A Mixed Methods Analysis of the Implementation and Uptake of the Human Papillomavirus Vaccination of Adolescent Girls in Lusaka, Zambia

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A thesis submitted to the Faculty of Health Sciences, University of Witwatersrand, in fulfilment of the requirements for the degree

of PhD in Public Health

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DECLARATION

I, Mwansa Ketty Lubeya, declare that this thesis is my original, unaided work. It is being submitted for the degree of Doctor of Philosophy at the University of the Witwatersrand, Johannesburg, South Africa. It has not been submitted before for any degree or examination at any other University or institution.

Signed: Date 22nd October 2024

God is never late; his timing is always perfect.

I dedicate this thesis to my parents, Dackson Ngosa Lubeya and Agness Chibuye Lubeya, my siblings, my husband, Siamulunge, and my children: Felistus, Chibwili, Nthibe, Moobola, Ngosa, Mutinta, and baby Elina Luyando.

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4. **Lubeya MK**, Chibwesha CJ, Mwanahamuntu M, Mukosha M, Frank S, Kawonga M. "When you get the HPV vaccine, it will prevent cervical cancer; it will act as a shield": Adolescent girls' knowledge and perceptions regarding the human papillomavirus vaccine in Zambia. Frontiers in Health Services. 2023;3.

5. **Lubeya MK,** Chibwesha CJ, Mwanahamuntu, Mukosha M, Vwalika B, Kawonga M. Determinants of the Implementation of Human Papillomavirus Vaccination in Zambia: Application of the Consolidated Framework for Implementation Research. *Vaccines* ***2023*** https://www.mdpi.com/2076-393X/12/1/32

6. **Lubeya MK,** Mwanahamuntu M, Chibwesha CJ, Mukosha M, Kawonga M. Selecting and Tailoring Implementation Strategies to Improve Human Papillomavirus Vaccine Uptake in Zambia: A Nominal Group Technique Approach. Vaccines (Basel). 2024 May 15;12(5):542. doi: 10.3390/vaccines12050542. PMID: 38793793; PMCID: PMC11126122.

Newspaper article arising from this PhD

Low HPV vaccine uptake: Need for more sensitisation 28 June 2023, Zambia Daily Mail

QUOTES

"Women are not dying because of diseases we cannot treat. They are dying because societies have yet to make the decision that their lives are worth saving."

Professor Mahmoud Fathalla

"Through cost-effective, evidence-based interventions, including human papillomavirus vaccination of girls, screening and treatment of precancerous lesions, and improving access to diagnosis and treatment of invasive cancers, we can eliminate cervical cancer as a public health problem and make it a disease of the past."

Dr Tedros Adhanom Ghebreyesus

Abstract

Background and rationale: Cervical cancer is the most common female cancer in sub-Saharan Africa compounded by the high prevalence of HIV among women of reproductive age. The human papillomavirus (HPV), mainly transmitted sexually, and persistent infection with oncogenic strains is a necessary cause of cervical cancer. The HPVs largely cause mild and self-limiting disease in those who are immunocompetent.

In 2006, the World Health Organisation (WHO) approved the use of highly effective and immunogenic HPV vaccines for prepubertal girls aged 9 to 14 years, naive to sexual intercourse. Further, in 2020 WHO launched the global call for cervical cancer elimination which includes vaccinating 90% of girls by age 15 by 2023. These policies focus on improving cervical cancer primary prevention.

Despite the known vaccine effectiveness and policy pronouncements, uptake remains low in many LMICS including Zambia, where there is a cervical cancer highly prevalent. The low HPV vaccine uptake is partly due to low levels of knowledge about HPV and HPV vaccines, myths and misconceptions, and vaccine mistrust. Implementation barriers, such as low adoption, human resource constraints, and coordination, hinder the successful implementation of the HPV vaccination.

Zambia shares a high burden of cervical cancer, yet HPV vaccine uptake is low. The demonstration project conducted between 2013-2017 reported suboptimal coverage. Additional health facility data for 2021 and 2022 after national rollout of the vaccination reported uptake of only 30% among 14-year-old eligible adolescent girls. Factors leading to this low uptake and implementation determinants are not very well understood in the Zambian context.

Therefore, this PhD aimed to understand factors associated with the uptake and implementation of the HPV vaccination of adolescent girls in Lusaka and select and tailor strategies based on their acceptability and feasibility to mitigate identified barriers.

Methodology: This research was embedded in behavioural and implementation research with multiple stakeholders. Based on existing literature, the social-ecological model (SEM) was used to develop the conceptual framework to ensure the study was deeply grounded in theory. The health belief model (HBM) and consolidated framework for implementation research (CFIR) were used to explore participants' behavioural and implementation dimensions, respectively, at the different levels of the SEM.

A mixed methods approach was employed, incorporating semi-structured interviews with adolescents, parents, teachers, and healthcare workers and a cross-sectional survey of parents. Thematic analysis and descriptive statistics were used to analyse the data, guided by the CFIR and the HBM. The nominal group technique (NGT) was used to achieve stakeholder consensus on feasible and acceptable implementation strategies to increase HPV vaccine uptake.

Secondly, a scoping review was conducted following an a priori protocol to understand the implementation strategies used to increase HPV vaccination of adolescent girls in the broader context of SSA. To have clear and replicable definitions, all the identified implementation strategies were coded according to the Expert Recommendation for Implementation Change (ERIC) taxonomy, grouped into clusters, and recorded their perceived feasibility and importance.

Results: This PhD identified low awareness and misinformation as significant barriers to vaccine uptake among adolescents and parents. Cultural beliefs, fears about infertility, and logistical challenges within the healthcare system were substantial obstacles. Teachers and healthcare workers pointed to inadequate training and resources as crucial limitations in program implementation.

Frequently used implementation strategies in SSA from the scoping review included building a coalition, changing service sites, distributing educational materials, conducting educational meetings, developing educational materials, using mass media, involving patients/relatives and families, promoting network weaving, staging implementation scale-

up, accessing new funding, promoting adaptability, and tailoring strategies. According to expert consensus, most of the identified implementation strategies were multifaceted and of high importance and feasibility.

Conclusion: The PhD highlights the need for targeted health education campaigns, access to clear information, improved coordination between stakeholders, and the development of flexible delivery models to reach out-of-school girls. Future research should evaluate the effectiveness of the proposed strategies to assess their impact on vaccine uptake in Lusaka, Zambia and within the region.

PhD Contributions

This PhD has illuminated factors associated with parental consent for daughters' HPV vaccination, where HPV and HPV vaccine knowledge, sociocultural factors, and socioeconomic status play an important role. The voices of adolescents have also been illuminated regarding their knowledge and attitudes towards HPV and HPV vaccination.

Despite having low knowledge of the vaccine and facing many barriers, adolescents have positive attitudes towards the HPV vaccine, which holds promise for increased HPV vaccine uptake in the future. Additionally, this PhD provides contextual evidence on HPV vaccine implementation determinants (identified by key stakeholders—teachers and healthcare workers using CFIR) and implementation strategies for addressing these determinants.

The findings further contribute to the evidence base in Zambia to align with WHO policies, such as the strategies for eliminating cervical cancer in our lifetime and the Immunisation Agenda 2030. Therefore, the findings from this PhD are important in improving HPV vaccine uptake.

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Structure of the Thesis

This PhD is by publication and comprises six papers. Four original papers, a scoping review, and a scoping review protocol have all been published in different open-access international journals.

This thesis has three main parts. Part one consists of chapters one, two, and three, while part two consists of the empirical findings from each of the sub-studies of this PhD, i.e.,

Chapters four to eight. Part three is the general discussion, conclusion, and implications for policy and future research, i.e., Chapter nine.

Chapter one provides the background, problem statement, significance of the study, conceptual framework, study aims and specific objectives. Chapter two is the literature review. Chapter three provides a summary of the methodology by objective, which is detailed in the individual results in chapters four to eight.

Chapter four includes paper one, a qualitative study exploring the knowledge and perceptions regarding HPV and HPV vaccination among vaccine-eligible adolescent girls in the Lusaka district and ascertaining the implications of these findings for vaccine acceptability and uptake. This paper was published in the Frontiers in the Health Services Section of the Health Policy and Management Journal in 2023 with an impact factor of 0.38.

Chapter five presents paper two, which reports the factors influencing parental consent to their daughter's HPV vaccination within the Lusaka district. Parents of adolescents were included in the survey to get insights around the consent process. This work was published in the Vaccines Journal in 2023 with an Impact factor of 5.2.

Chapter six includes paper three, which presents perspectives on determinants of HPV vaccine implementation among healthcare workers and teachers in Lusaka, Zambia, who are involved in the HPV vaccination programme. The manuscript was published in the Vaccines Journal in 2023 and has an Impact factor of 5.2.

Chapter seven includes papers four (scoping review protocol) and five (scoping review), which were done to understand implementation strategies used to increase HPV vaccine uptake for adolescent girls in SSA. The scoping review was published in the Vaccines Journal in 2023, with an Impact factor of 5.2, while the scoping review protocol was published in the PLOS ONE Journal in 2022, with an Impact factor of 3.7.

Chapter eight presents paper six, highlighting the work on selecting and tailoring implementation strategies using the NGT to overcome stakeholder-perceived barriers to HPV vaccination identified in papers 1-3. The effectiveness of the strategies was not evaluated. The manuscript was published in 2024 in the Vaccines Journal with an impact factor of 5.2.

Chapter nine provides a general discussion, policy and future research implications, and a conclusion. It also offers insights into how this PhD answered the objectives and reflects on this thesis's theories and emerging themes, and conceptual framework.

Author contributions

All the work that is contained in this PhD was led by me and I am the primary and corresponding author on all the papers emanating from this PhD. I conceptualised the overall methods to address the research questions with the support of my supervisors.

I oversaw the application and obtained regulatory approvals from Zambia, South Africa, and the USA because my PhD was a collaborative effort between the universities of these countries. Additionally, I was responsible for submitting progress reports to the ethics committees.

I was responsible for data collection, analysis, and first-draft manuscripts before sharing them with the other co-authors and supervisors. As a corresponding author on all the papers, I submitted the manuscripts to journals upon approval from co-authors. I led the process of responding to reviewers' comments from the different journals in collaboration with supervisors to satisfy the Journal editors.

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List of Abbreviations

CFIR-Consolidated framework for implementation research

DNA-Deoxyribonucleic acid

HBM-Health belief model

HIV-Human immunodeficiency virus

HPV-Human papillomavirus

IA2030-Immunisation agenda 2030

LMIC-Low- and middle-income countries

NCCSP-National Cancer Control Strategic Plan

SSA-sub-Saharan Africa

UNESCO- United Nations Educational and Social Cultural Organisation

VLPs-Virus like particles

WHO-World Health Organisation

ZAMPHIA-Zambia Population-based HIV/AIDS Impact Assessment

ZDHS-Zambia Demographic Health Survey

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Contextual definition of terms

Acceptability: Perception among stakeholders that the HPV vaccine implementation strategies are agreeable and satisfactory and perception by consumers that the HPV vaccine is satisfactory.

Adolescent—A young person aged between 10 and 19. In this study, the term will be used for girls aged 15 to 18.

Adoption**—**The proportion and representativeness of settings that adopt a given policy or program can be interchangeably referred to as uptake of an intervention, in this case, HPV vaccination.

Coverage-The number of individuals on the sampling frame divided by the estimated number of elements in the target population.

Feasibility-Extent to which intervention can be carried out in a particular setting.

HPV Vaccine- a substance used to stimulate the production of antibodies and provide immunity against the human papillomavirus, which acts as an antigen without inducing the disease.

HPV Vaccination- the act of giving a person the HPV vaccine to protect them against HPV infection.

Implementation process- The process of putting a decision or plan into effect; execution.

Parent-One who nurtures or raises a child or a relative who plays the role of guardian.

Reach is defined as the proportion of eligible individuals participating in the intervention.

CHAPTER ONE: INTRODUCTION

This chapter provides the background, problem statement, and study significance, including the aim and specific objectives. It describes the burden of cervical cancer, HPV distribution, and HPV vaccine uptake and implementation, including the barriers and facilitators to vaccination. The chapter also critiques the available literature on HPV vaccination implementation.

1.1 Background

1.1.1 Global and Regional context

Global statistics for 2022 show that over 350,000 women died from cervical cancer [1] with sub-Saharan Africa (SSA) bearing a disproportionate share of this burden (120,000 new cases per year) compounded by higher rates of HIV prevalence [2, 3] and limited healthcare resources. Despite the latest global report on cancers indicating that cervical cancer is the fourth highest among female cancers, it is the most frequent female cancer in Southern Africa, with an age-standardised incidence of 43.1/100000 [4, 5].

There are more than 200 species of HPV categorised into low-risk which cause diseases such as anogenital warts, and high-risk types, which are oncogenic [6]. HPV is a double-stranded DNA virus with icosahedral particles consisting of protein capsid. The virus codes for eight proteins, two forming the outer cover. The necessary cause of cervical cancer is persistent infection with high-risk strains of HPV. About 99.7 % of cervical cancers are caused by HPV, and types 16 and 18 account for approximately 70% of cervical cancer cases [7].

Globally, the point prevalence of HPV infection is estimated at 11–12% and is twice as high (22-24%) for SSA [8-11]. HPV is spread via skin-to-skin contact and sexual intercourse, infecting mucous membranes, with approximately 75% of sexually active people getting infected [12]. The process from infection to the development of invasive cancer when there is a breach in the basement membrane can take between 10 to 20 years [13].

This explains why the cancer peaks in middle age with an infection which could have occurred early in the sexual life of women. The infection is usually self-limiting and is cleared by a competent immune system; only about 20% of Infections persist [13]. Following exposure to high-risk HPV, the viral genome may integrate into the genome of the human differentiating epithelial cells, resulting in early protein expression [14].

This long latency creates unique opportunities in the prevention of cervical cancer, making it one of the few cancers that can be prevented through vaccination, screening, and early detection and treatment [15]. Figure 1.1 shows the natural history of HPV.

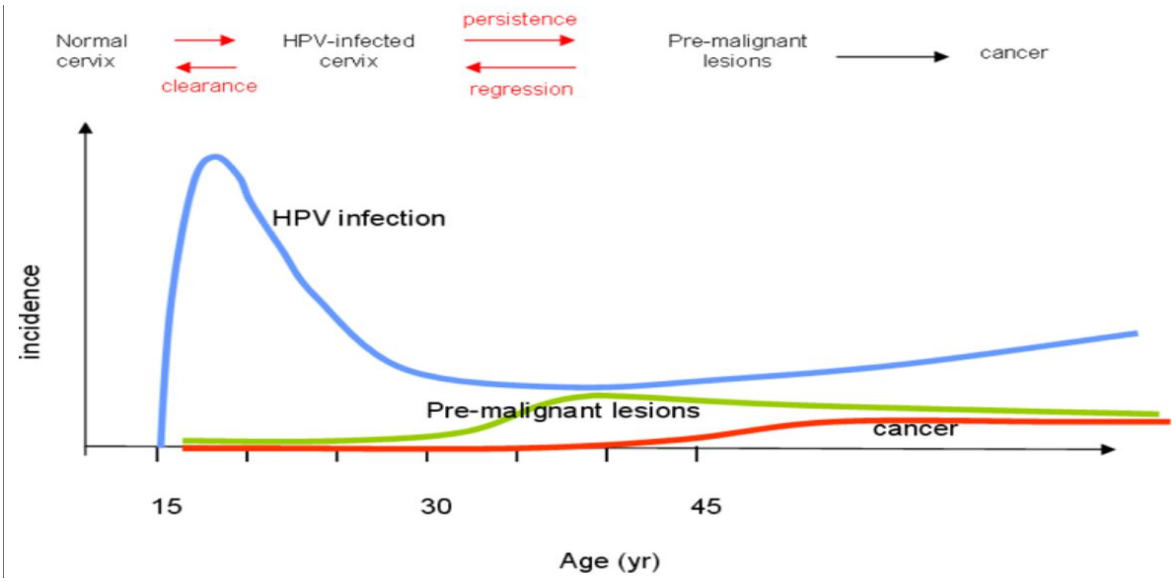

Figure 1.1 Natural history of human papillomavirus

Different sexually transmitted infections have been known to thrive with the HPV, and one example of a well-studied co-infection is that with human immunodeficiency viruses (HIV) [3]. Coupled with the high HIV infections, SSA women suffer a disproportionately high incidence of cervical cancer due to the co-infection with HIV and HPV [2, 3]. Women living with HIV are up to six times more likely to develop cervical cancer compared to HIV negative counterparts [2].

Furthermore, women living with HIV are at an increased risk of persistent HPV infection, having larger and more challenging to treat precancerous lesions and ultimately progressing quickly to cervical cancer [3, 16, 17]. A general lack of population-based cervical cancer screening programs within SSA further accentuates the problem [3, 18-22]. The role of highly active antiretroviral therapy (HAART) in the progression of the premalignant seems promising based on current evidence [2, 23].

In response to the global burden of cervical cancer, particularly in low and middle-income countries (LMICs), the World Health Organisation (WHO) has prioritised its elimination as a public health problem. The WHO's tri-pillar elimination strategy, introduced in 2020, sets ambitious goals for all countries to achieve by 2030 [24].

The strategy entails that 90% of girls are fully vaccinated with the HPV vaccine by the age of 15; 70% of women screened using a high-performance test by the age of 35, and again by the age of 45; 90% of women with pre-cancer treated and 90% of women with invasive cancer managed [25].

This elimination strategy highlights the importance of high HPV vaccination coverage integrated with regular screening programs, as well as providing timely treatment for those diagnosed with cervical cancer. In HIV-endemic areas, where women are at greater risk for persistent HPV infections and cervical cancer progression, achieving these goals is crucial for reducing mortality.

Regarding HPV vaccination, in 2006, the WHO approved its use for prepubertal girls aged 9 to 14 before their sexual debut to prevent HPV-related cancers [26]. The immunogenicity and efficacy of the HPV vaccine in reducing HPV vaccine-related infections and cancers in both HIV-infected and non-infected populations is very high, as shown in multiple studies [27-30].

The vaccines' mechanism of action is the production of neutralising antibodies for those who are naïve to sexual intercourse but are at increased risk of getting infected in their early years of sexual debut [31]. Over 98% of recipients develop an antibody response to HPV types in respective vaccines [32]. Estimates show that vaccination of adolescent girls against HPV can prevent 690,000 cases of cervical cancer and 420,000 deaths [33, 34].

There are currently three licensed HPV vaccine types: Bivalent, quadrivalent and nonavalent, which protect against strains16 & 18 and 6,11,16 & 18 and 6,11,16,18,31,33,45, 52 & 58, respectively [32]. The bivalent and quadrivalent vaccines were approved for use in 2006 for girls and 2011 for boys, then nine valent was licensed for use in 2014 for both girls and boys aged 11 years and older, including men and women up to age 26 without prior vaccination history [35].

Evidence has evolved on the effectiveness of two doses [35] from the initial three and now a single dose has been proven to be effective and recommended for adolescents aged 15 years and younger [36]. For adolescent girls older than 15 years or those immunocompromised e.g., due to HIV infection, a three-dose regimen is still recommended [36]. This shift to a single dose is poised to increase coverage as it reduces the cost of full vaccination, human resource constraints and multiplicity of facility visits [37].

A meta-analysis focused on high-income countries found that coverage of at least 50% among females decreased HPV-related conditions by 68%, with evidence of herd immunity [38]. In contrast, female coverage below 50% decreased HPV-related conditions by 50% without conferring herd immunity [30], a common picture in SSA.

From a policy perspective, the WHO has called for the development of complementary HPV vaccination strategies to identify and access both in- and out-of-school girls to maximise vaccination coverage [39]. A high vaccination coverage is necessary to reduce cervical cancer incidence. However, HPV vaccination uptake remains low, particularly in SSA, which bears the highest burden of cervical cancer in the world [40].

As of 2021, pooled global data shows that only 15% of girls are vaccinated at the population level within the targeted eligible girls, and SSA only contributing 1% to this total [40]. In a global systematic review and other literature, it was noted that in LMICs, coverage for completing the HPV vaccine dose regimen ranged between 1.1%-2.4% [12, 34]. Possible reasons for low coverage include social, behavioural, health system, and implementation factors [12, 34.].

An estimated 70% of eligible girls still live in countries which have not yet adopted or introduced national HPV vaccination programmes [40]. LMICs have introduced the HPV vaccine slower than high-income countries, where coverage is 77% [40, 41]. Bruni et al. (2021) identified systemic barriers to HPV vaccination in LMICs, including sociocultural barriers, such as vaccine misinformation and stigma [41].

1.1.2 The Zambia context

Zambia shares a high burden of cervical cancer with an age-standardized incidence rate of 71.5 per 100000 women and a mortality rate of 49.4 per 100000 women years [1]. This is compounded by the high prevalence of HIV among women of reproductive age. Women in Zambia carry a disproportionately higher prevalence of HIV than men [42] .

For example, the 2021 Zambia Population-based HIV Impact Assessment (ZAMPHIA) survey reports an HIV prevalence of 14% among women of reproductive age compared to 8% among male counterparts of similar ages [42]. In a study done in Zambia among 145 women living with HIV, 97% of them had evidence of cervical, vaginal HPV DNA with

multiple HPV types (two to five types), with greater prevalence in those with CD4 count below 200ul [43].

The national HPV vaccine rollout program in Zambia began in 2019, 14 years after the WHO prequalified it [44]. The introduction of the HPV vaccine in Zambia was initiated through a demonstration project conducted between 2013 and 2017 [45]. The project was conducted in selected districts within Lusaka province, primarily targeting 10-year-old girls or those in grade 4 [45]. The delivery model was predominantly school-based; complemented by community-based campaigns and health clinics.

The vaccine used in this demonstration project was Cervarix, a specific bivalent vaccine that protects against HPV types 16 and 18**,** which are responsible for most cervical cancer cases [7]. The campaigns were not continuous but occurred annually, with a second dose delivered in month two and the last one 6-12 months after the first. The Ministry of Health coordinated the program with various health partners such as the WHO, Churches Association of Zambia and Gavi [45].

1.2 Statement of the problem

Zambia, with its high burden of cervical cancer and HIV, introduced its national HPV vaccination program in 2019, 14 years after the WHO first recommended the vaccine. However, the nation faced challenges scaling up its vaccination program, especially in achieving the WHO target of 90% vaccination coverage for adolescent girls aged 15 by 2030 [25].

The HPV vaccine demonstration project that ran between 2013 and 2017 achieved lower-than-expected coverage, with only 59% of eligible girls vaccinated in the first year (2013) and 58% in the second year (2014) [46]. The coverage was lowest for out-of-school girls at 12% overall [46]. These coverage rates fell short of the program's target of 70%, reflecting the broader challenges facing Zambia's immunisation efforts.

Health facility data from 2021 and 2022 showed suboptimal coverage of as low as 39% for dose completion. [47]. Like with other vaccines in Zambia, there is heterogeneity in HPV vaccine coverage [48]. During the 2019 inaugural national HPV vaccine implementation, coverage figures were reported as low as 6.9 % for out-of-school girls and 25% for in-school girls in some areas [49].

Several factors contributed to the suboptimal results in the demonstration project. First, logistical issues coordinating school-based vaccine delivery between the Ministry of Health and Education resulted in missed vaccination opportunities [45]. Additionally, there was initial uncertainty within the Ministry of Health regarding where the HPV vaccination program should be housed—whether in the Child Health Unit or another department—further complicating early implementation [45].

The GAVI evaluation (2016) highlighted several critical areas for improvement, including better logistics management and data reconciliation to ensure accurate forecasting of vaccine demand [46]. Furthermore, Zambia's heavy reliance on external funding, particularly from GAVI and other donors, was identified as a significant barrier to the long-term sustainability of the HPV vaccination program [46].

Other barriers experienced in Zambia during the national rollout include poor sensitisation, belief in myths and misinformation, low levels of knowledge and, lately, the COVID-19 pandemic [47, 50]. In Zambia, of the girls aged 14 to 15 years, 14.8% are out of school, and 19.2% of these come from the poorest of families [51], adding to low national HPV vaccine uptake.

Despite the suboptimal demonstration coverage and little understanding of reasons and strategies to overcome barriers, Zambia proceeded to roll out the national HPV vaccination programme in 2019. The lack of a deeper understanding of user-side and vaccine implementation barriers and the application of specific strategies to overcome the barriers could explain why, as of 2020, some districts, like Kalumbila, only reached 25% of the targeted adolescents [49].

Many stakeholders are involved in the HPV vaccination cascade, including implementers (teachers and healthcare workers who play a key role) and users (parents and adolescent girls). Vaccine delivery strategies focusing on a school-based model entail healthcare workers and teachers collaborating to deliver the vaccine. Research on factors associated with HPV vaccine implementation and uptake among adolescent girls in Zambia is limited [52].

Furthermore, since vaccine uptake requires acceptance of the vaccine by parents and adolescent girls, a deeper understanding of the barriers to vaccine uptake amongst these stakeholders is needed but is lacking. This demands research to understand the factors associated with low HPV uptake, including user-side and implementation-related factors. Understanding these factors is essential to designing strategies to overcome the barriers.

Therefore, this study aimed to bridge the gap in the literature by understanding HPV vaccine implementation barriers and user-side barriers to vaccine uptake. Furthermore, this study aimed to identify barriers and develop tailored, context specific strategies to improve HPV vaccine coverage and uptake and ultimately contribute to improved overall coverage. However, the effectiveness of these tailored strategies was not evaluated in this PhD.

1.3 Significance of the study

Achieving the WHO elimination goals is only possible with scientists and communities understanding and identifying solutions to barriers that limit HPV vaccination coverage. Identifying implementation determinants and user-side barriers to uptake is an important step that allows researchers and stakeholders to develop context-specific strategies for addressing these barriers. Therefore, identifying which implementation strategies are acceptable and feasible in the Zambian context for different stakeholders is particularly important to reach all vaccine-eligible adolescents regardless of school status.

This PhD brings a nuance by engaging multiple stakeholders to give representative views and high-quality evidence to increase HPV vaccination uptake [53, 54]. The use of mixed methods to illuminate the interaction of factors influencing HPV vaccine implementation and uptake bolstered by a scoping review adds critical information to the body of knowledge on HPV vaccination [55]. Further, this study used standard definitions for terminologies and theoretical frameworks, making findings comparable and consistent.

Evidence generated from this research has the potential to influence policy by tailoring HPV vaccination strategies based on specific stakeholder needs and attain high success rates, as shown by other SSA countries like Rwanda [56]. Further, the findings serve as formative research for successful program implementation.

1.4 Overall aim, specific objectives, and conceptual framework

1.4.1 Overall aim:

To understand factors associated with the implementation and uptake of the HPV vaccination for adolescent girls in Lusaka and tailor implementation strategies to identified barriers.

1.4.2 Specific objectives

1. To explore factors influencing the acceptability and uptake of the HPV vaccine among adolescent girls in Lusaka, Zambia

2. To determine factors associated with parental consent to vaccinate their adolescent daughters against HPV in Lusaka, Zambia

3. To explore barriers and facilitators to HPV vaccination implementation experienced by healthcare workers and teachers in Lusaka, Zambia

4. To understand implementation strategies used to increase HPV vaccination uptake of adolescent girls in sub-Saharan Africa using a scoping review

5. To develop and explore the feasibility and acceptability of context-specific strategies to overcome identified barriers amongst different stakeholders in Lusaka, Zambia

1.4.3 Conceptual framework

Theoretical and conceptual frameworks are key in ensuring that a study is easier to interpret and comparable to other studies in a particular field [57, 58]. This PhD used various theories to respond to the study's objectives and to develop a conceptual framework. Considering the dynamics of this research, which premised that the factors influencing coverage operate at multiple levels.

The enquiry was embedded in both behavioural and implementation research with multiple stakeholders. The SEM was used as the overarching conceptual framework, and various theories and frameworks were then used to explore behavioural and implementation issues, respectively [57]. It was important to understand how various factors interact at different levels to influence HPV vaccine uptake by adolescent girls to ensure that the study is deeply grounded in theories [57].

This mixed-methods research uses the health belief model (HBM) as a theory to understand behavioural factors related to adolescent vaccine uptake and parental consent [59]. The consolidated framework for implementation research (CFIR) was used to systematically understand the barriers to HPV vaccine implementation from the implementer's perspective [60, 61], and the Expert Recommendation for Implementation Change (ERIC) taxonomy was used to code implementation strategies with stakeholders [62].

For objectives 1 and 2, the HBM formed part of the basis for data collection, management, and analysis. The HBM has been used widely to study health behaviour at both individual levels and as a proxy, e.g., parents accepting the HPV vaccine for daughters [63-65]. The HBM constructs include perceived susceptibility, perceived severity, perceived benefits, perceived barriers, self-efficacy, and cues to action [66]. According to Champion VL et al. (2008) these are defined as follows [66]

Perceived Susceptibility refers to beliefs about the likelihood of getting a disease or condition. For example, a girl must believe there is a possibility of getting cervical cancer before she is interested in getting the HPV vaccine.

Perceived Severity: Feelings about the seriousness of contracting an illness or of leaving it untreated include evaluation of both medical and clinical consequences, such as death, and social consequences, such as social relations. The combination of susceptibility and severity has been referred to as perceived threat.

Perceived Benefits: Even if a person perceives personal susceptibility to a serious health condition, whether this perception leads to behaviour change will be influenced by the person's beliefs regarding the perceived benefits of the various available actions for reducing the disease threat.

Perceived Barriers: The potential negative aspects of a particular health action, perceived barriers, may act as impediments to undertaking recommended behaviour.

Cues to action; strategies to activate readiness; a cue can be as fleeting as a sneeze or the barely conscious perception of a poster.

Objective 3 used the CFIR, which is a frequently used determinant framework exploring factors influencing the implementation of evidence-based health-related interventions [61]. CFIR is important in understanding stakeholder needs to increase and sustain high levels of vaccine acceptability and uptake [67].

The original CFIR is composed of five major domains and 39 distinct constructs; the domains are intervention characteristics, outer setting, inner setting, characteristics of the individuals involved, and the process of implementation [61]. The updated CFIR maintained the same number of domains but renamed some while adding constructs and sub-constructs to improve the clarity and ease of use [60].

"The CFIR provides a pragmatic structure for approaching complex, interacting, multilevel, and transient states of constructs in the real world by embracing, consolidating, and unifying key constructs from published implementation theories" [61].

The conceptual framework is summarised in Figure 1.2

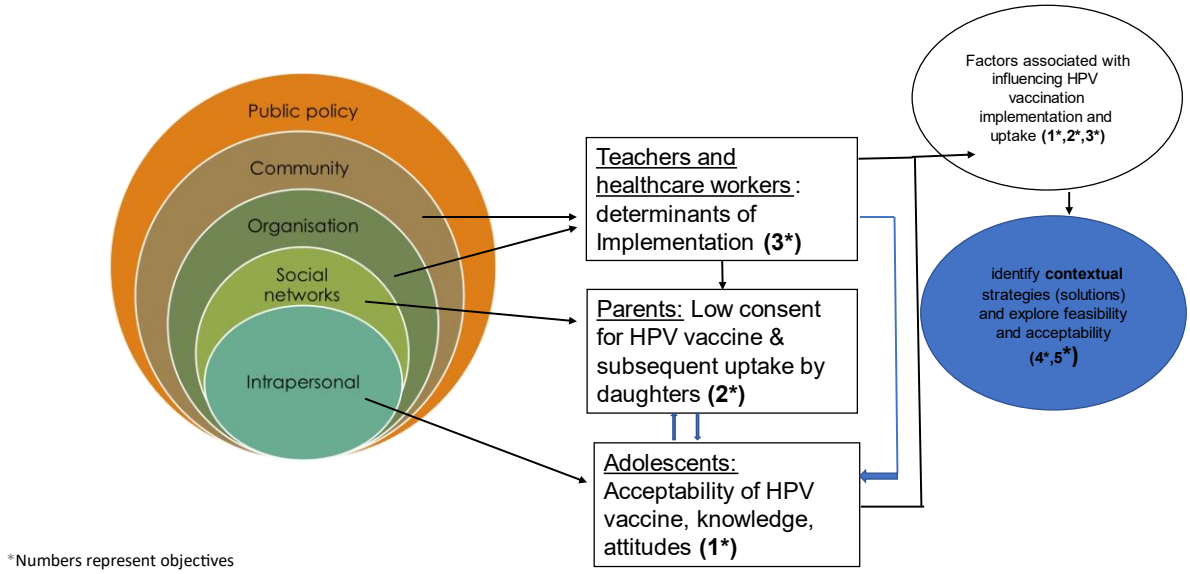

Figure 1.2 Conceptual framework

The ERIC taxonomy was used to code identified strategies in the scoping review and in selecting and tailoring strategies objectives 4 &5. The strategies developed in objective 5 were not evaluated for effectiveness.

CHAPTER TWO: LITERATURE REVIEW

This chapter examines the available literature on HPV vaccination acceptability, uptake, and implementation at the global, regional, and Zambian levels. Following the SEM, the literature review focuses on the acceptability, uptake, and implementation of the HPV

vaccine, stating the perspectives of multiple stakeholders (adolescents, parents, and healthcare workers).

2.1 Human papillomavirus vaccine knowledge, acceptability, and uptake among adolescent girls

Adolescents are the centre of HPV vaccination as primary recipients; hence, they play a crucial role in successfully implementing the vaccination. Because the lower age for vaccine initiation is around nine years, as per recommendation, adolescents may be missed in studies focusing only on parents who are their custodians. The other issues that may affect their participation include consent for the vaccine and consent to participate in studies [68].

In studies where they have been included, there are varied reasons for the barriers faced and facilitators for HPV vaccine uptake. A qualitative study done in Zambia in among vaccine eligible adolescents reviewed that low levels of knowledge, fear of infertility and other myths and parental consent were among the factors hindering vaccine uptake [69].Other studies have also identified these similar barriers [68, 70-77].

Further, Kisaakye et al. (2018), in their study in Lira district of Uganda among 460 girls, found that positive attitudes and education level were among the factors associated with 3-dose HPV vaccine uptake and series completion [78]. Generally, there is a lack of knowledge about HPV, the HPV vaccine and the relationship with cervical cancer and its prevention [79].

Watson-Jones et al. (2012) conducted a case-control study in Tanzania and found that girls who actively refused the vaccine had poor knowledge of the location of the cervix (aOR 2.65; 95%CI 1.17–6.01 for somewhere in reproductive system; aOR 3.37; 95%CI 1.62–6.99 for not known or somewhere else. Others did not know that the HPV vaccine could prevent cancer (aOR 2,73; 95%CI 0.91–8.13 for mentioning screening, condoms or no sex; aOR 1.78; 95%CI 1.04–3.06 for not known or methods excluding vaccination, screening, condoms or no sex) [80].

This could be partly related to the lack of school education generally on reproductive health among adolescents and the failure of parents to discuss these issues with their daughters. Additionally, myths and misinformation and school absenteeism create significant barriers to access.

In SSA, a good proportion of girls are out of school; for example, according to the UNESCO 2014 data, there were about 18.6 million out-of-school girls and a further five million not consistently attending school [34]. Therefore, there is a heightened risk of out-of-school girls contracting cervical cancer due to missed opportunities to be vaccinated.

Further, out-of-school girls are more prone to suffer other health-related problems such as missed early childhood vaccines, early marriages, age-discordant couples, and teen pregnancies [34]. In Zambia, 212,525 girls aged 6-15 are not in school. Rural and poorer children are also more likely to be out of school [51].

2.2 Parental HPV vaccination acceptability and consent

Parents play a pivotal role in vaccine uptake due to consent issues before vaccine administration. There is high interest by parents to vaccinate their daughters across different studies in Africa, as shown by high acceptability levels of the HPV vaccine [12, 63, 81]. The downside is that, due to varied barriers, neither acceptability nor intention translate into the actual behaviour of vaccine uptake.

Newman conducted a global systematic review and meta-analysis and found a pooled parental HPV vaccine consent for daughters and sons of 41.5% [30]. Further, a longitudinal study done in Eldoret, Kenya, found parental acceptability of 88.1% at baseline, but only 31.1% managed to vaccinate daughters, and 51.2% of parents who had accepted to vaccinate daughters could not as practical barriers obstructed them [82].

Some social-cultural barriers include parents feeling that the children are too young to receive the vaccine, myths around vaccine causing infertility, low perceived risk of HPV

infection, parental concern about the child not being sexually active, concern about the safety of the vaccine, thinking that vaccination will encourage sexual activity, lack of information, parental preference to wait till children are older, insufficient knowledge and information [12, 48, 50, 68, 83-86].

Misinformation about the vaccines has detrimental effects; for example, Cambodia, which had seen high uptake of the HPV vaccine of about 80% during the first four years of implementation, has suffered a high setback, with vaccination dropping to as low as 5% in 2016 [87]. This was due to a psychogenic disease suffered by more than 600 girls in Carmen de Bolivar, Colombia, which was wrongly associated with the HPV vaccine [87].

Further, the Japanese government suspended the active recommendation of the HPV vaccine after negative media reports about side effects experienced by some girls, resulting in a severe decrease in vaccine coverage from 70% to about 1% [88].

Facilitators of vaccination play a pivotal role in vaccine uptake; for example, most parents of adolescent girls are keen to receive the vaccination on recommendation by a physician or friend [64, 89]. Parents' health behaviour and beliefs towards the vaccine remain important in the vaccine delivery. Social mobilisation through government officials and champions generates high demand, complemented by positive media coverage around vaccine-related issues are key [88].

Despite the perceived high acceptability of the HPV vaccine by parents, uptake remains low and does not match the acceptability. For example, Perlman et. al. (2014) conducted a systematic review on willingness and acceptability of the HPV vaccine in SSA and found that acceptability in most countries across multiple stakeholders was classified as high or moderate [90]. Further, Vermandere et al., (2014) found parental acceptability of 87.1% at baseline and actual uptake of 31.1% post-implementation in Eldoret, Kenya [82].

2.3 Implementing the human papillomavirus vaccination programme in sub-Saharan Africa

As of 2019, about 112 countries were implementing national HPV vaccination programs, and just about 17 of these were from sub-Saharan Africa (SSA), including Zambia [41]. Most of the national implementation of HPV vaccination in SSA has taken place within the last 3-5 years. The first SSA country to have introduced national HPV vaccination was Rwanda, and it reached one of the highest completion rates globally, surpassing most high-income countries [56].

Countries that have implemented the vaccination program are already showing more benefits through herd immunity within the populations [91] GAVI has supported different demonstration projects for LMICs with the HPV vaccine and cold chain facilities [46]. The rationale for demonstration projects was for countries to learn how to introduce the HPV vaccination on a smaller scale before a national rollout [92].

The implementation also requires addressing several important contextual factors, such as provider attitudes, professional behaviour, and the service system. Strategies need to be employed carefully to increase the success of implementation [93]. Existing barriers, such as low adoption, acceptability, and feasibility, hinder the successful implementation and uptake of the HPV vaccine, reducing Its effectiveness in preventing HPV-related diseases, including cervical cancer [93].

Implementation science is a multidisciplinary field that studies methods and strategies to promote the systematic adoption and integration of evidence-based interventions into practice. It aims to bridge the gap between research and practice by identifying the most effective and efficient ways to implement innovations in real-world settings Implementation science recognises that the success of implementation efforts depends on the context in which they are implemented [62].

