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COSTS OF HPV VACCINATION IN GAVI-ELIGIBLE COUNTRIES: A CASE STUDY OF ZIMBABWE

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COSTS OF HPV VACCINATION IN GAVI-ELIGIBLE COUNTRIES: A CASE STUDY OF ZIMBABWE

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I. Abstract

COSTS OF HPV VACCINATION IN GAVI-ELIGIBLE COUNTRIES: A CASE STUDY OF ZIMBABWE

By Anna Hidle

Background: This study is an ingredients-based empirical cost analysis (guided by the WHO Cervical Cancer Prevention and Control Costing Tool (C4P)) of the HPV vaccination demonstration project that was carried out in two districts of Zimbabwe in 2014-2015. Funding support for the analysis was provided by GAVI, the Vaccine Alliance. The primary vaccination delivery strategy was school based. The target population was 6,508 ten-year-old-girls who received doses of the HPV vaccine based on e 2-dose schedule, following the World Health Organization (WHO) updated recommendations. **Methods:** Incremental costs attributable to the HPV vaccination demonstration project were included in the analysis. Financial and economic costs were collected by activity and, under guidance of the WHO C4P tool, categorized as either an introduction or recurrent cost. Financial costs are the monetary outlays from the Ministry of Health and Child Care (MOHCC). Economic costs are the MOHCC financial costs plus the monetary and in-kind contributions from other partners plus in-kind costs from the MOHCC. Costs were collected and presented in current year US$. **Results:** For both districts, both cohorts, 9,003 doses were administered and 4,412 Fully Immunized Girls (FIGs) were vaccinated. The total financial cost of the HPV vaccination demonstration project in Zimbabwe was US$256,074 and the total economic cost was US$703,534. The financial cost per Fully Immunized Girl (FIG) was US$58.04 and the economic cost per FIG was US$159.46. The total financial cost per dose was US$28.44 and the economic cost per dose was US$78.14. School-based delivery produced the lowest service delivery cost per FIG (financial cost: US$6.89; economic cost: US$28.25) when compared to other points (health facility and outreach). School based delivery also had the lowest service delivery cost per dose (financial cost: US$3.38; economic cost: US$13.84) as compared to other points (health facility and outreach). **Conclusion:** The costs per dose and per FIG (financial and economic) in Zimbabwe's HPV vaccination demonstration project were higher than costs seen in other countries. During the HPV vaccination demonstration project in Zimbabwe many lessons were learned that can inform planning for national scale-up.

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III. List of Tables/Figures/Annexes

Tables

Figures

Annexes

IV. Table of Contents

I. Introduction

Introduction and Rationale

In Zimbabwe (population: 14 million), an estimated 4.37 million women age 15 and older are at risk of developing cervical cancer (Bruni et al., 2014). With 2,270 new cases each year and 1,451 deaths, cervical cancer is the most frequent cancer among women and the leading cause of morbidity from all cancers in Zimbabwe (Government of Zimbabwe, 2013). The Zimbabwe National Health Strategy and the Zimbabwe National Cancer Prevention and Control Strategy have set comprehensive cancer prevention and control as a priority (Manangazira, 2016). One objective of Zimbabwe's non-communicable diseases strategic plan is to reduce morbidity and mortality from cancer (Manangazira, 2016). Human Papillomavirus (HPV) is necessary for the development of cervical cancer. It is estimated, that in Zimbabwe, around 20% of women carry HPV sub-type 16 (World Health Organization, 2014) (Bruni et al., 2014). HPV sub-types 16 and 18 cause approximately 70% of cervical cancer globally ("Human papillomavirus vaccines: WHO position paper, October 2014," 2014).

In 2014, Zimbabwe began an HPV vaccination demonstration project with grant funding through GAVI, The Vaccine Alliance (GAVI). One of the GAVI funding requirements was to perform a cost analysis of the HPV vaccination demonstration project (GAVI The Vaccine Alliance, 2015a). This thesis reports results from a cost analysis of the GAVI-funded HPV vaccine demonstration project in Zimbabwe. These cost analysis results may help inform decision making by the Ministry of Health and Child Care (MOHCC) in Zimbabwe about whether to initiate nationwide scale-up of HPV vaccination for target populations.

Problem Statement

As of 2013, GAVI has offered funding for HPV vaccination demonstration projects to 20 countries. Conducting a cost analysis of the demonstration project is one of the evaluations required as a condition of GAVI support. These evaluations are conducted primarily to inform programmatic decisions by Ministries of Health, GAVI, and other implementing partners, and not as academic research; results from these cost evaluations are therefore not expected to be routinely published in the peer-reviewed literature. HPV vaccination demonstration projects help countries prepare for the challenges and expected costs for a nationwide roll-out of the vaccine (Hanson, Eckert, Bloem, & Cernuschi, 2015). Information on the expected costs (e.g. procurement, training, social mobilization & IEC, monitoring and evaluation (M&E), supervision costs) is needed to help countries consider and plan for different delivery strategies and forecast the resources needed to scale-up to national HPV vaccination roll-out.

Purpose Statement

This thesis will help the MOHCC in Zimbabwe to analyze the costs, both financial and economic, of the HPV vaccination demonstration project implemented in two districts from 2014-2015. The analysis will fulfill one of GAVI's requirements of receiving an HPV vaccination demonstration project for the MOHCC in Zimbabwe - a cost analysis.

Research Questions

- What is the cost per Fully Immunized Girl (FIG) and per dose of the HPV vaccination demonstration project in Zimbabwe?
- What are the introduction and recurrent costs associated with the HPV vaccination demonstration project in Zimbabwe?

- What is the difference in service delivery cost between school-based vaccination, health facility based vaccination and outreach based vaccination?
- What are some of the challenges that occurred in the HPV vaccination demonstration project in Zimbabwe?

Significance Statement

This cost analysis will help inform decision making by Zimbabwe's MOHCC around the possible addition of the HPV vaccine to the country's National Immunization Program (NIP). It will guide the MOHCC in financial budgeting for national scale-up as well as resource planning moving forward.

Definition of Terms

General Terms

- GAVI, The Vaccine Alliance (GAVI) –An international organization committed to lowering costs and financing vaccines for low and middle-income countries (LMICs). Committed to provide HPV vaccination demonstration projects to countries who meet the requirements.
- Human Papillomavirus (HPV) – Viral infection that is common in both males and females that can cause lesions that can progress to cancer ("Human papillomavirus vaccines: WHO position paper, October 2014," 2014).
- WHO Cervical Cancer Prevention and Control Costing (C4P) Tool– A tool developed by the World Health Organization (WHO) to help with costing the HPV vaccination demonstration projects as well as estimating national scale-up in GAVI funded countries. The C4P tool allows for the input of start-up, recurrent and capital costs. The outputs expected are cost per fully immunized girl (FIG), cost per dose administered and cost per delivery strategy (Hutubessy et al., 2012).

Glossary of Terms

- Fully Immunized Girl (FIG) – A girl receiving full 2 doses of HPV vaccine within the recommended time schedule.
- National Immunization Program (NIP) – A national program implemented by a Government that adds vaccines to the national recommended vaccine schedule.
- Expanded Program on Immunization (EPI) – An initiative established by the World Health Organization (WHO) in 1974 to develop and expand immunization programs throughout the world.
- Information, Education, and Communication (IEC) - Strategies, approaches and methods used to promote desired positive health behaviors.
- Child Health Days / Child Days Plus - Campaign delivery of a package of services available at no financial cost to the mother or the child.

Economic Terms

- Analytic Horizon – "The period of time after an intervention ends, during which costs and outcomes accrue and are measured" (Zaza, Briss, & Harris, 2005).
- Annualization – "Division of total costs by life expectancy of the good, used to work out the cost of a capital good over its lifetime" (World Health Organization, 2016).
- Capital Items – "Goods that last longer than one year such as equipment" (World Health Organization, 2016).
- Cost Analysis (CA) – "An economic evaluation technique that involves the systematic collection, categorization, and analysis of program costs" (Zaza et al., 2005).
- Depreciation – "Amount of capital used during one year" (World Health Organization, 2016).

- Economic Costs – "Estimates all costs of an intervention, regardless of the source of funding, so that the opportunity cost of all resources is accounted for in the analysis, includes in-kind and donor contributions. Takes into account resources are tied up for one activity and are not available for other purposes (opportunity cost). Also allows for the fact that people prefer receiving goods and services now rather than later in the future (time preference) and includes discounting for capital items)" (World Health Organization, 2016).
- Economies of Scale – The reduction in the cost per unit due to an increase in production. In action economies of scale can be reflected as "the cost per person of the program might be less than if it were aimed at a smaller population" (Zaza et al., 2005).
- Financial Costs – The monetary funds expensed in exchange for a good or service. The C4P tool describes financial costs as "…the actual monetary flows of the buyer such as the Ministry of Health. Does not include the value of resources already paid for such as personnel time" (World Health Organization, 2016).
- Incremental Analysis – "…the process of estimating the additional cost per unit of outcome" (Shiell, Donaldson, Mitton, & Currie, 2002).
- Ingredients - Resources
- Introduction Costs – "…are initial one-time programmatic activities and include micro-planning, initial training activities, and initial sensitization/IEC. These are treated as capital costs in economic costing" (World Health Organization, 2016).
- Marginal Cost – "the additional cost associated with producing one more unit of output" (Shiell et al., 2002).
- Opportunity costs – "The cost of an alternative that must be foregone in order to pursue a certain action" (World Health Organization, 2016).

- Perspective - "The viewpoint of the bearers of the costs and benefits of an intervention (e.g. society, government, healthcare providers, business, or clients)" (Zaza et al., 2005).
- Present Value – "The current value of goods or services, usually applied to costs of outcomes expected in the future" (World Health Organization, 2016).
- Recurrent Costs – Costs of "goods of items used in the delivery of a service of intervention that lasts less than a year, e.g. personnel salaries" (World Health Organization, 2016).
- Shared Cost – Costs that are shared among programs, (e.g. transportation, supply chain) (World Health Organization, 2016).
- Straight-line Depreciation – "This type of depreciation assumes that all of the benefit from the capital good is worked out evenly throughout its lifetime; it involves annualizing the total costs but does not discount" (World Health Organization, 2016).
- Useful life years – The estimated period of time a good is to be useable for its given purpose.

II. Literature Review

Introduction

This literature review has four major sections: 1) Cancer and Human Papillomavirus (HPV) information inclusive of prevalence and burden both globally and in Zimbabwe; 2) background information about HPV vaccines; 3) GAVI, The Vaccine Alliance (GAVI) and its commitment to HPV vaccination demonstration projects including the GAVI application requirements to apply/receive a HPV vaccination demonstration project; 4) costs reported for previous HPV vaccination demonstration projects, inclusive of Fully Immunized Girl (FIG) cost estimates primarily in other African countries. This literature review will provide the reader with previous estimates of costs of HPV vaccination demonstration projects that have already occurred giving vital information on what we may expect to see from the cost analysis of the Zimbabwe HPV vaccination demonstration project.

Global Cervical Cancer

Cancer is the leading cause of death worldwide, (Torre et al., 2015) with an estimated 14.1 and 8.2 million new cancer cases and deaths, respectively, in 2012 (International Agency for Research on Cancer, 2013). Cervical cancer due to HPV claims 266,000 women every year. Most of these deaths occur in LMIC countries. These deaths are estimated to rise by 2035 to 416,000 (GAVI The Vaccine Alliance, 2015b). An increasing burden is within the 82% of the world's population who live in LMICs. This burden is expected to increase as populations grow, age and adapt to known cancer-causing behaviors and lifestyles (Torre et al., 2015).

