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Adolescent HPV vaccination: empowerment, equity and ethics

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ABSTRACT

Despite the great promise offered by human papillomavirus (HPV) vaccines to reduce disease burden and promote socioeconomic and gender equality, their implementation into national programmes has been slow. The vaccination of adolescents against a disease that may have serious consequences much later in life requires special consideration to the principles and processes of informed consent. Accumulating experiences from implementations in many countries indicate a need to examine ethical considerations related to adolescent vaccination. However, frameworks that integrate legal, development- and rights-based considerations in adolescent vaccination policies, while taking into account practical realities of HPV vaccination programmes, are currently lacking. We argue that principles of autonomy, social justice and gender equality have impacts on adolescent immunization that go beyond mere acceptance of vaccination and place greater demands on what constitutes meaningful informed consent, with implications for the provision of age- and context-appropriate information, vaccine financing and gender-based vaccination policies. Independent of cost-effectiveness considerations, we find a strong case to support universal HPV vaccination of girls that is free at the point of use and, where feasible, to extend vaccination to boys under the same financing schemes.

Abbreviations: HPV: Human papillomavirus; STI: Sexually transmitted infections; WHO: World Health Organization

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Background

The World Health Organization (WHO) recommends vaccination of girls aged 9–14 years against human papillomavirus (HPV).¹ Effective HPV vaccines have been available for over 10 years and have been shown to reduce the risk of cervical infection with high-risk HPV types by over 90%, and the risk of genital warts by over 80% among women who receive a full course of vaccination.¹ HPV vaccination programmes aimed at girls in this age group are likely to be highly cost-effective in most settings.² But despite notable successful national HPV immunization programmes, both in high- and low-income countries, HPV vaccination has yet to be introduced nationally in many countries, including most countries in Africa and Asia.³ Half a million cervical cancer cases and a quarter of a million cervical cancer deaths are caused by HPV worldwide each year.⁴ Of these, more than 80% occur in low- and middle-income countries, and women in the most economically productive age groups are disproportionately affected.⁵ HPV vaccine implementation is thus not simply an urgently-needed public health intervention – it is a development and equity issue.

Challenges affecting the roll-out and uptake of HPV vaccination have been described from numerous countries. Although these differ widely between settings, they include, among others, lack of infrastructure to support a national programme, insufficient political will, high vaccine

procurement and delivery cost at the national level, and inadequate involvement from healthcare professionals in recommending the vaccine at the provider level.^{6,7} Additionally, HPV vaccines have met resistance from certain groups who express a lack of confidence in or distrust of these vaccines, because they are perceived to be relatively new, are (inaccurately) portrayed as unsafe and ineffective, and are given to adolescents to protect against a sexually-transmitted infection, which may raise unwelcome discussions regarding adolescent sexual behavior.^{7,8}

HPV vaccination is recommended before the age of sexual debut, because the vaccine is expected to be less effective after an individual is exposed to HPV. HPV vaccine is unique in that, although consent to vaccinate adolescents is typically sought from those with parental responsibility, the benefits to individuals in terms of cancer prevention are not apparent until several decades later, once those adolescents have already reached the legal age of consent and when it may be too late to vaccinate. This is in stark contrast to vaccinations delivered in early childhood, which are primarily intended to protect against infections in the first few years of life, when children cannot reasonably be expected to make informed decisions about their healthcare.

Vaccination of adolescents requires additional considerations for the principles and processes of informed consent,

not least for school-based programmes in which vaccination is administered without the presence of parents or legal guardians. The WHO has issued considerations regarding consent for vaccination in children and adolescents,⁹ but these do not address certain issues specific to HPV vaccination. Existing position papers and considerations regarding adolescent vaccination pay particular attention to legal aspects of consent in minors.^{9,10} Others have argued for the importance of adopting a rights-based approach to adolescent vaccination,¹¹ in line with the United Nations Convention on the Rights of the Child, which emphasizes children's rights to have their best interests considered in societal decisions, to achieve optimal survival and development, to express opinions freely, to have access to information and act on it, to have their privacy respected, and to have access to the highest standard of healthcare.¹² More broadly, the Sustainable Development Goals underpin a global commitment to policies that reduce gender and economic inequality. Despite these individual guidelines and global goals, frameworks that integrate these legal, development- and rights-based considerations in adolescent vaccination decisions, while taking into account the practical realities of HPV vaccination programmes, are currently lacking.

