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Scaling up human papillomavirus vaccination: a conceptual framework of vaccine adherence

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Abstract

This review article provides a conceptual framework for human papillomavirus (HPV) vaccine acceptance and adherence, with a focus on improving understanding of the sociocultural factors impacting vaccine adherence behaviour. We include a systematic review of the slowly expanding literature on HPV vaccine acceptability and uptake in developed nations, as well as the relatively few publications from poorer nations, where more than 80% of global cervical cancer related deaths occur and where the vaccine will probably have the largest impact. We suggest that this conceptual framework will not only improve our understanding of HPV vaccine uptake and adherence, but it may also guide future sociobehavioural research geared towards improving adherence to the HPV vaccine and other multi-step vaccines in a young population at risk for sexually transmissible infections.

Additional keywords

adolescents; development; sexually transmissible infection

Overview

The discovery that certain oncogenic strains of human papillomavirus (HPV) are associated with uterine, vulvar, vaginal, anal and oropharyngeal cancers prompted the development of two effective vaccines that hold enormous promise for preventing HPV-associated malignancies, particularly in regions of the world where cytology based screening programs

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Conflicts of interest

None declared.

are inaccessible.^{1–5} While HPV vaccine efficacy has been clearly demonstrated in clinical trials,⁶ it remains unclear if the vaccine will achieve full impact at a population level. Optimal vaccine implementation will depend upon vaccine uptake and adherence.

Prior research has shown that adherence to biomedical prevention strategies has been suboptimal due to low perceived risk of infection and lack of immediate benefits.^{7,8} Vaccine specific adherence has proven to be challenging, particularly for adolescents.⁹ Completion rates of multi-step vaccines among adolescents, including vaccines against varicella, hepatitis A and hepatitis B (HBV), can be as low as 40–50%, despite acceptance of the first dose.^{10,11} Failure to complete the full vaccine schedule can mean the difference between a vaccine's success and its failure, as in the case of the HBV vaccine, where vaccine non-completion was associated with a higher risk of developing hepatocellular carcinoma.¹² These findings highlight the importance of understanding how to increase vaccine adherence among adolescents to optimise vaccine efficacy, particularly in settings with a high prevalence of sexually transmissible infections (STIs).

In this paper, we propose a model for understanding HPV vaccine uptake and completion. We suggest that this conceptual framework will not only offer a way to understand HPV vaccine adherence better, but it may also provide a basis for further sociobehavioural research on both the HPV vaccine and other multi-step vaccines targeting youth at high risk for STI acquisition.

Understanding vaccine adherence

Vaccine adherence starts with vaccine acceptance. Factors such as individual beliefs about susceptibility, perceptions of vaccine effectiveness, family and parental attitudes, sexual and cultural practices, provider attitudes and reactions to qualities of the vaccine program (e.g. cost and availability of the vaccine) can all affect vaccine acceptance.¹³ In the case of the HPV vaccine, issues relating to vaccine affordability and the infrastructure associated with implementation have also been important focal points for research on vaccine acceptance.^{14–17}

As has been shown in prior HBV vaccine studies and studies assessing willingness to participate in an HIV vaccine trial,¹⁸ HPV vaccine acceptability depends on both the caregivers' and adolescents' perceived vulnerability of disease acquisition, and their willingness to be vaccinated.¹⁹ To address the issue of cost, certain countries such as the UK and Australia have led the way in delivering HPV vaccines in free school-based settings. Data from the UK (in which 71% of girls received at least one HPV vaccine dose),²⁰ and Australia (the first country worldwide to commence with a government funded universal HPV vaccine program in 2007)²¹ show very high rates of vaccine acceptance,²² and a subsequent decline in presentations of genital warts.²³ While these findings suggest that attitudinal factors may play a minor role in vaccine uptake when pragmatic obstacles are removed or minimised, other studies report the significant effect of 'normative beliefs' – specifically a measurement of a participant's belief that her medical provider, her parents and others would approve of her receiving the HPV vaccine – as a key factor associated with vaccine uptake.²⁴ This finding is consistent with several studies demonstrating that social norms predict both intention to be vaccinated and vaccination itself.^{25–27}

While this expanding literature on HPV vaccine acceptability and uptake in developed nations provides important information,^{28,29} it may not be universally applicable to less developed nations, where the vaccine is likely to have the largest impact and where more than 80% of the cervical cancer related deaths occur globally.^{30–33} In some settings, school-based programs may not reach the target audience, particularly if girls are not attending school during their adolescent years. In addition, universal access may be challenging in

nations where funding for vaccines is limited and critical supplementation through global organisations, such as the Global Alliance for Vaccines and Immunisation (GAVI), is required.³⁴

Literature on immunisation in developing countries shows the complexity of achieving vaccine acceptance in nations with severe economic and political constraints.^{35,36} The only study published to date on HPV vaccine acceptability in South Africa shows the difficulties of introducing a new technology in an environment of limited health care capacity and resources.³⁷ In addition, it highlights the need for clear messaging. While the authors point out that an HPV vaccine would probably be well received, several individuals interviewed suggested marketing the vaccine as a ‘cancer vaccine’ instead of an ‘STI vaccine’, as a means of minimising opposition. In addition, a few community respondents feared that a South African HPV vaccine might be ‘inherently inferior’, based upon concerns that vaccines used in South Africa are often ‘not of the same standard as first world countries or in the private sector’.