Context includes factors such as the organisational culture, resources, policies, and leadership support within a specific setting. The WHO is making frantic pronouncements

to ensure that cervical cancer is eliminated by the next century [94], this is only possible if there is a deliberate effort to harness scientific evidence emanating from the worst-hit parts of the world, such as LMICs, so that even when generalisations are made, they will be representative [91].

The implementation strategies for HPV vaccination should be adapted from an ideal setting to a real-world setting to achieve set targets. Various interventions have been used in different setups to increase HPV vaccine uptake. These include changing the usual vaccination site from health facilities only, to include community outreach posts such as schools However, this puts a big challenge on hard-to-reach communities where girls are likely to fall prey to early marriages, which is compounded by poor health-seeking behaviour [34].

Other implementation strategies included engaging multiple stakeholders and enhancing collaboration between the Ministries of Health and Education, EPI managers and the community. Others include identifying champions such as political leaders, educating communities and social mobilisation [95-98].

There is a dearth of published data on the review of HPV vaccine uptake and implementation evaluations of strategies used following national roll-out programs for HPV vaccination in SSA. Most available data lacks African studies [12, 99]. There is also a general lack of use of models and frameworks to make the data more replicable and comparable. Frameworks like the ERIC taxonomy has been useful to group and define implementation strategies [62].

With most SSA countries adopting the school-based approach to delivering HPV vaccine, where healthcare workers and teachers play an active role. This type of strategy means that healthcare workers must leave their health centres to administer the vaccine [52]. Teachers take on further responsibilities, which may include broadcasting the dates of vaccine delivery, getting consent from parents and assent from the girls, registering eligible girls as well as helping girls to queue up on the day of vaccination [100].

Vermandere and Masika et al. found a lack of knowledge about the HPV virus and HPV vaccine and cervical cancer among teachers who mostly must rely on healthcare workers to attend to parents' concerns [100]. This implies that, on the other hand, healthcare workers need to be highly knowledgeable and intentional in recommending the vaccine and passing on positive messages [56, 89].

In studies done among physicians, their levels of knowledge about this HPV vaccine are relatively low. Astron, in his study, found that only 30% of doctors in India knew the HPV vaccine, and 34% of these would recommend it [12]. In a qualitative study done in Mozambique evaluating system-level barriers and facilitators, healthcare workers indicated a strain on organisational human resources, demanding many sacrifices from individuals [52].

In conclusion, the literature review in this thesis focuses on Human Papillomavirus (HPV) vaccination, particularly the uptake and the implementation in low- and middle-income countries (LMICs), including Zambia. The synthesised findings from the literature underscore the complexity of HPV vaccination implementation in Zambia. The low vaccine uptake, influenced by logistical, cultural, and informational barriers, highlights the necessity of context-specific strategies.

CHAPTER THREE: METHODOLOGY

This chapter briefly introduces the methodology, the research design, methods, study context, sampling methods, and selection of studies for the scoping review.

3.1 Study design

A mixed methods approach of qualitative and quantitative approaches was used in this study. The mixed methods approach, which combines qualitative and quantitative data collection, is ideal for addressing the complex and multi-faceted nature of HPV vaccine uptake and implementation. It allows for in-depth exploration of individual experiences and

perceptions and identifies broader patterns on these issues that may influence vaccine coverage.

The quantitative approach allowed for a numeric description of the question and to determine relationships between variables of interest to establish relevant relationships. Qualitative data gave meaning to the findings; it explained the why of an observed phenomenon which cannot be explained quantitatively [101].The mixing of methods expanded the breadth and depth of understanding. [102]. The study adopted a concurrent triangulation design.

The design was structured into two phases. In the first phase, the study gathered insights from key stakeholders, including users (adolescents, parents) and implementers of the HPV vaccine (healthcare workers and teachers) to understand acceptability and user-side factors that may influence the uptake of the vaccine (objectives 1&2) and implementer-perceived factors (objective 3). This investigation was framed within the SEM, which examines factors at multiple levels, from individual behaviour to broader organisational and societal influences.

Using this design, the first part of the study was formative (Objectives 1-3), whose findings informed the development of context-specific implementation strategies to overcome barriers faced with HPV vaccination implementation (objective 5). The feasibility and acceptability of these tailored strategies were explored through focus discussions using the nominal group technique with relevant key stakeholders.

The methods are discussed in each results chapter. It is important to note that the scoping review was done to get insights into how the SSA region implements HPV vaccination and not to develop strategies among the key stakeholders. Community members came up with strategies which they felt were feasible and acceptable.

Notably, the study did not seek to evaluate the effectiveness of these strategies in practice. Rather, the primary aim was to assess the acceptability of the proposed strategies from the perspectives of multiple stakeholders involved in the HPV vaccination program. This phase focused on the feasibility and acceptability of these strategies and provided a foundation for future research and implementation efforts.

Instead, the research aimed to understand whether these strategies are perceived as acceptable and feasible by the stakeholders most directly involved in the vaccination program. This focus on stakeholder input helps ensure that any future interventions are grounded in local realities and have the support of those responsible for implementing them.

3.2. Study Setting

This study was conducted in Lusaka district of Zambia, the capital city located in the southern central part of the country with a provincial population of approximately a population of 1,747,152 million people, 417.9 km2 area and a population density of 4181/km2 [103] out of the 19.47 million national population. During the national HPV vaccine launch in 2019, about 331,154 14-year-old teenage girls were eligible for dose one, 212,509 in 2020 and 420,704 in 2021 [47].

Lusaka district has six administrative subdistricts: Chawama, Chelston, Chilenje, Chipata, Kanyama and Matero. Healthcare facilities within these subdistricts provide the HPV vaccine to eligible adolescent girls. The number of girls vaccinated is determined using school registers, headcount, and Zambia Statistics Agency, while community volunteers and civil societies identify out-of-school girls.

Lusaka, the capital city of Zambia, was strategically selected as the study site for this research due to several critical factors that make it a focal point for understanding the challenges and opportunities related to HPV vaccination. Lusaka has been at the forefront

of Zambia's HPV vaccination initiatives, including the initial demonstration project and national rollout efforts.

As a result, the city's healthcare infrastructure has experience with the HPV vaccination program, making it a valuable setting for evaluating current strategies' effectiveness and identifying implementation gaps. The involvement of schools, healthcare facilities, and community organisations in these initiatives provides a rich environment for assessing the roles of various stakeholders in influencing vaccine uptake.

The HPV vaccine is given from health facilities and outreach posts such as schools and other community amenities to capture both in-school and out-of-school girls. Information on the vaccine and vaccination dates is shared with parents using flyers, educational materials, television adverts, radio programmes and school letters. Due to the age of the eligible girls, parental consent is required to opt-out. However, if parents decline and the girl is willing to be vaccinated, the vaccine is given.

3.3 Overall Approach (summary)

The study focused on three groups distinct groups of participants within Lusaka, Zambia: adolescent girls, parents, healthcare workers and teachers.

The first group comprised adolescent girls 15-18 years recruited through schools and community settings, with the sampling including both vaccinated and unvaccinated girls. This approach enabled the study to explore the factors influencing their decision-making around HPV vaccination, providing a more comprehensive view of the challenges and facilitators affecting vaccine uptake.

The second group, parents, included those with daughters aged 15 to 18 years. These parents were purposively selected to provide insights into their perceptions of the HPV vaccination and the factors influencing their decision to consent. Understanding their

viewpoints was vital, given the influential role parents play in the health decisions of their adolescent children.

The third group comprised healthcare workers and teachers previously participating in the HPV vaccination implementation. Their involvement was crucial in understanding the practical aspects of vaccine implementation, including the barriers and facilitators they encountered. Those selected had direct experience with the HPV vaccination, which allowed the study to gather in-depth insights into the delivery and implementation aspects of the vaccine rollout.

Recruitment was conducted through local community outreach and healthcare facilities. This method facilitated the inclusion of parents from diverse backgrounds, providing a wide range of attitudes and beliefs about the HPV vaccine. The rest of the methods are detailed in each paper's results section. References for literature cited in each results chapter appear within the references section of the paper itself and not necessarily in the references section of this thesis. The approach to this PhD is summarised in Figure 3.1 and Table 3.1.

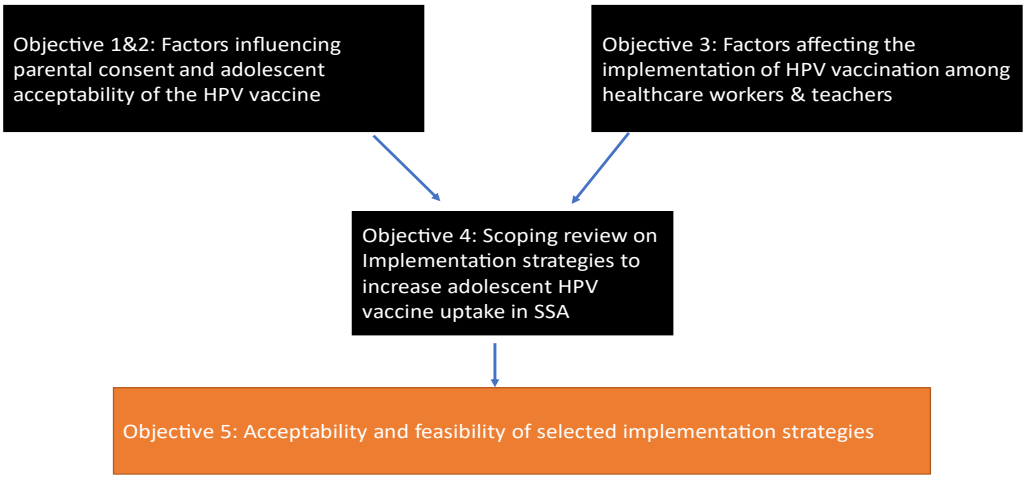

Figure 3.1: Thesis diagram

Table 3.1. Objectives and a brief description of how each was achieved

Sn	Objective	Description
1	To explore factors influencing the acceptability and uptake of the HPV vaccine among adolescent girls in Lusaka, Zambia	A qualitative study applying the health belief model to explore Adolescent girls (aged 15-18 years) beliefs regarding the HPV vaccine
2	To determine factors associated with parental consent to HPV vaccination of daughters	This quantitative survey targeted vaccine-eligible adolescent parents since the programme launch. The health belief model was used to explore parental attitudes and associated factors regarding consent to vaccinate daughters.
3	To explore barriers and facilitators of HPV vaccination implementation of adolescent girls among healthcare workers and teachers	A qualitative study using the CFIR to explore healthcare workers' and teachers' perspectives of implementation barriers and facilitators
4	Scoping review to understand implementation strategies used to increase HPV vaccination for adolescent girls	The ERIC compilation (an implementation science framework) was used to guide the scoping review and categorise identified strategies.
5	To tailor implementation strategies to identified barriers to HPV vaccination implementation	The nominal group technique was used as a participatory approach with respective groups of stakeholders to identify implementation strategies that would be feasible and acceptable to use for addressing barriers identified in objectives 1, 2 and 3

3.4 Ethical considerations

Ethical clearance was obtained from the University of Zambia Biomedical Research Ethics Committee (UNZABREC) Ref: 1609-2021, the Human Research Ethics Committee (HREC-Medical) at the University of the Witwatersrand Ref: M21/04/73, and a waiver was obtained from the University of North Carolina at Chapel Hill. The Ministries of Health and Education granted access to healthcare facilities and schools. The study was registered with Zambia National Health Authority (NHRA) as a local mandate.

Participants provided written informed consent before participating in the study. The research had no major risks to participants, except that some participants could have felt uncomfortable discussing personal matters. Confidentiality was observed, and study participants were free to withdraw from the study at any time without any negative implications. Participants were free to skip questions they were not comfortable answering.

As per ethical guidelines, adolescents below 18 years who were legally considered minors obtained consent from their parents or legal guardians. Additionally, the assent of the adolescent participants was required to ensure that they understood the purpose of the study and were willing to participate. Adolescents were given an age-appropriate information sheet explaining the study in clear, accessible language. This two-step process ensured that the minors' participation was informed and voluntary.

Given the involvement of healthcare workers and teachers, ensuring they did not feel coerced into participating was paramount. The study was introduced to these participants with a clear emphasis on the voluntary nature of their involvement. They were reassured that their participation or non-participation would not impact their professional standing or working relationships.

In settings where group interviews were conducted, a careful approach was taken to ensure that individuals did not feel pressured to share personal opinions or experiences

if they were uncomfortable doing so. All participants were informed that they could opt out of specific questions or activities without consequences, reassuring them.

Confidentiality was paramount in this study, and specific steps were taken to protect participants' identities. Participants were reminded of the importance of maintaining confidentiality within the group and encouraged not to discuss any personal details shared during the session. However, the limitations of confidentiality in group settings were acknowledged, and participants were made aware that complete confidentiality could not be guaranteed in these cases.

CHAPTER FOUR: “When you get the HPV vaccine, it will prevent cervical cancer; it will act as a shield:” Adolescent girls’ knowledge and perceptions regarding the human papillomavirus vaccine in Zambia.

Mwansa Ketty Lubeya, Carla Chibwesha, Mulindi Mwanahamuntu, Moses Mukosha, Simone Frank, Mary Kawonga

Adolescent girls are primary recipients of the HPV vaccine for the prevention of cervical cancer and other HPV related conditions. The acceptance and uptake of the HPV vaccine may be significantly impacted by the knowledge and attitudes of adolescent girls about HPV and the vaccination. However, there is a gap on the implications of knowledge and attitudes on HPV vaccine acceptability and uptake. The health belief model was used as a guide to understand HPV and HPV related perceptions among adolescent girls in Lusaka, Zambia. The manuscript has been published in Frontiers health management.

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"When you get the HPV vaccine, it will prevent cervical cancer; it will act as a shield": adolescent girls' knowledge and perceptions regarding the human papillomavirus vaccine in Zambia

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Introduction: The human papillomavirus (HPV) vaccination is an important preventive measure for HPV-related conditions such as cervical cancer. In 2019, Zambia introduced a free national HPV vaccination program for 14-year-old girls. However, the adolescents' knowledge and perceptions regarding the HPV vaccine are not well understood. Therefore, this study aimed to understand adolescent girls' knowledge and perceptions regarding the HPV vaccine and discuss its acceptability and uptake implications.
Methods: We conducted a qualitative study in the Lusaka district between June 2021 and November 2021 using semi-structured interviews with adolescent girls aged 15–18 years regardless of their HPV vaccination status. Interviews were transcribed verbatim, and NVIVO 12 was used for data management and analysis. We coded transcripts deductively and inductively based on emerging themes. Perceptions were coded using the health belief model constructs.
Results: We interviewed 30 adolescent girls to reach saturation. Seventeen girls reported having received at least one dose of the HPV vaccine. Participants expressed variable knowledge and awareness about HPV and the HPV vaccine. Participants exhibited positive attitudes towards the HPV vaccine and perceived it as beneficial. However, there were multiple perceived barriers to vaccination, such as the need for parental consent, not being in school, concerns about vaccine side effects, and belief in myths and misinformation
Conclusion: The adolescent girls in this study showed variable knowledge and positive attitudes toward the HPV vaccine despite the many perceived barriers. To support increased HPV vaccine acceptability and uptake among adolescent girls in Zambia, it is critical to actively engage stakeholders involved in HPV vaccination, such as adolescents and their parents, and debunk myths and misconceptions about HPV vaccination. Health education in schools and communities should be implemented to increase knowledge about HPV and HPV vaccination among adolescents and their parents.

KEYWORDS

HPV vaccine acceptability, HPV vaccine uptake, COVID-19 vaccine, health belief model, parental consent, myths and misinformation, cervical cancer

Background

The World Health Organization (WHO) recommends that the human papillomavirus (HPV) vaccine be included in national vaccination programs to prevent cervical cancer and other HPV-related conditions (1). Persistent infection with HPV causes benign conditions such as genital warts and malignancies such as cervical cancer, anogenital cancers (anal, vulva, penile), and head and neck cancers. HPV is a risk factor for the development of cervical cancer, with types 16 and 18 commonly identified in approximately 70% of all cervical cancers (2). By far, cervical cancer is most common in Low and Middle-Income Countries (LMICs), with a disproportionately larger burden in sub-Saharan Africa (SSA) (1). In 2020, there were over 600,000 new cases of cervical cancer globally, with approximately 330,000 related deaths, most of which were reported from LMICs (1).

Like many other SSA countries, Zambia has one of the highest cervical cancer incidences and mortality rates in the world (2) and faces many challenges in treating those diagnosed with the disease since most of them present in late stages (3). According to the Global Cancer Observatory, Zambia cervical cancer-related incidences and mortality stand at 65.5 and 43.4 per 100,000 (1) making it one of the most common cancers in the country.

Persistent infection with HPV and rapid progression to malignancy is characteristic in women co-infected with the Human Immunodeficiency Virus (HIV), especially in high epidemic regions like Zambia (4–6). Women living with HIV are six times more likely to have cervical cancer than those without HIV with about 63.8% of women with cervical cancer and HIV residing in Southern Africa (7). The 2021 Zambia Population-based HIV/AIDS Impact Assessment (ZAMPHIA) reported a National HIV prevalence of 11% among people aged 15 years and older, however, when disaggregated by sex, women bear a higher prevalence of 13.9% while it is 8% in males (8). This further puts women at an increased risk of having persistent infection with HPV leading to cervical cancer.

In 2018, the WHO recognized cervical cancer as a public health problem and announced a strategy for its elimination by setting triple targets to be achieved by 2030 (9). According to this strategy, the first target entails that 90% of girls should be fully vaccinated against HPV by age 15 years and this is the focus of this paper. There is overwhelming evidence of the safety and effectiveness of the HPV vaccine as a primary prevention for cervical cancer (10).

The HPV vaccine is primarily recommended for adolescents aged 9–14 years (11), however, most countries in SSA are currently implementing girls-only programs (12). In contrast, high-income countries (HIC) have commenced gender-neutral programs for both girls and boys as the HPV vaccine is more accessible (11). Countries that have implemented national HPV vaccination programs, deliver vaccinations in various settings such as schools, health facilities, community outreach posts, or a combination of different platforms (13, 14).

Since 2019, Zambia has been offering the two-dose HPV vaccine to 14-year-old girls 12 months apart, following a demonstration project done between 2013 and 2017 in Lusaka Province (15). The national HPV vaccination program is campaign-based, conducted annually during the first round of Child Health Week (CHWk1), lasting six days from Monday to Saturday, after which walk-in vaccinations are at the health facilities for those who could have missed out during the campaign. The primary vaccination platforms include static at health facilities and outreach at schools and other community points. However, uptake has been low owing to different factors such as parental refusal, beliefs in myths and misinformation, school closures due to the COVID-19 pandemic and its prevention measures (15). Zambia's reported coverage for dose one in 2019 was 75%, which dropped to 39% in 2021 owing to some of these highlighted factors (16, 17).

Understanding adolescents' knowledge and perceptions of the HPV vaccine is critical. Despite adolescents being the primary recipients (18), they are frequently left out in decision-making and research. In Zambia, most research has focused on other stakeholders, such as parents (6, 17, 19–22) and healthcare workers (22, 23) with very few studies focusing on adolescent girls as participants (24), despite being important stakeholders. The available literature has scanty information on adolescent girls' knowledge and perceptions regarding the HPV vaccine and this is likely to impact acceptability and uptake (25).

Therefore, adolescents' attitudes regarding the vaccine should be explored as a first step, to ensure the success of the HPV vaccination program as they are key stakeholders. This study is partly framed within the health belief model (HBM), a well-known and frequently used theory commonly used for exploring perceptions that may influence health-seeking behaviour such as HPV vaccine acceptability and uptake (26–29).

Methods

Study design and setting

We conducted an exploratory qualitative study using semi-structured interviews with adolescent girls between June 2021 and November 2021 within selected schools and health facilities of Lusaka district, the capital city of Zambia. The primary site for HPV vaccination is the school, as most adolescents within the target age group are found in schools. The Ministries of Health and General Education collaborate in implementing the HPV vaccination program. The number of eligible girls is determined using school registers, headcount, and Central Statistics Office figures (Now Zambia Statistics Office). At the same time, community health workers identify out-of-school girls in a door-to-door fashion or through civil societies and these girls receive the vaccine from health facilities or community outreach points.

Sampling

In the first stage, schools enrolling adolescent girls aged 15–18 years within the subdistricts of Lusaka were sampled purposively as those participating in the HPV vaccination program. Thereafter, girls aged 15–18 years were selected based on their eligibility to receive the HPV vaccine, regardless of their vaccination status. The selection of this age group was based on Zambia's national HPV vaccination policy rolled out in 2019, which currently targets 14-year-old girls for dose one (30), which was preceded by a demonstration project between 2013 and 2017 targeting 9- and 10-year-old girls out of school or school grade 4 pupils (31). The included schools were sampled conveniently with a combination of public, community, and private schools. The communities served by the various schools are primarily urban either in low, medium, or high-density areas.

Eleven schools were included with a minimum of two eligible girls per school selected to participate in the study. Although participants in our study were not asked about their socioeconomic status, a recent study within the same setting which focused on parents showed that most participants were either in the middle or lower wealth quintiles (17). The researchers met the headteachers to get access to the schools to sample eligible girls. Adolescent girls were identified either through the class teacher or the focal point teacher for school health-related activities. The potentially eligible girls were met during class break times slated at different times of the day.

Out-of-school girls were identified with the help of community health volunteers. Information about the study was given to the girls, and if they were willing to participate, information sheets and consent forms were presented in English or Local language in a sealed envelope for the girls to deliver to their parents for consent purposes. The girls were asked to return the forms once the parents reviewed them, and those who agreed to participate signed the informed consent form. Assent to participate in the study and interview audio recordings were obtained from the adolescent girls after parental consent.

Data collection

The semi-structured interview guide consisted of questions and probes that focused on socio-demographics; knowledge of HPV and the HPV vaccine, perceptions regarding the HPV vaccine, vaccination status (whether they had received at least one dose of the HPV vaccine), willingness to vaccinate for those not vaccinated or motivation for those vaccinated, and suggestions related to increasing HPV vaccine uptake. We explored knowledge and awareness by asking participants what they knew about HPV, what type of conditions it causes, if they knew about cervical cancer or genital warts and how they can be prevented, and how to prevent transmission. The questions regarding the HPV vaccine were whether they have heard about it, when it is given and how, and its purpose. To assess perceptions regarding the HPV vaccine, we used the HBM.

The HBM was developed in the early 1950s as a cognitive theory to predict health-seeking behavior (32). The original HBM postulates that for an individual to take a health-related action, they should perceive the disease as severe, perceive their susceptibility to the disease, believe that it is beneficial to take preventative action (HPV vaccination, in this case), and not perceive significant barriers to taking the health action (32). Two other constructs were added; self-efficacy (one's own confidence to engage in the behavior) and cues to action (specific triggers to action). Cues to action may be internal such as experiencing symptoms, or external such as receiving advice from friends, family members, or health care providers (32).

Some of the questions asked to the participants based on the HBM included; how likely are you to get infected with HPV, how severe would the HPV infection be if you got infected, what do you think are the benefits of getting the HPV vaccine, and what are the barriers to getting the HPV vaccine. See Table 1 for details.

An iterative process was used to develop and refine the interview guide. The guide was initially piloted using two interviews, after which edits were made to increase comprehension of the questions and improve clarity. Interviews took place in a private room on school premises for school girls and within health facilities for out-of-school girls. Interviews were conducted by one of the authors (MKL), experienced in conducting qualitative interviews and research related to HPV and HPV vaccination.

The interviewer's identity (MKL) as a medical doctor at the highest-level referral hospital in Lusaka could have potentially influenced the mutual relationship with participants and could have influenced how questions were asked. Further, the adolescents could easily feel the power difference and withhold information thinking the interviewer knows it all. The interviewer tried as much as possible to explain her current role as a researcher with a primary role in collecting data. To help the interviewer to be neutral, a reflexivity journal was maintained. Interviews were conducted in the local language, Cinyanja, or English, depending on the participants' preference.

TABLE 1 Examples of questions asked under each of the health belief model constructs.

HBM construct	Example question
Perceived susceptibility to HPV infection	How likely do you think are you to get infected with HPV?
Perceived severity of HPV infection	How severe would the HPV infection be if you got infected?
Perceived benefits of HPV vaccination	What do you think are the benefits of getting the HPV vaccine?
Perceived barriers to HPV vaccination	What are the possible things that can prevent you from receiving the HPV vaccine?
Cues to receive the HPV vaccine	What motivated you to get the HPV vaccine or why do you intend to get the HPV vaccine? (Depending on vaccination status or willingness to vaccinate)
Self-efficacy on getting the HPV vaccine	Could you please tell me more about your belief in your ability to receive the HPV vaccine?

All interviews were audio recorded using a voice recorder and transcribed verbatim.

Participants were allocated unique identification numbers to ensure anonymity during data analysis and discussion of results. All data were anonymized and kept securely. Data were collected until saturation was achieved. Saturation in this case was defined as a point where no additional data was obtained (33). This rigorous data collection process was used to assure dependability.

Data management and analysis

All interviews were transcribed verbatim by trained research assistants shortly after the interview; each transcript was checked for accuracy by one of the authors by listening to segments of the audio recording. Demographic data were collected to record the characteristics of the girls. Completed and final transcripts were imported into NVIVO 12.0 for data management and analysis.

Thematic analysis was used to identify emerging themes using a six-step approach: (a) familiarisation with the data through close reading of transcripts and memoing, (b) generating initial codes and developing a codebook, (c) searching for themes, (d) reviewing themes, (e) defining and naming themes, and (f) writing up the findings (34). Even though the study was framed within the HBM, thematic analysis was the most ideal approach to capture all aspects of data deductively and inductively. Other studies using the HBM as the guiding framework have used thematic analysis (35).

Transcripts were read thoroughly to understand what the adolescent girls were expressing, and memoing was used to reflect on the data and the analysis process. To assure confirmability, data was checked and rechecked throughout data collection and analysis. The initial codebook was developed (based on the HBM constructs for perceptions deductively) and codes were derived from the memoing process. Coding is an important step in data analysis, as it adds meaning to the data. Initially, one co-author (MKL) coded four transcripts to pilot the codebook, and a second co-author (SF) reviewed the transcripts, any disagreements in coding were discussed until consensus was reached or with a third co-author (MK), this member checking was done to ensure credibility of the data analysis.

The codebook was further refined through this iterative process until it was stable. Health belief model constructs were used as deductive codes. Using the finalised codebook, the rest of the transcripts were coded by MKL. Coded excerpts were then arranged into sub-themes and later themes. Data related to HBM constructs were coded deductively, while other emerging themes were coded inductively (34).

The standards for reporting qualitative research have been followed in the writing of this manuscript (36).

Ethical considerations

The study was conducted as per the national and international ethical principles in dealing with minors in research. Ethics approval was obtained from the University of Zambia Biomedical Research Ethics Committee (UNZABREC) Ref: 1609-2021, University of the Witwatersrand University Health Research Ethics Committee (HREC Medical) Ref: M21/04/73. A waiver was obtained from the University of North Carolina (UNC) Ethics Committee. Permission was sought from the Ministries of Health and General education and the heads of institutions for the study sites. The study was further registered with the Zambia National Health Research Authority (NHRA). Minors were only allowed to give assent and participate in the study after informed parental consent. Compensation of $5 was given to all participants for their time. The completed assent and parental informed consent forms and interview transcripts were stored separately. Participants were free to withdraw from the study without repercussions, and confidentiality was observed.

Results

We invited 35 girls to participate in the study. Four girls were ineligible to participate due to lack of parental consent, and one girl was ineligible due to her age (<14 years old, invited by error) and we reached saturation at 30 participants. Of the 30 participants interviewed (age range: 15–18 years old), 17 had received at least one dose of HPV vaccine and 27 were enrolled in school (**Table 2**). We categorized findings related to the following themes: knowledge about HPV and HPV vaccination, perceived susceptibility to HPV infection, perceived severity of HPV infection, perceived benefits of HPV vaccination, perceived barriers to HPV vaccination, cues to HPV vaccine uptake, self-efficacy, and participants' suggestions to improve HPV vaccine uptake.

Knowledge about HPV and HPV vaccine

Participants displayed varying knowledge about HPV and HPV vaccination. Some were knowledgeable about HPV, its consequences, and the role of vaccination. However, some were not aware or knew very little, especially the unvaccinated girls:

> *What I know about the HPV vaccine is that it can protect me from having cervical cancer.* ***A7, vaccinated***

One unvaccinated girl mentioned having easy access to a health facility, but had no information about the HPV vaccine:

> *The place to access the vaccine is quite near, but I don't know anything about the HPV vaccine.* ***A8, unvaccinated***

TABLE 2 Participants characteristics.

Participant ID	Sub-district	Age	School	School grade	School type	Vaccinated?
A1	Kanyama	17	Yes	8	Public	No
A2	Matero	15	Yes	9	Public	Yes
A3	Matero	15	Yes	7	Public	Yes
A4	Chelston	18	Yes	12	Public	Yes
A5	Chelston	16	Yes	7	Public	No
A6	Chilenje	15	Yes	11	Private	No
A7	Chelston	15	Yes	9	Quasi	Yes
A8	Chelston	15	Yes	9	Public	No
A9	Kanyama	16	Yes	9	Private	Yes
A10	Chelston	16	Yes	8	Private	Yes
A11	Chelston	16	Yes	7	Public	No
A12	Chawama	16	Yes	8	Private	Yes
A13	Chelston	15	Yes	9	Public	Yes
A14	Kanyama	17	Yes	8	Public	Yes
A15	Chawama	15	Yes	7	Community	Yes
A16	Chawama	15	Yes	7	Community	Yes
A17	Chawama	15	Yes	8	Private	Yes
A18	Chawama	16	Yes	10	Public	No
A19	Chawama	15	Yes	7	Community	Yes
A20	Chilenje	16	Yes	8	Private	No
A21	Chawama	17	Yes	11	Public	No
A22	Chawama	17	Yes	11	Public	Yes
A23	Chawama	16	Yes	10	Public	Yes
A24	Chipata	18	Yes	10	Public	No
A25	Chipata	17	Yes	9	Public	No
A26	Chipata	15	Yes	6	Public	No
A27	Chilenje	16	No	NA	NA	No
A28	Chilenje	16	No	NA	NA	No
A29	Chilenje	15	No	NA	NA	Yes
A30	Chipata	15	Yes	8	Public	Yes

While another unvaccinated girl expressed fear due to a lack of awareness:

> *We (adolescent girls) are all scared… because we don't really know what the vaccine is really about.* ***A27, unvaccinated***

Both vaccinated and unvaccinated participants discussed HPV as a sexually transmitted infection. They also discussed the increased risk of cervical cancer for those who are unvaccinated:

> *I know that uh it's transmitted through sexual intercourse (…) it is found on the foreskin like those men who are not circumcised yet do have sex, and I know that it attacks the cervix of the womb (…) I knew that this is a virus that usually comes from men and I learnt that it is usually on the foreskin of the penis (…) when it comes to a woman it is something some kind like it is foreign, so it reacts. But what I know is that it doesn't usually react, first takes some time and then it is going to develop into cervical cancer.* ***A21, unvaccinated***

> *This virus is usually found in men at the foreskin, and it is transmitted sexually into the vagina. It won't react that much the same that day, but it will maybe some years (…) that's where cervical cancer comes in.* ***A22, vaccinated***

Perceived susceptibility

Adolescent girls who reported that they were not sexually active but were thinking about future sexual encounters such as marriage or non-consensual sex such as rape were more conscious about the dangers of HPV and so believed they were more vulnerable to HPV infection. However, some girls felt they were not susceptible to HPV infection as they were not sexually active, hence did not feel the need to take the HPV vaccine until they were older and sexually active. Adolescent girls discussed circumstances beyond their control, such as being raped, which could put them at risk of infection with HPV. Further, there was an inclination towards men being carriers of HPV and not women.

> *There are so many ways in which us girls can get the virus (…) like if we get raped, and you (we) can get the virus. So, it is very important that we get the vaccine so that even when I get the devastating news that I have been raped, at least I will not get the HPV.* ***A14, vaccinated***

> *Because if I am not really on the safe side, I can get married to someone who has got that HPV because from what I know is that it is coming from men. So, for example, my husband*

> *might have it if I do not have any knowledge about It, and I might end up having cervical cancer.* ***A21, unvaccinated***

However, when an unvaccinated girl was asked about her risk of being infected with HPV, she said she would not get the virus "because I am not sexually active." ***A28, unvaccinated***.

While a vaccinated girl had this to say:

> *Abstinence is the best way, that's what I'm practicing so that I can't get the HPV and maybe others can use condoms if they are married.* ***A13, vaccinated***

Perceived severity of HPV infection

Some adolescents reported a higher perception of the severity of HPV infection especially when they were aware of its negative repercussions such as someone getting cervical cancer or experiencing other related health problems including death. Additionally, some perceived that their performance and participation in academic and career-related activities may be affected hence impacting their future professional prospects. Participants reported that their sense of self-worth may suffer as a result of worries about potential health effects and career progression.

> *It will affect me as I have a dream of becoming an engineer, but if I have this disease (cervical cancer), I can't go further in achieving my goals.* ***A23, vaccinated***

> *We were told not to sleep with boys as we would get the virus which doesn't go away until you die.* ***A1, unvaccinated***

Perceived benefits of HPV vaccination

Adolescent girls, regardless of their vaccination status, perceived HPV vaccination as being beneficial. Protection against cervical cancer was the primary benefit that participants discussed. Participants reported that the benefits of the HPV vaccine provided one with a feeling of safety, especially that the vaccine was known to be safe and effective.

> *The vaccine is very important to us, it prevents us from getting the cervical cancer. At some point we can be sexually active but if we never had that vaccine, HPV can be easily transmitted into us coz (sic) it comes as a foreign material. So as for that when you get the (HPV) vaccine it will prevent cervical cancer (hmm), it will act as a shield of course.* ***A22, vaccinated***

> *I can say I have not seen any bad side with these uh vaccinations coz (sic) it is just there to prevent those diseases that I might have in future, like cervical cancer, so just better to secure the future.* ***A21, unvaccinated***

Perceived barriers to HPV vaccination

There were several barriers reportedly experienced by both vaccinated and unvaccinated. These were coded as subthemes, namely: parental refusal to give consent, belief in myths and misconceptions, negative peer influence, being out of school, and perceived vaccine side effects.

Parents play a key role in the vaccination of their children, as they must consent for them due to their age. Even when adolescent girls may want to get the vaccine, the final decision comes from the parents. Participants reported conflict between mothers and daughters, as some adolescents were willing to receive the vaccine but were discouraged or stopped by parents, especially mothers.

> *Some (adolescents) think it's good, but their parents don't. So, there may be a bit of conflict between the two owing to the fact that most of my friend's parents are not educated and hence don't understand the importance of the vaccine, unlike us students who come here and understand the advantage of getting the vaccine. So, others think it's good while others don't.* ***A13, vaccinated***

> *My mum just refused me from getting the vaccine but I really wanted to get the vaccine I heard the effects of this disease (cervical cancer) and really wanted to get the vaccine, but my mum refused.* ***A20, unvaccinated***

In addition, participants reported that peers also influenced their reactions to the vaccine:

> *Well, at my previous school, I was willing to get injected, but after I transferred to this school, I started getting discouraged because of the comments they (peers) used to make such as they are just collecting your blood to take it elsewhere.* ***A17, vaccinated***

One participant indicated that some adolescent girls choose not to vaccinate because their peers say that one might get other diseases*: "you will be opening the door to other illnesses."* ***A27, unvaccinated***.

Belief in myths and misinformation were reported amongst both the vaccinated and unvaccinated girls. These myths seem to be perpetuated by different members of the community (including parents and peers) sharing false information, instilling fear in some girls. The most common myth was that the vaccine is meant to sterilize girls.

> *Then there some who say you are not supposed to get the vaccine because you will never have children, you will be barren for the rest of your life.* ***A7, vaccinated***

> *They get wrong information from the community. Some say you may die after taking the vaccine (…) they are told that they have*

> *just come to kill us all because there are a lot of females in our population.* ***A27, unvaccinated***

The misinformation was worsened by the introduction of the COVID-19 vaccine, where the community assumed that adolescents were secretly being inoculated with the COVID-19 vaccine within the pretext of administering the HPV vaccine.

> *Others are scared of the injections they think it's the COVID vaccine.* ***A2, unvaccinated***

> *They think it is expired, harmful, and that it's the corona vaccine (…) that it's harmful because they have seen fake information on the internet, that the vaccine can kill, the whites want to kill Africans (…).* ***A13, vaccinated***

Other myths included the belief that the vaccine can cause illness or death:

> *Some were saying that oh maybe these people they are just here to get the blood for this what uh witchcraft activities so they want us to donate our blood. There will be that, they will put us into satanism.* ***A22, vaccinated***

> *I think there may be effects like paralysis of my arm or falling ill, or that I may have a sore at the site of injection that won't go away and later turn into a cancer (…). They (adolescents) get wrong information from the community. Some say you may die after taking the vaccine… they are told that they have just come to kill us all because there are a lot of females in our population.* ***A27, unvaccinated***

Another barrier expressed by adolescents was that the vaccination program was biased toward school-going girls:

> *They (out-of-school girls) cannot have anyone to go and educate them about the HPV virus that's the disadvantage for most of them. They are taken into early marriages without consent so that can also prevent them from learning about it (HPV vaccine), and there is no one to educate them.* ***A13, vaccinated***

Perceived side effects of HPV vaccine

Some adolescent girls perceived that the HPV vaccine had variable side effects some of which could lead to permanent dysfunction of some body parts which discouraged some from receiving the vaccine.

> *It was painful at first then I was uh something was itching so yeah it was very painful at first and then it stopped in three to two days.* ***A23, vaccinated***

> *Then also that you may experience headaches and stomach-aches (…) generally feeling ill.* ***A8, unvaccinated***

Cues to HPV vaccination

Participants mentioned getting a recommendation from parents and friends to receive the HPV vaccine. These served an important role as they helped ease and allay fears that eligible adolescents could have.