While others have used ethical¹³ and social justice¹⁴ perspectives to explore the scope and financing of HPV vaccination programmes, we seek to extend these views in light of accumulating experiences from implementations in an increasing number of countries. In this paper, we argue that HPV vaccination is unlike other vaccinations currently administered to adolescents, both in its purpose and the long-term benefits and consequences of vaccination, and that this has far-reaching implications that make greater demands on the informed consent process. We therefore begin with an examination of what constitutes informed consent in the context of adolescent HPV vaccination and the implications for information provision and models of consent. We subsequently discuss the consequences that these greater demands on the informed consent process have for both vaccine financing and gender-based vaccination policies in adolescents.

Consent

In certain areas of healthcare, precedent exists to consider and respect adolescents' increased capacity for making healthcare decisions, including access to sexual and reproductive health services. In some settings, adolescents have legal rights to seek contraceptive advice, access diagnosis and treatment for sexually transmitted infections (STI), or seek pregnancy termination without parental knowledge or consent if they are deemed to be sufficiently mature and intelligent to understand the nature and implications of a proposed intervention. These are based on the common law rules of Gillick competence (in the UK) or the mature minor doctrine (in the US and Canada), or similar jurisdiction-specific statutory law.

Adolescents' rights in the area of vaccination have received less attention. Whether adolescents should have the right to self-consent for HPV vaccination is a subject of debate,¹⁵ despite it being an intervention for STI prevention.¹¹ In settings where Gillick competence may provide the legal basis for

adolescent self-consent, immunization providers have been found to be reluctant to vaccinate without obtaining written parental consent first.¹⁶ However, the epidemiological characteristics of HPV as an infection that has major health consequences predominantly in women, the potential for an adolescent vaccine to prevent disease beyond the age of majority, and the increasing capacity of adolescents to make informed decisions regarding their own healthcare, supports a greater role for adolescents in decision-making and consent for vaccination. The limited available empirical evidence from studies in adolescents indicates that a substantial fraction of individuals aged 10 to 15 years consider themselves sufficiently mature to make vaccination decisions^{17,18} and that, from adolescents' perspectives, cooperation with vaccination does not equate to consent.¹⁸ Another study found that children above the age of 11 years can be considered fully competent in medical decision-making and using age as a guide for decision-making capacity is reasonable.¹⁹

Adolescents' decision-making capacity should not in itself ethically or legally justify their decisional authority,²⁰ as there may be good reasons in a given society or context to invest decisional authority in parents or ensure their involvement for certain healthcare decisions. For example, vaccinations other than HPV are commonly administered to adolescents, including booster doses of diphtheria, tetanus and pertussis vaccines, and in some settings meningococcal and seasonal influenza vaccines. These serve three main functions – to counter waning immunity in individuals, immunize individuals who may have been missed earlier, or prevent outbreaks in higher-risk settings like schools and universities. These functions have implications that have bearing on the nature of consent for vaccination, which is generally granted by parents. Firstly, booster doses are, in most individuals, interventions that have already been administered in similar form earlier in life, and are thus part of completing a course of a vaccination to which parents have already consented. Secondly, particularly in the case of infections transmitted through the respiratory route or through close contact, the prevention of outbreaks is a collective responsibility; individual adolescents have limited agency to prevent exposure to or transmission of influenza virus or *Bordetella pertussis*, for example, and so cannot be expected to bear responsibility for outbreak prevention. In this circumstance, we believe there is a stronger ethical case for the responsibility of consent to rest primarily with parents or those with legal authority.