Concern over ‘inferior care’ has also been seen in studies examining HIV vaccine acceptability in Johannesburg. Despite data showing a high degree of willingness among Soweto youth to participate in an HIV vaccine trial,³⁸ many factors, including mistrust of health systems, science and the government, have been shown to impact participants’ desire to receive a proposed vaccine.³⁹ Ongoing formative research on vaccine acceptability will be of particular importance in these resource-limited settings where factors such as health service delivery, funding through international donors and a political will to improve immunisation rates, along with other sociocultural factors, may ultimately impact vaccine uptake.^{40–42}

Upon attainment of vaccine acceptability, vaccine adherence is the next component in vaccine implementation. In the case of a multi-step vaccine like HPV, adherence entails the completion of three doses, which is required to reach peak geometric mean titres, enabling a robust immune response.^{43,44} Vaccine adherence can be challenging to achieve, even in settings where vaccine initiation is high. In Australia, the school vaccination program delivered over 100 000 doses of the HPV vaccine by November, 2007 with 70–80% acceptance of the first dose.⁴⁵ Completion rates, however, only ranged from 55% to 77% for the third dose. In the USA, national estimates indicate that uptake in 2007 among adolescent girls aged 13–17 was 25% for the first dose and 6.9% for completion of the three-dose series.⁴⁶ Studies of smaller USA populations have shown wide variation in HPV vaccine completion, ranging between 0.2% and 58%.^{47–49} A recent study in the USA examining HPV vaccine utilisation among adolescent girls seen in university-based paediatric, family medicine or gynaecology clinics highlights the need for further research focussing on cost and racial disparities to understand factors influencing vaccine adherence.⁵⁰ Researchers found that series completion rates for the adolescent cohort overall was quite low (only 15% received all three doses among a subpopulation who had a full year to initiate and complete the vaccine series), and that African Americans and those on public health insurance were less likely than those of other races or those with private health insurance to complete the HPV series.

There is also much to learn about vaccine adherence from the experience of administering the HBV vaccine to high-risk adolescents. Similar to HPV, HBV is an oncogenic virus that has an effective preventive vaccine requiring multiple doses.⁵¹ Barriers to vaccine adherence among adolescents range from structural barriers, such as lack of transportation or health insurance, to perceived barriers, such as inability to access healthcare facilities.⁵² While these problems are faced by adults in the same settings, adolescents often lack the experience to overcome them.⁵³ Vaccine adherence has clinical implications, as evidenced

by a recent study investigating the impact of the universal Taiwanese HBV vaccine program (launched in 1984) on the prevention of hepatocellular carcinoma (HCC). It demonstrated vaccine non-completion was significantly associated with a higher risk for developing HCC than vaccine completers (odds ratio = 4.32, 95% confidence interval = 2.34 to 7.91).⁵⁴

While vaccine completion is an essential part of vaccine efficacy for both vaccines, there are important differences, including the fact that a two-dose schedule is possible in HBV vaccination when an adult dose (two times higher than an infant dose) is being used.^{55,56} In addition, a notable study on HBV vaccination in intravenous drug users does not entirely extrapolate to the target group for an HPV vaccine.^{57,58} Despite these differences, research on the uptake and adherence to the HBV vaccine can provide important information for further sociobehavioural studies focussing on the HPV vaccine.

Challenges associated with vaccines targeting an adolescent population

While the optimal target population for the HPV vaccine is likely to vary by country, based upon the age of sexual debut, it is likely to mirror current trends in developed nations – specifically adolescents between the ages of 10 and 14 years, with the goal of maximum efficacy in populations previously unexposed to its viral subtypes.^{59–61} Vaccine coverage in this age group (particularly in the older age range) remains suboptimal, even in developed nations such as the USA, where an estimated 93% of adolescents have a primary source for health care.⁶² In developing nations, rates of vaccination can potentially be even lower, given that vaccinating pre-adolescents and adolescents is a relatively new phenomenon, and regular health care visits for immunisations at this age are often not well established.⁶³

Reasons for poor vaccine uptake and adherence in the adolescent population are often driven by factors relating to both the caregiver and the adolescent. Poor caregiver–child communication, higher caregiver stress, lower caregiver quality of life and worse caregiver cognitive functioning are all factors that can impact adolescent adherence to health behaviours.⁶⁴ A recent HPV vaccine acceptability study highlighted the importance of caregivers in adolescents' willingness to be vaccinated.¹⁹ Researchers found that female caregivers' vaccination acceptability was associated with vaccine acceptability for their daughters, as were maternal beliefs about their daughters' likelihood of getting HPV.

Most vaccine-related decision-making occurs within the family unit, by one or more caregivers, and largely depends upon the caregivers' perceptions of the child's risk of exposure.⁶⁵ This framework may leave adolescents particularly vulnerable because many caregivers incorrectly assume their children are at low risk for acquiring an STI. Caregiver misperceptions mirror adolescent beliefs of invulnerability.⁶⁶ Unfortunately, potentially flawed assumptions about adolescent sexual behaviour may cloud decision-making, and prevent a child from accepting and adhering to a vaccination schedule.¹³ A successful vaccine program will need to address this complex interplay between familial, developmental and psychosocial factors influencing adherence in the adolescent population.

In addition, adolescent-specific factors impact adherence. These factors include: a lack of self-efficacy, stigma associated with a specific illness and an inability to consider future medical consequences into decision-making processes due to misperceptions of invulnerability and low risk.⁶⁶ A recent qualitative study focussing on barriers to adolescent vaccination in the USA showed that parent–child relationships, cognitive development, autonomy, time spent in school, relationship with 'medical homes', legal status and likelihood of having medical insurance all impacted adolescents' ability to accept and complete a multi-step vaccine.⁶⁷ Based upon these data, it is clear that a multi-factorial approach to understanding vaccine uptake and adherence in adolescents is necessary to improving vaccine completion rates.