There are drastic differences between high income and LMICs when it comes to cervical cancer rates. In sub-Saharan Africa, there are 34.8 new cases and 22.5 cancer deaths per 100,000 women per year compared to North America with 6.6 and 2.5, respectively (International

Agency for Research on Cancer, 2013). While cervical cancer is only the fourth most common cancer in the world, the burden is most notable in sub-Saharan Africa (International Agency for Research on Cancer, 2013). Eastern Africa (which includes Zimbabwe) has both the highest incidence and mortality from cervical cancer of all regions in sub-Saharan Africa with 42.7 and 27.6, per 100,000, respectively (Torre et al., 2015).

In LMICs, it is estimated that 444,500 women were newly diagnosed with cervical cancer with 230,200 estimated deaths from cervical cancer in 2012 (Torre et al., 2015). Globally, there are an estimated 527,600 and 265,000 new cases and deaths respectively in 2012 (Torre et al., 2015). LMICs have a disproportionate burden of both cervical cancer cases (70%) and deaths (90%) (International Agency for Research on Cancer, 2013) (Torre et al., 2015).

Patterns in the newest global data from 2013 identify that cervical cancer is among a list of cancers that should be given prevention and control priority (International Agency for Research on Cancer, 2013). Systematic cervical cancer screening has led to a decrease in morbidity and mortality from cervical cancer in high-income countries (Hanson et al., 2015). While cervical cancer can have devastating effects financially and economically, regardless of the setting, there are prevention and control efforts to minimize such costs (International Agency for Research on Cancer, 2013).

Global HPV Burden

Human papillomavirus (HPV) is the main cause of cervical cancer (GAVI The Vaccine Alliance, 2015a) and the HPV vaccine is recommended by the WHO as a cost-effective strategy to combat cervical cancer. The WHO recommends that countries add the HPV vaccine to their national immunization program (NIP) ("Human papillomavirus vaccines: WHO position paper, October 2014-Recommendations," 2015).

Invasive cervical cancers are most commonly attributable to HPV sub-types 16 and 18, the most common sub-types of HPV (Hanson et al., 2015) (World Health Organization, 2014). Sub-types 16 and 18 cause approximately 70% of cervical cancers globally (World Health Organization, 2014). Twelve sub-types of HPV have been identified as high-risk to humans, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59, with two others potentially high-risk, 68 and 73. 70-90% of HPV infections, of all sub-types, are asymptomatic and resolve themselves within a period of a few years. However, persistent HPV infection or multiple type infection, may progress to cervical cancer. The period of time between infection and progression of invasive carcinoma is typically 10 years or more (International Agency for Research on Cancer, 2012) ("Human papillomavirus vaccines: WHO position paper, October 2014," 2014).

Zimbabwe Cervical Cancer and HPV Burden

Currently, in Zimbabwe, 4.37 million women, age 15 and older are at risk of developing cervical cancer. With 2,270 new cases each year and 1,451 deaths, this is the most frequent cancer among women and the leading cause of morbidity from all cancers in Zimbabwe (Bruni et al., 2014) (Government of Zimbabwe, 2013). Cervical cancer is the 1st cause of all cancer in women in Zimbabwe and the 2nd most frequent cancer for women between the ages of 14 and 44, in Zimbabwe (Bruni et al., 2014).

Zimbabwe has both higher incidence and mortality rates as age increases than both Eastern Africa and the world (Bruni et al., 2014). Estimated premature deaths and disability due to cervical cancer in 2008 accounted for 35,119 estimated disability-adjusted life years, 33,498 years of life lost, and 1,621 years lived with disability in Zimbabwe. These estimates are higher than both Eastern Africa (721, 684 and 38) and the World (293, 264 and 28) estimates (Bruni et al., 2014).

Studies indicate that for women in Eastern Africa HPV infection sub-type 16 is carried by 20.3% of the population at any given time (Bruni et al., 2014). When assessing the burden of cervical cancer within Eastern Africa, 4.7% of the population have normal cytology. For women with low-grade cervical lesions 22.7% have HPV sub-types 16 and/or 18. For women with high-grade lesions, 18.2% are estimated to have HPV sub-types 16 and/or 18. For women with cervical cancer, 79.6% are estimated to have HPV sub-types 16 and/or 18 (Bruni et al., 2014). The most common HPV sub-types in Zimbabwe are 16 (61.2%) 18 (18.4%) 33 (38.4%) 31 (4.1%) and 35 (1.0%) (Government of Zimbabwe, 2013).

HPV Vaccine

Human papillomavirus (HPV) vaccination provides an opportunity for LMICs to implement prevention of cervical cancer (Hanson et al., 2015). WHO recommends that cervical cancer prevention, including HPV vaccines, should be a priority ("Human papillomavirus vaccines: WHO position paper, October 2014-Recommendations," 2015). Administering the HPV vaccine, recommended by the WHO, could avoid 70% of cervical cancer cases (GAVI The Vaccine Alliance, 2015b).

HPV vaccines were introduced in high income countries in 2006, yet it has been a major challenge to introduce them in LMICs mostly due to high prices per dose. GAVI has reduced vaccine prices for LMIC within the last ten years. Currently, the GAVI subsidized HPV vaccine prices stand at less than US$5 per dose (Hanson et al., 2015), which does not include procurement (freight and transportation) costs. While the price per dose of the vaccine is the most obvious hurdle that is faced by LMICs, many other challenges exist as well.

The challenge of delivering to a non-traditional (above the age of 5) population can be a hurdle, as many countries have never delivered a vaccine to this age group. The target age

recommendations from WHO are girls between 9 and 13 years of age because HPV vaccine is more efficacious before initial exposure to HPV by sexual debut ("Human papillomavirus vaccines: WHO position paper, October 2014-Recommendations," 2015). The creation of new vaccine infrastructure to reach this population may include an integrated health strategy focused on adolescent programs. An integrated health strategy could serve many purposes such as the provision of tetanus boosters, deworming medication, nutrition and education about a variety of topics including drugs, pregnancy and sex (Adefuye, Broutet, de Sanjose, & Denny, 2013).

Additional challenges could range from the required additional cold chain for the vaccine in some settings, to the follow-up required for the vaccine which requires multiple doses of the vaccine needed for a FIG. Communication of the need for the HPV vaccine and its disease prevention effects in the future requires effective communication of all parties to relay these benefits (Adefuye et al., 2013). The challenges to introduce the vaccine are numerous but the benefits to gain are worth such efforts.

There are currently two vaccines prequalified by WHO for GAVI HPV vaccination demonstration projects: Cervarix™ and GARDASIL® (Hanson et al., 2015). The bivalent Cervarix™ vaccine is a prophylactic vaccine manufactured by GlaxoSmithKline. It is protective regarding HPV types 16 and 18, which cause approximately 70% of cervical cancer cases. The recommended injection schedule of Cervarix™ is 0, 1, and 6 months (de Sanjose et al., 2012). The quadrivalent Gardasil® vaccine provides protection against HPV types 16 and 18 as well as additional protection against HPV types 6 and 11 (Hanson et al., 2015). It is still recommended that women receive cervical cancer screening regardless of vaccination to prevent other HPV type infections (de Sanjose et al., 2012).

HPV vaccine introduction should be implemented alongside behavior education, training of health personnel, and information about screening practices, diagnosis, and treatment of cervical cancer. Alongside vaccination, access to screening, diagnostics, and treatment for cervical cancer are key in reducing mortality. Reaching this adolescent population allows for possible integration of adolescent health services, however, if integration of services is not possible, it is not recommended to delay vaccination. WHO recommends that all girls in the recommended target age group (9-13 year olds) be vaccinated against HPV; however, for a country considering phased introduction of the HPV vaccine, priority should be given to populations that may be harder to reach with screening later after adolescence ("Human papillomavirus vaccines: WHO position paper, October 2014-Recommendations," 2015) (Hanson et al., 2015) (Adefuye et al., 2013).

The WHO Strategic Advisory Group of Experts (SAGE) made recommendations for a 2-dose HPV schedule in the beginning of 2014 (Hanson et al., 2015). WHO currently recommends a 2-dose schedule with 6 month interval between doses for girls younger than 15. It is recommended that there be no more than a 12-15 month interval between doses; if dose interval is less than 6 months, a 3rd dose is recommended. A 3-dose interval is also recommended for girls known to be HIV positive ("Human papillomavirus vaccines: WHO position paper, October 2014," 2014). As of 2013, it is estimated that 4.1% of 15-24 year olds are living with HIV in Zimbabwe, although with very few young people getting tested, it is estimated to be higher (AVERT, 2013). The goal of giving 10 year old girls, and not older girls, the HPV vaccination is to reach them before being exposed to HPV (Centers For Disease Control, 2015).

It is predicted that the 2-dose schedule provides protection from certain types of HPV infection of 20 years or more ("Human papillomavirus vaccines: WHO position paper, October

2014," 2014). Laprise et al suggests that the HPV vaccine given in a 2-dose schedule is cost-effective if the protection of the vaccine lasts ten years. The same is true of a 3-dose schedule if the protection lasts 30 years (Laprise et al., 2014) Goldie et al projects that if 10 consecutive years of HPV vaccine is given to 10 year old girls in sub-Saharan Africa, more than 1 million cases of cancer could be averted. For countries classified as East African countries, vaccination with 70% coverage could avert 17 deaths per 1000 women (Goldie et al., 2008).

The cost-effectiveness study (in GAVI-eligible countries) found that with HPV sub-types 16 and 18 vaccination implemented in Zimbabwe could produce a reduction of lifetime risk of cervical cancer would be 53.4% and 6,684 Disability Adjusted Life-years (DALYs) would be averted (Goldie et al., 2008). The incremental cost-effectiveness ratio of International Dollars/DALY used shows that at both 25 and 50 International dollars per FIG, it could still be cost-effective to vaccinate (Goldie et al., 2008). This would mean that even if costs per FIG were high in Zimbabwe, they may still be cost-effective.

Other vaccines/health interventions that have the ability to be delivered to this population during integrated services with the HPV vaccine are child health days plus (A. Levin, Wang, Levin, Tsu, & Hutubessy, 2014) (C. E. Levin et al., 2013) tetanus toxoid vaccine, deworming intervention (GAVI The Vaccine Alliance, 2015b) and other appropriate adolescent health interventions (GAVI The Vaccine Alliance, 2015a).

GAVI Application for HPV Vaccine Introduction

Although there are numerous benefits to HPV vaccination there are still many barriers to HPV vaccines in LMICs. One of these barriers is cost (Adefuye et al., 2013). To combat this barrier GAVI began rolling out funding for HPV vaccination demonstration projects for HPV vaccination to eligible countries in 2013, giving 7 countries, that year, the opportunity to provide

the HPV vaccine (Torre et al., 2015) (GAVI The Vaccine Alliance, 2015b). Kenya conducted the first HPV vaccination demonstration project, while Rwanda had the first GAVI national roll-out of the HPV vaccine proving its previous ability to meet GAVI's requirements (GAVI The Vaccine Alliance, 2015b). Rwanda proved in its inaugural year that reaching this adolescent population with a vaccination was possible, by achieving 93% HPV vaccination coverage (Adefuye et al., 2013).

GAVI has offered support to 23 countries, 20 of which have or will have implemented HPV vaccination demonstration projects by 2015, targeting more than 400,000 girls around the world for HPV vaccination. All 23 countries are implementing school based vaccination as the primary strategy, with mixed strategies (school based, health facility based, integrated approach and a mix of the previous) to reach out of school girls. (Hanson et al., 2015). By the end of 2015, it was estimated that one million girls have been vaccinated due to the GAVI HPV vaccination demonstration project. It is anticipated that the WHO recommended change from a 3-dose to a 2-dose schedule will assist in reducing costs associated with vaccination and will reduce cost for countries involved. (GAVI The Vaccine Alliance, 2015b).

