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Integration of other services with human papillomavirus vaccination; lessons from earlier in the life course highlight the need for new policy and implementation evidence ☆

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ABSTRACT

Integration of vaccination against human papillomavirus (HPV) with other essential health services for adolescents has been proposed in global strategies and tested in demonstration projects in low- and middle-income countries (LMIC). Published experiences, global guidance, and one key example, the implementation of "HPV Plus" in Tanzania, all demonstrate the need for greater operational evidence to guide future implementation and policy.

Review of experiences earlier in the life course, integrating post-partum family planning with infant immunization, show lessons from 13 LMICs that can apply to provision of adolescent health information and services alongside HPV vaccination. Three distinct models of integration emerge from this review comprising: 1) multiple tasks and functions by health staff providing vaccination and other care, or 2) secondary tasks added to the main function of vaccination, or 3) co-location of matched services provided by different staff. These models, with strengths and weaknesses demonstrated in family planning and immunization experiences, apply in different ways to the three main platforms used for HPV vaccination: school, facility or community.

For HPV vaccination policy and programming, an initial need is to combine the existing evidence on vaccine service delivery – including coverage, efficiency, cost, and cost-effectiveness information – with what is known on how integration works in practice; the operational detail and models employed. This synthesis may enable assessment which models best suit the different service delivery platforms. An additional need is to link this with more tailored local assessments of the adolescent burden of disease and other determinants of their well-being to develop new thinking on what can and cannot be done to integrate other services alongside HPV vaccination.

New approaches placing adolescents at the center are needed to design services tailored to their preferences and needs. The potential synergies with cervical cancer screening and treatment for older generations of women, also require further exploration. Coordinated action aligning HPV vaccination with broader adolescent health and wellbeing will generate social, economic and demographic benefits, which in themselves are sufficient justification to devote more attention to integrated approaches.

Abbreviations: HPV, Human papillomavirus; LMIC, Low- and middle-income country; WHO, World Health Organization.

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1. Introduction

Integration of other essential health services with immunization can increase coverage and access. Integration features as a priority in the global Immunization Agenda 2030 (IA2030) [1], as well as Gavi, the Vaccine Alliance's 2021–2025 strategy to deliver on equity, transformative approaches to gender, and leaving no one behind [2]. Both are closely linked to life course vaccination, a concept exemplified by vaccination of adolescent girls against human papillomavirus (HPV). In this commentary, we discuss the application of implementation lessons across the life course to HPV vaccine integration. We call for the establishment of a stronger policy and measurement agenda across the outcomes, operations, and service delivery models of integration, better tailored to country setting.

2. Integration of HPV vaccine with other services is an established priority, but programmatic evidence is needed in LMICs

When vaccinating girls against HPV, linking information and services relevant for adolescent health has been explored in HPV vaccine demonstration projects such as in Tanzania [3], and other low- and middle-income countries (LMICs) [4,5], whose resource-constrained settings are the focus of this commentary. The importance of taking every opportunity to promote and sustain adolescent health [6] is well established. Conversely, integration of HPV vaccine into existing child or school health programs, where such programmes exist in sufficient strength, has been important for efficiency and coverage [7,8].

Repeated reviews [7,8] have consolidated HPV vaccine introduction experiences, with limited description of where some non-vaccination services have been integrated. A systematic analysis has described adolescent health interventions with likely health benefits, focused on those that may prove feasible during school-based vaccination [9]. The World Health Organization (WHO) published guidance in 2014 on HPV vaccine integration [10] consistent with this evidence, and a 2018 WHO integration resource guide describes platforms suited to adolescent health alongside HPV vaccination [11]. What is missing is clear description of how these work in practice, and what policy is supportive, although one review across 17 African countries did capture reports of commonly linked services. This listed experiences with health education (including reproductive or sexual health topics), deworming medicine distribution, and other vaccines; and less commonly nutritional supplements or checks on growth or vision [12].