We see four key distinctions in the case of HPV vaccination that differentiate it from these other adolescent vaccines. Firstly, HPV vaccination is intended to reduce the risk of infection and disease from a sexually-transmitted infection, exposure to which is less institutionally-dependent and may happen not just in adolescence but well beyond the legal age of consent. Secondly, alternative ways exist to prevent HPV infection, including abstaining from sexual activity and safer sex practices to reduce infection risk. Implicit in these alternatives are issues of gender and power relations that are relevant when assessing their effectiveness, as well as a need to recognize that contextual factors may moderate one's ability to negotiate sexual interactions that may influence individual risk of infection. Greater agency over these alternatives

means greater responsibility to self and to others, but also means that individuals should be better informed about those responsibilities, so that they can make more informed decisions when choosing among a set of alternative or complementary preventive measures. Thirdly, HPV vaccination has implications for health needs and behaviors in later life, particularly cervical cancer screening. Fourthly, the major disease manifestation, cervical cancer, primarily occurs in adulthood, when its impact is particularly acute, as it affects women at a time in their life when they are typically at their most economically productive and when they may also bear responsibility over others, including children. These considerations augment the case for allowing adolescents to have greater influence in vaccination decision-making and consent, rather than placing responsibility solely on parents.

It is important to note, however, that both Gillick competence and the mature minor doctrine prescribe the need for parental involvement unless it is contrary to the best interests of the minor.²¹ Examples are when the parents are unavailable or unwilling to provide consent when the minor would like to receive an intervention, would benefit from it, and would otherwise be harmed if it were withheld. This ethico-legal understanding notwithstanding, the moral need to include adolescents in the informed consent process is particularly strong for HPV vaccination, given the potentially serious implications in the later life of an adolescent being denied vaccination. There is therefore a strong case favoring the active involvement of adolescents and the inclusion of their views in the informed consent process, even in jurisdictions where parental consent is the default requirement for general medical care. The exact mechanism of consent for HPV vaccination may vary between settings and may involve opt-in or opt-out, written or verbal, implicit or explicit approaches. Regardless of the specific mechanism and legal responsibility for consent, adolescent involvement in HPV vaccination should go beyond the moral concept of pediatric assent, which in the context of large-scale vaccination programmes may often be taken as a child's acceptance of vaccination. Involving adolescents in the informed consent process means that adolescents should be free to express their views regarding their own vaccination, be entitled to have those views heard, have influence over the decision of whether or not to vaccinate, and share in the responsibility for that decision.

Our practical recommendations are as follows. In settings where written consent is required and where there is legal basis, adolescents should be allowed to self-consent to HPV vaccination as a right. Alternatively, a dual consent approach with equal weight given to parent and adolescent decisions could be implemented, particularly if there is general reluctance among providers or adolescents themselves to rely on adolescent self-consent alone. In all settings, adolescents, including those without decision-making capacity, should be adequately informed about the benefits and consequences of HPV vaccination, as well as what they should expect during the vaccination process itself. Importantly, information should be age-appropriate. Evidence from both high- and low-middle income settings indicates that there is a need to improve awareness and knowledge of HPV vaccination among adolescents.^{22,23} In an evaluation of the school-based HPV vaccination programme in Australia,

adolescents reported that although information on the vaccine was provided, this was targeted at adults and not easy for adolescents themselves to comprehend.²⁴ Furthermore, information provided to adolescents should include considerations of the benefits and risks of vaccination, the consequences of a decision to vaccinate or not vaccinate, and the implications for cancer screening later in life. In addition, the potential impact of vaccine delivery itself should be communicated.²⁵ Few studies have sought to understand HPV vaccination programmes from the perspective of adolescents being vaccinated. Studies from Australia reported a number of challenges in the delivery of school-based HPV vaccination, including anxiety among students resulting from fear of injection pain, having to wait for extended periods, as well as difficulties in maintaining privacy.²⁴ The latter could be particularly important for HPV vaccine, as pregnancy status may need to be determined at the time of vaccination, the unintentional disclosure of which could result in individuals being stigmatized and could have serious legal ramifications in some settings. Anxiety resulting from the spread of rumors among students has also been reported by some studies,²⁶ while in some settings mass psychogenic events resulting from large-scale HPV vaccination have been documented.^{27,28} Integrating respect for privacy as a key aspect in the processes of consent and delivery, and targeting information at adolescents could directly address these issues and make adolescents better informed about what to expect during the vaccination process.