> *I went home to ask my mum if I could get the vaccine, then she said go back! Go and take the vaccine coz (sic) it may protect you somehow as you are growing (…) I was encouraged by my mum to say the vaccine is good that's how I got motivated. I know since mum is concerned about this let me just do it.* ***A22, vaccinated***

> *My friend is the one who told me to say, next time when they come (vaccinators) you just have to do it, she (a friend) has been encouraging me (…).* ***A21, unvaccinated***

Self-efficacy in getting the HPV vaccine

Adolescents showed willingness to take the necessary steps to get the vaccine, and expressed confidence in their own abilities to get vaccinated:

> *I think it just with my own motivation coz (sic) I think the health post they are always open (uh hmm) so any day I can just go there (and get the vaccine) yes, coz (sic) even now so I am out of class I have knocked off, I can go and get the vaccine.* ***A21, unvaccinated***

> *I was strongly encouraged and I have that boldness that's how I got the vaccine.* ***A22, vaccinated***

Participants' suggestions for increasing HPV vaccine uptake

Adolescents had several suggestions for increasing HPV vaccination amidst mixed messages. Some suggestions related to increasing knowledge and awareness of HPV vaccination by making information about HPV vaccination more accessible within communities through social mobilization campaigns, including information on HPV within the school curriculum and active involvement of politicians:

> *It should be more like a topic. They should put in a subject like science. Teachers make us understand coz (sic) me I have heard of it and many grade 11s have heard of it. But what of these grade 4s? They only know STIs like HIV. If you ask any child to say what kind of STI do you know, they mention HIV.* ***A21, unvaccinated***

> *Even the vice president needs to say something about the vaccine, encourage the young girls to get the vaccine so that they don't get diseases such as cervical cancer.* ***A15, vaccinated***

Some adolescents felt that parents and out-of-school girls should be educated more about the HPV vaccine:

> *Well, maybe talking to parents about the benefits of the vaccine, and assure them that nothing bad will happen when their daughters take it.* ***A15, vaccinated***

> *(…) they (Out of school) can be informed by community sensitisation on the advantages of being vaccinated.* ***A28, unvaccinated***

Discussion

This study set out to understand adolescent girls' knowledge and perceptions regarding HPV and the HPV vaccine and discuss its acceptability and uptake implications. The adolescent girls showed variable knowledge of HPV and HPV vaccination as more vaccinated girls were aware of HPV, its transmission route, and the outcome of infection. The attitudes towards the vaccine were generally positive among our study participants. The adolescent girls generally perceived the HPV vaccine as beneficial to limit the spread of HPV and prevent conditions like cervical cancer.

However, several barriers to receiving the HPV vaccine were highlighted, such as lack of parental consent, negative peer influence, belief in myths and misinformation, confusion, and misconceptions around the relationship of the HPV vaccine to the COVID-19 vaccine. Knowledge levels and positive perceptions play an important role in the acceptability of HPV vaccination, however, strategies to overcome the perceived barriers should be identified and implemented to actualize a high uptake (37, 38).

We found that adolescent girls in our study had positive perceptions towards the HPV vaccine, which is likely to increase its acceptability and uptake. Similarly, a qualitative inquiry conducted in Uganda found that girls with good attitudes towards the HPV vaccine widely accepted it despite most of them not having been vaccinated (39). This finding of positive perceptions regarding the HPV vaccine among Zambian adolescent girls holds promise as it could be used to reinforce positive messages about the vaccine to improve future uptake. HPV vaccine uptake remains low in Zambia, for 2021, only 39% and 31% of the eligible girls had received dose one and dose two respectively (16). Therefore, much effort is required to ride on these positive attitudes, because previous studies showed that in some instances, high acceptability did not translate into high HPV vaccine uptake (40, 41).

There was variable knowledge about HPV in general, the route of HPV transmission, and the HPV vaccine itself. Some girls were knowledgeable, while others were not even aware of HPV and its vaccine. In the extant literature, low levels of knowledge (42) have been found in different settings and many times have contributed to low HPV vaccine uptake (43). Similarly, a qualitative study done in the UK early into the HPV vaccination program showed low levels of HPV vaccine knowledge among the recipients (44). Within SSA, a recent study done in Tanzania found low levels of knowledge among adolescents, parents, and teachers, especially before the HPV vaccine was integrated with other health programs (45). Additionally, a quantitative study among Brazilian adolescent girls (46) and a systematic review among European adolescents (47) showed low levels of knowledge.

Therefore, low knowledge of HPV and HPV vaccine is a common feature in different parts of the world and is implicated as one of the contributors to low global HPV vaccination (40). For Zambia, these findings of mixed knowledge among participants in the capital city could be explained by the program being in its infancy, and hopefully, as it matures, more people may be aware through access to information about the HPV vaccine. Therefore, in our study context, culturally appropriate and contextualized strategies could be implemented with the aim of raising awareness and improving knowledge, and subsequently improving HPV vaccine uptake (37).

Examples of strategies include messages around the HPV vaccine packaged in an easy-to-understand format and language using the most accessible platforms: door-to-door campaigns, churches, markets, schools, and health facilities to ensure widespread information sharing. We also suggest that a quantitative inquiry be conducted to measure the actual levels of knowledge using validated tools.

While our participants expressed willingness to recommend the vaccine or intent to get vaccinated, there were some perceived barriers such as lack of parental consent, belief in myths and misconceptions, and negative peer influence. While parental support was viewed as an enabling factor for adolescent girls to receive HPV vaccination, parental refusal to consent was perceived as a significant barrier.

These findings align with other studies showing that parents, specifically mothers, play a key role in influencing the health-related behavior of their daughters (48). When mothers said no, girls did not get the vaccine. In this study, parental refusal superseded the final decision even when girls were willing to receive the vaccine. However, daughters' parental consent for HPV vaccination in the Zambian context is implied with an opt-out approach, there are no legal requirements for vaccination. Therefore, in a situation where the adolescent insists on receiving the vaccine in the absence of parental consent, the vaccine is given (49).

Our study also showed that when mothers expressed support or encouragement, there was no resistance by the girls. This indicates that mothers would be an essential target group for strategies aiming to increase HPV vaccine uptake in our study setting. Parents and elders in general are held in high esteem, especially in conservative cultures in the African context, and decisions regarding their children are usually final without any further discussion as they are perceived to be in the best interest of the child (50, 51).

Contrary to these findings within the HPV vaccination space, parents in Zambia have actively vaccinated their infants with

other childhood vaccines such as oral polio vaccine, Diphtheria, and tetanus vaccines. There has been a gradual increase and sustainable coverage in the period 2000–2018 owing to strong communication, collaboration, and coordination in the background of strong health systems (52). Therefore, considering the relative novelty of the HPV vaccine in Zambia, applying strategies that have been used to improve other vaccine coverage may be necessary (38, 52). Additionally, further studies to understand factors influencing parental decision-making for their daughter's vaccination should be considered to aid in mitigating experienced barriers (17).

There were several myths about the HPV vaccine discussed by adolescent girls in our study, some of which have been reported frequently in the literature. These myths included the vaccine causing infertility (53) and (54) the Western world attempting to eliminate the African population, vaccines being experimental and not safe (44), and the COVID-19 vaccine being given to adolescent girls instead of the HPV vaccine (16). Beliefs in vaccine myths are rampant globally and the HPV vaccine has not been spared (54, 55). Parents who hold fast to myths and misconceptions coupled with low education levels are more likely to decline vaccinating their daughters (56), and as reported in our study, beliefs in myths and misinformation discourage adolescent girls from adopting preventive interventions.

Such findings are worsened by anti-vaccine movements present among society, healthcare workers, and various media platforms misleading many citizens (57). Counter and positive context-specific messages are key in ensuring constant debunking of these myths and misconceptions such as the HPV vaccine does not cause ovarian insufficiency as early claims were based on case reports (58). Dispelling myths and misinformation is, however, not easy, and health education alone is not sufficient, implementing multiple context specific strategies is of paramount importance (37).

In our study, peers were reported to have mixed roles to encourage or discourage vaccination most probably due to the variations in levels of knowledge. These findings on the role of peer influence are not unique to our study but have been elicited elsewhere (59, 60). Adolescence is a period where there is a lot of succumbing to "peer pressure" as adolescents seek a sense of belonging and validation by peers. In some instances, school vaccination programs have led to mass psychogenic effects and this has negatively affected the vaccination programs (61). Therefore, with active engagement and education, peers can play a critical role in increasing HPV vaccine uptake if they are knowledgeable and they themselves have experienced vaccination.

Some of our participants had a low perceived risk and susceptibility to HPV infection, which appears to be a common finding for people who are not sexually active (35). The asymptomatic nature of early HPV infection and marketing of the vaccine as a prevention for sexually transmitted disease in contrast with other childhood vaccines could contribute to this perception. A study in Ghana on risk perception for developing cervical cancer also showed lower risk perception compared to the actual risk (62). Therefore, ongoing education for adolescent girls and parents on HPV virus infection disease progression is of paramount importance. These key stakeholders must be educated on the importance of the HPV vaccine being given before they become sexually active.

Strengths and limitations

This study has some strengths in that the voices of the primary HPV vaccine recipients have been illuminated. Out-of-school adolescents and those in hard-to-reach areas are rarely included in studies. We included out-of-school girls hence increasing the transferability of our findings in situations with in-school and out-of-school girls.

The use of the HBM as a guiding framework could be a basis for future quantitative research among adolescent girls with a view to ascertain whether some of the perceptions and experienced barriers are associated with HPV vaccine uptake and how they could be mitigated. Further, even though the current national guidelines entail a girls-only vaccination program, a future study involving boys is necessary because as the vaccine becomes more available, gender-neutral HPV vaccination will become policy.

To the best of our knowledge, this is the first study exploring knowledge, perceptions, and suggestions to increase the HPV vaccine from the perspective of adolescent girls in Zambia since the launch of the national program in 2019. It reinforces the earlier findings by other researchers among multiple stakeholders of low to moderate knowledge, positive attitudes, and perceived barriers amid high acceptability and low HPV vaccine uptake. It is important for policymakers to consider suggestions made by adolescent girls for the continued program implementation.

Our study is not without limitations. This study is qualitative and the participants were purposively sampled, therefore our results may vary with other settings if we randomly sampled a higher number of adolescent girls. This study enrolled participants in a single setting (Lusaka, Zambia), further investigation may be needed to confirm whether findings are generalizable to other settings, hence may affect transferability. These findings are however, still relevant within the Zambian context, and could still be useful in other sub-Saharan African countries.

Further, this study did not ask the girls what their HIV status was, therefore there is no information that is specifically about HIV keeping in mind the increased risk of HPV acquisition and cervical cancer development among people living with HIV.

We do not report differences in health beliefs between sub-groups as our goal was not to achieve saturation in the subgroups of vaccinated and unvaccinated, as well as in-school and out-of-school girls. We focused on the emerging themes from the whole data set other than the disaggregated data as girls were not sampled in that way. Additionally, there were only three out-of-school girls.

To address these limitations, we have included a thorough explanation of the sampling methods, discussed our findings

within the context of existing literature, supported findings with quotes from our interviews reached saturation within our sample, and engaged in an iterative data collection and analysis process, thus increasing the dependability and transferability of findings.

Conclusion

For the first time since the nationwide roll out of the HPV vaccination program in Zambia we have highlighted the knowledge and perceptions of adolescent girls regarding the HPV vaccine, illuminating factors that may influence HPV vaccine acceptability and uptake in Zambia, from the perspective of adolescent girls. Our findings on adolescent perceptions are similar to those other earlier studies in Zambia have found with different stakeholders.

The knowledge that the HPV vaccine can provide long-term protection may improve uptake. There are still urgent issues that need to be addressed such as myths and misinformation, and lack of parental consent to vaccinate daughters. To promote greater knowledge and boost vaccination uptake, ongoing efforts must be made to offer correct information, address misinformation, and improve understanding by adolescents and parents on HPV infection and the advantages of HPV vaccination.

Additionally, we recommend that future studies enroll adolescent girls based on school status and to reach saturation considering that out-of-school girls are difficult to just as has been shown in this study, despite their high vulnerability to HPV infection and its consequences.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by University of Zambia Biomedical Research Ethics Committee (UNZABREC) Ref: 1609-2021, University of the Witwatersrand University Health Research Ethics Committee (HREC Medical) Ref: M21/04/73. A waiver was obtained from the University of North Carolina (UNC) Ethics Committee. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin. Written informed consent was obtained from the individual (s), and minor(s)' legal guardian/next of kin, for the publication of any potentially identifiable images or data included in this article.

Author contributions

Conceptualization, ML, MK, MMw, CC; methodology, ML, MK, MMw, MMu, SF, and CC; formal analysis, ML, MK, and SF; data curation, ML, MK, and SF; writing–original draft preparation, ML; writing–review and editing, ML, MK, MMw, SF, MMu, and CC; funding acquisition, ML and CC; project administration, ML. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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CHAPTER FIVE: Correlates of parental consent to human papillomavirus vaccine uptake by their adolescent daughters in Zambia: Application of the health belief model

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Parental consent continues to play an important role in the HPV vaccination process due to the age of primary vaccine recipients. Available data has shown that the acceptability of the HPV vaccine is high. However, this does not match the actual uptake. There is limited available data to understand this mismatch. This paper aimed to understand whether health beliefs and knowledge are associated with parental consent in Lusaka, Zambia. The health belief model was used as a guiding framework to develop the data-collecting tool that was administered in a survey of parents of vaccine-eligible adolescent girls. The paper is published in Vaccines Journal.

Article

Correlates of Parental Consent to Human Papillomavirus Vaccine Uptake by Their Adolescent Daughters in ZAMBIA: Application of the Health Belief Model

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Abstract: Parental consent for adolescent human papillomavirus (HPV) vaccine uptake is important; however, refusal is prevalent. Therefore, this study aimed to understand factors associated with parental consent for their adolescent daughter's HPV vaccination. A cross-sectional study was conducted in Lusaka, Zambia, between September and October 2021. We recruited parents from different social settings. The means and standard deviations or median and interquartile ranges were used as appropriate to summarise continuous variables. Simple and multiple logistic regression models were fitted with robust estimation of standard errors. The odds ratios are presented with 95% CI. Mediation analysis was conducted using a generalised structural equation model. The study enrolled 400 parents, mean age 45.7 years [95% CI, 44.3–47.1]. Two hundred and fifteen (53.8%) parents reported consenting to their daughters' HPV vaccination, and their daughters received it. None of the health belief model (HBM) construct scores showed an independent association with parental consent. Higher, compared to lower wealth index (AOR; 2.32, 95% CI: 1.29–4.16), knowing someone with genital warts (AOR = 2.23, 95 CI: 1.04–4.76), cervical cancer screening uptake (AOR = 1.93, 95% CI: 1.03–3.62) were associated with increased odds of parental consent. This study highlights factors influencing parental consent for their daughters' HPV vaccination. Ongoing sensitisation programs are important to improve their decision-making.

Keywords: human papillomavirus vaccination; HPV vaccine; human papillomavirus; genital warts; knowledge; mediation analysis; socio-economic status; cervical cancer screening; generalised structural equation modelling; sub-Saharan Africa

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1. Introduction

The human papillomavirus (HPV) vaccine is one of the greatest inventions in preventing HPV-related conditions. HPV is sexually transmitted, with a significant proportion of sexually active people getting infected in their lifetime [1]. Infection transmission is highest during sexual debut [1]. The point prevalence of HPV infection is estimated at 11–12% globally and 22–24% for sub-Sahara Africa (SSA) [2]. The World Health Organisation (WHO) prequalified the use of the HPV vaccine among adolescent girls in 2006 since it is

more efficacious if administered before sexual debut [3]. From inception, the number of vaccine manufacturers was limited; however, manufacturers from China (bivalent Cecolin®, Xiamen Innovax Biotech Co., Ltd., Xiamen, China) and India [a quadrivalent vaccine from Serum Institute of India-pending prequalification] have come on board in a bid to improve the supply [4,5]. The available HPV vaccines offer protection against prespecified strains; however, cross-protection does occur [6]. HPV vaccines currently on the market include the bivalent (16, 18), quadrivalent and (6, 11, 16, 18) nine-valent (6, 11, 16, 18, 31, 33, 45, 52, 58) [7].

The HPV vaccine is safe and effective for the primary prevention of cervical cancer, which has high morbidity and mortality in sub-Saharan Africa (SSA) [8]. Studies have also shown that the HPV vaccine could be therapeutic in women already infected with high-risk types of HPV 16, 18 and 31 [9]. The World Health Organisations' global strategy to eliminate cervical cancer is set to be operationalised by achieving three targets by 2030 which are; (i) 90% of girls aged 15 years are fully vaccinated against HPV, (ii) 70% of women of reproductive age screened for cervical cancer at least twice at 35 and 45 years with a high-performance test (iii) 90% of women with pre/cancers receive appropriate treatment [10]. Therefore, it is prudent to deliberate nationally to work towards these targets. The primary focus of this paper is on the first target of the global strategy on the use of HPV vaccines among adolescent girls for cervical cancer prevention in Zambia.

Zambia has one of the world's highest cervical cancer incidence rates of 65.5 per 100,000 women and a mortality of 43.3 per 10,000 women, accounting for 23% of all new cancers in the country in 2020 [11,12]. With this high incidence, Zambia is among the first countries in SSA to have introduced a free national cervical cancer screening program, initially targeting women living with human immunodeficiency (WLHIV), later including HIV-negative counterparts [13,14], however screening uptake remains low [15]. Co-infection with HIV and HPV increases the persistence of high-risk HPV infections, rendering WLHIV at an increased risk of developing cervical cancer [14,16]. Furthermore, Zambian women of reproductive age suffer a disproportionately higher incidence of HIV than their male counterparts, increasing the risk of contracting cervical cancer [17]. Literature has shown that WLHIV are up to six times more likely to have cervical cancer than women without HIV [18].

To complement the efforts made through cervical cancer screening, Zambia introduced a campaign-based free national HPV vaccination program in 2019 restricted to a single age cohort of 14-year-old girls with a two-dose regimen, 12 months apart [17]. However, there are challenges of low HPV vaccine uptake; for example, dose one coverage was 78% in 2019, reducing drastically to 39% in 2021 [19]. Some of the reasons implicated in this low uptake include beliefs in myths and misinformation about the HPV vaccine, such as; it can cause infertility, HPV vaccination is viewed as a process of initiation into satanism, school closures due to the COVID-19 pandemic hence schools not accessible as a delivery platform, belief in myths around the COVID-19 vaccine, poor social mobilisation, parents' lack of awareness and non-willingness to consent for daughters' vaccination [19,20].

HPV vaccination in Zambia is non-mandatory; parental consent is required with or without the parent's presence at the point of vaccination. WHO has guided the consent process for eligible adolescents to be reviewed according to country guidelines; hence informed parental consent may be written, verbal or implied [21]. Parental consent plays a critical role in the HPV vaccination process for adolescent girls deemed too young to consent for themselves. Although the HPV vaccine is highly efficacious and safe, vaccine refusal among parents of adolescents is prevalent [22].

Since its national rollout, there has been a paucity of data on factors influencing parental HPV vaccination consent in the Zambian context. In addition, mechanisms that potentially drive parental HPV vaccination consent have not been explored. Previously, Lui et al. [23] reported high HPV vaccine acceptance among female parents in a hypothetical study done in Lusaka, Zambia, before the national rollout. However, this did not match the current low uptake of 39% in 2021, for example [19]. Other regional studies have shown

that even when girls are eligible, they do not receive the HPV vaccine due to non-consent by their parents, posing a considerable barrier to vaccination [24].

Understanding factors influencing parental consent to HPV vaccination, such as beliefs, knowledge, and attitudes, is critical in developing targeted strategies to increase HPV vaccine uptake among adolescent girls [25,26]. Therefore, to understand parents' beliefs and attitudes that influence consenting to HPV vaccine uptake for daughters, we used the health belief model (HBM) as a guiding framework. The HBM is a cognitive model with six constructs: perceived susceptibility, perceived severity, perceived benefits, perceived barriers, self-efficacy, and cues to action [27]. The HBM has been used extensively in health behaviour research to explain the uptake of health interventions such as HPV vaccination uptake [28–30], COVID-19 vaccination hesitancy [31] and cervical screening uptake [32]. However, there are conflicting results in the literature, possibly due to contextual variations such as geographical location, cultural aspects, sample size and study design [33]. We, therefore, included in our analysis other factors such as socio-demographic characteristics, HPV & HPV vaccine knowledge, cervical cancer screening and HIV status, which have been found to predict HPV vaccine consent behaviours [28].

To our knowledge, HBM has not been used previously in Zambia in the context of parental consent for HPV vaccination. Therefore, we hypothesised that parents with higher perceived severity, perceived benefits, perceived susceptibility, higher self-efficacy, more cues to action and lower perceived barriers would be more likely to consent to their daughters' HPV vaccination [29]. Further, based on the findings from earlier studies in Zambia [34,35], we hypothesised that parents with higher knowledge of HPV and HPV vaccine would be more likely to consent to their daughter's vaccination. Lastly, we hypothesized that the effect of HPV and HPV vaccine knowledge levels on parental consent might be mediated by different HBM constructs, as shown in the conceptual diagram in Figure 1.

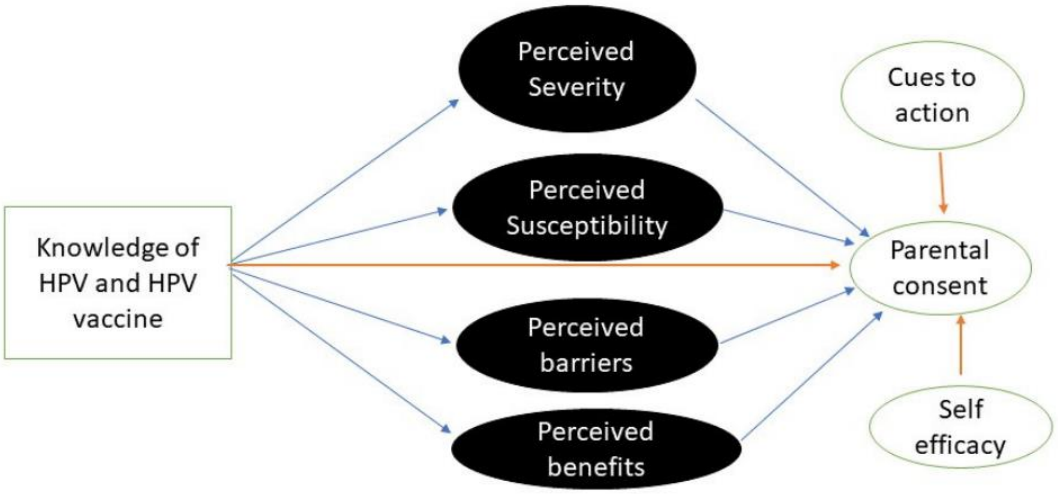

Figure 1. Knowledge directly (⟶) affecting parental consent to vaccinate their daughter or mediated indirectly (⟶) by 4 HBM constructs. At the same time, the other 2 HBM constructs directly affecting (⟶) the outcome.

2. Materials and Methods

2.1. Study Design and Setting

We conducted a cross-sectional study between September and October 2021, in Lusaka district, the capital city of Zambia, with a population of 1,747,152 million people, 417.9 km^2 area and a population density of 4181/km^2 [36]. The district is divided into six subdistricts:

Chilenje, Chawama, Chelston, Chipata, Matero and Kanyama. Primary healthcare facilities within the subdistricts have the task of offering the HPV vaccine to adolescent girls based on the catchment population. During the 2019 vaccine rollout program, 331,154 teenage girls (14 years old) were eligible for dose one and 212,509 in 2020 and 420,704 in 2021 [19].

The target number of adolescent girls for HPV vaccination is determined using school registers from the Ministry of General Education, headcount, and Central Statistical Office figures. Community health workers and civil societies additionally identify out-of-school girls. The HPV vaccination program is campaign based, conducted during the first round of child health week (CHWk1), lasting about six days from Monday to Saturday. The CHWk1 is a biannual event that aims to catch up on vaccinations for children under five years from health facilities and outreach/mobile sites. Additionally, for HPV vaccination, schools are used, making it a mixed approach to capture both in-school and out-of-school girls.

The district health director and health facilities work closely with the Ministry of General Education and schools in planning. Vaccination dates are shared with the school by the district health team so that teachers can prepare for the activity and girls can inform their parents in addition to community and mass media messages. Information sharing with parents varies, ranging from flyers, educational materials, television adverts, radio programs and letters.

The parental consent approach is opt-out, meaning consent is implied unless a girl categorically mentions that her guardians refused; most private schools, however, use the opt-in approach, which requires written parental consent before vaccination [37]. However, if parents decline and the girl is willing to be vaccinated, her wish supersedes parental consent, and the vaccine is given. Healthcare workers play the role of administering the vaccine and educating different stakeholders, whereas teachers play the role of registering and organising the eligible girls, including informing parents. Girls living with HIV take the first HPV vaccine dose with their peers, the intermediate dose from the health facility during the routine anti-retroviral therapy clinics, and the third dose at 12 months when their peers receive the second dose.

2.2. Sampling and Sample Size Considerations

Based on similar studies' estimates [28], we assumed that 267 participants would be sufficient to estimate the proportion of parents who would consent to vaccinate their daughters with precision ±5%. In addition, the sample gave us over 80% power to detect an absolute difference of 20% between consenting and non-consenting parents to vaccinate their daughters as statistically significant at the 5% level between these two equally sized groups.

A two-stage sampling technique was used to enroll respondents. In the first stage, we stratified Lusaka into six sub-districts. Then we randomly selected two zones in each sub-district using probability proportion to zone size. In the second stage, a random sample of 30 respondents per zone was drawn from various social settings, such as markets, saloons, and barber shops, until we reached 400 participants clustered within 12 zones. We inflated the final sample size to 400 participants after accounting for the assumed moderate design effect of 1.5 to counter the loss in precision caused by the clustering of respondents in the 12 zones.

2.3. Data Collection and Variables

Face and content validity of the questionnaire was ascertained by Obstetrician/Gynaecology consultants through a consultative process. We developed an interviewer-administered questionnaire based on the literature [29,38]. The questionnaire was developed in English and translated into one local language (Chinyanja) by a qualified local translator. We did not back-translate the questionnaire at analysis since all the questions were quantitative. We piloted the questionnaire among 33 participants in three sub-districts of Lusaka who were later excluded from the final analysis.

A screening question was asked if the potential participant had a daughter aged 15–18 years. If not, the interview was terminated. This age group was selected because the HPV vaccination program in Zambia targets 14-year-old adolescent girls for dose 1. Therefore, we anticipated that an age range of 15–18 years would give a sample of parents with daughters who would have been eligible to receive the first dose or completed the vaccination schedule during the HPV vaccination demonstration (2013–2017) [20,39] or national roll-out (2019) [40] HPV vaccination programs.

The outcome variable was parental consent for the HPV vaccine for daughters measured on a binary scale (yes = 1, no = 0). The primary exposure variable was the HBM constructs scores. The total scores for the HBM constructs were calculated using the following steps: For each item within the HBM constructs, the numeric values chosen by each respondent, with a five-point Likert scale, were added. Responses were coded such that higher scores indicate a greater level of the relevant construct (strongly disagree = 1, disagree = 2, neutral = 3, agree = 4, strongly agree = 5) and the reverse for perceived barriers. The total possible scores per construct were as follows; (a) perceived susceptibility (3 items = 15), (b) perceived severity (4 items = 20), (c) perceived benefits (4 items = 20), (d) perceived barriers (8 items = 40), (e) self-efficacy (4 items = 20), and (f) cues to action (2 items = 10). Knowledge of HPV (18 items) and HPV vaccine (24 items) scale had three options (true/false/don't know). We assigned a zero for "false/don't know" and a one for "true" options.

In addition, the study measured HPV and HIV-related parental characteristics, including ever screening for cervical cancer (females) (yes = 1, no = 0), parental HIV status (negative = 0, positive = 1, prefer not to say/don't know = 3), the daughter's HIV status (negative = 0, positive = 1, prefer not to say/don't know = 3), and knowing someone with cervical cancer or other HPV-related cancers (yes = 1, no = 0), Socio-demographics included age (continuous), sex (male = 0, female = 1), marital status (single = 0, married = 1) employment(yes = 1, no = 0) and socio-economic status (wealth index as proxy).

The socio-economic status variables used for calculating the wealth index included; source of drinking water, type of toilet, house ownership, employing anyone, use of electricity, type of cooking fuel used and ownership of any of the following; fridge, laptop, television, motorcycle, scooter, mobile phone, watch, livestock, land phone, car, agricultural land, washing machine [41].

Data collectors were trained over five days to understand the questionnaire, the study protocol and the use and configuration of the Open Data Kit (ODK) for data collection (https://getodk.org/). ODK is a free mobile-based platform with four tools serving different functions, namely, Aggregate, Build, Collect and Voice [42]. We used ODK Collect, which can run on Android-based devices and supports multiple methods of transforming data and other services for online and offline use. Further, ODK collect allows building forms in multiple languages, which can be used interchangeably within and between participants with a button click [42]. Due to its multiple advantages, ODK has been widely used in HPV vaccination research in other resource-constrained regions like Tanzania [43] and Senegal [44].

Thus, after piloting the study questionnaire, we changed the data collection platform from google forms to ODK, allowing participant data to be collected offline and uploaded to the database whenever internet connectivity was available. We efficiently used multiple languages based on participants' preferences.

A debriefing meeting about the study was held with the health facility staff, teachers, and community healthcare workers to disseminate information regarding this research. Study participants were sampled from community settings with the help of community healthcare workers. Interviews were conducted in a quiet and private place convenient for the participant, such as community halls. After the interviews, participants were given educational materials on HPV vaccines obtained from the Ministry of Health to bridge the knowledge gap. In addition, participants were allowed to give feedback about the interviews at the end of each session.

2.4. Data Management and Analysis

We used password-locked Android-based mobile tablets to collect and submit data to an online Ona server. Data collection was managed using ODK Aggregate, an intermediate platform for the server and later downloaded into Excel. Data collection was monitored daily by the principal investigator, checked for consistency, cleaned, transferred, and analysed in STATA version 17/BE (Stata Corp., College Station, TX, USA). All analyses accounted for the clustering of respondents within the zones using robust estimation of standard errors (which was achieved using the Stata commands to analyse survey data). In addition, the analysis accounted for the stratification by sub-districts within Lusaka province.

The item scores were summed to create a score for six HBM constructs scales and one knowledge scale. The means and standard deviations or median and interquartile ranges were used as appropriate to summarise continuous variables (age, the six HBM construct scores and knowledge score) and report whether the respondent consented to vaccinate their daughter.

Simple logistic regression models were fitted with robust estimation of standard errors with "consent to vaccinate daughter" as the response variable and one of the predictor variables at a time, to assess for any association between the predictor variable and consent to vaccinate daughter. Afterwards, a multivariable logistic regression model was fitted with six HBM construct scores (priori), and other variables found significant at a 20% level from the univariable logistic regression model. Variables were dropped from the multivariable model sequentially until only important variables remained. Finally, interactions between six HBM construct scores and modifying variables that remained in the final model were considered individually. The Hosmer Lemeshow test was done to assess the goodness of the model fit. The odds ratios are presented with 95% confidence intervals.

Using principal component analysis, we used household assets and other related characteristic variables to calculate the wealth index as a proxy for socio economic status [26]. The wealth index was categorised into five social economic quintiles (poorest, poorer, middle, richer, richest) [28] and further dichotomised (poorest, poorer, middle = poor, richer, richest = rich) for analysis owing to the small sample size.

Further, generalised structural equation modelling was conducted to understand the interrelationships between variables and assess mechanisms of association [45]. Direct, indirect, and total effects were studied to understand the mechanism through which knowledge affected parental consent to vaccinate daughters, part of which could occur through the HBM constructs. The effect of knowledge (exposure variables) on parental consent to vaccinate daughters (outcome variable) while controlling for HBM constructs was the direct effect, while the indirect effect occurred because knowledge affects the HBM constructs, which in turn affect parental consent to vaccinate daughters. Direct and indirect effects together formed the total effects on the outcome. All models independently adjusted for other co-variates, including age, sex, socio-economic status, marital status, and education levels. Odds ratios were used to estimate measures of effect. Bootstraps (52) replications were used to compute standard errors for the effects estimates [45].

The writing of this manuscript was guided by the STROBE statement checklist [46].

3. Results

We enrolled 400 participants; 215 (53.8%) reported consenting to the HPV vaccine for their daughters, and all reported that their daughters received it. The demographic characteristics and total knowledge scores are summarised in Table 1.

Table 1. Socio-demographic characteristics and knowledge scores of participants [a].

Variable	Total Sample N = 400 (%)	Parental Consent to Vaccinate a Daughter	
		No, *n* = 185	**Yes, *n* = 215**
Age years mean [95% CI]	45.7 [44.3–47.1]	46.3 [44.1–48.6]	45.3 [43.6–47.1]
Sex			
Male	50 (12.5)	24 (13.1)	26 (12.0)
Female	350 (87.5)	161 (87.0)	189 (87.9)
Marital status			
Married	264 (66.0)	121 (65.6)	143 (66.5)
Single	136 (34.0)	64 (34.5)	72 (33.5)
Education level			
None/primary	181 (45.3)	89 (48.1)	92 (42.8)
Secondary/Tertiary	219 (54.8)	96 (51.9)	123 (57.2)
Employment			
Unemployed	330 (82.8)	160 (86.5)	170 (79.1)
Employed	70 (17.3)	25 (13.5)	45 (20.9)
Daughter goes to school			
Yes	352 (88.0)	157 (84.8)	195 (90.7)
No	48 (12.0)	28 (15.1)	20 (9.3)
Wealth index			
Poorest/poorer/middle	245 (61.3)	124 (67.0)	121 (56.3)
Richer/richest	155 (38.8)	61 (33.0)	94 (43.7)
Total HPV/HPV vaccine knowledge mean score	11.1 [10.0–12.2]	9.0 [7.4–10.7]	12.7 [11.1–14.3]

Key: 95% CI-95% confidence interval, wealth index α = 0.74, Kaiser-Meyer-Olkin = 0.81.

Health Belief Model constructs scores according to parental consent to vaccinate their daughter.

Figure 2 shows that consenting and non-consenting participants had similar mean scores for all HBM constructs.

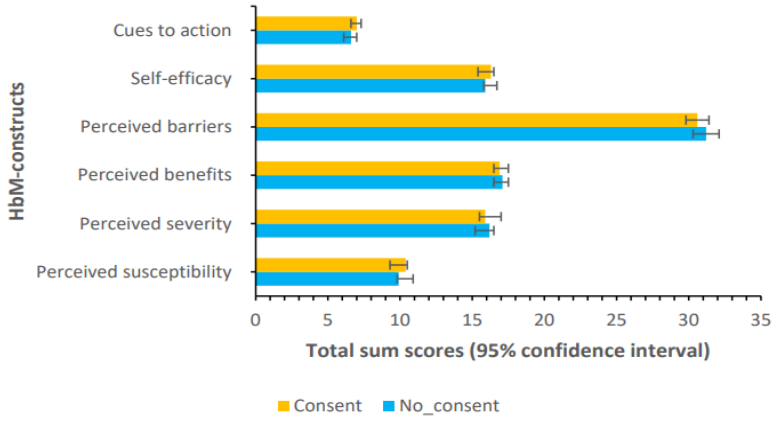

Figure 2. HBM constructs scores according to consent to vaccinate daughter: error bars are 95% confidence intervals.

3.1. HPV and HIV-Related Characteristics

A higher proportion of female participants who consented to vaccinate their daughter had screened for cervical cancer compared to non-consenting parents. Participants who knew their HIV status as positive, knew someone with cervical or HPV-related cancers or

someone who has had genital warts were more likely to consent to daughters' vaccination Table 2.

Table 2. HPV and HIV-related characteristics of participants [a].

Characteristic	Total Population N = 400 (%)	Parental Consent to Vaccinate a Daughter		*p*-Value
		No, *n* = 185 (%)	Yes, *n* = 215 (%)	
Ever been screened for cervical cancer? *n* = 350				0.001
Yes	247 (70.6)	99 (61.5)	148 (78.3)	
No	103 (29.4)	62 (38.5)	41 (21.7)	
Know someone with cervical cancer?				0.370
Yes	167 (41.8)	72 (39.3)	95 (43.8)	
No	233 (58.3)	111 (60.7)	122 (56.2)	
Know someone with other HPV-related cancer, e.g., vulva, penis, oral				0.011
Yes	43 (10.8)	12 (6.6)	31 (14.3)	
No	357 (89.3)	173 (93.5)	184 (85.6)	
Know someone with genital warts?				<0.001
Yes	85 (21.3)	23 (12.4)	62 (28.8)	
No	315 (78.8)	162 (87.6)	153 (71.2)	
Intent to vaccinate other daughters				0.843
No	31 (7.8)	15 (8.1)	16 (7.4)	
Yes	291 (72.8)	132 (71.4)	159 (74.0)	
Not sure	78 (19.5)	38 (20.5)	40 (18.6)	
Daughter's HIV status? *n* = 319				0.193
Negative	311 (97.5)	127 (96.2)	184 (98.4)	
Positive	8 (2.5)	5 (3.8)	3 (1.6)	
HIV status *n* = 320				0.036
Negative	200 (62.5)	94 (69.1)	106 (7.6)	
Positive	120 (37.5)	42 (30.9)	78 (42.4)	

[a] Values are given as a number (percentage) unless indicated otherwise, N = 400 unless otherwise stated. Wald test was used to calculate *p*-values.

3.2. Correlates of Parental Consent to Vaccinate Daughter

In the univariable logistic regression model, we found that wealth index, knowledge score, knowing someone with cervical cancer or other HPV-related cancers, knowing someone with genital warts and living with HIV were associated with providing consent to vaccinate the daughter. When adjusting for variables that were significant at a 20% level in the univariable model, the multivariable logistic regression showed that HPV/HPV vaccine knowledge, ever knowing someone with HPV-related cancer and none of the HBM construct scores were independently associated with consent to vaccinate the daughter (Table 3).

Table 3. Adjusted associations between predictors and parental consent to vaccinate daughter.

Variable	COR [95% CI] [a]	*p*-Value	AOR [95% CI]	*p*-Value
Socio-demographics				
Age (years)	0.99 [0.97–1.01]	0.413		
Sex				
Male	Ref			
Female	0.54 [0.28–1.03]	0.063		
Marital status				
Married	Ref			
Single	1.04 [0.62, 1.72]	0.890		
Education				
None/Primary	Ref			
Secondary/Tertiary	1.07 [0.64–1.73]	0.789		
Employment				
Employed	Ref			
Unemployed	1.49 [0.76–2.91]	0.245		
HPV/HPV vaccine knowledge mean score	1.04 [1.01–1.06]	0.004		
Wealth index				
Poorest/poorer/middle	Ref		Ref	0.005
Richer/richest	1.93 [1.16–3.21]	0.011	2.32 [1.29–4.16]	
Health Belief Model constructs				
Perceived susceptibility score	1.04 [0.97, 1.12]	0.241	1.05 [0.96–1.14]	0.262
Perceived severity score	0.97 [0.91, 1.04]	0.486	0.98 [0.91–1.06]	0.590
Perceived benefits score	0.99 [0.90–1.09]	0.835	1.06 [0.94–1.19]	0.321
Perceived barriers score	0.98 [0.94–1.02]	0.313	0.96 [0.90–1.01]	0.108
Self-efficacy	1.04 [0.96–1.12]	0.356	0.98 [0.88–1.09]	0.726
Cues to action	1.08 [0.98–1.20]	0.128	1.05 [0.92–1.19]	0.492
HPV and HIV-related characteristics				
Ever known anyone with cervical cancer	1.14 [0.70, 1.86]	0.588		
Ever known anyone with HPV-related cancers	2.60 [1.22, 5.55]	0.013		
Ever screened for cervical cancer	2.32 [1.43, 3.80]	0.001	1.93 [1.03–3.62]	0.041
Ever known anyone with genital warts	2.54 [1.32–4.87]	0.005	2.23 [1.04–4.76]	0.039
Daughters' HIV status				
Negative	Ref			
Positive	0.64 [0.13, 3.01]	0.567		
Parental HIV status				
Negative	Ref		Ref	0.078
Positive	1.93 [1.09, 3.42]	0.024	1.07 [0.01–1.36]	

Note: COR-crude odds ratios, AOR-adjusted odds ratios. [a] Values are given as a number (percentage) unless indicated otherwise

3.3. Mediation Effect of Knowledge on Parental Consent for HPV Vaccination

Mediation analysis was performed to explore and assess if HBM constructs are a mechanism through which knowledge levels affect parental consent choices. Knowledge levels were significantly associated with parental consent as a direct effect; however, the indirect effects of knowledge (mediated through HBM constructs) were not significant (Table 4). All other covariates: socio-economic status, marital status, and education level, were not significantly associated with parental consent to vaccinate their daughters or any of the HBM constructs.

