the most common viral infection affecting the reproductive tract and is contracted

through contact with genital skin, mucous membranes, or bodily fluids that are infected. It can be transmitted through sexual intercourse, including oral sex. Although most HPV infections are asymptomatic and resolve spontaneously, persistent infections of specific high-risk HPV types, such as HPV-16 and HPV-18, may result in precancerous lesions, progressing to invasive carcinoma if left undetected and untreated. Persistent infection with HPV is a necessary cause of cervical cancer and comprises 84% of all HPV-related cancers, accounting for 8% of all female cancer deaths in 2012. Oropharyngeal and anogenital cancers are also associated with HPV infection in both sexes.[5]

This possibility of HPV infections progressing to cancer thus demands prevention and protection against re-infections. When it comes to prevention, the WHO recommends that HPV vaccines should be included in national immunization programs, with cervical cancer prevention as priority for HPV immunization. Vaccination of girls prior to their sexual debut would be the optimal prevention. All three licensed HPV vaccines, namely bivalent, quadrivalent and nonavalent, are safe, with similarly excellent efficacy and effectiveness profiles. These all work against HPV-16 and HPV-18, which are associated with 71% of cervical cancers globally. Bivalent and quadrivalent vaccines provide cross-protection to other HPV types which are associated with 13% of cases, while nonavalent vaccines provide protection against those associated with 18% of cases.[5]

Based on a meta-analysis, the global HPV prevalence is estimated to be 11.7% among women with normal cytological findings, with Southeast Asia having a prevalence of 14%. This is among the highest globally, coming after sub-Saharan Africa with 24%, Latin America and the Caribbean with 16.1%, and Eastern Europe with 14.2%.[5]

HPV prevalence was high in all regions for men but showed varied rates from low-risk men with 1% to 84%, and from 2% to 93% among those considered as high-risk, such as sexually-transmitted infection clinic attendees, HIV-positive men (especially those who have sex with men, which have the highest prevalence), and male partners of women with abnormal cytology or HPV infection.[5]

More than 85% of cervical cancer cases are from less developed regions, accounting for 12% of all cancers in women[5]. Despite the

efforts of countries to implement HPV immunization programs from 2006 to 2014, a study states that only 1% of the estimated targeted 118 million women were from low-income or lower-middle-income countries. This disparity is even more pronounced with an estimated only 2.7% of women aged 10-20 years in less developed regions receiving the full course of vaccine, compared to the 33.6% from more developed regions[6].

Rationale

Given the varying prevalence of HPV infection and cervical cancer across different demographics and the influential role of vaccine hesitancy, there is a need to identify the factors that affect vaccine acceptance to aid in developing guidelines for improved administration. These guidelines would address the social determinants of health, which by the definition of the WHO, are conditions that cause health inequities or "the unfair and avoidable differences in health status within and between countries[7]." Health is multifactorial, and it requires that its different aspects (including various beliefs, circumstances, and resources) be accounted for in order to improve health outcomes and reduce health inequities.

Due to the limited number of studies in the Philippines concerning this matter, this study takes the opportunity to look at its neighboring countries from Southeast Asia that have similar contexts, beliefs, and circumstances.

Objective

This study aims to determine the factors that influence the general acceptance of Southeast Asians towards HPV vaccination and as a secondary objective, to suggest considerations in the creation of interventional and delivery strategies to increase HPV vaccine uptake.

Methods

A structured literature review was used to synthesize research evidence on factors influencing HPV vaccination in Southeast Asia. This review type was selected due to heterogeneity of literature with relevance to context and the lack of available comprehensive literature. The reviewers followed the reporting guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Extension for Scoping Reviews (PRISMS-ScR)[8].

Online databases including PubMed were used for the literature search. Search terms included: (1) vaccine confidence; (2) vaccine acceptance; (3) vaccine hesitancy; (4) HPV; and (5)

Southeast Asia. The search was limited to full-text, peer-reviewed articles published in English, involving human participants, between January 2009 and March 2020. Quantitative, qualitative and mixed-method studies were included. Papers were excluded if they were not about vaccines, not localized to Southeast Asia (e.g. Cambodian-American parents, Vietnamese-American women), clinical trials (e.g. immunogenicity), and focused on the prevalence, incidence, and clinical progression of HPV. A four phase flow diagram was used to assist and represent the selection, inclusion, and exclusion of research papers. All three authors examined the titles and results of the publications independently to exclude studies that did not fit the inclusion criteria. The authors then conducted data extraction and independently evaluated all eligible publications. A narrative summary was used to present the results of the review.