Vaccine financing

Equitable access to HPV vaccines within and between settings is intrinsically linked with social justice, given the potential of these vaccines to address serious medical, economic and social challenges arising from cervical cancer in women. Access to vaccines, however, is intimately linked to vaccine financing and cost. Studies of young women and parents of adolescents repeatedly find that high vaccine cost is a major barrier to HPV vaccination.^{29,30} Malmqvist et al. discuss ethical considerations for various possible models for financing adolescent HPV vaccination, ranging from an individual-initiated model in which vaccination is paid for entirely out-of-pocket, to a fully publicly-funded model mandating vaccination of both girls and boys.¹³ We do not repeat these here, but argue that greater involvement of adolescents in vaccination decisions additionally has important consequences for vaccine financing. Giving adolescents greater agency in vaccination decisions through appropriate information provision and self-consent, dual consent or shared decision-making processes, may become moot in situations in which financial constraints affect the decision. By and large, adolescents do not have the means to pay for healthcare interventions, so financial barriers to vaccine access introduce severe asymmetries to adolescents' say in vaccination decision-making, since adolescents are unable to pay for the vaccine even if they wish to have it, while parents might discourage or refuse vaccination on the basis of cost. This severely impinges on adolescents' autonomy (their governance over their own body and health), since it introduces the potential for vaccination decisions to be dependent on affordability, over which adolescents generally have no control.

Decisions based on individual affordability could also have other negative impacts. In school-based programmes where HPV vaccines are not provided for free, inequity in vaccine access has the potential to introduce stigma among students in lower income groups. At the population level, individuals' inability to pay for HPV vaccine is likely to further widen health and financial disparities based on gender and socio-economic position, particularly in settings where access to cancer screening is also limited.³¹ By contrast, analyses indicate that publicly-funded HPV vaccination is likely to promote greater equity by affording proportionately greater health benefits to lower income groups. Publicly-funded HPV vaccination programmes have also been shown to result in higher coverage compared with programmes in which individuals pay out of pocket.²⁹ Higher coverage is likely to have additional benefits, including indirect protection of unvaccinated individuals through herd immunity and encouraging vaccination as normative behavior. Conversely, having to pay for the vaccine may give individuals the impression that it is less of a priority compared with other publicly-funded vaccines.

Gender-based vaccination

Among countries with national adolescent HPV vaccination programmes, only a minority have extended universal vaccination to adolescent boys. In some countries, the vaccine is recommended for adolescent boys, but whether it is publicly funded or paid for out of pocket may depend on sub-national vaccination policies or insurance coverage. In still other countries, HPV vaccine may be licensed for adolescent boys, but must be paid for out of pocket, regardless of whether public financing exists for vaccination of adolescent girls. Arguments in favor of girls-only vaccination are based on the fact that females are disproportionately affected by the health effects of HPV, that heterosexual males will be largely protected from HPV infection by herd immunity if vaccine coverage in females is sufficiently high, as well as lack of conclusive evidence regarding the cost-effectiveness of extending vaccination to boys.³²

Cost-effectiveness analyses weigh up the cost of implementing a new vaccination programme against the societal burden of avoidable morbidity and mortality. Such analyses are increasingly used to provide objective metrics for informing vaccination policies. In settings with large private health sectors, however, cost-effectiveness assessments may be less clear cut, because while the state is usually responsible for decisions regarding vaccine introduction, the costs of vaccination and the healthcare costs of avoidable illness may be shared by a mixture of public financing, private insurance and out-of-pocket payments. Cost-effectiveness analyses generally do not capture how much these different actors are willing to pay to avoid illness, or broader societal benefits resulting from greater gender equity and reduced socioeconomic disparities. Furthermore, given a certain disease burden, vaccine efficacy profile and price, cost-effectiveness is dependent on a minimum level of vaccination coverage being reached, which is more difficult to achieve if the programme is not publicly funded and implemented. Current evidence indicates that increasing coverage in girls is more

cost-effective than offering gender-neutral vaccination, as girls only vaccination offers direct protection against cervical cancer and indirectly protects males against HPV infection. Extending vaccination to boys could be cost-effective in settings with low vaccination coverage in girls.^{33,34} Particularly in settings where female HPV vaccination coverage is modest and difficult to increase, there may be a strong scientific case for extending vaccination to boys with the same financing mechanisms as those available for vaccinating girls.