Countries must meet eligibility requirements to qualify for GAVI assistance for HPV vaccines. To receive national support, criteria must be met of "Gross National Income per capita (GNIpc) of US$1580 (or less) and a Diphtheria-Tetanus-Pertussis third dose (DTP3) coverage of at least 70% as for all other vaccines, but to have also demonstrated the ability to deliver a multi-dose vaccine to at least 50% of a target population of 9-13 year old girls in an average district size" (Hanson et al., 2015). Many countries do not meet one or both of these requirements. However for countries that have yet to meet these GAVI requirements, an alternative pathway was created to provide previously ineligible countries a way to receive support by way of

applying for a GAVI HPV vaccination demonstration project. In addition to the aforementioned requirements, countries must, in an application, show their ability to reach this population. These steps encourage such countries to create a comprehensive "national cervical cancer prevention and control strategy" listing HPV vaccine as their primary prevention method (Hanson et al., 2015).

It is assumed that through the HPV vaccination demonstration projects, implementing countries are more prepared for national scale-up by seeing the challenges of vaccination and having a plan in place to deal with such challenges. GAVI tries to ensure that the demonstration project offers lessons learned by requiring project evaluation by implementing countries. These project evaluations are a Post-introduction evaluation (PIE), a coverage survey, and a costing analysis (presented in this thesis) (GAVI The Vaccine Alliance, 2015b).

Although national scale-up is the goal from a HPV vaccination demonstration project, it has been shown in previous HPV vaccination demonstration projects that compiling lessons learned has been taking longer than expected. Therefore, GAVI currently offers bridging support to countries transitioning from demonstration to national scale-up so vaccination can continue vaccination between the demonstration project and application/approval for national scale-up (GAVI The Vaccine Alliance, 2015b). To apply for national scale-up of the HPV vaccine, countries conducting HPV demonstration projects must deliver the vaccine to a cohort of girls in the age range of 9-13, implement the demonstration project in at least one district with an existing EPI program and achieve coverage of at least 50% of the target population that receive the number of doses required to be designated a FIG (GAVI The Vaccine Alliance, 2015a). The first countries to initiate the HPV vaccination demonstration project demonstrated coverage from 60-90% (GAVI The Vaccine Alliance, 2015b).

GAVI does not cover port of entry costs, but covers the costs of vaccines up to that point. GAVI will provide a cash grant for district costs of start-up and operations up to 80% for vaccine introduction expecting the implementing country to contribute 20% of programmatic costs for countries to demonstrate ownership over the HPV vaccination demonstration project (Hanson et al., 2015).

Providing the vaccine to a non-traditionally vaccinated population presents many challenges, which can be addressed through a HPV vaccination demonstration project, prior to the addition of HPV vaccines to the National Immunization Plan (NIP). Findings can be presented and leveraged to national policymakers to influence national scale-up (Hanson et al., 2015). At national scale-up, GAVI and the country co-finance the vaccine purchase, with the degree of co-financing depending on Gross National Income (GNI) per capita. Early evaluation of the demonstration projects suggest that vaccination is feasible even in low resource environments (GAVI The Vaccine Alliance, 2015b), such as Zimbabwe.

Framework for Costing GAVI-supported HPV Vaccination Demonstration Projects

The financial costs, as defined by the WHO C4P costing tool, were defined as incremental monetary expenditures by a Ministry of Health during the demonstration project (World Health Organization, 2016). The economic costs are defined as incremental monetary contributions from a Ministry of Health as well as partners outside of the Ministry of Health (e.g., cost of vaccine and procurement), and the monetized value of in-kind resources from the Ministry of Health and partners utilized during the HPV vaccination demonstration project, inclusive of personnel time, volunteer time, and use of existing vehicles (World Health Organization, 2016). Including economic costs allows for an assessment of what non-monetary resources were utilized in the HPV vaccination demonstration project (World Health

Organization, 2016). It is expected that because this target population (10 year old girls) is not traditionally reached with vaccines the costs will be different from the delivery costs of other vaccines (World Health Organization, 2016).

HPV Vaccination Coverage

Within GAVI-eligible countries, results from five demonstration cost analysis results were available. These demonstrations took place in India (2009), Uganda (2009), Vietnam (2009), Tanzania (2011), and Rwanda (2012). Delivery strategies were school based (class based and age based), health facility based, integrated with other health programs or interventions and a mix of the aforementioned strategies (LaMontagne et al., 2011). Examples of integrated strategies include delivery with deworming and tetanus toxoid vaccine (GAVI The Vaccine Alliance, 2015b). These countries reported various coverage rates, delivery strategies and costs to reach this traditionally unreached population with vaccinations.

All strategies reported high coverage except for the first year of a child-days-plus program in Uganda (53%) through an age based strategy (LaMontagne et al., 2011). Vaccination coverage was 89% in Uganda through a school based strategy (LaMontagne et al., 2011). In India, a combined school and health facility based strategy was used that yielded a coverage between 77-88%. Vietnam achieved 99% coverage with a health facility based project (LaMontagne et al., 2011). Rwanda reported 97% coverage with a subsequent 2% drop out for each the 2nd and 3rd doses (Ngabo et al., 2015). Except for the child health days plus program, these HPV coverage figures look similar to coverage figures in high-income country settings (LaMontagne et al., 2011). The coverage figures suggest that reaching girls in schools with vaccines can be effective. It is of note that girls who are absent on the day of vaccination or out-

of-school girls should be considered when choosing a delivery strategy (LaMontagne et al., 2011).

It is highly speculative how best to reach out-of-school girls. Levin et al. suggest targeting them effectively will be different in different contexts suggesting that outreach points could be one solution or mass vaccination in countries with low density (A. Levin et al., 2014). As well, GAVI demonstration guidelines specify that countries provide the same opportunities for vaccination of hard to reach girls in the target population and suggest doing this by having alternate times/places that these girls can go beside the primary delivery strategy to receive vaccination, as well as suggest including these activities in the budget (GAVI The Vaccine Alliance, 2015a). These coverage results and lessons learned can help inform delivery strategies and policy regarding the delivery of HPV vaccines in low-resource settings (de Sanjose et al., 2012).

Delivery Strategies and Costs from prior HPV Vaccination Projects

A cross-sectional study was conducted in India, Uganda, and Vietnam, which included a population-based household survey adapted from the WHO infant immunization survey (LaMontagne et al., 2011). The HPV immunization demonstration project in Tanzania used a school based strategy broken up into age based delivery or class based delivery (Quentin et al., 2012). Peru also conducted a HPV demonstration project but was not GAVI-eligible (C. E. Levin et al., 2013). Rwanda's delivery of the HPV vaccine qualified as GAVI-eligible, but was not a GAVI demonstration project as Rwanda had secured funding for national introduction (Ngabo et al., 2015).

School based strategy

School based vaccination strategy both in Uganda and Vietnam reported financial costs of US$2.10 and US$1.62 respectively, excluding procurement of vaccine costs. As expected, adding economic costs produced higher costs per FIG in both Uganda and Vietnam increasing to US$3.15 and US$2.08 respectively. In both Uganda and Vietnam using only a school based strategy yielded higher costs than an integrated outreach strategy (integrating the vaccination with other health programs or services) in Uganda and a health facility strategy in Vietnam (C. E. Levin et al., 2013). Peru, which also conducted a school based vaccination demonstration project reported financial costs per FIG, without vaccine procurement cost, of US$2.08. When including economic costs, FIG increased to US$3.88 (C. E. Levin et al., 2013).

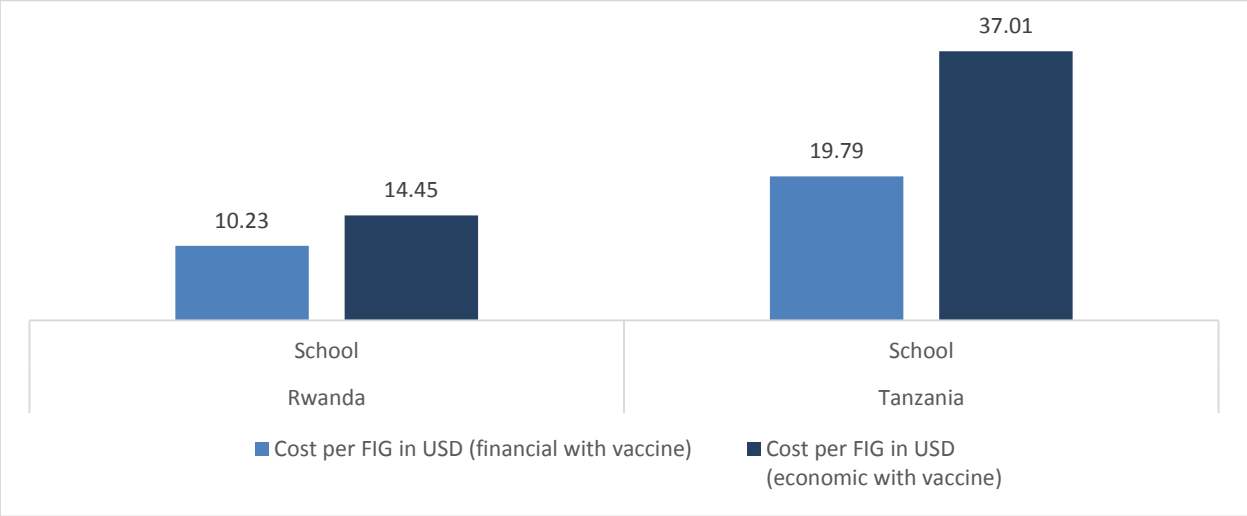
Levin et al reported that for HPV vaccination demonstration projects, the average introduction costs in school based delivery ranged from US$1.49 (India) to US$18.49 (Vietnam) per FIG (C. E. Levin et al., 2013). Average recurrent costs using school based delivery, the range was US$1.00 (India) to US$13.08 (Tanzania) per FIG (C. E. Levin et al., 2013).

Rwanda's main delivery strategy was through schools (grade 6 girls) while its secondary delivery strategy was through health facilities (3% of girls reached in health facilities). The financial cost of delivery per dose was US$3.37 not including vaccine procurement, while a figure inclusive of vaccine procurement was not reported. The financial cost of delivery in health facilities per FIG was $10.23 not including vaccine procurement and US$11.93 including vaccine procurement. The economic cost of delivery per dose (not including vaccine procurement) was US$4.76. Per FIG, the financial cost of delivery is US$10.23 not including vaccine procurement and US$11.93 including it. For economic delivery cost per FIG, US$14.45

including vaccine procurement and US$35.66 including vaccine procurement (Figure 1) (Ngabo et al., 2015).

Hutubessy et al find that including the vaccine, the financial cost per dose is US$19.79 and economic cost per dose is US$37.01. The cost per dose inclusive of the vaccine is financial cost of US$5.68 and economic cost of US$10.62. Vaccine procurement was the highest share of costs for both financial and economic categories as Tanzania moved towards national scale-up, while the highest financial cost during the introduction phase (3 regions being vaccinated) was social mobilization/IEC materials followed by training. These delivery costs were a 3-dose strategy. They suggest that to lower costs of delivery, school programs should be integrated, including treatment for Schistosoma mansoni, deworming programs and/or other school based health interventions. More information to assess costs of interventions to this population is needed (Hutubessy et al., 2012).

Figure 1. HPV national vaccine introduction and delivery (cost per FIG) (Ngabo et al., 2015) (Hutubessy et al., 2012).



Age based strategy versus Class based strategy

An age-based strategy is to vaccinate all girls based on age cut offs (e.g. all 10 year olds as of a certain date) as opposed to a class-based strategy (e.g. vaccinating all girls in grade 4).

Quentin et al found that for Mwanza region in Tanzania, age based strategy costs per FIG were higher, in both urban and rural settings than for a class-based approach. Procurement of vaccine was the highest cost in all scenarios. In urban facilities cost per FIG class-based and age-based FIG was US$66 and US$100 respectively. In rural facilities cost per FIG class-based and age-based FIG was US$78 and US$107. This was primarily due to rural schools having higher transportation costs (Quentin et al., 2012).