Finding and Discussion

Search Results and Sources of Evidence

The database search returned 58 publications (see **Figure 1**). After exclusion and identification of additional records, 41 original research publications were included for qualitative analysis and extraction of dominant themes relating to HPV vaccine acceptance.

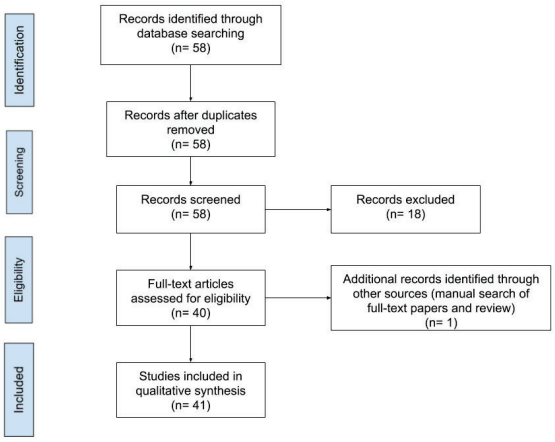

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram

Summary of Included Studies

The 41 studies covered seven Southeast Asian countries, distributed as follows: Malaysia (n=12), Vietnam (n=12), Thailand (n=8), Indonesia (n=3), Singapore (n=3), Cambodia (n=2), and the Philippines (n=1).

Collectively, these studies delved into a variety of topics, all related to the objective of the scoping review. The following outcomes were measured: knowledge of HPV, acceptance or attitudes towards HPV vaccination, factors influencing one's attitude towards HPV vaccination, and the effectiveness of interventions and

delivery strategies in increasing vaccine uptake. The majority of the studies measured at least two of the aforementioned outcomes; a few were specific to each outcome. In spite of the variety of outcomes being measured, the strong interplay among them could still be observed, along with general trends amid different demographics.

Health Literacy Assessment

As a way to gauge the context of the participants, most of the studies began by assessing their knowledge of HPV, particularly the vaccine and the relationship of the virus to cervical cancer. Generally, the participants were given a "low to moderate" rating in terms of knowledge on HPV as evidenced by the twelve studies[9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20] with participants of "low knowledge," eight studies[21, 22, 23, 24, 25, 26, 27, 28] with participants of "moderate knowledge," and just one study[29] with participants of "high knowledge." It is important to note, however, that the level descriptors used were not standardized; the researchers came up with their own criteria assessing their participants. Most of the studies measuring knowledge included asking participants if they have heard of HPV (and related terms) before.

The discussion can be further enriched by unveiling the respective contexts of some of the studies. In terms of demographics, almost all of the studies were conducted on women: mothers, adults, and young adolescents. Some studies delved into confounding factors by considering specific contexts, such as students taking medical/health science tracks and women living in rural areas. A few studies conducted research on other stakeholders of immunization programs, including educators, healthcare providers, and community and religious leaders.

Marginalized and rural communities[11, 13, 16] were found to be less knowledgeable about HPV—all studies of which are classified under the "low knowledge" category. One study that focused on a marginalized community involved sex workers in Cambodia, reporting that only 23.6% of participants had heard of HPV upon initial assessment. After administering an educational intervention, 90% of the participants were capable of answering HPV-related questions correctly, thus demonstrating the quintessential role of such strategies in addressing lack of knowledge on HPV[9]. Meanwhile, a cross-sectional survey that was conducted among Malaysian women found that those from universities, signifying urban

communities, had greater knowledge on HPV compared to those living in rural areas[30]. This is worth noting because of the comparative nature of its findings, relative to the three other studies conducted in rural areas, measuring knowledge as an outcome.

Among the participants with higher knowledge of HPV, there were two notable factors observed: sex and background in medicine/healthcare. Two studies, both conducted on Malaysian university students, found that while students were moderately knowledgeable about HPV, females had a significantly higher mean knowledge score in comparison to males, possibly due to the HPV disease profiles that are more common to women[23, 31]. It was also found that students from health-related colleges outperformed all other colleges[23]. This is further supported by one study in which medical students were assessed to have "high knowledge" on HPV[29].