Notwithstanding these cost-effectiveness considerations, strong arguments exist for extending universal, publicly-funded HPV vaccination to adolescent boys based on principles of autonomy, social justice and gender equity.¹³ Although the health burden from HPV disproportionately affects women and the priority should be to increase vaccination coverage in girls, an argument could be made that adolescent boys should reasonably expect the direct benefits of vaccination rather than rely on indirect protection that depends on the vaccination and sexual behavior of others. In addition, HPV still causes a substantial disease burden in men. A recent study from the United States found a 3-fold higher prevalence of oral HPV infection in men compared with women,³⁵ and men have a higher risk of certain HPV-related cancers, such as head and neck cancers, that are increasing in incidence in many regions.⁴ While burden in heterosexual men may be decreased given high female HPV vaccine coverage, the existence of certain male groups at higher risk of HPV infection and disease, such as men who have sex with men, could be an argument in favor of more equitable strategies specifically focusing on these groups. However, identifying individuals in these groups during early adolescence may be difficult and could have legal implications in some settings, while delaying vaccination until after sexual debut is likely to decrease vaccine effectiveness.

Secondly, while women may experience the bulk of HPV-related disease burden, both men and women contribute to HPV transmission. Given that there is no substantive gender difference in the profile of HPV vaccines in terms of safety and effectiveness against HPV infection, implementing girls-only vaccination places the burden for HPV prevention overwhelmingly on women. Men benefit from indirect protection when female vaccination coverage is high without taking on any potential risks (albeit minimal) associated with vaccine adverse effects, despite the existence of a means for them to contribute to prevention of HPV infection and disease. Such 'free-riding' seems at the very least to be morally questionable. Extending universal vaccination to adolescent boys promotes their ability to contribute to a public good that leads to a net benefit for each individual person vaccinated, and which would not make the community worse off in general from a public health ethics perspective.³⁶

Finally, much controversy regarding HPV vaccination and reluctance to vaccinate has resulted from societal perceptions that vaccination encourages earlier sexual debut, increases sexual activity or promotes risky sexual behavior, particularly among adolescent girls. Numerous studies have failed to provide evidence for such behavioral changes in either gender.^{37,38} By contrast, studies have found support for HPV vaccination of boys from community members, parents and healthcare providers,

who consider this an important way to emphasize boys' responsibilities toward sexual health and reduce gender-based stigma surrounding sexual activity.³⁹ Indirectly, therefore, a gender-neutral approach promotes the moral norm of a shared responsibility in all adolescents regardless of gender, while reducing misconceptions of girls as having principal responsibility for HPV transmission and prevention, potentially increasing consent for vaccination and improving vaccine uptake.

Conclusions and recommendations

Adolescent consent for HPV vaccination is intrinsically related to vaccine financing and principles of health and gender equity. Respect for adolescents' autonomy requires that due consideration be given to how vaccine financing impinges on adolescents' capacity to influence decisions about their own future health. Furthermore, commitments to reducing global health inequalities need to recognize the unique role that HPV vaccines can play in promoting both health and gender equity. On this basis, we believe that there are strong ethical and scientific grounds in support of universal vaccination of adolescent girls against HPV that is free at the point of use. In settings where it is feasible, extending vaccination to adolescent boys should be considered on the basis that these are likely to bring about societal benefits beyond simply cost-effectiveness, including promoting adolescent vaccination as normative behavior, reducing gender-based stigma related to vaccination, and a sense of shared responsibility for HPV prevention. Where vaccine coverage among girls is low and difficult to increase, these arguments are further strengthened by increased cost-effectiveness of extending vaccination to both genders. Where HPV vaccination is not fully publicly funded but financed partly through subsidies or reimbursements, there is a strong equity argument for making HPV vaccines available to both girls and boys through the same financing mechanisms.

