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Improving skills and institutional capacity to strengthen adolescent immunisation programmes and health systems in African countries through HPV vaccine introduction

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ABSTRACT

Several African countries have recently introduced or are currently introducing the HPV vaccine, either nationwide or through demonstration projects, while some countries are planning for introduction. A collaborative project was developed to strengthen country adolescent immunisation programmes and health systems in the African Region, addressing unique public health considerations of HPV vaccination: adolescents as the primary target group, delivery platforms (e.g. school-based and facility based), socio-behavioural issues, and the opportunity to deliver other health interventions alongside HPV vaccination.

Following a successful “taking-stock” meeting, a training programme was drafted to assist countries to strengthen the integration of adolescent health interventions using HPV vaccination as an entry point. Two workshops were conducted in the Eastern and Southern African Regions. All countries reported on progress made during a final joint symposium.

Of the 20 countries invited to participate in either of the workshops and/or final symposium, 17 countries participated: Angola, Botswana, Ethiopia, Kenya, Malawi, Mauritius, Mozambique, Namibia, Rwanda, Seychelles, South Africa, South Sudan, Swaziland, Tanzania, Uganda, Zambia and Zimbabwe. Countries that are currently implementing HPV vaccination programmes, either nationally or through demonstration projects, reported varying degrees of integration with other adolescent health interventions. The most commonly reported adolescent health interventions alongside HPV vaccination include health education (including sexually transmitted infections), deworming and delivering of other vaccines like tetanus toxoid (TT) or tetanus diphtheria (Td).

The project has successfully (a) established an African-based network that will advocate for incorporating the HPV vaccine into national immunisation programmes; (b) created a platform for experience exchange and thereby contributed to novel ideas of revitalising and strengthening school-based health programmes as delivery platform of adolescent immunisation services and other adolescent health interventions, as well as identifying ways of reaching out-of-school girls through facility and community based programmes; and (c) laid a foundation for incorporating future adolescent vaccination programmes.

1. Introduction

Cervical cancer is responsible for about 275,000 deaths every year worldwide, with the highest burden occurring in the developing world [1]. While persistent infection with a high-risk HPV type (e.g. 16/18/31/33/45/52/58/35/59/56/51/39/68/73/82) is a necessary cause for the development of cervical cancer [2], not all women with high-risk HPV infection will progress to cervical cancer.

Cervical cancer is the second most frequent cancer in African women based on crude incidence rates [3]. The annual number of new cervical cancer cases is 45,676 in Eastern Africa and 8652 in Southern Africa, with 28,197 and 4721 annual deaths from cervical cancer respectively [3].

HPV vaccines are powerful tools in the prevention of cervical cancer. Three vaccines, based on virus-like particles (VLPs), are currently on the market. The bivalent vaccine (Cervarix®) contains VLP antigens for HPV types 16/18 and is formulated with the adjuvant AS04 (3-O-desacyl-4'-monophosphoryl lipid A and aluminium salt). The quadrivalent vaccine (Gardasil®) contains VLP antigens for HPV types 16/18, as well as non-oncogenic HPV types 6/11 which cause genital warts, and is formulated with the adjuvant aluminium hydroxyl-phosphate sulphate [4,5]. Cross-protection has been shown for the bivalent vaccine against HPV types 31/33/45; while the quadrivalent vaccine showed cross-protection against HPV31 [6–10]. A recent meta-analysis, including both the bivalent and the quadrivalent vaccines, indicated cross-protection at population-level against HPV type 31 [11]. The nine-valent HPV vaccine contains VLP antigens for HPV types 6/11/16/18/31/33/45/52/58 [12], and is currently under review for prequalification by the World Health Organization (WHO). The bivalent and quadrivalent vaccines are currently being used in national immunisation programmes in the African region.

Both the bivalent and the quadrivalent vaccines were initially licensed in a three-dose schedule, to be administered intramuscularly at 0, 1 and 6 months and 0, 2 and 6 months respectively. The recommended target group is 9–14 year-old girls prior to becoming sexually active [4]. Based on immunological non-inferiority data of a two-dose schedule compared to a three-dose schedule, the European Medicines Agency (EMA) approved a two-dose schedule for the bivalent vaccine for girls up to 14 years of age in December 2013 [13]. The quadrivalent vaccine was subsequently licensed for a two-dose schedule for boys and girls up to 13 years of age in February 2014 [14]. These approvals contributed to a recommendation made by the Strategic Advisory Group of Experts on immunisation to WHO to update the HPV vaccination schedule. Currently, WHO recommends a two-dose

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schedule for girls younger than 15 years of age; while the three-dose schedule remains valid for girls older than 15 years of age or for high-risk groups such as immune-compromised individuals [4]. This recommendation is valid for the bivalent, quadrivalent and nine-valent HPV vaccines.