Table 4. Mediation effect of knowledge on parental consent for HPV vaccination.

	Mediators							
	Perceived Barriers		**Perceived Susceptibility**		**Perceived Severity**		**Perceived Benefits**	
Effects	**OR [95% CI]**	***p*-Value**	**OR [95% CI]**	***p*-Value**	**OR [95% CI]**	***p*-Value**	**OR [95% CI]**	***p*-Value**
Total	2.37 [1.62–3.47]	<0.001	2.39 [1.58–3.61]	<0.001	2.39 [1.45–3.93]	0.001	2.38 [1.53–3.71]	<0.001
Indirect	0.98 [0.95–1.01]	0.297	1.01 [0.97–1.04]	0.777	1.0 [0.97–1.03]	0.901	1.0 [0.97–1.03]	0.993
Direct	2.42 [1.66–3.52]	<0.001	2.37 [1.57–3.59]	<0.001	2.38 [1.45–3.90]	0.001	2.39 [1.52–3.74]	<0.001

All models independently adjusted age, sex, SES, marital status, and education levels. Bootstraps (50) replications were used to compute standard errors for effects estimates.

4. Discussion

This study found that over half of our sample participants provided parental consent for the daughters' HPV vaccination. We framed our study within the HBM based on its usefulness in exploring vaccination behaviour. However, we did not find any significant associations between HBM constructs and parental consent for the daughter's HPV vaccine uptake, associated factors included; having screened for cervical cancer, knowing someone with HPV-related conditions, socio-economic status and marginally for those living with HIV.

Parental consent to daughters' HPV vaccination was 53.8%, and their daughters vaccinated, giving an uptake of 53.8% amongst our sample. This uptake is higher than the 39% [19] coverage reported during the same period at the national level. This could be because our data is regional and may not be generalized countrywide. However, 53.8% HPV vaccine uptake is still lower than the recommended 70% for population herd immunity to be achieved [6]. Additionally, the girls' attitudes may affect HPV vaccine uptake, which could be influenced by myths, misinformation, and parental refusal [18].

Parental consent plays a crucial role in HPV vaccination as daughters believe and act upon what their parents tell them. An earlier hypothetical study done in Lusaka, Zambia, before the HPV vaccination demonstration project (2013–2017) and national rollout of the HPV vaccination (2019) showed that 100% of the parents intended to vaccinate their daughters or themselves [23]. On the contrary, another study in Lusaka, Zambia, after the HPV demonstration project, reported that only 6.5% of parents had vaccinated their daughters [35]. These studies show an extremely stark contrast to our finding, which could be because we reported parental consent and actual HPV vaccine uptake other than intent in a broader national HPV vaccination program. Yu et al. [47] reported similar findings among African American parents with a similar sample size. Our results on parental consent are below the expected average, this could be explained by limited knowledge of HPV and HPV vaccine among parents and the volumes of circulating myths and misinformation about vaccines in general and the HPV vaccine, accentuated by the COVID-19 pandemic [19]. Information about the current national HPV vaccine coverage shows a drop from 75% in 2021 to 39% in 2021 [19].

We did not find any differences in HBM construct scores between consenting and non-consenting parents, as earlier hypothesized. Similarly, Vermandere and others found no differences regardless of the daughter's vaccination in a selected cohort of parents in Kenya [28]. However, there are other studies which have contrasting results in different regions. For example, Krawcyzk et al. [29], in a study done in Canada, found that perceived severity, perceived susceptibility, cues to action and low perceived barriers were associated with parental vaccination of adolescent children. Another study in Nigeria reported that cues to action, such as recommendations by healthcare providers and friends/relatives, predicted HPV vaccination [48].

The plausible explanation could be that we had low awareness of HPV and HPV vaccine in our cohort, and people are unlikely to commit to or have firm perceptions/beliefs about what they do not know. Therefore, people empowered with knowledge may be able to give a well-informed position. Further, inherent within the HBM framework and previous literature, the constructs' relationship was assumed linear without variable ordering, which is considered a more complex approach [49].

Combined high knowledge of HPV and HPV vaccine was associated with vaccination in univariate analysis. However, this was not significant after adjusting for possible confounders. Similarly, in mediation analysis, knowledge was a statistically significant direct factor associated with parental consent for daughters, but not indirectly through the HBM constructs. Knowledge plays a key role, as low levels may predispose one to hold fast to myths and misinformation. In other studies, parental knowledge is highly associated with the willingness to vaccinate daughters [34,35,50]. Like our findings, a study in Sweden did not find any differences in knowledge between consenting and non-consenting parents [51].

The possible explanation is that the HPV vaccine is relatively new in Zambia, despite an earlier demonstration project; hence some parents may not be knowledgeable about it. Further, the HPV vaccination program is campaign-based, and mass media messages and other activities to raise awareness only occur briefly before and during the activity. Therefore, it is important to consider ongoing messaging that can be reinforced during vaccination [52].

This study revealed that the rich were more likely to consent to the HPV vaccine than the poor. Similarly, a study in Uganda based on demographic health data found that those in the middle wealth quintile were more likely to vaccinate their daughters [53]. Another study showed that people with a low SES are less likely to initiate and complete vaccination due to a delay in receiving and comprehending health messages [54]. Notwithstanding, people with low SES yet are most affected but continue with low uptake of health interventions such as the HPV vaccine.

We found that HIV-positive parents are more likely to vaccinate their daughters in univariable and marginally in multivariable analyses. There has been an emphasis on cervical screening WLHIV, especially in high-burdened regions like Zambia, to reduce the burden of cervical cancer [55]. As such, cervical cancer screening and education are intensified to increase WLHIV's uptake of screening services [56]; hence more are likely to know about other preventative measures like HPV vaccination.

Therefore, it is not surprising that WLHIV and those who have screened for cervical cancer are more likely to consent to their daughter's vaccination based on their exposure to information on HPV and the HPV vaccine's benefits. Wigfall et al. [57] reported that among WLHIV, those who were aware that HPV caused cervical cancer were more likely to be aware of the HPV vaccine. Further, women screened for cervical cancer were more likely to consent to their daughter's HPV vaccination. An earlier study in Zambia reported similar findings that cervical cancer screening was significantly associated with daughters' HPV vaccination [35].

5. Strengths and Limitations

This is one of the first studies in Zambia regarding parental consent for the HPV vaccine since the national rollout, framed in a well-recognised model. Even though the data is regional and collected from the capital city, the study can serve as a pilot, which can be scaled up to get a nationally representative sample. Using the health belief model is important as understanding results framed in theories is easier.

The HBM has been widely used as a cognitive theory; hence this study adds evidence to the existing literature on circumstances where the behaviour of interest, as in this case, may not be directly influenced by the HBM constructs [49]. Further, our use of the generalized structural equation model overcomes the limitations of the standard structural

equation model, which assumes a normal distribution of variables [45]. Additionally, we could simultaneously compare the direct and indirect effects of multiple interacting factors.

This study is without limitations; firstly, it was done in the Lusaka district hence the results may not represent the rest of the country, affecting the external validity. Secondly, recall bias could exist as some adolescents' vaccination period was as far back as two years. However, parents usually have a good memory for a child's health-related issues. Thirdly, girls could have received the vaccine without parents knowing since the current approach is opt-out, and the girl's desire is considered primarily. Therefore, these girls may have been reported as not-vaccinated by parents when the converse was true. Fourth, non-consenting parents may have reported consenting for their daughters due to social desirability since the questionnaire was interviewer-administered.

Fifth, this data was collected during the COVID-19 pandemic when there was a lot of mistrust around the COVID-19 vaccine, which could have significantly heightened the barriers in both groups during our data collection. Finally, the data was collected when the behaviour of interest, HPV vaccination, had already occurred. Therefore, the hypothesis can only be adequately tested where beliefs are known to have existed before the behaviour they are to determine; otherwise, individuals' perceptions could be modified in areas relevant to HPV vaccination. There is the potential that vaccination status may have led to selective exposure or recall bias, thus suggesting reverse causality.

6. Conclusions

This study has highlighted modifiable correlates of parental consent for adolescent HPV vaccination, which include socio-economic status, cervical cancer screening uptake and knowledge. Equity in vaccination programs should be prioritised as the rich are more likely to consent and get the vaccine and more likely to have screened for cervical cancer.

Focus on raising community awareness on the role of HPV vaccination in preventing cervical cancer, especially among those from low socio-economic status, should be a priority to improve future programming and uptake. Equitable access to the provision of the HPV vaccine is essential to reduce the gap between the rich and the poor. Further, education on the relationship between HPV and cervical cancer and the preventive role of HPV vaccination should be integrated into the screening programs. This approach may improve knowledge levels among parents. Additionally, at the policy level, the feasibility of having ongoing HPV vaccination should be explored as it may improve access; Zambia can take a leaf from countries like Senegal [44].

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CHAPTER SIX: Determinants of the implementation of human papillomavirus vaccination in Zambia: Application of the consolidated framework for implementation research

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Teachers and healthcare workers play a key role in the HPV vaccination programme, especially given that outreach sites include schools. However, the determinants of vaccine delivery are not well known within the Zambian context, exposing a gap in successful implementation. Understanding the implementation determinants is key to improved coverage. Therefore, this chapter focuses on factors influencing the implementation of HPV vaccination by teachers and healthcare workers.

Implementation science focuses on evidence-based practice, and this chapter systematically unveils some of the implementation determinants of HPV vaccination in Zambia from the perspectives of key stakeholders in HPV vaccine delivery. The CFIR, one of the most frequently used implementation research frameworks, was used as a guide. The use of the CFIR is critical to understanding stakeholder needs to increase and sustain high levels of vaccine coverage.

vaccines

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Article

Determinants of the Implementation of Human Papillomavirus Vaccination in Zambia: Application of the Consolidated Framework for Implementation Research

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Abstract: Cervical cancer can be prevented, primarily by the administration of the human papillomavirus (HPV) vaccine. Healthcare workers (HCWs) and teachers play important roles when schools are used for vaccine delivery; however, challenges exist. This study aimed to understand the barriers and facilitators to HPV vaccination that are perceived by HCWs and teachers. Guided by the consolidated framework for implementation research (CFIR), key informant interviews were conducted in Lusaka district between June 2021 and November 2021 using a semi-structured questionnaire. Recorded interviews were transcribed verbatim and imported into NVIVO 12 for data management and analysis. We coded transcripts inductively and deductively based on the adapted CFIR codebook. We reached saturation with 23 participants. We identified barriers and facilitators across the five CFIR domains. Facilitators included offering the HPV vaccine free of charge, HPV vaccine effectiveness, stakeholder engagement, and timely planning of the HPV vaccination. Barriers included vaccine mistrust due to its perceived novelty, low levels of parental knowledge, myths and misinformation about the vaccine, lack of parental consent to vaccinate daughters, lack of transport for vaccination outreach, lack of staff incentives, and inadequate sensitisation. Using the CFIR as a guiding framework, we have identified implementation barriers and facilitators to HPV vaccination among HCWs and teachers. Most of the identified barriers are modifiable, hence it is prudent that these are addressed for a high HPV vaccine uptake.

Keywords: HPV vaccination; CFIR; implementation determinants; teachers; healthcare workers; COVID-19 vaccine; barriers; facilitators; parental consent; myths and misinformation

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1. Introduction

The cervical cancer caused by high-risk human papillomavirus (HPV) types is the fourth most common cancer globally, with global estimates of 604,127 cases and 341,831 deaths for women [1]. However, most of these cancer cases occur in low- and middle-income countries (LMICs), where cervical cancer is the most common cause of cancer-related death. Furthermore, the risk of developing cervical cancer is increased by HIV co-infection by about six times compared with women living without HIV [1,2]. The

burden of cervical cancer in sub-Saharan Africa (SSA) is worsened by the high prevalence of HIV/AIDS among women of reproductive age [3].

Zambia is a country with a very high cervical cancer age-standardised incidence of 65.5 per 100,000 women and a mortality of 43.4 per 100,000 women. [1,4]. Furthermore, the national prevalence of HIV in Zambia is about 12%; however, when disaggregated by sex, the prevalence in women is higher (14%) than in men (8%) [5]. The HIV epidemic further puts women at an increased risk of cervical cancer even when on antiretroviral therapy [6–10].

On the other hand, cervical cancer is one of the few preventable cancers, due to HPV vaccination, screening, and early treatment. However, in Zambia, HPV vaccine and cervical cancer screening coverage are low [11,12], just like in many SSA countries [2], leading to the late presentation of cervical cancer worsened by late diagnosis and delayed treatment at the only national chemoradiation centre [13].

HPV vaccination for adolescent girls intended for the primary prevention of cervical cancer was launched in 2019 in Zambia [12]. The vaccine coverage rates range from 31–76% for both doses 1 and 2, with some regions consistently reporting low figures [14]. The target group for HPV vaccination in Zambia is adolescent girls aged 14 years; the vaccination is delivered through static (health facilities) and outreach points (schools and within the communities) targeting in-school and out-of-school adolescent girls [12].

Multiple stakeholders are involved in HPV vaccine delivery, including teachers and healthcare providers. Teachers play a role in recruiting the in-school girls and sending information to parents, as well as in other activities such as ensuring order and filling out vaccination cards [12]. Primarily, healthcare professionals play a critical role in promoting HPV vaccination. Their duties range from planning, administering the vaccine, offering health education, entering data in the vaccination cards, and monitoring recipients for adverse events following immunisation. The aim is to maximise vaccination coverage and safeguard the adolescents' health, however, this comes with challenges. The barriers to vaccinating HPV-vaccine-eligible girls span different aspects such as those related to the system and those related to the community [15–17].

Examples of barriers are: constraints on human resources, especially in outreach practice, as some members of staff must remain at the health facility to continue with other routine activities [18]; pockets of the eligible population that are hard to reach [19]; financial support to acquire logistics [15]; low levels of knowledge among healthcare workers, teachers, and parents of adolescents and belief in myths and misinformation [20]. Implementation facilitators include knowledgeable healthcare workers who can discuss the vaccine confidently and recommend it [21], stakeholder engagement, and adequate social mobilisation [15]. However, barriers and facilitators to HPV implementation are not well known in the Zambian context, where HPV vaccine coverage remains lower than the recommended threshold for herd immunity and there is high cervical-cancer-related incidence and mortality. Understanding the barriers is important for the development of appropriate strategies for this context and to enhance implementation success.

The successful implementation of HPV vaccination for adolescent girls is poised to increase coverage and reduce the incidence of HPV-related conditions such as cervical cancer in countries such as Zambia with high related morbidity and mortality. Therefore, this study aimed to understand the implementation determinants of HPV vaccination among teachers and healthcare workers in Lusaka, Zambia using the consolidated framework for implementation research as a guiding framework (CFIR) [22]. CFIR is one of the most widely used frameworks for exploring implementation determinants, especially in health-related research [23].

2. Materials and Methods

2.1. Study Design

This was a qualitative study with healthcare workers and teachers involved in the HPV vaccination program, as key informants.

2.2. Study Setting

The study was conducted within health facilities and schools that are located within the six sub-districts of Lusaka. Further details about the study setting and how the HPV vaccination program is implemented in Zambia are reported elsewhere [12].

2.3. Sampling

In the first stage, nine schools within the six sub-districts of Lusaka were sampled purposively if they were participating in the HPV vaccination program and six health facilities servicing the selected schools were sampled. In the second stage, we purposively sampled teachers and healthcare workers who were involved in the HPV vaccination program implementation. Not all teachers and healthcare workers found at these facilities participate in the HPV vaccination program. Participants were given information about the study and those who agreed to participate signed informed consent forms. Additional consent was obtained for interview audio recordings.

2.4. Data Collection

We developed an interview guide consisting of 50 questions, sub-questions, and a variable number of probes adapted from the CFIR website (www.cfir.org) to assess barriers and facilitators as perceived by teachers and healthcare workers. Demographic data about the participants were collected, and other data were based on the CFIR constructs. Some of the CFIR questions focused on the characteristics of the HPV vaccine, cost implications for the vaccination program, community response, stakeholder engagement, organisational incentives, and working relationships with colleagues. The CFIR is a determinant framework made up of five domains with 39 CFIR constructs and sub-constructs that reflect the variables most likely to influence the implementation of evidence-based interventions [22]. Recently, based on feedback from users, the CFIR has been updated to 48 constructs and 19 sub-constructs while maintaining the five domains [24].

We defined and contextualised our study according to the updated CFIR within the five domains as follows: the innovation domain included factors related to the HPV vaccine and HPV vaccination program, the inner setting domain included factors related to the organisational context (the health facilities and schools), the outer setting domain included adolescent girls, parents, and the community, the individuals domain included the characteristics of teachers and healthcare workers such as public health nurses, general nurses, and midwives, and the implementation process included processes for planning and executing the HPV vaccination program.

We developed and refined the interview guide using an iterative process. The interview guide was piloted using two interviews and minor edits were made to increase comprehension and make the guide more succinct, this continued throughout the data collection process.

Participants were recruited purposively based on their involvement in the HPV vaccination program. Key informant interviews took place in a private room within the school premises for teachers and within health facilities for healthcare workers. The interviews were conducted between June and November 2021; the specific timing and date of the interviews were dependent on the availability of the participants. Interviews were conducted in English and recorded using a voice recorder.

To ensure anonymity during data analysis, each participant was allocated a unique identifier. Data were collected until theoretical saturation was reached [25]. We used this process of rigorous data collection to assure dependability.

2.5. Data Management and Analysis

Trained research assistants transcribed all the interviews verbatim, whereas one of the co-authors checked for accuracy by listening to segments of the audio recording. NVIVO 12.0 was used to manage and analyse the collected data. We used thematic analysis to identify emerging themes as described by Braun and Clarke [26]. Some studies guided

by the CFIR have also used a similar data analysis approach, considering that CFIR use is flexible and can be used according to context and study design [27–29].

Data were checked thoroughly during data collection and analysis for confirmability. The publicly available CFIR codebook based on the original CFIR was adapted and updated using the updated CFIR [24] and used to deductively code the data. One of the authors (MKL) coded initial transcripts, which were then reviewed by another co-author (MK) until consensus was reached to ensure the credibility of the data analysis process.

The standards for reporting qualitative research (SRQR) tool was used to guide the writing of this manuscript [30].

3. Results

We interviewed a total of 23 participants from the six sub-districts of Lusaka, of whom 12 were teachers. Twenty participants were female (Table 1).

Table 1. Characteristics of participants.

Sn	Age	Sex	Profession
001	35	Female	Teacher
002	50	Female	Midwife
003	48	Male	Teacher
004	49	Female	Midwife
005	54	Female	Teacher
006	44	Female	Teacher
007	42	Female	Teacher
008	39	Female	General nurse
009	60	Female	Midwife
010	41	Female	Public health nurse
011	43	Female	Teacher
012	36	Female	Public health nurse
013	25	Female	General nurse
014	30	Female	Registered nurse
015	47	Female	Midwife
016	57	Female	Teacher
017	54	Male	Teacher
018	45	Male	Teacher
019	46	Female	Teacher
020	28	Female	Teacher
021	22	Female	Teacher
022	37	Female	Public health nurse
023	35	Female	Midwife

The results are reported as facilitators and barriers for each theme (CFIR domain) and broken down into sub-themes, as shown in Table 2.

Table 2. Summary table of results: CFIR domains and implementation determinants.

Sn	Domain	Facilitators	Barriers
1.	Innovation characteristics	• HPV vaccine effectiveness • HPV vaccine given free of charge • Ability to pilot the HPV vaccination before national scale-up	• Innovation evidence base: community mistrust about the effectiveness of the HPV vaccine
2.	Outer setting	• Stakeholder engagement	• COVID-19 pandemic • Myths and misconceptions • Lack of parental consent
3.	Inner setting	• Positive relationships with workmates • Training of staff involved in implementing the HPV vaccination	• Inadequate funding • Lack of transport during implementation • Lack of appropriate information, education, and communication materials
4.	Individual's domain	• Having opinion leaders support HPV vaccination • Identifying HPV vaccination champions • Individual competence in HPV vaccination	
5.	Implementation process domain	• Planning early • Education sessions for implementers and users • Engaging HPV vaccine users	

3.1. HPV Vaccine Characteristics Domain

The innovation in the context of this research is the HPV vaccine. Participants reported more facilitators than barriers regarding the HPV vaccine.

There were many ways in which the participants reported the characteristics of the HPV vaccine as facilitators to its implementation. Some of the perceived facilitators of the HPV vaccine included the prior demonstration project and the vaccine being given free of charge and including accurate information about its effectiveness.

3.1.1. HPV Vaccine Trialability (HPV Demonstration Project)

Zambia had its demonstration programme for the HPV vaccine between 2013 and 2017, which was perceived as a success by the participants.

> The pilot study was first done in 2013. We were told that we were to give those girls between the age of 9 and 14 but later were changed to those in grade 4. The first pilot we did was very successful as we didn't have any complaints from mothers or the clients themselves. 009 Midwife

3.1.2. HPV Vaccine Is Offered Free of Charge

Zambia is one of the countries benefiting from the Gavi alliance; it receives subsidised vaccines that are later given to eligible girls free of charge.

> So, some of the parents come back to appreciate as they don't pay for the medicine (HPV vaccine) 021 Teacher

3.1.3. HPV Vaccine Evidence Base

Participants perceived that the known benefits of the HPV vaccine, such as prevention of cervical cancer, made them confident to implement the programme.

> (. . .) because we are sure we can fight cervical cancer, it is very effective as we are giving the girls to help us fight cervical cancer. 018 Teacher

Regarding barriers associated with the HPV vaccine, participants reported some myths within the communities that were perceived as a barrier.

3.1.4. Myths and Misinformation about the HPV Vaccine

There are deeply rooted myths about the HPV vaccine that prevent the community from accessing the HPV vaccine. Participants reported having some resistance from the community due to these myths. The most prominent was that girls who receive the HPV vaccine will be infertile and thus they would shun it for fear of not bearing children in the future.

> Ah the vaccine at first was very difficult because some parents were saying "Why are you targeting our children from 9 years to 14–15 years? This means you want our children in the coming generation not to come and have, to come and bear children." 002 Midwife

3.2. Outer Setting—Community

Within the outer setting, which includes the community and in which the inner setting exists, more barriers than facilitators were reported by the participants.

Collaborative efforts within the community were among the facilitators experienced.

3.2.1. Partnerships and Connection

Participants reported that having partnerships within the community facilitated the HPV vaccination program, such as councillors who serve as gatekeepers for the communities.

> The main stakeholders we work with are the ward councillors who are the owners of the village because whenever you have to go into the community you have to involve those. Then we also have the health neighbourhood committees in our units who help us with sensitisation issues. Then we also have the teachers in schools because we know that they can sensitise. 012 Public health nurse

There were some perceived barriers to HPV vaccination within the community which included low levels of parental knowledge, lack of parental consent to vaccinate daughters, belief in myths and misinformation and other large-scale occurrences such as the COVID-19 pandemic.

3.2.2. Critical Incidents Such as the COVID-19 Pandemic

The COVID-19 pandemic was an unexpected global event that the entire globe battled with. Participants reported that the COVID-19 pandemic prevention measures, such as lockdowns and vaccination, had an impact on the HPV vaccination programme. Participants perceived the pandemic as a barrier to HPV vaccination as the myths around the COVID-19 vaccines had a negative effect on the HPV vaccine as well. Some parents felt that their daughters were being given the COVID-19 vaccine under the pretext that it was the HPV vaccine.

> Because of this COVID-19, most of the parents are not interested in having their children vaccinated thinking we are giving them the COVID-19 vaccine (...) Some say you will become a zombie after some years, some say that they will never have children after vaccination whilst others say you will have blood clots. Those myths are still in the community. I remember before COVID-19, even if not all the children would get parental consent, the number was higher than when we started giving the COVID-19 Vaccine. 004 Midwife

3.2.3. Local Attitudes in the Community

The low levels of knowledge on HPV and the HPV vaccine posed a challenge to the vaccination program. Participants reported that parents did not trust the HPV vaccine due to a lack of knowledge and hence they withheld consent for their daughters' HPV vaccinations.

> The other challenge is parental consent. We need to educate parents even as we educate their children. So, there is that challenge of them not having the knowledgeon the HPV vaccine. 017 Teacher

> Some parents refuse the children from getting vaccinated as they don't know its benefits so if only they were to be sensitised, and that would make things easier. 007 Teacher

3.3. Inner Setting Domain

Regarding the internal environment, which in this case was the health facility and the schools, some barriers and facilitators were reported. The reported facilitators included relational connections and access to information about HPV through workshops.

Some reported facilitators included strong relationships within teams and access to knowledge about the HPV vaccine.

3.3.1. Relational Connections among Implementers

Participants reported that having relational connections with other workmates were seen to make the work easier, as there were consultations between old and new nurses.

> We have good teamwork. If we don't understand something we ask each other together with the new nurses. 004 Midwife

3.3.2. Access to Knowledge and Information about the HPV Vaccine

Training sessions on HPV vaccination for teachers and healthcare workers were viewed as important in information dissemination to the implementors as well as vaccine users.

> We had a workshop here where the doctors came, it was a one-day workshop. So, they came with some books and we were told how to go about it (. . .) they talked about the meaning of HPV; how someone can get it, and the dangers of it if one is not vaccinated, and they talked a lot. They also talked about parents with negative attitudes towards the vaccine and told us to talk to them about the benefits of their children receiving it. 018 Teacher

3.3.3. Materials and Equipment

On the other hand, there were some barriers that were perceived in the inner setting, such as the limited availability of materials and funding. Some logistics were not in place, such as vehicles and fuel to ensure that outreach vaccination posts were accessed on time to maximise on the HPV vaccination delivery.

> So, you find that there is only one vehicle that is supposed to take the team to schools and the same vehicle is also supposed to run other errands for the hospital. 009 Midwife

3.3.4. Funding for HPV Vaccination

Community volunteers play a role in supporting the HPV vaccination program. The participants felt that having some funding set aside to provide incentives for these volunteers was important for the success of the program. Incentives could take the form of money or other attire for certain weather conditions.

> For us to make sure that this programme is a success, we have to sensitise and for that to work we need the PA system, we need batteries for the megaphone it's not just a matter of using the PA system, we need also need people to also go door to door. So, the foot soldiers (community volunteers) need to be given something as an incentive because, at the end of the day, they would want to eat because it won't be effective sensitisation (. . .). 014 Registered nurse

3.4. Individuals Domain

This theme focuses on individuals with influence on the attitudes and behaviours of others regarding the HPV vaccine. There were some facilitators reported such as having the support of opinion leaders and other members of the community.

Within the individuals domain, participants reported that some facilitators of HPV vaccination included the involvement of opinion leaders and implementation leaders.

3.4.1. Opinion Leaders

Opinion leaders were reported to play a role in the program implementation by encouraging their followers to take the vaccine. People often listen to these leaders and follow what they say. Support from opinion leaders in the vaccination process was viewed as a facilitator to the success of the program. These opinion leaders represented political, traditional, and religious circles:

> We have the churches, the church leaders are the ones helping us to sensitise(. . .) even the marketeers, the chairpersons of these markets because once you go to them, they sensitise them then you find people coming to us. We also use traditional healers. Politicians are also very influential, so we would also go to the MPs [Member of parliament] to help us with sensitisation. So those are the stakeholders we have been using. 009 Midwife

3.4.2. Implementation Team Members

Participants reported that individuals collaborating and supporting implementation were viewed as facilitators to the HPV vaccination. These offered support in different ways, ranging from sensitisation to data collection.

> So, we also have champions in communities, we would say in each unit, we would choose a champion for HPV so that one will spearhead even the sensitisation, and registering of pupils, and that makes coordination easier when we collect data from them. We also have champions in schools. Without them, we can barely run the program as a good. 012 Public health nurse

3.4.3. Characteristics Sub-Domain (Capability)

Some participants reported that having been trained made them more comfortable to participate in the HPV vaccination program.

> I went for training which I completed I was at UTH [University Teaching Hospital] where I was offered a certificate in cervical cancer screening (...) I have also participated in sensitisation on the transmission of HPV in our catchment area. 002 Midwife

3.5. Implementation Process Domain

This domain represents the implementation process itself and includes strategies and activities used to implement HPV vaccination. Participants described facilitators as planning early, i.e., in advance of the actual vaccination dates to select the eligible girls and community sensitisation using various platforms. Additionally, the tailoring of strategies to mitigate some known pre-existing barriers, as well as active engagement with the parents and adolescent girls. were perceived as facilitators.

3.5.1. Planning for HPV Vaccination

Participants reported that timely planning and sensitising communities using various platforms was a facilitator, as it made the actual delivery much more manageable.

> In each school, before starting the programme... we (healthcare workers) would go to a particular school and give the teachers a task to count how many girl children were between the ages of 9 and 14 who were eligible for the vaccine. They would give us (healthcare workers) the number and we would also ask

> them to give us the date when they expected us to go and vaccinate because we wanted the teachers to also educate the girl child as they are very influential to these girls and their parents. 009 Midwife

3.5.2. Tailoring Strategies to the Local Context

Tailoring implementation strategies to mitigate known barriers, such as a low level of knowledge about HPV, was perceived as a facilitator. This was the case for implementers as well as users.

> Yes, that education can be given to the parents because what we used to do some time back, we had drama, so we would go out like at the marketplace where those people are found we would go there at the market, and we would have drama teaching people on what exactly would happen if someone had cervical cancer and we would take posters that shows exactly what the cervical cancer is and the normal cervix is so by doing that, people were educated on that one, and that's what resulted for the parents to bring the children for vaccination. 002 Midwife

3.5.3. Engaging HPV Vaccine Recipients

Participants reported that various strategies were used to attract end users, such as community sensitisation in public spaces about the HPV vaccine among the parents and the girls regardless of school status.

> We use the schools and markets (. . .) to also cater for those that are not in school as everyone passes through the market. We also use markets during sensitisation. Mothers in the market are mostly there from 6 a.m. to around 20 h (8 p.m.), so they can also get the information and decide to bring their children. 004 Midwife.

3.6. Participants' Suggestions

To have some local and home-grown solutions through stakeholder engagement, participants were asked to make suggestions on possible ways to improve the HPV vaccine coverage. Some suggestions on how best the program can be implemented were given by participants. The suggestions focused largely on the use of multimedia platforms and community gatherings such as churches to raise awareness within the outer setting. Other suggestions included sensitisation and equipping teachers with the correct information way before the actual vaccination dates.

> Yes, the TV, and radio, and they can also do that by using mobile network carriers like MTN or Airtel to be sending out awareness texts. Then the church also must be involved by making announcements in church which helps some people make better decisions with such issues. Change is a process, until one day they all decide to know the benefits of the vaccine. So, we don't have to wait for the program to start and then start sensitising, it has to be a continuous thing. 004 Midwife

> The teachers also need to be sensitised because as teachers, they can explain better to their pupils, unlike the child only having basic information at the last minute which makes it difficult to explain themselves to the parents. 001 Teacher

4. Discussion

This study reported on determinants for the implementation of HPV vaccination in Zambia framed in the five CFIR domains. The identified facilitators included offering the vaccine free of charge, the HPV vaccine being readily available, and the inclusion of stakeholders, including healthcare workers and support staff, teachers, religious leaders, parents, adolescent girls, and media personnel in the different stages of implementation. The identified barriers across these domains included: mistrust around the HPV vaccine due to its perceived novelty, lack of information and education materials in local languages, low levels of parental knowledge, myths and misinformation about the HPV vaccine,

lack of parental consent to vaccinate daughters, lack of transport for vaccination outreach purposes, lack of staff incentives, and inadequate sensitisation.

We found that giving the vaccine free of charge and it being readily available were perceived as facilitators of the vaccination program. In Zambia, the HPV vaccine has been given free of charge to eligible adolescent girls during both the demonstration project and the national rollout program supported by Gavi, the vaccine alliance [31]. However, this privilege is not cross-cutting for sub-Saharan Africa, as in some countries such as Nigeria, users must pay for the HPV vaccine, creating a barrier to uptake [32].

Similar to our findings, vaccine recipients have reported free vaccination as one of the main facilitators of HPV vaccination [33]. However, this facilitator is overshadowed by a myriad of barriers [17], leading to a low HPV vaccine uptake within the region [15]. Therefore, policy regulations should promote free and sustainable HPV vaccine provision for equitable access, especially in regions with high cervical cancer morbidity and mortality, to achieve the goals set by the WHO for cervical cancer elimination [34].

Including key stakeholders in the HPV vaccination implementation process was another reported facilitator in this study. The vaccination process requires cooperation and collaboration from multiple stakeholders for it to be successful [35]. For example, healthcare workers play a central role [21,36]; when schools are used for outreach, school staff are key [12]; political figures play the role of champions [37]; and community and religious leaders are trusted and when they approve of the vaccine, their followers are receptive [19]. Parents of adolescent girls should consent to the vaccination of their children, who are usually below the age of legal consent [12], even when most countries are implementing an opt-out approach [38]. On the other hand, adolescents themselves should be knowledgeable about the vaccine and have good attitudes towards it [39,40], hence it is necessary to improve their knowledge [41].

Therefore, when the stakeholders are supportive of HPV vaccination, uptake is enhanced. These findings are further supported by a systematic review of sub-Saharan health system constraints and facilitators, which revealed that in countries where there is multiple stakeholder engagement, the programs had better implementation outcomes [15].

Some barriers to HPV vaccination implementation were reported in this study. For example, there was a lack of trust in the vaccine, as it was perceived as a new and untested innovation; this was compounded by a lack of educational materials in local languages. Similarly, a study on ethnic minorities in the UK found that language and understanding of information and consent forms about HPV were difficult to understand for persons with low literacy, which was a barrier that impeded parental consent [42]. On the other hand, parental non-consent and worry about the novelty of the HPV vaccine were reported in other setups [43–45] (just like what was reported here) as hindrances to uptake.

In our recent study in this same setting, we found that 54% of parents of adolescent girls consented to vaccinating their daughters [12]. This is despite the WHO encouraging an opt-out parental consent approach or contextualising the consent process to country-specific requirements [38]. Some of the factors associated with parental consent for daughters included high knowledge levels about HPV vaccine, higher socioeconomic status, and parental HIV status (positive). These challenges are not unique to Zambia [46,47] and are encountered in many other settings [48–50].

Therefore, continued education and information sharing in easy-to-understand language to the parents of vaccine-eligible girls is key to increasing vaccine trust.

Financing for logistics during implementation was another identified barrier by our study participants, despite the vaccine being readily available. Examples included transportation to outreach points and a lack of incentives for community-based volunteers who are not on routine government salaries. This seems to be a similar situation to Mbale, Uganda where low financing was deemed as a barrier to service delivery in the absence of non-governmental organisations supporting the HPV vaccination program [18]. Therefore, national governments should be encouraged and compelled to increase national health financing, which will include sustainable funding for vaccination programs [51].

Our study participants reported inadequate social mobilisation and myths and misinformation in the implementation process of HPV vaccination. Critical information did not reach the intended groups, which could have deepened myths and misinformation, making users shy away from the vaccine altogether. Communication strategies on HPV vaccination that are tailored to specific stakeholder groups are effective in the African context [16], other low-income countries [52], and high-income countries [53–55] Effective communication helps in debunking and countering the myths and misinformation that have been rampant with many vaccines including the HPV vaccine [56].

5. Limitations

This study was conducted within Lusaka district to obtain insights into the HPV vaccination program. However, the results could be applied to other parts of the country and within the region due to their credibility and transferability.

6. Conclusions

We identified facilitators and barriers at the provider, interpersonal, and practice levels as perceived by healthcare workers and teachers in Zambia. Additionally, this study demonstrated the dynamic interplay between these factors by using the five CFIR domains. Therefore, context-relevant implementation strategies for mitigating the modifiable identified barriers and enhancing the facilitators are important for improving HPV vaccine coverage, which will protect future generations of women from cervical cancer and other HPV-related conditions. Additionally, a high HPV vaccine coverage entails the attainment of herd immunity and ultimately elimination [57–59]. Future research on identifying the implementation strategies that are effective in this setup is key [35,60].

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Institutional Review Board Statement: International ethical standards were followed in the conduct of this study. The study was conducted in accordance with the Declaration of Helsinki. The University of Zambia Biomedical Research Ethics Committee (UNZABREC) Ref: 1609–2021 and the University of the Witwatersrand Health Research Ethics Committee (HREC) Medical Ref: M21/04/73 both granted their clearance. The University of North Carolina (UNC) Ethics Committee granted a waiver. For the study sites, approval was requested from the Ministry of Health and Ministry of General Education as well as the specific heads of institutions. The Zambia National Health Research Authority (NHRA) also registered the study. The signed informed permission forms from participants and the interview transcripts were kept apart. Participants' privacy was protected, and they were allowed to leave the study at any time without facing any repercussions. Confidentiality was maintained.

Data Availability Statement: Data are available on reasonable request from the corresponding author as this work is part of an ongoing PhD.

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CHAPTER SEVEN: Implementation strategies used to increase human papillomavirus vaccination uptake by adolescent girls in sub-Saharan Africa: A scoping review

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According to IS concepts, implementation strategies are essential for successful implementation. There is limited evidence on the strategies used in SSA to enhance the uptake of the HPV vaccine. This paper addressed this gap. This chapter focuses on the scoping review, which aimed to get an overview of what implementation strategies have been used in SSA to increase HPV vaccination for adolescent girls. To standardise the definitions of the implementation strategies and make them more replicable, we framed the definitions within the ERIC taxonomy and grouped them into distinct clusters. This paper was published in the Vaccines Journal.

PLOS ONE

STUDY PROTOCOL

Implementation strategies to increase human papillomavirus vaccination uptake for adolescent girls in sub-Saharan Africa: A scoping review protocol

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Abstract

Introduction

The human papillomavirus (HPV) is sexually transmitted and infects approximately 75% of sexually active people early in their sexual life. Persistent infection with oncogenic HPV types can lead to malignant conditions such as cervical cancer. In 2006, the World Health Organisation approved the use of an efficacious HPV vaccine for girls aged 9 to 14 to prevent HPV-related conditions. Despite the HPV vaccine being available for about 15 years, dose completion remains as low as 20% in sub-Saharan African (SSA) countries implementing the vaccination program compared to 77% in Australia and New Zealand. A fraught of barriers to implementation exist which prevent adequate coverage. Achieving success for HPV vaccination in real-world settings requires strategies to overcome implementation bottlenecks. Therefore, a better understanding and mapping of the implementation strategies used in sub-Saharan Africa to increase HPV vaccination uptake is critical. This review aims to identify implementation strategies to increase HPV vaccination uptake for adolescent girls in sub-Saharan Africa and provide a basis for policy and future research, including systematic reviews to evaluate effective strategies as we accelerate the elimination of cervical cancer.