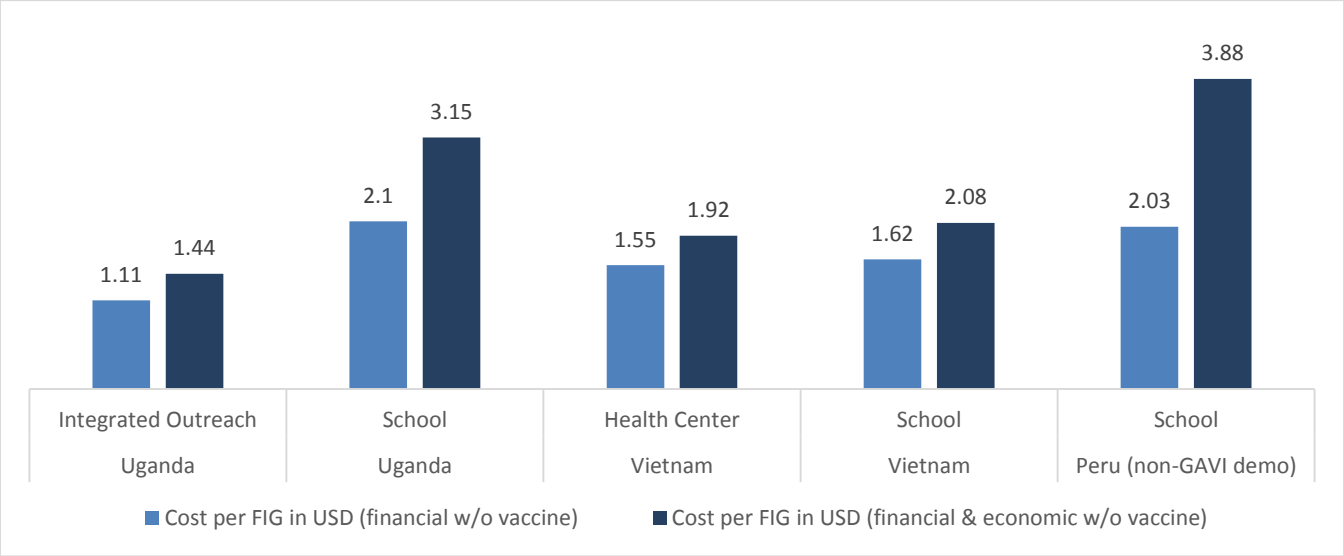
Health Facility based strategy

Vietnam was able to deliver a health facility based HPV vaccine demonstration project that reported cost per FIG at US$1.55 without the vaccine, and US$1.92 including the vaccine (C. E. Levin et al., 2013). Vietnam reported 99% coverage using a primary health facility based strategy (LaMontagne et al., 2011).

Integrated Outreach based strategy

Uganda implemented their HPV vaccination demonstration project integrated with child health days plus. They reported costs of US$1.11 per FIG not including the HPV vaccine and US$1.44 excluding the vaccine price (Figure 2) (C. E. Levin et al., 2013). An integrated health services approach could provide a unique platform to deliver interventions to this population and give needed opportunities to provide other health services as well. This could include tetanus boosters, deworming medication, future vaccines, and educational programs regarding issues facing young people (e.g. drugs, pregnancy, and sexually transmitted infections) (Adefuye et al., 2013). Using an integrated approach allows for the potential reduction in delivery costs as they can be shared among programs/projects.

Figure 2. HPV vaccination demonstration project cost by delivery strategy - Cost per FIG (C. E. Levin et al., 2013).



Cost per FIG

Levin et al found that the financial cost per FIG was US$1.11, US$2.10, US$1.55, US$1.62 and US$2.01 without the additional cost of the vaccine, respectively in each of the reported countries (Figure 2) (C. E. Levin et al., 2013). The financial and economic cost (without the cost of vaccine) per FIG was US$1.44, US$3.15, US$1.92, US$2.08 and US$3.88 (Figure 2) (C. E. Levin et al., 2013).

Quentin et al found the total cost per FIG in urban schools was US$66 for class based delivery and was US$100 for aged based delivery, for one district in Tanzania (Quentin et al., 2012). Rural schools reported total cost per FIG of US$78 and US$107, respectively. It is noted that rural schools had higher delivery costs per FIG due to higher transportation costs (Quentin et al., 2012). Quentin et al also noted that the number of girls vaccinated per school affected costs dramatically (Quentin et al., 2012). While the cost of the HPV vaccination demonstration project cost in Mwanza was exceptionally high (2011), national introduction costs were estimated to be

much lower in Tanzania (2011 through 2015) when considering the cost per dose and cost per FIG (Quentin et al., 2012) (Hutubessy et al., 2012).

Scale-up Cost versus HPV Vaccination Demonstration Project

Quentin et al noted that for the HPV vaccination demonstration project in Tanzania in one district the costs per FIG were very high, however when scaled-up, costs reduced per FIG significantly. For instance "…economic scaled-up costs per fully-immunized girl through class-based delivery in Mwanza Region, including the cost of vaccine, were estimated at US$26.00" (Quentin et al., 2012).This is considerably less than the pilot project which estimated the cost to be between a range of US$66 and US$78 (Quentin et al., 2012).

Summary of current problem and study relevance

From the literature reviewed regarding costs of GAVI supported HPV vaccination demonstration projects around the world, many different costs exist dependent upon delivery strategies in different contexts. The cost analysis in this thesis will report cost estimates for Zimbabwe regarding its GAVI supported HPV vaccination demonstration project. This will allow for costs and delivery strategies to be compared based on settings. Lessons learned will also be reported that will provide critical knowledge to countries in similar settings as they look to begin a demonstration project. Lessons learned and costs reported will also be critical to Zimbabwe as they look forward and consider national scale-up of HPV vaccination.

IV. Zimbabwe HPV Demonstration Project Methodology

Introduction

This analysis presents both financial and economic costs of an HPV vaccination demonstration project that took place in two districts of Zimbabwe. This cost analysis is aimed to guide Zimbabwe on the budgeting of national scale-up of the HPV vaccine.

Procedures

Data were collected from September 2015 to March 2014 by a cost analysis team. The team included the MOHCC's Director of Epidemiology and Disease Control, an economist from the MOHCC, and two economists from the CDC's Global Immunization Division in Atlanta. Primary data was collected on type, quantity and unit cost of resources utilized under each activity and sub-activity for project implementation.

Data were primarily collected through in-person consultations and secondarily by phone and e-mail. Data collection forms were utilized during the consultations based on the C4P tool. Follow-up interviews were conducted for data clarification purposes. These interviews involved MOHCC staff at all levels (national, provincial, district, and health facility) and the two local NGOs.

During in-person consultations and follow-up interviews, any relevant programmatic and financial documents were collected. These documents were internally reviewed and were used as secondary data source references. These documents included vaccination reports, work plans, and budgets. Zimbabwe's GAVI application for the HPV vaccination demonstration project was also used as a reference.

Zimbabwe HPV Vaccination Demonstration Project

GAVI granted support to the Zimbabwe MOHCC in October 2013, to conduct an HPV vaccination demonstration project. This support included direct financial support in the amount of US$170,000. The funds were received by the MOHCC in 2014. On top of the direct financial support, technical support was also offered to Zimbabwe's MOHCC from international partner organizations, which were separately funded by GAVI. GAVI required that the MOHCC of Zimbabwe provide at least 20% of the program operation costs of the HPV vaccination demonstration project (GAVI The Vaccine Alliance, 2015a). The two-dose vials of the bivalent Cervarix™ HPV vaccine was procured by United Nations Children's Fund (UNICEF) with no costs to the MOHCC (Government of Zimbabwe, 2013). GAVI intended that the demonstration project would allow Zimbabwe to test different vaccine delivery strategies to reach the target population not formally reached by current vaccination strategies (ten-year-old-girls). One of the demonstration projects intentions was to test these strategies and better understand the costs and resources needed prior to implementing nationwide scale-up of the HPV vaccine.

The HPV vaccination demonstration project was managed (owned) by Zimbabwe's MOHCC, although support (in addition to GAVI) was given from numerous partners, including UNICEF, the World Health Organization (WHO), the Program for Appropriate Technology in Health (PATH), and the U.S. Centers for Disease Control and Prevention (CDC). Partner contributions included the Adolescent Interventions Assessment conducted by UNICEF, the Post-Introduction Evaluation (PIE) funded by WHO, the Coverage Survey funded by UNICEF and WHO with technical support from PATH, and the cost evaluation (this report) conducted with technical assistance from CDC and WHO. Other partners offered field support to the project, including GlaxoSmithKline (GSK), the Maternal & Child Health Integrated Program

(MCHIP) with ELMA, the United Nations Population Fund (UNFPA), Médecins Sans Frontières' (MSF) and the Southern African AIDS Trust (SAT). These partners offered field support that was inclusive of but not limited to assistance of supervision of service delivery by use of a vehicle and support in the creation of IEC materials. Any outlays (both financial and economic) that were not from GAVI or the MOHCC were costed in the economic cost category.

Zimbabwe carried out the HPV vaccination demonstration project in two districts: Beitbridge District in Matabeleland South Province and Marondera District in Mashonaland East Province. Both districts were selected because of the representation of two major ethnic groups in Zimbabwe (the Ndebele and the Shona) and their high diphtheria, tetanus, and pertussis (DTP) vaccination coverage (Government of Zimbabwe, 2013). Each of the districts have experience vaccinating school children during previous outbreaks (H1N1 and measles), as well as each district currently has school health programs that provide a potential platform for integrated delivery of the vaccine with other health interventions in the future (Government of Zimbabwe, 2013). It is expected that the lessons learned by these two districts will be informative in planning and decision making when considering possible national scale-up of the HPV vaccine.

Two Harare based NGOs contracted for the HPV demonstration project were: Community Working Group on Health (CWGH) in Marondera District and Women and AIDS Support Network (WASN) in Beitbridge District. The local NGOs were contracted by the MOHCC to conduct social mobilization/IEC activities, mobilize and sensitize communities prior to vaccination, and to identify out of school girls. The sensitization meetings conducted by the NGOs were intended to help identify out-of-school girls and to develop strategies for where this segment of the target population could receive the vaccination.

CWGH and WASN distributed informational pamphlets/consent forms to the parents of the 10-year-old girls in order to gain consent from the parent/guardian for the vaccination. The girls were then instructed to bring their consent form to their place of vaccination. These informational pamphlets/consent forms (IEC materials) were created in English, Shona, Ndebele and Venda. The MOHCC developed a training manual and IEC materials with assistance of the Strategic Advisory Group (SAG) for the HPV vaccine. Training for supervisors took place at the national level and training for vaccinators took place in both districts.

Population and Sample

The target population was ten-year-old girls who resided within the two districts within the vaccination period. Two cohorts of girls were vaccinated in each district between September 2014 and November 2015. Two doses of the bivalent Cervarix™ vaccine were given to each eligible girl. A girl who received both a first and second dose of the HPV vaccine was considered a fully immunized girl (FIG). Under Zimbabwe's delivery strategy adopted for the demonstration project, the second cohort's first dose was given concurrently with the first cohort's second dose. Marondera District implemented a primarily school-based vaccination delivery strategy with a secondary strategy of offering the vaccines in health facilities. While Beitbridge District implemented a primarily school-based strategy with a secondary strategy of delivering vaccines at health facilities and at outreach points in the community.

The cost analysis included all incremental financial and economic costs incurred at the national and district level to implement the HPV vaccination demonstration project in the two selected districts (Beitbridge and Marondera).