Reducing the number of doses of HPV vaccination could have significant positive public health implications. Given the challenges in reaching adolescent girls with a three-dose schedule in some settings, as well as the high cost of the HPV vaccine, a two-dose schedule might be more effective in reaching a higher vaccination coverage compared to a three-dose schedule, as well as in reducing costs of the vaccine and vaccine delivery. Several countries in the African region are currently implementing HPV vaccination programmes using a 2-dose schedule, either nationally or through demonstration projects. African countries that initially started to deliver a 3-dose HPV vaccination schedule, have now moved to a 2-dose schedule. As of August 2017, 7 countries (Botswana, Lesotho, Mauritius, Rwanda, Seychelles, South Africa and Uganda) have introduced the HPV vaccine nationwide and 20 countries through demonstration projects (Benin, Burkina Faso, Cameroon, Cote d'Ivoire, Ethiopia, Gambia, Ghana, Kenya, Liberia, Madagascar, Malawi, Mali, Mozambique, Niger, Senegal, Sierra Leone, Tanzania, Togo, Zambia, Zimbabwe).

2. Rationale of the project

Around 1 in 6 persons globally is an adolescent: i.e. 1.2 billion people are aged 10–19 years. Behavior and health decisions taken in adolescence can have consequences on morbidity and mortality later in life; therefore, protecting young people from health risks is key for the prevention of health problems later in adulthood [15].

Being a vaccine targeting adolescents, countries are faced with many challenges introducing the HPV vaccine, as most African countries do not have strong and/or functional adolescent health or school-based vaccination programmes in place. The HPV vaccine is the first vaccine to face unique public health considerations and challenges involving an older target age group (9–14 year-olds instead of infants and young children), delivery platforms (the majority being school-based instead of primary health care facilities), involvement of multiple authorities at country level (at least two key ones being Ministry of Health (MoH) and Ministry of Education (MoE)), socio-behavioural issues (gender issues as girls are being targeted, parental consent, and the stigma of HPV being a sexually transmitted infection) and health benefits (long delay of benefits as cervical cancer takes many decades to develop, hence it takes time to demonstrate control and impact).

Given that the African region is lagging behind with introducing HPV vaccination programmes, a regional collaborative project was developed with the overall objective of strengthening regional capacity in adolescent health using HPV vaccination as an entry point. At the start of the project in 2014, of the 47 countries in the WHO African Region, only 5 countries had introduced HPV vaccination nationwide, while only 15 countries were implementing demonstration projects. The specific objectives of the project included to: (a) promote successful and effective introduction of the HPV vaccination programme to improve both country and regional capacity; (b) share best practices and challenges for introduction of the HPV vaccination programme, including the need for multi-sectoral approach, information, education and communication (IEC), social mobilization, etc.; and (c) strengthen country adolescent immunisation programmes and health systems in the African Region using the HPV vaccine as a case study.

School-based immunisation is most commonly used in the Americas (27 countries), and least commonly used in the African and the South-East Asian Regions, being used in only 11 and 3 countries respectively [16]. In addition, a survey by UNICEF and WHO revealed that most countries with a school-based immunisation approach deliver tetanus and diphtheria toxoids most frequently. Where an adolescent vaccination programme is in existence in low- and middle-income countries, the coverage data for this age group is often unknown [16,17].

3. Potential adolescent health interventions to be included with HPV vaccination

Given the challenges in dealing with adolescents who rarely attend primary health care facilities, the ability to deliver multiple interventions along with the HPV vaccine could serve as an entry point to increase adolescents' access to health care and services. Several health-related interventions could potentially be integrated with HPV vaccination programmes. Potential interventions alongside with HPV vaccination can be summarized in 4 categories: screening; information/skills building; commodity delivery; and other vaccines [15,18]. The selection of other adolescent health interventions to be integrated with HPV vaccination and their potential benefits are subject to a range of factors: e.g. the vaccination schedule, ease of delivery of the adolescent health intervention, and epidemiology of the main health problems affecting adolescents [15]. Table 1 summarizes a list of adolescent health interventions that can potentially be integrated with HPV vaccination.