Designing a conceptual framework for HPV vaccine adherence

Theories of health behaviour can offer *a priori* predictions about beliefs likely to impact uptake and adherence to an HPV vaccine. Models have been successfully used to better understand and explain both health promotion behaviours and illness prevention behaviours.^{68,69} To inform future research on HPV vaccination, we developed a theoretical framework to organise potential determinants of HPV vaccine uptake and adherence behaviour. Our framework, which we are titling ‘The Vaccine Perceptions, Acceptability and Adherence Model’ is based on a systematic review of the literature focussing on vaccine acceptability and uptake, using theory to identify predictors of HPV vaccine uptake and adherence, emphasising the populations most affected by cervical cancer.

We have based our approach of adapting conceptual models to new cultural settings on the heuristic model advocated by Ware *et al.*⁶⁸ who suggest that adapting a model to a new setting based on empirical research will lead to more effective public health interventions than creation of a *de novo* model. The framework displayed here is intended to act as a first step towards improving vaccine adherence research, particularly in regions of the world where STIs are endemic. Further formative research and testing is necessary to refine this model, in order to identify which, if any of these constructs drive behaviour.

For our literature review, the lead author searched PubMed/MEDLINE and other electronic databases from 1995 to 2009 (the approximate time frame during which HPV was known to cause cervical cancer), as well as electronic conference proceedings of the recent HPV-related conferences, for articles related to HPV vaccine uptake and adherence. The focus was on likely barriers and facilitators, identified from behavioural theory, among adolescents and their caregivers. Since federal approval of the vaccine was not granted until 2007, we were only able to examine actual uptake in the latter years of our search. Search terms included: human papillomavirus (and variants such as HPV); AND adherence* and attitude* and uptake* and barrier* and knowledge* and risk perception*; AND vaccine*. We also searched the reference sections of included articles.

In addition, given the limited number of articles available discussing HPV vaccine adherence, we decided to expand our search and look at models of understanding adherence as a concept, via a review of medication adherence literature. While this uncovered an extensive amount of literature, we ultimately felt that adherence to a preventive measure such as vaccination was too different from treatment adherence (as in the case of HIV medication). We therefore only included one reference in the text to medication adherence – specifically showing that adherence, as a general concept, can be challenging in adolescents. Inclusion criteria for our searches were an examination of awareness, knowledge or attitudes related to HPV vaccine, and reporting original data in English.

By using these search terms, we generated over 400 research papers. We focussed on how factors such as acceptability, awareness, knowledge and beliefs (of both the adolescent and the caregiver) influenced actual behaviour in the later years of our search. We then considered descriptive, methodological and contextual factors from each relevant study to gain an understanding of what research has already been done in this field. We identified key themes (discussed below) through this literature relating to factors influencing uptake and adherence of the HPV vaccine.

For our model constructs, we examined literature from both clinical psychology and public health, focussing on a range of validated models that have been developed over the past several decades that have been used to elucidate the interactions of variables affecting individual health-seeking processes.^{70,71} Research driven by sociobehavioural theory has been previously used to examine acceptability and desirability of vaccines in Diseases of the

Most Impoverished Program, as well as predictors of HPV vaccine acceptability before its introduction.^{44,72} Our review emphasises the Health Belief Model.⁷³ The constructs in this model – including perceived risk, perceived effectiveness of the vaccine, perceived barriers to vaccine uptake and adherence, and cues to action (situational factors that trigger one to get vaccinated or adhere to a vaccine regimen) – have been previously shown to be important predictors of vaccination.⁷⁴

While behaviourist models of health-seeking, such as the Health Belief Model, are highly relevant in the context of immunisation uptake, they can neglect the complex relationships among individuals, sociocultural and political-economic conditions. This potential shortcoming is of particular relevance in resource-limited settings where perceptions of vaccines (and of health care systems, in general) may be very different from a Western context, where behaviourist theories originate and where individualistic factors are emphasised. An integrated and dynamic framework that recognises both the cultural and economic forces at play is therefore required to analyse HPV vaccine uptake and adherence in resource-limited settings.

Our model incorporates information from our literature review as well as the theories mentioned above, recognising that HPV vaccine acceptability and adherence are shaped by structural and sociocultural factors that inform both the individual adolescent and her caregiver – influencing the perceived risk of disease acquisition and perceived effectiveness of the vaccine. Barriers to vaccine acceptability, along with cues to action (which we term ‘facilitators’), will impact vaccine uptake. In the case of vaccine adherence, an additional step, with a new set of barriers and facilitators to adherence behaviour, is involved that is informed by both the adolescent’s and caregiver’s experience with the first point of care, along with evolving community beliefs about the HPV vaccine. This is framed within an environmental context that informs decision making for both the adolescent and the caregiver.

A brief illustrative example demonstrates the model. Information sent to an adolescent regarding an HPV vaccine as part of an educational campaign can influence both perceived risk and perceived effectiveness of a vaccine. Factoring in the youth’s past behaviours, particularly the level of engagement with the health care system and her history of vaccinations, along with sociodemographic factors and social norms, both barriers and facilitators to vaccine initiation are generated. In low-income settings, it is important to recognise that structural factors, such as costs related to this vaccine and transportation to get to the clinic, may trump the individual’s ability to initiate vaccination, even if perceived effectiveness of the vaccination is high. These factors continue to influence vaccine adherence, with the added dimension of personal history with the vaccine (e.g. side-effects associated with the first dose, cost of the first visit) and the health care system, as well as the evolving community beliefs regarding perceived risk of disease acquisition and perceived risk and effectiveness associated with the vaccine.

Both individual and caregiver factors are essential in a vaccination targeting adolescents. We have therefore indicated an ongoing exchange between these two as part of the process of both vaccine initiation and vaccine adherence. Caregivers’ perceptions of cervical cancer severity, along with their beliefs regarding the likelihood of HPV acquisition, are weighed against perceived barriers to HPV vaccination, stigma associated with discussions relating to sexuality and concerns about vaccine side-effects. These beliefs are connected to a caregiver’s trust of the health care system in general, and trust in vaccinations as effective prevention strategies. The caregiver’s impact on the ultimate decision to vaccinate will likely correlate with his or her relatedness to the adolescent and to the daughter’s health care provider, and feelings about the daughter’s current or future sexuality.