Research Design

Cost Analysis Design

This economic and financial cost analysis used a retrospective empirical ingredients-based design. The analysis only takes into account the incremental or additional resources needed to add the HPV vaccination demonstration project to an established immunization program (World Health Organization, 2016). The financial costs represent monetary outlay or expenditures from the MOHCC while the economic costs represent MOHCC monetary and non-monetary expenditures (e.g. personnel time) and non-monetary outlay including personnel time and donated monetary and in-kind goods and services from implementation partners (including the vaccine) (World Health Organization, 2016).

Financial and economic costs were collected from the resources (i.e., ingredients) utilized for each major activity under the HPV vaccination demonstration project as defined by the C4P tool. These activities include: micro-planning, vaccine (procurement of vaccine and supplies), training, social mobilization/IEC, service delivery, supervision, monitoring, and evaluation, other, and cold chain supplementation (World Health Organization, 2016). These activities were categorized as introduction costs or recurrent costs according to the definitions used in the C4P tool and C4P guide (World Health Organization, 2016). Introduction costs are costs that are expected to last longer than one year, and were defined to include the activities of social mobilization/IEC materials, micro-planning and training of supervisors and vaccinators. Introduction costs are expected to be needed only during the initial phase of introduction of a new vaccine into the NIP. Therefore these costs are annualized over a period of time to serve as the vaccine introduction period. Introduction costs were then depreciated over the assumed useful life years of introduction (5 years). Recurrent costs are items expected to last less than one

year and were defined to include the activities of procurement of vaccines and related supplies, service delivery, and supervision, monitoring and evaluation. Recurrent costs are costs that are expected to continue throughout the project.

Cost Analysis Sites and Population

The cost analysis included all incremental costs (financial and economic) that were incurred at the national and district level to implement the HPV vaccination demonstration project within two selected districts (Beitbridge and Marondera). All doses administered to all girls in both cohorts during the HPV vaccination demonstration project were used for calculating the cost per dose and the cost per FIG.

Cost Analysis Time Frame and Analytic Horizon

This cost analysis collected costs that were incurred from March 2014 to March 2016. This time frame was the implementation period of the HPV vaccination demonstration project, beginning with the first activities that took place (HPV SAG meetings, national level micro-planning) through the last activity (report writing). The analytic horizon for calculating total costs and unit costs per dose and per FIG was over the entire implementation time period (March 2014 to March 2016).

Costs Included and Excluded

The cost analysis included the costs of the resources (i.e., ingredients) utilized under each activity as defined by the C4P tool (World Health Organization, 2016). Data collection followed the list of resource costs that could potentially be included under each activity as defined in the C4P tool guidance (This information available at: http://www.who.int/immunization/diseases/hpv/cervical_cancer_costing_tool/en/)); however, only a subset of the resources from C4P guidance were actually used under each activity as

implemented in Zimbabwe's demonstration project and were included in this cost analysis (Annex 1). Differences were due to (i) the organizations that provided the resource in the Zimbabwe setting (e.g., resources that would have been included under financial costs had they been paid for by the MOHCC were instead included under economic costs only because they were provided by an external partner), (ii) certain types of listed resources not being utilized in Zimbabwe's project implementation based on the strategy adopted (e.g., television spots), or (iii) data limitations (e.g., economic cost of in-kind vehicle use). For the financial cost analysis, the resource costs that were included in this cost analysis were for MOHCC outlays using GAVI grant funding, including: per diem, transportation (and fuel), vaccination supplies (safety boxes and cotton swabs) materials and supplies, personnel salaries and benefits paid for directly from the GAVI grant, venue rental and communication. For economic costs, costs included in this cost analysis were the same as those for the financial cost analysis, plus financial outlays and in-kind resources from external partners and from the MOHCC not paid for by the GAVI grant, including: personnel salaries and benefits that were not captured directly by the GAVI grant, use of existing vehicles, the vaccine itself and procurement of vaccine (including freight, transportation and syringes) and share of time of in-kind vehicle use. The organization that paid each cost or provided each resource was identified in the course of data collection; however, it was not an aim of the analysis to present the costs by funding source beyond the division between financial and economic costs. Costs excluded from the analysis were the costs of routine operation of the health system and immunization program in Zimbabwe that were not new/additional (incremental) and costs related to conducting the cost analysis itself.

Valuation of In-Kind Resources

Personnel time was estimated using an annual salary plus benefits (given by the MOHCC Human Resources department), which was then divided by 222 working days in a year, resulting in a per day salary estimate. Salaries were given from the MOHCC by cadre, therefore each unique salary was not known explicitly. The number of days that each cadre spent per activity was collected through interviews, data collection forms, and review of registries. Volunteer time was valued using a minimum wage estimate given by the MOHCC. The minimum wage estimate used was the lowest paid MOHCC employee salary given by Human Resources (annual salary plus benefits of US$5,352).

The 2016 HPV vaccine purchase price (per dose) was listed as US$4.60 (GAVI The Vaccine Alliance, 2015a). This figure excludes airport clearance and transportation to central vaccine stores (CVS). These costs were therefore added to the cost analysis for a total price per dose estimate for procurement and vaccine together. The number of vaccines received by the MOHCC covered two doses of the target population including a standard 25% buffer stock, a minimum set by GAVI (Government of Zimbabwe, 2013).

In-kind donations of vehicles were valued at an average cost of the vehicle used based on the average new sale price of that type of vehicle within Zimbabwe. It was assumed that the vehicle would not have a resale value, the discount rate used was 5% and 5 useful life years of the vehicle was assumed. With the use of this information the vehicles were annuitized using 222 working days per year. A total financial cost per vehicle estimated was calculated using the number of days the vehicle was used per project activity.

Instruments

WHO Cervical Cancer Prevention and Control Costing Tool (C4P)

The WHO C4P tool was created by the WHO to help LMIC's assess the implementation of cervical cancer interventions from both the programmatic and policy levels. While the Cervical Cancer Screening and Treatment module is still being developed, the HPV Vaccine module is available for use (both for demonstration projects and national scale-up). The C4P tool entails 4 major levels of data collection (national, provincial, district, and health facility/service delivery) (Hutubessy et al., 2012). Data collection forms were adapted from the creators of the WHO C4P tool and adapted for use in data collection. The C4P tool that was used to guide data collection was the WHO C4P tool version2, last updated in January of 2015. A user-guide to the WHO C4P tool is available online at: (http://www.who.int/immunization/diseases/hpv/cervical_cancer_costing_tool/en/) (World Health Organization, 2016).

Plans for Data Analysis

Data were imported into an Excel spreadsheet based on the WHO C4P tool for analysis. Costs of this analysis are presented as financial and economic costs for the HPV demonstration project in Zimbabwe. They were disaggregated into total introduction cost, total recurrent cost, cost per dose given and cost per FIG. The cost per FIG and cost per dose (both financial and economic) are the total cost of the project divided by the number of FIGs and number of doses administered. The cost per dose was calculated using a two dose vial of the bivalent Cervarix™ vaccine. Vaccine costs were inclusive of freight charges and syringes. The total cost per two dose vial was then divided by two to obtain a price per single dose. All costs were collected and presented in current year US$ and were not adjusted for inflation over the two year

implementation period. This cost analysis is aimed to cost the entirety of the HPV vaccination demonstration project in Zimbabwe. This cost analysis presents actual costs as implemented, even when the implementation deviated from what was planned (e.g., reaching fewer vaccination points).

Ethical Considerations

IRB was reviewed and determined unneeded for the analysis conducted by CDC and funded by GAVI. Technical assistance was requested by Zimbabwe's MOHCC. IRB was unneeded because it did not use human subjects as research or collect any personally identifiable information.

V. Results

Introduction

The cost analysis findings of the Zimbabwe HPV vaccination project that was implemented in two districts of Zimbabwe are presented in this section. Research questions for this cost analysis were: the total cost per FIG and per dose, recurrent cost and introduction costs, service delivery costs per strategy and challenges associated with the HPV vaccination demonstration project in Zimbabwe. All costs are presented as both financial (monetary outlay from MOHCC) and economic costs (monetary outlay from the MOHCC plus monetary outlay and in-kind resources from partner organizations plus a valuation of personnel time) (World Health Organization, 2016).

Findings

Vaccination Points

The primary delivery strategy of both districts was school-based. Beitbridge administered the HPV vaccine at 70 schools (increasing from 69 to 70 schools when a new school opened between the delivery of the first and second dose in cohort 1) and Marondera at 96 schools (Table 1). Both districts used health facilities as a secondary strategy to deliver the vaccine, at 17 health facilities in Beitbridge and 23 health facilities in Marondera. Beitbridge also visited 47 outreach points with vaccination teams as a secondary strategy to deliver the vaccine. Both health facility and outreach vaccination were used primarily to reach out-of-school girls. In cohort 2, dose 2, Beitbridge reached fewer points (for all strategies) overall. If no dose 1 vaccinations were given at the location, the vaccination location was not reached because it was expected that no girls would be there to vaccinate with dose 2.

Table 1. Number of Vaccination Points

Delivery	School Points		Health Facilities		Outreach Points
District	Beitbridge	Marondera	Beitbridge	Marondera	Beitbridge
Cohort 1 dose 1	69	96	17	23	47
Cohort 1 dose 2 & Cohort 2 dose 1	70	96	17	23	47
Cohort 2, dose 2	66	96	10	23	7

Target Population, Doses Administered, and Number of Fully Immunized Girls (FIGs)

For both doses combined for cohort 1, the target population was 3,743 girls. The first doses administered were 2,641, giving coverage of 71% (Table 2). For cohort 1 second dose the target population was the girls that received the first dose of 2,641, doses administered were 2,479 with a coverage of 94%. FIG for the first cohort was 2,149. For cohort 2 first dose the target population was 2,765, the doses administered were 1,950 giving a first dose coverage of 71%. For cohort 2 second dose the target population was the girls that received the first dose of 1,950, doses administered were 1,933 for second dose coverage of 99%

The two districts administered a total of 9,003 doses to a target population of 6,508 eligible ten-year-old girls. This resulted in 4,412 FIGs. Total coverage for the entire HPV vaccination demonstration project was 68%. This was calculated by dividing the total number of FIGs by the total target population. The cohort and total project coverage rates are less than the individual dose coverage due to missed girls in the target population during the first dose and dropout between first and second doses.

Table 2. Target Population, Doses Administered, and Fully Immunized Girls (FIGs)

Cohort	Dose	Target Population	Doses Administered	Coverage by Dose (%)	Coverage by Cohort (%)	FIGs per cohort
1	1	3,743	2,641	71%		
1	2	2,641	2,479	94%	66.2%	2,479
2	1	2,765	1,950	71%		
2	2	1,950	1,933	99%	69.9%	1,933
	Total	6,508±	9,003		68%†	4,412

±Total Target Population = cohort 1 dose 1 + cohort 2 dose 1
†Coverage rate for Total = Total FIGs/Total Target Population

Financial and Economic Cost per Category

The total financial cost of the HPV vaccination demonstration project in Zimbabwe was US$238,224 (Table 3 & Figure 3). The financial cost of Zimbabwe's HPV vaccination demonstration project was funded 71% by GAVI funds and co-financed 29% by the MOHCC, which exceeds the GAVI requirement for country contribution of 20% of program operation costs.

The largest share of financial costs per activity was for social mobilization/IEC at US$58,109 accounting for 24.4% of the financial resources (Table 3 & Figure 3). Factors that contributed heavily to this category were the cost of reprinting IEC materials following a change in the initial vaccination launch dates from May to September 2014, and a change in the number of doses as well as the involvement of both MOHCC district health promotion personnel and NGOs with social mobilization during the vaccination periods. To account for these changes districts/NGOs had to re-visit previously visited points for community sensitization with updated information. Districts had lower costs to reach the sensitization points due to their more central location in the district as compared to the Harare-based NGOs which incurred higher transportation/accommodation costs to reach the points. Following social mobilization/IEC in descending order was financial cost of training (US$55,196, 23.2%), service delivery

(US$41,206, 17.3%), supervision, monitoring and evaluation (US$36,513, 15.3%), other (US$44,349.00, 18.6%), micro-planning (US$2,690, 1.1%), and vaccines (US$ 161, 0.1%).