Materials and methods

This scoping review will consider studies pertaining to implementation strategies to increase HPV vaccination uptake for adolescent girls in sub-Saharan Africa. Studies targeted at different stakeholders to increase adolescent vaccine uptake will be included. Studies using interventions not fitting the definition of implementation strategies as defined by the refined compilation of implementation strategies from the Expert Recommendations for

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Implementing Change project will be excluded. MEDLINE (via PubMed), Embase, CINAHL (via EBSCO), Scopus and Google Scholar will be searched. Two independent reviewers will screen titles and abstracts for studies that meet the review's inclusion criteria, and the full text of eligible studies will be reviewed. Data will be extracted from eligible studies using a structured data charting table developed by this team for inclusion by two independent reviewers and presented in a table and graphical form with a narrative summary.

Introduction

The human papillomavirus (HPV) is sexually transmitted and affects approximately 75% of sexually active people early in their sexual life [1, 2]. There are more than 200 species of HPVs categorized into low-risk (causing warts) and high-risk types (causing cancers) [3]. The point prevalence of HPV infection is estimated at 11–12% globally and 22–24% for sub-Sahara Africa (SSA) [4–7]. HPV infection is mainly asymptomatic and transient, with approximately 90% cleared in immunocompetent people but persists in about 10–20% [2]. Immunocompromised people, such as those living with HIV, are more likely to have persistent HPV infections, which usually progress more rapidly to pre-cancers and cancers than the general population [8]. Cancers caused by HPV include vaginal cancer, vulvar cancer, and anal cancer, as well as some head and neck cancers like oropharyngeal cancer and cervical cancer which is highly prevalent in SSA [5].

In 2006, the World Health Organisation (WHO) approved HPV vaccines for prepubertal girls aged 9 to 14 years, naïve to sexual intercourse to prevent HPV-related conditions [2]. There are currently four licensed HPV vaccines classified as bivalent, quadrivalent and nonavalent based on the number of targeted HPV strains [9]. From 2006 to 2014, three doses were recommended to complete the vaccination schedule; however, evolving evidence has shown that two doses are effective, therefore, WHO recommends two doses for girls below the age of 15 [10], with ongoing studies showing promise for an efficacious and cost-effective single-dose HPV vaccine [11]. Therefore, the three-dose schedule is now reserved for girls older than 15 years or the immunocompromised, including people living with HIV [9]. The reduced number of doses is envisioned to boost vaccine coverage and reduce barriers to vaccination, such as multiple visits to the health facility, human resource demand and vaccine cost [12–15].

Despite the HPV vaccine being available for about 15 years, dose completion remains as low as 20% in SSA for countries implementing the vaccination program compared to 77% in Australia and New Zealand [16]. Barriers to HPV vaccination have been identified within SSA, and implementing national programs remains challenging at both initiation and sustainability levels [17]. Some identified barriers to HPV vaccine uptake include; individual, structural, economic, community/social, and cultural issues [14, 18]. Further, systematic health system constraints occur in many SSA countries, including but not limited to service delivery, low levels of knowledge among health care workers, financing, vaccine communication, and community engagement [19]. There is a dire need at the global level to increase HPV vaccine uptake with the accelerated global strategy for cervical cancer elimination, whose target is to fully vaccinate 90% of girls aged 15 years by 2030 [20].

The impact of HPV vaccination in reducing HPV-related diseases is evident in high-income countries which introduced national immunization programs earlier. For example, a meta-analysis of fourteen high-income countries implementing the HPV vaccination program reported a reduction in the prevalence of HPV 16 and 18 by 83% among girls aged 13–19 years and by

66% among women aged 20–24 years with significant cross-protection from HPV 31, 33 and 45 [21]. Furthermore, emerging data from the UK has shown that cervical cancer has almost been eliminated ten years after implementing the HPV vaccination of adolescent girls aged 12–13 years [22]. However, many SSA countries are still trailing behind in implementing the national HPV vaccination under a backdrop of low uptake in countries that have already implemented the program despite having the highest HPV-related morbidity and mortality [12, 23].

The point of the HPV vaccination programme is to get vaccines to those who need to receive them and mitigate future preventable diseases such as cervical cancer. For interventions such as the HPV vaccination to achieve success (intervention effectiveness) in a real-world setting, they must be implemented well and in ways that can reach the target groups. This often requires implementation strategies to overcome any implementation bottlenecks [24]. According to Powel and others, an implementation strategy is "a systematic intervention process to adopt and integrate evidence-based health innovations into usual care" [24]. Therefore, to successfully implement the HPV vaccine and harness the benefits, implementation strategies should be tailored to a real-life situation. For example, a study by Chigbu et al. [25] in Nigeria used educational intervention [implementation strategy] to increase HPV vaccine uptake for adolescent girls from 0.9% to 33.2% in a pre and post-design method. Another study done in South Africa used multiple implementation strategies such as building a coalition, conducting educational meetings, conducting educational outreach visits, developing educational materials, distributing educational materials, mandate change, obtaining and using consumers feedback and saw adolescent HPV vaccine uptake of up to 87% [26]. A systematic review by Niccolai et al. [27], including studies from the USA, reported implementation strategies such as reminder and recall systems, physician-focused strategies, school-located programs, and social marketing to have improved HPV vaccination coverage among adolescents. Another systematic review focused on high-income countries identified reminders, education and training, information delivery and communication campaigns, feedback on coverage data, financial incentives and school-based interventions as strategies which increased adolescent HPV vaccination [28].

There is a consensus among researchers that implementation strategies in one region may not necessarily work in another; therefore, implementation strategies should be tailored according to the context in which they will be implemented in a real-life context [24]. Therefore, it is urgent to have evidence from SSA, one of the regions with the highest burden of HPV infection and align with the global strategy for eliminating cervical cancer [20]. Therefore, this scoping review aims to identify implementation strategies used in SSA to increase HPV vaccine uptake for adolescent girls. The findings of this review will provide systematic evidence and an opportunity for policymakers to link the identified implementation strategies to the systematic barriers to HPV vaccination implementation. In addition, the findings will form a basis for future research, including systematic reviews to understand which implementation strategies are effective in SSA in tandem with the recommendations by the WHO Africa region leadership [17].

A preliminary literature review was conducted in December 2021 inPubMed, Scopus, Google Scholar, and JBI evidence synthesis database; no similar scoping review has been done or is underway in the context of SSA. Even though a narrative review was conducted on the HPV vaccine in SSA in 2020, focusing on ten years of HPV vaccination research in Tanzania [29]. However, a narrative review uses an implicit process to compile evidence and has weaknesses such as lack of systematic selection of studies and likely to reinforce authors' preconceived ideas and experiences, leading to bias [30]. On the other hand, our scoping review will be comprehensive with explicit inclusion and exclusion criteria and will transparently synthesise the available evidence to minimize similar limitations.

Review question

What implementation strategies have been used to increase the uptake of HPV vaccination for adolescent girls in sub-Saharan Africa?

Objective

To identify implementation strategies used to increase HPV vaccination uptake for adolescent girls in sub-Saharan Africa and provide a basis for future systematic reviews to evaluate effective strategies.

Materials and methods

The proposed scoping review will follow the updated Joanna Briggs Institute (JBI) methodology for scoping reviews [31]. This scoping review is registered in Open Science Framework projects [32].

Inclusion criteria

Participants. Participants will include all stakeholders involved in the cascade of HPV vaccination, such as studies on adolescent girls aged 9–14 years as the primary recipients and those aged 15–19 years who may be eligible for subsequent doses. This scoping review will also include studies focusing on parents/guardians of adolescent girls as they are involved in the consent process for the vaccination of their daughters. Further, studies involving healthcare workers will also be included considering that healthcare providers play a crucial role in recommending and administering the vaccine to eligible adolescent girls. Finally, studies involving teachers and other community leaders will also be considered.

Concept. We will include studies that used at least one of the implementation strategies defined by the refined compilation of implementation strategies from the Expert Recommendations for Implementing Change (ERIC) project [33] to increase the uptake of HPV vaccination. The ERIC expert panel achieved consensus on 73 discrete implementation strategies, including their definitions. Some examples of these implementations strategies include; i) conduct educational meetings, defined as "hold meetings targeted toward different stakeholder groups to teach them about the clinical innovation," ii) build a coalition, defined as "recruit and cultivate relationships with partners in the implementation effort," iii) access new funding defined as "access new or existing money to facilitate the implementation" [33]. The ERIC project classification has been used in scoping reviews in other health fields such as dementia [34, 35] and costing of implementation strategies [36] scoping reviews in preference to other taxonomies as it is more detailed with a conceptually clear description of strategies.

Considering that not all interventions may be reported as implementation strategies, we will read through all the studies mentioning interventions to check which ones meet the definitions by the ERIC project and classify them during data charting. Studies including interventions other than those based on the refined compilation of implementation strategies from the ERIC project will be excluded.

Context. This review will consider studies done in sub-Saharan Africa aimed at improving the uptake of the HPV vaccine among adolescent girls.

Types of sources

This scoping review will consider experimental and quasi-experimental study designs, including randomized controlled trials, non-randomized controlled trials, before and after studies and interrupted time-series studies. In addition, analytical observational studies, including

prospective and retrospective cohort studies, case-control studies and analytical cross-sectional studies, will be considered for inclusion. We will also consider descriptive observational study designs and qualitative studies. In addition, systematic reviews that meet the inclusion criteria will also be considered, depending on the research question. Text and opinion papers will also be considered.

Search strategy

An initial limited search of MEDLINE (PubMed), EMBASE and Scopus was undertaken to identify articles on the topic. The text words contained in the titles and abstracts of relevant articles and the index terms used to describe the articles were used to develop a full search strategy for MEDLINE (PubMed) (S1 Appendix). The search strategy will aim to locate both published and unpublished studies. The search strategy, including all identified keywords and index terms, will be adapted for each included database and information source. The reference list of included sources of evidence will be screened for additional studies. The section for similar articles will also be searched on MEDLINE (PubMed).

Studies published in any other language besides English will not be included as the teams' competence does not go beyond the English language. Studies published starting in 2006 will be included as this was when WHO approved the use of the HPV vaccine among prepubertal girls; the search will include studies published until December 31st 2021.

The databases to be searched include MEDLINE (via PubMed), EMBASE, CINAHL (Cumulative Index to Nursing and Allied Health Literature) (EBSCO) and Scopus. Grey literature citations (unpublished, nonpeer review data sources including conference proceedings, abstracts and dissertations) indexed by any databases searched will be reviewed with other peer-reviewed publications using the same inclusion and exclusion criteria. Google Scholar is useful, particularly in grey literature search, despite its limitations. Systematic reviews have traditionally assessed the first 50 search results from Google Scholar to complement searches from other databases [37, 38]. Therefore, we will review the first 50 hits from the Google Scholar search engine for possible inclusion. A medical librarian/ information specialist will guide the search.

Following the search, all identified studies will be collated and uploaded into Endnote X9 (Clarivate Analytics, USA) and duplicates removed, after which they will be imported into the Joanna Briggs Institute System for the Unified Management, Assessment and Review of Information (JBI SUMARI) [39]. Two independent reviewers will screen titles and abstracts for assessment against the inclusion criteria for the review. Potentially relevant studies will be retrieved in full, and their citation details using JBI SUMARI. Two independent reviewers will assess the full text of selected citations in detail against the inclusion criteria. The scoping review will record and report reasons for excluding full-text studies that do not meet the inclusion criteria. Any disagreements that arise between the reviewers at each stage of the study selection process will be resolved through discussion or with a third reviewer if consensus is not reached. The search is planned to start on 31st May 2022. The search results will be reported in full in the final scoping review and presented in a Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for scoping reviews (PRISMA-ScR) flow diagram [40].

Data extraction

Data will be extracted from papers included in the scoping review by two independent reviewers using a data extraction chart developed by the reviewers (S2 Appendix). The data extracted will include; the first author, year of study, year of publication, country, the title of the article,

article type, study design (where applicable), sample size, implementation strategy(ies), targeted stakeholders, type of program (national program/demonstration/subpopulation, the funding source for the vaccine, HPV vaccine coverage/uptake, limitations and strengths. The draft extraction chart will be piloted on five included pieces of evidence and revisions made if necessary. The draft data extraction tool will further be modified and revised as necessary during data charting from each included evidence source. Modifications will be detailed in the scoping review. Authors of included papers will be contacted to request missing or additional data, where required; if no response is received within two weeks, available data will be used in the best possible way.

Data presentation

The scoping review reporting will align with the PRISMA-ScR [40]. The extracted data will be presented in a table or graphical form to align with the study objectives. These will accompany a narrative summary of how the findings relate to the research question and objectives.

Discussion

A narrative summary of findings will be provided and discussed.

Limitations

Firstly, this scoping review will only focus on studies done in English; hence may miss other important research conducted in other languages. Secondly, the expert panel involved in developing the ERIC taxonomy was drawn from the USA and North America; hence some strategies may be more applicable to North American settings. However, the original compilation drew from taxonomies developed in other contexts [33]. Thirdly, some studies may not explicitly define the interventions as implementation strategies, however, this will be mitigated by a thorough review of all identified interventions against the definitions of implementation strategies by the ERIC project. Finally, this scoping review will not include studies that examined interventions in girls who are 20 years or older.

Supporting information

S1 Appendix. PUBMED search.
(DOCX)

S2 Appendix. Sample data charting tool.
(DOCX)

S3 Appendix. PRISMA ScR checklist.
(DOCX)

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S1_Appendix 1 PUBMED SEARCH 26.01.2022.

Search	Actions	Details	Query	Results	Time
#6			Search: ((((#1) AND (#2)) AND (#3)) AND (#4)) AND (#5)	142	07:38:37
#5			Search: ((((((

Search	Actions	Details	Query	Results	Time
#3			Search: ((Human papillomavirus vaccination) OR (HPV vaccination)) OR (HPV immunisation)	18,234	07:34:36
#2			Search: (Implementation strategies) OR (interventions)	9,425,631	07:33:47
#1			Search: ((((((Girls) OR (parents)) OR (Teachers)) OR (Health care providers)) OR (health professionals)) OR (doctors)) OR (nurses)	3,168,662	07:31:21

S2: Sample data charting form

SAMPLE DATA CHARTING FORM

First Author full names	Country of study	Year of publication	Title	Type of programme	Study design	Sample size	Targeted stakeholder	Frame work for data collection	Age of girls/school grade	Age of girls out of school	Data collecting tool	Implementation strategies	Funding source for the vaccine	HPV vaccine coverage/uptake

S3 Checklist: Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Implementation strategies to increase human papillomavirus vaccination uptake for adolescent girls in sub-Saharan Africa: A scoping review protocol	1
ABSTRACT			
Structured summary	2	Abstract provided	1
INTRODUCTION			
Rationale	3	This review will provide a basis for policy on increasing uptake of HPV vaccine for adolescent girls and future research including effectiveness systematic reviews	4
Objectives	4	Review question What implementation strategies have increased the uptake of HPV vaccination for adolescent girls in SSA? Objective: To identify implementation strategies to increase HPV vaccination uptake for adolescent girls in sub-Saharan Africa and provide a basis for future systematic reviews to evaluate effective strategies.	5
METHODS			
Protocol and registration	5	Protocol registration https://osf.io/gfd7s/.	5
Eligibility criteria	6	We intend to capture all research papers published in English on implementation strategies including various stakeholders (parents, adolescent girls, teachers and	5

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
		community leaders between January 2006 and December 2021	
Information sources*	7	The databases to be searched include MEDLINE (via PubMed), EMBASE, CINAHL (Cumulative Index to Nursing and Allied Health Literature) (EBSCO) and Scopus. Grey literature citations will also be searched including Google scholar	5
Search	8	Provided as S1	S1 Appendix 1
Selection of sources of evidence†	9	Two independent reviewers will assess articles for inclusion by screening titles, abstracts ad full text	7
Data charting process‡	10	The data extracted will include specific details about the participants, concept, context, study methods and key findings relevant to the review question. The draft charting tool will be piloted on 5 included pieces of evidence and revisions will be made as necessary during the process of data charting from each included evidence source. Modifications will be detailed in the scoping review. Authors of papers will be contacted to request missing or additional data, where required, if no response is received, available data will be used in the best possible way. Data charting will be done by two independent reviewers.	7
Data items	11	Also provided as S2 1. First author 2. Year of study 3. Year of publication 4. Country(ies)	8

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
		5. Title 6. Type of program 7. Study design (where applicable) 8. Sample size 9. Targeted stakeholders 10. Framework 11. Age of girls/ school grade 12. Implementation strategies 13. Number of implementation strategies 14. Funding source 15. HPV vaccine uptake 16. HPV vaccine coverage	
Critical appraisal of individual sources of evidence§	12	NA	NA
Synthesis of results	13	The extracted data will be presented in table or graphical forms to align with the study objectives. These will be accompanied by a narrative summary of how the findings relate to the research question and objectives.	8
RESULTS			
Selection of sources of evidence	14		Click here to enter text.
Characteristics of sources of evidence	15		Click here to enter text.

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Critical appraisal within sources of evidence	16		Click here to enter text.
Results of individual sources of evidence	17		Click here to enter text.
Synthesis of results	18		Click here to enter text.
DISCUSSION			
Summary of evidence	19	Objective: To identify implementation strategies to increase HPV vaccination uptake for adolescent girls in sub-Saharan Africa and provide a basis for future systematic reviews to evaluate effective strategies.	8
Limitations	20	This scoping review will only focus on studies done in English hence may miss other important research done in other languages, further only strategies focusing on uptake of the vaccine for girls only will be considered, yet there could be other strategies used for vaccine uptake among boys	8
Conclusions	21		Click here to enter text.
FUNDING			
Funding	22		Click here to enter text.

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.
* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.
† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).
‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.
§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence

that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMAScR): Checklist and Explanation. Ann Intern Med. 2018;169:467–473. doi: 10.7326/M18-0850.

vaccines

MDPI

Review

Implementation Strategies Used to Increase Human Papillomavirus Vaccination Uptake by Adolescent Girls in Sub-Saharan Africa: A Scoping Review

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Abstract: Barriers to successful implementation of the human papillomavirus vaccination exist. However, there is limited evidence on implementation strategies in sub-Saharan Africa (SSA). Therefore, this scoping review aimed to identify implementation strategies used in SSA to increase HPV vaccination uptake for adolescent girls. This scoping review was guided by Joanna Briggs Institute guidelines for scoping reviews and an a *priori* protocol and reported based on the Preferred Reporting Items for Systematic Reviews and Metanalysis for Scoping Reviews (PRISMA-ScR). We searched PubMed, EMBASE, CINAHL, Scopus, Google Scholar, and gray literature. Two independent reviewers screened article titles and abstracts for possible inclusion, reviewed the full text, and extracted data from eligible articles using a structured data charting table. We identified strategies as specified in the Expert Recommendation for Implementing Change (ERIC) and reported their importance and feasibility. We retrieved 246 articles, included 28 of these, and identified 63 of the 73 ERIC implementation strategies with 667 individual uses, most of which were highly important and feasible. The most frequently used discrete strategies included the following: Build a coalition and change service sites 86% (24/28), distribute educational materials and conduct educational meetings 82% (23/28), develop educational materials, use mass media, involve patients/relatives and families, promote network weaving and stage implementation scale up 79% (22/28), as well as access new funding, promote adaptability, and tailor strategies 75% (21/28). This scoping review shows that implementation strategies of high feasibility and importance were frequently used, suggesting that some strategies may be cross-cutting, but should be contextualized when planned for use in any region.

Keywords: HPV vaccine uptake; cervical cancer elimination; HPV immunization; implementation strategies; feasibility; scoping review; ERIC taxonomy; adolescent HPV vaccination; Africa

check for updates

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1. Introduction

The human papillomavirus (HPV) primarily affects human beings and is one of the most common sexually transmitted agents affecting approximately 3 out of 4 sexually active people early in their sexual life [1,2]. Generally, the point prevalence of HPV infection is

estimated at 11–12% globally and 22–24% for sub-Saharan Africa (SSA) [3–6]. There are several strains of HPV (>200) categorized into low-risk and high-risk types [7].

Cancers caused by HPV include anal, penile, oropharyngeal, vulval, and the commonest being cervical cancer, which has the highest incidence in SSA [4]. Paradoxically, SSA has low cervical cancer screening uptake [8,9] and delayed diagnosis and treatment [10]. Furthermore, women living with the Human Immunodeficiency Virus (HIV) are more likely to have persistent HPV infections, with more rapid progression to malignancies [11], even in women on antiretroviral therapy [12–14].

Primary prevention of cervical cancer is possible with the HPV vaccination of prepubertal girls aged 9 to 14 years before sexual debut [2]. Currently (2023), the available licensed HPV vaccines are classified as bivalent, quadrivalent, and non-valent based on the number of targeted HPV strains [15]. Evolving evidence has shown that fewer doses are effective, prompting the World Health Organization (WHO) to recommend one to two doses for girls aged 9–20 years and one to two doses for those aged 21 years or older with a 6-month interval [16,17]. The three-dose schedule is indicated in immunocompromised adolescents, such as those living with HIV, due to limited evidence in this population [15,17]. The reduced number of doses shows promise in increasing HPV vaccine uptake by mitigating barriers, such as multiple visits to the health facility, loss to follow-up, cost of the vaccine and its delivery, and human resource [18–21].

The benefits of HPV vaccination are evident in high-income countries which introduced national HPV vaccination programs earlier. A meta-analysis including fourteen high-income countries implementing the HPV vaccination program reported a reduction in the prevalence of HPV 16 and 18 among adolescent girls and young women [22]. Similarly, the United Kingdom shows that cervical cancer has almost been eliminated after 10 years of the national HPV vaccination of adolescent girls [23].

On the contrary, many SSA countries are yet to implement national HPV vaccination programs and further challenged by low vaccine uptake in implementing countries [18,24]. Some identified barriers to HPV vaccine uptake include individual, structural, economic, community/social, and cultural issues [20,25] and, recently, the COVID-19 pandemic [26]. Furthermore, systemic health system constraints occur in many SSA countries, including low levels of knowledge among various stakeholders, financing, vaccine communication, and community engagement [27,28].

There is an urgent need at the global level to increase HPV vaccine uptake, a priority of the WHO accelerated global strategy for cervical cancer elimination, with targets set for 2030 [29]. The WHO strategy has the following triple targets; 90% of girls by the age of 15 years should be fully vaccinated with the HPV vaccine, 70% of women by age 35 years should be screened with a high-performance screening test and again screened at 45 years of age and 90% of women with pre-cancer treated and 90% of invasive carcinoma managed properly [29].

Considering the long-standing need to increase HPV vaccination coverage in SSA and now with the pronouncement of WHO cervical cancer elimination strategy to achieve success in different real-world settings, implementation strategies are necessary to overcome bottlenecks and reach the target groups. Implementation strategies are "a systematic intervention process to adopt and integrate evidence-based health innovations into usual care" [30]. Some examples of implementation strategies are to; distribute educational materials, build a coalition, conduct educational meetings, change service sites, and obtain and use consumer feedback [31–33]. The need to better understand and evaluate the implementation of evidence-informed HPV vaccination programs in high-burden regions, such as SSA has been recognized in policy statements [29] and synthesized literature [34]. Therefore, it is important to know the breadth and depth of ongoing implementation strategies in SSA used to increase HPV vaccination uptake for cervical cancer prevention.

A systematic review by Mavundza et al. [34] on effective interventions to increase HPV vaccine uptake was limited to controlled randomized trials performed in high-income countries despite having the primary goal of reviewing data from all income brackets.

Studies from low- and middle-income countries did not meet the inclusion criteria as most were considered poorly designed. We conducted a preliminary systematic search of online databases, which showed that no recent systematic or scoping review has been undertaken or was underway in SSA to describe implementation strategies used to increase HPV vaccine uptake and their effectiveness. We, therefore, elected to conduct a scoping review as an ideal methodological approach to achieve our aim [35] to identify and map the identified implementation strategies used in SSA for increasing HPV vaccination for adolescent girls according to the compilation of Expert Recommendation for Implementation Change (ERIC) [36] and the corresponding nine clusters [37] as a starting point.

Research question: What implementation strategies have been used to increase human papillomavirus vaccination by adolescent girls in sub-Saharan Africa?

2. Materials and Method

This scoping review followed the Joanna Briggs Institute (JBI) updated methodology for scoping reviews [38] and an *a priori* protocol [39].

2.1. Inclusion Criteria

2.1.1. Participants

We included studies aiming to increase HPV vaccine uptake by adolescent girls; however, these implementation strategies often target various stakeholders. Therefore, participants included adolescent girls, parents/guardians, healthcare providers, teachers, key community leaders, politicians, and policymakers.

2.1.2. Concept

We included studies that used at least one of the 73 implementation strategies defined by the ERIC taxonomy [36] to increase the uptake of HPV vaccination by adolescent girls.

The second step of the ERIC compilation validated the distinctness of the 73 strategies and organized them into nine clusters: 1. Use evaluative and iterative strategies, 2. provide interactive assistance, 3. adapt and tailor to context, 4. develop stakeholder interrelationship, 5. train and educate stakeholders, 6. support clinicians, 7. engage consumers, 8. utilize financial strategies, and 9. change infrastructure [37]. The 73 strategies were later rated based on relative importance and feasibility and supported by the formation of go-zone quadrants based on perceived feasibility and importance: (I) Strategies with high importance and feasibility, (II) high feasibility low importance, (III) low importance and feasibility, and (IV) high importance low feasibility according to Waltz et al. [37].

2.1.3. Context

This review considered only studies carried out in SSA aimed at increasing the uptake of the HPV vaccine by adolescent girls.

2.2. Types of Sources

We considered all study designs, peer-reviewed studies, gray literature, and reports. Narrative literature reviews and articles including multiple countries were included if they had country-specific data for any SSA country and met the inclusion criteria [39]. We read through all the articles mentioning interventions to check which ones met the definitions by the ERIC taxonomy.

2.3. Search Strategy

We initially searched PubMed, EMBASE, and Scopus to identify articles on adolescent HPV vaccination, guided by a medical librarian. The text words in the titles and abstracts of relevant articles and the index terms used to describe the articles were used to develop a full search strategy for PubMed (Supplementary Table S1). This search strategy, with all identified keywords and index terms, was adapted for each included database and information source: PubMed, EMBASE, Cumulative Index to Nursing and Allied Health

Literature (CINAHL), Google Scholar, and Scopus. Gray literature citations (unpublished, non-peer review data sources including conference proceedings, abstracts, and meetings) were reviewed with other peer-reviewed publications using the same inclusion and exclusion criteria.

The reference lists of included sources of evidence were screened for additional studies. Similar articles in PubMed were also searched. Studies published in other languages besides English were excluded due to the teams' limited competence. We included studies published from January 2006, when WHO approved the use of the HPV vaccine among prepubertal girls through December 2021.

2.4. Sources of Evidence Selection

Data from identified articles were collated and uploaded into Endnote X9 (Clarivate Analytics, Philadelphia, PA, USA), removed duplicates, and imported the rest of the studies into the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI: JBI, Adelaide, Australia) [40]. Two independent reviewers (MKL and MM) screened titles and abstracts and assessed the full text of selected citations in detail against the inclusion criteria. Full-text studies and articles that did not meet the inclusion criteria were excluded. Reasons for exclusion are provided in Figure 1. Any disagreements between the reviewers at each stage of the study selection process were resolved through discussion or with a third reviewer (any of MK, CC, or MM#) if consensus was not reached.

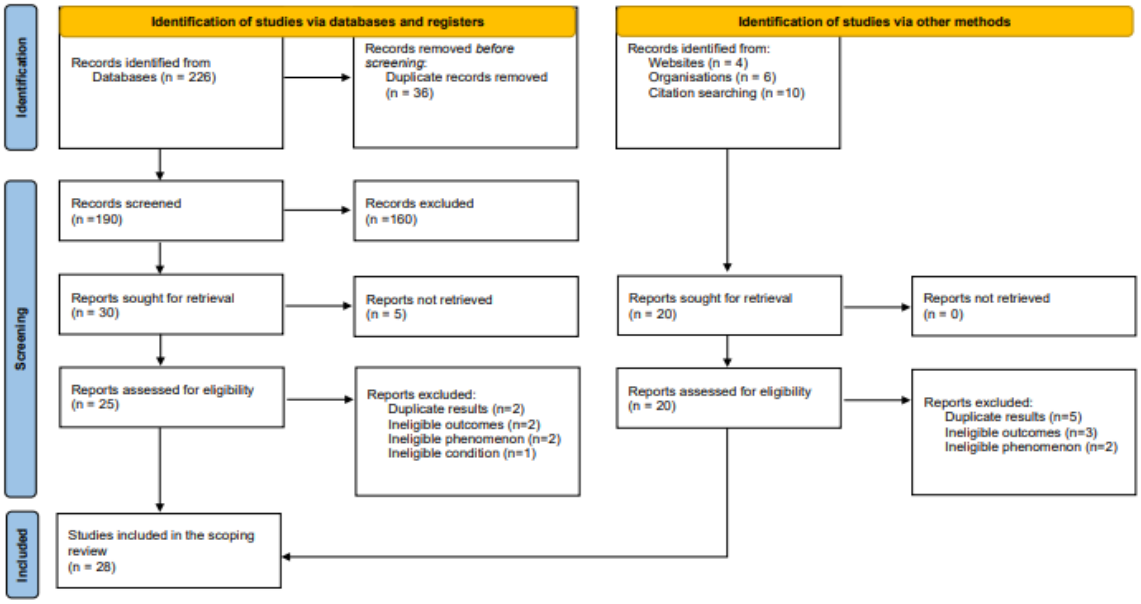

Figure 1. PRISMA flow chart adapted from http://www.prisma-statement.org/ accessed on 16 June 2023.

Sources of information for the implementation strategies included surveys within vaccination programs or Expanded Programs for Immunization managers, government documents, community surveys, registers for HPV vaccinations, HPV training manuals, micro plans, training reports, and support supervision reports. The search results are presented in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Review (PRISMA-ScR) flow diagram [41] in Figure 1.

2.5. Data Extraction and Charting

Data from the included papers were extracted and summarized by two independent reviewers (MKL and MMW) and checked by MK using a data extraction chart developed by this team. The extracted data included the first author's name, year of publication, country of study, the title of the article, article type, study design (where applicable), targeted stakeholders, and type of program (national program/demonstration/subpopulation).

The draft extraction chart was trialed on five included papers by (MKL, MMW, and MM). The revisions included (i) clarifying the sample size to be that of the eligible girls other than study participants as this was dynamic and not consistently reported; (ii) not to report the framework for data collection as this was rarely reported.

A meeting was held among MKL, MK, MWM, and MM to pilot the coding process of the ERIC strategies on three included studies. Three reviewers (MKL, MWM, and MM) independently coded and charted data for the specific ERIC implementation strategies and their allocated codes (1 to 73) along with the corresponding ERIC cluster (1 to 9). Co-authors MKL and MWM iteratively and inductively coded other strategies which emerged but could not neatly fit into the ERIC compilation [42]; these were verified by MK.

2.6. Data Analysis and Presentation

The extracted data are presented in table form to align with the study objectives and accompanied by a narrative summary. The identified strategies were mapped onto the ERIC compilation, grouped into the ERIC's nine conceptually relevant clusters, and mapped to the four go-zones to understand their relative importance and feasibility rating according to Waltz et al. [37]. This scoping review is written according to the PRISMA-ScR checklist (Supplementary Table S2).

3. Results

3.1. Characteristics of Included Studies

Our search yielded 246 articles and finally included 28 studies as shown in the Prisma flow chart in Figure 1. Most articles included multiple countries $n = 8$ [43–50], while the rest included single countries as follows: South Africa $n = 3$ [51,52], Malawi $n = 2$ [53,54], Tanzania $n = 2$ [55,56], Uganda $n = 2$ [57,58], and one each for Botswana [59], Cameroon [60], The Gambia [61], Ghana [62], Mozambique [63], Nigeria [64], Rwanda [65], Senegal [66], Togo [67], Zambia [68], and Zimbabwe [69].

A significant amount of data was from demonstration projects, $n = 14$ [43–46,50,51,54, 57,58,61,63,67,68,70] followed by other sub-national research projects $n = 7$ [31,52,53,55,60, 62,64], national programs $n = 5$ [48,56,65,66,69], and two had mixed data sources [47,49]. Of the national vaccination programs identified, 26 had international financial support to acquire the vaccines delivered free of charge to eligible girls. Half of the reported funding was from Gavi, the vaccine alliance (14/28). Most of the included articles were research papers $n = 18$ [31,43–45,47–49,51–55,57,60,62,66,69], followed by reports $n = 5$ [56,58,59,61,68], evaluations $n = 3$ [46,63,67], and perspectives $n = 2$ [50,65]. Publication year ranged from 2011 to 2021 with no articles identified for 2022, 2019, and 2014. About a third of the studies $n = 8$ were published in 2021 [48,49,53,56,62,66,67,69], $n = 2$ in 2018 [31,63], $n = 3$ in 2017 [45,54,64], $n = 2$ in 2016 [47,50], $n = 4$ in 2015 [52,57,61,70], $n = 3$ in 2013 [44,51,68], $n = 4$ in 2012 [46,55,60,65], and $n = 2$ in 2011 [43,58]. See Table 1 for details.

Table 1. Characteristics of included articles.

First Author Name; Year [Reference]	Title of Article	Country of Study	Type of Data Source	Type of Program	Targeted Stakeholder	School Grade/Age of Girls	Funding Agency
Binagwaho, Agnes; 2012 [65]	Achieving high coverage in Rwanda's national human papillomavirus vaccination program	Rwanda	Perspective	National	Policymakers, Non-governmental organizations, Donor community, Clergy, Teachers, Healthcare workers, parents, adolescent girls, community health workers	Grade 6 or 12 years	Merck
Casey, Rebecca M.; 2021 [66]	National introduction of HPV vaccination in Senegal: Successes, challenges, and lessons learnt	Senegal	Research—cross sectional	National	Policymakers, healthcare workers, nongovernmental organizations, parents, adolescent girls	9 years	The Gavi
Chigbu, Chibuike O.; 2017 [64]	The impact of community health educators on uptake of cervical and breast cancer prevention services in Nigeria	Nigeria	Research—pre- and post-design	Sub-national	Nurses	9–13 years	Out of pocket
Delany-Muretwe; 2018 [31]	Human papillomavirus vaccine introduction in South Africa: implementation lessons from an evaluation of the national school-based vaccination campaign	South Africa	Research—cross sectional	National program	District leaders, EPI Leaders, Healthcare workers, teachers, defense forces, nursing schools, politicians, journalists	Grade 4 or 9–13 years	The Gavi
Drokow, Emmanuel K.; 2021 [62]	The Impact of Video-Based Educational Interventions on Cervical Cancer, Pap Smear, and HPV Vaccines	Ghana	Research—pre- and post-design	Sub-national research	Parents	N/A	The Gavi
Engel, Danielle; 2021 [67]	Promoting adolescent health through integrated human papillomavirus vaccination programs: The experience of Togo	Togo	Evaluation	Demonstration in two districts	Technical partners, healthcare workers, adolescents, family members, community health workers	Grade 5 or 10 years	The Gavi
Galagan, Sean R.; 2013 [44]	Influences on parental acceptability of HPV vaccination in demonstration projects in Uganda and Vietnam	Uganda/Vietnam	Research—cross sectional	Demonstration program in two districts	Parents	Grade 5 or 10 years	The Gavi
Gallagher, Katherine E.; 2017 [45]	Lessons learnt from delivering HPV vaccine in 45 LMICs	45 LMICs (SSA countries included)	Research—Ecological study	Demonstration program	Policymakers, healthcare workers, non-governmental organizations, parents, adolescent girls	9–18 years	Variable
Jones, Amy; 2021 [53]	Using branded behavior change communication to create demand for the HPV vaccine among girls in Malawi: An evaluation of Girl Effect's Zathu mini magazine	Malawi	Research—pre- and post-design	Sub-national research	Girls, parents, and influencers	9 years	N/A

Table 1. *Cont.*

First Author Name; Year [Reference]	Title of Article	Country of Study	Type of Data Source	Type of Program	Targeted Stakeholder	School Grade/Age of Girls	Funding Agency
Kabakama, Severin; 2016 [47]	Social mobilization, consent, and acceptability: A review of human papillomavirus vaccination procedures in low- and middle-income countries	37 LMICs (SSA countries included)	Literature review	LMICs—National and sub-national	Girls, parents, and influencers	Variable, routine	Variable
Ladner, Joe; 2016 [50]	Experiences and lessons learned from 29 HPV vaccination programs implemented in 19 low- and middle-income countries, 2009–2014	LMICS (SSA countries included)	Perspective	Demonstration program	parents, community, government, multiple	9–13 years	Global Access Program
Ladner, Joel; 2012 [46]	Assessment of implementation of HPV vaccination programs in eight of the lowest-income countries (SSA—Cameroon and Lesotho)	LMICs—Cameroon and Lesotho included	Program evaluation	Demonstration program	Policymakers, educators, healthcare workers	9–13 years	Global Access Program
LaMontagne, Scott D.; 2021 [69]	HPV vaccination coverage in three districts in ZIMBABWE following the national introduction of a schedule of 0 to 12 months among girls aged 10 to 14 years	Zimbabwe	Research—cross sectional	National program	Parents	Multi-age cohort (10–14 years)	The Gavi
LaMontagne, D. Scott; 2011 [43]	Human papillomavirus vaccine delivery strategies that achieved high coverage in low- and middle-income countries	LMICs/Uganda	Research—cross sectional	Demonstration in two districts	Healthcare workers, community mobilizers, Parents, Adolescent girls	9–14 years	Merck and Co./Glo-xosmithl-ine
Moodley, Indres; 2013 [51]	High uptake of Gardasil vaccine among schoolgirls aged 9–12 years participating in an HPV vaccination demonstration project in KwaZulu-Natal, South Africa	South Africa	Research—cross sectional	Demonstration, one province	Nurses, teachers, religious, district health, district education health	9–12 years	Research grant
Mpuru, Alex; 2021 [56]	National introduction of human papillomavirus (HPV) vaccine in Tanzania: Programmatic decision-making and implementation	Tanzania	Report	National	EPI TWG, policymakers, politicians, religious leaders, healthcare workers, community health volunteers, school personnel, media personnel	14 years	The Gavi

Table 1. *Cont.*

First Author Name; Year [Reference]	Title of Article	Country of Study	Type of Data Source	Type of Program	Targeted Stakeholder	School Grade/Age of Girls	Funding Agency
Msyamboza, Kelias P.; 2017 [54]	Implementation of human papillomavirus vaccination demonstration project in Malawi: Successes and challenges	Malawi	Research—cross sectional	Demonstration program in two districts	Healthcare workers, policymakers, parents	Grade 4 or 9–13 years out-of-school	The Gavi
Mugisha, Emmanuel; 2015 [57]	Feasibility of delivering HPV vaccine to girls aged 10–15 years in Uganda	Uganda	Research—cross sectional	Demonstration project in two districts	District leaders, EPI Leaders, Healthcare workers	Grade 5 or 10 years	Glaxosmithkline Biologicals SA
Program for Approriate Technology in Health; 2011 [58]	HPV Vaccination in Africa, lessons learnt from a pilot program in UGANDA	Uganda	Report	Demonstration project in two districts	Policymakers, planners, teachers, community members, adolescent girls, parents	Grade 5 or 10 years	Glaxosmithkline biologicals SA
Raesima, Mmakgomo M.; 2015 [59]	Human Papillomavirus Vaccination Coverage Among School Girls in a Demonstration Project—Botswana, 2013	Botswana	Report	Demonstration program, one district	Teachers, parents, adolescent girls, and healthcare workers	Grades 4 to 6 or >9 years	Pink Ribbon Red Ribbon
Snyman, Leon; 2015 [52]	The Vaccine and Cervical Cancer Screen project 2 (VACCS 2): Linking cervical cancer screening to a two-dose HPV vaccination schedule in the South West District of Tshwane, Gauteng, South Africa	South Africa	Research—cross sectional	Sub-national Gauteng and Western provinces	Adolescents and female parents	Grades 4 to 7 or 9 years	Manufacturer donation
Soi, Catherine; 2018 [63]	Human papillomavirus vaccine delivery in Mozambique: identification of implementation performance drivers using the Consolidated Framework for Implementation Research (CFIR)	Mozambique	Evaluation	Demonstration—three regions	Healthcare workers, policymakers, community leaders	Grade 4	The Gavi
Tsu, Vivien; 2021 [48]	National implementation of HPV vaccination programs in low-resource countries: Lessons, challenges, and future prospects	LMICs (SSA countries included)	Literature review	National programs	Journalists, healthcare workers, teachers, parents, community leaders, adolescent girls	Variable, routine	Variable

Table 1. *Cont.*

First Author Name; Year [Reference]	Title of Article	Country of Study	Type of Data Source	Type of Program	Targeted Stakeholder	School Grade/Age of Girls	Funding Agency
Wamai, Richard; 2012 [60]	Assessing the effectiveness of a community-based sensitization strategy in creating awareness about HPV, cervical cancer, and HPV vaccine among parents in North West Cameroon	Cameroon	Research—cross sectional	Regional—one district	Parents	9–13 years	Church donation
Watson, Deborah-Jones; 2012 [55]	Human papillomavirus vaccination in Tanzanian schoolgirls: Cluster-randomized trial comparing two vaccine-delivery strategies	Tanzania	Research—cluster randomized trial	Regional research in two districts	Teachers, Adolescents, Parents	Grade 6 or 12 years	Wellcome trust
Whitworth, Hilary; 2021 [49]	Adolescent Health Series: HPV infection and vaccination in sub-Saharan Africa: 10 years of research in Tanzanian female adolescents—narrative review	SSA	Literature review	Regional—SSA	Policymakers, teachers, healthcare workers, parents, adolescent girls	N/A	N/A
World Health Organisation; 2013 [68]	Human papillomavirus (HPV) vaccine introduced in Zambia	Zambia	Report	Demonstration in three districts	Policymakers, teachers, healthcare workers, parents, adolescent girls	Grade 4 or 10 years	The Gavi
World Health Organisation; 2015 [61]	First Lady launches the HPV vaccine project for the prevention of cervical cancer	The Gambia	Report	Demonstration project in two districts	Political figures, policymakers, parents, adolescent girls	9–13 years	The Gavi

3.2. Characteristics of the Eligible Adolescent Girls

The target adolescents' age group varied from 9 to 18 years or grades four to seven. One study used the recommended multi-age cohort outside demonstration projects [69]. Other studies for countries introducing national programs used a single-age cohort of 9-year-old girls [66] or 14-year-old girls [56].