Our central argument focuses on what should be understood to constitute meaningful informed consent in the context of HPV vaccination, which we take to include the provision of age-appropriate information regarding the benefits, consequences and process of HPV vaccination, as well as the active inclusion of adolescents' views in vaccination decisions, regardless of existing legal frameworks of consent. Our arguments and conclusions are therefore not limited to any specific setting. The extent to which adolescents are actively involved in decision-making about HPV vaccination, beyond simply pediatric assent, is difficult to assess and may (perhaps appropriately) vary across families. Further research in this area and experience from HPV vaccine implementing countries will be highly informative for developing guidance on how best to respect adolescents' autonomy and privacy while safeguarding their best interests throughout the consent and vaccine delivery processes. The consent process should at the very least include age-appropriate information for adolescents on benefits and consequences of vaccination, as well as information regarding what to expect during the process of vaccine delivery. Although the role of adolescents in spreading negative perceptions about vaccination has been well documented,^{26,40} adolescents' potential role in promoting positive attitudes to vaccination, for example through the

sharing of positive vaccination experiences with unvaccinated peers, has received little attention and warrants further research. Valuing and empowering adolescents in this way not only affirms their role as engaged and active contributors to decision making, but also fulfills a strategic objective of the Global Vaccine Action Plan that "*individuals and communities understand the value of vaccines and demand immunization as both their right and responsibility*".

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References

1. World Health Organization. Human papillomavirus vaccines: WHO position paper, May 2017. *Releve Epidemiologique Hebdomadaire*. 2017;92(19):241–68.
2. Jit M, Brisson M, Portnoy A, Hutubessy R. Cost-effectiveness of female human papillomavirus vaccination in 179 countries: a PRIME modelling study. *Lancet Global Health*. 2014;2(7):e406–414. doi:10.1016/S2214-109X(14)70237-2.
3. Bruni L, Diaz M, Barrionuevo-Rosas L, Herrero R, Bray F, Bosch FX, de Sanjosé S, Castellsagué X, et al. Global estimates of human papillomavirus vaccination coverage by region and income level: a pooled analysis. *Lancet Global Health*. 2016;4(7):e453–463. doi:10.1016/S2214-109X(16)30099-7.
4. International Agency for Research on Cancer. GLOBOCAN 2012: estimated cancer incidence, mortality and prevalence worldwide in 2012. [accessed 2018 Jan 04] http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx.
5. de Martel C, Plummer M, Vignat J, Franceschi S. Worldwide burden of cancer attributable to HPV by site, country and HPV type. *Nt J Cancer*. 2017;141(4):664–70. doi:10.1002/ijc.v141.4.
6. Howard N, Gallagher KE, Mounier-Jack S, Burchett HED, Kabakama S, LaMontagne DS, Watson-Jones D, et al. What works for human papillomavirus vaccine introduction in low and middle-income countries? *Papillomavirus Res*. 2017;4:22–25. doi:10.1016/j.pvr.2017.06.003.
7. Markowitz LE, Tsu V, Deeks SL, Cubie H, Wang SA, Vicari AS, Brotherton JML, et al. Human papillomavirus vaccine introduction—the first five years. *Vaccine*. 2012;30(Suppl 5):F139–148. doi:10.1016/j.vaccine.2012.05.039.
8. Ferrer HB, Trotter C, Hickman M, Audrey S. Barriers and facilitators to HPV vaccination of young women in high-income countries: a qualitative systematic review and evidence synthesis. *BMC Public Health*. 2014;14:700. doi:10.1186/1471-2458-14-700.
9. World Health Organization. Considerations regarding consent in vaccinating children and adolescents between 6 and 17 years old. 2014; [accessed 2018 Jan 01]. http://www.who.int/immunization/programmes_systems/policies_strategies/consent_note_en.pdf.
10. English A, Ford CA, Kahn JA, Kharbanda EO, Middleman AB. Adolescent consent for vaccination: a position paper of the society for adolescent health and medicine. *J Adolesc Health off Publ Soc Adolesc Med*. 2013;53:550–53.