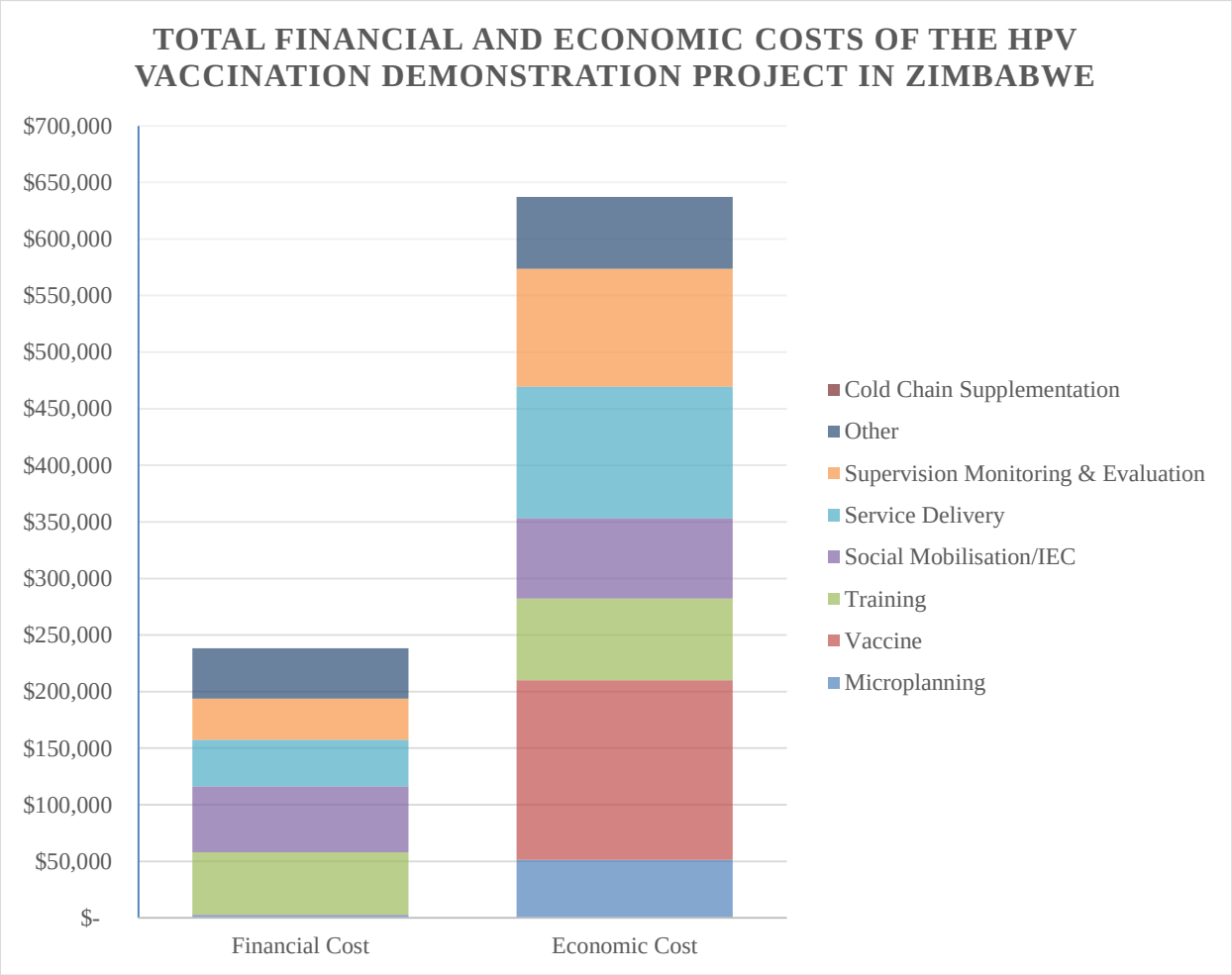
The total economic cost of the HPV vaccination demonstration project in Zimbabwe was US$637,306. The largest share of economic costs per activity was vaccine at US$158,726, using 24.9% of total economic resources (Table 3 & Figure 3). Following in descending order was activities is economic cost of service delivery (US$116.309, 18.3%), supervision, monitoring and evaluation ($103.955, 16.3%), training ($ 72,353, 11.4%), social mobilization/IEC (US$ 71,017, 11.1%), other (US$63,728, 10.0%) and micro-planning (US$51,218, 8.0%). Economic costs included monetary and in-kind donations and the cost of a variety of personnel contributing to the activities (salaries).

Cold chain was reported as sufficient during the HPV vaccination project from all levels, therefore no major improvements were added to existing cold chain capacity for attributable to the HPV vaccination project.

Table 3. Total Financial and Economic Cost per Activity ($ and %)

Activity	Financial Cost		Economic Cost	
	US$	%	US$	%
Micro-planning	2,690	1.1	51,218	8.0
Vaccine	161	0.1	158,726	24.9
Training	55,196	23.2	72,353	11.4
Social Mobilization/IEC	58,109	24.4	71,017	11.1
Service Delivery	41,206	17.3	116,309	18.3
Supervision, Monitoring and Evaluation	36,513	15.3	103,955	16.3
Other	44,349	18.6	63,728	10.0
Cold Chain Supplementation	0	0.0	0	0.0
Total cost of HPV Vaccination Demonstration Project	**238,224**	**100**	**637,306**	**100**

Figure 3. Total Financial and Economic Costs of the HPV Vaccination Demonstration Project in Zimbabwe; by Activity



Introduction Costs

Total financial introduction costs (inclusive of micro-planning, training, social mobilization/IEC and other) were US$125,822 (Table 4). Total economic introduction costs were US$221,929. Assuming these introduction investments last for a period of 5 years, the annualized introduction costs were financial cost of US$25,164 and economic cost of US$51,260. The highest financial cost of introduction was training (US$55,196). Training took place at both the national level for supervisors and at the district level for service delivery

personnel. The highest economic cost of introduction was training as well (US$72,353). The economic cost of training included personnel time (salaries).

For social mobilization IEC, under the sub-activity IEC support, the cost of developing HPV materials was supposed to be included in this category based on the WHO C4P tool guidance. However, the creation of training materials was included instead in the other category under HPV SAG Meetings (5). These five meetings were partially attributed to the creation of HPV support materials (brochures, pamphlets, training manuals, tally sheets, vaccination cards, etc.). The meetings were included in the other cost introduction category because while the HPV SAG meetings were responsible for the creation of the IEC support materials, they also included other crosscutting activities such as planning and sensitization. The other introduction category included costs that were not attributable to any particular activity category but were considered introduction costs. The highest cost within the other category was the launch of the HPV vaccination (financial cost: US$22,752; economic cost: US$23,233). The total cost of the other costs category was financial cost of US$ 42,660 and economic cost of US$ 60,773.

Table 4. Detailed Introduction Costs by Activity and Sub-Activity

Activity and Sub-Activity	Financial Cost (US$)	Economic Cost (US$)
Micro-planning		
National Micro-planning	0	34,840
District Micro-planning	2,690	16,378
Total Micro-planning costs	**2,690**	**51,218**
Training		
Training of Supervisors	20,031	28,191
Training of Service Delivery Personnel	35,165	44,162
Total Training Costs	**55,196**	**72,353**
Social Mobilization/IEC		
Social Mobilization	25,276	37,585
IEC Support	0	0
Total Sensitization and IEC Support Costs	**25,276**	**37,585**
Other Costs		
Cost of Launch	22,752	22,752
Review of Monitoring Tools	4,000	4,000
Stakeholders Meeting	11,165	19,417
Report Writing Meeting	4,743	8,448
HPV SAG Meetings (5)	0	6,156
Total Other Costs	**42,660**	**60,773**
Total Introduction Costs	**125,882**	**221,929**
Annualized Introduction Costs*	***25,164***	***51,260***

**Assuming introduction investments last for 5 years.*

Recurrent Costs

Recurrent cost totals were US$112,402 for financial costs and US$415,377 for economic costs (Table 5). For recurrent financial costs, the biggest share of cost was service delivery (US$41,206). This included all strategies; financial delivery costs for school visits at US$30,303, health facility vaccinations at US$6,035 and outreach visits (only conducted in Beitbridge district) at US$4,868. It is expected that school visits would be the biggest cost of service delivery because there were more school visits than health facility static points or outreach points. Total financial delivery costs (inclusive of both districts) were US$41,206.

The biggest share of economic recurrent costs was for vaccine (US$116,309). The economic cost of the vaccine included vaccines (procurement, freight and transportation), syringes (procurement and freight), safety boxes and cotton swabs. The vaccine and syringes were procured by UNICEF and therefore not a direct monetary outlay from the MOHCC. The financial costs for the vaccine incurred by the MOHCC were for the safety boxes and cotton swabs. The bivalent Cervarix™ vaccine was cost at US$5.06 per dose (inclusive of freight and transportation to CVS) and US$5.12 per dose when syringe costs (procurement and freight) were added. The number of doses procured and included in this cost analysis by UNICEF was 31,000.

Table 5. Detailed Recurrent Costs: Financial and Economic

Activity and Sub-Activity	Financial Cost (US$)	Economic Cost (US$)
Vaccines		
Vaccines (including freight and transportation)	0	156,860
Syringes	0	1,705
Safety Boxes	122	122
Cotton Swabs	39	39
Total Vaccine Costs	**161**	**158,726**
IEC Materials		
IEC Materials Printing	32,833	33,432
Total IEC Materials	**32,833**	**33,432**
Service Delivery		
School Visits	30,303	98,783
Health Facility Vaccinations	6,035	6,731
Outreach Visits	4,868	10,795
Total Service Delivery Costs	**41,206**	**116,309**
Supervision Monitoring & Evaluation		
Supervision	29,250	79,924
Monitoring	7,263	7,263
Evaluation	0	16,768
Total Monitoring, Supervision and Evaluation Costs	**36,513**	**103,955**
Other		
Other Recurrent Costs	1,689	2,955
Total Other Costs	**1,689**	**2,955**
Total Recurrent Costs	**112,402**	**415,377**

Total financial introduction costs (US$125,822) were higher than total financial recurrent costs (US$112,402) (Table 6). This can be explained by the adoption of a 2-dose schedule following adherence to WHO recommendations (2-dose schedule of the vaccine is non-inferior to a 3-dose schedule). Planning and community mobilization/IEC was initially carried out with a 3-dose schedule but prior to administration of the vaccine, the schedule changed. Costs as a result of the change were reprinting IEC materials, social mobilization, training, and micro-planning meetings. For these reasons higher introduction costs were found than what was to be

expected. Total economic introduction costs (US$221,929) were lower than total economic recurrent costs (US$415,377) reflecting the inclusion of the HPV vaccine and procurement.

Total Financial and Economic Cost per FIG and Cost per Dose

The total financial cost per FIG (inclusive of vaccine) was US$53.99 and the total economic cost per FIG was US$144.45 (Table 6). The total financial cost per dose was US$26.46 and the total economic cost per dose was US$70.79. At all vaccination points, cohort 1's second dose and cohort 2's first dose were delivered concurrently. The total cost of the vaccine is the total costs minus any costs under the vaccine category. Financial costs of the vaccine included safety boxes and cotton swabs. Economic costs of the vaccine included financial cost plus the cost of the vaccine (procurement, freight and transportation) and syringes (procurement and freight).