3.3. Vaccine Delivery Approaches

Some studies indicated reaching out-of-school girls through community sensitization and active tracing by community healthcare workers [48,54,56,63,65,68]. Other studies only focused on school delivery approaches [31,59]. In some studies, there were multiple locations where girls could access the vaccine, such as from schools and health facilities for out-of-school girls or school girls who missed the vaccine offered at school [48,50,56,65]. In some instances, HPV vaccination delivery was integrated with other health programs, such as deworming, vitamin A supplementation, nutrition counselling, infectious diseases prevention, tetanus toxoid vaccination, and other sexual health reproductive education [43,54,56,65,67].

3.4. Implementation Strategies According to ERIC Compilation

We identified 63 of the 73 ERIC implementation strategies across the 28 studies, while 10 were not reported in any article (Supplementary File Table S3). All included studies reported using multifaceted implementation strategies, which indicates combining two or more strategies. The most commonly reported discrete strategies were to build a coalition $n = 24$ [43,45,46,48–52,54,56,58,59,61,63,65–70], change service sites $n = 24$ [31,43,45–52,54,56–61,63,65–70], conduct educational meetings $n = 23$ [31,43–52,56,58,59,62–70], distribute educational materials $n = 23$ [31,43–48,50–52,56–60,62–67,69,70], develop educational materials $n = 23$ [31,43–48,50–53,56–60,63–67,69,70], promote network weaving $n = 22$ [31,43–51,54,56–59,61,63,65–67,69,70], stage implementation scale up $n = 22$ [31,43–48,51,52,54,56–59,61,63,65–70], use mass media $n = 22$ [31,44–49,51,53,56–59,63–65,67–70], tailor strategies $n = 21$ [31,44–51,53,54,56–59,63,64,66–69], and access new funding ($n = 21$) [31,43,45,46,48–52,54,56,58,59,61,63,65–70]. Other strategies were coded inductively as they were used frequently but could not neatly fit into the ERIC taxonomy, such as investment in a system to report and manage Adverse Events Following Immunization (AEFI) and applying an opt-out approach to parental consent to vaccinate daughters.

Table 2 shows the distribution of the identified implementation strategies within the nine ERIC clusters and the frequency of their use within the articles [37], this is detailed in Supplementary Table S4. All strategies within cluster 1 (use evaluative iterative and strategies), cluster 2 (provide interactive assistance), cluster 5 (Train and educate stakeholders), and cluster 7 (Engage consumers) were used at least once. Majority of the reported strategies of high importance and feasibility categories were within cluster 1: use evaluative and iterative strategies; cluster 4: develop stakeholder interrelationships; and cluster 5: train and educate stakeholders.

Table 2. Implementation strategies used by cluster.

Implementation Strategies Cluster	Total No. of Strategies within Each Cluster	Strategies Used per Cluster across 28 Papers No. (%)	Total No. of Times Strategy Identified by Scoping Review
1. Use evaluative and iterative strategies	10	100% (10/10)	113
2. Provide interactive assistance	4	100% (4/4)	51
3. Adapt and tailor to context	4	75% (3/4)	45
4. Develop stakeholder interrelationships	17	94% (16/17)	164
5. Train and educate stakeholders	11	100% (11/11)	131
6. Support clinicians	5	80% (4/5)	26
7. Engage consumers	5	100% (5/5)	65
8. Utilize financial strategies	9	44% (4/9)	27
9. Change Infrastructure	8	63% (5/8)	46

3.5. Targeted Stakeholders for Implementation Strategies

Stakeholders involved were varied within the included studies. Most articles included more than one stakeholder group, e.g., policymakers, politicians, healthcare workers, community volunteers, teachers, parents, and adolescent girls n = 23 [31,43,45–54,56–59,61,63,65–69], while others focused on exclusively specific stakeholders, such as parents n = 3 [45,60,62], healthcare workers n = 2 [63,64], or adolescents n = 1 [55].

4. Discussion

This scoping review aimed to identify implementation strategies to increase HPV vaccination of adolescent girls in SSA and map them according to the ERIC compilation. Majority of the identified implementation strategies were of high importance and feasibility falling within ERIC clusters 1, 4, and 5. Furthermore, most studies reported multifaceted implementation strategies which combine discrete strategies, and none neatly fit into blended strategies, which have been described as "multiple strategies packaged as a protocolized or branded implementation intervention" [30].

Strategies under the cluster of train and educate stakeholders were among the most frequently used. However, there is mixed evidence on the value of education strategies to increase the uptake of interventions generally and for HPV vaccination [71]. A recent systematic review carried out in India to measure the impact of educational interventions identified three studies focusing on educational interventions, and only one of these showed an increase in HPV vaccine uptake [72]. Contrary to this, a systematic review conducted in the USA reported that education by authoritative sources to parents increased HPV vaccine uptake by youths [73]. This is not surprising as knowledge has also been implicated as one of the barriers to HPV vaccination, suggesting that educational interventions may be of value if combined with other strategies and contextualized to a specific population.

We recently demonstrated that knowledge levels in a population of parents in Zambia affected their consent to vaccinate their adolescent daughters against HPV [28]. Additionally, an interventional study using educational presentations to teachers, healthcare workers, and parents on various aspects of HPV and HPV vaccines found that increased knowledge increased vaccine uptake and acceptance of the HPV vaccine [74]. Therefore, a systematic review on educational intervention and knowledge levels among different stakeholders will be key to understanding the value of education-related interventions in the HPV vaccination space in SSA to change the current landscape.

We found that multiple stakeholders worked together across the different studies, which was under the strategy "build a coalition," cluster to develop stakeholder's interactions. For example, healthcare workers played a pivotal role in administering the vaccine, and thus ought to be knowledgeable and have positive attitudes toward the vaccine [75], as their recommendation plays a crucial role in vaccine uptake across many geographical areas [76,77]. Teachers, as well, served as a conduit between the implementers and the user side in terms of information sharing and obtaining consent from the parents and assent from the girls. Ministries of health and education, including vaccination bodies, non-governmental organisations and the communities worked together to achieve a common goal of increasing HPV vaccination. Understanding the stakeholder landscape and networking during the planning and implementation of HPV vaccination programs is key to successful implementation.

As expected, given the scope of our review, we did not find the strategies that SSA countries used to navigate the HPV vaccination roll-out during the COVID-19 pandemic. To date, the available evidence shows that some LMICs rolled out national HPV vaccination programs during the COVID-19 pandemic. In contrast some SSA countries, such as Cameroon, had their HPV vaccine introduction programs interrupted during the same period [48]. Therefore, data are urgently needed to halt the drop in vaccine uptake experienced, negating the gains made earlier. However, it is unclear if the implementation strategies could be applied to the SSA context, where the HPV uptake dropped due to school closures and misinformation around the COVID-19 pandemic [26].

Generally, there were fewer articles reporting implementation strategies for national HPV vaccination rollout programs despite reports of 17 countries currently implementing these programs [8]. There is a need for these data close to real-life settings considering that over 55 demonstration projects have already been carried out [78].

The change in service site which falls within the "change infrastructure" cluster was one of the most frequently used strategies. This was mostly seen as delivering HPV vaccines in schools outside the usual health facility settings. Most studies acknowledged that large numbers of adolescents targeted for the vaccine are found in schools, favouring this platform [43,48,68]. Additionally, combining strategies in the school vaccination program has been found to be useful. For example, a study conducted in the United States of America on interventions to increase HPV vaccination reported that school-based vaccination combined with community education of parents and adolescents showed a significant increase in the intervention group [79]. Other studies have even intimated that schools should be used as primary vaccination sites due to vast experience and proof of success [48,80].

However, school-based delivery poses a challenge for reaching out-of-school girls who may be more vulnerable to early sexual debut and exposed to HPV infection in early discordant marriages [81]. Some studies we identified in this scoping review did not include out-of-school girls in their demonstration programs [59]. Finding out-of-school girls in the face of heavily school-based HPV vaccination continues to be challenging, and more literature and experiences should be shared to inform policy.

The most frequently used strategies under the cluster "adapt and tailor strategies" were to promote adaptability and tailor strategies. A systematic review and meta-analysis on effective communication strategies to increase HPV vaccination uptake among adolescent girls in SSA reported that tailoring communication interventions to specific stakeholders yielded positive results [82]. The review reported that the most effective communication strategies included those which educate the population about the HPV vaccine, facilitate decision-making on vaccine uptake and community ownership of the vaccination process.

Therefore, promoting, and tailoring strategies in the use of the HPV vaccine in SSA implies developing tactics specific to the region's circumstances and problems. Addressing issues, such as culturally appropriate communication, scarce resources, inadequate health-care facilities, and low knowledge is part of this. To guarantee that HPV vaccination is successful and ongoing, adaptation needs to be encouraged.

We identified monitoring of side effects as an implementation strategy outside the ERIC compilation. HPV vaccination can result in transient minor side effects, such as pain and redness on the injection site. This scoping review found that active management of side effects was used in some settings to increase HPV vaccination. Occurrences, such as mass hysteria among vaccine-eligible adolescents have been erroneously associated with the HPV vaccination [82]. These unfounded reported side effects have resulted in some countries, such as Japan and Cambodia to have very low HPV vaccine uptake compared to the initial levels when the programs were launched [83,84]. Effectively dealing with adverse events is crucial for HPV vaccine acceptability and uptake.

However, the HPV vaccine is not the only vaccine marred with misinformation about Adverse Events Following Immunization. Other vaccines, such as Diphtheria, Tetanus, and Pertussis, and Measles, have suffered a similar fate [85]. Gains made are quickly lost amid misinformation, for example, in Ireland, groups of parents started sending out wrong information; fortunately, these were countered promptly [86]. A similar trend was noted in Senegal among healthcare workers [66]. Therefore, general messaging around vaccines improves understanding and increases end-user confidence across multiple stakeholders.

Even though the cluster with strategies to "utilize financial strategies" was not frequently used and deemed to be of both low feasibility and importance by the initial expert consensus, access new funding and fund and contract for clinical innovation were deemed important though less feasible. Therefore, the non-feasibility of raising new funding in SSA may explain the presence of funders, such as Gavi, the vaccine alliance, Merck, Bill and

Melinda Gates Foundation, GlaxoSmithKline, PATH, and others, that have made it possible to increase vaccination in many SSA countries by supporting the supply chain; therefore, partially, or completely removing the cost to the end users. However, concern remains whether the Gavi-supported countries will sustain the HPV vaccination program when they transition to self-financing due to the high cost of the vaccine and its implementation [87].

5. Limitations

Scoping reviews are ideal to determine the scope of literature on a given topic as we have established here; however, there are some inherent limitations. We did not synthesize the findings or assess the methodological quality and risk of bias for included studies, according to guidance by the JBI methodology for scoping reviews [38]; therefore, the findings should be used with caution when guiding policy statements. Additionally, the expert panel involved in developing the ERIC taxonomy was drawn from the US and North America; however, the original compilation was drawn from taxonomies developed in other contexts; therefore, the strategies are applicable in SSA [36]. Finally, we only included studies reported in English, and thus may have missed other important research reported in other languages.

6. Conclusions

This scoping review has mapped and provided a broad overview of implementation strategies used to increase HPV vaccination uptake in SSA using the ERIC compilation and reported research gaps unique to SSA. Implementation and sustainability of the HPV vaccination remain challenging, as shown by low global levels of HPV vaccine uptake, which is lowest in SSA. We present clearly defined discrete implementation strategies to ease replication and understanding of findings. Most strategies used were of high importance and feasibility, which indicates that they could be adapted within the SSA to increase HPV vaccine uptake for adolescent girls.

We found low availability or reporting of implementation strategies for national HPV vaccination rollout programs, even though 17 countries in SSA are currently implementing this program [8]. Most studies reported on demonstration projects and small studies, which served as a learning point before full scale up which was under the cluster of "use evaluative and iterative strategies". Improved reporting of implementation strategies by national programs is needed to learn lessons from similar contexts considering that most SSA countries are now planning or are introducing national HPV vaccination programs. Furthermore, these studies should be well designed with clearly defined strategies for better evaluations and comparisons across studies and settings.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/vaccines11071246/s1 and captioned as Supplementary Materials for the scoping review. Table S1: PubMed search strategy; Table S2: PRISMA-ScR checklist; Table S3: Identified strategies per study according to ERIC compilation; Table S4: Implementation strategies used ERIC clusters according to feasibility and importance.

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CHAPTER EIGHT: Selecting and tailoring implementation strategies to improve human papilloma virus vaccine uptake in Zambia: A nominal group technique approach

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Tailoring implementation strategies and ensuring stakeholder participation are important in achieving implementation success. Every context is unique, and a one-size-fits-all approach may not effectively address the specific needs, beliefs, and barriers within that setting. Stakeholder participation is also crucial in the implementation process. Involving key stakeholders, such as community members, healthcare providers and policymakers allows for a more comprehensive and collaborative approach.

The landscape in Zambia is not clear on the role of stakeholders in tailoring strategies since the vaccination demonstration program and national roll out. This chapter focuses on sharing on the process of engaging multiple stakeholders in identification and prioritisation of barriers to HPV vaccination, and selection of contextual strategies for addressing these barriers in the Zambian setting.

The different stakeholder groups included in this research were adolescent girls, parents, teachers, and healthcare workers. The nominal group was used as a method to build consensus among the respective groups. Selected and tailored strategies were prioritsed based on their perceived acceptability and feasibility amongst the stakeholders.

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Selecting and Tailoring Implementation Strategies to Improve Human Papillomavirus Vaccine Uptake in Zambia: A Nominal Group Technique Approach

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Abstract: The human papillomavirus (HPV) vaccine is effective in cervical cancer prevention. However, many barriers to uptake exist and strategies to overcome them are needed. Therefore, this study aimed to select and tailor implementation strategies to barriers identified by multiple stakeholders in Zambia. The study was conducted in Lusaka district between January and February 2023. Participants were purposively sampled from three stakeholder groups namely, adolescent girls, parents, and teachers and healthcare workers. With each of the stakeholders' groups (10–13 participants per group), we used the nominal group technique to gain consensus to tailor feasible and acceptable implementation strategies for mitigating the identified contextual barriers. The identified barriers included low levels of knowledge and awareness about the HPV vaccine, being out of school, poor community sensitisation, lack of parental consent to vaccinate daughters, and myths and misinformation about the HPV vaccine. The lack of knowledge and awareness of the HPV vaccine was a common barrier across the three groups. Tailored strategies included conducting educational meetings and consensus-building meetings, using mass media, changing service sites, re-examining implementation, and involving patients/consumers and their relatives. Our study contributes to the available evidence on the process of selecting and tailoring implementation strategies to overcome contextual barriers. Policymakers should consider these tailored strategies to mitigate barriers and improve HPV vaccine uptake.

Keywords: feasibility; acceptability; barriers; cervical cancer elimination; Zambia; knowledge; myths and misconceptions; implementation strategies

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1. Introduction

Human papillomavirus (HPV) vaccination serves as a primary prevention strategy in reducing the global incidence of cervical cancer to less than 4/100,000 women, referred to as the elimination of cervical cancer [1]. In 2020, the World Health Organisation (WHO) issued a global call with three specific targets to be achieved by 2023 to make progress towards the elimination of cervical cancer as a public health problem [1]. The specific targets include the following: "90% of girls fully vaccinated with HPV vaccine by age 15 years, 70% of women are screened with high-performance test by 35 years of age and

again by 45 years of age, 90% of women with precancer treated and 90% of women with invasive cancer managed" [1]. Thus, the focus of this paper is on the first strategy.

The current global statistics for the HPV vaccine show that uptake of this important vaccine remains very low, especially in very vulnerable communities of adolescent girls [2–4]. The implementation of the HPV vaccination has been faster in high-income countries compared to low-income countries, with a global population coverage of 15% [2] owing to multiple challenges [5–12]. Systematically reviewed data from 2006 to 2014 showed that in more developed regions, 33.6% of females aged 10–20 years received the full course of vaccine compared with only 2.7% in less developed regions [13].

Zambia has not been spared from low HPV vaccine coverage due to various barriers [5,14–17] despite having one of the highest cervical cancer-related morbidity and mortality rates in the world [18–20]. The high incidence is further compounded by the high prevalence of HIV among women of reproductive age, late presentation to health facilities, and delayed diagnosis [21–25] despite the country having a robust cervical cancer screening program since 2006 [26–28]. Since 2019, the HPV vaccine in Zambia has been offered for free to a single cohort of 14 year old girls in health facilities and outreach facilities such as schools, where most eligible girls are found. A detailed description of the implementation of the HPV vaccination in Zambia is published separately elsewhere [5].

To achieve the goal of high HPV vaccination adoption and successfully contribute to the global call for cervical cancer elimination [1], the immunisation agenda of 2030 [29], and the sustainable development goals, evidence-based implementation strategies are important to mitigate contextual barriers to HPV vaccine implementation. Implementation strategies are actions for promoting the use of research evidence and evidence-based interventions (such as the HPV vaccine) in real-world practice [30]. For instance, physician training, assessment, and feedback are specific strategies shown to be effective in increasing HPV vaccine reach and uptake. Specific actions may include strategies targeting providers as well as educating patients and parents. Implementation strategies should be tailored to a particular context for them to be relevant as strategies which have been used in a particular set up may not necessarily apply to another context [31,32].

There are several implementation strategies which have been used for implementing HPV vaccination programs in SSA [33,34]. However, the selection and tailoring of strategies to contextual implementation barriers are underdeveloped [31]. Tailoring in this study was defined as a selection of implementation strategies to address contextual barriers which may influence the uptake of the HPV vaccine. In Zambia, there has been limited effort in engaging key stakeholders in the process of identifying implementation barriers and selecting and tailoring strategies for overcoming these. This paper addresses this gap.

We used the nominal group technique (NGT) [35] to identify stakeholder-perceived-specific barriers to HPV vaccination and tailor feasible and acceptable strategies to mitigate these barriers through consensus building. The NGT is proven to be beneficial in program planning including in healthcare [36,37]. Participants in a group come up with solutions which represent the groups' preferences [38]. Therefore, in this study, we used the NGT to obtain stakeholder consensus on the most important barriers to HPV vaccination implementation and uptake [5,39]. Stakeholders further tailored implementation strategies to mitigate the identified barriers while prioritising strategies based on their perceived feasibility and acceptability.

2. Materials and Methods

2.1. Study Setting

The study was conducted within the six administrative subdistricts of Lusaka District, Zambia, between January and February 2023. This setting was selected as it was one of the regions where the HPV vaccination demonstration project was conducted between 2013 and 2017 and hence has some experience with the HPV vaccine. Healthcare facilities located within these subdistricts have the mandate to offer the HPV vaccine to eligible

adolescent girls. The study setting is detailed elsewhere in a study conducted with this set up [5,39].

2.2. Study Design

We used the NGT for consensus building among the different stakeholders [35]. The nominal group technique is a structured method for group brainstorming that encourages contributions from everyone and facilitates quick agreement on the relative importance of issues, problems, or solutions. The process prevents the domination of the discussion by a single person as may happen in focus group discussions. The NGT typically includes 4 steps as listed below:

1. Silent generation of ideas in writing (independently).
2. Recording of ideas (round robin-no discussion at this point).
3. Discussion of listed ideas (carried out for clarity of all ideas).
4. Voting to enable ranking of priority ideas.

2.3. Participant Selection

Adolescent girls were sampled from schools and the communities in the study setting where the broader formative research was conducted [39]. Parents were sampled from the communities and social settings, while healthcare workers and teachers were sampled from health facilities and schools, respectively. The sampling procedure is detailed in the formative research we conducted in this same setting [39]. Participants were sampled purposively to select participants likely to give the most information about barriers to HPV vaccination in their context and to select and tailor implementation strategies based on their feasibility and acceptability. Some of the participants had taken part in the formative research.

2.4. Data Collection and Analysis

The data collection process involved three facilitators. One facilitator took field notes, whilst the other presented the questions and the third one managed the group. Stakeholder-specific homogenous groups were invited to the meeting on different dates. The meetings took place either in community halls or school halls. About 10–13 participants were selected per group to allow for an organised discussion as well as diversity within the participants [36].

The data collection sessions were divided into two parts. Part one included the identification and voting for the most pertinent barriers as perceived by each particular stakeholder group in addition to those identified in the formative research, whose results are published elsewhere [5]. During the introduction of the activity, barriers were defined as things that may hinder or affect their willingness to vaccinate, give consent to the vaccination, or receive the HPV vaccine depending on the specific stakeholder group. Part two included selecting and tailoring implementation strategies suggested by the participants and later coding these strategies with the expert recommendation for the implementation change (ERIC) taxonomy [40].

2.4.1. Part 1: Selecting Barriers

Step 1: Generating ideas—identification of barriers

A stakeholder-specific question on barriers to HPV vaccination was written down on a piece of manilla paper stuck onto the wall and was read out to the participants (Table 1).

A total of 15 minutes were given for participants to write as many perceived barriers as possible on a piece of paper. The facilitators went round to ensure that the instructions were clear to the participants. The rationale was to see the consistency in the barriers elicited in the formative stage and to ascertain if additional barriers would come up.

Table 1. Questions asked for identification of barriers.

No.	Stakeholder	Question
1	Adolescents	What are the barriers experienced by adolescent girls in receiving the HPV vaccine?
2	Parents	What barriers are experienced by parents to consent for their daughter's HPV vaccination?
3	Healthcare workers and teachers	What are the perceived barriers for the implementation of the HPV vaccination program?

Step 2: Recording of barriers

This step is also referred to as a round-robin recording of ideas. Each participant was asked to read out the barriers they had written down, and these were written on a mounted manilla paper by one of the facilitators. A discussion of the barriers was not permitted at this point.

Step 3: Discussing identified barriers

Participants were asked to explain what they understood about the written barriers. Each barrier was discussed to ensure that there was clarity on its importance. The facilitators constantly asked participants if there were any barriers that needed to be clarified. The identified barriers were later summarised with consensus and written down on a mounted manilla paper. The barriers identified in the formative research were also considered by participants.

Step 4: Voting on important barriers

Participants were asked to copy down the summarised barriers and vote independently and silently, giving a maximum score to the most important barrier and a score of 1 to the least important barrier based on the total number of barriers. Each participant read out the scores, which were recorded on a score sheet and were later summed up. The three most important barriers (with the highest total score upon voting) were then written down to be used in the subsequent step for selecting and tailoring implementation strategies.

2.4.2. Part Two: Tailoring of Strategies Based on Important Barriers

Like in part one, the NGT was again used to gain consensus on which implementation strategies would be ideal to mitigate each of the prioritised barriers. A stakeholder-specific question on strategies which can be used to overcome the identified barriers to improve HPV vaccination adoption by adolescent girls was written down on a piece of manilla paper and read out to the participants.

The question was as follows: what strategies can be used to overcome barriers identified in the HPV vaccination program? Participants were asked to copy the top three barriers and write down as many strategies as possible which could be used to mitigate each one of the three barriers prioritised in the previous steps, separately. They were asked to write down barriers they perceived to be feasible and acceptable. This was conducted independently and silently in approximately 15 min. The identified implementation strategies were later coded using the ERIC taxonomy [40] for reproducibility purposes.

The selection and tailoring of the implementation strategies followed the four steps of the NGT as described in part one to match the barriers to implementation strategies based on the perceived feasibility and acceptability. All the interactions were written down on manilla paper and stuck around the room for reference. Additionally, the discussions were recorded and transcribed for an accurate reference of the discussion. The top three most important barriers were listed by the stakeholder groups, and each was tailored to three implementation strategies. The final selected implementation strategies were coded using the ERIC taxonomy to increase replicability.

3. Results

The characteristics of the participants are presented in table form for each of the different stakeholder groups.

3.1. Adolescent Girls

There were 13 girls who were purposively sampled to participate in this study. Of these, eight were in school and five were out of school. Five girls had received at least one dose of the HPV vaccine. The mean age was 15 years. (Table 2).

Table 2. Characteristics of adolescent girls.

No.	Age	Goes to School?	School Grade	Received at Least One Dose of HPV Vaccine
1	16	Yes	11	Yes
2	15	Yes	10	No
3	15	Yes	10	No
4	15	Yes	9	Yes
5	15	Yes	9	No
6	16	Yes	11	No
7	15	Yes	10	No
8	15	Yes	9	Yes
9	15	Yes	9	No
10	15	Yes	9	No
11	18	No	NA	No
12	18	No	NA	Yes
13	18	No	NA	Yes

The identified barriers were as follows, with the vote count in brackets: the lack of knowledge and awareness about the HPV vaccine/program (78); the lack of school attendance (63); parents not consenting to vaccination (61); myths and misconceptions such as the HPV vaccine is an experiment, vaccination is an initiation into satanism, the HPV vaccine can bring cancer, someone can become lame after receiving the HPV vaccine, and misinformation about cervical cancer prevention (51); external influence by friends and families (49); COVID-19 pandemic—some adolescents thought the vaccine was for COVID-19 rather than HPV infection prevention (34); and fear of vaccine side effects (32). The top three barriers with the highest votes were identified and tailored to implementation strategies. The most feasible and acceptable strategies were voted for as shown in Table 3.

3.2. Parents Who Have Adolescent Girls

Thirteen parents were invited and participated in the NGT to select and tailor implementation strategies. The mean age was 46, and six were male (46%), seven had at least secondary education (54%), nine were employed (69%), 11 had school-going vaccine-eligible girls (85%), and five parents confirmed that their daughter had received at least one dose of the HPV vaccine (38%) (Table 4).

Table 3. Identified barriers and tailored strategies by adolescent girls.

No.	Identified Barriers	Possible Implementation Strategies (Points)	Final Selected Implementation Strategies Tailored to Barriers—Voted on Based on Feasibility and Acceptability	Tailored Implementation Strategies Coded According to the ERIC Taxonomy [40]
1	Lack of knowledge and awareness about the HPV vaccine/program	- Use of TV, radio, flyers, newspapers, and social media to share information (65) - Conducting community educational meetings (63) - Educate adolescent girls in and out of school about HPV vaccine (58) - Conducting door-to-door campaigns on HPV vaccine (57) - Share information directed at adolescents (37)	- Use of TV, radio, flyers, newspapers, and social media to share information about HPV vaccine - Conducting community educational meetings - Educate adolescent girls in and out of school about HPV vaccine	- Use mass media - Conduct educational meetings - Involve consumers/patients and their families
2	Lack of school attendance	- Implement the free education policy (69) - Build more schools in communities (58) - Announce on TV, radio, and social media (52) - Increase school awareness and importance (39) - Create books on HPV vaccination (28) - Make more programs throughout the year (26)	- Implement the free education policy (69) - Build more schools in communities (58) - Announce on TV, radio, and social media (52)	- Purposely reexamine the implementation - Change service sites - Use mass media
3	Lack of parental consent to vaccinate daughters	- Educate parents on the advantages of the HPV vaccine (34) - Conduct door-to-door campaigns (33) - Parents should encourage children to get vaccinated (32) - Share information with parents (31)	- Educate parents on the advantages of the vaccine (34) - Conduct door-to-door campaigns on the HPV vaccine - Parents should encourage children to get vaccinated	- Conduct educational meetings - Increase demand - Involve patients/consumers and family members

Table 4. Demographic characteristics of the parents.

No.	Age (Years)	Sex	Education Level	Employment	Child in School?	Child Vaccinated
1	28	Male	Primary	Yes	Yes	Yes
2	49	Male	Secondary	Yes	Yes	No
3	44	Female	Secondary	Yes	Yes	No
4	68	Male	Primary	No	Yes	Yes
5	60	Male	Secondary	No	Yes	No
6	23	Male	Secondary	No	Yes	No
7	34	Male	Tertiary	No	Yes	Yes
8	49	Female	Tertiary	Yes	Yes	Yes
9	25	Female	Secondary	No	Yes	No
10	52	Female	Secondary	No	No	No
11	54	Female	Primary	No	Yes	No
12	50	Female	Primary	No	Yes	No
13	59	Female	Secondary	No	No	Yes

The identified barriers with participant scores for each barrier were as follows in order of importance and vote counts in brackets, the lack of knowledge and awareness about the HPV vaccine (72), inappropriate venues set up for the vaccination (45), myths and misconceptions (44), timing of the HPV vaccination (44), COVID-19 pandemic (35), and the lack of resources (33). The three most important barriers were then matched with implementation strategies voted based on feasibility and acceptability (see Table 5).

Table 5. Selecting and tailoring of strategies to identified barriers by parents.

No.	Identified Barriers	Possible Implementation Strategies (Points)	Selected Implementation Strategies Voted on Based on Feasibility and Acceptability	Tailored Implementation Strategies Coded According to the ERIC Taxonomy
1	Lack of knowledge and awareness about the HPV vaccine	- Coordinate health workers to work with the community (20) - Use of drama groups to raise awareness - Conduct door-to-door education on vaccines (27) - Offer incentives for vaccination program stakeholders (45) - Involve parents/girls (38) - Community education in places like schools, bars, and markets (36) - Distribute fliers and brochures which have information about vaccines to raise awareness (36)	- Offer incentive for vaccination program stakeholders (45) - Involve parents and girls (38) - Community education in places like schools, bars, and markets (36)	- Alter incentive for those involved in the vaccination - Involve patients/consumers and their families - Conduct educational meetings
2	Inappropriate venue set up for vaccination	- Secure a good place for vaccination which is near the target population (22) - Secure tents for vaccination venues for more privacy (14)	- Secure a good place for vaccination which is near the target population (22) - Secure tents for vaccination venues for more privacy (14)	- Change service site - Change physical structure and equipment

Table 5. *Cont.*

No.	Identified Barriers	Possible Implementation Strategies (Points)	Selected Implementation Strategies Voted on Based on Feasibility and Acceptability	Tailored Implementation Strategies Coded According to the ERIC Taxonomy
3	Myths and misinformation	- Educate people in the community about the HPV vaccine (41) - There should be more health talks in schools, markets, and churches (26) - Use of communication media like radio and television programs and drama to raise awareness (27) - Involve girls and parents (17)	- Educate people in the community about the HPV vaccine (41) - Use of communication media like radio and television programs and drama to raise awareness (27) - There should be more health talks in schools, markets, and churches (26)	- Conduct education meetings - Use of mass media - Change in service sites

3.3. Teachers and Healthcare Workers

For the teachers and healthcare workers group, the total number of participants was 10. Six were teachers while four were nurses (Table 6).

Table 6. Characteristics of teachers and healthcare workers.

No.	Age	Sex	Profession
1	48	Female	Nurse midwife
2	36	Female	Nurse
3	40	Female	Nurse midwife
4	42	Female	Nurse midwife
5	28	Male	Teacher
6	45	Female	Teacher
7	26	Male	Teacher
8	39	Male	Teacher
9	33	Female	Teacher
10	30	Female	Teacher

The identified barriers in order of importance were as follows: myths and misinformation in the community (104), the poor sensitization of teachers and healthcare workers (83), the lack of information dissemination programs to the community (81), the lack of knowledge and sensitization among teachers and healthcare workers (70), the lack of materials on HPV vaccine (70), language barriers during community sensitization (69), the lack of communication between teachers and healthcare workers (68), the age restriction for eligible girls (68), inadequate human resources (49), teachers prohibiting pupils from getting vaccinated (41), private schools not allowing vaccination teams in their premises (39), and the COVID-19 pandemic (e.g., vaccine and restrictions) (38). Table 7 shows the selection process of the strategies.

Table 7. Selecting and tailoring of strategies by teachers and healthcare workers.

No.	Identified Barriers	Selected Implementation Strategies (Points)	Final Tailored Implementation Strategies Voted on Based on Feasibility and Acceptability	Tailored Implementation Strategies Coded According to the ERIC Taxonomy
1	Myths and misinformation in the community	- Adequate sensitization to the community, e.g., churches and schools using drama, music, and megaphones for community - Health education in churches, schools, and markets on HPV vaccine - Create one-on-one rapport with parents - Involve local celebrities and public figures - Give an incentive to those receiving the vaccine - Use local languages when sensitizing and simplifying reading materials on HPV vaccine - Conducting door-to-door sensitization with the help of community volunteers	- Use local languages when sensitizing and simplifying reading materials on the HPV vaccine (43) - Health education meetings in churches, markets, and schools on HPV vaccine (35) - Adequate sensitization to the community, e.g., schools and churches using drama, music, radio, and megaphones (33)	- Distribute educational materials on the HPV vaccine - Conduct educational meetings on the HPV vaccine - Use mass media
2	Lack of knowledge and poor sensitization among teachers and healthcare workers	- Conduct workshops for teachers and healthcare workers before the HPV vaccination exercise (40) - Provide more materials on the HPV vaccine (21) - Build teacher–healthcare worker rapport through communication on health matters (35) - Review what is discussed in meetings, e.g., quarterly (26) - Each head of department from the school should be part of the sensitization team (34) - Provide certificates of competence for those trained in giving HPV vaccinations (26)	- Conduct workshops for teachers and healthcare workers before the HPV vaccination exercise (40) - Build teacher–healthcare worker rapport through communication on health matters (35) - Each head of department from the school should be part of the sensitization team (34)	- Conduct ongoing training - Promote network weaving - Facilitation
3	Lack of information dissemination programs to the community	- The Ministry of Health should have strategies for disseminating information on radio and TV before a program starts (35) - Involve the school and clinic administration to come up with strategies to be used in the communities concerning HPV vaccination (26) - Provide handouts on HPV in various local languages (36) - Teachers should sensitize pupils to HPV for them to teach their parents (28) - Come up with short videos and movies about HPV to post on social media (34) - Make use of newspapers and magazines (26) - Engage influencers to educate people on HPV (39)	- Engage influencers to educate people on HPV vaccine (39) - Provide handouts on HPV in various local languages (36) - The Ministry of Health should have strategies for disseminating information on radio and TV before a program starts (35)	- Build a coalition - Distribute educational materials - Use mass media

4. Discussion

Implementation strategies based on the identified barriers were successfully selected and tailored by multiple stakeholders using the NGT. There was an overlap between the implementation strategies and barriers between the groups. Both parents and adolescent girls voted for a lack of knowledge about HPV and the HPV vaccine as the most important barriers. Myths and misinformation were among the top three most important barriers for the parents' group and teacher/healthcare group.

The barriers identified by the stakeholders are summarised as follows: low levels of knowledge and awareness, being out of school, poor sensitisation, the lack of parental consent, and myths and misinformation. These types of barriers have been frequently reported in various regions [41–48]. Based on these barriers, the selected and tailored implementation strategies were to conduct educational meetings and consensus-building meetings, use mass media, change service sites, reexamine implementation strategies, involve patients/consumers and their families, and alter the incentives.

Most of these tailored strategies are frequently used within SSA to increase HPV vaccinations and they are of high feasibility and importance, according to our recent scoping review [33]. In this study, all three stakeholder groups commonly suggested the use of educational strategies to mitigate barriers such as low awareness and knowledge about the HPV vaccine, the lack of parental consent, the poor dissemination of information about HPV vaccines, and myths and misinformation.

Educational strategies have been used in many setups [33,49,50] even though their value is debatable in some cases [51]. Some innovative educational strategies have, however, been found to be effective. For instance, Drokow et al. [52] used a video-based education intervention to increase the knowledge and uptake of cervical cancer screening and HPV vaccinations and the increase in both was statistically significant. Another study in an urban clinic in the USA used an educational video to educate parents of adolescent girls. Girls whose parents watched the educational video were three times more likely to be vaccinated at the end of a seven-month period [53].

In a quasi-experimental study in Malawi, a mini magazine was created for vaccine-eligible adolescent girls to provide educational information and create household conversations around the HPV vaccine. The study found a positive correlation between the consumption of the mini magazine and HPV vaccine uptake among the girls [54]. Additionally, that study involved the primary HPV vaccine recipients sharing information with their parents to help them buy into the HPV vaccination program, similar to an implementation strategy suggested by our stakeholders in this study to involve patients/consumers and their relatives.

The suggestion by various stakeholders to implement educational strategies could be partly explained by the recent introduction of the HPV vaccine at the national level (2019), sharing information with key stakeholders once a year during the vaccination campaign, with most information and education materials being available mainly in English. Therefore, considering that educational strategies are not always effective, culturally sensitive educational information should be packaged in ways which are effectives such as videos, comics, and magazines [54,55].