11. Nathawad R, Goldhagen J. A child rights and equity-based framework to advance policy and practice related to adolescent consent to vaccines. *J Adolesc Health off Publ Soc Adolesc Med.* 2014;54(5):619. doi:10.1016/j.jadohealth.2014.02.007.
12. United Nations General Assembly. Res 44/25, convention on the rights of the child. 1989; Accessed 2013 Dec 24. <http://www.un.org/documents/ga/res/44/a44r025.htm>.
13. Malmqvist E, Helgesson G, Lehtinen J, Natunen K, Lehtinen M. The ethics of implementing human papillomavirus vaccination in developed countries. *Med Health Care Philos.* 2011;14(1):19–27. doi:10.1007/s11019-010-9285-9.
14. Thompson A. Human papilloma virus, vaccination and social justice: an analysis of a Canadian school-based vaccine program. *Public Health Ethics.* 2013;6(1):11–20. doi:10.1093/phe/pht010.
15. Agrawal S, Morain SR. Who calls the shots? The ethics of adolescent self-consent for HPV vaccination. *J Med Ethics.* 2018. doi:10.1136/medethics-2017-104694.
16. Audrey S, Batista Ferrer H, Ferrie J, Evans K, Bell M, Yates J, Roderick M, MacLeod J, Hickman M, et al. Impact and acceptability of self-consent procedures for the school-based human papillomavirus vaccine: a mixed-methods study protocol. *BMJ Open.* 2018;8:3. doi:10.1136/bmjopen-2017-021321.
17. Katahoire AR, Wani JA, Murokora D, Mugisha E, LaMontagne DS. Acceptability of HPV vaccine among young adolescent girls in Uganda: young people's perspectives count. *Int J Child Adolesc Health.* 2013;6:211.
18. Rylance G, Bowen C, Rylance J. Measles and rubella immunisation: information and consent in children. *BMJ.* 1995;311(7010):923–24. doi:10.1136/bmj.311.7010.923.
19. Hein IM, De Vries MC, Troost PW, Meynen G, Van Goudoever JB, Lindauer RJ. Informed consent instead of assent is appropriate in children from the age of twelve: policy implications of new findings on children's competence to consent to clinical research. *BMC Med Ethics.* 2015;16(1):76. doi:10.1186/s12910-015-0067-z.
20. Salter EK. Conflating capacity and authority: why we're asking the wrong question in the adolescent decision-making debate. *Hastings Center Report.* 2017;47(1):32–41. doi:10.1002/hast.666.
21. Coleman DL, Rosoff PM. The legal authority of mature minors to consent to general medical treatment. *Pediatrics.* 2013;131(4):786–93. doi:10.1542/peds.2012-2470.
22. Patel H, Jeve YB, Sherman SM, Moss EL. Knowledge of human papillomavirus and the human papillomavirus vaccine in European adolescents: a systematic review. *Sex Transm Infect.* 2016;92(6):474–79. doi:10.1136/sextrans-2015-052341.
23. Salwa M, Abdullah Al-Munim T. Ethical issues related to human papillomavirus vaccination programs: an example from Bangladesh. *BMC Med Ethics.* 2018;19(Suppl 1):39. doi:10.1186/s12910-018-0287-0.
24. Braunack-Mayer A, Skinner SR, Collins J, Tooher R, Proeve C, O'Keefe M, Burgess T, Watson M, Marshall H, et al. Ethical challenges in school-based immunization programs for adolescents: a qualitative study. *Am J Public Health.* 2015;105(7):1399–403. doi:10.2105/AJPH.2014.302280.
25. Kabakama S, Gallagher KE, Howard N, Mounier-Jack S, Burchett HED, Griffiths UK, Feletto M, LaMontagne DS, Watson-Jones D, et al. Social mobilisation, consent and acceptability: a review of human papillomavirus vaccination procedures in low and middle-income countries. *BMC Public Health.* 2016;16(1):834. doi:10.1186/s12889-016-3517-8.
26. Brabin L, Roberts SA, Stretch R, Baxter D, Elton P, Kitchener H, McCann R, et al. A survey of adolescent experiences of human papillomavirus vaccination in the Manchester study. *Br J Cancer.* 2009;101(9):1502–04. doi:10.1038/sj.bjc.6605362.