Table 6. Total cost for Introduction and Recurrent costs; per dose and per FIG

Cost Category	Financial Cost (US$)			Economic Cost (US$)		
	Total	**Per dose±**	**Per FIG***	**Total**	**Per dose±**	**Per FIG***
Introduction Cost	125,821.68	13.98	28.52	221,929.43	24.65	50.30
Recurrent Cost	112,402.36	12.48	25.48	415,376.57	46.14	94.15
Total Cost	**238,224.04**	**26.46**	**53.99**	**637,306.00**	**70.79**	**144.45**
Total Cost (without Vaccine**)	***238,063.01***	***26.44***	***53.96***	***478,579.97***	***53.16***	***108.47***

± Total Doses administered: 9,003
*Total FIG: 4,412
**Vaccine includes costs of vaccine (inclusive of freight and transport), syringes, safety boxes, and cotton swabs.

Service Delivery Cost per Strategy

The cost of FIG vaccinated at school (financial cost US$6.89; economic cost US$22.46) is less than the cost of a FIG (for financial and economic costs) of other strategies (health facility and outreach points) (Table 7 & Table 8). This was due to far more FIGs vaccinated at in schools (4399) as compared to health facilities (9) and outreach points (4). Both FIG and per dose costs

were higher at both health facilities and outreach points due to few girls being vaccinated at these points.

The command center and data collection costs were weighted and divided among the delivery strategies as all service delivery points incurred these costs. Economic costs were higher in schools because mobile teams comprised of nurses and drivers had to reach each school and schools were the most common point visited for vaccination. The economic costs for health facilities were minimal; personnel time (salaries/minimum wage estimates) was included for village health workers and the small amount of personnel time contributed to nurses. An estimate of (20) minutes to vaccinate 1 girl was used (given by the district MOHCC staff) and few girls were vaccinated in health facilities (17 doses).

Table 7. Financial Cost of Service Delivery by Strategy: Total, per Dose, and per FIG

Cost Category	Doses given	FIGs	Financial Cost (US$)		
			Total	**Per dose**	**Per FIG**
School	8,978	4,399	30,303.14	3.38	6.89
Health Facility	17	9	6,035.33	355.02	670.59
Outreach Point	8	4	4,867.53	608.44	1,216.88
Total Cost	**9,003**	**4,412**	**41,206.00**	**4.58**	**9.34**

Table 8. Economic Cost of Service Delivery by Strategy: Total, per Dose, and per FIG

Cost Category	Doses given	FIGs	Economic Cost (US$)		
			Total	**Per dose**	**Per FIG**
School	8,978	4,399	124,288.36	13.84	28.25
Health Facility	17	9	6,755.06	397.36	750.56
Outreach Point	8	4	14,066.68	1,758.33	3,516.67
Total Cost	**9,003**	**4,412**	**145,110.09**	**16.12**	**32.89**

Service Delivery Cost per Cohort

Three runs of vaccination delivery were conducted in each district. The first run conducted was cohort 1 dose 1. The second run conducted was both cohort 1 dose 2 and cohort 2 dose 1 concurrently. The third run was cohort 2 dose 2 For Beitbridge, total financial service delivery costs decreased across vaccination runs (run 1 US$8,643; run 2 US$6,864l; run 3

US$5,239) (Table 9 & Table 10). The price per dose reflects the number of doses that were given in each run, therefore, for run 2, where a higher number of doses were given, the cost (both financial and economic) was the lowest. Alternatively, the highest cost per dose (both financial and economic) was seen in the run where the fewest doses were given (e.g. run 3 for both Beitbridge and Marondera).

Table 9. Service Delivery Cost per Cohort and Dose: Total and per dose; Marondera

Run	Cohort	Dose	Doses Given	Financial Cost (US$)		Economic Cost (US$)	
			Marondera	Marondera		Marondera	
				Total	Per dose	Total	Per dose
1	1	1	1,285	6,820	5.31	23,023	17.92
2	1, 2	2, 1	2,194	6,820	3.11	23,573	10.74
3	2	2	1,038	6,820	6.57	23,531	22.67
Total			4,517	20,460	4.53	70,126	15.53

Table 10. Service Delivery Cost per Cohort and Dose: Total and per dose; Beitbridge

Run	Cohort	Dose	Doses Given	Financial Cost (US$)		Economic Cost (US$)	
			Beitbridge	Beitbridge		Beitbridge	
				Total	Per dose	Total	Per dose
1	1	1	1,356	8,643	6.37	17,376	12.81
2	1, 2	2, 1	2,235	6,864	3.07	16,206	7.25
3	2	2	895	5,239	5.85	12,600	14.08
Total			4,486	20,746	4.62	46,182	10.29

VII. Discussion / Conclusion

Introduction

The costs presented in this analysis demonstrate that there were costs associated with reaching this new population (ten-year-old girls) with vaccines in the HPV demonstration project in Zimbabwe. These costs provided learning opportunities for Zimbabwe regarding delivery strategies, budgeting and allocating resources for national scale-up, but also presents the opportunity to compare costs found in previous GAVI-eligible HPV demonstration vaccination projects and to critically analyze the WHO Cervical Cancer Prevention and Control Costing (C4P) Tool.

Cost Drivers of Zimbabwe's HPV Vaccination

When comparing costs across countries it is important to note that the costs found in Zimbabwe were associated with a 2-dose vaccination delivery schedule (not a 3-dose vaccination schedule that was found in other published papers) and the service delivery costs of run 2 (cohort 1 dose 2 and cohort 2 dose 1) were given concurrently. This is not a limitation of the study because it was the unique delivery to Zimbabwe. However, for this reason when comparing Zimbabwe's findings with findings from other published studies there is limited comparability.

Financial and Economic Costs

In Zimbabwe the highest financial cost was social mobilization/IEC (US$58,109) followed by training (US$55,196). Hutubessy et al found that the highest financial cost during the introduction phase (3 regions being vaccinated) was social mobilization/IEC materials followed by training (Hutubessy et al., 2012). The highest economic cost was vaccine procurement in Zimbabwe because UNICEF procured the vaccine and syringes (which included freight and transportation. This was therefore categorized as an economic cost. UNICEF

procured 31,000 doses of the vaccine, which was far more than the doses delivered (9,003), thus increasing economic costs.

Driving social mobilization/IEC costs in Zimbabwe were the costs of reaching sensitization points for the contracted Harare based NGO's. MOHCC staff took over conducting sensitization visits after cohort 1 dose 1 (first run), due to lack of funds, after GAVI grant had been exhausted. The cost of reaching sensitization points by the NGO's were higher than the cost of MOHCC staff reaching these same points (especially in Beitbridge due to distance and needed accommodation). MOHCC staff were able to reach points at lower costs per visit then the NGOs.

Introduction and Recurrent Costs

Total financial introduction costs were higher than total financial recurrent costs in Zimbabwe. Financial introduction cost per FIG in Zimbabwe was US$28.52. Levin et al found that the financial introduction costs ranged from US$1.49 (India) to US$18.49 (Vietnam) per FIG for a 3-dose schedule (C. E. Levin et al., 2013). Introduction costs were influenced by the change in the WHO recommendations resulting in Zimbabwe shifting from a 3-dose vaccination schedule to a 2-dose vaccination schedule. Work had begun both at the national and district level planning for a 3-dose schedule. After the dose schedule changed, work that had already occurred, including printing of IEC materials, visiting of vaccination points for social mobilization, training, and micro-planning meetings had to be re-done. IEC materials were re-printed, social mobilization points were re-visited, and information had to be re-disseminated to communities, trainees and planning staff. All of these subsequently increased the financial and economic cost of introduction activities

The financial recurrent cost per FIG in Zimbabwe was US$25.48. Levin et al. found that the average recurrent costs ranged from US$1.00 (India) to US$13.08 (Tanzania) per FIG for a

3-dose schedule (C. E. Levin et al., 2013). Zimbabwe delivered a mixed strategy (school, health facility, outreach points), which increased costs of service delivery (a recurrent cost). Recurrent costs were increased due to the aforementioned dose change from 3-doses to 2-doses after the WHO changed their recommendations. Therefore IEC materials (US$32,833) were printed twice. Had they been only printed once, costs would have been reduced. As well, recurrent service delivery costs were influenced by the composition of vaccination teams. This included mobile teams (reaching school and outreach points) of two to three (Beitbridge) or four (Marondera) nurses plus a driver, VHWs, school coordinators, command center personnel (two in Beitbridge, three in Marondera), data collectors, and one or two nurses at static health facility locations. For health facility delivery, per diems (sitting fees) were given to health facility personnel, while very few vaccinations actually took place there. The composition of the service delivery teams affected financial recurrent service delivery costs based on per diems and economic recurrent costs based on personnel time (estimated by cadre level salaries and benefits).

Cost per Fully Immunized Girl (FIG)

For Zimbabwe's HPV vaccination demonstration project, the financial and economic costs per FIG were higher than those reported in previously reported GAVI-eligible HPV vaccination demonstration projects, which is to be expected when comparing a 2-dose to 3-dose schedule. Zimbabwe's financial cost per FIG was US$53.99 including the vaccine and US$53.96 excluding the vaccine. For financial costs, Ngabo et al estimated the financial cost per FIG of $10.23 (Ngabo et al., 2015). Levin et al, reported financial costs per FIG in Uganda and Vietnam of US$2.10 and US$1.62 (excluding procurement of vaccine costs) (C. E. Levin et al., 2013). In

Tanzania, Quentin et al found total cost per FIG in rural sites ranged between US$78.00 and US$107.00 (Quentin et al., 2012).

Zimbabwe's relatively higher financial cost per dose and per FIG than other published studies may also reflect the relatively small target population concurrently with long distances to vaccination points. This consequently resulted in higher costs for both transportation and per diem costs to reach all vaccination points.

Service Delivery; Cost per dose in Schools

Zimbabwe's school-based delivery financial cost per dose of US$3.38. Rwanda's school based strategy produced the financial cost of delivery per dose of US$3.37 (Ngabo et al., 2015). Zimbabwe's school-based delivery costs for economic per dose of US$13.84. For school based strategy in Rwanda the economic cost per dose was US$4.76 (not including vaccine) (Ngabo et al., 2015)

Quentin et al reported findings that delivering the HPV vaccine in urban Tanzanian schools as opposed to rural schools was a major cost driver per dose and per FIG (Quentin et al., 2012). For urban schools, cost per FIG was US$66 for school based delivery in Tanzania and was US$100 for aged based delivery, while rural schools were US$78 and US$107, respectively (Quentin et al., 2012). While Zimbabwe's analysis was not broken up to estimate costs of urban vs. rural, it was found that in Beitbridge in particular (which is a mostly rural district), costs of reaching vaccination points were higher, which echoes the work of Quentin et al. School vaccination in Zimbabwe was where most (>99%) girls were vaccinated. Therefore the costs per dose and per FIG for school based delivery were significantly lower than delivery through any other strategy (health facilities or outreach points).

Quentin et al suggested that the number of girls vaccinated per school affected the costs of vaccination (Quentin et al., 2012), which is similar to what Zimbabwe also found based on the high cost per dose and per FIG of vaccinating in health facilities and outreach points. While these points (health facilities and outreach points) were utilized to try and reach out-of-school girls, very few out-of-school girls were reached. Both districts reported that in some cases out-of-school girls re-enrolled in school following community sensitization as well as some out-of-school girls reported to school during vaccination day to receive vaccination. For both financial and economic costs of service delivery, per diems and personnel time were a cost driver with many cadres contributing to service delivery (nurses, village health workers (VHWs), data collection personnel, drivers, command center staff).

Integration of Services

Many of the published papers on HPV vaccination projects discussed the need for further research on cost sharing when delivering the HPV vaccination. Hutubessy et al mentioned that integration of services could lower costs to this population (Hutubessy et al., 2012). Levin et al presented costs for Uganda's integrated health program using child health day's that lowered costs (C. E. Levin et al., 2013). While Zimbabwe did not deliver the HPV vaccine using an integrated approach the literature shows that this could be an effective way to share costs among programs and lower the costs of service delivery across the board.