Further, to increase knowledge and awareness, the reach of adolescent girls and debunking myths and misinformation, the implementation strategy of the use of mass media was frequently selected. This strategy has also been widely used to increase HPV vaccinations [33,56–59]. For example, in Rwanda, announcements about the HPV vaccine were made via newspapers, magazines, and radio as part of the communication strategy [60]. Rwanda has one of the highest HPV vaccine uptakes in the world.

Additionally, a systematic review and meta-analysis on communication strategies used to increase HPV vaccine uptake among adolescents in SSA found that community meetings, information posters, flyers, television, radio, and newspapers were useful to increase HPV vaccine completion [61]. Therefore, the use of mass media in disseminating information plays a key role in reaching different stakeholders and increasing HPV vaccine

uptake [48,62,63]. The other advantage for Zambia to implement such an approach is that mass media platforms use the different local languages to deliver information which can be useful to increase HPV vaccine uptake.

The strategy about changing service sites was tailored to the barriers related to being out of school and inappropriate vaccination venues to make the HPV vaccine more accessible and ultimately increase uptake. In most SSA countries including Zambia, schools serve as the key primary sites for HPV vaccination [33,64,65]. School delivery has advantages such as reaching more eligible girls [66–69] and is more cost effective. However, this disadvantages out-of-school girls who are mainly found in hard-to-reach locations [70–73].

In most instances, despite out-of-school girls being more vulnerable, they are difficult to find during vaccinations [74,75]. Further, most school-girls are frequently absent from school despite being enrolled in schools [76]. Therefore, community outreach posts such as markets and community posts suggested in this study, stakeholder mobilisation, and other innovative ideas should be a policy priority to ensure that out-of-school girls are reached [77,78].

Our study makes a useful contribution, highlighting the perspectives of some key contextual stakeholders for HPV vaccine uptake, but further research is needed to generate more definitive evidence to inform decisions on which strategies to adopt in this setting. For instance, our NGT research could be repeated with broader groups of stakeholders in this setting (including programme managers and health administrators at facility and higher levels) to gain perspectives from a broader and more comprehensive group of stakeholders and see if there is consistency in the results with those from adolescents/parents/teachers/health workers in our study. Furthermore, future research could use the qualitative findings of our study to develop a quantitative survey and administer this on a larger sample of stakeholders, asking them to identify feasible strategies aligned to the contextual determinants in this setting. Future research could then use a longitudinal research design to test whether the identified tailored implementation strategies are feasible, acceptable, and increase HPV vaccine uptake (implementation effectiveness) in the Zambian context.

Strengths and Limitations

This study has strengths in that it builds on previous formative research and has engaged multiple stakeholders including out-of-school girls and creates a foundation for future research in Zambia and the region. The use of the NGT ensured that a rapid group consensus was achieved on common barriers. Additionally, the strategies selected were based on the context of the participants' perception of feasibility and acceptability. Further, the ERIC taxonomy was used to code the identified strategies for easy replication and communication.

This study is not without limitations. Firstly, we documented barriers and strategies using the ranking method, rather than using frequency of use. However, the original NGT recommends ranking, which has also been used widely. Secondly, the sample size is small and non-random, which limits generalisability. Thirdly, the group consensus approach used may be skewed by dominant voices. However, the participants were aware of the HPV vaccine, and they all participated fully. Finally, though the study appropriately obtains the perspectives of key stakeholders involved in delivering or receiving the HPV vaccine, these participants selected strategies based on their experiences and perceptions rather than on evidence of whether their chosen strategies improve vaccine uptake.

5. Conclusions

Implementation strategies should be tailored to the context where they are being implemented. In this study, key stakeholders were involved in identifying barriers important to them as well as selecting and tailoring the implementation strategies to these contextual barriers. The barriers identified are not unique to the Zambian setting. However, this process shows the important barriers to adolescent girls, parents, and teachers and

healthcare workers in this set up. There was some between-group variation regarding what barriers were most important.

The common barrier identified by all stakeholders was low awareness and knowledge about the HPV vaccine. Hence, from the perspective of our stakeholders, more educational strategies and other tailored strategies should be implemented. However, there is room for further research work to generate evidence for decision making on strategies to adopt in the Zambian context.

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CHAPTER NINE: General discussion and conclusion

9.1 Introduction

This chapter reflects on research themes that emerged from this PhD in line with some global policies such as the WHO 90-70-90 global cervical cancer elimination strategy. Qualitative and quantitative data from the different results chapters converged to strengthen findings that point to several recommendations.

9.2 Implications for HPV vaccine acceptability and uptake

Adolescent girls are the primary recipients of the HPV vaccine therefore involving them in research to understand their knowledge and attitudes plays a critical role in acceptability and uptake. In this PhD, low knowledge regarding HPV and HPV vaccine and its effect on vaccination was a cross cutting issue among the different stakeholders, just like in other set ups [104].

Adolescent girls showed variable levels of knowledge during our qualitative inquiry, which may influence their acceptability and uptake of the vaccine [104]. On the other hand, parents who had lower knowledge levels were less likely to consent for their daughters' vaccination [68]. in Chapter six of this thesis, teachers and healthcare workers also reported low levels of knowledge among themselves as well as the communities they served as a hindrance to the HPV vaccination.

These findings are not unique to the Zambian context, other regions are also faced with low levels of knowledge about the HPV and HPV vaccination [90, 104], even though acceptability has been high [63, 105-107]. This PhD strengthens available data that low levels of knowledge are a great hindrance to the uptake of the HPV vaccine as well as successful implementation of the programme to increase coverage.

Consistent efforts in educating communities on HPV and the HPV vaccine and massive sensitisation using acceptable platforms and language are key. Information should be

shared routinely rather than only when there are campaigns, especially for out-of-school girls and communities. Chapter 7 highlights feasible and acceptable implementation strategies to improve knowledge among stakeholders.

Therefore, policymakers should strategise on how best these strategies deemed to be feasible and acceptable can be implemented in the Zambian context [108] as well as within the region. Once the strategies have been enacted, their implementation effectiveness can be measured (by assessing their effect on implementation outcomes, such as acceptability and feasibility), as can their effect on reported HPV vaccination uptake.

9.3 Insights gained from study stakeholders.

There was broad consensus among stakeholders on the importance of HPV vaccination as a tool for preventing cervical cancer, which is one of the leading causes of cancer-related deaths among women in Zambia. Parents and healthcare workers acknowledged the potential of the vaccine to save lives, especially in a high-prevalence HIV setting where the risk of developing cervical cancer is elevated. This consensus is in line with global recognition of the HPV vaccine as a key public health intervention, particularly in countries where cervical cancer screening programs are not widely available [40].

Additionally, there was agreement on the need for better communication and education about the vaccine. Stakeholders across all groups identified gaps in public health messaging, with many pointing out that current communication strategies do not effectively address the concerns of parents or adolescents. Studies from other African countries have similarly highlighted the importance of tailored, culturally sensitive communication strategies to improve vaccine uptake [109].

While there was general agreement on the importance of the HPV vaccine, stakeholders had differing views on how best to improve coverage. Parents, for instance, were more concerned with the safety of the vaccine and how it would affect their daughters' future

fertility. This concern was more prominent among rural and less-educated parents, suggesting that socio-cultural factors may influence parental attitudes toward vaccination.

In contrast, healthcare workers and teachers were more focused on the logistical challenges of delivering the vaccine, such as inadequate resources and the burden of additional responsibilities. These divergent perspectives reflect stakeholders' different roles in the HPV vaccination program and varying access levels to information. The differences in perspective may also be attributed to varying levels of trust in the healthcare system.

Parents, particularly those from lower socioeconomic backgrounds, may be more skeptical of government health initiatives due to past experiences of healthcare failures or misinformation. Healthcare workers, on the other hand, are likely to understand the scientific rationale behind the vaccine better and may not share the same concerns as parents. This highlights the need for more effective engagement with communities to build trust in the health system and address the specific concerns of different stakeholder groups.

One key finding from the quantitative analysis was that parental education level, access to healthcare services, and knowledge about HPV were significant predictors of vaccine uptake. However, the qualitative interviews revealed more nuanced barriers that were not fully captured in the quantitative data, such as the cultural stigma surrounding discussions of sexual health and the pervasive fear that the vaccine could lead to infertility.

These qualitative insights help explain why, despite high levels of awareness, actual vaccine uptake remains suboptimal in some communities. The integration of these findings highlights complementary and contrasting results between the two data streams. While the quantitative data showed a clear link between knowledge and vaccine uptake, the qualitative data revealed that knowledge alone is insufficient in overcoming deeply embedded cultural barriers.

This challenges us to develop strategies that are not solely focused on increasing knowledge but also address these socio-cultural factors. These complementary findings underscore the need for multifaceted interventions, combining educational campaigns with community engagement initiatives that address cultural beliefs and misconceptions about the vaccine, thereby engaging policymakers in finding practical solutions.

9.4 Implications for the Field and Existing Literature

The findings from this thesis contribute to the broader literature on HPV vaccination in low- and middle-income countries (LMICs), particularly in SSA. Prior studies in LMICs, such as those conducted in Kenya and Uganda, have similarly highlighted the role of parental consent, access to healthcare, and educational campaigns in improving vaccine uptake. [78] [82]. Further, this aligns with research from Tanzania, where Watson-Jones et al. (2012) found that addressing cultural concerns is as important as increasing knowledge when promoting HPV vaccination [83].

Moreover, the study's findings add to the growing body of evidence that school-based vaccination programs, while effective in reaching in-school girls, need to be complemented by community outreach efforts to address the needs of out-of-school girls. This supports the findings from Rwanda’s successful national HPV program, which utilised a combination of school-based and community-based strategies to achieve high vaccine coverage [56].

9.5 Implications for social and behaviour change communication

Communication and social mobilisation play a key role in vaccination uptake. Planning for vaccination should be mandated other than it being done within a short time for vaccination implementation to earn confidence and buy-in from key stakeholders. Myths such as the vaccine causing infertility or cervical cancer itself or is a form of initiation into Satanism and side effects reported out of proportion are still very persistent, increasing vaccine hesitancy [68].

In the event of negative media publicity on adverse events following immunisation, counter messages should be quickly circulated by those in charge. For example, the COVID-19 vaccines suffered misinformation and disinformation, but strategies were quickly implemented. According to a systematic review by Anna S. Whitehead et al. (2023), a promising approach to curb COVID-19 vaccine misinformation included communicating the weight of evidence around vaccines and related myths [110].

Well-trained teams should always be on hand to execute this task; otherwise, with so many sources of information mainly on social media, may perpetuate misinformation and cause disinformation to spread widely [111]. The impact of negative marketing and sensationalising such stories negatively affects immunisation programmes. Therefore, planning early with a clear communication plan should include strategies to deal with vaccine-hesitant groups and misinformation.

Social mobilisation is needed to reach as many girls as possible in Zambia regardless of school status. Specific implementation strategies to reach the poor, such as community mobilisation through mass media and drama within markets where lots of people are found regardless of socioeconomic status [112]. HPV related educational materials should be distributed in an ongoing manner to protect future women from contracting cervical cancer[113].

9.6 Strategies for enhancing vaccination implementation and uptake in Zambia.

Zambia is one of the 195 countries subscribing to the WHO and hence implements policies that they declare and advise. This PhD brought out modifiable factors that should be addressed to be on course with achieving the various set global targets, such as the WHO cervical cancer elimination strategy pillar one of HPV vaccination. Hence, context-specific interventions should be implemented to mitigate the identified barriers.

The evidence from this study could inform the development of a comprehensive local HPV elimination strategy. Caution should be taken to generalize the findings as this study was

only done in Lusaka. However, It is recommended that policymakers should test the effectiveness of the tailored strategies selected by the stakeholders on a large scale.

9.7 Reflection on the contribution and challenges of existing frameworks

The SEM, HBM, and CFIR provided a strong theoretical foundation for this study. The Social-Ecological (SE) model and the additional frameworks selected for this study, such as the CFIR and the Health Belief Model (HBM), were instrumental in exploring factors influencing HPV vaccination uptake in Lusaka.

The SEM provided a multi-level perspective, enabling the study to capture the complex interplay between individual behaviour, social relationships, and organisational practices. It helped demonstrate how factors at different levels—such as the intrapersonal (adolescents' knowledge and attitudes), interpersonal (parental influence), and organisational levels (teachers and healthcare workers)—interacted to affect vaccine uptake.

This multi-layered approach allowed for identifying specific barriers and facilitators at each level, contributing to a richer understanding of the underlying issues. The application of the SEM also facilitated the development of targeted recommendations for improving vaccine uptake, such as the need for enhanced communication at both the family and community levels.

However, the SEM was less effective at accounting for the impact of socio-political factors, such as governmental policy constraints and funding shortages, which may have played a more significant role in vaccine implementation challenges. Policymakers were not among the study participants. Additionally, while the model provided a valuable framework for identifying different influences on vaccine uptake, it did not fully elucidate the interconnections between these levels.

HBM helped to understand how perceptions of risk, benefits, and barriers influenced vaccine acceptability among adolescents and their parents. This model proved effective in exploring individual-level decisions, particularly in highlighting the role of perceived susceptibility to HPV and cervical cancer in shaping parental and adolescent attitudes. While the HBM effectively explained how perceived risks and benefits influenced parental consent, it did not fully account for the role of cultural beliefs in shaping health behaviour.

The HBM typically focuses on individual perceptions of health risks and benefits. However, this study found that cultural factors, such as community-level myths and religious beliefs, were just as crucial in determining vaccine acceptability. This suggests that the HBM may need to be supplemented with additional theoretical perspectives that better capture the influence of culture and social norms on health decisions, especially in LMICs.

Similarly, the CFIR helped identify organisational barriers to vaccine implementation, such as the lack of coordination between the Ministry of Health and Education. However, the framework's focus on formal organisational processes somewhat overlooked the informal networks and social dynamics within schools and communities that significantly influenced program delivery. Teachers, for instance, noted that their ability to promote the vaccine was often influenced by their relationships with parents and community leaders, highlighting the importance of informal social structures in program success.

9.8 Implications for future research

The findings from this PhD have implications for future research and improve the implementation of HPV vaccination programs. The focus should be developing and evaluating innovative community engagement strategies to increase awareness and understanding of HPV and the vaccine. Multiple stakeholders play different roles in the vaccination cascade; hence, they should be involved in implementation decision-making.

For uptake to improve, key stakeholders should be aware of the HPV and HPV vaccines and be actively involved in evidence generation. Raising awareness could include

community-based campaigns, social media interventions, or partnerships with local leaders and organisations to disseminate accurate information and address misconceptions.

The next critical step in future research would be to evaluate whether the proposed implementation strategies—which emerged from discussions with adolescents, parents, healthcare workers, and teachers—can lead to improved vaccine coverage in Lusaka applicable to other regions of Zambia, particularly in rural and peri-urban settings where healthcare access and vaccine delivery systems may differ significantly from urban areas like Lusaka.

This evaluation would allow for measuring the strategies' impact on vaccination rates and identifying barriers to their effective implementation. Such research would provide a more substantial evidence base to determine whether these context-specific strategies are feasible and successful in achieving higher coverage rates. Further, policy analysis is another key recommendation for future research as this PhD did not focus on policymakers.

9.9 Conclusion

This PhD has highlighted various barriers and facilitators to HPV vaccination as shared by multiple stakeholders. The findings provide insights into the HPV vaccination program in Zambia and the experiences of multiple key stakeholders. Most importantly providing stakeholder-identified specific feasible and acceptable implementation strategies that are tailored to address contextual barriers to improve HPV vaccination implementation and uptake amongst adolescent girls in Zambia.

The findings from this PhD are important in improving HPV vaccine uptake in Zambia, a country grappling with high cervical cancer morbidity and mortality. The findings further contribute to the evidence base in Zambia to align with WHO policies such as the global

call for eliminating cervical cancer in our lifetime. Therefore, I recommend policymakers take a keen interest in measuring the effectiveness of the tailored strategies.

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APPENDICES

Appendix 1:

Participant information sheet (adolescents)

Study title: A mixed methods analysis of the implementation and uptake of the human papillomavirus vaccination of adolescent girls in Lusaka, Zambia

Adolescents' ICF: VERSION 1 March 2021

Principal Investigator: Dr. Mwansa K. Lubeya

Principal Investigator Department: Public Health

Greeting

Good day, my name is ……., I'm part of a team conducting research on HPV vaccination for adolescent girls in Lusaka, Zambia

Introduction

The human papillomavirus (HPV) is a tiny germ that infects human beings, and sometimes, this infection can lead to warts or cancer of different body parts. A vaccine prevents people from getting this infection, and it's called the HPV vaccine. In 2019, Zambia started offering this vaccine to girls aged 14years regardless of whether they go to school or not. We understand that girls have to talk with their parents before they

could receive the vaccine. Further, we know that health care workers, e.g., nurses work with teachers to deliver messages about the HPV vaccine during the vaccination period.

We are therefore looking at different aspects that may affect receiving of the vaccine by adolescent girls. Feel free to ask questions where you are not clear.

Invitation to participate in this study

You are invited to participate in this study because you are within the age group recommended to receive the HPV vaccine. We would like to understand why some girls accept and receive the HPV vaccine while others don't. This document gives you information about the study.

Once you understand what the study is about, and if you agree to take part, you will be asked to sign a consent form, and a copy will be given to you to keep. Your parents/guardians know about the study and are willing to have you participate if you so wish. It is important for you to know that even if your parents have allowed you to participate, the ultimate decision will be made by you.

Why is this study being done?

This study will help explain why girls have been receiving the HPV vaccine or not and their reactions towards it. After understanding the issues which prevent girls from accessing the vaccine, we will attempt to suggest possible solutions to overcome the problems faced.

What is involved in the study?

You will be required to participate in an interview between June 2021 and December 2021. If you do not know what the HPV vaccine is, further details will be given during the interview.

How many people will take part in this study?

Approximately 12-15 girls in Lusaka, Zambia, aged 15-18 years, will participate in this study.

What do I have to do if I take part in this study?

You will be interviewed about your feelings towards the HPV vaccine.

How long will I be in this study?

The interview will take approximately 30 to 45 minutes to complete

What are the risks of being involved in the study?

There is minimum risk involved in taking part in this study. Some questions regarding your health may be embarrassing or intimidating. You are free to skip questions that you may not feel comfortable answering.

What are the benefits of being in the study?

There are no immediate benefits; however, the information gathered will help with under possible ways of having more girls get vaccinated against HPV, therefore, reducing cancers that are caused by this germ.

What are my rights as a research participant?

Participation is voluntary. You can refuse to participate and discontinue participation at any time without any punishment, or need to provide a reason.

Will I be reimbursed for participating in this study?

There is no payment associated with participation in this study. You will receive R75 for your refreshment

What are the costs to me?

There is no cost to you.

Confidentiality: Efforts will be made to keep personal information confidential. Absolute confidentiality cannot be guaranteed.

What happens to the information collected for research?

All information collected will not be told to anyone outside the research team, your name and other specific details about you will not be on the collected data. The audio recording will be kept in a secure password protected computer. If results are published

all data collected in the course of the study will be securely retained for two (2) years, and six (6) years, if there is no publication. Thereafter data will be destroyed accordingly.

What are the outputs of this study?

Once this study is completed, scientific publications will arise to attain a PhD in public health. If you wish to receive the results, they will be accorded to you.

Contact details for the research team

For further information, please contact the Principal Investigator: Dr. Mwansa Ketty Lubeya Phone: +260955108465 E-mail: ketty.lubeya@unza.zm

Contact details of HREC administrator and chair

This study has been approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, Johannesburg (“Committee”). A principal function of this Committee is to safeguard the rights and dignity of all human subjects who agree to participate in a research project and the integrity of the research.

If you have any concern over the way the study is being conducted, please contact the Chairperson of this Committee, who is Professor Clement Penny, on telephone number 011 717 2301, or by e-mail on Clement.Penny@wits.ac.za. The telephone numbers for the Committee secretariat are 011 717 2700/1234 and the e-mail addresses are Zanele.Ndlovu@wits.ac.za and Rhulani.Mukansi@wits.ac.za

Thank you for reading this participant information sheet

Appendix 2

Participant assent sheet for minors*

Study title: A mixed-methods analysis of the implementation and uptake of human papillomavirus (HPV) vaccination of adolescent girls in Lusaka, Zambia.

1. I have been given a Participant Information Sheet for Minors, which explains what this study is about;
2. The study was explained to me and I understand what will happen if I take part;
3. I was given time to ask any questions I wanted to and was happy with the answers I was given;
4. I understand that I will not benefit from the study, should I agree to take part. I also understand that I will not be paid to take part in the study; taking part will not cost me anything either;
5. I have been given a range of contact details, repeated below, should I require further information at a later stage, or have any cause for concern over anything which is done to me during the study; and
6. I understand that even if I agree to take part in the study, I can change my mind later and stop being a part of the study
7. My parent(s) or guardian(s) know that I have been invited to take part in the study. They agree that I may do so, but the decision to take part is also mine.

Contact details:

Dr Mwansa Ketty Lubeya, Principal Investigator, telephone no. +260955108465, or by e-mail at ketty.lubeya@unza.zm

Dr Mary Kawonga, Supervisor 1, on telephone no. +27117172575, or by e-mail at mary.kawonga@wits.ac.za

Prof Carla Chibwesha, Supervisor 2, on telephone no +2772744789 or by email at Carla.chibwesha@med.unc.edu

Prof Mulindi Mwanahamuntu, Supervisor 3 on telephone +26096887236 or email at mmulindi@hotmail.com

Professor CB Penny, Chairperson of the Human Research Ethics Committee (Medical) at the University of Witwatersrand, on telephone no. 011 717 2301, or by e-mail at Clement.Penny@wits.ac.za.

Ms. Z Ndlovu or Mr Rhulani Mkansi, Committee Secretariat, telephone nos.: 011 717 2700 or 1234, or by e-mail at: Zanele.Ndlovu@wits.ac.za or Rhulani.Mkansi@wits.ac.za

Name of Participant: _____

Date: _____

Place: _____

Signature or mark: _____

Name of Parent or Guardian: _____

Date: _____

Place: _____

Signature or mark: _____

Witnessed by:

Name of Witness: _____

Signature: _____

Date: _____

Appendix 3: Assent form for audio recording qualitative interviews

Study title*:* A mixed-methods analysis of the implementation and uptake of human papillomavirus (HPV) vaccination of adolescent girls in Lusaka, Zambia.

I hereby assent to audio recording of the interview

I understand that:

- The recording will be stored in a secure location (a locked cupboard or password protected computer) with restricted access to the researcher and the research supervisor.
- The recording will be transcribed and any information that could identify me will be removed,
- The recordings will be erased within either (a) two (2) years of the publication of the research findings, or (b) six (6) years, if no publications arise from this research
- Anyone wishing to access this information in the future will first have to obtain the approval of the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, Johannesburg
- Direct quotes from my interview, without any information that could identify me, may be cited in the research report or other write-ups of research.

Name of Participant: _____

Date: _____

Place: _____

Signature or mark: _____

Name of Parent or Guardian: _____

Date: _____

Place: _____

Signature or mark: _____

Witnessed by:

Name of Witness: _____

Signature: _____

Date: _____

Appendix 4

Parents information sheet to allow daughters to participate in the study

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Study title: A mixed-methods analysis of the implementation and uptake of the Human Papillomavirus vaccination of adolescent girls in Lusaka, Zambia

Parents' ICF: VERSION 2 June 2021

Principal Investigator: Dr. Mwansa K. Lubeya

Principal Investigator Department: Public Health

Greeting

Good day, my name is …….. I'm part of a team conducting research on human papillomavirus (HPV) vaccine delivery. Parents play a key role in facilitating the uptake of the HPV vaccine by daughters. We would like to understand different factors that are associated with adolescent girls receiving or not receiving the HPV vaccine.

Introduction:

Your daughter is being invited to participate in this study. This document gives you information about the study. Once you understand what the study is about, and if you agree that your daughter takes part, you will be asked to sign this form, and a copy will be given to you to keep. Your daughter will also individually sign another form to indicate that she has also agreed in her own capacity.

Why is this study being done?

This study sets out to understand factors associated with parents consenting for HPV vaccine uptake for daughters in Lusaka and develop context-specific strategies to overcome the experienced barriers.

Invitation to participate:

Your daughter is being invited to participate in this study, but will need your permission to do so. All necessary information will be given to her before she makes a choice to participate

What is involved in the study?

Infection with HPV can cause self-limiting disease, however persistent infection is known to cause genital warts and cancers such as cervical, anal, oral and vulva. However, a vaccine is available to help prevent these infections and ultimately reduce number of people getting HPV related cancers like cervical cancer. The vaccine is known to be effective, especially if given to girls before they become sexually active. In 2019, a two dose HPV vaccine schedule was introduced for girls aged 14years in Zambia. Through this research, we would like to understand how girls feel and think about this vaccine.

This will be a cross-sectional qualitative study targeting girls aged 15-18 years. The girls will be invited to participate in an interview between June 2021 and December 2021

How many people will take part in this study?

Approximately 12-15 girls aged 15-18 years will participate in this study.

What should my daughter do if she has to take part in this study?

Your daughter will be interviewed following an interview guide. Questions will be asked regarding social demographic characteristics, knowledge and attitudes about HPV and HPV vaccine

How long will she be in this study?

The interview will take approximately 30 to 45 minutes to complete

What are the risks of being involved in the study?

There is very little risk involved in taking part in this study. Some questions regarding her health-seeking approach may be intimidating. She will be free to skip questions that she may not feel comfortable answering and can withdraw from the study at any point without any consequences.

What are the benefits of being in the study?

There are no immediate benefits; however, the information gathered will help understand possible ways of having more girls get vaccinated against HPV. She will be given information on the study while involved in the project and after the results are available.

What are the rights for research participants?

Participation is voluntary, there will be no punishment for refusal to participate. She may discontinue participation at any time without any punishment, and without giving a reason. Anonymity can usually be guaranteed in questionnaires but not completely with interviews

Will she be reimbursed for participating in this study?

There is no payment associated with participation in this study, however a R75.00 reimbursement will be given for your daughter's refreshments

What are the costs to for the participant?

There is no cost associated with participating in this study.

What is a certificate of confidentiality?

Confidentiality: Efforts will be made to keep personal information confidential. Absolute confidentiality cannot be guaranteed. Personal information may be disclosed if required by law.

Organisations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the Research Ethics Committees and the South African Health Products Regulatory Authority (SAHPRA) (where appropriate).

What happens to the information collected for research?

If results are published all data collected in the course of the study will be securely retained for two (2) years, and six (6) years, if there is no publication. Thereafter data will be destroyed accordingly.

What are the outputs of this study?

Once this study is completed, scientific publications will arise for attainment of a PhD in public health. If you wish to receive the results, indicate accordingly

Contact details for research team

Further information please contact the Principal Investigator: Dr. Mwansa Ketty Lubeya Phone: +260955108465 Email: ketty.lubeya@unza.zm

Contact details of REC administrator and chair

This study has been approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, Johannesburg (“Committee”). A principal function of this Committee is to safeguard the rights and dignity of all human subjects who agree to participate in a research project and the integrity of the research.

If you have any concern over the way the study is being conducted, please contact the Chairperson of this Committee who is Professor Clement Penny, on telephone number 011 717 2301, or by e-mail on Clement.Penny@wits.ac.za. The telephone numbers for the Committee secretariat are 011 717 2700/1234 and the e-mail addresses are Zanele.Ndlovu@wits.ac.za and Rhulani.Mukansi@wits.ac.za

Thank you for reading this Participant Information Sheet.

Appendix 5:

Consent sheet for daughter's participation in research

Study title*:* A mixed-methods analysis of the implementation and uptake of the Human Papillomavirus vaccination of adolescent girls in Lusaka, Zambia

I have been given a Participant Information Sheet which explains the nature and processes involved in this study, which is attached hereto;

1. I was given time to read it, or had it read to me, in the language I best understand
2. I was given time to ask any questions I wanted to and found any answers given to me to be reasonable and satisfactory
3. I believe I fully understand why the study is being conducted and what the intended outcomes will be
4. I understand that there will be no immediate benefit to me, should I agree to participate, nor will I receive any payment; conversely, participation will not cost me anything but my time
5. I understand that, even if I initially consent to take part in the study, I may subsequently withdraw at any time and would not be required to give any reasons; if that happened, any data collected about me for the purposes of the study would immediately be destroyed, unless I give consent for it to be retained

6. I have been given a range of contact details, listed below. If I require further information or become concerned about any aspect of this study. I am free to speak to any of these contacts.

Contact details:

Dr Mwansa Ketty Lubeya, Principal Investigator, telephone no. +260955108465, or by e-mail at ketty.lubeya@unza.zm

Dr Mary Kawonga, Supervisor 1, on telephone no. +27117172575, or by e-mail at mary.kawonga@wits.ac.za

Prof Carla Chibwesha, Supervisor 2, on telephone no +2772744789 or by email at Carla.chibwesha@med.unc.edu

Prof Mulindi Mwanahamuntu, Supervisor 3 on telephone +26096887236 or email at mmulindi@hotmail.com

Professor CB Penny, Chairperson of the Human Research Ethics Committee (Medical) at the University of Witwatersrand, on telephone no. 011 717 2301, or by e-mail at Clement.Penny@wits.ac.za.

Ms. Z Ndlovu or Mr Rhulani Mkansi, Committee Secretariat, telephone nos.: 011 717 2700 or 1234, or by e-mail at: Zanele.Ndlovu@wits.ac.za or Rhulani.Mkansi@wits.ac.za

Name of Participant: _____

Date: _____

Place: _____

Signature or mark: _____

Witnessed by:

Name of Witness: _____

Signature or mark: _____

Date: _____

Appendix 6:

Consent sheet for audio recording of daughter's qualitative interview

Study title: A mixed-methods analysis of the implementation and uptake of the Human Papillomavirus vaccination of adolescent girls in Lusaka, Zambia

1. I have been given a Participant Information Sheet which explains the nature and processes involved in this study, which is attached hereto

2. I was given time to read it, or had it read to me, in the language I best understand

3. I was given time to ask any questions I wanted to and found any answers given to me to be reasonable and satisfactory

4. I believe I fully understand why the study is being conducted and what the intended outcomes will be, as well as that the interview will be recorded

5. I understand that there will be no immediate benefit to me, should I agree to participate, nor will I receive any payment; conversely, participation will not cost me anything but my time

6. I understand that, even if I initially consent to take part in the study, I may subsequently withdraw at any time and would not be required to give any reasons; if that happened, any data collected about me for the purposes of the study would immediately be destroyed, unless I give consent for it to be retained

7. I have been given a range of contact details, listed below. If I require further information or become concerned about any aspect of this study. I am free to speak to any of these contacts.

Contact details:

Dr Mwansa Ketty Lubeya, Principal Investigator, telephone no. +260955108465, or by e-mail at ketty.lubeya@unza.zm

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Prof Mulindi Mwanahamuntu, Supervisor 3 on telephone +26096887236 or email at mmulindi@hotmail.com

Professor CB Penny, Chairperson of the Human Research Ethics Committee (Medical) at the University of Witwatersrand, on telephone no. 011 717 2301, or by e-mail at Clement.Penny@wits.ac.za.

Ms. Z Ndlovu or Mr Rhulani Mkansi, Committee Secretariat, telephone nos.: 011 717 2700 or 1234, or by e-mail at: Zanele.Ndlovu@wits.ac.za or Rhulani.Mkansi@wits.ac.za

Name of Parent: _____

Date: _____

Place: _____

Signature or mark: _____

Witnessed by:

Name of Witness: _____

Signature or mark: _____

Date: _____

Appendix 7

Adolescents' interview guide

Study title: A mixed-methods analysis of the implementation and uptake of the Human Papillomavirus vaccination of adolescent girls in Lusaka, Zambia mixed-

Short demographic history

Age: Name of school: School grade:……..

Residence: Vaccination status:

Number of vaccine doses received: Date (s) of vaccination …….

Introduction

Good day, my name is……Thank you for agreeing to participate in this study and to have the interview recorded. Just to share a bit of background, infection with HPV can be cleared by the body or cause conditions such as genital warts and cancers like cervical, anal, oral and vulva. However, a vaccine is available to help prevent these infections and ultimately reduce number of people getting HPV related conditions. I will be interviewing you today about the human papillomavirus vaccine. Once again, the information gathered will remain confidential and only be used for the purposes of this research.

Do you have any questions before we start the interview?

1. Please tell me about yourself and your family.

Probe: Who do you live with?

Probe: How many sisters and brothers do you have?

Probe: Age, school grade if in school

2. Have you ever heard about the human papillomavirus? (Information will be available for those who may not know about HPV)

Probe: Where did you get this information is from

3. What diseases does the HPV cause? (Cervical cancer, genital wart)

Probe: Do you know about cervical cancer?

Probe: Do you know about genital warts?

4. What do you know about vaccines?

Probe: Have you ever received any vaccine?

Probe: If yes, what vaccine did you receive?

Probe: What was the vaccine for?

5. Please tell me, before today, did you know about the HPV vaccine? (Information will be available for those who may not know about it)

Probe: If yes, what do you know about it?

6. Have you received the HPV vaccine?

Probe: How old were you when you received the vaccine?

Probe: When did you receive the vaccine

7. What do your friends think about the HPV vaccine?

Probe: Those who did not receive the vaccine?

Probe: Those who received the vaccine?

8. What do you think about adolescent girls with HIV getting the vaccine?
9. How likely are you to get diseases related to HPV if you don’t get vaccinated?

Probe: Genital warts?

Probe: Cervical cancer?

10. What do you think would happen to you if you do not get the vaccine?

Probe: Get cervical cancer or genital warts

Probe: Die from cervical cancer

11. What do your parents think about the HPV vaccine?

Probe: They are okay with it

Probe: They do not agree with it

Probe: What do your teachers say about the HPV vaccine?

12. What are the possible things that can prevent you from receiving the vaccine?
13. What motivated you to get the vaccine (Depends on participant vaccination status) If vaccinated:
14. What are your feelings about the vaccine?
15. How did your body feel like after receiving the vaccine?
16. probe: Any side effects fever, pain at injection site, swelling
17. If the response is no: Do you ever wish to get the vaccine in future?
18. Would you recommend others to get the HPV vaccine?

Probe: Give reason for your answer

19. What should be done to ensure that many girls get the HPV vaccine?
20. Do you have any questions about this interview?

We have come to the end of this interview; I may come back to you if I need any further information. Thank you.

Appendix 8

Participant information sheet for quantitative research

Study title: A mixed-methods analysis of the implementation and uptake of human papillomavirus vaccination of adolescent girls in Lusaka, Zambia.

Parents' ICF: VERSION 1 12 July 2021

Principal Investigator: Dr. Mwansa K. Lubeya

Principal Investigator Department: Public Health

Good day, my name is ……., I'm part of a team conducting research on human papillomavirus (HPV) vaccine delivery. We would like to understand the factors that lead parents to consent to vaccinate their daughters or not.

Introduction

Infection with HPV can cause self-limiting disease as well as cancers such as cervical, anal, oral and vulva. However, a vaccine is available to help reduce these infections and ultimately reduce number of people getting HPV related cancers. The vaccine is known to be effective especially if given to girls before they become sexually active. In 2019, The HPV vaccine was introduced in Zambia for adolescent girls. The girls are scheduled to receive 2 doses of 12 months apart. The first dose is given at 14 years and the second dose at 15years of age. Through this research, we would like to understand why some parents choose to vaccinate their daughters and why others choose not to.

Invitation to Participate

You are being invited to participate in this study because you have a daughter aged 15 to 18 years. This document gives you information about the study. Once you understand what the study is about, and if you agree to take part, you will be asked to sign this form and a copy will be given to you to keep.

Why is this study being done?

There are many factors at play with regards to HPV vaccination. In 2019, Zambia rolled out a free national HPV vaccination program, targeting 14-year-old girls. Parental consent is required for the vaccination besides the assent by the girls. Parents play a key role in decision making for their daughters. This study sets out to understand factors associated with parents consenting for HPV vaccine uptake for daughters in Lusaka and develop context-specific strategies to improve uptake of the vaccine.

What is involved in the study?

This will be a cross-sectional quantitative arm of the study, targeting parents whose daughters are aged 15-18 years, assumed to be age for full immunisation. Participants will be required to complete a pre tested questionnaire, data will be collected between June 2021 and December 2021

How many people will take part in this study?

Approximately, 330 parents in Lusaka, Zambia. The minimum age of participants will be 18 years.

What do I have to do if I take part in this study?

A questionnaire will be administered by research team however; you will have an option to complete the questionnaire yourself or the research team will do it for you. Questions will be asked regarding social demographic characteristics, social economic status, knowledge about HPV and HPV vaccine, attitudes towards HPV vaccination for daughters will be explored.

How long will I be in this study?

The questionnaire will take approximately 30 to 45 minutes to complete

What are the risks of being involved in the study?

There is very little risk involved in taking part in this study. Some questions regarding your health seeking behaviour maybe embarrassing. You are free to skip questions that you may not feel comfortable answering, besides you can withdraw from the study at any point without any consequences.

What are the benefits of being in the study?

There are no immediate benefits, however the information gathered will help with understanding possible ways of having more girls get vaccinated against HPV. You will be given information on the study while involved in the project and after the results are available.

What are my rights as a research participant?

Participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which you may be entitled. You may discontinue participation at any time without penalty, or any requirement to provide a reason. Anonymity can usually be guaranteed in questionnaires.

Will I be reimbursed for participating in this study?

There is to be no payment associated with participation in this study, however a R75 will be given for your refreshments

What are the costs to me?

There is no cost associated with participating in this study.

What is a certificate of confidentiality?

Confidentiality: Efforts will be made to keep personal information confidential. Absolute confidentiality cannot be guaranteed. Personal information may be disclosed if required by law.

Organisations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the Research Ethics Committees and the South African Health Products Regulatory Authority (SAHPRA) (where appropriate).

What happens to the information collected for research?

If results are published all data collected in the course of the study will be securely retained for two (2) years, and six (6) years, if there is no publication. Thereafter data will be destroyed accordingly.

What are the outputs of this study?

Once this study is completed, scientific publications will arise for attainment of a PhD in public health. If you wish to receive the results, indicate accordingly

Contact details for research team

For further information please contact the Principal Investigator: Dr. Mwansa Ketty Lubeya Phone: +260955108465 Email: ketty.lubeya@unza.zm

Contact details of REC administrator and chair

This study has been approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, Johannesburg (“Committee”). A principal function of this Committee is to safeguard the rights and dignity of all human subjects who agree to participate in a research project and the integrity of the research.

If you have any concern over the way the study is being conducted, please contact the Chairperson of this Committee who is Professor Clement Penny, who may be contacted on telephone number 011 717 2301, or by e-mail on Clement.Penny@wits.ac.za. The telephone numbers for the Committee secretariat are 011 717 2700/1234 and the e-mail addresses are Zanele.Ndlovu@wits.ac.za and Rhulani.Mukansi@wits.ac.za

Thank you for reading this Participant Information Sheet.