4. Activities

The project was implemented from May 2014 until December 2016, and covered five major activities: a launch symposium, stakeholders meeting, two workshops and a final symposium. Since the project aimed to strengthen regional capacity in adolescent health using HPV vaccination as an entry point, experts from the immunisation and adolescent health programmes, non-communicable disease programme, school health programme, and any other relevant key stakeholders were targeted.

In total 20 countries were invited to participate in the project. Invitations to government officials were addressed to the MoH Permanent Secretary or Director-General of Health of the respective countries, for clearance and identification of relevant delegates to participate in the workshops and symposia. The project received high-level approval, and generated high-level advocacy and awareness on accelerating prevention of HPV-related diseases.

Table 1
Potential adolescent health interventions to be included with HPV vaccination [15,18].

Intervention category	Possible complementary interventions
Screening	Vision screening (if referral/glasses available & affordable)
Provision of information	HPV information Reproductive and sexual health education; HIV prevention, condom promotion Promotion of physical exercise Prevention of mosquito borne diseases Menstrual hygiene education Warnings on substance abuse (tobacco, alcohol, drugs)
Commodity delivery	Anti-helminthic treatment Insecticide treated bed nets for malaria prevention Iron and folic acid supplementation Provision of condoms for those engaged in sexual activity Menstrual hygiene products
Vaccines	Td booster Hepatitis B Meningococcal Typhoid Rubella

A stakeholders meeting was organised in March 2015, in Pretoria, South Africa; following an opening symposium (57 delegates), highlighting the current status, best practices and gaps in HPV vaccine introduction. During the stakeholders meeting, a roadmap to deliver the training programme was drafted. The objectives of the stakeholders meeting included: (a) Compile/develop training materials that can be easily adapted to specific country needs and used as national resources; and (b) Develop a common framework to guide cascading of training in various countries, with the overall objective of promoting successful and effective introduction of HPV vaccination and other adolescent health interventions. The stakeholders meeting was attended by 22 delegates from Belgium, Congo-Brazzaville, Ghana, Senegal, South Africa, Swaziland, Switzerland, Uganda, United Kingdom, Zambia and Zimbabwe.

Two workshops “Implementing HPV vaccination in Africa: opportunities for strengthening adolescent health” were organised during the project time; the first one in October 2015, in Johannesburg, South Africa; the second one in March 2016, in Nairobi, Kenya. The objectives of the respective workshops included: (a) Promote successful and effective introduction of HPV vaccination and other adolescent health interventions; (b) Create a multi-disciplinary resourceful team of experts to support and advocate for the introduction of HPV vaccines and other adolescent health interventions; and (c) Increase synergy between academics, educators and Ministries of Health to revive and strengthen school-based health programmes as delivery platforms of adolescent immunisation services.

The workshop in South Africa was attended by 54 delegates. Nominated country delegates included: representatives of the MoH of Botswana, Malawi, South Africa, Swaziland, Zambia and Zimbabwe; representative of the Ministry of Primary and Secondary Education of Zimbabwe; WHO representatives of Malawi, Mozambique, Namibia, South Africa and Zimbabwe. Facilitators were from: WHO, Gavi, South African Medical Research Council (SAMRC) and academia (University of Cape Town, Stellenbosch University, University of the Witwatersrand, University of the Free State, South African Vaccination and Immunisation Centre (SAVIC)/Sefako Makgatho Health Sciences University (SMU), London School of Hygiene and Tropical Medicine and Network for Education and Support in Immunisation (NESI)/University of Antwerp).

The workshop in Kenya was attended by 66 delegates. Nominated country delegates included: representatives of the MoH of Ethiopia, Kenya, Mauritius, Mozambique, Seychelles, Tanzania and Uganda; representatives of Mekelle and Jimma University (Ethiopia), and Manhiça Health Research Centre (Mozambique). Other participants came from the East Africa Centre for Vaccines and Immunisation (ECAVI), Kenya Paediatric Association, academia (Kenya Medical Training College, Cheikh Anta Diop University, Universitas Padjadjaran, ICAP Columbia University), MoH Oman, and industry. Facilitators were from: WHO/Regional Office for Africa (AFRO), WHO/Kenya, WHO/IARC, Gavi, PATH, SAMRC, Kenya Medical Research Institute, and academia (Aga Khan University, University of Nairobi, University of the Free State, SAVIC/SMU, NESI/University of Antwerp).