WHO Cervical Cancer Prevention and Control Costing (C4P) Tool

The WHO Cervical Cancer Prevention and Costing (C4P) tool was created as an Excel-based module to help LMICs assess the resources utilized for HPV vaccination. The C4P tool is still in its developmental phase and version 2 was utilized to help guide this analysis. The tool had many advantages to it. If a country were to know the inputs (at a unit cost level) of the

demonstration project, the tool can be a user-friendly way to estimate total costs and cost per dose and per FIG in a transparent way. The tool is best suited to a country setting in which implementation of each strategy and cohort occurs separately, to reduce challenges of allocating shared costs across strategies and cohorts. The C4P tool can be a helpful way for countries to decide how to deliver the vaccine during the planning phase, allowing for monetary and resource planning before delivering the vaccine using a particular strategy (school, health facility, outreach, integrated, mixed approach).

While the C4P tool was useful in many ways, a number of challenges were noted during its use for the Zimbabwe HPV demonstration project cost analysis. For example, the C4P tool allows only a single value for some inputs, such as assuming that for each delivery (run) of vaccine administration the unit costs were the same each time. However, for Zimbabwe, the dose schedule changed, sensitization teams had different composition (NGOs vs. MOHCC), a different number of points were reached on different runs, different per diems were given per cadre, etc. This posed major challenges when the tool was structured to accept only a single average costs of transportation and per diems. To address this challenge, additional calculators ("plug ins") could be added to the C4P tool (especially for transportation costs) to increase the tool's usability for a wider non-specialist audience. As well, this single cell entry approach does not give the user a way to calculate the fact that some vaccination points take more or less resources to reach. Including service delivery as an average cost per point gives less room for interpretation when assuming that each point incurred the same amount of costs.

The C4P tools use of the word "introduction" may be confusing to both users of the tool and those trying to interpret the C4P outputs. These costs may not necessarily be introductory costs for all countries (e.g. social mobilization visits may be a recurrent cost in Zimbabwe with

the use of consent forms which would need to be explained to a parent or guardian). It may also be hard to estimate how long introductory costs will last (in years).

In order to use the C4P tool for retrospective empirical costing, the user must have more than a basic background on the calculation of both financial and economic costs. The tool, which can provide a very straightforward costing of what may happen for a planning phase, is less well-suited to calculate retrospective costs of real-life scenarios of vaccine delivery that are less straightforward. As countries may adjust and change their approach in the course of the demonstration project due to lessons learned in order to produce optimal service delivery, a more flexible tool and greater capacity in economic evaluation may be needed to accurately capture the costs incurred during more complex and evolving implementation approaches. GAVI currently funds the provision of technical assistance to countries implementing HPV vaccination demonstration projects; involvement of the partners providing technical assistance on cost analysis of the demonstration project beginning with the planning phase could allow the country teams to think through the most cost-effective strategies of delivery and to collect data in a more organized and accurate fashion.

Limitations and Delimitations

The cost analysis results should be interpreted while considering several limitations. This analysis was conducted retrospectively and project implementation staff were asked to recall information from the HPV vaccination demonstration project that happened in the past. For some of the information no written record was available (e.g. personnel time). Therefore these given estimates are subject to recall bias, which may have caused an overestimate of economic costs.

While personnel time spent on activities was estimated by project implementation staff, salaries were collected from the MOHCC Human Resource department. These were salaries per

cadre and not exact salaries specific to the exact person involved with the program activity. Therefore the salary levels assumed may be different than actual salary level. These economic costs used annual salary plus benefits and minimum wage estimates. For the HPV SAG meetings, it was assumed that all members of the SAG committee were present as only one register was collected to estimate the economic costs of all meetings. Therefore it is possible that HPV SAG meeting economic costs are overestimated. During the vaccination period Marondera District experienced high staff turnover, therefore the costs may be underestimated due to unknown costs from departed personnel. The Central Vaccine Stores and implementing districts were unable to give waste attributable to the vaccine although they did estimate that the cost was negligible.

Service delivery costs were reported from project implementers (MOHCC) as lump sum costs. Therefore the lump sums were divided per strategy and weighted by the number of points visited of each type (school, health facility, outreach point) by run. This method does not allow for an estimated unit cost of reaching each point. In reality, it is likely to have been more costly to reach some vaccination points (e.g. those that were further distances). In both districts multiple points were reached on the same day, however fuel costs were given in a lump sum, therefore this assumption was made in the absence of knowing the cost of reaching each particular point.

Costs were collected, presented and analyzed in current year US$. Therefore costs from 2014, 2015 and 2016 are presented in this analysis. No adjustment for inflation was performed.

The contributions made to the HPV vaccination demonstration in Zimbabwe as a whole may be underestimated due to incomplete recall from project implementers. This includes both from the MOHCC and implementing partners. Efforts were made by the costing team to obtain

any available information regarding financial outlays and in-kind resources that were used during the project implementation. However, when the $170,000 project funds from GAVI were spent (following the first run), resources (both monetary and in-kind) from the MOHCC and partner organizations were used to continue implementation (run 2 and 3). When this transition from GAVI money to MOHCC and partner organizations occurred, less precision took place to track these incremental costs attributable to the HPV vaccination demonstration program.

VIII. Implications / Recommendations

This cost analysis provides new evidence regarding the resources required to deliver HPV vaccines among a non-traditionally vaccinated population, ten-year-old girls. The HPV demonstration project in Zimbabwe provided an opportunity to understand the implementation dynamics and cost drivers of different delivery strategies. The lessons learned from the demonstration project can help inform the Zimbabwe MOHCC's decision on budgetary and resource requirements around possibly adding the HPV vaccine to the NIP.

Lessons Learned / Recommendations for Zimbabwe

Reaching out-of-school girls

One major challenge during Zimbabwe's HPV vaccination was reaching out-of-school girls. Very few out-of-school girls were identified and subsequently vaccinated. Both NGO's and MOHCC personnel at the district level reported that out-of-school girls were hard to identify in the districts and that families would send their ten-year-old girl to school upon hearing that people were looking for them. Marondera District reported that they facilitated transportation to the nearest school on vaccination day if an out-of-school girl was identified, to allow her to receive vaccination. If these implications about finding out-of-school girls are true for the rest of Zimbabwe, it would be advantageous for Zimbabwe to re-examine offering health facility and outreach point delivery as the primary way to reach out-of-school girls when planning for national scale-up.

Exploring locally-based service providers to reduce costs

Harare based NGOs were contracted by the MOHCC to conduct social mobilization within the districts as well as to identify out-of-school girls during the first run of vaccine delivery. After the first run, MOHCC district personnel took over sensitization duties. In

Beitbridge district, a one-time training to school health coordinators / school headmasters on sensitization was offered, so the MOHCC staff would not have to make trips to each school for sensitization purposes. However, both of the contracted NGOs were Harare based and therefore had higher transportation and accommodation costs than MOHCC district personnel did to reach these points, as they are working in the district already. This was especially true of Beitbridge District which is 635 km from Harare. MOHCC district level personnel were also present for some of the NGO sensitization visits.

Allowing the MOHCC's existing districts' Expanded Program on Immunization (EPI) to conduct sensitization and community mobilization could reduce costs. As well, shifting tasks from higher ministry staff to school coordinators and village health workers (VHWs) could also further reduce staff costs to allow for less visits for community sensitization. The same could be said of localized supervision from the provincial and district level instead of national level MOHCC personnel.

Addressing operational issues to improve coverage rates and reduce costs

Operational issues were identified when consulting with program implementers during the cost analysis data collection which reduced coverage rates within the districts. Marondera District reported that some ten-year-old girls within schools did not have their consent forms signed; reasons given were religious objection, didn't know about the vaccination, skeptical due to change in vaccination schedule (3 to 2-doses) and date changes or use of the word "demo", thinking that it was an experiment on their children. These girls could not be vaccinated because they did not have a signed consent form from a parent or guardian. This requirement produced lower coverage rates, which therefore increased the serviced delivery cost both per dose and per FIG.

Some doses were scheduled to be given close to a school break/holiday and end of the year examinations. This lowered coverage rates due to high rates of absenteeism from school. When considering vaccination scheduling in the future, schools should consider times during the school year when attendance is not affected by the aforementioned. As well, any changes in delivery personnel composition should be considered while weighting the programmatic implications such as coverage and quality of the HPV vaccination. Service delivery costs could be reduced by cutting down the size of both mobile and command center teams. This would therefore reduce both financial and economic costs of service delivery.

Consent form strategy as well as scheduled vaccination were both barriers to increasing coverage and cost drivers of the cost per FIG and cost per dose. As well, increasing the number of girls in the target population could also be advantageous. This could be done by increasing the age range or using a class strategy. These points should be considered when considering HPV national scale-up.

Conclusion / Next Steps

Adapting findings from this cost analysis of the HPV vaccination demonstration program is useful as Zimbabwe's MOHCC considers national scale-up of the HPV vaccine. Examining current strategies and expenditure of resources as well as implementing new strategies for particular cost drivers of the HPV vaccination demonstration project can guide where efficiency gains and cost saving strategies may be possible. MOHCC should assess the following choices while looking towards national scale-up in order to cost-effectively allocate resources for potential cost savings.

- Alternative strategies for reaching out of school girls will need to be explored. During the HPV vaccination demonstration, total service delivery cost per dose

and per FIG at both health facilities and outreach points were relatively high. This is due to few girls utilizing these methods for vaccination. The districts and contracted NGOs lessons learned about how and where to reach out or school girls should be considered when planning how to reach out of school girls during national scale-up

- The use of locally based service providers as opposed to Harare based service providers is a potential opportunity for cost savings. The HPV vaccination demonstration project demonstrated that national/Harare based personnel incurred higher costs of travel and per diems to reach locations for both social mobilization and supervision cost categories than more localized personnel. Task shifting these activities to local personnel has the potential to provide cost savings, especially when considering national scale-up.
- Operational issues should be considered when moving towards national scale-up to increase coverage rates. Time of year of vaccination, strategies to increase the number of signed consent forms and strategies to increase the target population (increasing age range or class strategy) are main points to consider to increase coverage rates.
- Reduction of vaccination personnel during service delivery is a cost driver that should be discussed during planning stages of national scale-up. This could have other implications during delivery that should be discussed when deciding if cost savings for service delivery is the biggest priority. Beitbridge and Marondera Districts experience offer valuable insight when deciding composition and total personnel needed for service delivery purposes.

- Finally, national scale-up should consider that rural districts will have higher financial and economic service delivery costs as opposed to urban districts due to the time and resources it takes to reach rural vaccination points.

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X. Annexes

Annex 1. Resource Costs Included in Cost Analysis per Activity as Implemented under Zimbabwe HPV Demonstration Project

	Financial Costs								Economic Costs							
Activity **Resource Costs Included**	**Micro-planning**	**Vaccine**	**Training**	**Social Mobilization/IEC**	**Service Delivery**	**Supervision, Monitoring & Evaluation**	**Other**	**Cold Chain Supplementation**	**Micro-planning**	**Vaccine**	**Training**	**Social Mobilization/IEC**	**Service Delivery**	**Supervision, Monitoring & Evaluation**	**Other**	**Cold Chain Supplementation**
Vaccine										x						
Vaccination supplies (syringes, safety boxes, etc.)		x								x						
Freight, customs, transport of vaccine and related supplies										x						
Personnel time (share of salaries and benefits)				x					x		x	x	x	x	x	
Per diem (lodging, meals)	x		x	x	x	x	x		x							
Fuel / Transportation fees	x		x	x	x		x									
Vehicle use (share of time)													x	x		
Equipment																
Other supplies/ materials	x		x	x			x		x			x			x	
Venue rental	x						x		x							
Communications							x								x	