Aside from the aforementioned implications of particular contexts to knowledge on HPV, it is also worth noting the type of information or the levels of understanding among certain demographics. One extensive qualitative study, conducted among several stakeholders, including children, parents, teachers, administrators, health workers, and community and religious leaders, found that although knowledge on HPV itself was limited, the gravity of cervical cancer and other HPV-related symptoms was acknowledged[25]. Another study on daughters and mothers in Vietnam found that mothers were more knowledgeable about cervical cancer and HPV, while the daughters were more knowledgeable about the HPV vaccine[24].

Health Literacy

Across most of the studies, the assessment of literacy was followed by determining its link to acceptance, the primary factor that this review aims to elucidate. In addition to knowledge, acceptance measures were typically found to be high. These findings were noted across different populations, particularly among parents[32, 21, 22, 10, 11, 12, 33, 14, 18, 34, 19], young women and students[22, 23, 31, 12, 29], adult women[22, 35, 13, 36, 27, 20, 37], health care professionals[38, 31, 28], teachers[39], sex workers[9], and different stakeholders (e.g., community and religious leaders)[25]. Although there is high acceptability regardless of demographic, the characteristics of the studied subgroups depict the association of knowledge, individual beliefs, and

health behaviors with vaccine acceptance.

Acceptance by parents, the most frequent demographic measured across studies, has been associated with their primary role in the decision-making process of vaccinating their children[25]. In the context of preventing cervical dysplasia, vaccination is most effective when given before sexual debut and HPV exposure. The Centers for Disease Control and Prevention (CDC) recommends administration of the vaccine to both boys and girls between the ages of 11 and 12 years, and as early as 9 years[40]. As a result, this window for vaccination often places the responsibility on the parents or guardians of the child. Additionally, acceptance of childhood vaccinations has been associated with parental HPV vaccine acceptance[32].

All studies that measured vaccine acceptance found a direct relationship with vaccine literacy. The operational definition of vaccine literacy overarches perceived susceptibility, knowledge of benefits, perceived seriousness of illnesses[27, 36], exposure to vaccine information in the form of intervention[9, 33, 37], knowledge that multiple partners increased risk[10, 41], and simply having heard of the virus and its associated disorders. The aforementioned study conducted on sex workers in Cambodia is an example of mass acceptance consequent to an educational intervention aiming to increase vaccine literacy[9]. This demonstrates the expected link between the two outcomes; however, several studies also found that low levels of literacy do not necessarily translate to lower acceptance[11, 13, 18]. One cross-sectional study done in Thailand found that despite being judged to have little knowledge on HPV vaccination, participants still exhibited high willingness to copay if the vaccine was not free[10]. Another study, set in rural Indonesia, found that parents were supportive of vaccinating their children, even if the majority had no knowledge of HPV[11]. Despite being autonomous agents, this phenomenon can be attributed to the passive acceptance that was found to be the norm in households and communities of low-resource settings, unless acted upon by external factors (e.g., sociocultural, economic, or environmental)[25, 33]. In contrast, another study found that there was no significant difference between the general attitude of women from urban and rural areas[30], which poses the possibility of overt bias among participants that claimed to be open to vaccination.

In discussing the relationship between literacy and acceptance, it is important to consider the reasons for vaccine hesitancy that stem from misconceptions, limited knowledge, and stigma on HPV. The reasons for refusal that have more to do with resources will be expounded on in the following sections. Several studies elicited the following reasons for vaccine hesitancy and decline of participation: possible side effects[33, 17, 18, 25], possible impact on fertility[33, 25], the possibility that it will not work[19], the embarrassment of getting screened by a male doctor[11], and the embarrassment of getting vaccinated per se[27, 30]. Most of the studies necessitated appropriate educational interventions to fill in gaps of knowledge on HPV vaccination, thus it is more sound to conclude that increasing literacy can address reasons behind vaccine hesitancy rather than entirely confirming a non-dynamic relationship between literacy and acceptance, which, as evidenced by the earlier studies, is subject to confounding variables.