Adolescent-specific factors, including developmental factors, may also impact vaccination. While a lack of executive function may falsely lead to feelings of immortality and therefore a diminished desire to obtain a vaccine, other factors such as high self-esteem and high self-efficacy may increase health-seeking behaviour and likelihood of vaccine initiation. The adolescent's mental health and social support are both important factors in behaviours associated with prevention of STIs.⁷⁵ Both the caregiver's and adolescent's beliefs about vaccine safety, along with knowledge of HPV and disease acquisition, will probably be informed by the environmental context. Message framing (gain v. loss or STI protection v. cervical cancer prevention) is an essential component of the environmental context and has been known to influence the intention to receive the HPV vaccine.⁷⁶ In addition, the media is an important component of the external environment that influences HPV vaccine uptake, and the tone (supportive of the vaccine v. alarmist) taken in the lay press can have a significant impact on vaccine acceptability.^{77,78} These factors are displayed in our model below. This model is intended to act as a first step towards improving vaccine adherence research, particularly in regions of the world where cervical cancer rates are high. Further formative research and testing is necessary to refine this model (Fig. 1) in order to identify which, if any, of these constructs drive uptake adherence, particularly in developing countries.

HPV vaccine adherence as a model for other multi-step vaccines targeting youth at risk for STIs

An improved understanding of factors influencing HPV vaccine adherence may guide other vaccine programs with similar target populations. Nowhere will this be more crucial than in the dissemination of a future HIV vaccine,⁷⁹ which will probably require adherence to a multi-step regimen.⁸⁰ While there are clear differences between an HPV vaccine that has proven efficacy and an experimental HIV vaccine that has yet to be fully realised, HPV and HIV share many important similarities.⁸¹ Both HIV-1 and oncogenic strains of HPV are STIs that cause immense morbidity and mortality from viruses that cause delayed but severe sequelae. In addition, both establish lifelong, persistent infections that disproportionately affect adolescents, women and disenfranchised populations in the developing world.⁸² Despite differences in knowledge and stigma relating to the diseases caused by these two viruses, behavioural research on the current HPV vaccine, particularly in resource-limited nations, can provide important information regarding a future HIV vaccine.

The parallels between HPV and HIV vaccinations are supported by a recent report by the International AIDS Vaccine Initiative (IAVI) stating that swift and efficient HPV vaccine introduction in developing countries will provide a valuable opportunity for AIDS vaccine researchers and advocates to learn from the HPV vaccine experience in planning for the introduction of future AIDS vaccines.⁸³ While research on the development of an HIV vaccine continues, it is clear that there will be tremendous pressure to implement a global vaccination campaign immediately once it is developed. By examining the factors that affect adherence to a multi-step HPV vaccination now, we can optimise HIV vaccine delivery and dissemination in high-risk populations once it becomes available.^{23,84–86}

Conclusion

By developing a conceptual framework for HPV vaccine adherence, we hope to inform future research on vaccine adherence among adolescents at high risk for STI acquisition. The analytic construct proposed here recognises forces such as structural and sociocultural factors effecting vaccine uptake and incorporates them into the model. This model also takes into account the target population and the role that caregiver involvement will play in acceptance of this vaccination. It provides a future direction for *research*. We caution

readers that most reviewed studies, when considered on their own, yield evidence of inadequate quality to direct future *interventions*. We do believe, however, that this work, taken in combination with other health behaviour theories and a body of empirical literature that continues to expand on HPV vaccine uptake and adherence, suggests that programs promoting vaccine uptake and adherence would benefit from optimising educational messaging (vaccine effectiveness) while addressing important sociocultural barriers for both adolescents and their caregivers. Ultimately, we believe our proposed conceptual model will aid in future research aimed at understanding barriers to vaccine uptake and adherence, and ultimately provide further information about means to overcome them, thus enabling millions to receive the benefits of vaccination.

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References

1. Muñoz N, Castellsagué X, de González AB, Gissmann L. Chapter 1: HPV in the etiology of human cancer. *Vaccine*. 2006; 24:1–10. [PubMed: 16122853]
2. Baden LR, Curfman GD, Morrissey S, Drazen JM. Human papillomavirus vaccine – opportunity and challenge. *N Engl J Med*. 2007; 356:1990–1.10.1056/NEJMe078088 [PubMed: 17494932]
3. Muñoz N, Bosch FX, de Sanjosé S, Herrero R, Castellsagué X, Shah KV, et al. International Agency for Research on Cancer Multicenter Cervical Cancer Study Group. Epidemiologic classification of human papillomavirus types associated with cervical cancer. *N Engl J Med*. 2003; 348:518–27.10.1056/NEJMoa021641 [PubMed: 12571259]
4. Parkin DM. The global health burden of infection-associated cancers in the year 2002. *Int J Cancer*. 2006; 118:3030–44.10.1002/ijc.21731 [PubMed: 16404738]
5. Coglianò V, Baan R, Straif K, Grosse Y, Secretan B, Ghissassi F. Carcinogenicity of human papillomavirus. *Lancet Oncol*. 2005; 6:204.10.1016/S1470-2045(05)70086-3 [PubMed: 15830458]
6. Muñoz N, Kjaer SK, Sigurdsson K, Iversen OE, Hernandez-Avila M, Wheeler CM, et al. Impact of human papillomavirus (HPV)-6/11/16/18 vaccine on all HPV-associated genital diseases in young women. *J Natl Cancer Inst*. 2010; 102:325–39.10.1093/jnci/djp534 [PubMed: 20139221]
7. Myers E, Huh WK, Wright JD, Smith JS. The current and future role of screening in the era of HPV vaccination. *Gynecol Oncol*. 2008; 109 (Suppl 1):S31–9.10.1016/j.ygyno.2008.02.001 [PubMed: 18482556]
8. Padian NS, Buvé A, Balkus J, Serwadda D, Cates W Jr. Biomedical interventions to prevent HIV infection: evidence, challenges, and way forward. *Lancet*. 2008; 372:585–99.10.1016/S0140-6736(08) 60885-5 [PubMed: 18687456]
9. Lehmann C, Benson PA. Vaccine adherence in adolescents. *Clin Pediatr*. 2009; 48:801–11.10.1177/0009922809336360
10. Heininger U, Loos K, Lorenz I, Rascher W. Compliance with recommended immunizations in adolescents. *Eur J Pediatr*. 2006; 165:671–6.10.1007/s00431-006-0161-9 [PubMed: 16705466]
11. Nelson JC, Bittner RC, Bounds L, Zhao S, Baggs J, Donahue JG, et al. Compliance with multiple-dose vaccine schedules among older children, adolescents, and adults: results from a vaccine safety datalink study. *Am J Public Health*. 2009; 99(Suppl 2):S389–97.10.2105/AJPH.2008.151332 [PubMed: 19797753]