In one example, Tanzania's national immunization program, with support from partners, instituted "HPV-Plus" [13], that advocates for adolescent health education, de-worming, nutrition and vision screening, alongside HPV vaccination in schools, health facilities and community outreach. Evaluations were underway in 2021, however reports from earlier in Tanzania's introduction highlight likely implementation challenges [3], and many working on HPV immunization [7,8,12,14], have called for better documentation of the processes that underpin optimal integration strategies. There is room to increase the quality of published evidence on what operational details drive success, and which models of HPV vaccine service integration are most feasible, cost-efficient and effective; especially at scale.

3. Integration experiences from earlier in the life course may inform integration of HPV vaccination

Integration of other services with vaccination in the first years of life has a longer history than HPV vaccination. A key supplement to *Vaccine* in 2012 documented examples of using the infant immunization platform to provide hearing screening, human immunodeficiency virus (HIV) services, vitamin A supplements, deworming, malaria treatment or bed-nets, family planning (FP), growth monitoring, and health education [15]. Since then, the evidence base has expanded most notably in integration of early infant diagnosis and treatment for HIV [16] and in FP information and services; the latter in particular providing operational insights, some of which can inform HPV vaccine integration efforts.

Post-partum FP education or contraceptive distribution alongside infant immunization has a rich array of published experiences from the past decade, with examples from Benin [17], Burkina Faso [18], Ethiopia [19,20], Ghana [21], India [22], Liberia [23,24], Malawi [25,26], Nigeria [27], Rwanda [28], Senegal [29], and Zambia [21]; or with an expanded package adding infant growth and nutrition services in Kenya [22,30] and Sierra Leone [31]. Most of these (all but [18,21,27]) measured encouraging outcomes showing benefits in FP knowledge, attitudes or behaviors, including contraceptive uptake. Where measured, this was without adverse impact on immunization services. Some experiences saw services shifting closer to the community [18–20,25], potentially relevant to integrated services for out-of-school girls. Some researchers [22,26], however, cautioned against unintended reduction in equitable coverage if integrating services only at facilities limits their availability to those who already have access.

Operational details were key to success or failure in FP-immunization integration; many of which are likely to apply to HPV vaccine integration. These drivers included: adequate staff numbers and time if vaccinators are to do additional tasks [18–21,24,27,30], sufficient training for new services such as counselling or referral [20,21,23,26–28,31], supporting staff with tailored job aids [21,23,27–29,31], infrastructure that promotes privacy and easy inter-departmental referral [23,30], alignment of service delivery times [23,25,27,28], harmonization of health records [31], coordinated reliable supply chains [23,25,30], and clear regular communications between immunization and reproductive health programme managers [18,23]. Social and gender inequalities also affect uptake, such as the need for a husband's approval delaying or obstructing contraception decisions [20,23,24,26,28]. This highlights the importance of formative exploration of social and cultural acceptability in intervention design, and for communications to avert confusion and distrust. In the short term, this may involve distinguishing immunization from other services with different sensitivities [21]; and in the longer-term by multi-sectoral alliances for advocacy, for example with religious or other social leadership [20].

4. Describing models of integration and service delivery platforms to guide future work

As well as the need for detailed planning and faithful implementation, these experiences illustrate the importance of choosing a model of integration that best matches the services to be integrated [25]. Below we discuss three main *models* of integrated service arrangements can be seen in the FP-immunization experiences; and their application to the different service delivery *platforms* relevant to HPV vaccine (see Fig. 1).

The first model involves staff, during vaccination sessions, taking on multiple tasks of equal importance, as in Malawi [26] or Ethiopia [20], where members of outreach teams were trained to vaccinate, as well as counsel on and provide contraceptives, among other services; a model perhaps suited to the lower clinic client numbers in rural outreach, and one that promoted equity. In Tanzania's implementation of "HPV-Plus" in three regions of the country [32], specifically trained nurses provide HPV vaccination, group