The first day of the respective workshops comprised of presentations highlighting key aspects of cervical cancer screening, HPV vaccines, adolescent health interventions, delivery platform for HPV vaccination, and effective communication strategies for building public trust in HPV vaccination. During the second day, each country presented their respective status of HPV vaccine implementation and other adolescent health interventions, grouped in three sessions: (a) countries with a national HPV vaccination programme; (b) countries with a demonstration project; and (c) countries planning for HPV vaccine introduction. During the third day country group presentations were made, highlighting for each country the strengths, gaps and challenges based on the feedback received during the individual country presentations on the second day. Countries also identified opportunities to collaborate in assisting each other in successful implementation of HPV vaccination and other adolescent health services. The last session of the workshop focused on monitoring and evaluation, the importance of a cancer registry and measuring the impact of HPV vaccination.

The final symposium “Strengthening HPV vaccination and adolescent health programmes in Africa” took place in November 2016, in Johannesburg, South Africa. The objectives of the symposium included: (a) Discuss recent advances in HPV vaccines and their use; (b) Discuss adolescent health interventions to be delivered alongside HPV vaccination; (c) Exchange lessons learnt and best practices regarding HPV vaccination and adolescent health services among participating countries; and (d) Strengthen a multi-disciplinary team of experts to support and advocate for the introduction of HPV vaccination and other adolescent health interventions in the African Region. The symposium was attended by 87 delegates. Representatives (MoH, MoE, WHO and academics) from 16 countries of the Eastern and Southern African Region participated in the symposium: Angola, Botswana, Ethiopia, Malawi, Mauritius, Mozambique, Namibia, Rwanda, Seychelles, South Africa, South Sudan, Swaziland, Tanzania, Uganda, Zambia and Zimbabwe. Facilitators came from the following organisations/institutions: WHO/AFRO, WHO/South Africa, WHO/IARC (France), Gavi (Switzerland), SAMRC, Centre for Infectious Disease Research in Zambia (CIDRZ) and academia (University of the Free State, SAVIC/SMU, University of Cape Town, University of Witwatersrand, Stellenbosch University, NESI/University of Antwerp). Additional delegates were from the pharmaceutical industry.

Of the 16 countries present, six had introduced the HPV vaccine nationwide. Seychelles and South Africa shared their overall experience, best practices and challenges with the introduction of the HPV vaccine; while Botswana, Rwanda and Uganda focused on monitoring and evaluation of their HPV vaccination programmes. Mauritius gave an update on their recent HPV vaccine introduction. Three countries (Malawi, Mozambique and Tanzania) gave updates on their respective HPV vaccine demonstration projects. Zimbabwe gave a comprehensive overview focusing on integrating other adolescent health interventions alongside HPV vaccination; while Zambia and Ethiopia shared their experiences and best practices regarding information, education and communication for building public trust in HPV vaccination. Namibia and Swaziland are planning for HPV vaccine introduction in 2017 and communicated their respective introduction plans.

5. Results

Of the 20 countries that were invited to participate in either of the workshops and/or the final symposium, 17 countries participated (85%). Of those, 15 countries gave a presentation, highlighting their current status of HPV vaccine introduction, including year of introduction, delivery platform and target age group. At the time of the final symposium, six countries had introduced the HPV vaccine nationwide; while seven countries were implementing demonstration projects. A summary of the current status of HPV vaccination and integration of other adolescent health interventions is presented in [Table 2](#).

Countries also shared their experiences related to government commitment, multi-sectoral collaboration, advocacy and social mobilization, training, data collection, monitoring and evaluation. Only a few examples are outlined below. The individual data are not presented as these are beyond the scope of this report.

Countries reported commitment at government level, collaboration between MoH and MoE, and strong programme leadership to be key for successful introduction of the HPV vaccine. All countries report strong commitment from their respective MoH and MoE to introduce the HPV

Table 2

Current status of HPV vaccine introduction and adolescent health interventions in Eastern and Southern African countries that participated in the project [as reported at workshops/symposium].