27. Buttery JP, Madin S, Crawford NW, Elia S, La Vincente S, Hanieh S, Smith L, Bolam B, et al. Mass psychogenic response to human papillomavirus vaccination. *Med J Aust.* 2008;189(5):261–62. doi:10.5694/mja2.2008.189.issue-5.
28. Domingues CMAS, AGK M, Pinto MFS. The introduction of HPV vaccines in Brazil: advances and challenges. *DST - J Bras Doenças Sex Transm.* 2015;27:67–72.
29. Rambout L, Tashkandi M, Hopkins L, Tricco AC. Self-reported barriers and facilitators to preventive human papillomavirus vaccination among adolescent girls and young women: a systematic review. *Prev Med.* 2014;58:22–32. doi:10.1016/j.ypmed.2013.10.009.
30. Pourat N, Jones JM. Role of insurance, income, and affordability in human papillomavirus vaccination. *Am J Manag Care.* 2012;18:320–30.
31. Crowcroft NS, Hamid JS, Deeks SL, Frank J. Human papilloma virus vaccination programs reduce health inequity in most scenarios: a simulation study. *BMC Public Health.* 2012;12:935. doi:10.1186/1471-2458-12-935.
32. Brisson M, Benard É, Drolet M, Bogaards JA, Baussano I, Vänskä S, Jit M, Boily M-C, Smith MA, Berkhof J, et al. Population-level impact, herd immunity, and elimination after human papillomavirus vaccination: a systematic review and meta-analysis of predictions from transmission-dynamic models. *Lancet Public Health.* 2016;1(1):e8–e17. doi:10.1016/S2468-2667(16)30001-9.
33. Ben Hadj Yahia MB, Jouin-Bortolotti A, Dervaux B. Extending the human papillomavirus vaccination programme to include males in high-income countries: a systematic review of the cost-effectiveness studies. *Clin Drug Investig.* 2015;35(8):471–85. doi:10.1007/s40261-015-0308-4.
34. Jiang Y, Gauthier A, Postma MJ, Ribassin-Majed L, Llargeron N, Bresse X. A critical review of cost-effectiveness analyses of vaccinating males against human papillomavirus. *Hum Vaccin Immunother.* 2013;9(11):2285–95. doi:10.4161/hv.25754.
35. Sonawane K, Suk R, Chiao EY, Chhatwal J, Qiu P, Wilkin T, Nyitray AG, Sikora AG, Deshmukh AA, et al. Oral human papillomavirus infection: differences in prevalence between sexes and concordance with genital human papillomavirus infection, nhanes 2011 to 2014. *Ann Intern Med.* 2017;167(10):714–24. doi:10.7326/M17-1363.
36. van den Hoven M. Why one should do one's bit: thinking about free riding in the context of public health ethics. *Public Health Ethics.* 2012;5(2):154–60. doi:10.1093/phe/phs023.
37. Kumakech E, Andersson S, Wabinga H, Musubika C, Kirimunda S, Berggren V. Cervical cancer risk perceptions, sexual risk behaviors and sexually transmitted infections among Bivalent Human Papillomavirus vaccinated and non-vaccinated young women in Uganda - 5 year follow up study. *BMC Women Health.* 2017;17(1):40. doi:10.1186/s12905-017-0394-y.
38. Mullins TLK, Rosenthal SL, Zimet GD, Ding L, Morrow C, Huang B, Kahn JA. Human vaccine-related risk perceptions do not predict sexual initiation among young women over 30 months following vaccination. *J Adolesc Health.* 2018;62(2):164–9. doi:10.1016/j.jadohealth.2017.09.008.
39. Noakes K, Yarwood J, Salisbury D. Parental response to the introduction of a vaccine against human papilloma virus. *Hum Vaccin.* 2006;2(6):243–48. doi:10.4161/hv.2.6.3391.
40. Turiho AK, Okello ES, Muhwezi WW, Harvey S, Byakika-Kibwika P, Meya D, Katahoire AR, et al. Effect of School-based Human Papillomavirus (HPV) vaccination on adolescent girls' knowledge and acceptability of the HPV vaccine in Ibanda district in Uganda. *Afr J Reprod Health.* 2014;18(4):45–53.