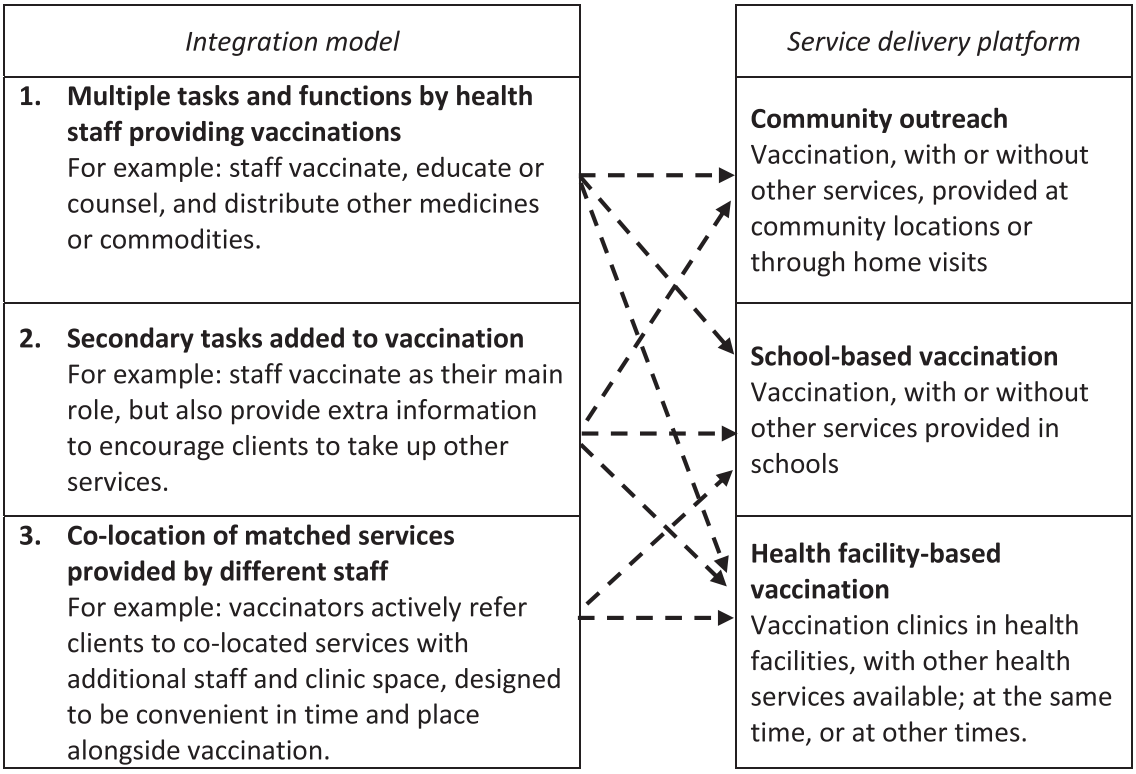

Fig. 1. Integration models and service delivery platforms. Integration models and service delivery platforms interact to describe who, when, and where integrated services are provided. Lines indicate potential application of integration model to service delivery platform.

education on adolescent sexual and reproductive health, and conduct screening for nutrition or visual difficulties.

The second model adds tasks that are secondary to the vaccinator's role, for example in Ghana and Zambia [21], where vaccinators were to provide extra information on FP during individual vaccination contacts. In this example the advice was deliberately brief so as to fit within busy vaccination clinics. No increase in contraceptive uptake was seen, most likely because the intervention was insufficient to change clients' behavior and/or because it was not implemented as designed. This sounds a cautionary note for HPV vaccine integration, for example when additional interventions, especially potentially complex counselling, are provided within the constraints of busy school-based or facility-based vaccination sessions [9]. However, in Togo [33], even short education sessions alongside HPV vaccination imparted new knowledge that could be retained by students, although the intervention was too short to measure outcomes in behavior change. There is a dearth, however, of published assessments of the outcomes of delivering potentially complex information on sexual and reproductive health alongside HPV vaccination at scale.

The third model expands both of the above with pro-active co-location of linked services. Examples come from for example in Liberia [23] and Rwanda [28] where vaccinators provided FP information and brief assessment of mothers' FP needs during vaccination. They then offered referral to FP services provided by other professional staff, in clinics that were arranged to be convenient in timing and location as part of the integration process. The successful co-delivery of information and services in Togo [33] combined the first and the third model, by having both educators and vaccinators working in close collaboration during vaccination sessions.