Stage in HPV vaccination introduction	Country year of introduction	HPV vaccine delivery platform	Adolescent health intervention alongside HPV vaccination
National HPV vaccination programme	Botswana 2015 Demo started in 2013	School-based (grades 5, 6, 7) and out-of-school girls aged 9–13 years	TT review of school health card
	Mauritius 2016 No demo	School-based (grade 5)	Booster dose tetanus and vision testing in grade 5 health education
	Rwanda 2011 No demo	School-based (grade 6) and out-of-school girls	Health education on hygiene, nutrition, infectious diseases and reproductive health
	Seychelles 2014 No demo	School-based (grade 6)	Incorporated into the School Health vaccination programme Sexual reproductive health/STI/HIV & AIDS Cancer prevention programme
	South Africa 2014 No demo	School-based (grade 4)	Health education deworming
	Uganda 2015 Demo started in 2008	School-based (grade 4) and out-of-school girls aged 10 years	TT deworming vitamin A
HPV vaccination demonstration project	Ethiopia 2015	School-based (grade 4) and out-of-school girls aged 10 years	Integration plan for reproductive health services with HPV during national scale up.
	Kenya 2013	1st demonstration project school-based (grade 4) 2nd demonstration project health facility based	Not reported
	Malawi 2013	School-based (grade 4) and out-of-school girls aged 10 years considering health facility based for national roll-out	IEC adolescent growth and development, menstrual hygiene, HIV/AIDS
	Mozambique 2014	10 year old girls (schools, health facility and community)	Health talks on the vaccination days
	Tanzania 2014	School-based (grade 4) and out-of-school girls aged 9 years	Deworming vision screening dental care
	Zambia 2013	School-based (grade 4) and out-of-school girls aged 10 years	Td health education on family planning and HIV prevention
HPV vaccination introduction plans	Zimbabwe 2014	School-based (grade 5) and out-of-school girls aged 10 years	Integrated with adolescent sexual and reproductive health programme
	Namibia planned 2017	Planned 9–13 year old girls through schools, health facility and outreach	N.A.
	Swaziland planned 2017	Planned school-based and health facility for out-of-school girls	N.A.

IEC: Information, education and communication; TT: Tetanus Toxoid; Td: Tetanus diphtheria.

N.A.: Not applicable.

vaccine. In South Africa, Mozambique and Tanzania for example, the launching ceremony was under the patronage of the first Ladies. Botswana and Seychelles, as well as other countries, identified the development of Technical Working Groups including representatives from different programmes, as a key component for successful implementation. Also, e.g. South Africa and Uganda stressed the importance of the involvement and commitment of partners to support the programme.

All countries mentioned the importance of a detailed communication and social mobilization plan, including provincial micro-plans. Local media was used to sensitize the population. Teachers, community and religious leaders, community healthcare workers, parents and girls were informed on the benefits of HPV vaccination. Community volunteers were used to reach out to people in different communities. In Zambia, for example, a community door-to-door and a church outreach programme were implemented, involving community workers and parents. Many countries reported challenges in reaching out-of-school girls. In Ethiopia, women's groups played a crucial role in mobilizing the out-of-school girls.

Overall, community response to the programme was high in all countries. In a few cases, parents did not allow healthcare workers to vaccinate, which was respected (e.g. Botswana). Tanzania reported some misconception of the HPV vaccine by some parents/guardians. In Mozambique, the majority of the girls (84.7%) accepted the vaccine. However, lack of knowledge, fear of pain and of adverse events (e.g. infertility), were described as barriers to acceptability for some girls.