12. Bailey CL, Smith V, Sands M. Hepatitis B vaccine: a seven-year study of adherence to the immunization guidelines and efficacy in HIV-1-positive adults. *Int J Infect Dis.* 2008; 12:e77–83.10.1016/j.ijid.2008.05.1226 [PubMed: 18723381]
13. Zimet GD, Liddon N, Rosenthal SL, Lazcano-Ponce E, Allen B. Chapter 24: psychosocial aspects of vaccine acceptability. *Vaccine.* 2006; 24(Suppl 3):S201–9.10.1016/j.vaccine.2006.06.017
14. Reynales-Shigematsu LM, Rodrigues ER, Lazcano-Ponce E. Cost-effectiveness analysis of a quadrivalent human papilloma virus vaccine in Mexico. *Arch Med Res.* 2009; 40:503–13.10.1016/j.arcmed.2009.08.004 [PubMed: 19853192]
15. Ault K, Reisenger K. Programmatic issues in the implementation of an HPV vaccination program to prevent cervical cancer. *Int J Infect Dis.* 2007; 11(Suppl 2):S26–8.10.1016/S1201-9712(07)60018-6 [PubMed: 18162242]
16. Goldie SJ, O'Shea M, Diaz M, Kim SY. Benefits, cost requirements and cost-effectiveness of the HPV16,18 vaccine for cervical cancer prevention in developing countries: policy implications. *Reprod Health Matters.* 2008; 16:86–96.10.1016/S0968-8080(08)32409-4 [PubMed: 19027626]
17. Zimet GD, Mays RM, Winston Y, Kee R, Dickes J, Su L. Acceptability of human papillomavirus immunization. *J Womens Health Gend Based Med.* 2000; 9:47–50.10.1089/152460900318957 [PubMed: 10718505]
18. de Bruyn G, Skhosana N, Robertson G, McIntyre JA, Gray GE. Knowledge and attitudes towards HIV vaccines among Soweto adolescents. *BMC Res Notes.* 2008; 1:76.10.1186/1756-0500-1-76 [PubMed: 18759973]
19. Fazekas KI, Brewer NT, Smith JS. HPV vaccine acceptability in a rural Southern area. *J Women's Health.* 2008; 17:539–48.10.1089/jwh.2007.0489
20. Brabin L, Roberts SA, Stretch R, Baxter D, Chambers G, Kitchener H, et al. Uptake of first two doses of human papillomavirus vaccine by adolescent schoolgirls in Manchester: prospective cohort study. *BMJ.* 2008; 336:1056–8.10.1136/bmj.39541.534109.BE [PubMed: 18436917]
21. Garland SM, Brotherton JM, Skinner SR, Pitts M, Saville M, Mola G, et al. Human papillomavirus and cervical cancer in Australasia and Oceania: risk-factors, epidemiology and prevention. *Vaccine.* 2008; 26(Suppl 12):M80–8.10.1016/j.vaccine.2008.05.041 [PubMed: 18945417]
22. Garland SM. Can cervical cancer be eradicated by prophylactic HPV vaccination? Challenges to vaccine implementation. *Indian J Med Res.* 2009; 130:311–21. [PubMed: 19901440]
23. Fairley CK, Hocking JS, Gurrin LC, Chen MY, Donovan B, Bradshaw CS. Rapid decline in presentations of genital warts after the implementation of a national quadrivalent human papillomavirus vaccination programme for young women. *Sex Transm Infect.* 2009; 85:499–502.10.1136/sti.2009.037788 [PubMed: 19837728]
24. Conroy K, Rosenthal SL, Zimet GD, Jin Y, Bernstein DI, Glynn S, et al. Human papillomavirus vaccine uptake, predictors of vaccination, and self-reported barriers to vaccination. *J Women's Health.* 2009; 18:1679–86.10.1089/jwh.2008.1329
25. Sturm LA, Mays RM, Zimet GD. Parental beliefs and decision making about child and adolescent immunization: from polio to sexually transmitted infections. *J Dev Behav Pediatr.* 2005; 26:441–52.10.1097/00004703-200512000-00009 [PubMed: 16344662]
26. Mok E, Yeung SH, Chan MF. Prevalence of influenza vaccination and correlates of intention to be vaccinated among Hong Kong Chinese. *Public Health Nurs.* 2006; 23:506–15.10.1111/j.1525-1446.2006.00590.x [PubMed: 17096775]
27. Daley MF, Crane LA, Chandramouli V, Beaty BL, Barrow J, Allred N, et al. Influenza among healthy young children: changes in parental attitudes and predictors of immunization during the 2003 to 2004 influenza season. *Pediatrics.* 2006; 117:e268–77.10.1542/peds.2005-1752 [PubMed: 16452334]
28. Marlow LA, Waller J, Evans RE, Wardle J. Predictors of interest in HPV vaccination: a study of British adolescents. *Vaccine.* 2009; 27:2483–8.10.1016/j.vaccine.2009.02.057 [PubMed: 19368790]
29. Reiter PL, Brewer NT, Gottlieb SL, McRee AL, Smith JS. How much will it hurt? HPV vaccine side effects and influence on completion of the three-dose regimen. *Vaccine.* 2009; 27:6840–4.10.1016/j.vaccine.2009.09.016 [PubMed: 19765398]