Other less common integration models include immunization advice or catch-up vaccination provided during other curative or preventive services. This was seen to some degree in Sierra Leone [31] where catchup vaccination was provided alongside childhood growth and nutrition services. Similarly, there is unexplored potential to promote HPV vaccination alongside cervical cancer screening, as explored in the systematic review also published in this supplement [34].

Beyond functional models discussed above, which describe who provides which service, the broader service delivery platform is critically important to HPV vaccine integration [11]. Most LMIC HPV vaccination programmes have either created school-based vaccination platforms [8] into which adolescent information and services can be integrated [9], or less commonly integrated vaccinations into pre-existing preventive care platforms, such as a school health service or child health weeks (as in Zambia) [7,8]. School-based delivery also illustrates the value a multisectoral engagement can bring to integration efforts, as highlighted in global guidance [10,11], in Tanzania [32] where education officials supported curriculum design and training, and in Togo [33], where the partnership provided educators to work alongside health staff.

Vaccination in health facilities is the other main platform where integration of additional services has been possible. For example, in Tanzania [32] the "HPV-Plus" integrated package is offered in both schools and facilities. Integration of highly clinical services, such as diagnosis and treatment of human immunodeficiency virus, may be better suited to health facility platforms, however no reviews to date have detailed analysis that differentiates integration packages by service delivery platform.

Reaching under-vaccinated communities including out-of-school girls has rested on promoting their attendance at facilities, supplemented in some countries by another platform: community outreach [7,8]. Multifunction health outreach teams, such as those used in Malawi [26] to integrate FP, other reproductive health and infant vaccination services, may offer lessons for reaching such girls with other services in addition to HPV vaccination. Multisectoral engagement seems critical to reaching this population;

such as with the education sector which may be critical in advocacy for and identification of out-of-school girls, and the collaboration with society leaders seen in some family planning experiences [20].

5. Implications for future efforts to integrated HPV vaccination with information and services for adolescents

An initial need is to combine the existing evidence on HPV vaccine service delivery across the three platforms – including coverage, efficiency, cost, and cost-effectiveness information – with what is known on the operational detail and models of integration. This synthesis may enable assessment of how HPV vaccine integration experiences can provide benefit, and which models best suit the different service delivery platforms. An additional need is to link this with assessment of the adolescent burden of disease and other determinants of their well-being (such as school completion) [35], tailored by setting, to start to refine both what is most feasible, and what will have the greatest impact when integrating information and services. Prospective work at scale may prove invaluable, for example in a set of countries representative of different types of adolescent health needs, using an implementation-oriented lens with a more people-centered focus. This could identify how to adapt existing, or develop new, policy models to optimize the health and economic impacts of the likely interventions. This can also consider key determinants such as the delivery platform, which packages of integrated services have best synergy, are most cost-effective, and which are most acceptable to providers and clients.

We also propose that future implementation research and programme evaluations take a more detailed and systematic approach to documenting the operational details (including costs), integration models, and service delivery platforms that are used when integrating information and services for adolescents with HPV vaccination. A more comparable set of measures may help to identify key points of feasibility and acceptability helpful to program managers deciding on service delivery arrangements at national and subnational levels. A richer description of intervention fidelity, "dosage", and reach, will also support assessment of feasibility, sustainability and the likely health impact; for example of sexual or reproductive health education. The evaluation of Tanzania's implementation of "HPV-Plus" will report late in 2021, and aims to help demonstrate which service delivery arrangements are likely to be most feasible in the long-term for Regional and District level programming.

Evidence is also needed as to what is most sustainable for national programs, for example the balance between school-, facility-, and community-based platforms, and the requirements for good quality integrated services. Application of tools, such as the module for costing adolescent health interventions in the United Nations OneHealth costing tool [36] can assist. Such evidence is needed to help countries using HPV vaccine now, and those contemplating introduction, for example on how to identify and overcome socio-economic barriers to accessing health services.