Vaccine-Related Factors

The economic aspect of demand is inextricable from vaccination, just as with any product. It is to no surprise then, that several studies deemed price the most pertinent factor in HPV uptake[38, 16], at the minimum highlighting its inverse relationship with acceptance[21, 23, 38, 11, 42, 13, 15, 16, 18, 41, 26, 34, 19, 37]. The desire to avail of a vaccine is limited by the ability to do so, which is dictated by the consumer's purchasing power, hence also household income[21]. Similar studies in two different countries, Vietnam and Malaysia, measured the willingness of parents to pay for the full course of HPV vaccinations. The participants of the study conducted in North Vietnam were willing to pay from a range of under $23 to $46[42], while the participants of the Malaysian study were willing to pay an average of $27.7[16]. The same study revealed that the market price was $342.85[16]. It is also important to note that both studies were conducted in rural areas, which may suggest relatively lower income households. Two more Malaysian studies, when juxtaposed, can point out the role of price in HPV uptake. The first study measured the prevalence of HPV vaccination among secondary school girls after a newly employed government intervention of providing free vaccines and actively promoting HPV vaccination in the media; the study concluded that free vaccination significantly increased uptake[43]. On the other hand, despite high awareness of HPV among adult women, low uptake persisted because there were no government

subsidies for adults, only school girls[15]. This brings forth the relationship between knowledge and uptake, in contrast to acceptance. Knowledge has a direct relationship with uptake but only to the extent that one has the resources and financial capabilities to get vaccinated. Apart from price, although not as pervasive across the studies, other vaccine-related factors include vaccine type, effectiveness, and duration of effectiveness. One study found that the quadrivalent HPV vaccine contributed to the most favorable scenario[38], while another found no significant difference between bivalent and quadrivalent in terms of acceptance[10]. Regarding effectiveness, one study found that effectiveness was deemed more important than duration of effectiveness[34]. Unfortunately, such factors were only discussed in the three mentioned studies, thus posing limitations on its generalizability.

Personal Factors

Upon reviewing the studies, several miscellaneous factors emerged; they can be categorized into personal and social factors. Compared to price and knowledge, these were not as pervasive across the studies, although many of them are related to the latter in terms of influencing acceptance. It has already been elucidated in the earlier sections that living in a rural area is associated with lower knowledge of HPV and lower purchasing power, but these do not translate to a negative attitude towards HPV vaccination[11]. Aside from location, the following factors were also touched upon: age, sex, religion, and ethnicity. For age, younger women were more willing to get vaccinated than older women[13, 41]. One study found that there was higher acceptance among women younger than 45 years old and that age was the strongest associated factor for acceptance[12]. This was hypothesized to have been associated with participants' sexual behavior, interest in health information, and beliefs prior to the release of the vaccine. According to the CDC, catchup vaccinations should be offered to all previously unvaccinated females aged 13 to 26 years, and are not recommended for adults aged 27 to 45 years due to minimal public health benefit[44]. The existence of age group specific recommendations is congruent with the need for greater acceptance among younger women and mothers. Consequently, this underscores the need for adequate, accessible, and appropriate health information. For sex, it was found that women were more willing to get vaccinated than men[31] and that mothers were more inclined to

vaccinate their daughters over their sons[19], again possibly due to the HPV-related disease profiles more common to women. In terms of religion, no association with acceptance has been established in any of the studies[39, 19]. With ethnicity, on the other hand, only one study, conducted in rural Malaysia, found that there was higher perceived embarrassment for HPV vaccination among the Malay and the Indians as compared to the Chinese, hence the need for interventions that are culturally specific[29].