30. Agosti JM, Goldie SJ. Introducing HPV vaccine in developing countries – key challenges and issues. *N Engl J Med*. 2007; 356:1908–10.10.1056/NEJMp078053 [PubMed: 17494923]
31. Wong LP. Physicians' experiences with HPV vaccine delivery: evidence from developing country with multiethnic populations. *Vaccine*. 2009; 27:1622–7.10.1016/j.vaccine.2008.11.107 [PubMed: 19100803]
32. Winkler JL, Wittet S, Bartolini RM, Creed-Kanashiro HM, Lazcano-Ponce E, Lewis-Bell K, et al. Determinants of human papillomavirus vaccine acceptability in Latin America and the Caribbean. *Vaccine*. 2008; 26(Suppl 11):L73–9.10.1016/j.vaccine.2008.05.027 [PubMed: 18945404]
33. Muñoz N, Franco EL, Herrero R, Andrus JK, de Quadros C, Goldie SJ, et al. Recommendations for cervical cancer prevention in Latin America and the Caribbean. *Vaccine*. 2008; 26(Suppl 11):L96–107.10.1016/j.vaccine.2008.05.062 [PubMed: 18945407]
34. Andrus JK, Sherris J, Fitzsimmons JW, Kane MA, Aguado MT. Introduction of human papillomavirus vaccines into developing countries – international strategies for funding and procurement. *Vaccine*. 2008; 26(Suppl 10):K87–92.10.1016/j.vaccine.2008. 05.003 [PubMed: 18847561]
35. Gauri V, Khaleghian P. Immunization in developing countries: its political and organizational determinants. Policy Research Working Paper 2769. World Development. 2002; 30:2109–32.
36. Loevinsohn B, Hong R, Gauri V. Will more inputs improve the delivery of health services? Analysis of district vaccination coverage in Pakistan. *Int J Health Plann Manage*. 2006; 21:45–54.10.1002/hpm.824 [PubMed: 16604848]
37. Harries J, Moodley J, Barone MA, Mall S, Sinanovic E. Preparing for HPV vaccination in South Africa: key challenges and opinions. *Vaccine*. 2009; 27:38–44.10.1016/j.vaccine.2008.10.033 [PubMed: 18977271]
38. de Bruyn G, Skhosana N, Robertson G, McIntyre JA, Gray GE. Knowledge and attitudes towards HIV vaccines among Soweto adolescents. *BMC Res Notes*. 2008; 1:76.10.1186/1756-0500-1-76 [PubMed: 18759973]
39. Sayles JN, Macphail CL, Newman PA, Cunningham WE. Future HIV vaccine acceptability among young adults in South Africa. *Health Educ Behav*. 2010; 37:193–210.10.1177/1090198109335654 [PubMed: 19509123]
40. Kaljee LM, Pack R, Pach A, Nyamete A, Stanton BF. Sociobehavioural research methods for the introduction of vaccines in the diseases of the most impoverished programme. *J Health Popul Nutr*. 2004; 22:293–303. [PubMed: 15609782]
41. Sherris J, Friedman A, Wittet S, Davies P, Steben M, Saraiya M. Chapter 25: education, training, and communication for HPV vaccines. *Vaccine*. 2006; 24(Suppl 3):S210–8.10.1016/j.vaccine. 2006.05.124
42. Andrus JK, Lewis MJ, Goldie SJ, Garcia PJ, Winkler JL, Ruiz-Matus C, et al. Human papillomavirus vaccine policy and delivery in Latin America and the Caribbean. *Vaccine*. 2008; 26:L80–7.10.1016/j.vaccine.2008.05.040 [PubMed: 18945405]
43. Bonanni P, Boccalini S, Bechini A. Efficacy, duration of immunity and cross protection after HPV vaccination: a review of the evidence. *Vaccine*. 2009; 27(Suppl 1):A46–53.10.1016/j.vaccine. 2008. 10.085 [PubMed: 19480962]
44. Joura EA, Kjaer SK, Wheeler CM, Sigurdsson K, Iversen OE, Hernandez-Avila M, et al. HPV antibody levels and clinical efficacy following administration of a prophylactic quadrivalent HPV vaccine. *Vaccine*. 2008; 26:6844–51.10.1016/j.vaccine.2008.09.073 [PubMed: 18930097]
45. Watson M, Shaw D, Molchanoff L, McInnes C. Challenges, lessons learned and results following the implementation of a human papilloma virus school vaccination program in South Australia. *Aust NZ J Public Health*. 2009; 33:365–70.10.1111/j.1753-6405.2009.00409.x
46. Centers for Disease Control and Prevention. Vaccination coverage among adolescents aged 13–17 years – United States, 2007. *MMWR Morb Mortal Wkly Rep*. 2008; 57:1100–3. [PubMed: 18846032]
47. Chao C, Slezak JM, Coleman KJ, Jacobsen SJ. Papanicolaou screening behavior in mothers and human papillomavirus vaccine uptake in adolescent girls. *Am J Public Health*. 2009; 99:1137–42.10.2105/AJPH.2008.147876 [PubMed: 19372507]