Measures of outcomes specifically attributable to improved integration are difficult at all levels, as are high-level measures of progress in integration. These have been attempted, however, in Immunization Agenda 2030 [1], and expanded upon in its January 2021 Framework for Action. The WHO and UNICEF also track co-delivery of vaccination with other intervention in schools through the Joint Reporting Form that countries submit annually; a review in trends in these measures would contribute significantly to assessing progress and opportunities in integration. Given that most programmes under consideration already track outcomes nationally and globally, it hoped that this may be achieved by better linkage of existing data, without any need to create a new complicated system.

One important area of consideration that fell outside the scope of this commentary is the potential for integration to generate demand for, and build confidence in, immunization and other adolescent health services. Interviews with adolescents in Uganda [37] demonstrated that receipt alongside other services was associated with significantly increased HPV vaccine uptake. While evidence is available on how to increase the acceptability of HPV vaccination in general, less well studied are the preferences of adolescents and their families for how services could be organized or which interventions they desire in an integrated package. As implied by many experiences collated above, this evidence also needs to consider the barriers raised by gender or social inequalities.

6. Conclusion

More work is needed on how to create effective, sustainable, and acceptable packages integrating HPV vaccination and adolescent health information and services. This requires clearer information on the matching of integration models with service delivery platforms (school, facility or community), their costs, and acceptability. New approaches placing adolescents at the center are needed to design services tailored to the particular adolescent health and well-being characteristics in different contexts. Essential operational detail includes documenting who provides integrated care, where and when, how adolescents' preferences are catered to, and how adolescents and communities can be better engaged. Critical to success are the broader long-term system and resource supports (programmatic, human and financial). The platform for care to adolescents is not yet sufficiently robust in many LMICs to serve all these needs, and it may be that an alliance across immunization, adolescent health and whole-of-life primary health care platforms is needed. The global integration working group that gave impetus to many post-partum FP-immunization experiences noted in 2018 that multiple stakeholders across reproductive health and nutrition (both maternal and infant) have as strong an investment in service delivery during early adolescence as does immunization.

It is also clear that elimination of cervical cancer as a public health problem requires vaccination, screening and treatment interventions to work in synchrony if those ambitious but achievable goals are to be realized and mortality reductions reached as soon as possible [38]. HPV vaccination platforms can do more, and current good practices need to be collected and analysed [34]. This has potential to benefit HPV vaccination, cervical cancer elimination, and broader adolescent health outcomes, and to align monitoring and evaluation of HPV vaccination with the integration aspirations in IA2030.

The potential gains for young people through stronger investment in adolescent health are enormous. Successful health interventions in adolescence generate a "triple dividend" from optimal health for adolescents themselves, healthier trajectories across the life course and a healthier start to life for the next generation [39]. Coordinated action towards adolescent health and wellbeing will further generate social, economic and demographic benefits, which in themselves are sufficient justification to devote more attention to integrated approaches.

CRediT authorship contribution statement

Christopher Morgan: Conceptualization, Methodology, Investigation, Project administration, Formal analysis, Writing – original draft, Writing – review & editing. **Mary Rose Giattas:** Conceptualization, Formal analysis, Writing – review & editing. **Taylor**

Holroyd: Conceptualization, Formal analysis, Writing – review & editing. **Anne Pfitzer:** Conceptualization, Formal analysis, Writing – review & editing. **Danielle Engel:** Conceptualization, Formal analysis, Writing – review & editing. **Anissa Sidibe:** Conceptualization, Formal analysis, Writing – review & editing. **Megan Holloway:** Conceptualization, Formal analysis, Writing – review & editing. **Paul Bloem:** Conceptualization, Formal analysis, Writing – review & editing. **Rebecca Fields:** Conceptualization, Formal analysis, Writing – review & editing. **Lora Shimp:** Conceptualization, Formal analysis, Writing – review & editing. **Somesh Kumar:** Conceptualization, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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