Social Factors

Compared to the personal factors that include a plethora of relatively unrelated elements, the social factors can be summarized through a qualitative study conducted among Chinese Singaporean women, that reported the role of passive and active acquisition in the decision-making process for HPV vaccination. Passive acquisition involves information from personal networks such as family and friends, while active acquisition involves information from credible sources such as medical pamphlets and health professionals[35]. Both rely on the peripheral route to persuasion (acceptance due to credibility over reason), which trades literacy for conformity in terms of HPV acceptance. These concepts are supported by studies that highlight the role of recommendations from healthcare providers[23, 36, 20] and partners[27, 13] in HPV acceptance, accounting for passive and active acquisitions, respectively. For active acquisition, gynecologists and general practitioners were found to be the most credible sources[20]. In line with active acquisition, a descriptive qualitative study in Vietnam also attributed an increase in support of HPV vaccination to the credibility that the government demonstrated in its implementation of the National Expanded Program of Immunization[33]. The same study also contextualized the concepts of passive and active acquisition by claiming that active decision-making is more common in urban areas[33]. For passive acquisition, the studies found that marital status had mixed findings, hence the conclusion that marital status is simply an avenue for decision-making in general, a factor that can increase or decrease vaccine acceptance[27, 13, 37], depending on other circumstances.

Interventions

Among the 41 studies, only a few specifically measured perception of outcomes after intervention[33, 43, 45, 46, 47], but the call for such strategies persisted as an overarching recommendation. School-based and national immunization programs

were found to be effective in significantly increasing HPV immunization[43, 47] with refusals mainly attributed to programmatic considerations such as absenteeism[45]. Nonetheless, it is our recommendation that such programs will only work with system preparedness[46] in the form of human resources and proper delivery of vaccines via cold chain[25]. In addition, access to transportation[37] and vaccine locations[18] were found to be barriers to immunization and thus need to be incorporated in the creation of delivery strategies.

Limitations of the Study

Measures of vaccine hesitancy, acceptability, and confidence have remained unstandardized, as a result of a lack of clear operational definitions. This may result in discrepancies between interpretations of similar variables. Vaccine acceptability must be sufficiently defined and described using standard tools to allow for analysis of the same unit. The failure to do so may lead to limited comparability of studies. Studies focusing on different demographics (age-groups, sexes, occupations, cultural groups, urban populations, rural populations), resource settings (e.g. developing countries), and sociocultural landscapes demand context-specific interpretations. In addition to extracting overarching themes, it is recognized that deeper analysis by subgroups must also be conducted to identify the reasons behind heterogeneity. Lastly, it must be noted that the significant number of cross-sectional study designs employed by the included studies only allow for descriptions of association and not causation. A number of studies also make use of self-administered questionnaires, which are subject to end aversion and positive skewing of results. Potential confounders affecting exposure and outcome must also be taken into account to include the many factors affecting decision-making.

Conclusions

After reviewing 41 studies on acceptance and attitudes of Southeast Asians towards HPV vaccination, it can be concluded that in spite of varying contexts, general trends can be established. In terms of HPV literacy, an overall level descriptor of “low to moderate” persisted throughout all the studies, with those from the rural and marginalized communities scoring the lowest and those with a background in healthcare scoring the highest. It is also worth measuring the type of information that specific demographics are unaware of so that educational

interventions can identify the gaps that need to be filled and address different levels of literacy in a community. Vaccine acceptance was generally high. It can be said that interventions that aim to increase literacy can address misconceptions that lead to vaccine hesitancy. It is wrong to claim, however, that there is a non-dynamic relationship between literacy and acceptance as there are other confounding variables at play, as evidenced by studies with high acceptance despite low literacy. A more sound conclusion would be that literacy has a direct relationship with uptake but is limited by one's resources to get vaccinated. This brings forth the role of price as the most crucial factor behind accessibility, as supported by interventions facilitating free vaccination found to be the most effective in vaccination uptake. Aside from literacy and price, personal factors such as location, age, and sex were found to be moderately linked to acceptance, while religion and ethnicity were found to have no association. The limited knowledge on such factors calls for the need of more culturally-specific research and interventions that would better grasp the contexts of their target communities. Social influence also played a large role in decision-making and was often dictated by the credibility of the source—physicians and the government for active acquisition, partners, friends, and family for passive acquisition. The majority of studies called for the need of intervention. The most effective strategies are school-based and national immunization programs. In addition to price, other factors that reduce accessibility such as lack of transportation and inconvenient vaccine locations must be addressed when creating interventional and delivery strategies that aim to increase HPV vaccine uptake.

Declarations

Ethics approval and consent to participate

Not applicable.

Availability of data and material

Not applicable.

Conflict of interests

All authors declare that they have no conflicting interests.

Funding

Not applicable.

Authors' contributions

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