48. Neubrand TP, Radecki-Breitkopf C, Rupp R, Breitenkopf D, Rosenthal SL. Factors associated with completion of the human papillomavirus vaccine series. *Clin Pediatr*. 2009; 48:966–9.10.1177/0009922809337534
49. Kahn JA, Rosenthal SL, Jin Y, Huang B, Namakydoust A, Zimet GD. Rates of human papillomavirus vaccination, attitudes about vaccination, and human papillomavirus prevalence in young women. *Obstet Gynecol*. 2008; 111:1103–10. [PubMed: 18448742]
50. Dempsey A, Cohn L, Dalton V, Ruffin M. Patient and clinic factors associated with adolescent human papillomavirus vaccine utilization within a university-based health system. *Vaccine*. 2010; 28:989–95.10.1016/j.vaccine.2009.10.133 [PubMed: 19925899]
51. Rots NY, Wijmenga-Monsuur AJ, Luytjes W, Kaaijk P, de Graaf TW, van der Zeijst BAM, et al. Hepatitis B vaccination strategies tailored to different endemicity levels: some considerations. *Vaccine*. 2010; 28:893–900.10.1016/j.vaccine.2009.10.125 [PubMed: 19932217]
52. Sneller VP, Fishbein DB, Weinbaum CM, Lombard A, Murray P, McLaurin JA, et al. Working Group on Vaccination of High-Risk Adolescents. Vaccinating adolescents in high-risk settings: lessons learned from experiences with hepatitis B vaccine. *Pediatrics*. 2008; 121:S55–62.10.1542/peds.2007-1115G [PubMed: 18174322]
53. Geber GM. Barriers to health care for street youth. *J Adolesc Health*. 1997; 21:287–90.10.1016/S1054-139X(97)00111-0 [PubMed: 9358291]
54. Chang MH, You SL, Chen CJ, Liu CJ, Lee CM, Lin SM, et al. Taiwan Hepatoma Study Group. Decreased incidence of hepatocellular carcinoma in hepatitis B vaccinees: a 20-year follow-up study. *J Natl Cancer Inst*. 2009; 101:1348–55.10.1093/jnci/djp288 [PubMed: 19759364]
55. Boland G, Beran J, Lievens M, Sasadeusz J, Dentico P, Nothdurft H, et al. Safety and immunogenicity profile of an experimental hepatitis B vaccine adjuvanted with AS04. *Vaccine*. 2004; 23:316–20.10.1016/j.vaccine.2004.06.006 [PubMed: 15530674]
56. Heron L, Selnikova O, Moiseieva A, Van Damme P, van der Wielen M, Levie K, et al. Immunogenicity, reactogenicity and safety of two-dose versus three-dose (standard care) hepatitis B immunisation of healthy adolescents aged 11–15 years: a randomised controlled trial. *Vaccine*. 2007; 25:2817–22.10.1016/j.vaccine.2006.12.021 [PubMed: 17276552]
57. Altice FL, Bruce RD, Walton MR, Buitrago MI. Adherence to hepatitis B virus vaccination at syringe exchange sites. *J Urban Health*. 2005; 82:151–61.10.1093/jurban/jti016 [PubMed: 15746385]
58. Lum PJ, Hahn JA, Shafer KP, Evans JL, Davidson PJ, Stein E, et al. Hepatitis B virus infection and immunization status in a new generation of injection drug users in San Francisco. *J Viral Hepat*. 2008; 15:229–36. [PubMed: 18233994]
59. Koulova A, Tsui J, Irwin K, Van Damme P, Biellik R, Aguado MT. A brief report: country recommendations on the inclusion of HPV vaccines in national immunization programmes among high-income countries, June 2006–January 2008. *Vaccine*. 2008; 26:6529–41.10.1016/j.vaccine.2008.08.067 [PubMed: 18805453]
60. Cutts FT, Franceschi S, Goldie S, Castellsague X, de Sanjose S, Garnett G, et al. Human papillomavirus and HPV vaccines: a review. *Bull World Health Organ*. 2007; 85:719–26.10.2471/BLT.06.038414 [PubMed: 18026629]
61. Villa LL, Costa RL, Petta CA, Andrade RP, Ault KA, Giuliano AR, et al. Prophylactic quadrivalent human papillomavirus (types 6, 11, 16, and 18) L1 virus-like particle vaccine in young women: a randomised double-blind placebo-controlled multicentre phase II efficacy trial. *Lancet Oncol*. 2005; 6:271–8.10.1016/S1470-2045(05)70101-7 [PubMed: 15863374]
62. Bloom B, Cohen RA. Summary health statistics for US children: National Health Interview Survey 2006. *Vital Health Stat* 10. 2007; 234:1–79. [PubMed: 17969822]
63. Harries J, Moodley J, Barone MA, Mall S, Sinanovic E. Preparing for HPV vaccination in South Africa: key challenges and opinions. *Vaccine*. 2009; 27:38–44.10.1016/j.vaccine.2008.10.033 [PubMed: 18977271]
64. Mellins CA, Brackis-Cott E, Dolezal C, Abrams EJ. The role of psychosocial and family factors in adherence to antiretroviral treatment in human immunodeficiency virus-infected children. *Pediatr Infect Dis J*. 2004; 23:1035–41.10.1097/01.inf.0000143646.15240.ac [PubMed: 15545859]