Appendix 9

Participant consent sheet (Parents)

Study title: A mixed-methods analysis of the implementation and uptake of the Human Papillomavirus vaccination of adolescent girls in Lusaka, Zambia

1. I have been given a Participant Information Sheet which explains the nature and processes involved in this study, which is attached hereto;
2. I was given time to read it, or had it read to me, in the language I best understand;
3. I was given time to ask any questions I wanted to and found any answers given to me to be reasonable and satisfactory;
4. I believe I fully understand why the study is being conducted and what the intended outcomes will be;
5. I understand that there will be no immediate benefit to me, should I agree to participate, nor will I receive any payment; conversely, participation will not cost me anything but my time;
6. I understand that, even if I initially consent to take part in the study, I may subsequently withdraw at any time and would not be required to give any reasons; if that happened, any data collected about me for the purposes of the study would immediately be destroyed, unless I give consent for it to be retained
7. I have been given a range of contact details, listed below. If I require further information or become concerned about any aspect of this study, I am free to speak to any of these contacts.

Contact details:

Dr Mwansa Ketty Lubeya, Principal Investigator, telephone no. +260955108465, or by e-mail at ketty.lubeya@unza.zm

Dr Mary Kawonga, Supervisor 1, on telephone no. +27117172575, or by e-mail at mary.kawonga@wits.ac.za

Prof Carla Chibwesha, Supervisor 2, on telephone no +2772744789 or by email at Carla.chibwesha@med.unc.edu

Prof Mulindi Mwanahamuntu, Supervisor 3 on telephone +26096887236 or email at mmulindi@hotmail.com

Professor CB Penny, Chairperson of the Human Research Ethics Committee (Medical) at the University of Witwatersrand, on telephone no. 011 717 2301, or by e-mail at Clement.Penny@wits.ac.za.

Ms. Z Ndlovu or Mr Rhulani Mkansi, Committee Secretariat, telephone nos.: 011 717 2700 or 1234, or by e-mail at: Zanele.Ndlovu@wits.ac.za or Rhulani.Mkansi@wits.ac.za

Name of Participant: _____

Date: _____

Place: _____

Signature or mark _____

Witnessed by:

Name of Witness: _____

Signature: _____

Date: _____

Appendix 10

Questionnaire for quantitative interviews

Study title: A mixed-methods analysis of the implementation and uptake of the Human Papillomavirus vaccination of adolescent girls in Lusaka, Zambia

Screening question: Do you have a daughter aged from 15 to 18 years? I) No ii) Yes

If yes interview proceeds, if not terminates

PART A: Social Demographic Characteristics

1. Age
2. Sex i) male ii) female
3. Marital status i) single ii) married
4. Level of education: i) primary ii) secondary iii) tertiary
5. Employment status: i) not employed ii) employed
6. Residential area ……
7. Monthly family income (Total amount in Zambian Kwacha) …….
8. Do you have a cell phone, car, fridge, TV, a house (Y/N)

PART B: HPV general knowledge (Answer: True/False/Don't know)

1. HPV is very rare
2. HPV always has visible signs and symptoms
3. HPV can cause cervical cancer
4. HPV can be transmitted through genital skin-to-skin contact
5. There are many types of HPV
6. HPV can cause genital warts
7. HPV can be passed on during sexual intercourse
8. HPV can cause genital warts
9. Men cannot get HPV
10. Using condoms reduces the chances of HPV transmission
11. HPV can be cured with antibiotics
12. Having many sexual partners

13. Most sexually active people will get HPV at some point in their lives
14. A person could have HPV for many years without knowing it
15. Having sex at an early age increases the chances of getting HPV
16. HPV can cause anal cancer
17. HPV is a bacterial infection
18. HPV can be transmitted via oral sex
19. HPV can cause cancer of the penis
20. HPV can be transmitted via anal sex
21. HPV infection always cause health problems
22. HPV can cause Oral cancer
23. A person with no symptoms cannot transmit the HPV infection
24. HPV infection is more severe in people living with HIV

PART C: HPV Vaccine knowledge scale (Answer True/False/Don't know)

1. The HPV vaccine requires at least 2 doses
2. PLWHIV need more doses of HPV vaccine
3. The HPV vaccine offers protection against all sexually transmitted infections
4. The HPV vaccines are most effective if given to people who have never had sex
5. Someone who has received the HPV vaccine cannot develop cervical cancer
6. The HPV vaccines offer protection against most cervical cancers
7. The HPV vaccine offers protection against genital warts
8. Girls who receive HPV vaccine do not need cervical cancer screening when older
9. The HPV vaccine protects you from every type of HPV
10. You can cure HPV by getting the HPV vaccine
11. The HPV vaccine is approved and recommended in Zambia for females aged 14
12. The HPV vaccine is currently not approved for males in Zambia
13. People living with HIV can receive the HPV vaccine

PART D: Assessing Parental Attitudes Using Health Belief Model

Perceived Susceptibility

	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
My daughter will likely get HPV.					
My daughter's chances of getting HPV in the next years are high					
I feel my daughter will get HPV sometime during her life.					

Perceived Severity

	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
The thought cervical cancer scares me.					
If my daughter developed cervical cancer her academics and career would be endangered.					
I'm afraid to even think of cervical cancer					
Cervical cancer is more serious than other diseases					

Perceived Benefits

	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
If my daughter receives the HPV vaccine, would not worry as much about her getting cervical cancer					
Receiving vaccinations will help prevent diseases					
Having the HPV vaccination is the best way for my daughter to prevent HPV and cervical cancer.					
Having the HPV vaccination will decrease daughters' chances of dying from cervical cancer					

Perceived Barriers

	Strongly agree	Agree	Neutral	Disagree	Strongly disagree

I don't know how to go about my daughter receiving the HPV vaccination					
I am afraid for my daughter to receive the HPV vaccine					
I don't understand the two-dose procedure.					
My daughter can become promiscuous if she receives the HPV vaccine					
My daughter can become infertile if she receives the HPV vaccine					
My daughter is too young to receive the vaccine					
The COVID-19 Pandemic affected my decision to get my daughter vaccinated					

Self-efficacy

	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
Healthcare workers recommended the vaccine					
My family & friends recommend the vaccine					

Cues to Action

	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
Healthcare worker recommended the vaccine					
My family & friends recommend the vaccine					

Part E

1. How old was your daughter at her last birthday?
2. Does your daughter go to school? i) No ii) Yes
3. What school grade is your daughter?
4. Did you consent for your daughter to receive the HPV vaccine? I) No ii) Yes
5. Give a reason for your answer in 5…….
6. Has your daughter received the HPV vaccine? I)No ii) Yes
7. If no to question 6, give a reason for your answer

8. If yes how many doses? I) No ii) yes
9. Do you intend to get HPV vaccination for your other daughters in future? I) No ii) Yes
10. Have you screened for cervical cancer? Female respondents only I) No ii) Yes
11. Do you know anyone with cervical cancer? I) No ii) Yes
12. Do you know anyone with other HPV-related cancers e.g. vulva, penile, anal or oral i) No ii) Yes
13. Do you know anyone with genital warts? I) No ii) Yes
14. Have you taken an HIV test in the last 3 months? I) No ii) Yes iii) Prefer not to answer
15. If yes what was the result i) Negative ii) Positive iii) I don't know iv) Prefer not to mention

Appendix 11

Teachers and healthcare worker's information sheet

Study title: A mixed-methods analysis of the implementation and uptake of the Human Papillomavirus vaccination of adolescent girls in Lusaka, Zambia

Principal Investigator: Dr. Mwansa K. Lubeya

Principal Investigator Department: Public Health

Greetings

Good day, my name is ……., I'm part of a team conducting research on human papillomavirus (HPV) vaccine delivery.

Introduction

Infection with HPV can cause self-limiting disease as well as cancers such as cervical, anal, oral and vulva. However, a vaccine is available to help reduce these infections and ultimately reduce number of people getting HPV related cancers. The vaccine is known to be effective especially if given to girls before they become sexually active. In 2019, The HPV vaccine was introduced in Zambia in 2019 for adolescent girls, with schools being the main delivery platforms.

The girls are scheduled to receive two doses of HPV vaccine 12 months apart. The first dose is given at 14 years and the second dose at 15years of age. The vaccine is meant to protect against cancers caused by the HPV such as cervical cancer. Through this

research, we would like to understand perceived barriers and facilitators to adoption, acceptability and reach by teachers and HCW

Invitation to participate in the study

You are being invited to participate in this study because you are involved in the HPV vaccination program. This document gives you information about the study. Once you understand what the study is about, and if you agree to take part, you will be asked to sign this form and a copy will be given to you to keep.

Why is this study being done?

Health care workers collaborate with teachers to deliver messages about the vaccine to the girls and during actual delivery of the vaccine. We would like to understand the barriers and facilitators to delivery of this vaccine by service providers and later develop context-specific strategies to overcome the experienced barriers.

What is involved in the study?

Participants will be interviewed via telephone or in person. Questions around the facility planning and individual planning will be asked. The interview will last about 1 hour. Data will be collected between June 2021 and December 2021

How many people will take part in this study?

Approximately 8-10 teachers and healthcare workers will participate in this study. The minimum age of participants will be 18 years.

What do I have to do if I take part in this study?

In depth interviews will be conducted. Since you are a key informant, questions will be asked regarding your social demographic characteristics, barriers and facilitators to HPV and HPV vaccine delivery, adoption and reach, will be explored. The interview will be audio recorded

How long will I be in this study?

The Interview will take approximately 1 hour to complete

What are the risks of being involved in the study?

There is very little risk involved in taking part in this study. Some questions may be intimidating. You are free to skip questions that you may not feel comfortable answering, besides you can withdraw from the study at any point without any consequences.

What are the benefits of being in the study?

There are no immediate benefits, however the information gathered will help with understanding possible ways of having more girls get vaccinated against HPV. You will be given information on the study while involved in the project and after the results are available.

What are my rights as a research participant?

Participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which you may be entitled. You may discontinue participation at any time without penalty, or any requirement to provide a reason. Anonymity can usually be guaranteed in questionnaires.

Will I be reimbursed for participating in this study?

There is no payment associated with participation in this study, however a R75 reimbursement will be given for your refreshments

What are the costs to me?

There is no cost associated with participating in this study.

One exception is if you agree that we can give out research information with your name on it. You may give written permission for an insurer, employer or other person to get copies of your study records.

Confidentiality: Efforts will be made to keep personal information confidential. Absolute confidentiality cannot be guaranteed. Personal information may be disclosed if required by law.

Organisations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the Research Ethics Committees and the South African Health Products Regulatory Authority (SAHPRA) (where appropriate).

What happens to the information collected for research?

If results are published all data collected in the course of the study will be securely retained for two years, and six years, if there is no publication. Thereafter data will be destroyed accordingly.

What are the outputs of this study?

Once this study is completed, scientific publications will arise for attainment of a PhD in public health, further findings will be disseminated to the public, service providers and policy makers. If you wish to receive the results, indicate accordingly.

Contact details for research team

Further information please contact the Principal Investigator: Dr. Mwansa Ketty Lubeya Phone: +260955108465 Email: ketty.lubeya@unza.zm

Contact details of REC administrator and chair

This study has been approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, Johannesburg (“Committee”). A principal function of this Committee is to safeguard the rights and dignity of all human subjects who agree to participate in a research project and the integrity of the research.

If you have any concern over the way the study is being conducted, please contact the Chairperson of this Committee who is Professor Clement Penny, on telephone number 011 717 2301, or by e-mail on Clement.Penny@wits.ac.za. The telephone numbers for the Committee secretariat are 011 717 2700/1234 and the e-mail addresses are Zanele.Ndlovu@wits.ac.za and Rhulani.Mukansi@wits.ac.za

Thank you for reading this Participant Information Sheet.

Appendix 12

Participant consent sheet (Health care workers & Teachers)

Study title*:* A mixed-methods analysis of the implementation and uptake of the Human Papillomavirus vaccination of adolescent girls in Lusaka, Zambia

1. I have been given a Participant Information Sheet which explains the nature and processes involved in this study, which is attached hereto;
2. I was given time to read it, or had it read to me, in the language I best understand;
3. I was given time to ask any questions I wanted to and found any answers given to me to be reasonable and satisfactory;
4. I believe I fully understand why the study is being conducted and what the intended outcomes will be;
5. I understand that there will be no immediate benefit to me, should I agree to participate, nor will I receive any payment; conversely, participation will not cost me anything but my time;
6. I understand that, even if I initially consent to take part in the study, I may subsequently withdraw at any time and would not be required to give any reasons; if that happened, any data collected about me for the study would immediately be destroyed, unless I give consent for it to be retained
7. I have been given a range of contact details, listed below. If I require further information or become concerned about any aspect of this study, I am free to speak to any of the provided contacts.

Contact details:

Dr Mwansa Ketty Lubeya, Principal Investigator, telephone no. +260955108465, or by e-mail at ketty.lubeya@unza.zm

Dr Mary Kawonga, Supervisor 1, on telephone no. +27117172575, or by e-mail at mary.kawonga@wits.ac.za

Prof Carla Chibwesha, Supervisor 2, on telephone no +2772744789 or by email at Carla.chibwesha@med.unc.edu

Prof Mulindi Mwanahamuntu, Supervisor 3 on telephone +26096887236 or email at mmulindi@hotmail.com

Professor CB Penny, Chairperson of the Human Research Ethics Committee (Medical) at the University of Witwatersrand, on telephone no. 011 717 2301, or by e-mail at Clement.Penny@wits.ac.za.

Ms. Z Ndlovu or Mr Rhulani Mkansi, Committee Secretariat, telephone nos.: 011 717 2700 or 1234, or by e-mail at: Zanele.Ndlovu@wits.ac.za or Rhulani.Mkansi@wits.ac.za

Name of Participant: _____

Date: _____

Place: _____

Signature or mark _____

Witnessed by:

Name of Witness: _____

Signature: _____

Date: _____

Appendix 13

Interview guide for Teachers and Healthcare workers

Study title: A mixed-methods analysis of the implementation and uptake of the Human Papillomavirus vaccination of adolescent girls in Lusaka, Zambia

Introduction

Good day, my name is ……Thank you for consenting to participate in this study and to have the interview recorded. I will be interviewing you today about your experiences with the delivery of the HPV vaccine. You have been selected to participate because you have been involved in the vaccination programme.

This interview will be recorded so that we capture everything you say.

Please tell me about yourself and your background in general.

Probe: Age, your profession, qualifications, duration in service and at the local facility

Please tell me about the specific role you played during the HPV vaccination.

Probe: Part of planning, distributing vaccines, administering the vaccine to girls, supporting to register eligible girls, writing vaccination cards, filling out the register, maintaining order of flow of girls during the programme

Please tell me about how vaccination programmes are conducted at your facility?

Probe: Target age group, location and duration

What other health related activities are undertaken at your school?

Probe: Tell me more about the structure and organisation of the other health programs. Whom do they target? How often do they happen and who is involved? (Teachers only).

1.0 INTERVENTION CHARACTERISTICS

1.1 Evidence Strength & Quality

What information (evidence) do you have that shows whether or not the HPV vaccination programme is working in your zone?

Probe: How does this knowledge affect your perception of the HPV vaccination programme?

What do influential stakeholders think of the HPV vaccination programme?

Probe: What do administrative or other leaders think of the HPV vaccination programme? Religious leaders, community leaders, school headteacher

1.2 Adaptability

What kinds of changes or alterations do you think you will need to make to the HPV vaccination programme so it will work effectively in your zone?

Probe: Do you think you will be able to make these changes? Why or why not?

1.3 Complexity

How complicated is the HPV vaccination program?

Probe: Please consider the following aspects of the intervention: duration, scope, intricacy and number of steps involved, and whether the intervention reflects a clear departure from previous practices.

1.4 Design Quality & Packaging

What is your perception of the quality of the supporting materials?

Probe: packaging, and bundling of the HPV vaccine for implementation?

Probe: Why do you hold those views?

What supports, such as online resources, marketing materials, or a toolkit, are available to help you implement and use the HPV vaccine?

Probe: How do you access these materials?

How will available materials affect implementation in your zone?

1.5 Cost

What costs were incurred to implement the HPV vaccination programme?

What cost were considered when deciding to implement the HPV vaccination programme?

2.0 OUTER SETTING

2.1 Participant needs & resources

To what extent is staff aware of the needs and preferences of the individuals being served by your organisation?

Probe: How "in touch" are staff and leadership with the individuals served by your organisation?

How do you think the adolescents and parents served by your organisation responded to the HPV vaccination programme?

Probe: Were the reactions warm or cold?

What barriers did the adolescents and parents face to participating in the HPV vaccination programme?

Probe: Timing, distance, vaccine shortages, parental refusal

Have you elicited information from participants regarding their experiences with the HPV vaccination programme?

Probe: What are their perceptions of the HPV vaccine?

Have you heard stories about the experiences of participants with the HPV vaccine?

Probe: Can you describe a specific story?

2.3 External Policies & Incentives

What kind of local, state, or national performance measures, policies, regulations, or guidelines influenced the decision to implement the HPV vaccination programme?

Probe: How will the HPV vaccination programme affect your organisation's ability to meet these measures, policies, regulations, or guidelines?

3.0 INNER SETTING

3.1 Structural Characteristics

How does the infrastructure of your organisation (social architecture, age, maturity, size, or physical layout) affect the implementation of the HPV vaccine?

Probe: How did the infrastructure facilitate/hinder implementation of the HPV vaccination programme?

Probe: How did you work around structural challenges? Any changes made?

3.2 Networks & Communications

Can you describe your working relationships with your colleagues?

Probe: With colleagues in your unit? in other units?

Can you tell me a story about a time you needed to work with others to solve a problem? Or to implement an intervention in the past or this HPV vaccination?

Probe: Can you describe your working relationship with leaders?

Probe: Your supervisor? Supervisors of other colleagues?

3.3 Culture

How would you describe the culture of your organisation?

Do you feel like the culture of your own unit is different from the overall organisation?

Probe: In what ways?

How do you think your organisation's culture (general beliefs, values, assumptions that people embrace) affected the implementation of the HPV vaccination program?

Probe: Can you describe an example that highlights this?

3.4 Implementation Climate

In your own opinion, what is the general level of receptivity in your organisation to implementing the HPV vaccination?

Probe: Why?

3.5 Tension for Change

Is there a strong need for this HPV vaccination?

Probe: Why or why not?

Probe: Do others see a need for the HPV vaccine?

3.6 Compatibility

How well does the HPV vaccination program fit with your values and norms and the values and norms within the organisation?

Probe: Values relating to interacting with adolescents and their parents e.g. shared-decision making vs. being more directive?

How well does the HPV vaccination fit with existing work processes and practices in your setting?

Probe: What are likely issues or complications that may arise?

Can you describe how the HPV vaccination programme has been integrated into current processes?

Probe: How will it interact or conflict with current programs or processes?

3.7 Relative Priority

What kinds of high-priority initiatives or activities are already happening in your setting?

Probe: What is the priority of getting the HPV vaccination implemented relative to other initiatives that are happening now?

Probe: Will the implementation conflict with these priorities?

Probe: Will the implementation help achieve (or relieve pressure related to) these priorities?

Probe: How will you juggle competing priorities in your own work?

3.8 Organizational Incentives & Rewards

What kinds of incentives are there to help ensure that the implementation of the HPV vaccination programme is successful?

Probe: What is your motivation for wanting to help ensure the implementation is successful?

3.9 Goals & Feedback

Has your organisation set goals related to the implementation of the HPV vaccination programme?

Probe: [If yes] What are the goals?

Probe: To what extent are organisational goals monitored for progress?

3.10 Learning Climate

To what extent do you feel like you can try new things to improve your work processes?

Probe: Do you feel like you have the time and energy to think about ways to improve things?

Probe: Did you feel valued/respected by your supervisor for the role you played?

3.11 Leadership Engagement

What level of endorsement or support have you seen or heard from leaders?

Probe: Who are these leaders and how has this affected thing so far? Going forward?

Probe: What kind of support have they given you? Can you provide specific examples?

Probe: What kind of support can you expect going forward? Can you provide specific examples?

Probe: What types of barriers might they create?

3.12 Available Resources

Do you expect to have sufficient resources to implement and administer the HPV vaccination programme?

Probe: [If Yes] What resources are you counting on? Are there any other resources that you received, or would have liked to receive?

Who do you ask if you have questions about the HPV vaccination programme or its implementation?

Probe: How available are these individuals?

4.0 Process

4.1 Planning

What have you done to get a plan in place to implement the HPV vaccination programme?

Can you describe the plan for implementing the HPV vaccination programme?

Probe: What is your role in the planning process?

Probe: Who is involved in the planning process? What are their roles?

What role has your plan for implementation played during implementation?

Probe: Was it used to guide implementation of the HPV vaccination programme?

4.2 Opinion Leaders

Who are the key influential individuals to get on board with this implementation?

Probe: Who are these influential individuals?

Who leads the implementation of the HPV vaccination programme in your organisation?

Probe: How did this person come into this role:

Why was this person chosen?

4.3 Champions

Besides the formal implementation leader, are there people in your organisation who are likely to champion (go above and beyond what might be expected) the HPV vaccination programme?

Probe: Were they formally appointed in this position, or was it an informal role?

Probe: What position do these champions have in your organisation?

Probe: How do you think they will help with implementation?

4.4 External Change Agents

Did someone (or a team) outside your organisation help you with implementing the HPV vaccination programme?

Probe: Can you describe this person/group?

Probe: How did they get involved?

Probe: What is their role?

Probe: What kind of activities will they be doing?

4.5 Key Stakeholders

What steps have been taken to encourage individuals to commit to supporting the HPV vaccination programme?

Probe: Who are the key individuals to get on board with HPV vaccination programme?

4.6 HPV vaccine eligible adolescents

How did you or your colleagues communicate to adolescents about the HPV vaccination programme?

Probe: How did they participate in the HPV vaccination?

Probe: How did they access the HPV vaccine?

4.7 Executing

Has the HPV vaccination been implemented according to the implementation plan?

Probe: [If Yes] Can you describe this?

Probe: [If No] Why not?

4.8 Reflecting & Evaluating.

Will you receive feedback reports about the implementation or the HPV vaccination programme itself?

Probe: Who will give this feedback?

Probe: How was results of the evaluation be distributed to stakeholders?

We have come to the end of this interview; I may get back to you if I need further clarification.

Thank you very much for your time.

Appendix 14

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Mrs Sandra Benn
E-mail: sandra.benn@wits.ac.za

07 December 2022
Person No: 2402093
TAA

Dr MK Lubeya
Women and Newborn Hospital
University Teaching Hospitals
Dept of OBS & GYNAE
P/BAG RW1X
10101
Zambia

Dear Dr Mwansa Lubeya

Doctor of Philosophy: Change of title of research

I am pleased to inform you that the following change in the title of your Thesis for the degree of **Doctor of Philosophy** has been approved:

From:	**A mixed-methods analysis of the acceptability, adoption, reach and uptake of human papillomavirus (HPV) vaccination of adolescent girls in Lusaka, Zambia**
To:	**A mixed-methods analysis of the implementation and uptake of the human papillomavirus vaccination of adolescent girls in Lusaka, Zambia**

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

Appendix 15

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Mwansa Ketty Lubeya

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M210473

NAME: (Principal Investigator)	Dr Mwansa Ketty Lubeya
DEPARTMENT:	School of Public Health Lusaka district schools and health facilities Zambia
PROJECT TITLE:	A Mixed Methods Analysis Of The Acceptability, Adoption, Reach And Uptake Of The Human Papillomavirus Vaccine Of Adolescent Girls In Lusaka, Zambia
DATE CONSIDERED:	30/04/2021
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr M. Kawonga, Prof C. Chibwesha and Prof M. Mwanahamuntu
APPROVED BY:	CB Penny Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	18/06/2021

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions.Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report.** The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **April** and will therefore be due in the month of **April** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

23RD JUNE 2021
Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix 16

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R49 Ms MK Lubeya

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M210473

NAME: (Principal Investigator)	Ms MK Lubeya
DEPARTMENT:	School of Public Health Medical School University
PROJECT TITLE:	*A mixed methods analysis of the implementation and uptake of the human papillomavirus vaccination of adolescent girls in Lusaka, Zambia* New study title noted on 2022/12/13
DATE CONSIDERED:	2021/04/30
DECISION:	Approved unconditionally
CONDITIONS:	
NOTE:	If contact information regarding student study participants is required, please contact the Registrar's office - <Nicoleen.Potgieter@wits.ac.za>
SUPERVISOR:	Dr M Kawonga; Profs C Chibwesha & M Mwanahamuntu
APPROVED BY:	CB Penny Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2021/06/18

This Clearance Certificate is valid for 5 years from the date of approval. An extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office secretariat on the 3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **April** and therefore reports and re-certification will be due in the month of **April** each year. Unreported changes to the study may invalidate the clearance given by the HREC (Medical).

Signature of Principal Investigator _____ Date _____

All correspondence should be addressed to the Provincial Health Director
Telephone: +260 211 256813
Fax: +260 211 256814
Telephone: +260 211 256815
Cell: +260 956 399643
+260 963 908260

Appendix 17

REPUBLIC OF ZAMBIA

MINISTRY OF HEALTH

In Reply please quote:

PHOLSK/101/8/1
File No.:.....

Lusaka Provincial Health Office
P.O. Box 32573
LUSAKA

26th April,2021

Dr Ketty Mwansa Lubeya
University of Zambia, School of Medicine
P O Box 50110
LUSAKA

RE: REQUEST FOR AUTHORITY TO CONDUCT RESEARCH

Reference is made to above subject matter.

Lusaka Provincial Health Office is in receipt of your letter requesting for permission to conduct a research titled: **"A Mixed-methods analysis of the acceptability, adoption, reach and uptake of Human Papillomavirus vaccination of adolescent girl in Lusaka, Zambia.**

My office is glad to inform you that it has no objection to your request provided that;

1. The relevant District Health Directors where the study is being conducted are fully appraised;
2. Progress updates are provided to Lusaka Provincial Health Office and the District Health Office biannually from the date of commencement of the study;
3. The final study report is cleared by NHRA before any publication or dissemination within or outside the country;
4. After clearance for publication or dissemination by NHRA, the final study report is shared with all relevant Provincial and District Directors of Health where the study was being conducted, University Leadership and all key respondents.

Kindly ensure minimum interruption in health service delivery to the selected health facilities you will undertake your research.

By copy of this letter, the district is advised to allow you undertake the above mentioned research and provide you with the relevant support.

Dr Bushimbwa TambaTamba
Public Health Specialist
For/Provincial Health Director
Lusaka Province.

REPUBLIC OF ZAMBIA
MINISTRY OF HEALTH
LUSAKA PROVINCIAL HEALTH OFFICE
26 APR 2021
PROVINCIAL HEALTH DIRECTOR
P. O. BOX 32573, LUSAKA

CC: The District Health Director – Lusaka

Appendix 18

NATIONAL HEALTH RESEARCH AUTHORITY

Ref No: NHRA00001/19/04/2021 Date: 19th April, 2021
The Principal Investigator Dr. Ketty Mwansa Lubeya,
University of Zambia, School of Medicine,
P.O. Box 50110,
Lusaka.
Dear Dr. Lubeya,

Re: Request for Authority to Conduct Research

The National Health Research Authority is in receipt of your request for authority to conduct research titled "A MIXED-METHODS ANALYSIS OF THE ACCEPTABILITY, ADOPTION, REACH AND UPTAKE OF HUMAN PAPILLOMAVIRUS VACCINATION **OF ADOLESCENT GIRLS IN LUSAKA, ZAMBIA."** I wish to inform you that following submission of your request to the Authority, our review of the same and in view of the ethical clearance, this study has been **approved** on condition that:
The relevant Provincial and District Medical Officers where the study is being conducted are fully appraised.
Progress updates are provided to NHRA quarterly from the date of commencement of the study;
The final study report is cleared by the NHRA before any publication or dissemination within or outside the country;
After clearance for publication or dissemination by the NHRA, the final study report is shared with all relevant Provincial and District Directors of Health where the study was being conducted, University leadership, and all key respondents.

Yours sincerely,
Prof. Godfrey BiembaDirector/CEO

National Health Research Authority

All correspondences should be addressed to the Director/CEO National Health Research Authority

Appendix 19

UNIVERSITY OF ZAMBIA
BIOMEDICAL RESEARCH ETHICS COMMITTEE

Telephone: 260-1-256067
Telegrams: UNZA, LUSAKA
Telex: UNZALU ZA 44370
Fax: + 260-1-250753
Federal Assurance No. FWA00000338

Ridgeway Campus
P.O. Box 50110
Lusaka, Zambia
E-mail: unzarec@unza.zm
IRB00001131 of IORG0000774

31st March 2021

Your REF. No. 1609-2021

Dr. Mwansa Ketty Lubeya,
University of Witwatersrand,
Faculty of Health Sciences,
South Africa.

Dear Dr. Lubeya,

RE: "A MIXED-METHODS ANALYSIS OF THE ACCEPTABILITY, ADOPTION, REACH AND UPTAKE OF HUMAN PAPILLOMAVIRUS (HPV) VACCINATION OF ADOLESCENT GIRLS IN LUSAKA, ZAMBIA" (REF. NO. 1609-2021)

The above-mentioned research proposal was presented to the Biomedical Research Ethics Committee on 31st March, 2021. The proposal is **approved**. The approval is based on the following documents that were submitted for review:

a) **Study proposal**
b) **Questionnaires**
c) **Participant Consent Form**

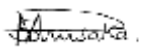
APPROVAL NUMBER : REF. 1609-2021

This number should be used on all correspondence, consent forms and documents as appropriate.

- **APPROVAL DATE : 31st March 2021**
- **TYPE OF APPROVAL : Fast Track**
- **EXPIRATION DATE OF APPROVAL : 30th March 2022**
  After this date, this project may only continue upon renewal. For purposes of renewal, a progress report on a standard form obtainable from the UNZABREC Offices should be submitted one month before the expiration date for continuing review.
- **SERIOUS ADVERSE EVENT REPORTING**: All SAEs and any other serious challenges/problems having to do with participant welfare, participant safety and study integrity must be reported to UNZABREC within 3 working days using standard forms obtainable from UNZABREC.
- **MODIFICATIONS**: Prior UNZABREC approval using standard forms obtainable from the UNZABREC Offices is required before implementing any changes in the Protocol (including changes in the consent documents).
- **TERMINATION OF STUDY**: On termination of a study, a report must be submitted to the UNZABREC using standard forms obtainable from the UNZABREC Offices.

- **NHRA:** You are advised to obtain final study clearance and approval to conduct research in Zambia from the National Health Research Authority (NHRA) before commencing the research project.
- **QUESTIONS**: Please contact the UNZABREC on Telephone No.256067 or by e-mail on unzarec@unza.zm.
- **OTHER**: Please be reminded to send in copies of your research findings/results for our records. You're also required to submit electronic copies of your publications in peer-reviewed journals that may emanate from this study. Use the online portal: unza.rhinno.net for further submissions.

Yours sincerely,



Sody Mweetwa Munsaka, BSc., MSc., PhD
CHAIRPERSON
Tel: +260977925304
E-mail: s.munsaka@unza.zm

Appendix 20

UNIVERSITY OF ZAMBIA
BIOMEDICAL RESEARCH ETHICS COMMITTEE

Telephone: 260-1-256067
Telegrams: UNZA, LUSAKA
Telex: UNZALU ZA 44370
Fax: + 260-1-250753
Federal Assurance No. FWA00000338

Ridgeway Campus
P.O. Box 50110
Lusaka, Zambia
E-mail: unzarec@unza.zm
IRB00001131 of IORG0000774

5th September, 2022.

REF. NO. 1609-2021.

Dr. Mwansa Ketty Lubeya,
University of Zambia,
School of Medicine,
Department of Obstetrics and Gynaecology,
P.O Box 50110,
Lusaka.

Dear Dr. Lubeya,

RE: REQUEST FOR RENEWAL FOR: "A MIXED-METHODS ANALYSIS OF THE ACCEPTABILITY, ADOPTION, REACH AND UPTAKE OF HUMAN PAPILLOMAVIRUS (HPV) VACCINATION OF ADOLESCENT GIRLS IN LUSAKA, ZAMBIA" (REF. No. 1609-2021)

We acknowledge receipt of your request for renewal and the enclosed Progress Report therewith.

Renewal is granted for a period of one year from 31st March 2022 to 30th March 2023.

Yours sincerely,

Sody Mweetwa Munsaka, BSc., MSc., PhD
CHAIRPERSON
Tel: +260977925304
E-mail: s.munsaka@unza.zm

Appendix 21

UNIVERSITY OF ZAMBIA BIOMEDICAL RESEARCH ETHICS COMMITTEE

Telephone: 260-1-256067 Ridgeway Campus

Telegrams: UNZA, LUSAKA P.O. Box 50110

Telex: UNZALU ZA 44370 Lusaka, Zambia

Fax: + 260-1-250753E-mail: unzarec@unza.zm

Federal Assurance No. FWA00000338 IRB00001131 ofIORG0000774

6th January, 2023.

Your Ref: 1609-2021

Dr. Ketty Mwansa Lubeya University Teaching Hospitals,

Department of Obstetrics and Objectives,Women and New Born Hospital, **Lusaka.**

Dear Dr. Lubeya,

RE: AMENDMENT TO CHANGE THE STUDY TITLE FOR: A MIXED-METHODS ANALYSIS OF THE ACCEPTABILITY, ADOPTION, REACH AND UPTAKE OFHUMAN PAPILLOMAVIRUS (HPV) VACCINATION OF ADOLESCENT GIRLSIN LUSAKA, ZAMBIA (REF. NO. 1609-2021)

We acknowledge receipt of your request for amendment to change the study title.

The amendment to change study title from “A mixed-methods analysis of the acceptability,adoption, reach and uptake of human papillomavirus (HPV) vaccination of adolescent girls inLusaka, Zambia” to “A mixed-methods analysis of the implementation and uptake of the Human Papillomavirus vaccination of adolescent girls in Lusaka, Zambia”, was **reviewed** and is**approved.**

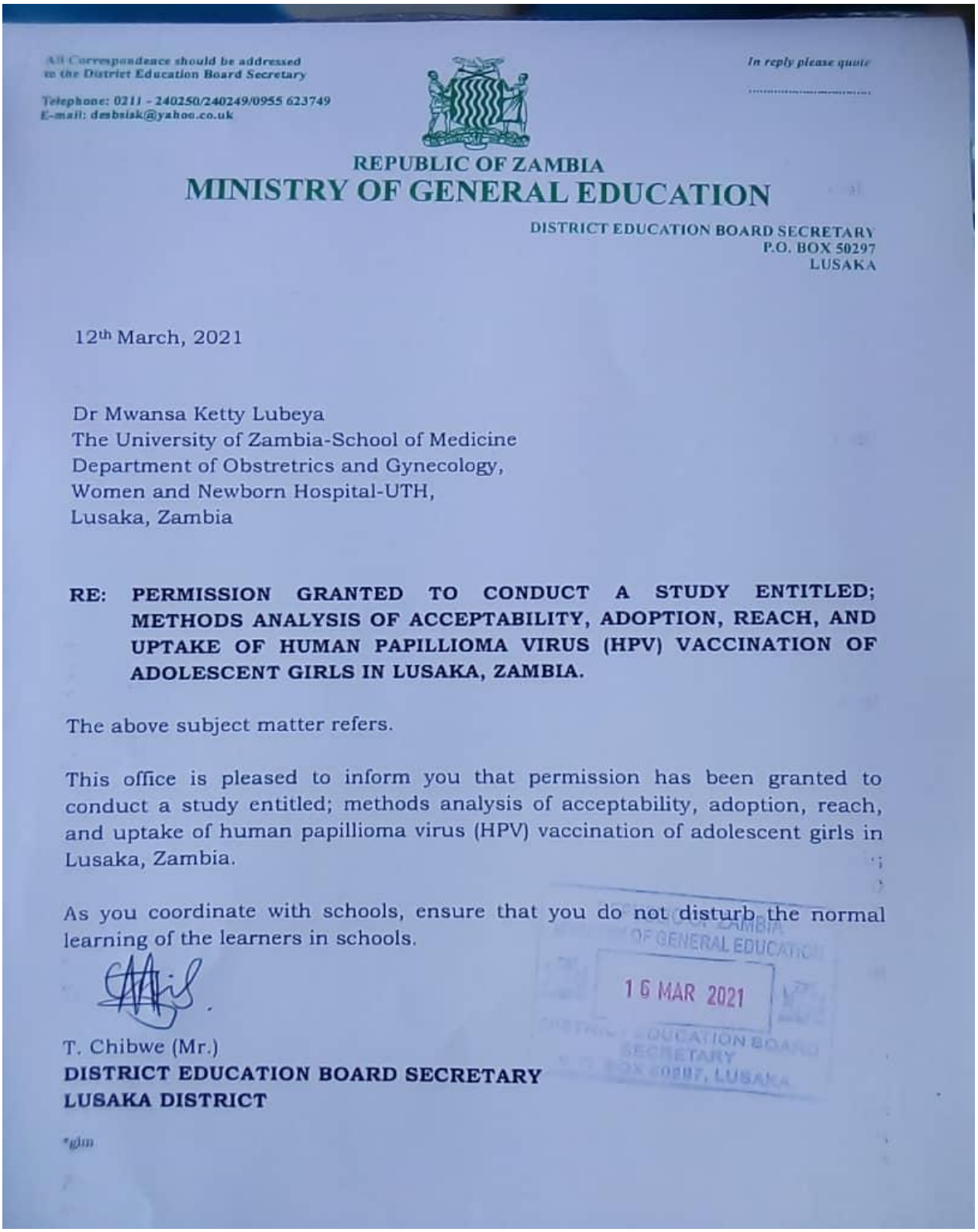
Yours sincerely,

Munsaka.

Sody Mweetwa Munsaka, BSc., MSc., PhD CHAIRPERSON

Tel: +260977925304 E-mail: s.munsaka@unza.zm

Appendix 21



All Correspondence should be addressed to the District Education Board Secretary

Telephone: 0211 - 240250/240249/0955 623749
E-mail: desbslak@yahoo.co.uk

In reply please quote .....

REPUBLIC OF ZAMBIA
MINISTRY OF GENERAL EDUCATION

DISTRICT EDUCATION BOARD SECRETARY
P.O. BOX 50297
LUSAKA

12th March, 2021

Dr Mwansa Ketty Lubeya
The University of Zambia-School of Medicine
Department of Obstretrics and Gynecology,
Women and Newborn Hospital-UTH,
Lusaka, Zambia

RE: PERMISSION GRANTED TO CONDUCT A STUDY ENTITLED; METHODS ANALYSIS OF ACCEPTABILITY, ADOPTION, REACH, AND UPTAKE OF HUMAN PAPILLIOMA VIRUS (HPV) VACCINATION OF ADOLESCENT GIRLS IN LUSAKA, ZAMBIA.

The above subject matter refers.

This office is pleased to inform you that permission has been granted to conduct a study entitled; methods analysis of acceptability, adoption, reach, and uptake of human papillioma virus (HPV) vaccination of adolescent girls in Lusaka, Zambia.

As you coordinate with schools, ensure that you do not disturb the normal learning of the learners in schools.

REPUBLIC OF ZAMBIA
MINISTRY OF GENERAL EDUCATION
16 MAR 2021
DISTRICT EDUCATION BOARD SECRETARY
P.O. BOX 50297, LUSAKA

T. Chibwe (Mr.)
DISTRICT EDUCATION BOARD SECRETARY
LUSAKA DISTRICT

*gm