6. Discussion

At the time of the final symposium, six countries had introduced the HPV vaccine nationwide; while seven countries were implementing demonstration projects. All of the countries use a school-based approach, while some countries also target out-of-school girls. Both Kenya and Malawi reported the high cost of school-based delivery of HPV vaccination as a challenge, and are considering the roll-out through health facilities. School-based vaccination has proven to be a reliable delivery platform [19], as shown by high coverage rates above 90% in Rwanda [20]. Australia (2007) and the UK (2008) were the first countries to introduce the HPV vaccine into their national immunisation programme, both using a school-based programme and reaching high coverage of above 70% with three doses [21]. The national HPV vaccination programme in Scotland reached annual high vaccination coverage of above 90% since its introduction in 2008 through school-based delivery in a three-dose vaccination schedule [7,22]. The USA introduced HPV vaccination through primary care providers but coverage was only 38% after the third dose in 2013 [21]. Another early adopter country, Uganda, through support from PATH, explored two possible strategies for the delivery of the HPV vaccine in demonstration projects: (1) offer the HPV vaccine as part of Child Days Plus; and (2) vaccinate girls at schools, making special efforts to reach out-of-school girls [23]. For the national roll-out, Uganda is using the school-based platform (grade 4) and targeting out-of-school girls aged 10 years. Many countries, however, indicated having difficulties in identifying the hard-to-reach and out-of-school girls; hence the need for research on how to reach those girls. This inevitably has an effect on data validity.

Countries reported varying degrees of delivering other adolescent health interventions alongside HPV vaccination. Referring to Table 1, the

reported adolescent health interventions can be summarized as follows: (1) screening: three countries provide screening; (2) provision of information: most of the countries provide health information; (3) commodity delivery: only three countries provide deworming tablets; (4) vaccines: four countries provide additional vaccines, mainly TT, during HPV vaccination. Two countries with current demonstration projects did not report on any other adolescent health intervention. Potential adolescent health interventions are summarized in a recent review article [24]. It is evident that each country should identify interventions that address the needs of the population and are feasible to integrate alongside HPV vaccination. In this respect, Zimbabwe, for example, took the opportunity to review its school health programme/policy to include a comprehensive adolescent health package. Zimbabwe identified three possible options: (1) A “Healthy Living Day” held on the same day as the vaccination programme; (2) Implementation of an adolescent health package which includes health inputs to the revised School Health Policy; (3) Combination of option 1 and 2. Stakeholders meetings are ongoing to decide which option to adopt.

Some lessons learned were identified during the project regarding HPV vaccination and adolescent health interventions, including: (a) School-based vaccination has the potential of reaching high coverage. School registers help to capture the target population. (b) School-based vaccination requires good coordination between MoH and MoE. (c) High commitment at government level and strong programme leadership are key to successful HPV vaccine introduction. (d) Early preparation and distribution of information, education and communication materials is crucial, and the materials should be translated in the local language. (e) Sensitize teachers, community leaders, parents and girls on the benefits of HPV vaccination. (f) Selection of adolescent health interventions should be based on local priorities.

The presentations and discussions also highlighted the need for more implementation research. While several ideas were discussed, the most urgent ones included to identify: (a) the most effective communication strategy and means to reach the hard-to-reach and out-of-school girls; (b) strategies that will achieve the highest coverage at the lowest cost; and (c) strategies to address cultural and social barriers against HPV vaccination and sexual and reproductive health education.

7. Conclusion

While countries are embarking on introducing HPV vaccination, they should be empowered to add other health interventions in order to strengthen overall adolescent health. The selection of adolescent health interventions should be based on local priorities. Countries in the Eastern and Southern African Region, that are currently implementing HPV vaccination programmes, either nationally or through demonstration projects, reported varying degrees of integration with other adolescent health interventions. School-based vaccination is the preferred delivery platform for HPV vaccination, as a high target population can be reached. It requires, however, good coordination between the MoH and the MoE. Information, education and communication are critical for building public trust and hence successful HPV vaccine introduction. The project clearly stressed the importance of collaboration between different programmes including: immunisation, adolescent health, school health, sexual and reproductive health and cancer control programmes.

This project has successfully (a) established a predominantly African-based network to advocate for incorporating the HPV vaccine into national immunisation programmes; (b) created a platform for experience exchange and thereby contributed to novel ideas of revitalising and strengthening school-based health programmes as delivery platform of adolescent immunisation services and other adolescent health interventions, as well as identifying ways of reaching out-of-school girls through facility and community based programmes; and (c) laid a solid foundation for incorporating future adolescent vaccination programmes.

Conflict of interest statements

Dr Dochez reports that the University of Antwerp receives educational grants from both the public and private sector to support the project NESI. Prof Burnett and Dr Musyoki report that SAVIC receives unrestricted educational grants from vaccine industry. Prof Mphahlele, Prof Were, Dr Mbola Mbassi and Dr Trovoada have nothing to disclose.

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