65. Bingham A, Drake JK, LaMontagne DS. Socio-cultural issues in the introduction of human papillomavirus vaccine in low-resource settings. *Arch Pediatr Adolesc Med*. 2009; 163:455–61.10.1001/archpediatrics.2009.50 [PubMed: 19414692]
66. Rosenthal SL, Kottenhahn RK, Biro FM, Succop PA. Hepatitis B acceptance among adolescents and their parents. *J Adolesc Health*. 1995; 17:248–54.10.1016/1054-139X(95)00164-N [PubMed: 8580126]
67. Ford CA, English A, Davenport AF, Stinnett AJ. Increasing adolescent vaccination: barriers and strategies in the context of policy, legal, and financial issues. *J Adolesc Health*. 2009; 44:568–74.10.1016/j.jadohealth.2008.11.015 [PubMed: 19465321]
68. Ware NC, Idoko J, Kaaya S, Biraro IA, Wyatt MA, Agbaji O, et al. Explaining adherence success in sub-Saharan Africa: an ethnographic study. *PLoS Med*. 2009; 6:e11.10.1371/journal.pmed.1000011 [PubMed: 19175285]
69. Williams GC, Niemiec CP, Patrick H, Ryan RM, Deci EL. The importance of supporting autonomy and perceived competence in facilitating long-term tobacco abstinence. *Ann Behav Med*. 2009; 37:315–24.10.1007/s12160-009-9090-y [PubMed: 19373517]
70. Bogart, LM.; Delahanty, DL. Psychological models. In: Boll, TJ.; Frank, RC.; Baum, A.; Wallander, JL., editors. *Handbook of clinical health psychology*. vol 3. Models and perspectives in health psychology. Washington DC: American Psychological Association; 2004. p. 249-89.
71. Fishbein, M.; Ajzen, I. *Belief, attitude, intention and behavior: an introduction to theory and research*. Reading, MA: Addison-Wesley; 1975.
72. Brewer NT, Fazekas KI. Predictors of HPV vaccine acceptability: a theory-informed, systematic review. *Prev Med*. 2007; 45:107–14.10.1016/j.ypmed.2007.05.013 [PubMed: 17628649]
73. Becker MH. The health belief model and personal health behavior. *Health Educ Monogr*. 1974; 2:324–508.
74. Brewer NT, Chapman GB, Gibbons FX, Gerard M, McCaul KD, Weinstein ND. A meta-analysis of the relationship between risk perception and health behavior: the example of vaccination. *Health Psychol*. 2007; 26:136–45.10.1037/0278-6133.26.2.136 [PubMed: 17385964]
75. Sales JM, Milhausen RR, Wingood GM, DiClemente RJ, Salazar LF, Crosby RA. Validation of a parent-adolescent communication scale for use in STD/HIV prevention interventions. *Health Educ Behav*. 2008; 35:332–45.10.1177/1090198106293524 [PubMed: 17200099]
76. Gerend MA, Shepherd JE. Using message framing to promote acceptance of the human papillomavirus vaccine. *Health Psychol*. 2007; 26:745–52.10.1037/0278-6133.26.6.745 [PubMed: 18020847]
77. Hilton S, Hunt K, Langan M, Bedford H, Petticrew M. Newsprint media representations of the introduction of the HPV vaccination programme for cervical cancer prevention in the UK (2005–2008). *Soc Sci Med*. 2010; 70:942–50.10.1016/j.socscimed.2009.11.027 [PubMed: 20064682]
78. Abdelmutti N, Hoffman-Goetz L. Risk messages about HPV, cervical cancer, and the HPV vaccine Gardasil: a content analysis of Canadian and U.S. national newspaper articles. *Women Health*. 2009; 49:422–40.10.1080/03630240903238776 [PubMed: 19851946]
79. Newman PA, Lee SJ, Duan N, Rudy E, Nakazono TK, Boscardin J, et al. Preventive HIV vaccine acceptability and behavioral risk compensation among a random sample of high-risk adults in Los Angeles (LA VOICES). *Health Serv Res*. 2010; 44:2167–79.10.1111/j.1475-6773.2009.01039.x [PubMed: 19780857]
80. Rerks-Ngarm S, Pitisuttithum P, Nitayaphan S, Kaewkungwal J, Chiu J, Paris R, et al. MOPH-TAVEG Investigators. Vaccination with ALVAC and AIDSVAX to prevent HIV-1 infection in Thailand. *N Engl J Med*. 2009; 361:2209–20.10.1056/NEJMoa0908492 [PubMed: 19843557]
81. Weiss RA. On viruses, discovery, and recognition. *Cell*. 2008; 135:983–6.10.1016/j.cell.2008.11.022 [PubMed: 19070561]
82. UNAIDS. *AIDS epidemic update*. Geneva: Joint United Nations Programme on HIV/AIDS; 2007.
83. IAVI Publications. *Current HPV vaccines and future AIDS vaccines: common challenges and unprecedented opportunities*. New York: IAVI; 2008. Available online at: <http://www.iavi.org/publications-resources/pages/publicationdetail.aspx?pubid=15af74c1-c0b1-4a9b-a87a-8dec767740d2> [verified November 2009]

84. Heise LL, Elias C. Transforming AIDS prevention to meet women's needs: a focus on developing countries. *Soc Sci Med.* 1995; 40:931–43.10.1016/0277-9536(94)00165-P [PubMed: 7792632]
85. d'Cruz-Grote D. Prevention of HIV infection in developing countries. *Lancet.* 1996; 348:1071–4.10.1016/S0140-6736(95)11031-3 [PubMed: 8874461]
86. Esparza J, Osmanov S, Pattou-Markovic C, Toure C, Chang ML, Nixon S. Past, present and future of HIV vaccine trials in developing countries. *Vaccine.* 2002; 20:1897–8.10.1016/S0264-410X(02) 00062-2 [PubMed: 11983240]

Fig. 1.
The Vaccine Perceptions, Accountability and Adherence Model.